

Nutritional Medicine

**A Vital Partner of 21st Century medicine
With special reference to the case of
Cyprus**

(Volume II. Evidence of Achievement)

**A project submitted to
Middlesex University in
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EVIDENCE OF ACHIEVEMENT

TITLE: NUTRITIONAL MEDICINE-A VITAL PARTNER OF 21st CENTURY MEDICINE

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INTRODUCTION

This book is the outcome of an action research carried out within the context of a Professional Doctorate thesis in Nutritional Medicine with Middlesex University. The major aim of the project was to build up evidence to support the author's advocacy for the role of Nutritional Medicine (or as otherwise termed, Nutritional Therapy¹) as a vital partner of 21st century medicine, particularly in the area of prevention and treatment of chronic disease. The research was conducted in Cyprus, with reference to the worldwide context of the provision of healthcare, and critically investigated a number of issues related to the provision of healthcare, including the reasons hiding behind the rising incidence of chronic disease, and the extent to which Nutritional Medicine can contribute to its containment by offering solutions not currently provided. Four different methodologies were used, in an attempt to enhance through triangulation the validity and reliability of the findings of the research. The knowledge obtained from a profound review of a volume of publications was contrasted, compared and updated with fresh knowledge created by the research in Cyprus.

The first methodology was an analytical extensive review of a volume of existing literature, including articles, books, treatises, journals, clinical studies, experiments, systematic reviews and meta-analyses, official statistics and various other documents. Aiming to enhance the objectivity of the results and to strengthen the arguments needed to support the aims of the project, particularly due to the author's role as an insider researcher, the review of literature was conducted in its largest, by far, part within work published by researchers and scholars from the medical community itself –not rarely being the outcome of self-evaluation and reflective practice. The inquiry was profound and pervasive at all levels –national (Cyprus) and international- and extended into both the depth and breadth of time, in search of evidence of the academic perspective on a number of critical issues relevant to the aims of the project. Historical retrospection into the roots and the pathway of evolution of scientific medicine were considered an important part of the research in order to identify the epistemologies that supported medical practice throughout the ages until the present times, as well as the influence of ideas on the development of medical thought. A number of treatises of the ancient Greek

¹ Nutritional Therapy is an alternative term for Nutritional Medicine currently used to denote the applied form of Nutritional Science as a therapeutic modality

philosophers were, among other publications, critically reviewed in their original ancient Greek language-mainly Ionian¹- since the ancient Eastern part of the Mediterranean is identified by several historians as the cradle of Scientific Medicine. The insights gained from searching through the original ancient Greek treatises were contrasted and compared with their translations provided by other translators/commentators.

A survey, conducted within the adult population of the five, government controlled, districts of Cyprus, during the period October-December 2008, with the support of the the Center of European and International Affairs of the University of Nicosia, was the second methodology used. The survey aimed at gaining insights of public opinion on a number of important issues related to the provision of healthcare in Cyprus including: perceptions of health; determinants of disease; needs, desires and expectations of people; coincidence between treatment order and treatment preference; perceived treatment success; and lifestyle habits. The third methodology aimed at evaluating the political perspective, as extracted from the analysis of personal Interviews with a number of Cypriot key actors, selected on the basis of their power to influence -directly or indirectly- the workings and politics of the health sector of Cyprus. The interviews, were conducted during the months November 2007 and December 2008, using semi-structured and open-ended questions and the majority of them were subjected to discourse analysis in an attempt to extract, not only factual information on existing and planned policies, but also the views, deeper beliefs, prejudices, and hidden motives of the respondents, as well as a perspective of how commodities of power are distributed within the wider area of the provision of healthcare in Cyprus. The last methodology was a qualitative analysis and cross-case synthesis of fifty randomly selected patient cases from the author's clinical practice aiming to evaluate nutritional medicine practice and how this compares, where it coincides with, and where it differs from, contemporary medical practice

The results of the research analysed, synthesised and triangulated, were compared and contrasted with the work of other researchers and are presented in this book in seven Parts as follows:

¹ Ionia: Ancient Greek territory now known as Minor Asia

PART I: IDENTIFYING THE PROBLEM.

A high awareness is evident at all levels –political, academic, and medical- for the rising incidence of chronic disease, which appears increasingly at lower ages and amongst the most deprived groups of the population, indicating socioeconomic status as a strong predictor of disease. It appears that, in spite of the unprecedented progress in several areas of the provision of healthcare, people do not become healthier, although they do, admittedly, live longer. The new terms HALE (*Healthy Life Expectancy*) and DALYs (*Years Lost from Premature Death plus Years lived with a Disability*) figure in most reports and people suffering from more than one chronic health problems simultaneously appear to be the rule rather than the exception. Cyprus occupies the second lowest position in the HALE indicator in Europe, with its citizens losing an average of 9.7 years to illness and disability, which is about 12.5% of their lives. An interesting account is provided in this part on what health means to people and to what extent ‘perceived health’ coincides with factual health as promoted by contemporary health systems.

PART II: THE EVOLUTION OF MEDICAL THOUGHT- A critical historico-philosophical review

A tribute to the strong influence of ideas on science, this Part represents a critical historico-philosophical review of the evolution of medical thought during the last two millennia. The historical review stretches back in time, a few centuries B.C. in the Eastern part of the Mediterranean, where the rise of scientific thought among the first, widely known as ‘Presocratic’, thinkers of the Classical Era of ancient Greece, is accompanied by a significant epistemological debate. The search for ‘what the world is made off’ and ‘what reality is’ gives rise to different, often antithetical, theories which in turn provide the basis for the establishment of the first medical schools of antiquity. The ideas of the Presocratics, espoused and further expanded by the great philosophers of Classical Greece, are promoted to the following generations. Following the pathway of evolution of medicine throughout the ages, different periods and their relation to the development of medical thought are evaluated. The Dark Ages with the strong influence of the dogmas of Christianity on all science is followed by the Medieval Awakening which coincides with the rise of the Byzantine medicine. With the advent of the Renaissance followed by the Scientific Revolution, scientific medicine takes a new turn along its pathway of evolution. The centuries that follow are characterised by an unprecedented

development in all fields of medical science and technology. A detailed account of these developments demonstrates the miracles achieved by Biomedicine in surgery, pathology, genetics, medical technology and pharmacopoeia, which they would have not been achieved without the rigorous application of the Newtonian scientific method of cause and effect and the Cartesian analytical thinking and reductionism. This Part provides also a brief overview of a number of worldwide known eastern philosophical systems such as Buddhism, Taoism, Hinduism, and Traditional Chinese Medicine (*which recently appear to have worth-noting parallelisms with twentieth century scientific developments in quantum mechanics and the Relativity Theory*) (A/N: this issue is not discussed in this book).

PART III: CONTEMPORARY HEALTHCARE -A CRITIQUE

A critical evaluation of a number of issues related to the provision of healthcare, particularly in the area of prevention and treatment of chronic disease, is attempted in this Part. In view of the volume of evidence in literature demonstrating an inversely proportional relationship between the unprecedented development in all fields of healthcare and the optimisation of health (*as discussed in Part I*), this part embarks on a critical examination of the reasons hiding behind the fact that more and more people, at increasingly lower ages, and from the lower socioeconomic strata of the population, suffer with multiple co-existing chronic health problems. Most of the times these problems appear to be effectively 'managed' rather than eradicated.

Criticisms target a number of long-established practices in the provision of healthcare such as: the emphasis on an impersonal model of care which focuses on particular diseases rather than the whole patient; a narrow conception of the determinants of disease, ignoring those falling outside the boundaries of the health sector, such as lifestyle habits, psychosocial effects, socioeconomic factors and environmental exposures; the overemphasis on specialisation to the detriment of continuity of care and the family doctor who traditionally used person-centred approaches; and the exclusive use of drug and surgery treatments, largely underplaying the therapeutic power of other factors in the patient's life, including diet and lifestyle. Aiming to enhance the objectivity of this Part, most of the publications reviewed represented self-criticisms and reflective practice by medical scholars and practitioners.

PART IV: THE WHOLISTIC NUTRITIONAL MODEL OF MEDICINE

This part elaborates on the identity of Nutritional Medicine and the medical epistemology which supports nutritional therapeutic interventions. Brief historical retrospection reveals that Nutritional Therapy in the ancient world was an important component of the newly born Scientific Medicine along with Pharmaceutical and Surgical Medicine, and it continued to be applied by medical doctors until the nineteenth century, when it was largely abandoned (although not entirely). The turn of the twentieth century coincides with the revival and redefinition of Nutritional Medicine, which aspires to fill a gap in the provision of healthcare, particularly in the area of prevention and treatment of chronic disease. An overview of how the science of Genomics relates to nutrition is offered in this Part, with special reference to the role of Nutrigenetics and Nutrigenomics as the sciences that study the genetic variations and gene polymorphisms and how gene expressions are regulated and modified by different nutrients in different humans under different conditions.

PART V: PUSHING FORWARD THE BOUNDARIES OF HEALTHCARE

This part focuses on the new philosophy in healthcare as proposed by medical and other academics and as appears to be materialising at different levels of the society with the advent of the twenty first century. A number of policies at the international and the European Union level are evident towards a new more person-centred healthcare, with the inclusion of non-conventional medicines, along with Biomedicine, into the national health systems. At the educational level, more and more universities enhance their medical programmes with new psychosocial and more person-centred therapeutic methods. The public appears eager for a new model of healthcare by resorting more and more to alternative methods of treatment, often in conjunction with their medical treatments, in an effort to find more effective solutions to their multiple chronic health problems. Apparently, this is a critical moment in the history of healthcare systems of the Western World, a turning point at which important decisions need to be taken at all levels, political, social, and medical. Academic literature abounds of proposals for new models of healthcare, Wholistic, Multidisciplinary, Integrated, Functional and

Biopsychosocial, all having Biomedicine as their basic component but are more patient- rather than disease-centred, and all resting upon the same epistemological framework: *wholism, functionality, and biochemical individuality*.

PART VI: NUTRITIONAL MEDICINE PRACTICE IN THE NEW PARADIGM

Within this epistemological fervour, Nutritional Science in its applied form, termed Nutritional Medicine or Nutritional Therapy, appears to offer solutions as a science that possesses the credentials to transcend the borders between disciplines. Sound evidence allows no doubt that the human body is a nutritional reality and this has been largely ignored by the current paradigm of healthcare. The volume of scientific research demonstrating the therapeutic role of diet and lifestyle in chronic disease is huge and increasingly rising. This part demonstrates with several evidence-based examples how nutrients can work either alone or synergistically with medical treatments to promote health and reverse disease. An account is also offered on how Nutritional Medicine is practiced, including a detailed example from the author's clinical practice, and on the rationale for nutritional supplementation, demonstrating the reasons for which people become deficient in nutrients, including exposure to endogenous and exogenous sources of oxidative stress. This part includes a number of examples of common chronic diseases, such as cardiovascular disease, neurodegenerative diseases, autoimmune diseases and cancer, and how these can be prevented and/or reversed by effective nutritional interventions, either alone or in conjunction with medical treatments, demonstrating the power of synergistic applications and consequently the vital role of Nutritional Medicine within contemporary medical practice

PART VII: NUTRITIONAL RESEARCH-A CRITIQUE

This part attempts to explain the reasons hidden behind the fact that, in spite of the volume of evidence-based research on the therapeutic effect of nutritional interventions, this information is not readily available and it is often ignored and/or underplayed by healthcare providers. Several scholars and researchers attempt to provide explanations on the limitations and weaknesses of nutritional research posed by the particular nature, the unique characteristics, and the complexity of the field of nutrition, which make this area of research different from that of pharmaceutical research. Factors mentioned are,

baseline exposure, nutrient status, bioequivalence, bioavailability, multiple and interrelated biological functions of a nutrient, undefined nature of nutrient intervention and uncertainties in assessing dose-response relationships. Recommendations for improving nutritional research are provided also in this part, as proposed by academics and researchers.

PART I

IDENTIFYING THE PROBLEM

CHAPTER I

HEALTH AND DISEASE FACTS

'...it is the looming epidemics of heart disease, stroke, cancer and other chronic diseases that for the foreseeable future will take the greatest toll in deaths and disability. It is vitally important that the impending chronic disease pandemic is recognised, understood and acted on urgently.'

World Health Organisation 2005

The first decade of the twenty first century is characterised by a high awareness of the need of urgent action in order to contain the rapidly spreading pandemic of chronic disease, which is reported as a major cause of death and disability worldwide, (WHO [2003i, 2003iii, 2004i, 2004ii, 2005i, 2006, 2006iii, 2006iv, , 2007, 2007i, 2007ii, 2007viii, 2007xi, 2008; 2008i, 2008ii]; WHO Europe [2006, 2008, 2008i, 2008ii]; EU [2005;2007ii]; Evans et al. 2001; Yach et al. 2004; Wolf & Akesson 2001; Mathers & Loncar 2006; Davis & Wagner 1999; Lopez et al., 2006; Ramsey et al 2008; Zimmet 2000). The World Health Organisation experts, recognising the 'enormous human suffering caused by non-communicable diseases' (WHO 2008), express high concern for the future of humanity, which is threatened by the 'looming epidemics of heart disease, stroke, cancer and other chronic diseases that for the foreseeable future will take the greatest toll in deaths and disability', (WHO 2005). The new terms DALYs (*Years lost from premature death plus the years lived with a disability*) and HALEs (*Healthy Life Expectancies*) figure in most reports, (WHO [2005i; 2006iv]; Woolf & Akesson 2001; Davis & Wagner 1999; Mathers & Loncar 2006; WHO Europe [2008i, 2008ii]). Colin Mathers and Dejan Loncar, researchers of the World Health Organisation claim that it may be the case that YLD (*years lived in disability*) will become an increasing proportion of total DALYs over the next thirty years, (Mathers & Loncar 2006). At the turn of the twentieth century, Ronald Davis, medical doctor and North American Editor of the British Medical Journal, and colleagues, in a special issue of the British Medical Journal devoted to chronic disease and the challenges presented to its management, referred to an *epidemiological transition*, during which people gain years of life, alas in disability (DALYs), and which is rapidly spreading from the rich countries, who have already completed the transition, to the rest of the world. Drawing from official reports and statistics, they demonstrated then that, about 691 million people worldwide had high blood pressure, 165 million suffered from

rheumatoid arthritis, and 29 million from dementia, while diabetics was estimated to increase from 135 million to 300 million by 2025, (*Davis & Wagner 1999*). With the advent of the twenty first century warnings appear to significantly increase. Estimates show that deaths from chronic diseases –half of which occur prematurely in people under 70 years of age, (*WHO 2005*)- are expected to increase by 17% worldwide, and 25% in the Eastern Mediterranean, over the next 10 years, (*WHO 2008*); cardiovascular diseases, cancers, diabetes and chronic respiratory diseases are reported as the ‘world’s biggest killers’, (*WHO 2008*); ischaemic heart disease and depressive disorders are estimated to be among the three leading causes of the burden of disease in 2030, (*Mathers & Loncar 2006*); the number of new cancer cases and deaths are expected to increase by 70% by 2030, (*Zarocostas 2010*); osteoarthritis is the fourth most frequent cause of disability worldwide in women, (*Woolf & Akesson 2001*), while osteoporosis, which was responsible for 1.7 million fractures in 1990, is expected to cause 6 million fractures by 2050, (*WHO 2003iii*). More than 180 million people worldwide suffer with diabetes, a figure estimated to more than double by 2030, with deaths from diabetes –almost half of them occurring in people under the age of 70 years- expected to increase by more than 50% worldwide, and by more than 80% in upper-middle income countries, (*WHO 2008*).

Cyprus ranks very high among the other countries of the developed world in the burden of chronic disease. While in its 2007 Annual Report the Cyprus Ministry of Health reports that the estimated Life Expectancy of 81.7 and 77.0 years for females and males respectively, is favourably compared with other developed countries, (*MOH 2008, table 2, p.14*), the World Health Organisation indicates in its reports that Cypriots have the second lowest Healthy Life Expectancy (HALE) in Europe. Cypriots lose an average of 9.7 years to illness, which is the 12.5% of their lives and which represents the difference between Life Expectancy (LE) and Healthy Life Expectancy. This loss is more than two years more than the Eur-A¹ average (7.3 years) and the Eur-B+C² average (7.6 years), (*WHO 2006iv, fig. LE & HALE*,

¹ Eur-A, comprising 27 countries in the WHO European Region with very low child and adult mortality: Andorra, Austria, Belgium, Croatia, **Cyprus**, the Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, the Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland and the United Kingdom; (27 countries) (*WHO 2006iv*)

² Eur-B+C, comprising 26 countries in the Region: Eur-B (17 countries with low child and adult mortality: Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Montenegro, Poland, Romania, Serbia, Slovakia, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Turkmenistan and Uzbekistan) and Eur-C (9 countries with low child but high adult mortality: Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Moldova, the Russian Federation and Ukraine). (*WHO 2006iv*)

p.5). Drawing from the work of other researchers, it appears that Cyprus is included in the high risk regions for cardiovascular disease, (*Zachariadou et al. 2008*), which accounts for 40% of deaths in Cyprus, (*MOH 2008, p.15*) and for 21.1% of total DALYs¹ (*WHO 2006iv*), and it is reported as the major cause of death among the Cypriot population, (*MOH 2008, p.15; Golna et al 2004, fig 4, p.9*). It is expected to retain its prevalent position at least until the year 2030, (*WHO 2007xi fig. p.1*). Cypriot women occupy the second highest position in deaths from pulmonary and other heart diseases in Europe (Eur-A), (*WHO 2008, graph p.40*). Cancer, which is reported as the second cause of death among Cypriots (10% of deaths), (*MOH 2008, p.15*), killed 14.1% of Cypriots in 2005 and this percentage is expected to increase in the next two decades, (*WHO 2007xi fig. p.1*). Previous studies show that 62.9% of Cypriot men and 46% of women suffer from high cholesterol, (*Golna et al 2004*). Neuropsychiatric disorders appear as the second highest cause of disability among Cypriots, accounting for 19.4% of total DALYs for females and 15.8% for males, (*WHO 2006iv, table, p.6*). *Golna et al. (2004)*, report that 20% of the general population in Cyprus suffers from a psychiatric disorder, 15% from general anxiety and 7% from depression.

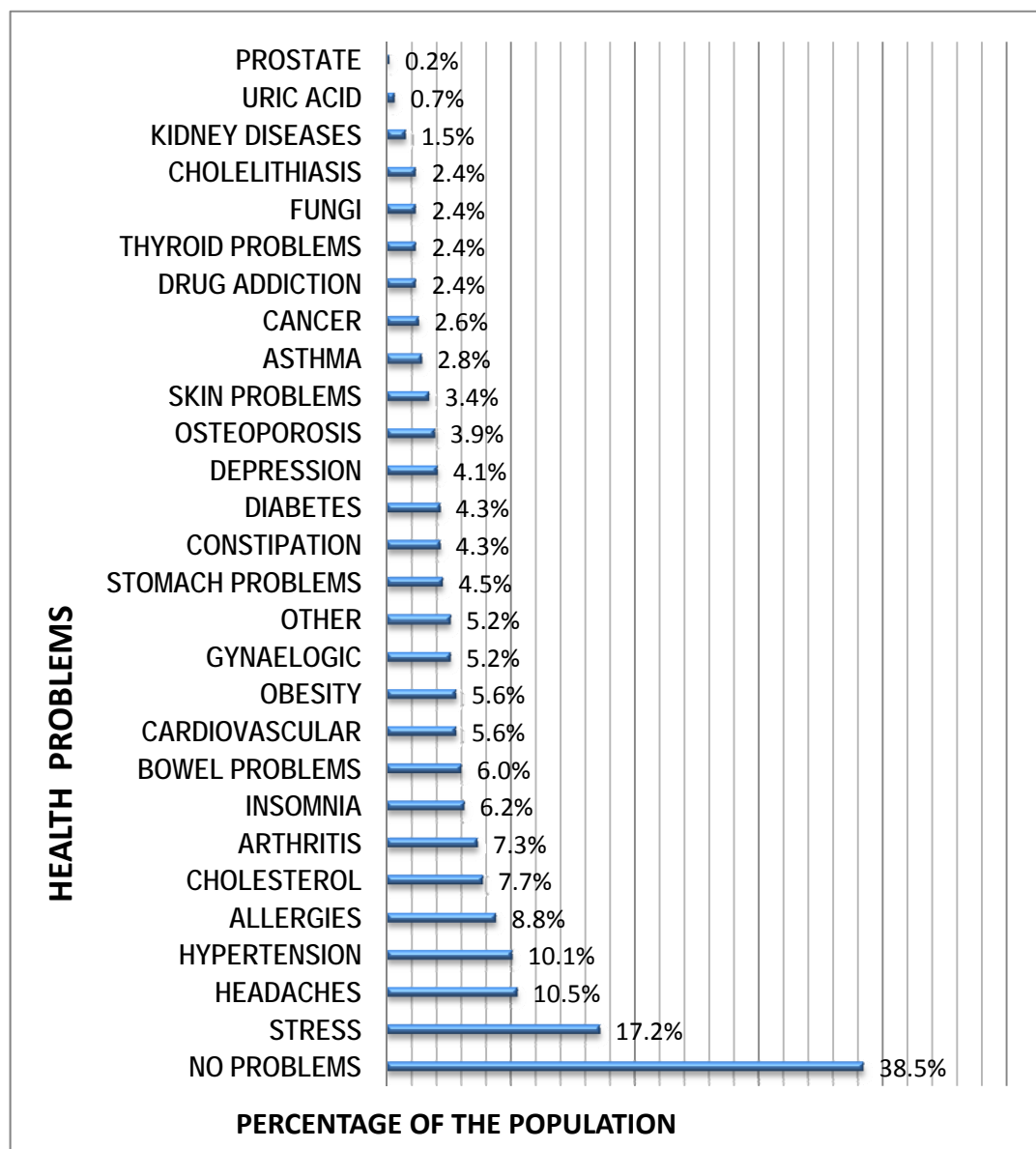
Almost all key actors of Cyprus interviewed by the author demonstrated awareness of the rising incidence of chronic disease in this country. Concerns were particularly raised by the Officials of the Ministry of Health for the rising incidence of child obesity, stating that action is already being taken through a series of programmes. The Officials of the Health Insurance Organisation (HIO), which was set up under Law in 2001 with a mission to implement a new National Health System stated that action is in their future plans, when the new system is established. Some of the politicians referred to a number of measures and plans for action promoted by their parties/associations towards the Government. In particular, the representative of one of the Patients' Associations expressed high concerns for the rapidly increasing incidence of diabetes in Cyprus, referring to an epidemiological study in 2004 which demonstrated that diabetes affects more than a tenth (10.3%) of the population. Further concerns were raised that this percentage is much higher because many people do not know they are diabetic, and special awareness

¹ DALYs: the number of years lost from premature death plus the years lived with a disability. The DALY combines in one measure the time lived with disability and the time lost owing to premature mortality. One DALY can be thought of as one lost year of healthy life. (*WHO 2006iv*)

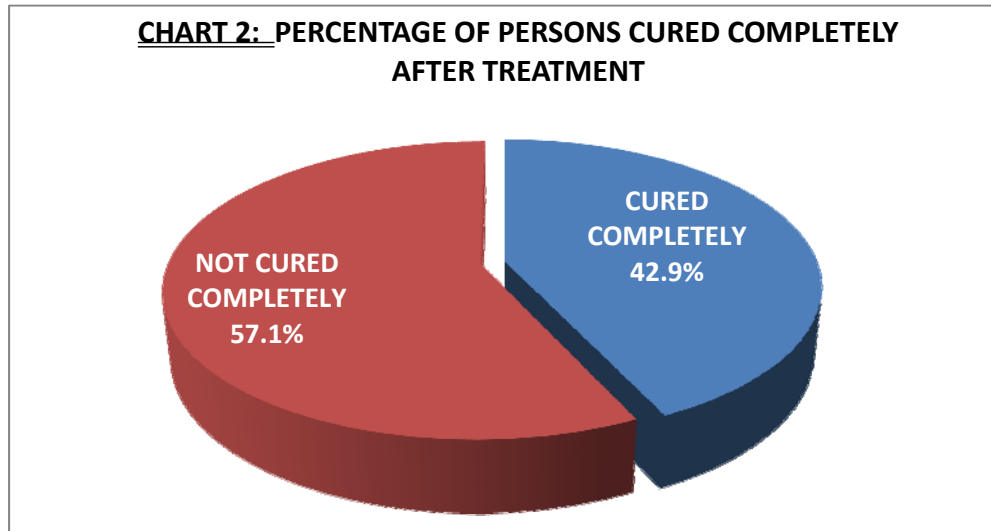
was demonstrated about child diabetes being the result of unhealthy diet, child obesity and sedentary life.

Furthermore, the present Survey demonstrated a less than optimum health status amongst Cypriots. In the question 'Do you suffer or suffered in the past from any of the following health problems?' (Appendix 1, Question 16), 61.5% of Cypriots stated as suffering now or suffered in the past from one or more health problems, while 38.5% of them stated as never had in the past, or have now, any health problems, (Chart 1: Percentage of the population with health problems).

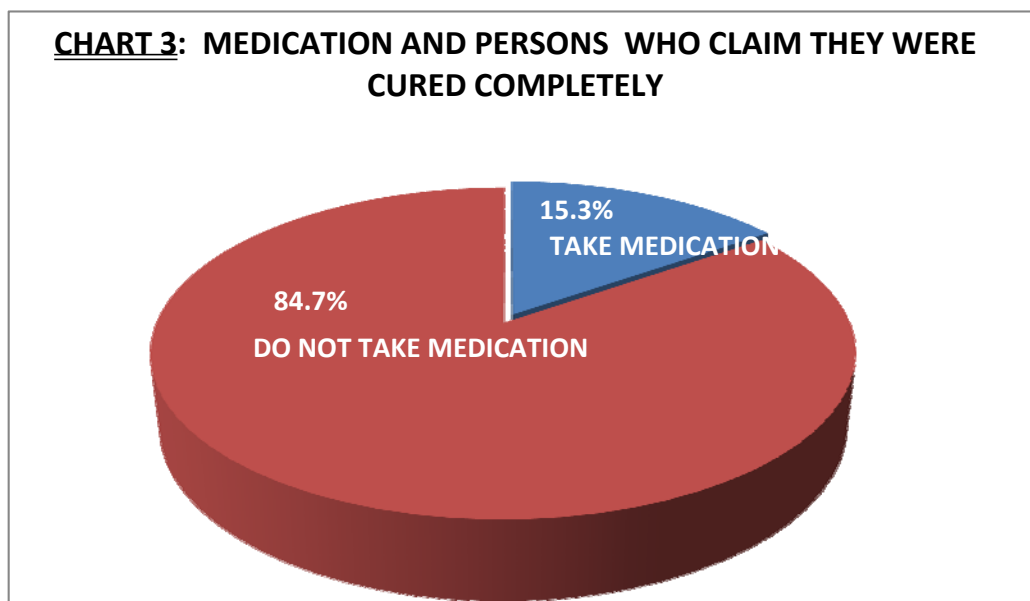
CHART 1: PERCENTAGE OF THE POPULATION WITH HEALTH PROBLEMS



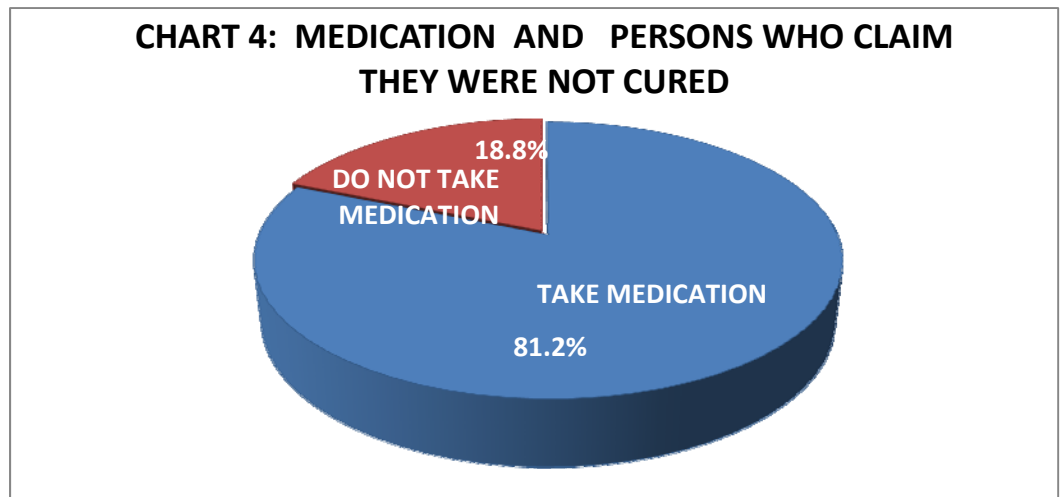
Further cross tabulation of the results, however, revealed significant facts not observable at first sight. In particular 57.1% of those who stated that were treated for one or more health problems also stated as 'not cured completely' while only 42.9% of them stated as 'cured completely' (Chart 2: Percentage of persons cured completely after treatment)



From those stating as 'cured completely' 15.3% continue to take medication (Chart 3: Medication and persons who claim they were cured completely). In other words only 36.3% of those who were treated for one or more health problems stated as 'completely cured' and 'not taking any medication', (84.7% X 42.9%).



This confirms that almost two thirds of people treated for their chronic health problems were not cured completely, or believe they were cured but still take medication, demonstrating that their health is not at optimum levels. Furthermore, from those stating as 'not completely cured after treatment' 81.2% are still under medication, while 18.8% stopped their medication without being cured, (Chart 4: Medication and persons who claim they were not cured)

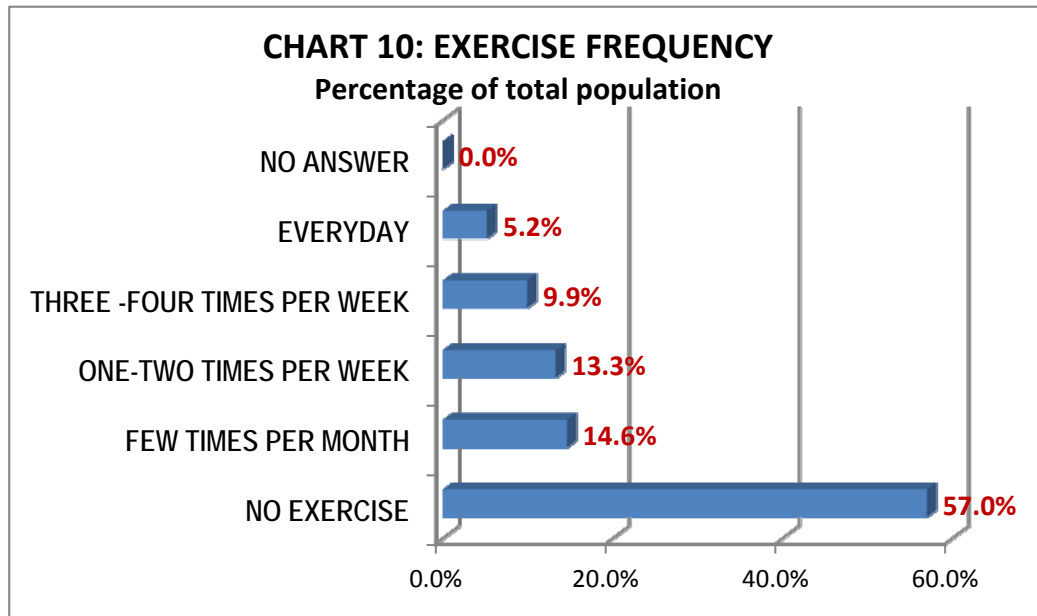


The fact that chronic disease occurs increasingly at lower ages, was also evident from the research in Cyprus which demonstrated that some common chronic health problems appear at all ages without discrimination. In table below (Table 2: Correlations between age and health problems), some health problems do not show any significant correlation with aging: These include asthma, prostate, depression, bowel problems, skin problems, headaches, stress, allergies, and constipation. Worth noting is that at this last list most psychologically-based problems are included such as depression and stress.

TABLE 2: CORRELATIONS BETWEEN AGE AND HEALTH PROBLEMS

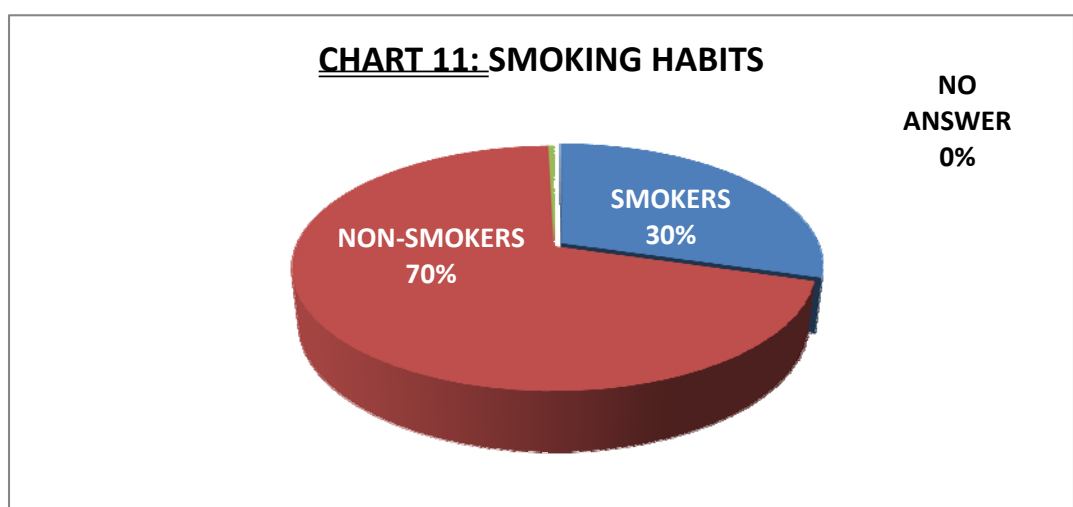
HEALTH ISSUE	PEARSON CORRELATION	SIGNIFICANCE (2-TAILED)	CONCLUSION
HYPERTENSION	0.322	0	YES AT 0.01 LEVEL
CARDIOVASCULAR	0.276	0	YES AT 0.01 LEVEL
ARTHRITIS	0.260	0	YES AT 0.01 LEVEL
HYPERCHOLESTEROLEMIA	0.241	0	YES AT 0.01 LEVEL
OSTEOPOROSIS	0.232	0	YES AT 0.01 LEVEL
DIABETES	0.225	0	YES AT 0.01 LEVEL
OTHER PROBLEMS	0.138	0.003	YES AT 0.01 LEVEL
THYROID PROBLEMS	0.134	0.004	YES AT 0.01 LEVEL
OBESITY	0.125	0.007	YES AT 0.01 LEVEL
DRUG ADDICTION	0.125	0.007	YES AT 0.01 LEVEL
FUNGI	0.115	0.013	YES AT 0.05 LEVEL
INSOMNIA	0.112	0.016	YES AT 0.05 LEVEL
STOMACH PROBLEMS	0.104	0.024	YES AT 0.05 LEVEL
CHOLELITHIASIS	0.102	0.028	YES AT 0.05 LEVEL
URIC ACID	0.101	0.03	YES AT 0.05 LEVEL
KIDNEY DISEASES	0.098	0.035	YES AT 0.05 LEVEL
GYNAECOLOGICAL	0.096	0.038	YES AT 0.05 LEVEL
CANCER	0.096	0.038	YES AT 0.05 LEVEL
PROSTATE	0.086	0.064	NO
ASTHMA	0.056	0.225	NO
DEPRESSION	0.040	0.39	NO
BOWEL PROBLEMS	0.035	0.45	NO
SKIN PROBLEMS	0.033	0.482	NO
HEADACHES	0.024	0.602	NO
STRESS	0.008	0.856	NO
ALLERGIES	-0.003	0.951	NO
CONSTIPATION	-0.084	0.072	NO

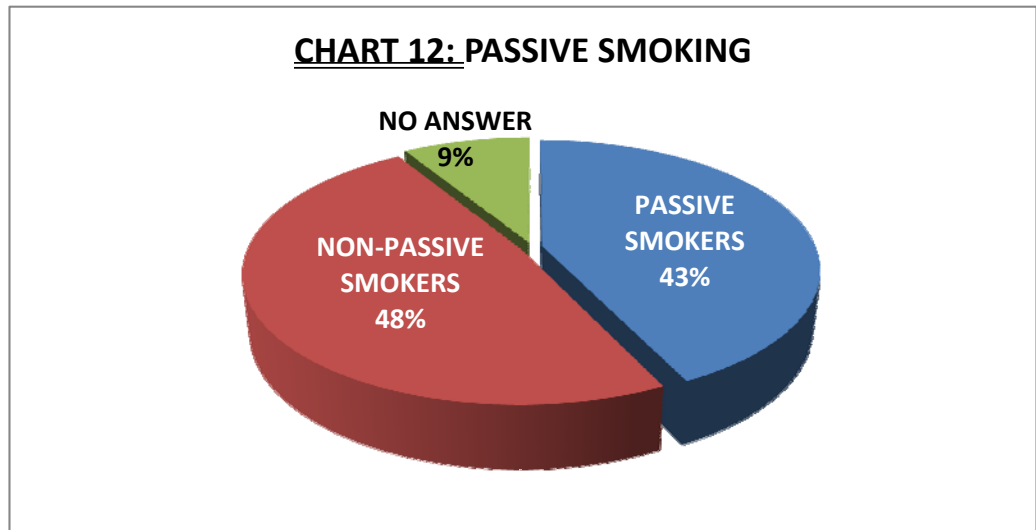
Furthermore, Cypriots appear to have adopted very unhealthy lifestyle habits, having abandoned their traditional Mediterranean diet, for unhealthy fatty food, (Golna et al 2004; Antoniadou 2005), ‘pushing up the prevalence of diseases that demand expensive therapies’, (Antoniadou 2005;) Researchers report an increase of the ‘new epidemics’, such as cancer and cardiovascular disease, ‘as a by-product of modern lifestyle’, (Golna et al. 2004). The Survey confirmed the tendency to sedentary and unhealthy lifestyle habits. It was particularly demonstrated that more than two thirds of the Cypriot population (71%), never exercise (57.0%), or exercise only a few times per month (14.6%), with only 15.1% stating that they exercise regularly at least three times weekly, (Chart 10: Exercise frequency).



Things appear to worsen year by year, if one compares the results of previous studies. In particular, the epidemiological survey of the Ministry of Health (Annual Report 2001) had shown that 32.2% of the population had a totally sedentary lifestyle (Golna et al 2004). Two years later the Ministry's Health Survey (2003) demonstrated that 63.8% never exercise, and the majority of the rest (27.3%) do some kind of light exercise, such as walking and bicycling at least four hours weekly.

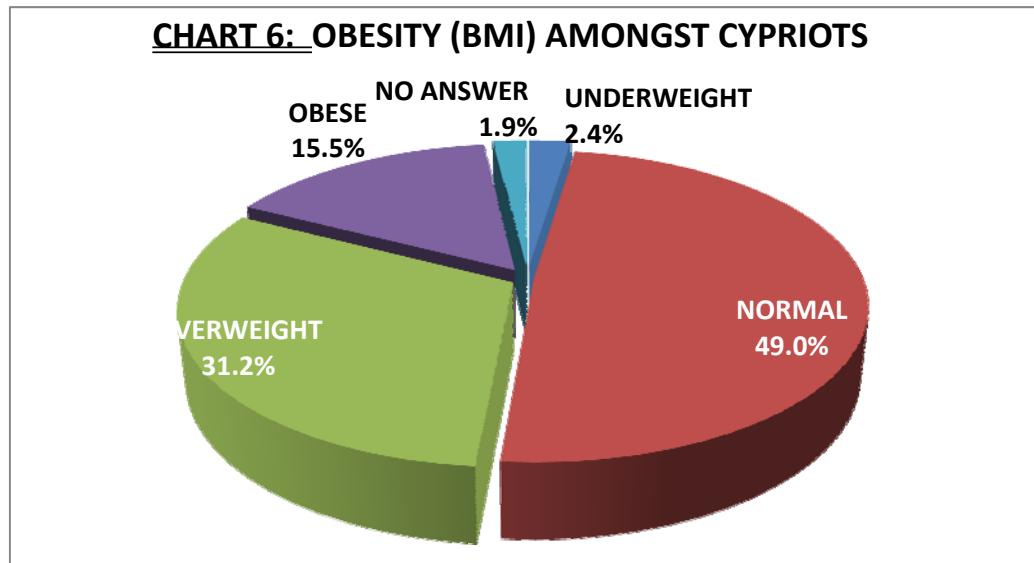
The same trend is true for smoking. In the present Survey it was shown that 29.6% of Cypriots are active smokers, while 46.9% state passive smokers, (both percentages based on those who replied) (Chart 11: Smoking habits & Chart 12: Passive smoking).





Previous studies had shown that 23.9% of the population smoked daily, (*Cyprus Statistical Service 2003; Golna et al., 2004*). This percentage was then estimated to be 68% higher than the EU average, (*Antoniadou 2005*). A more recent study by Kareklas et al., (2007) demonstrates a worsening of the condition. The study was carried out among freshmen college students and the results showed that only 39% reported not smoking, 39% smoke frequently, 10% smoke infrequently and 3% used to smoke in the past. The researchers found also that the rates of female smokers are higher than those of males. (*Karekla et al., 2007*)

In addition levels of obesity within the Cypriot population, particularly among men, have reached an epidemic level, (*Savva et al. 2007*) and are significantly higher among other Europeans. In 2001, 44.3% of males and 29.7% of females were obese or overweight, (*Golna et al. 2004, fig.7, p. 14; Antoniadou 2005*) while more recent studies reveal that one in two adults and at least one in four preadolescent children are overweight or obese, (*Lazarou et al. 2008; WHO 2008*). The present Survey verified the high incidence of obesity (as body mass index), with almost half of the Cypriot population (47.6%) appearing to be overweight or obese (31.2% and 15.5% respectively), (Chart 6: Obesity (BMI) amongst Cypriots).



Strong positive correlations between obesity (as Body Mass Index) and chronic disease were evident in literature, (Nguyen et al., 2009; Smith et al., 2009; PSC 2009; Coogan et al., 2009; Parsons et al., 2009), as well as a strong link between elevated waist circumference and chronic disease, (Elsayed et al 2008; Lemieux et al 2007; Blackburn et al 2009); without of course failing to acknowledge the fact that not all chronic diseases emerge from obesity, (Real et al 2006; Nikolakakis et al 2008; Yanik et al., 2009; Wise et al. 2005; Schwartz et al 2000; Foster et al 2008; Elsayed et al 2008). The present Survey revealed a strong relation between obesity (as Body Mass Index) and many of the most common chronic diseases. Significant positive correlations at the 0.01 level (2-tailed) were found between obesity and hypertension, high cholesterol, cholelithiasis, depression, fungal infections, diabetes, arthritis, cardiovascular disease, and insomnia, and at the 0.05 level (2-tailed) between obesity (as Body Mass Index) and cancer, thyroid problems, and digestive problems. A particularly strong positive correlation was found between obesity and drug addiction, demonstrating that obese people are more prone to drug dependency. Many chronic health problems, however, equally common amongst the Cypriot population, were found to have no specific correlation with obesity demonstrating the importance of other than obesity factors of disease (*discussed further down*). These include: osteoporosis, asthma, prostate, headaches, skin problems, uric acid, bowel problems, stress, kidney, gynaecological problems, constipation and allergies. (Table 1b: Correlation between BMI and health problems).

TABLE 1b: CORRELATION BETWEEN BMI AND HEALTH PROBLEMS

HEALTH PROBLEM	PEARSON CORRELATION	SIGNIFICANCE (2-TAILED)	CONCLUSION
DRUG ADDICTION	0.320	0	YES AT 0.01 LEVEL
HYPERTENSION	0.263	0	YES AT 0.01 LEVEL
HYPERCHOLESTEROLEMIA	0.195	0	YES AT 0.01 LEVEL
CHOLELITHIASIS	0.177	0	YES AT 0.01 LEVEL
DEPRESSION	0.173	0	YES AT 0.01 LEVEL
FUNGI	0.156	0.001	YES AT 0.01 LEVEL
DIABETES	0.149	0.001	YES AT 0.01 LEVEL
ARTHRITIS	0.146	0.002	YES AT 0.01 LEVEL
CARDIOVASCULAR PROBL	0.135	0.003	YES AT 0.01 LEVEL
INSOMNIA	0.130	0.005	YES AT 0.01 LEVEL
CANCER	0.113	0.015	YES AT 0.05 LEVEL
THYROID PROBLEMS	0.099	0.032	YES AT 0.05 LEVEL
STOMACH PROBLEMS	0.095	0.041	YES AT 0.05 LEVEL
OSTEOPOROSIS	0.081	0.081	NO
ASTHMA	0.075	0.107	NO
PROSTATE	0.057	0.218	NO
HEADACHES	0.050	0.278	NO
OTHER PROBLEMS	0.046	0.319	NO
SKIN PROBLEMS	0.042	0.364	NO
URIC ACID	0.041	0.381	NO
BOWEL PROBLEMS	0.031	0.508	NO
STRESS	0.030	0.525	NO
KIDNEY DISEASES	0.015	0.751	NO
GYNAECOLOGIC PROBL	-0.008	0.869	NO

CHAPTER II

PERCEPTIONS OF HEALTH

‘What health is’ or, more specifically, ‘what health means’ to people, has always been a subject of contention amongst scholars. An interesting account of how illness is perceived by different people is offered by Debbie Bean and her colleagues from the Department of Psychological Medicine at the University of Auckland in New Zealand. The researchers, in a comparative study amongst Europeans, South Asians and Pacific Islanders, have found five dimensions in the perception of illness, on the basis of Leventhal’s Self-Regulation model: 1) ‘identity’: perceptions of the label and the symptoms of the illness; 2) ‘timeline’: perceptions of the length of the illness; 3) ‘cure/control’: perceptions of the curability or controllability of the illness; 4) ‘consequences’: perceptions of the consequences of the illness; and 5) ‘cause’: perceptions of the cause of the illness (*Bean et al 2007*). Goode & Mavromatas (2008) refer to peoples’ perception of obesity as a problem of appearance or ‘not looking as good’, rather than as a health problem. The researchers claim that, the fact that commonly offered clinical options include reduced-calorie diets, appetite suppressors, and stomach stapling, verifies the fact that conventional approaches fail to address the multitude of underlying factors of obesity such as cellular metabolic imbalances, nutritional deficiencies, as well as psychosocial parameters, (*Goode & Mavromatas 2008*). According to Professor John Starr at the Geriatric Medicine Unit in Edinburgh University in the UK, and his colleague Linda Marsden, the term ‘health’ is much broader than the term ‘disease’. The researchers refer to the 2001 World Health Organisation’s definition of health as ‘a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity’, (*Starr & Marsden 2008*). On the same issue, Francois Gremy Professor of Public Health at European Union official research claims that the World Health Organisation’s definition of “Health” as a ‘state of complete welfare’ is ‘an asymptotic state impossible to reach, and the sole fashion to struggle for health is to systematically reduce and eliminate the causes of no-health’ (*Gremy 2005*). Ivan Illich (1995), historian and philosopher, in his book *Limits to Medicine*, defines ‘health’ as ‘an everyday word that is used to designate the intensity with which individuals cope with their internal states and their environmental conditions.’ In addition, he claims that health

levels of a population are at the optimum when ethical and political actions promote those environmental and cultural conditions needed by people to live a life of constant autonomous healing, rather than intense technical manipulation , (*Illich 1995, pp.6-8*).

The controversy over the definition of 'health' can be traced as far back in history as the ancient Hellenic era, in the writings of the great thinkers of antiquity who are widely recognised by historians as the pioneers of scientific thought, (*Ligeros 1937; Magee 1998; Arieti 2005*). In his treatise *On Ancient Medicine*, Hippocrates criticises the physicians of his time who graduated from the medical school of Knidos¹, for not distinguishing between symptoms and causes, when treating a patient (*Hatzopoulos 1992i, p.80, 11*)² and Galen, a few centuries later, also attacks the graduates of Knidos for the categorisation of diseases and for acting on the assumption that 'the whole was merely the sum of its parts' and 'if these parts were treated each in and for itself, the health of the whole organism would be eventually restored', (*Brock 1916, p.xxvi*). For Galen health was synonymous with *eukrasia*³, which denotes the good internal balance of the whole body whereas the opposite, *dyscrasia*⁴ was at the heart of all disease⁵, (*Goold 1916, p.188, 121*). Aristotle also employed a functional view of health emphasising in his work *Metaphysics II* on the importance of viewing a being as a whole entity with a reason and a cause for its existence and not just as a sum of its constituent parts⁶. Even Plato, who espoused a philosophy which was based on a dichotomy between 'real' and 'ideal' entities, believed that health is a function of symmetry, balance and harmony of the whole organism, (*Hatzopoulos 1992xiii, pp.204-7, 82*), and stressed the importance of restoring health by allowing illness to run its course and not using different medicines to treat the different phases of the same disease.⁷

¹ The medical school of Knidos was older than the Hippocratic school of Cos. Euryphon is considered to be the author of *Κνίδια Γνώμαι* the most representative work of Knidos which has not been saved but references to it are made by Hippocrates and Galen (*Lypourlis 2000i*)

² 'Σκέψασθαι δε χρὴ διὰ τίνος προφάσεως αὐτέοισι ταῦτα ξυνέβη', (*Hatzopoulos, (1992i, p.80, 11)*)

³ Ευκρασία= ευ (good) + κράση (The totality of the physical and psychological characteristics of an individual), (*Bambiniotis 2002*)

⁴ Δυσκρασία=Δυς-κράση

⁵ Ουδέ γὰρ δι' ἄλλο τι δυνατόν γίνεσθαι τὴν δυσκρασίαν αἰτίαν τῶν πρώτων νοσημάτων ἀλλ' ἢ διὰ τὴν ευκρασίαν διαφθειρομένην, (*Goold, 1916, p.188, 121*)

⁶ 'Πάντων γὰρ ὅσα πλείω μέρη ἔχει καὶ μὴ ἔστιν οἶον σωρὸς το παν ἀλλ' ἔστι τι ὅλον παρὰ τα μόρια, ἔστι τι αἰτίον', (*Hatzopoulos 1992xxii, [H,p.136, [1045a,9-10]*)

⁷ 'τρόπος οὖν ο αὐτός καὶ τῆς περὶ τα νοσήματα συστάσεως. ἦν ὅταν τις παρὰ τὴν εἰμαρμένην τοῦ χρόνου φθεῖρη φαρμακείαις, ἅμα ἐκ σμικρῶν μεγάλα καὶ πολλὰ ἐξ ὀλίγων νοσήματα φιλεῖ γίνεσθαι', (*Hatzopoulos 1992xix, p.226, 89c*)

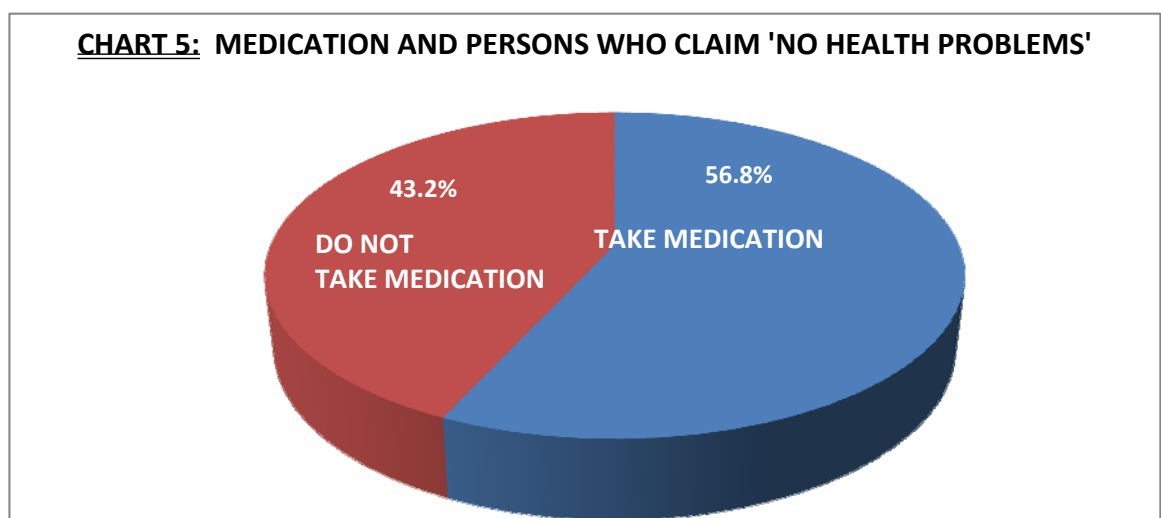
Apparently, the view of 'health', as the elimination of symptoms through their effective 'management' rather than 'complete cure', often with the long-term use of one or more medications has been established into the perceptions of the common people, (*Davis & Wagner 1999; Rastegar 2005*). Ronald Davis, medical doctor and North America editor of the *British Medical Journal*, and his colleagues, claim that the goals of prevention and early cure of chronic disease are 'often not met' allowing medical systems with no other option than the 'management' of chronic conditions, (*Davis & Wagner 1999*). Stephen Brown, assistant professor at the Department of Health Education in Southern Illinois University, Carbondale and his colleagues, in a study with 1178, 9-13year old students in seven states, found, among other results, that kids believed that they can do little to affect their future health, therefore had little interest in and desire to follow what they were taught about health. The researchers claim that 'health literacy involves more than the ability to navigate the health care system or follow doctors' directions, and refer to the Institute's of Medicine suggestion for seeing health literacy in an 'ecological framework' which is influenced by three different systems: 1) the healthcare system, 2) the culture of the society, and 3) the educational system, (*Brown et al 2007*).

Furthermore, recent officially conducted research in the European Union showed that the majority of European citizens perceive their health as very good, (*EU 2009i-Table: Health Perceptions; Harbers 2008- Table: Perceived General health*), in spite of the fact that studies demonstrate high disability rates (DALYs¹), and low healthy life expectancies (HALE) in most countries (*WHO [2002ii, 2003i, 2003iii, 2004i, 2005. 2005i; 2006; 2006iv, 2007i, 2007ii, 2007ix; 2007xi, 2008, 2008i, 2008ii]; WHO Europe [2006, 2008; 2008i; 2008ii]; Yach et al. 2004; Saultz & Lochner 2005; Hjortdahl 1992; Rastegar 2005; Shepherd 2009; Antoniadou 2005; Golna et al. 2004; Zachariadou et al. 2008; Woolf & Akesson 2001; Calman 1994; Starfield 1980; Davis & Wagner 1999; Mathers & Loncar 2006; Zimmel 2000*). Results from previous research in Cyprus have shown similarly optimistic perceptions: In the survey conducted by the Cyprus Ministry of Health in 2002 with 8375 Cypriots, the majority of the sample (73.2%) reported being in 'very good' (36.9%) or 'excellent' (36.3%) health, with only 6.3% reporting 'so-so' health and a very small 2% stating 'not good' health, (*Golna et al 2004*). Similarly, in the survey conducted by the Cyprus Statistical Service in December 2003, 80.8% of Cypriots considered their health status 'good' or 'very good' (*Cyprus Statistical Service 2003*). The same was true for a more recent

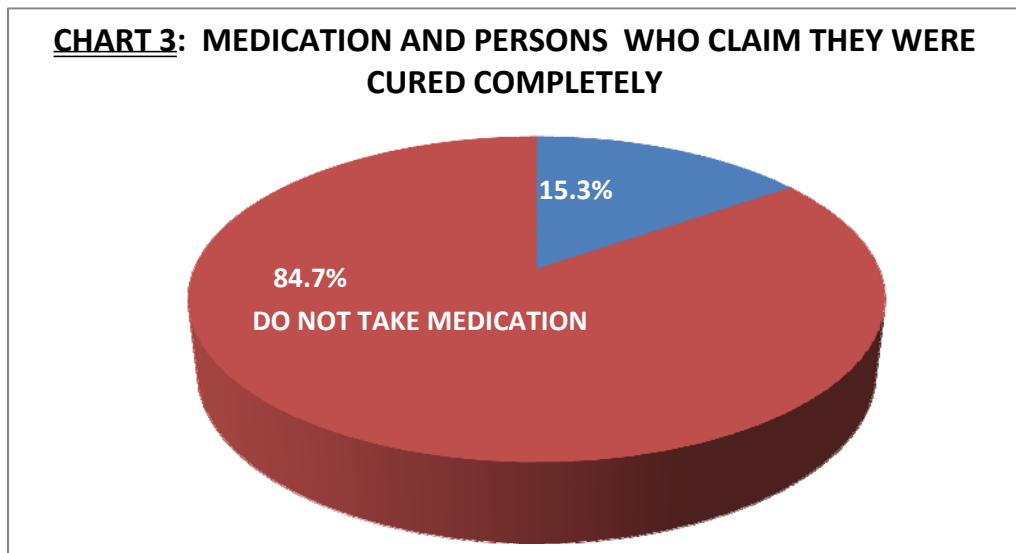
¹ DALYs: Disability-Adjusted Life Years (Years lost to ill health and premature death [*WHO 2008ii*])

European Union research which demonstrated that 81% of Cypriots reported 'good' or 'very good' health, ranking among the first four of the 27 European countries, (*EU 2009: Table: Health Perceptions*).

Contrasting and comparing facts and perceptions demonstrates significant contradictions, if one considers the health facts of Cypriots cited in the previous chapter, (Part I, Chapter 1). Recalling some of this evidence: Cypriots have the second lowest Healthy Life Expectancy in Europe, cardiovascular disease accounts for 40% of deaths in the country and 21.1% of total DALYs, cancer killed 14.1% of Cypriots in 2005, more than one fifth of the population suffers with hypertension, 62.9% of men and 46% of women suffer from high cholesterol, and neuropsychiatric disorders appear as the second highest cause of disability among Cypriots. The present Survey verified this paradox emerging from the gap between facts and perceptions and confirmed the prevalence of the 'management' rather than the 'cure' perception of health among Cypriots. A significant proportion of the population (38.5%) stated that they 'never had or have any health problems', as demonstrated in Part I of this Part, (Chart 1: Percentage of the population with health problems). However, further cross-tabulation of the results of the survey demonstrated a number of paradoxes. The first paradox is that, 56.8% of those stating as 'never had or have any health problems', take medication, confirming the long-term 'management' of a health problem with medication being perceived as 'cure', or 'no health problem', (Chart 5: Medication and persons who claim have no health problems)

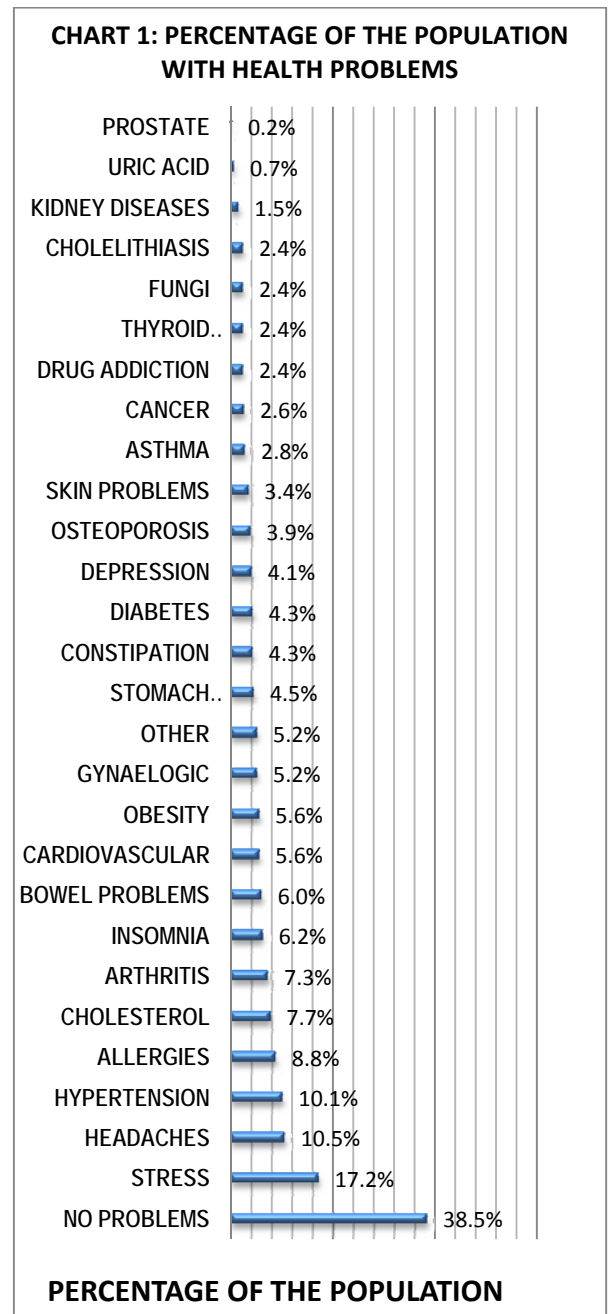
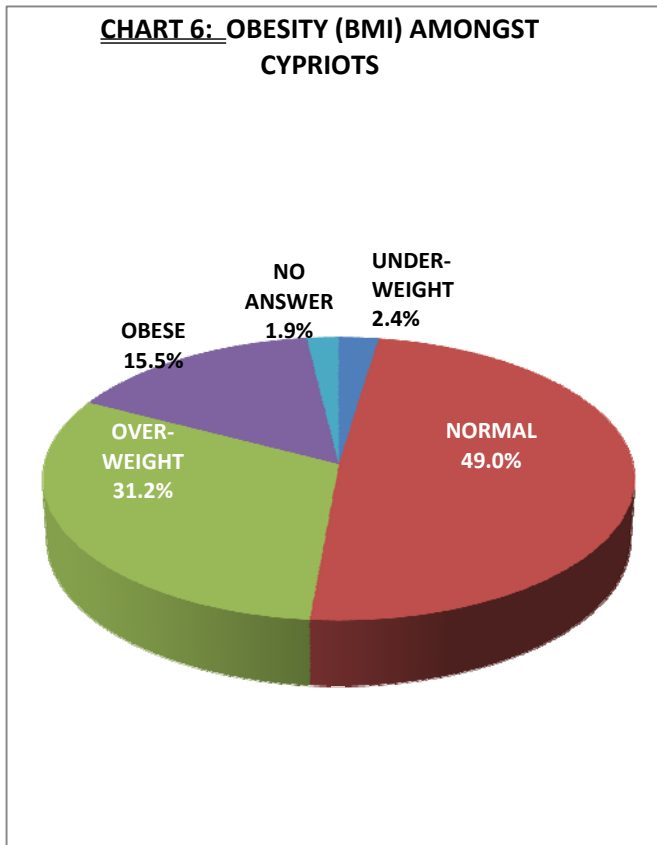


Another paradox is that 15.3% from those who 'have or had problems' and also stated as 'completely cured' after treatment of their health problem (s), still take medication (Chart 3: Medication and persons who claim they were cured completely):



These paradoxes – appear to explain the low reported levels of some chronic diseases in the Survey (much lower than official statistics above), such as only 7.7% stating as suffering with high cholesterol and 10.1% with hypertension, as demonstrated above in Chart 1: Percentage of population with health problems. Apparently taking long-term medication that reduces cholesterol and hypertension is perceived as 'cure'. The example of hypertension, which is considered by official reports as one of the 'most frequent long-standing health problems faced by Cypriots', (*Cyprus Statistical Service 2003*) and which is widely known to be successfully controlled, to a large extent, with life-long medication, is characteristic of the view that eliminating the symptoms equals to 'free of disease'. The high use of medication for the control of cardiovascular disorders, as is hypertension, is confirmed by official statistics which show that 41.5% of prescribed drugs in Cyprus are used for cardiovascular problems (heart, blood vessels or blood pressure), (*Cyprus Statistical Service, 2003*). Worth noting is the use of analgesics (painkillers), typical medicines for symptom relief, which represent the 46.6% of prescribed medicines in Cyprus, (*Cyprus Statistical Service 2003*).

Another paradox identified by this research relates to a contradiction between the actual percentages of obese Cypriots (15.5%), which was derived by working out height and weight values, (Chart 6: Obesity (BMI) amongst Cypriots) and those derived from their statements (5.6%) as in Chart 1: Percentage of the population with health problems. (See both charts compared in the following page). This paradox demonstrates once again the difference between definitions and perceptions of health.



PART II

THE EVOLUTION OF MEDICAL THOUGHT

**A critical historico-philosophical
review**

CHAPTER I

EPISTEMOLOGY: A PHILOSOPHY OF KNOWLEDGE AND LIFE

“Medicine is the daughter of time; we cannot fully appreciate its advancement, unless we turn back to the earliest traditions of the most remote inventions of science”

Fr. Z. Ermerins¹

Two major healing traditions appear to have supported world medical practice throughout the ages: **the Eastern**, influenced by the Asian-Pacific philosophy closely dependent to religious schools of thought such as Buddhism, Taoism and Hinduism; and **the Western**, underpinned by the Greco-Roman philosophy and quite independent from religious and mystical influences, (*Zunin & Wong 2006; Pizzorno & Murray 2007-2011*) (*this of course being true only before the discovery of the twentieth century physics*). Literature abounds of terms used to denote therapeutic approaches based on different conceptual frameworks of medical thought. Some of the most frequently used are: **Conventional, Modern, Biomedicine, Allopathic, Biopsychosocial, Alternative, Complementary, Integrative, Nutritional, Traditional, Holistic² or Wholistic³, Natural, Naturopathy, Homeopathy, Orthomolecular, Biological, Functional, Bioelectromagnetics, Reiki, Ayurvedic, Unani Tibb and others.** (*Balch & Balch 2000; Ballentine 1978; Capra 1982; Connelly 1994; Cushman & Hoffman 2004; Tovey et al 2005; Sheenan & Hussain 2002; Bodane & Brownson 2003; Zarcone 2003; Critchley et al 2000; Galland 2005; Garrow et al. 2000; Glenville 2001; Goldberg et al., 2002; Hyman et al. 2005; Jamison 1999; Jones 2005; Jones et al 2005; Jones & Quinn 2005; Lamb 2005; Liska et al 2004; Micozzi 2001; Mitchell & Cormack 1998; Murray et al. 2005; Pfeiffer 1987; Pizzorno & Murray 2006; Plaskett 2004 (i-xv); Quinn & Jones 2005; Rappay 1996; Reckeweg 1991; Roy 1999; Schmid 1991; Sudak 2005; Thiel 2000; Trivieri & Anderson 2002; Vithoulkas 1980; Werbach & Moss 1999; WHO 2003ii; Lypourlis 2000; Hatzopoulos 1992*). In the western world the prevalent academic view classifies all therapeutic traditions under two major categories:

¹Franciscus Zacharias Ermerins (1808-1871), quoted in Ligeros (1937)

² The word ‘Holistic’, commonly used to denote wholistic approaches, is taken as written by Goldberg et al., (2002)

³ The author uses the word ‘Wholism’ instead of ‘Holism’, which is commonly used to denote wholistic approaches, to avoid any connection with divine or spiritual concepts. As its title denotes, the Wholistic Nutritional Medicine Society of the UK adopts the same policy. For accurate referencing, however, the term ‘Holistic’ is used often in the text when quoted in phrases from other authors.

1. **Conventional or Modern Medicine, or Biomedicine, or Allopathic Medicine**, , widely accepted as the dominant medical system in the contemporary western world for the last three centuries.
2. **Non-Conventional (NCMs) or Complementary and Alternative medicines (CAM)** the umbrella for all therapies that are considered ‘non-biomedical’ (including *Traditional Medicine*).

The influence of philosophy into all fields of science, including medicine, is widely recognised by the academic world (Arieti 2005; Armstrong 1935[i-ij]; Balme 1991; Bennett 2001; Blackburn [1996;2005]; Brock 1916; Brock 1923; Capra 1982; Craik, 2009; Einstein & Infeld 1938; Flood 1996; Forster 1961[i-ii]; Goold & Balme 1991; Goold & Potter 1995; Goold & Smith 1994; Goold [1916; 1928]; Goold 1961[i-iii]; Goold 1988[i-ii]; Hatzopoulos 1992[i-xxii]; Henderson [1931; 1933; 1970]; Henderson 1923[i-ii]; Henderson 1935[i-iii]; Jeste & Vahia 2008; Jones 1923[i-ii]; Jones 1931; Kant 2004; King 2001; Ligeros 1937; Lypourlis [2000; 2001]; Magee 2005; Mallinger 1998; Mbitsakis 1978; Peck [1942; 1961; 1965; 1970]; Pentzopoulou & Petrou 2001; Potter 1988[i-ii]; Reid 1996 ; Smart 2000; Smith 1994; Tredenick [1933; 1935]; Vallance 1990; Vorning 1997; Vryonis 1989; Withington 1928; Yu-Lan 1976, p.2) and no investigation into the roots of any discipline can be considered valid and reliable if it fails to take into account the epistemological imprints of particular philosophical values and doctrines. Philosophy in general, and epistemology¹ in particular, provides the framework, within which new knowledge is constantly built, debated, disputed, discredited, and rebuilt, and represents the ‘watch dog’ against any attempt to restrict this knowledge within taken-for-granted boundaries.

History informs us that the great philosophers of Hellenic antiquity believed that the study of philosophy² was sought, not for some practical reason but, solely for the sake of knowledge³, and this was possible only for those who had secured all the essentials for life (often referred to as *aristocrats*). To the words of Aristotle:

‘If men studied philosophy to avoid ignorance, it is obvious that they delved into this activity for the sake of knowledge and not for some practical reasons. The course of events confirms this fact, that philosophy was sought only after people had secured all the necessities of life and pleasure⁴

Tredenick 1933, p12: Aristotle Metaphysics I, 982b [22-24]

¹ Epistemology: derived from the Greek word επιστήμη (episteme)=science, deals with the nature of science and knowledge (Arieti 2005)

² Philosophy: from the two Greek words φίλος=friend, and σοφία=wisdom (φιλο-σοφία)

³ To the words of Aristotle: ‘ἄστ’ ἐπερ διά το φεύγειν την ἄγνοιαν ἄφιλοσόφησαν, φανερόν ἔτι διά το ἐδέσθαι το ἄπίστασθαι ἄδίκων και οἱ χρήσεώς τινος ἔνεκεν, (Hatzopoulos 1992xxi, p.52 [982b20-21]),

⁴ σχεδόν γάρ πάντων ἄπαρχόντων τῶν ἄναγκαίων και προς ἄστῶννην και διαγωγῆν ἄ τοιαύτη φρόνησις ἄρξασθο ζητεῖσθαι) (Hatzopoulos 1992xxi, p.52 [982b22—24])

However retrospection into the history of science -and of humanity in general- allows no doubt that this was written under the strong influence of the doctrines of the different philosophical traditions. Bryan Magee, philosopher and politician of the twentieth century, who devoted his book *The Story of Philosophy* to prove that science was born from philosophy, views philosophy as the pursuit of truth stretching as far as our logos¹ can take us and can only be alive through dialogue, critique, exchange of arguments, and constant questioning of the fundamental principles of our existence and experience, (*Magee 2000, p. 6-7*). Albert Einstein and Leopold Infeld in a prologue to their treatise *The Evolution of Physics*, -a tribute to the strong influence of ideas on the explanation of physical phenomena- state that their intention is to describe, in simple easily comprehensible words, the effort of human spirit to find the relation between the world of ideas and the world of physical phenomena, and to demonstrate the driving forces hiding behind the effort of science to invent ideas to correspond to the realities of our world, (*Einstein & Infeld 1938; Mbitsakis 1978*). Professor Fung Yu-Lan, known as the father of Neo-Confucianism, in a chronicle of Chinese thought stretching from the third millennium until the twentieth century scientific revolution, claims that philosophising is 'thinking reflectively on life' and from this type of thinking emerge all theories of life, the universe, and knowledge, (*Yu-Lan 1976, p.2*).

¹ Our reason

CHAPTER II

THE EASTERN TRADITION: AN OVERVIEW

In spite of the fact that a significant number of scholars identify the word philosophy, - from the Greek words 'philos' (φίλος)=friend + 'sofia'(σοφία)=wisdom- with Classical Greece and, very often, the term 'ancient philosopher' brings to mind the philosophers of the Hellenic antiquity, adequate evidence exists to verify that the roots of philosophy are traced several centuries before the Hellenistic era, in the Far Eastern part of the world, particularly in India and China. A brief historical overview of major eastern philosophies is adequate to discredit the popular western view of the sole ancient Greek scientific heritage and allows no doubt that several people of the past, such as the Hindu, the Chinese, the Iranians in Mesopotamia, the Babylonians, and the Assyrians, demonstrate impressive epistemological and scientific achievements dating several centuries –often millenniums- before the Greeks (*Capra 1982; Ligeros 1937*). In many of these areas, philosophy dominates all life until the present time and is considered to be at the basis of all knowledge, (*Yu-Lan 1976; Capra 1982*). In the case of China, for example, philosophy 'has been every educated person's concern' and it is the first subject taught to children when they first go to school, (*Yu-Lan, 1976, p.1*).

Hinduism

Hinduism is one of the oldest religious traditions that it is still alive, -the oldest written texts date about two millenniums BC-, (*Jeste & Vahia 2008; Flood 1996*), and it represents 'a large and complex socio-religious organism consisting of innumerable sects, cults and philosophical systems', (*Capra 1982*). Simon Blackburn, Professor of Philosophy at the University of Cambridge, attributes to the Vedic period (1500-700BC) the oldest written Hindu scriptures, known as the Upanishads, (*Blackburn 2005*), which contain the essence of Hindu philosophy and have inspired India's scholars for more than twenty five centuries (*Capra 1982*). Ninian Smart, Emeritus Professor of Comparative Religion and Religious Studies at the University of California, identifies the roots of Hindu philosophy in the

ancient hymns of the Vedas¹ influenced by the Aryan culture that inhabited India fifteen centuries BC, (*Smart 2000*). The ultimate reality in Hinduism, the essence or 'soul' of all things is the Brahman, manifested in the individual human soul as Atman. The Brahman which is infinite and beyond all concepts gives Hinduism its monistic² character, (*Capra 1982*), and is paralleled with the Parmenidian³ One, (*Blackburn 2005*), which represents a deterministic view of an eternal and indestructible reality and a universe as a continuous, unchangeable, motionless reality, (*Magee 1998; Blackburn 2005*). For Hinduism there are two diametrically opposite worlds: the one perceived by our senses, the Empirical World, and the Real World, which represents the ultimate, unchangeable reality hidden behind the Empirical World (*Magee 1998*), -a philosophy espoused several centuries later by Plato and Socrates, and much later by Kant and Schopenhauer. According to Indian philosophy, all things and events around us are not realities of nature; they are just the result of our perceptions. According to Fritzof Capra, high-energy physicist, researcher, and author of many books based on the philosophical implications of modern science, the essence of Hinduism lies in realizing that 'we are all part of the same reality' which is the Brahman and any one believing that can be separated and act independently of their environment is bound by Karma⁴. Liberation from Karma can be materialised by joining the Brahman through a number of rituals, such as meditation and Yoga (from Yoke=to join), (*Capra 1982, p.102*). The early centuries AD are considered as the main period of the formation of classical Hinduism and its major orthodox schools -three pairs of which were widely recognised. These are the *Nyaya-Vaisesika*, the *Mimamsa-Vedanta* and the *Yoga-Sankhya*. The latter is widely applied now in the western world for its therapeutic effects on both the physical and mental/emotional parts of the body. Yoga developed initially on a metaphysical basis but obtained atheist character throughout the ages until the modern times, (*Smart 2000*). In the medieval period Yoga evolve as a meditational exercise with the name *Hatha Yoga*, placing emphasis on transcendental purification through 'higher flights of meditation, (*Smart 2000, p.42*), in antithesis to its sister system *Sankhya* which has an intellectual content and emphasises *gnosis* (knowledge)

¹ Vedas: a collection of ancient scriptures written by anonymous sages in ancient Sanskrit, the sacred language of India during the period 15th -7th centuries BC, which followed the migration of Aryan people into the Hindu valley. The Vedic philosophy is mainly included in the concluding sections of the *Vedas*, known as the *Upanishads* (*Blackburn 2005; Capra 1982*)

² Monism: the doctrine of one principle, one causal factor, one unchanging reality. From the Greek word *μόνος*=single

³ Parmenides of Elea: Prosocratic known for his statement: 'Ἐν τῷ πᾶν' =there is only One unified whole

⁴ Karma: a universal law of cause and effect (*Blackburn, 2005*), the force of creation, that supports action in a universe in which all are dynamically interconnected', (*Capra 1982*)

Buddhism

Buddhism, being the dominant spiritual tradition, in different versions, in several countries of Asia, including Indochina, Sri Lanka, Nepal, Tibet, China, Korea and Japan, (Capra 1982), is considered by many as a breakaway from the ancient Hindu tradition, since it rejects the orthodox Vedic authority, (Smart 2000). It emerged initially in India by Siddhartha Gautama, the so called *Buddha*, (Blackburn 2005), around the sixth century BC, coinciding with the birth of ancient Greek philosophy in the Eastern part of the Mediterranean but also with other 'spiritual and philosophical geniuses', such as Confucius and Lao Tzu in China and Zarathustra in Persia, (Capra 1982). Buddhist epistemology is both spiritual/metaphysical and material at the same time, (Smart 2000; Capra 1982), based on radical empiricism, or experientialism, (Suzuki 1968)¹, describing reality as perceived empirically by the individual consciousness but endorsing to the oneness of an ultimate reality the *Dharmakaya* (as the Brahman for Hindu), which is reflected in the human mind as the enlightened wisdom (*bodhi*), (Capra 1982). Buddhism views the world and every individual as a 'cloud of impermanent events' rejecting the theory of an eternal, unchangeable *atman* (soul) wandering through the cosmos in an endless process of successive reincarnations, (Smart 2000, p.17). For Buddha the doctrine of impermanence is at the heart of all life. People suffer because they cling to fixed forms (*maya*) and resist flow and change in life; and they get frustrated by confining reality into fixed categories created by the mind, getting trapped into a vicious circle (*samsara*) of a never-ending chain of cause and effect (*karma*), (Capra 1982). Buddha offers a way out of suffering and reincarnations through self-development to reach *Buddhahood*, a state of total liberation (*nirvana*) from false notions of a separate self and from the bondage of *karma*, (Capra 1982). The psychological character of Buddhist philosophy is also evident in the work *World Philosophies* of Ninian Smart, in which Buddhism appears to emphasize recollection and pureness through self-analysis, introspection and self-control, and to view the individual as composed of bodily expressions, perceptions, feelings, dispositions, and conscious events, (Smart 2000, pp.17-18). One should not ignore, however, that Buddhism, apart from its intellectual side it has also a religious consciousness expressed as transcendental wisdom (*prajna*), faith, love and compassion, (*Karuna*), (Capra 1982).

¹ Quoted by Capra (1982)

Taoism

'Reasoning will not make men wise in it [knowledge]

Chuang Tzu¹

Taoism² represents one of the two major schools of thought, –the other being Confucianism³– which occupy the two poles on the spectrum of Chinese philosophy. Confucianism, being more of a moral philosophy, centres on human heartedness and righteousness, (Yu-Lan 1976) and supports a life based on social organisation, common sense, and practical knowledge, (Capra 1982). Yu-Lan, argues that the most striking difference between the Chinese and other people in the world is the fact that ethics (especially Confucian ethics) are the dominant feature of their culture, rather than religion, and claims that philosophy offers access to values, higher and purer from imagination and superstition, without the need of taking ‘the roundabout way provided by prayers and rituals’, (Yu-Lan, 1976, p. 5-6). Taoism, on the other hand, is more mystically oriented and more relevant for the comparison with modern physics; it attributes an intrinsically dynamic quality to the world, which is seeing in a continuous flow and change which occurs in a cyclic nature; Taoism is concerned with the discovery of human happiness through Tao, which is the *Way* to natural order; it employs mystical intuition in the observation and explanation of nature; it is characterised by a deep mistrust in conventional reasoning and analytic method; it rejects social etiquette and moral standards as artificial constructs of man; (Capra 1982), and stresses the unity of humanity with the universe which, when lost, gives way to the rise of the necessity for moral laws and systems of ethics, (Blackburn 2005). This is what Lao-Tzu⁴, the originator of Taoism, meant when he stated: ‘When Tao is lost only then does the doctrine of virtue arise’, (Blackburn 2005). Taoism represents the attempt of Chinese thought to liberate the search of knowledge from conventional reasoning, following instead an intuitive pathway to wisdom (Capra 1982).

¹ Chuang-Tzu: lived two centuries after Lao-Tzu and is regarded as the author of the second important –after Lao-tzu’s Tao Te Ching– and much larger Taoist book named Chuan-Tzu. Noteworthy, both books are considered to be collection of Taoist writings by more than one authors, (Capra 1982, p.115)

²Tao=Way or Process or Order. The ultimate, indefinable reality and as such is considered by Capra (1982) as the equivalent of the the Hinduist Brahman and the Buddhist Dharmakaya. Originated from Lao Tzu

³ Confucius or Kung Fu Tzu, (551-479 BC): the most celebrated teacher of poetry, history, and moral philosophy of Chinese history, espoused a philosophy which emphasized morality, righteousness, living within the structures of social order, (Blackburn 2005)

⁴ Lao Tzu (Old Master): the originator of Taoism, who lived in the 6th century BC and is regarded the author of Tao Te Ching, a short book of aphorisms regarded as the main Taoist scripture, (Capra 1982)

TRADITIONAL MEDICINES

A brief overview of number of the most important medical traditions found in different areas of the world, many of them based on the philosophies espoused by the major schools of thought described above, are cited below. Worth noting is that most of those so called 'unconventional' therapeutic practices of the western world, that qualify as Complementary and Alternative Medicines (CAM) have strong links with the Eastern Healing Tradition with Asian-Pacific philosophical and religious influences. They are grouped under the title Traditional Medicine, which appears to dominate the primary health care of most traditional societies, in which a major part of the Earth's population lives. (*WHO 2000; 2003ii*). The World Health Organisation estimates that up to 80% of indigenous people use traditional forms of medicine. A few of the most important of traditional medicines are listed below

Traditional Chinese Medicine (TCM)

TCM is the classical medicine of China. China's healthcare system places emphasis on preventive services and on integration of Western and Traditional medicines, (*Dong & Phillips 2008; Chen 2008*). TCM is based on traditional Chinese medical theories and uses locally grown natural therapeutic plants (more than 2000 species are identified), animal tissues, and minerals. The approaches to diagnosis and treatment are wholistic, focusing on the complex interrelationships within the human body and its constant interactions with its environment, (*Critchley et al., 2000*). Its roots can be traced several thousand years back in time and similarities to the ancient Greek four-element theory are detected by scholars. Researchers argue that the only differences between TCM's herbal means of treatment and those used by Western or modern medicines relates to the fact that the latter have been scientifically proved while the former are based on wisdom handed over from generation to generation. (*Critchley et al., 2000*). Daniel Reid, a leading authority on Chinese Medicine identifies the cornerstones of Chinese civilization, in which medicine had central importance, in the Central Plain of the Yellow River in northern China, (confirmed by recent archaeological excavations) at least five thousand years ago, around the thirtieth century BC. The tribal *shamans*, or 'medicine men', of that time used wild herbs for healing after testing them and categorizing them. Archaeological excavations revealed references to thirty six diseases and their herbal cures, inscribed on tortoise shells and

oracle bones, dating from the ancient Yin dynasty around the fifteenth century BC, (*Reid 1996*). The Chou Dynasty, which takes the sceptres from the Yin in the twelfth century BC and reigns until the third century BC, is identified with the golden age of Chinese philosophy (*Capra 1982*) and the period when medicine becomes an independent profession, (*Reid 1996*). Craik (2009) claims that, in spite of the fact that little documentary evidence exists for Chinese Medicine before the Han dynasty (2nd century BC), the *Neijing*¹, the monumental *Classic of Internal Medicine*, existed long before that -even though its date is disputed, (*Craik, 2009*). The two antithetical schools of thought in Chinese philosophy, Confucianism and Taoism, are in fact considered complementary, as 'two opposite poles of one and the same human nature' (*Capra 1982, p.114*). This view falls within the boundaries of the philosophical doctrine of the *yin* and *yang*, which are the two end poles which set the limits for the cycles of change. Hence, any situation that develops to an extreme point will eventually become its opposite. Modesty and avoidance of excesses prevents development of extremes. The theory of opposites finds application in traditional Chinese medicine where illness is seen as a disruption of the balance between the *yin* and *yang* in the human body (*Capra 1982*). The causes of disease are traced by Traditional Chinese Medicine to functional disharmony in the energy system of the body which is a function of the interdependence between the Three Treasures –physical body, energy, and mind. The germ theory of disease, according to which bacteria are omnipresent, absorbed by our food and drink, inhaled by the air we breathe, but cannot survive in our bodies if they don't find a fertile matter on which they subsist, lies at the heart of Traditional Chinese Medicine for the last five thousand years and it is espoused and taught in the West by the Schools of Naturopathy.

Traditional Indian Medicine: Traditional Indian Systems of Medicine (ISM)

ISM include *Ayurveda*, *Siddha*, *Homoeopathy*, *Unani*, *Yoga*, and *Naturopathy*, and are practised along western Biomedicine. They are all holistic, emphasising on prevention and using natural means for therapy. Practitioners of ISM study in recognised by the state universities and constitute the majority of all registered medical practitioners in India. *Ayurveda*, which is a holistic approach and it dates back to the Vedas², is the most popular system with the highest number of hospitals, beds and practitioners.

¹ *Neijing Suwen* or *Huangdi Neijing* or *Basic Questions of Internal Medicine* was composed by the Yellow Emperor who reigned during the 26th – 25th c. BC, (*Chinese Medicine 2010*)

² Ancient Hindu scriptures, 1500 BC-500 BC

Homeopathy, the second most practised Indian medical system, uses highly diluted remedies based on the law 'like cures like'. The rest of the traditional systems rank far below and include: *Unani Tibb*, widespread mostly among Muslim Indians; *Siddha* a very ancient, similar to *Ayurveda*, system from South India; *Naturopathy*, based on Ayurvedic principles but, conforming to the laws of nature, uses only dietary means entirely rejecting medicines; and *Yoga* which is not an actual system of medicine as it promotes general health and well-being through exercise and meditation, (Welchhoff 2006). Zarccone 2003 writes that the Indian medical tradition shares with the Chinese tradition the theory of breath and breathing and is closely connected with *Yoga*, (Zarccone 2003)

Traditional South Asia Medicine-Unani Tibb

*Unani Tibb*¹ means Ionian Medicine and it is a system of medicine practiced today in India, Pakistan and Bangladesh along with modern European Biomedicine, Homoeopathy and other traditional systems². *Unani Tibb* was transmitted in South Asia by the Arabs and Persians during the medieval period. It is based on the theories of Hippocrates and Galen with influences from the Persians Ibn Sina³ and Rhazes⁴ (Sheenan & Hussain, 2002; Welchhoff 2006).

Traditional African Medicine (TAM)

It was influenced by the wholistic ancient Greek theories of *humoral medicine*. In Tanzania traditional leaders are legalised and a traditional medicine research unit operates in the University of Dar Es Salaam. (Juntunen et al., 2000;).

Tibetan medicine

It is a complex system with influences from the Chinese and Indian medical thought. It highly values the role of diet and cooking in health and disease, and is referred to as 'an art of living' with ethical, aesthetic and cultural dimensions'. (Zarccone 2003).

¹ Unani or Yunani =Ionian (ancient Greek territory, now known as Minor Asia); Tibb: medicine in Arabic. Also known as Islamic Tibb

² Examples are Ayurveda and Siddha

³ Latinised name Avicenna, 980-1037 A.D, Persian doctor and philosopher, known as the Father of scientific Medicine in the East

⁴ Ar-Razi, Muhammad ibn-Zakariyya 865-923 A.D. Persian doctor, alchemist and philosopher

CHAPTER III

CLASSICAL GREECE

The Presocratics (c.6th - c.5th B.C)

Focussing on the evolution of medical thought, from the prevalent western historian perspective, demonstrates the roots of scientific medicine into the philosophical doctrines of the Presocratic Thinkers¹ of ancient Ionia of Greece a few centuries BC. Medicine in this part of the world before this period, as it appears in the writings of Hesiod² and Herodotus³, and in the Epics of Homer⁴, was practiced by the Asclepian centres. These, scattered all over ancient Greek territory, were established by Asclepius, who lived around 1250 BC. In the Asclepians - the most famous being at Olympia, Akragas, Corinth, Piraeus, Cos, Pergamum and Epidaurus- treatments offered included, among others, hydrotherapy, surgery, and herbal medicine. Moss (2000), refers to an abundance of evidence, including marble reliefs and inscriptions of surgical instruments, which verify that Asclepius practiced surgery. References are made by the historian Diodorus (1954)⁵ and the Trojan architect and engineer Apollodorus (1921)⁴¹. James Arieti, medical academic and historian, in his work *Philosophy in the Ancient world*, claims that theocratic perceptions and treatments, using the healing power of dreams and invoking the curative powers of gods, as used by the Asclepian sanctuaries, were never abandoned by the modern world but continue to exist along with scientific medicine, (Arieti 2005). Nevertheless, there is no doubt that the Wise Thinkers of the Eastern part of the Mediterranean attempted to overthrow the mantles of prejudice and mysticism and to explain their world through physical laws and mathematics. Scholars identify the birth of deductive reasoning during this time, in the tendency of the Ionian philosophers to develop explanations from a number of axioms (Arieti 2005).

Epistemological conflicts in the newly born scientific thought are evident among the philosophers of this time. The search for 'what the world is made off' and 'what reality is'

¹ The philosophers that lived before Socrates during the period c. 600-c.400BC and attempted systematically cosmology (Blackburn 2005).

² Greek oral poet who live around the c.8th-7th BC

³ Greek historian, who lived in the c.5th BC

⁴ Greek epic poet who lived around the c.12th-13th BC

⁵ Quoted in Moss 2000

gives rise to different, often antithetical, theories. Aristotle in his treatise *Metaphysics I* informs us that Thales the Milesius, known as the first philosopher, believed that the world was made of Water in different forms and densities, while Diogenis the Apollonian considered that Air was the basic substance in different densities. Empedocles supported the view that all matter consists of *Four Elements*: Fire (*Pyr*), Air (*Aer*), Earth (*Gaea*), and Water (*Hydor*) which are kept in harmony with the interaction of the two opposite forces of *love* and *strife*. Heraclitus from Ephesus, who also adopted the theory of the *Four Elements*, but with *Fire* predominating, believed in a continuous motion and transformation of all things in the universe. He is well known for his characteristic phrases: '*ta panta rei*' ('everything is in a state of flux'), and '*it is impossible to step into the same river twice*'. Both Heraclitus and Empedocles believed in the *transmigration* of souls and in the harmony brought by the reconciliation of opposite forces. Parmenides of Elea adopted a diametrically opposite to Heraclitus view of the world, which he saw as eternal, unchanging, indivisible and indestructible, his theory summarised in his famous short phrase: '*All is one*'¹. Xenophanes from Colophon postulated that reality is only a construction relative to our experiences and thus there is no absolute truth, while Pythagoras from Samos, who also believed in *metempsychosis*², attempted to explain the world using mathematical equations. The Pythagorean ideas were espoused and expanded by Plato into his theory of the genesis of the world. Leucippus and Democritus, known as the first atomists³, claimed that all things consist of individual, indestructible atoms existing in empty space, a theory strongly in line with the Parmenidian deterministic doctrine of a static universe, and diametrically opposite to the Empedoclean belief of a continuously changing and transforming world. Socrates, a prominent figure in the Platonian dialogues, employed a philosophy of the world on the basis of critical self-reflective reasoning and constant questioning of conventional ethics and taken-for-granted values and principles. Socrates, who is thought to have lived in the fifth century BC and served as a soldier in the Peloponnesian War, was equipped with exceptional dialectical skills, which he used to transmit knowledge and virtue to his followers. His

¹ ἅν τ' ἅν'

² The cycle of reincarnation

³ From the Greek word ἀ-τομον=cannot be divided

monumental phrase: *'I know only one thing, that I know nothing'*¹, is characteristic of his phenomenal wisdom and virtue.

A significant part of the academic community believe that the doctrines of the Presocratics provided the archetypes for all western philosophy and science. The great philosophers that succeeded them in the period, which extended a few centuries before and after the advent of Christianity, used the Presocratic theorems as cornerstones to build their epistemological paradigms and there is no doubt that this wisdom was transmitted through generations to the present time. Aristotle, Plato, Hippocrates, and Galen were among the pre-eminent intellectual figures of this era who expanded and organized the Presocratic wisdom into particular branches of scientific knowledge, while the last two developed these ideas into a specific science of medicine. Arieti (2005) claims that, although doctoring is as old as civilization, only the Greeks developed a purely rational way of looking at the world from which medicine became a science, (Arieti 2005). Evidence of the medical epistemology of the different schools of medical thought that flourished within the spirit of the Ionian Revolution are found in the Hippocratic Corpus and the writings of Galen, and to a lesser extent in Aristotle and Plato. The most important were the medical school of Croton, established and led by Pythagoras of Samos, Alcmaeon of Croton, Democedes, Democritus, etc; the medical schools of Knidos with Euryphon and Chrysippos; and the medical school of Cos with Hippocrates. Each one of the schools formed their own theories of the causes and symptoms of disease on the basis of their different systems of thought regarding the nature of man and its environment, (Ligeros 1937). Spyros Vryonis, Professor of History at the New York University, in a lecture on *The Medical Unity of the Mediterranean World in Antiquity and the Middle Ages*, stresses the strong influence of Ionic science on them, drawing from the fact that, although the schools were within the Doric dialect, their writings were recorded in Ionic, (Vryonis 1991).

¹ Ἔν οἶδα ὅτι οἶδέν οἶδα'

The medical school of Croton-Alcmaeon (c.5th B.C)

The first school of Greek medicine was established by Alcmaeon in the city of Croton in Ionia in the fifth century BC –although some identify it a little earlier around the second half of the sixth century B.C, (Debernardi et al., 2010). A volume of medical and philosophical works are attributed to Alcmaeon, however since they have not been preserved, all knowledge available on this school of thought -found fragmented in Aristotle, Galen, Plutarch, Calcidius, Stobaeus and others- is disputed by different scholars, (UMDL 2005). Vryonis (1989) refers to a lost medical treatise, the *Concerning Nature*¹, written in Ionian language by Alcmaeon, in which he identifies the doctrine of *Isonomia Dynameon* (*Equilibrium of Forces*)² in the human body, as the major determinant of health and disease, (Vryonis, 1989,p.14). Scholars believe that he was a pupil of Pythagoras, and that he practiced anatomical dissection on animals. If our information is correct, Alcmaeon was one of the most eminent medical theorists of antiquity, with a great contribution to the study of medicine. He attributed a central role to the brain, as the most intelligent part of the body, and established the connection between the brain and the sense organs, (Debernardi et al., 2010). He is thought to have been the first to have dealt with the internal causes of illnesses, suggesting that health was a function of both the internal balance between opposing humours of the body as well as of the surrounding environment, nutrition, and lifestyle of the individual, (Vryonis 1991; Ligeros 1937; King 2001; UMDL 2005). A. Debernardi and colleagues at the Department of Neurosurgery, Niguarda Cà Granda Hospital, Milan, Italy, claim that the medical school of Croton was ‘the most famous in Magna Graecia’ in which scientific and experimental practices were used for the first time in the examination of the diseases of the human body, (Debernardi et al., 2010). According to Helen King, Professor of the History of Classical Medicine in the University of Reading, Alcmaeon used the word *Isonomia* -which is commonly used by political science to denote *equality of rights*- to emphasise the fact that health is a sort of democracy contrary to the ‘monarchy’ of disease, in which excess of one quality suppresses the others, (King 2001, p.8). It is not clear whether his anatomical dissections were carried out on animals or humans, however he is considered to be the first to identify the Eustachian tubes, (UMDL 2005).

¹ Περί Φύσεως: Peri Physeos

² Ἴσωνομία Δυνάμεων

The medical school of Cnidus-Euryphon (c.5th B.C)

The second school is the medical school of Cnidus which appears to have been established by Euryphon,- who is mentioned by Diogenis Laertius, Ruffus of Ephesus and Coelius Aurelianus, (*Ligeros 1937; Vryonis 1989*). Scholars identify strong influences on the Cnidian thought from Egyptian medicine. A characteristic example of Egyptian medicine relates to the aetiology and treatment of, what we call today, reflux regurgitation. According to this theory, traces of which are found in the Cnidian school, the genesis of this disease is attributed to the poisoning of the body from the excess food in the stomach which remains undigested and becomes putrefied (*Vryonis 1989*). In general, Euryphon appears to have an identical to the Egyptian medical thought approach to pathology and therapy. The Hippocratic Corpus, as transferred to Alexandria, during the age of Ptolemy the I, contained a volume of texts on the medical thought of the school of Cnidus which was in disagreement with that of Cos, (*Vryonis, p.17*). References in the Hippocratic Corpus and the writings of Galen demonstrate the Cnidians as more concerned with the symptoms rather than the causes with strong influences from Egyptian medical thought in pathology and therapy (*Vryonis 1989*). According King (2001) the Hippocratic Corpus contains a volume of work attributed to Cnidian doctors and this can explain the difference in approach between different texts in the corpus, (*King 2001*). A coherent system of medicine was developed in the school of Cnidus with detailed branches of anatomy, physiology, clinical description and pathology, regimen and therapy, surgery and gynaecology, (*Vryonis 1989*). Vryonis, drawing from the writings of Herodotus, acknowledges a significant Egyptian component in the medical thought of Cnidus which together with the schools of Croton and Cos contributed to the transformation of medicine from the Asclepian therapeutics to more scientific approaches, (*Vryonis, 1989*). Kleantis Ligeros, medical academic and historian, refers to Littré's¹, emphasis on the important contribution of this school to the method of observation. In the third book of the Cnidian School, '*Des Affections Internes*', reference is made to pleuritic resonance and friction and to the rhonchus or rale, which is most observable in some pleuritic conditions in the presence of fluid, (*Ligeros 1937, pp.379-380*). Demetrios Lypourlis, Professor Emeritus at the Aristotelian University of Thessaloniki,

¹ Eminent French scientist (quoted in Ligeros 1937)

claims that the medical school of Cnidus would have retain the most important place in the history of medical thought if Cos was not lucky enough to give birth to Hippocrates, (*Lypourlis 2000, p.239*). The Cnidian school was fiercely attacked by Hippocrates and Galen for approaching treatment of disease ‘from a static perspective’ and for attaching significance ‘to the trivialities of diagnosis of the symptoms’, (*Brock 1916, p.xi*). Galen writes that the Cnidian doctors have identified several diseases of each organ including, seven for the gallbladder, twelve for the urinary bladder, four for the kidneys, four jaundices, and three tuberculoses (*Lypourlis 2000, p.240*).

The medical school of Cos- Hippocrates (c.5th – c.4th B.C)

Our knowledge of Hippocratic medicine emerges from the Hippocratic Corpus and the writings of Galen. References are also found in the works of the historian Thucydides, the tragic writer Euripides, and the philosophers Plato and Aristotle. Hippocrates, widely known in the western world as the Father of medicine, was the first to coin the term doctor-philosopher claiming that all the elements of philosophy, such as unselfishness, humbleness, modesty, authority of opinion, judgement, presence of mind, gnosis of the useful and necessary for life, unprejudiced mind and divine superiority, are found also in medicine¹. According to Eleni Theodosopoulou, Associate Professor at the Nursing School of the University of Athens, Hippocrates is frequently referred to as the first rationalist medical thinker who ‘differentiated medicine from magic’, (*Theodosopoulou 2010*) and attacked charlatans and quacks who used charms to treat disease. Worth noting, however, is the introduction to the Hippocratic Corpus, by Odysseas Hatzopoulos and his philological team of experts, in which they underline an important fact: that Hippocrates used three sources of knowledge, the first being the *intellect (dianoisis)* the second the *senses (aestheseis)* and the third the *intuition (diaesthesia) or revelation (apokalypsis)* (*Hatzopoulos 1992ii, pp.16-17*). Scholars highlight the fact that this latter one, the *intuition*, has been strongly rejected as a way of learning by the scientific community of the western world, whereas it predominates as a source of knowledge in the East, (*Capra 1982*)

¹ In the exact words of Hippocrates in the treatise, Περὶ Ἐπισημοσύνης: ‘καὶ γὰρ ἐνὶ τὰ πρὸς σοφίην ἐν ἐτηρικῷ πάντα, ἐφιλαργυρίῃ, ἐντροπῇ, ἐρυσθήσις, καταστολή, δόξα, κρίσις, ἐσυχίη, ἐπάντησις, καθαριότης, γνωμολογίη, ἐπιδησις τῶν πρὸς βίου χρηστῶν καὶ ἐναγκαίων, ἐκαθαροίης, ἐπεμπόλησις, ἐδαισιδαίμονίη, ἐπεροχὴ θεία’ (*Hatzopoulos 1992i, [5]p.180*)

Hippocrates who rejected the possibility of any entity to be composed of only one element, developed further the doctrine of the *Four Elements (Fire, Air, Earth, and Water)* of Heraclitus and Empedocles to formulate his theory of the *Four Humours, Blood, Phlegm, Earth,, Water*¹ –which was subsequently espoused by Aristotle and expanded, five centuries later, by Galen. According to this theory, which is presented analytically in the *Nature of Man*² treatise, (Hatzopoulos 1992iv, p.145-179), humans are made of four humours *blood, phlegm, yellow bile and black bile*, which correspond to the four elements of the Presocratics as follows:

- | | | |
|--------------------|-------------------|------------------------------------|
| 1. Fire (Pyr) → | Warm (Psychron) → | Blood (Haema), |
| 2. Air (Aer) → | Cold (Thermon) → | Phlegm (Phlegma), |
| 3. Earth (Gi) → | Dry (Xiron) → | Yellow bile (Xanthe Chole), |
| 4. Water (Hydor) → | Moist (Ygron) → | Black bile (Melaena Chole), |

The quantity, colour, warmth, coldness, dryness and moisture of the four humours as well as the harmonic and balanced relationship in between them are at the basis of health and disease. A few lines from the *Nature of Man* treatise are characteristic of this theory:

*‘The body of man has in itself blood, phlegm, yellow bile and black bile; these make up the nature of his body, and these are responsible for his feelings of pain and being healthy. He is, moreover, enjoying the best health, when these elements are in the correct proportions as regards their quantities, power, and volume, as well as their intermixture but he is in pain when any one of these elements exists in excess or in deficiency or is isolated and it is not compounded with the others inside the body*³

(Hatzopoulos 1992iv, p.154 [4])

Hippocratic medical philosophy was essentially wholistic, taking into consideration the multitude of interactions taking place every moment inside the body of each individual and the complex interrelationships with its surrounding environment. In his treatise *Airs*

¹ Αἷμα, Φλέγμα, Γῆ, ὕδωρ

² Περί φύσιος ἄνθρωπου

³ ‘Το δε σῶμα τοῦ ἀνθρώπου ἔχει ἐν εωυτῷ αἷμα καὶ φλέγμα καὶ χολήν ξανθὴν τε καὶ μέλαιναν, καὶ ταῦτ’ ἐστὶν ἀπὸ τῶν φύσιος τοῦ σώματος, καὶ διὰ ταῦτα ἐλγέει καὶ ἰγιάει. ἰγιάει μὲν οὖν μάλιστα, ἐκόταν μετρίως ἔχῃ ταῦτα τὰς πρὸς ἀλλήλα κρήσιος καὶ δυνάμιος καὶ τοῦ πλήθους, καὶ μάλιστα μεμιγμένα. ἐλγέει δε ἐκόταν τι τούτων ἐλασσον ἢ πλέον ἢ χωρισθὲν ἐν τῷ σώματι καὶ μὴ κεκρημένον ἐ τοῖσι ξύμπτασιν. (Hatzopoulos 1992iv, p.154 [4])

*Waters Places*¹, Hippocrates advises the doctors of his time, that if they wish to apply the right medicine they need to proceed as follows: when they visit their patients, to study carefully not only their specific health problem but also where and how they live, the effect each season has in their area, the winds –from which direction they come, if they are cold or warm and if they are common to many areas or particular to their area- and the waters, their taste and weight and their effects². Hippocrates had a deep belief in the inherent self healing power of the human body, which had the potential to cure from any illness, with the use of natural therapeutic means which would allow the disease to run its course. This is described by Brock as ‘*Giving Nature a chance*’, (Brock, 1916, p.xi). These views were in sharp antithesis to the Cnidian school with its categorisation of diseases, and its view of the body merely as a sum of its parts which if treated separately the health of the whole body will be restored, (Hatzopoulos [1992i; 1992 vi]; Brock 1916; Goold 1916).

In the first paragraph of his treatise *Regimen in Acute Diseases*³, (*Peri Diatit Oxion*) (Hatzopoulos 1992vi [pp. 25-26, 1; Jones 1923ii, pp.62-65]), Hippocrates does not rule out the possibility that some of the Cnidian doctors were aware that an illness can have a multitude of phases until it runs its course⁴ and he praises them for their significant contribution to the science of medicine with their listing of the different phases of each disease; however, he expresses his disagreement with the usefulness of this work when it comes to treatment of the patient, drawing their attention to the fact that labels are good enough only in explaining the symptoms of the different phases of the disease; and therefore to avoid basing their diagnosis only on superficial manifestations and to be careful when deciding for what treatment each individual patient needs on the basis of the diagnosis of symptoms⁵, since similar symptoms may not have the same deeper cause and patients with identical symptoms may need different treatments, (Hatzopoulos 1992vi [pp. 24-26, 1]). Hippocrates also supported the view that the practice of using the same medicine to treat

¹ Περί Αέρων Ἐδάτων Τόπων,

² Ἐητρικὴν ἔστις βούλεται ἔρθῃς ζητέειν, τάδε χρή ποιέειν. Πρῶτον μὲν ἐνθυμέεσθαι τὰς ἔρας τοῦ ἔτεος, ἃ τι δύναται ἐπεργάζεσθαι ἑκάστη. Ὁ δὲ γὰρ οἰκασίν ἑλλήλῃσιν οἰδέν, ἑλλά πούλυ διαφέρουσιν αὐταί τε ἐφ’ ἑωυτέων και ἐν τῇσ μεταβολῃσιν. Ἐπειτα δε τὰ πνεύματα τὰ θερμά τε και τα ψυχρά, μάλισα μὲν τὰ κοινὰ πῆσιν ἐνθρώποισιν, Ἐπειτα δε και τὰ ἐν ἑκάστη χώρῃ ἐπιχώρια ἑόντα. Δεῖ δε και τῶν ἑδάτων ἐνθυμέεσθαι τὰς δυνάμιας. Ἐσπερ γὰρ ἐν τῷ στόματι διαφέρουσι και ἐν τῷ σταθμῷ οἰττω και η δύναμις διαφέρει πούλυ ἑκάστου.’ (Lypourlis 2000, p.112-144 [1])

³ Περί διάιτης ἑξέων= Regimen of acute diseases

⁴ ‘Τὰς μέντοι πολυτροπίας τὰς ἐν ἐκάστη των νοῦσων και την πολυσχιδίην αὐτέων οὐκ ἡγνόεον ἐνίοι’, (Hatzopoulos 1992vi[p. 26, 1)

⁵ ‘Ὀκόσα δε προκαταμαθῆιν χρη τον ιητρον, μη λέγοντος του κάμνοντος, τουτέων τα πολλά παρείται, ἄλλα ἐν ἄλλοισι, και ἐπίκαιρα ἐνια ἐόντα ἐς τέκμαρσιν. Ὀκόταν δε ἐς τέκμαρσιν λέγηται ως χρή ἑκάστα ιητρεύειν, ἐν τουτέοισι πολλά ἐτεροίως γιγνώσκω ἢ ως ἐκεῖνοι ἐπεξήεσαν.’ (Hatzopoulos 1992vi[p. 24, 1]; Jones 1823ii, p.62)

similar symptoms was the reason for which quacks succeeded in pretending to be doctors. 'It is naturally easy, he argued, for anyone to learn the name of the medicines used in each case'¹.

Hippocratic medicine was based on the fundamental principles of natural medicine, (as listed by Zunin & Wong 2010):

1. The healing power of nature (vis medicatrix naturae)
2. First do no harm (primum non nocere)
3. Find the cause (tolle causam)
4. Treat the whole person
5. Preventive medicine
6. Wellness
7. Doctor as teacher

In the Hippocratic treatise *Ancient Medicine*² the doctor is advised to search for all the factors that determine the existence of the patient before prescribing a treatment³, to investigate deeper than the symptoms⁴, and to never do harm to any patient⁵. Hatzopoulos (1992i) identify Pythagorean influences in this part of the Hippocratic Oath. According to the commentators, *euthanasia*⁶ -which was rejected by Hippocrates- was well known in antiquity and our ancestors frequently preferred to commit suicide rather than suffer from a tantalizing disease. Pythagoreans were the only ones who strictly forbade the use of this method (Hatzopoulos 1992i, p.315-16). The Pythagoreans were also against abortion and the Hippocratic Oath states clearly: *I will never give phthorion*⁷ to induce abortion⁸, (Hatzopoulos 1992i, p.34). Worth noting is Hippocrates belief to the strong link

¹ 'Οι γὰρ μὴ ἰητροὶ ἰητροὶ δοκέουσιν εἶναι μάλιστα δια ταύτας τὰς νόσους. Ρηίδιον γὰρ τὰ ονόματα ἐκμανθάνειν, οκοῖα νενόμισται προσφέρεσθαι πρὸς τοὺς τὰ τοιαῦτα κάμνοντας. (Hatzopoulos 1992vi| p. 28, 2; Jones 1923ii, p.66[VI6-9])

² Περί Ἀρχαίας Ἰητρικῆς

³ 'Ἐπεὶ τοῦτο γέ μοι δοκεῖ ἀναγκαῖον εἶναι παντὶ ἰητρῷ περὶ φύσιος ἐπιδέξασθαι, καὶ πάνυ σπουδάσαι αὐτῷ εἶσεται, ἔπειτα μὲν τῶν δεόντων ποιήσῃ, καὶ τί τέστιν ἄνθρωπος πρὸς τὰ ἐπιθιόμενα καὶ πινόμενα, καὶ αὐτὸς πρὸς τὰ ἄλλα ἐπιτηδεύματα, καὶ αὐτὸς ἐφ' ἑκάστου ἐκάστῳ συμβήσεται' (Lypourlis 2000 [20], p. 86)

⁴ 'σκέψασθαι δὲ χρὴ διὰ τίνος προφάσις ἀπέτοις ταῦτα ξυνέβη'

⁵ Ὁ δὲ δώσω δὲ οὐδέ φάρμακον οὐδενὶ ἀπτηθεὶς θανάσιμον, οὐδέ φηγήσομαι ξυμβουλίην τοιγόνδε' (Hatzopoulos 1992i, p.34) I shall never give poison even if I am asked to do so, I will never advice so

⁶ From the Greek words: εὖ (good) +θάνατος (death)=εὐθανασία

⁷ Fluorine: A poison of that time (a substance used to form fluoride used today to prevent tooth decay)

⁸ 'Ἐμοίως δε οὐδέ γυναικὶ πεσσόν φθόριον δώσω'

between the emotional and physical body. In his *Aphorisms*¹ he advises his student doctors to use drastic laxatives for the lower part of the bowel for those suffering from melancholy and, within the same conceptual framework, to do the opposite in antithetical cases², (*Hatzopoulos 1992*[9], p.256)

Notwithstanding the above, it should be noted that there exists an uncertainty as to which parts of the corpus were written by Hippocrates, if any, (*King 2001; Craik 2009; Vryonis 1989; Arieti 2005*). Scholars consent on the fact that there was no single author 'Hippocrates' and that the fifty to seventy surviving books attributed to Hippocrates are in fact written by different authors, (*Craik 2009; Arieti 2005*). Conflicting views are identified with some of the books attributed to Hippocrates being at odds with one another, and also within the writings of the same book, (*Craik 2009; Arieti 2005*). King refers to a set of fake letters attributed to Hippocrates –the *Pseudepigrapha*³– prepared by different writers from about the second century BC onwards, which they have provided the basis for many long-lasting legends about Hippocrates. However there seems to be a consensus for the existence of Hippocrates as a real person, as well as for the time the treatises were written which is the fifth and early fourth centuries BC, (*Vryonis 1989; Arieti 2005; Garrison 1929; Seelig 1908; Kempf 1905; Cordell 1904*).

As regards Hippocratic medicine, as expressed in the Corpus, scholars, although acknowledging its experimental, rational, and clinical character (*Seelig 1908*), they question the commonly held view that this was entirely free from mysticism and superstition, not even free from wrongly deduced dogmatic assumptions, in spite of his 'so extraordinarily great keenness of clinical observation' (*Seelig 1905*). M.G. Seelig, medical doctor and historian of the beginning of the twentieth century, in a geographico-historical retrospection into the evolution of medicine in the West, attacks Hippocratic humoral theory, questioning the rationality of the belief in an absolute proportion of the four elements as a function of health. Superstition, according to Seelig is based on a false observation, or on false deduction from a correct observation. Mysticism and superstition appear also in the medical schools that followed Hippocrates, such as the Alexandrian

¹ ἄφορισμοί

² 'τους δε μελαγχολικούς, αδροτέρως τας κα'τω τω αυτώ λογισμώ τανάντια προστιθείς'

³ Greek word: Ψευδεπίγραφα: fake letters

school, the Methodists, the Empiricists, the Encyclopaedists, the Pneumatics and the Eclectics, and permeates medical thought during the Roman time and the Dark Ages that followed, (*Seelig 1905*).

Plato: dualism: rationalism and mysticism (c.4th B.C)

It is worth noting that, while the basic characteristic of Hippocratic medicine was thought to be the rejection of theocratic and mystical perceptions, (*Arieti 2005; Vryonis 1989; Magee 1998; Ligeros 1937*) -which were not absent from the Pre-Socratic thought- these retain their place after Hippocrates. An inclination to religion and mysticism appears side by side with rationalism in the writings of Plato who adopted a dualistic view of the world. In an attempt to reconcile the Parmenidian One with the theory of Heraclitus '*everything is in a state of flux*' he promoted the theory of the two separate worlds: the Visible, always changing, world and the Ideal Invisible world which never changes, (*Arieti 2005*). Plato, like Heraclitus and Empedocles, believed in a series of lives and at the same time, like Pythagoras, attempted to explain the genesis and function of the world through physics and mathematics. A characteristic example is a phrase from *Timeus* in which his belief in the reincarnation of soul is evident: '*those men who were timid and unfair in their present life they will be reborn as women in their second life*¹, (*Hatzopoulos 1992xix, p.230 [90e]*). In his theory of the world, Plato adopted the Empedoclean doctrine of the four elements, Fire, Water, Earth and Air,² which he believed they continuously combined and transformed one to each other in a circular movement³. His conception of the creation of the world involves two causes, the *Divine (theion)* and the *Necessity (anangaion)*⁴. The Creator⁵ offers the basic substance, the *immortal soul (psyche)*, to the Gods, who are the divine bodies created by the Creator first, and who in turn synthesise it with the four Elements of the Universe, *Earth, Fire, Wind and Water* to create the *mortal body* with the promise

¹ 'τῶν γενομένων ἔνδρῶν ἔσοι δειλοί και τον βίον ἐδίκως διέλθον, κατά λόγον τον ἐξκότα γυναῖκες μετεφύοντο ἔν τῷ δευτέρῳ γενέσει.'

² πῦρ, ὕδωρ, γῆ, ἔραρας 'Τῶν δέ δή τεττάρων ἔν ἔλον ἐκαστον ἐλήφεν ἔ τοῦ κόσμου σύστασις' (*Hatzopoulos 1992xix, p.70 [32c]*),

³ '...κύκλον τε οἴτω διαδίδοντα ἐξ ἑλληλα, ἐς φαίνεται την γένεσιν'. (*Hatzopoulos 1992xix, pp.112-114 [49c-d]*)

⁴ 'διό δή χρή δύ' ἀπίας ἐθδη δορίζεσθαι, το μέν ἔναγκαῖον, το δε θεῖον,...' (*Hatzopoulos 1992xix, p. 170 [68e]*) and μεμειγμένη γάρ οἴν ἔ τοῦδε τοῦ κόσμου γένεσις ἐξ ἔνάγκης τε καί νοῦ συστάσεως ἐγεννήθη' (*Hatzopoulos 1992xix, p.108 [48a]*).

⁵ ο Δημιουργός

to return it back when is dead¹. The four elements *Fire, Water, Earth, and Air*, are in a state of complete disorder, as it happens in the absence of a Creator², and they are organised and formulated after being mixed with ideas and numbers³. Both the Creator in creating the *soul* and the Gods in synthesising the *body* employ mathematical reasoning using geometrical forms (triangles, circles, ratios and arithmetical multiplications and divisions) in combination with ideas, and in the case of the *body* with the Four Elements. The philosopher, on the creation of the *soul*, begins with the phrase: ‘and he [the Creator] began to divide as follows’⁴

The Pre-Socratic concept of the necessity of two opposite forces interacting for the materialisation of every function permeates all Platonic philosophy and it is characteristically evident in the two parts of the *soul*, the mortal and the immortal⁵, which the Gods placed in separate parts of the body so the mortal does not infect the immortal part⁶. Within the same conceptual framework, the Creator provided for genesis and death, both necessary for a harmonious world. The concepts *variable (meristos)* and *invariable (ameristos)* are frequently used to explain the creation of the world. To create for example the *soul* he used two diametrically opposite substances the *variable meristos* and the *invariable ameristos* which he mixes with a medium consisting of both the *variable* and the *invariable*, Hatzopoulos (1992xix) identify the difference with Christian philosophy, in which death was not included in the initial plans of the Creator, who made immortal beings until Eve and Adam made the mistake and became immortal. Therefore the dogma that death is the result of sin and not a natural parameter in the functioning of the world, which has dominated western thought for more than two millenniums, does not emerge from ancient Greek philosophy, (Hatzopoulos 1992xix, p.74[34c-35b]).

¹ ‘τό δέ λοιπόν ἔμελλε, ἠθανάτῃ θνητόν προσυφαίνοντες, ἠπεργάζεσθε ζῆα καὶ γεννῆτε τροφήν τε διδόντες ἀξίζαντες καὶ φθίνοντα πάλιν δέχεσθε’, (Hatzopoulos 1992xix, p.92 [41d])

² παντάσῃ γε μὴν διακείμενα ὡσπερ ἐξῆκος ἔχειν ἔπαν ἔταν ἔπιπῆ τινός θεός, (Hatzopoulos 1992xix, p.124 [53b])

³ οἴπτω δὴ τότε πεφυκότα τάττα πρῆτον διεσχηματίσατο ἐῖδεσι τε καὶ ἀριθμοῖς’ (Hatzopoulos 1992xix, p.124 [53b]).

⁴ ‘ἄρχετο δε διαρεῖν ἔδε. (Hatzopoulos 1992xix, p.74-79 [35b-36d).

⁵ οἱ δὲ [θεοὶ] μιμούμενοι, παραλαβόντες ἄρχῆν ψυχῆς ἠθανάτον, το μετὰ τοῦτο θνητόν σῆμα ἀπῆτ περιετόρνευσαν ἄχημά τε πῆν το σῆμα ἠδοσαν ἄλλο τε εἶδος ἔν ἀπῆτ ψυχῆς προσῆκοδόμου το θνητόν, δεινά καὶ ἔναγκαῖα παθήματα ἔχον’ (Hatzopoulos 1992xix, p.172 [69c]),

⁶ ‘καὶ διὰ τάττα, δὴ σεβόμενοι μαιίνειν το θεῖον, ἔτι μὴ πῆσα ἔν ἔνάγνη, χωρὶς ἔκείνου κατοικίζουσιν ἐξ ἔλλην τοῦ σώματος οἴκησιν το θνητόν’

All disease, for Plato, relates to deficiencies, excesses or displacement of the four elements¹. As regards mental and psychological disease, Plato strongly believes that this emerges from the excesses and stresses of the physical body². With his famous phrase, ‘nobody is bad at his own will’³, Plato expresses a strong belief to the theory that an individual can be bad only if his physical body is in a bad condition or because he was badly raised. Sorrows emerge from the bad condition of the body, which relate to the acid and salty *phlegm* and the bitter *bile* which when they cannot find ways out of the body, they mix their evaporations with the movement of the soul and create mental and psychological diseases, (Hatzopoulos 1992xix, pp.218-221[86-87]). On the basis of the same theory, Plato in his *Timeus* Hatzopoulos 1992xix, pp.218-226 [86-90]), advises people to exercise without excesses both the physical and the mental part of their body in order to have harmony between the two, which is important for the health of both, ‘and as regards health, disease, virtue and vice there is no valid symmetry other than that between the body and soul’⁴. (Hatzopoulos 1992xix, p. 220 [87d]). Similarly, in the next page he argues: ‘There is only one correct way keep disease away. We should never care for our soul without caring for the body, so that they don’t react between each other and to be in perfect balance and health’⁵. Plato endorses the Hippocratic theory that disease should be allowed to run its course claiming that if we interfere to cure disease with drugs before it runs its course, more serious diseases will follow, adding that diet rather than drugs is the appropriate means to use.⁶

¹τό δε τῶν νόσων ἕθεν συνίσταται, δὲλόν που και παντί. Τετάρων γάρ ἔντων γενῶν ἕξ ἔν συμπέτηγεν το σῆμα, γῆς πυρός ἕδατός τε και ἕέρος, τούτων ἔ παρά φύσιν πλεονεξία και ἔνδεια και τῆς χώρας μετάστασις ἕξ οἰκείας ἔπ’ ἔλλοτρίαν γινομένη, πυρός τε αἶ και τῶν ἕτέρων ἕπειδή γένη πλείονα ἔνός ἔντα τυγχάνει, το μη προσἔκον ἕκαστον ἕαυτἕ προσλαμβάνειν’ (Hatzopoulos 1992xix, p.204 [82a]).

² ἕδονάς δε και λύπας ἕπερβαλλούσας τῶν νόσων μεγίστας θετέον τῆ ψυχῆ’ (Hatzopoulos 1992xix, p.216 [86b]) (‘νοσοἕσαν και ἕφρονα ἕσων ἕπό τοἕ σώματος την ψυχῆν, οἕχ ἕς νοσἔν ἕλλ’ ἕς ἕκῶν κακός δοξάζεται’) (Hatzopoulos 1992xix, p.218 [86d]).

³ ‘κακός μέν γάρ ἕκῶν οἕδεις’ (Hatzopoulos 1992xix, p.218[86d])

⁴ ‘πρός γάρ ἕγιείας και νόσους ἕρετάς τε και κακίας οἕδεμία συμμετρία και ἕμετρία μείζων ἕ ψυχῆς αἕτἕς πρόσ σῆμα αἕτό.’ (Hatzopoulos 1992xix, p. 220 [87d])

⁵ ‘μία δἕ σωτηρία προς ἕμφω, μήτε την ψυχῆν ἔνευ σώματος κινεἔν μήτε σῆμα ἔνευ ψυχῆς, ἔνα ἕμυνομένω γίγησθον ἕσορρόπω και ἕγιἕ.’ (Hatzopoulos 1992xix, p. 222 [88b])

⁶ τρόπος οἕν ἕ αἕτός και τῆς περι τἕ νοσήματα συστάσεως. ἔν ἔταν τις παρά την εἕμαρμένην τοἕ χρόνου φθείρἕ φαρμακείας, ἕμα εκ σμικρἔν μεγάλα και πολλά ἕς ἕλίγων νοσήματα φιλεἕ γίγησθαι, διό παιδαγωγεἔν δεἕ διαίταις πάντα τἕ τοιαἕτα, καθ’ ἕσον ἔν ἕ τἕ σχολή, ἕλλ’ οἕ φαρμακεύοντα κακόν δύσκολον ἕρεθιστέον’ (Hatzopoulos 1992xix, p.226[89c-d])

Aristotle: teleology and functionalism (c.4th B.C)

Aristotle, who was a student of Plato, respected his predecessors and advocated the need to take into account earlier ideas expressed by other thinkers even if we don't agree with them.¹ Hence, while he adopted the doctrine of the four elements, Fire, Earth, Air and Water as the basic substances, he presented the theory of the Faculties (*Dynameis*) having four qualities: *Cold, Warm, Solid, and Fluid*², (*Goold 1961i, p.106 [646a13-17]*). These *Faculties* represented the matter of all composite bodies and the causes of all life and death, health and disease³. The harmonic blend of the four principles *Cold, Warm, Solid, and Fluid* is at the basis of all life for Aristotle. As in Hippocrates, the wholistic principle was at the basis of Aristotelian philosophy which postulated a functional approach to the human body. For Aristotle the wise man was that who had a wide knowledge of everything and was not specialised in something⁴. In the treatise *Parts of Animals* he claims: 'In the science of Nature it is the whole entity, the totality that concerns us and not its constituent parts which can never be found separately from their totality'⁵. And one frequently identifies in his writings his strong belief to the complex interrelationships and interactions between the physical, mental, and emotional parts of the body⁶ claiming for example that almost always, sad and pleasant events cause the body temperature to rise or fall⁷. Similarly, in the *Parts of Animals* he relates the consistency of the blood to intelligence claiming that the animals which have thinner and clearer fluids in their bodies have faster sensations and higher intelligence, although they are also more

¹ οὐ μόνον δε χάριν ἔχειν δίκαιον τούτοις ἐν τῶν κοινῶνσαιτο ταῦς δόξαις, ἀλλὰ συνεβάλοντό τι. Τὴν γὰρ ἔξιν προήσκησαν ἑμῶν (*Hatzopoulos 1992xxi, p.116 [993b12-14]*).

² Ψυχρόν, Θερμόν, Ξηρόν, Ὑγρόν

³ διό δεῖ λανθάνειν πῶς δεῖ τῶν φύσει συνεστῶτων τά μὲν θερμά λέγειν τά δε ψυχρά και τά μὲν ξηρά τά δ' ἄγρᾳ, ἔπει ἔτι γ' ἀπὸ ταῦτα σχεδόν και θανάτου και ζωῆς οἴκειν εἶναι φανερόν, ἔτι δ' ἔπνου και εγρηγόρσεως και ἐκμῆς και γήρωσ και νόσου και ἐγείας, (*Goold 1961i, p.122 [648b2-6]*).

⁴ Ἐπολαμβάνομεν δὴ πρῶτον μὲν ἐπίστασθαι πάντα τον σοφόν ὅς ἐνδέχεται, μη καθ' ἕκαστον ἐχοντα ἐπιστήμην ἀπὸ τῶν (*Hatzopoulos 1992xxi, p.52 [982a8-10]*)

⁵ και τον περί φύσεως περί τῶς συνθέσεως και τῶς ἐλης οἰσίας, ἀλλὰ μη περί τούτων ἢ μη συμβαίνει χωριζόμενα ποτέ τῶς οἰσίας ἀπὸ τῶν. (*Goold 1961i, p.100 [645a35-37]*).

⁶ A characteristic example is the following extract from *Movement of Animals*: 'Ἐλλοιοῦσι δ' αὖ φαντασίαι και ἀσθησεις και ἀπνοιαί. Αἱ μὲν γὰρ ἀσθησεις ἐκθῶς ἐπάρχουσιν ἐλλοιώσεις τινές οἰσαι, ἡ δε φαντασία και νόησις την πρᾶγμάτων ἐχουσιν δύναμιν. Τρόπον γὰρ τῶν το εἶδος το νοούμενον το τοῦ θερμοῦ ἢ ψυχροῦ ἢ ἐδέος ἢ φοβεροῦ τοιοῦτον τυγχάνει ἐν οἷον περ και τῶν πρᾶγμάτων ἕκαστον, διό και φρίττουσι και φοβοῦνται νοήσαντες μόνον. Ταῦτα δε πάντα πάθη και ἐλλοιώσεις εἰσίν. Ἐλλοιούμενων δ' ἐν τῷ σώματι τά μὲν μείζω τα δ' ἐλάττω γίνεται [...] ἔτι δε κατά θερμότητα ἢ ψύξιν ἢ κατ' ἄλλο τι τοιοῦτον πάθος ἐται γένηται ἐλλοιώσεις-περί την καρδίαν, και ἐν ταύτῃ κατά μέγεθος ἐναισθητῆ μορίῳ, πολλήν ποιεῖ τοῦ σώματος διαφορὰν ἐρυθρήμασι και χροῖτησι και φρικαίς και τρόμοις και τοῦς τούτων ἐναντίοις. (*Goold 1961ii, p.464[VII,701b17-34]*)

⁷ ὅστι δε τα λυπηρά κί ἔδέα πάντα σχεδόν μετά ψύξεώς τινος και θερμότητος, (*Goold 1961ii, p.464[VIII,702a 1-2]*)

timorous, while those with thicker blood are more powerful and passionate (Goold 1961i, p.138 [650b19-37])

Teleology (*teleologia*)¹ is a basic characteristic of Aristotelian philosophy and all bodies, functions, and concepts of life are determined by a purpose (*telos*). Within this conceptual framework falls Aristotle's functional approach to the human body, in which all its constituent parts exist and function for the sake of the whole. Arieti (2005) claims that modern neuroscience has already validated Aristotelian views of the composite unity of the human body, as against the Cartesian mind-body dualism. Aristotle, in contrast to Plato who view the soul as imprisoned in the body until death after which is released, had the view that there is a strong link between human chemistry and human behaviours. Similarly the causes of all events can be found by identifying the purpose for which these events occur. So, if we consider that the doctor places Health as his purpose when treating the patient, then we can explain the reasons for the particular means he uses for the treatment². Aristotle, along the same lines with Hippocrates, strongly criticised those practitioners and technicians who applied their scientific knowledge in practice without searching for the deeper causes³. Arieti underlines the inquiry into the causes of disease as one of the important features of Greek medicine, (Arieti 2005). Worth noting is that Aristotle espoused also the theory that harmony is brought by the interaction of opposites, a basic principle of Presocratic philosophy. In his *Metaphysics A* refers specifically to the Pythagorean principles and concepts which appear in pairs of opposites⁴, claiming that what is important to keep from this Pythagorean theory, which was also espoused by Alcmaeon of Croton⁵, is that opposites are at the base of genesis of all entities⁶. Reference is made also to Empedocles who considered the necessity of an opposite in everything in nature such as beauty and ugliness, good and evil, love and hate, (Hatzopoulos 1992xxi, pp.66-68 [985a])

¹ From the Greek word: Τέλος=aim, purpose

² Ἐμὲν ἰατρός τιν ἰαγίαν ἔδ' οὐκ οὐκ ὁδὸς τιν οὐκίαν, ἰποδιδόασι τοὺς λόγους καὶ τὰς ἀπτίας οὐκ ποιοῦσιν ἑκάστου, καὶ διότι ποιητέον οὐκίως. (Goold 1961i, p.56 [639b16-20])

³ Ἐτι τὸν ἑκτριβέστερον καὶ τὸν διδασκαλικώτερον τῶν ἀπτιῶν σοφώτερον εἶναι περὶ πῶσαν ἰπιστήμην, (Hatzopoulos 1992xxi, p.52 [982a13-15]) and (Ἐπεὶ δι φανερόν ἐτι τῶν ἑξ ἑρχῶς ἀπτιῶν δεῖ λαβεῖν ἰπιστήμην (τότε γὰρ εἰδέναι φαμέν ἑκαστον, ἔταν τιν πρώτην ἀπρίαν οὐκ ὠμέθα γνωρίζειν) (Hatzopoulos 1992xxi, p.52 [982a24-26]).

⁴ Ἐτεροι δε τῶν ἀπτιῶν τούτων τὰς ἑρχὰς δέκα λέγουσιν εἶναι τὰς κατὰ συστοίχίαν λεγομένας, πέρας [καὶ] ἰπειρον, περιπτόν [καὶ] ἰριτιον, ἑν [καὶ] πλήθος, διξιόν [καὶ] ἰρισιτερόν, ἑρρεν [καὶ] ἰθῆλυ, ἑρεμοῦν [καὶ] κινούμενον, εἰθῆ [καὶ] καμπύλον, φῆς [καὶ] σκότος, ἰγαθόν [καὶ] κακόν, τετράγωνον [καὶ] ἰτερόμηκες (Hatzopoulos 1992xxi, p.72 [986a22-26]).

⁵ Ancient Greek philosopher and medical theorist, pupil of Pythagoras. He was an early pioneer of dissection and the founder of the medical school of Croton

⁶ παρά μὲν οὐκ τούτων ἑμφοῦν τοσοῦτον ἑστι λαβεῖν, ἐτι τῶν ἀντία ἑρχαί τῶν ἑντων (Hatzopoulos 1992xxi, p.72 [986b2-4])

CHAPTER IV

MEDICAL THOUGHT AFTER HIPPOCRATES

The anatomical school of Alexandria (c.3th B.C)

It emerged in the third century BC during the reign of the Ptolemies in Egypt, and it was in sharp antithesis to Hippocratic medicine, attaching importance to the constituent parts rather than the whole of the body. Vryonis (1989) identifies a paradox: that the medical thought of the Coans was transferred to Alexandria -which remained the medical centre of the Mediterranean until the Arabic conquest in the seventh century AD- through the Hippocratic Corpus, (Vryonis 1989). The founders of this school were Heroclitus, a Greek physician from Chalcedon in Asian Minor, who studied medicine at the Hippocratic school of Cos, and Erasistratus, a Greek anatomist and physician from Chios¹, who carried out extensive studies on physiology and anatomy through dissection of dead human and animal bodies, (Vryonis 1989; Arieti 2005). According to Vryonis in the Hippocratic era there was a reservation of dissecting a dead body and this has inhibited further advancement of anatomy in the school of Cos. However, the changes that occurred in Greek philosophy after Hippocrates opened the way to this area of research and the Alexandrians practiced dissection, thereby greatly increasing the knowledge of anatomy and physiology. Plato promoted the idea of an immortal soul leaving the body after death, while Aristotle claimed that the body after death had no feelings, and thus no claims. Erasistratus at some point rejected completely the Hippocratic humoral physiology, which was, however, re-established later by Galen, within the context of a 'medical orthodoxy', (Vryonis 1989, p.23). According to Arieti (2005), in the period that followed the Alexandrians there was a decline in the study of the human body. He attributes this either in the reverence of the Romans for dead bodies or in the emphasis the Greek religions and philosophies placed on studying the soul rather than the body, (Arieti 2005, p.234).

It should be noted, however, that the genesis of Egyptian medicine is located by historians several centuries back in time long before the Presocratics' ontological

¹ An island along the coast of ancient Ionia

speculations appeared. The Edwin Smith Papyrus, the world's oldest surviving surgical text, was written in Egyptian hieratic script around the 17th century BCE, but probably based on material from a thousand years earlier. The papyrus is a textbook on trauma surgery, and describes anatomical observations and the examination, diagnosis, treatment, and prognosis of numerous injuries in exquisite detail. Scholars identify in the writings of ancient historians such as Homer¹, Herodotus² and Clement of Alexandria³, significant evidence on the considerable development of the practice of medicine in ancient Egypt, long before Hippocrates, (*Vryonis, 1991; Garrison 1929; Garland 1928; Thiel 2000*) -who is referred to as having studied in Egypt (*Thiel 2000*). Other sources, including references in the Greek and Roman classics, hieroglyphic inscriptions, and medical papyri, such as the Kahun⁴, the Ebers⁵ and the Edwin Smith Papyri⁶, demonstrate evidence of a highly developed medicine, with a strong element of rational aetiology, in ancient Egypt, (*Vryonis 1991*). Eugene Cordell, medical academic, President of the Medical and Chirurgical Faculty of Maryland, and Honorary Professor of the History of Medicine at the University of Maryland, at the beginning of the twentieth century, drawing from Celsus, claims that *lithotripsy*, which was used by surgeons by the end of the nineteenth century was invented and practiced by Ammonius of Alexandria, about 230 BC, (*Cordell 1904*). Spyros Vryonis refers to a pathological system in ancient Egyptian medicine which employed rational, non-religious, non-superstitious methods of diagnosis and therapy, (*Vryonis, 1991,p.13*). Surgeons and other medical professionals of different specialisations existed several millenniums BC, (*Garrison 1929; Garland 1928*) and, according to literature, the medical profession in Egypt was based on a combination between rationalism and mysticism, with the latter prevailing as Egyptian civilisation declined, (*Garland 1928*). According to Vryonis, there was a channelling of Egyptian medical theories into early Greek medicine, particularly in the early Cnidian school of medicine but also in the Hippocratic writings. The high specialisation in different areas of medicine promoted by the Cnidian doctors appears in Egypt at the time of Herodotus. Spyros Vryonis suggesting that Herodotus

¹ Ancient Greek Epic Poet (9th c. BC)

² Ancient Greek Historian (5th c. BC) from Halicarnassus (ancient Ionia), widely known as the Father of History

³ Theologian, philosopher and writer of the first centuries of the Christian Era

⁴ The Kahun Papyrus (around 2000BC): is the oldest text dealing with symptoms, diagnosis and treatment of gynaecological conditions

⁵ Ebers Papyrus (around 1559 BC): one of the two oldest preserved medical documents (the other being the Smith Papyrus),

⁶ The Edwin Smith Papyrus (around 1600BC): one of the most important document in the history of medicine, (*Garland 1928*) and the best preserved books on surgery and external medicine of Egyptian antiquity, (*Ligeros 1937*)

must have visited Egypt because he was very informative about that land quotes a passage from his writings (Vryonis 1991):

Medicine has been divided by them according to the following categories: Each physician is a (specialist) in one illness and in no more. (...) some are set up as ophthalmologists, others as (physicians) of the head; still others are dentists, some of the middle body cavities, and other of internal diseases.'

Herodotus¹

Medical thought during the three centuries before the advent of Christianity

A number of medical schools appear during the last three centuries before the advent of Christianity. These include:

The Epicureans appeared in the third century B.C as a new version of the Democritian atomic philosophy with influences from Plato. Epicurus (341-270BC), a Greek philosopher from Samos, -who moved to Athens where he established a secluded community called the 'Garden'- (*Blackburn 2005*), considered pleasure –intellectual rather than bodily- as the highest good in life. He is thought to have introduced a degree of chance in Democritian determinism, a theory emerging from his belief in the freedom of will which downgraded, in a way, the traditional view that supernatural powers determine all life, (*Brock 1916*). Epicureanism rejected immortality and mysticism as well as any possibility of afterlife and as a philosophy flourished for seven centuries. The Epicureans were against the fear of pain and death and promoted a crude and superficial way of regarding disease, showing little interests to its deeper causes, (*Moon 1923*). Epicurus himself died at age 71 from urinary calculus after having suffered for a long time and researchers refer to an exceptional description of his own terminal symptoms providing useful insights of the disease, which survived within the texts of subsequent medical practitioners, (*Bitsori & Galanakis 2004*). The Epicurean philosophy, suppressed during the Middle Ages, revived in the sixteenth and

¹ ii. 156, (quoted by Vryonis, 1991, p.11)

seventeenth centuries contributing significantly to the development of science and humanism, (Magee 1998).

The Empiricists, also in the third century BC, in Alexandria, violently attacked the theoretical or speculative practice of medicine, and promoted an, opposite to Hippocratic medical thought, theory according to which what should concern the doctor is not the cause of disease but its cure (Brock 1916). *Empiricism*¹, as a philosophy emphasises the importance of experience through sensory perception and evidence from observation and experiment, in obtaining knowledge in contrast to *rationalism* which relies on reason. Any *a priori* knowledge of innate or intuitive knowledge or general principles deduced from the use of reason is denied, (Blackburn, 2005) and hence empirical -medicine disregards universally applied scientific theories, relying solely on practice experience.

The Asclepiadeans, during the second and third centuries. Asclepiades was born in Bithynia of Minor Asia but practiced medicine most of his life in Rome. The medical theory of Asclepiades was based on the idea that all health is determined by the balanced movement of the basic particles (ἔναρμα στοιχεία) of the universe, and disease occurs when these particles collide. Brock (1916) claims that he was the introducer of Greek medicine in Rome, however as a mechanistic system with a disbelief in the self-healing power of the body, (Brock 1916, p.xiii). From a different perspective, Vallance (1990) views Asclepiades as ‘historically standing at a crucial point in the development of Greek medicine’ and his medical theory –not in existence any more- as forming the basis of ‘one of the most intriguing doctrinal disputes in ancient science’, (Valance 1990, p.2). Galen, in his treatise *Natural Faculties*², links the theory of *inharmonious particles*³ of Asclepiades with the Epicurean theory of *indivisible atoms*^{4,5} and strongly criticises those who reject the humoral theory of Hippocrates such as the atomists of the Alexandrian School, the Epicureans, and Asclepiades, whom he frequently scorns for his medicine⁶. He often, however, identifies contradictions and inconsistencies between Epicurus and

¹ From the Greek word εμπειρία=experience

² Περί Φυσικῶν Δυνάμεων

³ ἔναρμοι ἔγκοι,

⁴ Atom: ἄτομον in Greek is literally ἄ-τομον=non divisible

⁵ Ἐπικούρου μὲν οὖν καίτοι παραπλησίους ἔσκληπιιάδῃ στοιχείοις προς την φυσιολογίαν χρώμενος ἔμωσ ἔμολογεῖ...,(Goold 1916, p.71)

⁶ Ἐρ’ οὖν οὐ μαίνεσθαι νομιστέον ἀπτόν [τον Ἐλικιβιάδην] ἔπαντάσιν ἔπειρον εἶναι τῶν ἔργων τῆς τέχνης (Goold 1916, p.64[41]).

Asclepiades¹. Vallance claims that none of Asclepiades' works survived and his medical theories are known from contradictory accounts by non-sympathetic commentators, thereby rejecting Galen's connection between Asclepiadean and Epicurean theories. His view is that the fragility of Asclepiadean corpuscles point to a concept of matter (and void) far removed from the atomists, (*Vallance 1990*).

The Methodists, in the first century B.C, represented a school of physicians developed by the student of Asclepiades, Themison of Laodicea, epistemologically located between Hippocrates and the Empiricists. According to Brock (1916), the Methodist system was characterised by simplicity in both diagnosis and treatment. All diseases were classified in two classes those of *stasis*² and those of *flux*³ the former indicating a decrease of the natural secretions of the body, due to constriction of the minute channels or *pores* which traverse the tissues of the body, and the latter indicating an increase of them due to dilatation of the *pores*. Brock (1916), who parallels this practice with modern medicine's use of several labels standing for 'one and indivisible' entity 'to be treated by a definite and unvarying formula, uses the term 'the tyranny of names' to characterise the Methodist school of thought which looked at the disease as 'fixed and finite' entirely independent from the setting within which they developed (*Brock 1916, p.xv*)

Galen-the natural faculties of the organism (c.2th A.D)

Galen or Claudius Galenus, (*Γαληνός* in his mother language) was born at Pergamon⁴ in Ionia. Galen was famous as a physician and anatomist, but also as a philosopher and writer, charged with a huge body of medical writing divided into seven categories: anatomy, pathology, therapy, diagnostic and prognostic, the commentaries of Hippocrates, philosophy and grammar (*Vryonis 1989*). After he finished his studies in Greece, Ionia, and Alexandria, he spent most of his life in Rome, where he served as a physician in the court of Marcus Aurelius. King (2001) claims that 'it would be impossible for us to think of medicine in the Roman Empire without Galen of Pergamum, the most influential

¹ τὰ δ' Ἐπικούρου πάλιν ἐκ Σκληπιάδης ἐρχόμενος εἰς τὴν ἐκκολοθίαν, ἐς ἔκκεθρον οὐδὲ πᾶν τι φαίνεται φροντίζων', (Goold 1916, pp.80-81 [52].

² στέγνωσις

³ ρύσις

⁴In Mysia of Asia Minor, now Pergama, Turkey

and prolific of all the physicians of antiquity', (*King 2001, p.38*). Vryonis (1989) refers to Galen as 'an all-encompassing intellect, and as such was the best student and interpreter of the whole development of Greek medicine' (*Vryonis 1989, p.24*). Along the same lines, Simon Blackburn Professor of Philosophy at the University of Cambridge considers Galen's influence on medieval thought and medicine 'second only to that of Aristotle'. Similarly, Brock (1916) claims that 'it is essentially in the form of Galenism that Greek medicine was transmitted to after ages' (*Brock 1916, p.ix*), while a few years later, in an article in the British Medical Journal, he praises Galen's unique artistic method by which 'he chose the best elements from all the competing schools of medical thought and blended these elements into a unity'. In his letter to the editor he advocates for Galen's artistic method of handling material and his eclectic and synthesising abilities, emphasising on how clearly Galen 'saw this principle of artistic selection at work in the animal organism'. He specifically refers to the two of the most fundamental of Galen's 'Natural Faculties', the one of 'attracting the appropriate' (*dynamis elktiki tou oikeiou*¹) and the opposite of 'eliminating the appropriate' (*apokritiki tou allotriou*²) (*Brock 1923*).

Indeed, Galen frequently praises the artistic way by which *She* [the Nature] provided the organism with different *Faculties (Dynameis*³) each one of them performing a specific activity (*Energia*⁴) by which a specific Effect (*Ergon*⁵) is produced and *The Natural Faculties* treatise is permeated by this theory, which lies at the basis of all health and disease⁶. According to Galen, to examine which are these Faculties we should first identify their Effects (*Erga*)⁷. For example, the *blood making faculty*, the *digestive faculty faculty* of the stomach, the *pulsative faculty* of the heart and so on, every part of the body having a special faculty that corresponds to the function/activity (*Energia*) of that part and to a specific effect (*ergon*)⁸. Galen, whose medical thought was essentially wholistic, considered Hippocrates as being the first doctor and philosopher at the same time and

¹ δύναμις ἠλεκτική τοῦ οἰκείου

² ἀποκριτική τοῦ ἀλλοτρίου

³ Δυνάμεις

⁴ Ἐνέργεια

⁵ Ἔργον

⁶ Τοιαύτην δ' ὁσάν ἀπτήν ἐθεώς και δυνάμεις ἠπέλαβεν ἔχειν ἠλεκτικήν μεν τῶν οικείων, ἀποκριτικής δε τῶν ἀλλοτρίων και τρέφειν τε και ἀξείν ἀπτήν τα ζῶα και κρίνειν τὰ νοσήματα. (*Goold 1916, p.60[38-39]*).

⁷ 'ἐπερ ὁν μεθόδῳ μέλλοιμεν ἔξευρήσειν, ἔπόσαι τε και ἔποταί τινες ἀπ δυνάμεις ἐσίν, ἔπό τῶν ἔργων ἀπ τῶν ἔργκτέον.', (*Goold 1916, p.16[10]*).

⁸ εἶναί τινα λέγοντες ἔν ταῖς φλεψίν ἀματοποιητικήν, «ἔσαύτως δε κῆν τῷ καρδίῳ σφυγμικήν και καθ' ἔκαστον τῶν ἄλλων ἔδιαν τινά τῆς κατά το μόριον ἔνεργείας.', (*Goold 1916, p16 [9-10]*).

the first to develop such a strong awareness of Nature's works in relation to animals, and of the just way by which she performed them¹. He fully adopted and supported the Hippocratic doctrines claiming that these can be verified for their correctness and truth from research on the function of the animals.² More specifically, he incorporated the Hippocratic Humoral Theory into his theory of the Natural Faculties³, which was preserved through his writings up to the Byzantine period in which Alexandria was a centre of medical practice, (Vryonis 1989). 'He was also fully in accordance with the Hippocratic doctrine, which postulates that disease is a form of cleansing, a *crisis* (*krisis*)⁴ that leads to *catharsis* (*katharsis*)⁵, which should be allowed to run its course. This is evident in the function of the Eliminative Faculty⁶ as is the case of haemorrhoids or the female excessive menstruation⁷. Equally strong emphasis, Galen placed on preventive medicine⁸, wondering 'should we take care of the evacuation of the bile and ignore its genesis? As if it is not much easier to prevent its development rather than go into all the trouble of expelling it', (Goold 1916, p.168 [107]). For the origin of diseases he fully adopted the views of Hippocrates, whom he considered to be the first to identify the genesis of disease and the remedies for treatment, with Aristotle subsequently supporting and

¹ 'Ἐπιοκράτης μὲν οὖν ἐν ἔσμεν πατρῶν τε καὶ φιλοσόφων πρῶτος ἐπάντων, ἐς ἐν καὶ φιλοσόφων πρῶτος ἐπάντων, ἐς ἐν καὶ πρῶτος ἐπιγνοῦς τὰ τῆς φύσεως ἔργα, θαυμάζει τε καὶ διὰ παντός ἀπτήν ἔμνευε δίκαιαν ἐνομάζων καὶ μόνην ἐξαρκεῖν ἐς ἕπαντα τοῦς ζώοις φήσιν ἀπτήν ἐξ ἀπτής διδιδάκτως πράττουσαν ἕπαντα τὰ δέοντα. (Goold 1916, p.60[38]).

² 'Μαθεῖν δ' ἐνεστιν οὐ μόνον ἐξ ἐν οὐ τ ἐναντία τιθέμενοι διφέρονται τοῦς ἐναργῆς φαινομένοις, ἐς ἔσον ἐρθότητός τε καὶ ἐληθείας ἐκει τὰ ἐπιοκράτους δόγματα, ἐλλὰ κἄξ ἀπτήν τὴν κατὰ μέρος ἐν τῷ φυσικῷ θεωρίῳ ζητουμένων τὴν τ' ἄλλων ἐπάντων καὶ τὴν ἐν τοῦς ζώοις ἐνεργειῶν', (Goold 1916, p.48[30]).

³ ἐν οὐθ' ἐπιοκράτης οὐτε Διοκλῆς οὐτε Πραξαγόρας οὐτε Φιλιστίων ἐλλ' οὐδέ τὴν ἐρίστων φιλοσόφων οὐδεὶς κατεφρόνησεν οὐτε Πλάτων οὐτ' ἐριστοτέλης οὐτε Θεόφραστος... σύμπαντες οὐτοι θερμῶ καὶ ψυχρῶ καὶ φηρῶ καὶ ἔργῳ τοῦς μεν ἐς δρῶσι, τοῦς δ' ἐς πάσχουσι, τὰ κατὰ το σῆμα τὴν ζῶων ἐπάντων διοικεῖσθαί φασι καὶ ἐς το θερμόν ἐν ἀπτοῦς ἐς τε τὰς ἐλλας ἐνεργείας καὶ μάλιστ' ἐς τὴν τὴν χυμῶν γένεσιν το πλεῖστον δύναται', (Goold 1916, p.172 [111]).

⁴ Κρίσις

⁵ Κάθαρσις

⁶ '...ἐπιοκρτικὴν δε τὴν ἐλλοτριῶν καὶ τρέφειν τε καὶ ἀξίειν ἀπτήν τὰ ζῶα καὶ κρίνειν τὰ νοσήματα' (Goold 1916, p.60[38-39])

⁷ 'Ἐπί μεν γε χρονίαις ἀμμορροῖσιν ἐπισχεθείσαις ἐ διὰ κένωσιν ἐμετρον ἐς ψῆξιν ἐσχάτην ἐγαγούσαις τον ἐνθρωπον οὐχ ἐπαξ οὐδέ δις ἐλλὰ πολλάκις ἐδη τεθεάμετα συστάντας ἐδέρους, ἔσπερ γε καὶ γυναξίν ἐ τε τῆς ἐφ' ἐκάστῳ μηνί καθάρσεως ἐπώλεια παντελής καὶ ἐμετρος κένωσις, ἐταν ἀμμορραγήσωσί που' ἀπ μῆτραι σφοδρῆς, ἐπεκαλέσαντο πολλάκις ἐδερν καὶ τισιν ἀπτήν καὶ ἐ γυναικεῶς ἐνομαζόμενος ἐοῦς ἐς τοῦτ' ἐτελεῦτησε το πάθος', (Goold 1916, p.170 [109-110])

⁸ 'καὶ τῆς κενώσεως ἐρα φροντιστέον ἀπτής μόνης, ἐμελητέον δε τῆς γενέσεως; ἔσπερ οὐκ ἐμεινον ἐπάρχον μακρῶ το κωλύειν ἐπθύς ἐξ' ἀρχῆς γενεῖσθαί πλείονα τοῦ πράγματ' ἐχειν ἐκκενοῦντας',

expanding the Hippocratic views¹: Galen asserts that the doctrines of physiology, originated from Hippocrates, and were further developed by Aristotle and the Stoics²

Scholars view Galen as the ‘most influential and prolific of all the physicians of antiquity’ bringing together earlier medical theories and merging them with philosophy into a unique synthesis characteristic of his intellect, (*King 1981*). It is estimated that he wrote more than three hundred and fifty medical treatises, many of them lost and some surviving only in Arabic or Syriac languages, (*King 2001; Vryonis 1989*). According to Brock (1916) ‘Galen and Greek Medicine became synonymous, since much of his medical writings have come down to our epoch’, although it is recognised that much of his work is drawn from the labours of his predecessors, (*Brock 1916*). Fielding Garrison, medical academic and Lecturer at the History of Medicine at the John Hopkins University of Baltimore, claimed then that Galen was the ‘first great experimental physiologist before Harvey who adopted the Roman law-makers’ habit of codifying and systematizing knowledge, setting the pace of the great medical encyclopaedias of Byzantine, Arabian and Medieval periods, while his ‘mania for seeking the ‘why’ rather than the ‘how’ was instrumental for sterilizing the medicine of the West for nearly 1700 years (*Garrison 1929*). Historical evidence demonstrates that Galen greatly contributed to the channelling of Greek medical thought into Byzantine, Persian and Arab medical systems and from there to the Eastern part of the world -as well as its return back to the West. Galenic medicine dominated the medical thought of Europe until the appearance of the great figures of scientific medicine, Paracelsus, Vesalius, and Harvey whose theories undermined Galen’s medicine, (*Vryonis 1989*)

¹ ‘τῶν νοσημάτων τῆς γενέσεως καὶ τὰ τῶν ἰαμάτων τῆς ἐπιπέσεως ἑπικράτης μὲν πρῶτος ἰπάντων ἐν ἴσμεν ἑρθῆς ἐῖπεν, ἑριστοτέλης δε δεῦτερος ἑρθῆς ἐξηγήσατο’, (*Goold 1916, p.140[90]*)

² ‘...ἑλλ’ ἑτι μὲν τῆς ἑριστοτέλους φυσιολογίας οὐδέν ἑρασιστράτῃ μετέστιν, ἑ κατάλογος τῶν πορειρημένων ἑνδείκνυται δογμάτων, ἑ πρῶτου μὲν ἑπικράτους ἑν, δευτέρου δ’ ἑριστοτέλους, ρίτων δε τῶν Στωϊκῶν’, (*Goold 1916, p.144[92]*)

CHAPTER V

THE DARK AGES

The early medieval period-Christianity (c.1st-10th A.D)

A closer look at the period extending from Galen to the Scientific Revolution¹, allows not doubt that western medical thought –apart for a few gleams of advancement- remained in a stalemate for more than a millennium. The collapse of the Roman Empire² gives way to several centuries of scientific apraxia in the West -the so called Dark Ages- which end with the advent of the Scientific Revolution. According to Garrison (1929), ‘medieval clinical medicine, and with it the social status of the doctor, sank to an ‘almost unexampled degradation’ and the only medicine that developed during this time was Military Surgery in response to the exigencies of constant warfare between the Greeks and the Romans, as well as Public Hygiene to contain mortality and social inconvenience of the great epidemics, (*Garrison 1929*). M.G. Seelig, medical academic and historian at the onset of the twentieth century, in a geographico-historical retrospection into the evolution of medicine in the West, had claimed that during the Dark Ages medicine in Europe degenerated into ‘a thaumaturgical ritual of superstitious beliefs’ without ‘not even a glimmering remnant of the former beacon light of learning’, (*Seelig, 1908*). Seelig, who had argued a few years earlier that medicine ‘is not an exact science and its very inexactness is the spring and fountain head of false theorizing, leading to superstitions’ (*Seelig 1905*), views a force acting, during the medieval period, against the Hippocratic spirit - which had aimed at subjugating imagination to reason and at eradicating the mystic and superstitious elements from medicine, (*Seelig 1908*). Seelig, drawing from the clinician Boerhaave from Holland, claims that Galen, in sharp contrast with the eminent practicability of Hippocrates, used dialectic reasoning as ‘the nutcracker’ on all hard facts, causing, at the end of day, more harm than good for medicine. According to the Seelig, Galenic physiology established the belief that the only purpose of the physical body’s function was to serve the soul, (*Seelig 1905*) and, in general, Galenic medicine provided the

¹ 16th century AD (some see it earlier)

² The date of the fall of the Roman Empire is debated by different historians. The traditional date for its end is year 476 AD when the last emperor Romulus Augustulus was deposed by Goths, (*American Heritage Dictionary, 2009; Collins English Dictionary 2003*)

basis on which much of the superstition of the Dark Ages rested. The good elements of Galen's medicine -which prevailed in Europe for almost fourteen hundred years- are seen as being nullified by the leaguings of his medicine with philosophy, in a combination of Plato's idealism and Aristotle's rationalism into 'a maze' of Galenic dialectic reasoning, (Seelig 1905).

Magee (1998) views the period that followed the collapse of the western Roman Empire until the dawn of the Enlightenment in the fifteenth century as dominated by the Church which played a leading role in the development of civilisation. The works of the great philosophers of the ancient world were scrutinised to identify those doctrines that were in harmony with the principles of Christianity, (Magee 1998). Further advancing the argument, Fritzof Capra, high-energy physicist and author of many books on the philosophical implications of modern science, claims that the dualism of matter-soul, which occupied Western thought for more than two thousand years, was firmly based on the Church's strict adherence to an Aristotelian model of universe emphasising the lack of interest in the material world (Capra 1982, p. 26). Along the same lines George Engel, Professor of Psychiatry and Medicine at the University of Rochester School of Medicine, New York, drawing from Rasmussen, relates the reason the 'reductionist, dualistic biomedical model' evolved in the West with the Christian Church and its view of the body as a weak and imperfect vessel for the transfer of the soul from this world to the next, (Engel, 1977). The determinative role of the Christian Church in the redirection of scientific thought from Hippocratic rationalism is also emphasised by Godfrey Vesey, Emeritus Professor of Philosophy at the Open University and his colleague Paul Foulkes -who collaborated with Bertrand Russell on *Wisdom of the West*. In an attempt to demonstrate the spirit of the medieval period, the scholars single out the last sentence on the Holy Trinity, of Boethius¹: 'As far as you are able, join faith to reason', (where 'faith' stands for faith of Christian Revelation and 'reason' for pagan Greek philosophy) and 'the history of medieval philosophy is largely the history of this ability: 'as far as you are able...', (Vesey & Foulkes 1990). Manlius Boethius had translated Aristotle's logical works which, together with his own *Consolation of Philosophy*, provided the basis of medieval philosophy and influenced many subsequent philosophers and scholars such as Dante and Chaucer, (Arieti, 2005). Scholars view Neoplatonic and Stoic influences on the philosophy of Boethius, who

¹ Manlius Boethius(c.475-524 AD):

represented the last of the ancient philosophers, (*Magee, 1998; Arieti 2005, p.345*), before Europe plunged into darkness for several centuries again. **Neoplatonism** was a philosophical system, which rose at the same time with Christian philosophy, aiming to reconcile Aristotelian and Platonian philosophies, (*Seelig 1905; Magee 1998; Arieti 2005*). Its major exponent was Plotinos from Egypt, whose dualistic philosophy attempted to reconcile the Platonic transcendental world, apprehended by mind only, with the Aristotelian dynamic and changing world, as experienced by the senses. Neoplatonism had a great influence on Christian thought, (*Arieti, 2005; Magee 1998*). Magee believes that the debate between the Nominalists –emerging from the Platonic view of reality- and the Realists or Pragmatists –emerging from the Aristotelian view of reality-, which was the major characteristic of the Dark Ages, had serious consequences for theology, since it was connected with the mystery of the nature of the Holy Triad, (*Magee, 1998, p.58*). Seelig (1905), from a medical perspective, charges Neoplatonism with the flourishing of astrology, alchemy, necromancy and witchcraft during the early sixteenth century, (*Seelig 1905*)

The medieval awakening - Byzantine medicine (c.7th-c.14th A.D)

The so-called, ‘medieval awakening’ occurs, according to different historians, during the period extending from the beginning of the thirteenth century until the fall of Constantinople¹ to the Ottomans in 1453. Signs of this awakening, however, appear much earlier. Evidence demonstrates that the history of science had already found its way, once again, to the South-eastern part of Europe, this time to the new centre of civilisation of the western world, the Byzantium. The Byzantines, who resisted the materialism and cosmopolitanism of their predecessors the Romans, provided a fertile ground for the continuation of the Greek ideals and the tradition of scientific research, in spite of the theocratic and theological character of this era, (*Ligeros, 1937; Garrison 1929*). Medicine was among the sciences significantly improved in Byzantium, with new discoveries. Byzantine medicine, apart from its significant influence on Islamic medicine, provided the basis for

¹Byzantium an ancient Greek city founded by Greeks in the 7th century B.C, later renamed Constantinople, was the capital of the Byzantine Empire for more than one thousand years until its capture by the Ottoman Turks in 1453 and renamed in Turkish as Istanbul

the rebirth of medicine during the Renaissance in Europe. Prominent figures in Byzantine medical science include **Oribasius** (3rd or 4th c), who, under the orders of the Emperors of Byzantium, compiled much of the medical classical knowledge of ancient Greece into the so-called Oribasius Collection, -later translated into Latin, and into English and French during the Enlightenment in Europe; **Paul of Aegina** (7th c), great Byzantine surgeon and obstetrician, known for his emphasis on the practical aspects of medicine, especially surgery, and his important work *Medical Compendium in Seven Books*, which was used as a major medical textbook for eight centuries; **Theophilus Protospatharius** (7th c. AD), whose treatise *On Urines* with illustrations on techniques and divisions of uroscopy was translated and much used throughout the Greek East and the Latin West ; **Nicholas Myrepsos** (13th century AD) whose work was used as the principal pharmaceutical code by the medical community of Paris until the late seventeenth century; **Demetrios Pepagomenos** (13th c) whose works on gout were also translated in Latin; **John Actuarius** whose works on urine provided the foundation for later studies in this area; **Pedanius Dioscurides**, physician, pharmacologist and botanist, who wrote the *De Materia Medica* a compendium of all the *material medica* then known from Greek medicine and other sources (about six hundred plants and their medical uses are referred). This work is considered a precursor to modern pharmacopeia and a famous copy of it known as Vienna Dioscurides was prepared for the Byzantine emperors, and was in use until the sixteenth century, (Ligeros 1937; Cordell 1904; Scarborough 1985; Garrison 1929; Temkin 1962; The Rector et al 2009; Geanakoplos 1966; Carr 1920).

Historians refer to the medical school of the University of Constantinople in which medicine was for the first time taught as a scholarly subject, as well as to the medical institutions of Byzantium, similar to what we know today as hospitals. These had special wards for various types of diseases and systematic methods of treatment, in which medical specialists and assistants (*Archiatroi*: Chief Doctors (including women doctors, *hypougoi*: Nurses, and *ypiretai*: the servants), worked in an organised hierarchy, (Scarborough 1985; Temkin 1962; Geanakoplos 1966). Byzantine influences are found in the medical school of Salerno in Southwest Italy, already in place by ninth century AD, which developed to a high degree to become the centre of the revival of western medicine. Roger Salerno physician at the school was influenced by the treatises of the Byzantine doctors Aetius and Alexander of Tralles of the sixth century as well as Paul of Aegina of

the seventh century AD. (*Geanakoplos 1966*). Worth noting is that the school of Salerno was undermined after the eleventh century by the return of Galenism which was translated in Latin from its Arabian version –as Brock characterises it: ‘Greek medicine in oriental trappings’, (*Brock 1916, p.xx*). During this period, -at the same time when Galen assumes a supreme authority in medical education, referred to, by subsequent commentators, as the ‘Medical Pope of the Middle Ages’, (*Brock 1916, p.xxi*)- scientific thought ascribes mathematics a central role as a gateway to science, with Roger Bacon (13th century) recognising the importance of practical observation in the search for empirical truth, (*Magee, 1998*); and Thomas Aquinas (13th century), a highly influential scholastic philosopher and theologian, bestowed the title ‘the official philosopher of the Catholic Church’, introduces Hebrew and Islamic elements, in addition to Platonic and Neo-Platonic components, into Aristotelian philosophy, which blends with Christianity to formulate a new cosmotheory called *Thomism*, (*Magee 1998*). From this time onwards the criticisms of the scholastic philosophers Dun Scotus (12th c) and William of Ockham (13-14th c), against the philosophical doctrines of Aquinas, permeated by the spirit of empiricism, open the road to new scientific approaches to knowledge which were subsequently taken and expanded by Lock, Berkley and Hume, (*Magee, 1998*). The fourteenth century rising medical schools of Bologna, Padua, Paris, and Montpellier, base their teachings on the *Anatomia of Mondino di Luzzi*, which was strongly influenced, among others, by Galen and the Byzantines, (*Geanakoplos 1966*). Worth noting this period is the beginning of the demise of Galenic medical authority –some call it *autocracy*,(*Seelig 1905*)- which lasted for nearly fourteen centuries. King (2001), claims that Galen’s authority was ‘unassailable in Western medicine until the sixteenth century when a number of challenges threatened the so-called ‘Prince of Physicians’, (*King 2001*)

CHAPTER VI

THE SCIENTIFIC REVOLUTION

The Renaissance (c.14th-16th A.D)

The doctrine that only *observation* and *experience* can provide us with reliable and valid information about the world prevails over *logos* (reason) during the transitional period extending from the Dark Ages to the Scientific Revolution, and widely known as the Renaissance. *Logical syllogism* is necessary but not adequate enough in the search for knowledge. This era is characterised by revolutionary developments in science such as the Copernican¹ discovery of a sun-centred universe, replacing the old earth-centred Ptolemaic system which was supported by the Christian Church for more than a thousand years. This undermines the authority of the Bible in providing a valid and indisputable cosmotheory as expressed in psalmody 93 from the Bible: '*and [God] fixed the universe in such a way that cannot move*'². Alastair Rae, formerly lecturer at the School of Physics and Astronomy at the University of Birmingham and currently editor of the European Journal of Physics, in his book *Quantum Physics: Illusion or Reality* -reported by *The Sciences* (Aug. 1987) as a wonderful effort to explain the paradoxes of the twentieth century physics- identifies the sixteenth century and the discovery of the heliocentric theory of the universe by Copernicus with the onset of the modern scientific thought, which required observation and experiment, rather than philosophical or religious doctrines, as the criteria for all scientific truth, (Rae 1986). Similarly, Capra (1982) views Renaissance as the era when 'men began to free themselves from the influence of Aristotle and the Church', approaching for the first time the study of nature truly scientifically, with Galileo combining empirical knowledge with mathematics, (Capra 1982, p.27).

From this time onward medicine takes a new turn along its pathway of evolution, based on the new discoveries in anatomy which brought down Galenism and its anatomical errors, (Brock 1916). Brock (1916) claims that Galen, while combating the atomic explanation

¹ Nicolaus Copernicus (1473-1543): Polish astronomer who first developed the heliocentric theory of the universe, (Blackburn, 2005)

² 'και την οικουμένην εσπερέωσεν, ώστε δεν θέλει σαλευθει' (Magee 1998, p.65)

of physical processes, -such as the views of Erasistratus on the role of the calibre of the vessels in determining the secretion of fluids, and the mechanical support stomach walls provided to digestion- had nevertheless acknowledged the weaknesses of the theory, which postulates the absolute exemption of living bodies from the so-called 'mechanical laws', (*Brock 1916*). A major suspending factor, during this time, which interrupts the awakening, and redirects thought from the scientific pathway, is the appearance in Europe of three of the most threatening plagues in the history of humanity, *syphilis*, *the English sweat*, and *typhus exanthematicus*. All these spread widely, instigating superstition and irrational belief in demons and ghosts, even among some of the greatest thinkers of all times, such as Thomas Erastus, (*Seeling 1905*). King (2001) counts these historical incidences as among the challenges to Galenic medicine, since the new diseases, such as *syphilis* and *the English sweat* could not be found in Galen's manuscripts. Other challenges to Galenism mentioned by King include: the invention of the printing press which facilitated the translation and publishing of the complete Hippocratic corpus into Latin in the early sixteenth century, undermining the until then 'unassailable' (*King 2001*) Galenic authority; the travelling outside Europe and the discovery of new medicinal plants together with the loss of trust among travellers to the power of ancient medicine to hold all the answers when they were far from their native land; and the achievements of famous medical men such as Andreas Vesalius, Ambroise Pare, Philippus Theophrastus Paracelsus, and Michael Servetus, (*Seelig 1905; Brock 1916; Vryonis 1989; Garrison 1929*), which gave Galenic medicine the final blows.

References on the achievements of this time are found in the writings of medical scholars of the first decades of the twentieth century, (*Garrison 1929; Brock 1916*). Paracelsus established the first formal textbook on chemistry, the *Alchymia*, (*Garrison 1929*) while Michael Servetus was burned at the stake, as heretic, for his theory that blood passes through the lungs, on its way from the right to the left side of the heart, (*Brock 1916, pp. Xxii-xxiii*). An important medical treatise of this time, which represents one of the most influential works in the history of Western medicine, is the *De Humani Corporis Fabrica (On the Fabric of the Human Body)* conceived and written by the 28-year-old Andrea Vesalius (1514-1564), a professor at the University of Padua. Vesalius was both a learned scholar and a gifted innovative anatomist, (*King 2001; NLM 2010; Garrison 1929*). Vesalius's *De Fabrica* was so successful

and made him so famous that he was ultimately appointed as court physician to the Holy Roman Emperor Charles V. In his *De Fabrica* he discusses the structure, function, pathology, and names of the various parts of the body, not failing to acknowledge the contributions of his predecessor anatomists such as Galen, stressing though the importance of learning through hands-on dissection of the human body. Vesalius, who identified over two hundred anatomical errors made by Galen, offers comparative images of anatomic details between human and animal organs to demonstrate the mistakes of Galen's anatomy, which was based on dissection on animals and not humans. In particular, in spite of being fiercely attacked by Galenists, Vesalius managed to prove, among other things, that Galen's theory of the permeability of the interventricular septum of the heart was wrong. Similarly, he demonstrated that Galen had wrongly hypothesised that the network of veins at the base of the brain of animals existed also in humans, (*King 2001, NLM 2010*). King refers to a characteristic phrase said by Vesalius for Galen: 'he was deceived by his apes', (*King 2001, p.56*). *De Fabrica* provided very useful illustrations of all anatomical and surgical instruments that a medical practitioner would need for the dissections and for anatomy in general. Scholars claim that Vesalius, in spite of his disagreements in Galenic anatomy, he retained much of his physiology, especially the theory of the arteries and nerves carrying blood and spirit through the body. Vesalius was a pioneer in the study of inside of the brain recognising it as the centre of the nervous system, contrary to previous anatomists' views of the heart or the liver as the centre. (*NLM 2010*)

According to King (2001) during the two hundred years that passed between the fourteenth and the sixteenth centuries, some human body dissections were allowed by the church for specific reasons related to its aims, such as autopsies on saints' bodies to reveal anatomical Christian symbols on their internal organs, or when requested by lawyers needing to know the cause of a death. The next step was to allow dissections for educational purposes in the universities, carried out by a surgeon or a butcher and the professor pointing out the relevant parts -the whole process looking more like a religious ceremony rather than a proper anatomical lecture, (*King 2001*). Engel (1977) views in the Church's permission for the study of the human body, a 'tacit interdiction' against any scientific investigation of human mind and behaviour, two areas to remain strictly under its ecclesiastical domain. According to the Engel, the mind-body dualism, as expressed in

the scientific theorems of Galileo, Newton, and Descartes, was firmly pre-established 'under the imprimatur of the Church, (*Engel 1977*).

The rise of the mechanistic paradigm (c. 16th -18th)

The advent of the Scientific Revolution coincides with the findings of Johannes Kepler (1571-1630), who discovered the elliptic planetary motions, discrediting the theory of absolute symmetry in the universe; and those of Galileo (1564-1642) the first to observed the planets with a telescope, and who discovered, apart from the movement of the Earth, the isochronisms of the pendulum, and the theory that all bodies descend at the same velocity independently of their weights and with almost stable acceleration at 9.80m/sec, (*Magee 1998*). According to the *Theory of Relativity* of Galileo, 'if the laws of mechanics are valid for a specific System of Coordinates, then they are valid for any other System of Coordinates which moves smoothly in relation to the first System of Coordinates', (*Einstein & Infeld 1934, p.144*). Galileo established the principle of objectivity in science, advocating the method of systematic scientific observation and rejecting the reliability and validity of knowledge obtained through the senses, (*Magee, 1998*).

The search of absolute objectivity and the belief that everything is possible to be explained through observation and experiment on the basis of universally applied laws permeates all areas of scientific activity from this time onwards. Prominent figures of this paradigm were: Nicola Machiavelli (1469-1527) in politics with his *Hegemon* considered the Bible of *realpolitik*, and espoused by Hitler; Francis Bacon (1561-1626) genius in political matters and strong opponent to Aristotle, who postulated that from individual experiments generalisations can be induced which can be considered as laws (inductive syllogism) and oppositely from a general law individual cases can be predicted (deductive syllogism) and who drew attention to the unreliability of evidence obtained through sensual experience; Thomas Hobbes (1588-1679), who was considered the first modern materialist/empiricist (*Magee 1988*) and had characteristically asserted that matter is the only thing that truly exists and that all mental processes consist of movements of matter within the human skull. The medical significance of Hobbesian materialistic theory, which influenced several subsequent thinkers, lies in its influence in the area of human

psychology putting an end to the belief that mind is something abstract. On the basis of these views it is widely accepted today that there is a material base in mental processes, which cannot adequately be understood without reference to physics, (*Magee 1988*). A prominent figure of seventeenth century medical thought was William Harvey (1578-1657), an English physician and scientist (*Historian Magee informs us that he was the personal doctor of Francis Bacon*), considered as the founder of Modern Medicine (*Magee 1988*). His newly developed concepts, and most importantly his discovery of the circulation of the blood, which showed that the veins and arteries did not form separate systems, further discredited Galenic physiology according to which veins, arteries, and nerves were three separate systems with different functions (*King 2001, p.42*). Harvey's new discoveries provided the basis for a new epistemology of medicine, the widely known today Biomedicine or Modern Medicine, which is the prevalent medical system in most of the western world for the last four centuries. Eugene Cordell¹, medical doctor and Honorary Professor of the History of Medicine, had claimed at the turn of the nineteenth century that Harvey's explanation of the circulation was a 'purely mechanical one' derived from a logical syllogism, similar to that of Hippocrates, based on anatomical examination and comparison with various animals, since only the discovery of the microscope at a later time allowed Malpighi to observe the capillaries, (*Cordell 1904*). Edward Adams, medical doctor and historian, lists among the founders of modern medicine the anatomist James Winslow (1669-1760) for his *Exposition Anatomique de la Structure du Corps Humain* and his description of the brain as a secretory organ; Theophilus Bonetus (1620-1689) for his anatomical researches to discover the seats of diseases and his unique work *Sepulchretum*; and Morgagni as 'a bright star of a systematised Morbid Anatomy, who wrote his *De Sedibus* inspired by *Bonetus Sepulchretum*, (*Adams 1904*)

A famous contemporary to Galileo and Kepler was Rene Descartes (1546-1650), a French mathematician destined to be named by subsequent generations the 'founder father of modern philosophy', (*Blackburn 1996*). Descartes invented a deterministic theory of knowledge which postulated that it is possible to locate an undisputable starting point from which knowledge can rise, by the *method of doubt*. According to this method, every proposition whose truth can be doubted is suspended and the standards of acceptance

¹ Eugene F. Cordell: medical doctor, President of the Medical and Chirurgical Faculty of Maryland ; Honorary Professor of the History of Medicine; President of the Johns Hopkins Hospital Historical club

are gradually raised as one comes to doubt things like memory, sensual experiences, and even reason. Descartes in his famous 'Cogito ergo sum' ('*I think therefore I exist*') located the point of certainty in his own awareness of his existence, (Blackburn 1996). Cartesian philosophy was dedicated to a strict dichotomy between mind and matter, a distortion of the Platonic dualism of reality, entirely rejecting the Aristotelian functional view of body and soul as a unified whole. His method of analytical thinking, which dictated that the whole could be understood by breaking it up into its constituent parts and studying them separately, permeated all areas of scientific thought including medicine for the three centuries that followed. Bennett (2001, p.21), draws from Truesdell (1995,p.6)¹ the following characteristic phrase: 'While nearly all of Descartes's physics is wrong in detail, his grand attempt is the beginning of theory in the modern sense' (Bennett 2001). Descartes recognised the existence of a higher deity to which he left the responsibility of insoluble problems of nature related to the causal connection between substance and mind, (Blackburn 1996). Apparently Descartes 'placed no limits on how God might be expected to behave' since he did not believe that every 'Why?' could always receive a 'Because' and, as a result, the part of his physics on the collision of bodies he presented it as an outcome of God's actions. Bennett (2001) wonders on this theory:

'Why, then, should God not have acted in a different way which would make bodies conform to something like Newton's gravitational law? [...]. I cannot see that Descartes could answer this',

J. Bennet (2001): *Learning from Six Philosophers*

The deterministic principles of Descartes together with the discoveries of Kepler and Galileo were further developed and formulated into particular theorems to apply subsequently into all areas of human endeavour, by Isaac Newton (1642-1727), a highly talented man of exceptional intelligence, at the same time a physicist, mathematician, astronomer, alchemist and philosopher. Bennett (2001), refers to firm recent evidence which documents the belief that it was Descartes's views of nature as a great machine that were indoctrinated into Newton's laws of terrestrial and celestial motion, rather than, as previously thought, Galileo's and Kepler's. Drawing from other scholars (Whiteside 1974; Dijksterhuis 1961), he claims that the Cartesian worldview was first publicly presented by

¹ Quoted in Bennet 2001

Newton in his *Philosophiae Naturalis Principia Mathematica*, (Bennett 2001, p.21) a work considered to have placed the founding stone for the new paradigm of scientific method, which prevails until the present time. Newton is credited with numerous inventions and discoveries which have provided the basis on which the edifice of modern western science was built but also a cornerstone for the rise of the industrial revolution, (Blackburn 2005). Blackburn claims that, Newton, although the father of the 'age of reason', he was interested in theology and he devoted a lot of time in interpretation of the Bible and wrote extensively on religious concepts such as the *Observations upon the Prophecies of Daniel and the Apocalypse of St John* (Blackburn 2005). Worth noting is the tendency of Newton, similar to Descartes, to attribute to God unexplained phenomena in physics that could not be predicted on the basis of his laws. Reference is made to the general scholium at the end of book III of *Principia*, in which Newton argues that 'it is not to be conceived that mere mechanical causes could give birth to so many regular motions' pointing to the operations of God, (Blackburn 1996).

Notwithstanding these criticisms and many more that have risen since then, Isaac Newton is unquestionably one of the most prominent scientists of the world, the principal source of the classical scientific view of the world, (Blackburn 2005), characteristically called by Magee (1998), 'the Patriarch of Sciences', (Magee, 1998, p. 67), and by Hume 'The greatest and rarest' (Blackburn 2005). Among his works worth mentioning is the establishment of the idea that the function of the natural system is governed by laws that can be expressed by mathematical equations (justifying the Pythagoreans two millenniums later) which due to their invariable character gave the power of scientific prediction for the first time. The basic law of Newtonian mechanical science is based on the mathematical equation: $acceleration = force/mass$. This means that if no force acts on a specific mass no acceleration occurs and the body remains in its current state (rest or motion) (Bullock et al 1998). Newtonian explanations of physics were quantitative, in contrast to Aristotelian qualitative explanations of the physical world, (Bennett 2001) and, according to Magee (1998), the philosophy that suffered the strongest blow from this development in science was the Aristotelian. Capra (1982) parallels this mechanistic view of the world with the image 'of a monarchical God, who ruled the world from above by imposing his divine law on it', implying the strong influence of the Christian Church on its development (Capra 1982, p.27).

While criticising the mechanistic paradigm, he does not fail to acknowledge, however, the important contribution of Cartesian syllogism in the development of classical physics and technology. In particular, he highlights the fact that twentieth century physics, originated in the Cartesian split and in the Newtonian mechanistic world view and their development was possible only on the basis of this thought, (*Capra, 1982, p.28*).

CHAPTER VII

BIOMEDICINE

The evolution of the Biomedical Model (c.19th-20th)

According to Cody (2010), in America at the beginning of the nineteenth century, medicine was primarily 'domestically oriented', practiced by a friend or relative of the patient on the basis of William Buchan's Domestic Medicine (1769), John Wesley's Primitive Physic (1747) or John Gunn's Domestic Medicine (1830). By the middle of nineteenth century significant medical events of progress 'crowded one another in rapid succession, (*Garrison 1929*). Whereas the first medical school had been open in 1765 at the College of Philadelphia (the, later, University of Pennsylvania), proliferation of medical schools began actually in 1812. By 1850 forty two medical schools were in place, (Cody 2010).

At the same time in Europe medical practice as we understand it today was at its infancy divided between medical practitioners who have received technical education on one side and 'a host of empirics' without diplomas such as cuppers, lechers, old women, midwives, and herb-doctors, - the majority of them doing a 'thriving business' on the other side. Seelig (1905), drawing from Baas, describes in an apposite way the condition of the health sector of this transitional time.

'There existed during the very era of progress and enlightenment, two sets of physicians; one, the so-called regular set, made up of court, field, hospital and pest physicians, wound doctors, apothecaries, midwives, and nurses; and the other, a set of quacks, made up of old women, village ministers, dispensers of quack salves, urine prophets, peripatetic Jews, crystal gazers, gypsy fortune tellers, demon and devil banishers, soothsayers and rat catchers...'

M.G. Seelig, 1905

Medical Doctor and Historian

King (2001) confirms this situation, reporting that during this time there was an increasing tendency to resort to different newly appearing drugs rather than changes to diet and lifestyle habits, usually provided at a higher expense by the traditional Galenic healer who

spent time and brainwork to learn all about the patient's constitution and life. This led to the rise of a phenomenon referred to as the 'medical marketplace', where several quacks without university training presented drugs claiming to cure all diseases, which were much cheaper and easier rather than embarking on radical dietary and lifestyle changes. King refers to Van Helmont, a physician, chemist and physicist, who devoted a lot of work to invent new drugs to satisfy this market, (*King 2001, p.58-59*). E.J.Kempf, medical doctor and historian at the turn of the nineteenth century, believes that the rise of Homeopathy, with its main exponent being Samuel Hahnemann who advised the administration of medicines in infinitely minute doses, owes much to the practice of this time of taking unreasonably high dosages of drugs, -as Kempf describes it 'shot-gun prescriptions' of 'the vilest drugs', such as calomel, gamboges or saltpetre. He thinks that it is not strange that homoeopathy went to the other extreme, (*Kempf 1905*).

Medical historians refer to the first schools of modern medicine in Europe, which appear during this period and particularly to those of medical men whose contribution was great towards improvement of modern biomedical practice (*Kempf 1905; Garrison 1929*). According to Kempf (1905), the medical practitioners of that time were divided into three classes, physicians, surgeons and apothecaries. Percival Pott is referred to for his *Code of Ethics*, written in 1800, Dr MacBride for his *Introduction to the Theory and Practice of Physic*, Cleghorn for his book *Epidemical Diseases in Minorca*, and Ritty for his *Materia Medica*. In France, Antoine Louis as an authority in legal medicine; Sabatier for his writings in anatomy and surgery; Lietaud for his *Historia Anatomico-Medica* on morbid anatomy; Lorry for his treatise on *Melancholy* and his book on the diseases of the skin; Sauvages, possessor of the Montpellier medical school for his *Pathologica Methodica* and *Nosologia Methodica*; Venel, professor of *materia medica*, for his introduction of Chemistry in the faculty of Montpellier medical college and his analyses on many mineral waters of France; and Fouquet for his treatise on *pulse*. In Italy -'the nursery of modern medicine' according to Kempf - reference is made to great names such as Morgagni, Spallanzani, Fontana, Caldani, and Calvani. In the north of Europe, the University of Upsala in which the professors Linnaeus and Bergman are mentioned -the first as a great discoverer in Chemistry-, as well as Gaubius in the school of Leyden for his *Institutiones Pathologiae Medicinalis*; and the University of Gottingen in which Rudolph August Vogel taught

materia medica and Roederer *obstetrics*. In Austria under the encouragement of the Empress Maria Theresa, Van Swieten influenced DeHaen to establish a clinical school of medicine which maintains a high character until the present time. Reference is made to Zimmermann for his work on *dysentery*. Alexander Blackwell from Aberdeen famous for his *A Curious Herbal*, a leading book on *Materia Medica* containing over five hundred medicinal plants, (Kempf 1905)

In the science of anatomy special reference is made to Marie Francois Xavier Bichat, great anatomist and physiologist, author of nine important volumes, with treatises on membranes, on general and pathological anatomy. According to Kempf (1905), Bichat remained in history with the title, the 'Napoleon of Medicine', due to his great contribution for the progression of medical sciences. Bichat believed that *pathological anatomy* is the solid foundation of medical knowledge, overthrowing the speculative tendency in medicine. Others were Matthew Baillie from Scotland famous for his book *The Morbid Anatomy of Some of the Most Important Parts of the Human Body*; Marshall Hall from England for his doctrine of the *reflex* function of the nervous system; and Richard Bright for *morbid anatomy* of the internal organs. In the area of diagnosis reference is made to Leopold Auenbrugger, who invented the art of *percussion* using his ear and hand on the patient, later improved by Laennec with the invention of the *stethoscope*. Laennec is also known for the discovery of *auscultation* a method going hand in hand since then with *percussion* and his work *De l'Auscultation Mediate*, which is considered as having the greatest effect in the area of diagnosis than any other work published until then Laennec together with his posterity Skoda and Austin Flint are considered as establishing the art of physical diagnosis in the area of thoracic cavity. Further methods of physical diagnosis were added, such as *inspection*, *palpation*, *mensuration*, and *succession*, (Kempf 1905). Ligeros (1937), reminds us that this method was first introduced by Hippocrates, who shocked the patient on a rigid seat and applied his ear to the chest to listen to the succession sound in lung and abdomen -mentioned by Littre as a 'boiling sound', (Ligeros 1937, p.121)

In the area of surgery, reference is made to the surgeon and anatomist Pierre Joseph Desault who systematised and improved the practice and *armamentarium* of surgery. Desault had already by the eighteenth century instituted a clinical school of surgery in

Paris attracting large audiences of physicians and students from all the countries of the then civilised world. Others mentioned in this area include Francois Chopart known for the *amputation* bearing his name; Richter of Germany who enunciated the principle of *dressing wounds*; Jean Louis Petit who perfected the *screw tourniquet* and improved the art of *amputation*; Percival Pott from London, a distinguished surgeon, for his investigations on *angular curvature of the spine* –a deformity already known in antiquity-, mentioned in literature as *Pott's disease*; Sir Charles Bell, for his discoveries in the *nervous system* and for his invention of the science called *topographical anatomy*- a combination of anatomy and practical surgery- now taught in the medical schools; Antonio Scarpa in Italy, one of the greatest clinical surgeons in Europe, famous for his industrious, scholarly and artistic works, especially on the anatomy of the organs of smell and hearing, the supply of the heart with nerves, and the minute anatomy of the *bone*; Lazzaro Spallanzani from Italy for his work on the heart and blood circulation; William Cheseldem, English surgeon and anatomist who wrote *The Anatomy of the Human Body and the Osteography*, the former being the leading textbook in England for long time; Sir Astley Cooper, English surgeon and medical scientist, known for his work on *Hernia*, a great contribution to medical science on the topic, and for succeeding to elevate surgical operations from 'a series of frightful alterations, or hazardous compromises' to the position of dignified science, (*Kempf 1905*)

In the area of chemistry, Karl Wilhelm Scheele from Sweden discovered a number of chemical substances such as tartaric acid, chlorine, baryta, oxygen, glycerine, the arsenite of copper, and prussic acid (a deadly poison used in therapeutics); Leopold Gmelin from Gottingen compiled all knowledge in chemistry until his time in the *Handbuch der Chemie*, considered a classic in the literature of chemistry; Sir Humphrey Davy with his lecture 'On some chemical agencies of electricity' universally considered as one of the most valuable contributions to chemical science. He is credited with several discoveries of metals such as sodium barium, strontium, calcium, and magnesium, by decomposing compound substances, such as potash, soda, baryta, strontium, lime and magnesia. In the area of *anaesthesia* Sir Humphrey Davy used *nitrous oxide gas* (the 'laughing gas'), as an anaesthetic, while Pearson used the vapour of *sulphuric ether* for the relief of spasmodic affections of the respiratory passages and in the nineteenth century Sir James Simpson

used the our well known *chloroform* (Kemp 1905). The introduction of vaccination, initially for the immunisation against *smallpox* by Edward Jenner an English surgeon, anatomist, pathologist and experimenter, represent another important landmark in the history of modern medicine. Although preventive inoculation using the virus from sufferers with smallpox or from the cowpox was applied long before Jenner, he is credited with making a careful observation and deep study of the subject succeeding to transmit *vaccinia* from the cow to the human individual making them immune to *smallpox*, (Kemp 1905).

In physiology, Rene Dutrochet, from France is known for his research on *endosmosis* and *exosmosis*, terms related to the passage of fluids through the body and Joseph Black, from Scotland, eminent chemist and lecturer at the university of Glasgow known to science for his theory of 'latent heat'. The *microscope*, which was invented in the seventeenth century and further developed and improved in the eighteenth century allowed the observation of 'germs' in the blood ultimately leading to the formulation of the theory of the connection between specific bacteria and specific diseases. By the mid-nineteenth century two opposing theories were developed regarding the cause of disease: The *Germ Theory school*, or *Single-Agent Theory* advocated by Louis Pasteur, which postulated that specific diseases are caused by specific bacteria and killing them with a poisonous substance can cure the disease, and the *Nature Cure School* which supported the view that that bacteria are omnipresent, absorbed by our food and drink, inhaled by the air we breathe, but cannot survive in our bodies if they don't find a fertile matter on which they subsist. Pasteur's theory prevailed and became dominant providing the basis of modern medicine with its emphasis on fighting specific diseases rather than promoting a strong immune system and supporting the body's self-healing power to avoid invasion of the bacteria, (Proby 1975; Trivieri & Anderson 2002; Reid 1996; Pizzorno & Murray 2007-2011; Plaskett 2004). This theory, according to scholars have failed to explain the causes of diseases such as *cancer*, *arthritis*, *osteoporosis*, *arteriosclerosis* and many other degenerative conditions not related to germs, (Proby 1975; Trivieri & Anderson 2002; Reid 1996; Plaskett 2004; Thiel 2000). It even failed to provide adequate explanation 'why under precisely the same conditions of exposure to exactly the same germs, some people catch the disease and others do not, (Reid, 1996, p.49). Reid (1996), proposes the analogy of the garbage which whereas it always attracts flies, this does not mean that flies necessarily cause garbage. In fact, he claims,

the garbage becomes 'diseased' when the flies place their eggs because they find fertile conditions. Using pesticides to kill flies will not get rid of the garbage. The only solution is to 'clean up the garbage!' What, actually, pathogenic organisms need to thrive are specific conditions of temperature, humidity, pH, and other environmental factors, exactly as a good baker provides the right 'climate for fermentation of bread and wine maker for that of wine'. Reid asserts that Pasteur was aware of this truth and he wrote several references on the importance of the internal climate that predisposes tissues to infection by germs; however this part of his work 'has been swept under the carpet by the modern medical industry'. Interestingly, Pasteur recanted his germ theory before dying, acknowledging from his deathbed: 'the microbe is nothing! The terrain is all! (Reid 1996, p.50). A characteristic example refers to the fact that eighty percent of all humans carry the pneumonia bacillus in their lungs without problem 'as long as "favourable winds" prevail in the human energy system and the immune response remains strong' (Proby 1975, pp.36-37). Worth noting is Henry Proby's claim for studies demonstrating that in the mouth of a healthy two-month old infant almost all the bacteria known to medical science can be found, (Proby 1975, p.38). Within the same conceptual framework, the physician argues using the term *Disease Diathesis* that 'it is found that 'under identical conditions of exposure to draughts or infection, only a certain percentage of individuals will "take cold" or "catch disease"'. (Proby 1975; Trivieri & Anderson 2002; Reid 1996).

By the end of the nineteenth century bones could be observed through X-rays and the CAT and MRI scanners allowed the observation of soft tissues and the possibility to identify tumours and other lesions; improved knowledge of the roles of vitamins and minerals helped the elimination of the 'deficiency diseases'; and the Human Genome Project promoted the mapping of the genes. New drugs synthesised in the laboratory are added to, and often, replace or enhance those used by Hippocratic and Galenic doctors until then. In particular, the plant *willow bark* used until then for fever and pain, is synthesised and tested on animals and people in the second half of the nineteenth century and given the new name '*aspirin*'. From this time onwards new 'designer drugs' (King 2001, p.60), are created to target particular conditions. A worth noting development in the end of the eighteenth century is the change in the approach to treatment of the mad. The practice of putting the person in a *strait-jacket* is replaced by a 'moral therapy'

according to which the insane is approached and treated gently, with electricity and surgery added to the treatment of this problem by the middle of the twentieth century along with the use of newly discovered drugs effective for long-term treatment of mental illness. (King, 2001; Trivieri & Anderson 2002)

Several inventions and improvements to past inventions occur in the nineteenth century including the *stethoscope* in 1816, the *thermometer* in 1860, various methods of blood testing, such as Gowers' *haemocytometer* in 1877; the *ophthalmoscope*, *laryngoscope*, *endoscope*, *electricity*, the *X-ray apparatus* etc (Kempf 1905; Cordell 1904). The onset of the twentieth century is accompanied by a rapid development in different areas of medical science and technology, including new microscopes, electromagnetic apparatus, bacterial cultures, vaccines, X-rays, and by the 1930s the discovery of *antibiotics* (the first antibiotic, *penicillin*, discovered by Alexander Fleming in 1928, , which contributed greatly to the fight against the terrible acute infections of the past, (Drummen 2010)

The growth and achievements of Biomedicine

Researchers identify the definition of *Biomedicine*, as it first appeared in Britain, in Dorland's, 1923, Medical Dictionary as follows: "clinical medicine based on the principles of physiology and biochemistry" (Quirke & Gaudilliere 2008). According to Cozzens (2010), Biomedicine 'has often been invoked as the exemplar of strategic research', further explained as the fundamental science which prioritises biomedical research policies and contributes to the solution of practical problems, (Cozzens 2010). Others claim that the term *Biomedicine* 'resonated strongly with the priorities for medical research' of the British Medical Research Council, (MRC)¹, (Valier & Timmermann 2008), highlighting the coincidence of the invention of the name with the movement of the MRC away from public health concerns towards biological research, (Quirke & Gaudilliere 2008). Some view the post-Second World War transformation of medical research on the basis of statistical applications and probabilistic analysis of the aetiology of chronic disease in epidemiology, clinical trials, and laboratory experiments, as having changed the relationship between the clinical and

¹ Medical Research Council: Established in 1911

laboratory sciences. This is what was explained by Berlivet (2008) as ‘the statistician’s intrusion into clinical matters centred on the randomisation of therapeutic trials’, and by Jean-Paul Gaudilliere as the ‘experimentalisation of the clinic’, (*Berlivet 2008*). Quirke & Gaudilliere (2008) speak for a re-definition of ‘public health’ as essentially ‘hospital and drug-based’, and for medicine as becoming ‘curative rather than preventive’, with experimental science and biological science dominating all areas of medical practice (*Quirke & Gaudilliere 2008*), while Berlivet (2008) identify a shift from one regime of knowledge production to another on the basis of a ‘molecularization’ of medicine, (*Berlivet 2008*).

Nevertheless, despite criticisms for the heavy dependency of Biomedicine on medical research for the validation of its means and methods of treatment, (*Cozzens 2010; van Weel & Rosser 2004; Berlivet 2008*), a volume of literature highlights the remarkable achievements in several areas of medical practice and technology. Unprecedented developments in surgery, pathology, genetics, medical technology, and pharmacopoeia have occurred through the rigorous application of the scientific method of cause and effect, analytical thinking and reductionism, (*Cushman & Hoffman 2004*). In the area of experimental science, new systems of relations between science, technology and medicine led to the development of ‘a new way of knowing’, according to which life and its more basic processes are relocated at the level of the macromolecular structures –DNA and genes- and the area of aetiology of disease greatly expands to cover new enzymes, cancer viruses and inbred strains of mice, (*Quirke & Gaudilliere 2008*). The increasingly sophisticated understanding of the structure and function of amino acids, proteins, and peptides, as well as the maturation of recombinant DNA technologies, have led to the development of new peptide-based biomaterials, which possess significant physical, chemical and biological properties for application in Biomedicine and biotechnology. Areas of application include protein purification, drug delivery, tissue engineering, and surface engineering, (*Chow et al 2008*). Evidently, *omics*¹ studies in biomedical research have led to the emergence of new models of diagnosis and treatment of disease and to the identification of clues to possible pathogenic organisms, thereby allowing the development of new diagnostic tests and the adaptation of therapeutic responses, on the basis of a more personalised medicine, (*Reitman & Shadt, 2007*). Important insights, for example, have been offered over the past

¹ Refers to the area of study in Biomedicine ending in the suffix omics, such as genomics or proteomics

decade into the molecular basis of cancer, through analyzing gene expression in patient-derived tumour samples, (*Bodenreider & Burgun 2008*). According to researchers DNA microarrays (DNA chips), contribute to the classification of many tumour types, such as prostate cancer, brain cancer, lymphoma and others, and are used to monitor the gene expression of thousands of genes simultaneously across the entire human genome, (*Bodenreider & Burgun 2008*). Genomics have also opened the way to novel approaches to drug discovery, where prior knowledge of a target gene that is biologically relevant to a disease state, offers the basis for the discovery of a new drug. The new drugs are in turn used to modulate biological processes in cells, (*Bodenreider & Burgun 2008*).

In the area of biotechnology, the work of molecular biologists, biochemists, geneticists and virologists is greatly supported and promoted by the discovery of new tools and instrumental practices, such as the ultracentrifuge, the electron microscope, and electrophoresis, (*Quirke & Gaudilliere 2008*). Technologies such as radiography, ultrasonography, magnetic resonance imaging, and spiral or conebeam computed tomography, greatly enhance diagnostic capabilities by allowing visualisations of diseased organs, tissues, and ligaments, in different planes, in three dimensional volumetric reconstructions, (*Jackson 2002; Wadhwa & Kapila 2008*). The last five decades are identified with great advancements in biotechnology and the invention of nanotechnology which have surpassed all science fiction movies, (*Drummen 2010*). Nanotechnology, the science that uses the unique therapeutic capabilities of nanoparticles, through the manipulation of matter at the atomic scale –a microscopic level below 100nm- marks the transition from the classical Newtonian world, based on the properties of bulk materials, to the world of quantum mechanics. Quantum dots biotechnology, among other functions, facilitates the location of cancer cells and their therapy with the use of magnetic fluid hyperthermia; nanoparticles and nanoshells deliver highly sophisticated therapeutic drugs and concentrate the heat from infrared light to target specific cells, thereby minimising the damage to healthy surrounding cells, (*Drummen 2010*). The recent developments in biomedical *nanomagnetism* find broad applications in different areas of medicine, such as imaging, diagnosis and therapy and open new horizons in personalised medicine on the basis of synergies between chemistry, materials science, physics, engineering, biology and medicine. Researchers emphasise the unlimited possibilities *nanotechnology* offers in the

area of detection of disease at the earliest possible time before damages occur, and the important contribution of *nanomagnetics* in targeted and triggered drug release, that is delivering therapy 'at the right dose and at the right time' and, consequently, minimising toxicity to healthy cells, (*Krishnan 2010*). According to Bekyarova et al., 2009, the application of the principles of biology to *nanotechnology* offers incredible possibilities in the design and function of artificial devices and tremendous opportunities to manipulate living cells at the single molecular level. *Nanomaterials* find application in a variety of biomedical and biotechnological areas such as bone growth, enzyme encapsulation, biosensors and delivery of DNA into living cells. A century away from Edison's discovery of the intriguing properties of *carbon*, the discovery of the carbon *nanotubes*, the 'most promising of all nanomaterials', has attracted the attention of physicists, chemists and materials scientists, (*Bekyarova et al., 2009*).

The incredible progress of high performance computation technology is also stressed by researchers, which allowed the handling of a huge amounts of data of large size and complexity, such as *gene expression* and *proteomics data* generated from *DNA microarrays* and *mass spectrometry*, (*Carriero et al. 2005*). Research projects increasingly require high technology computation, biomedical informatics professionals and mathematicians to solve information problems in health care, and researchers 'spend less time in the their 'wet labs' gathering data and more time on computation', (*Bernstam et al., 2010*). Bernstam et al. (2010), identify *digital methodologies* such as the 'hallmark of tomorrow's Biomedicine' while Bodenreider & Burgun (2008), highlight the special computational needs emerging from the evolution of biomedical research from traditional clinical and biological investigations towards omics sciences and translational research. Omics studies, generate large number of measurements on a limited number of test subjects, contrary to traditional clinical trials which involve many subjects but only a few parameters measured, (*Bodenreider & Burgun 2008*).

PART III

CONTEMPORARY HEALTHCARE

A Critique

The unprecedented developments of the last century in all areas of medical science and technology outlined in Part II, juxtaposed to the evidence provided in Part I on the rising incidence of chronic disease, the increasing DALYs and YLD indicators, and the declining HALEs (Healthy Life Expectancies), provides grounds for a number of reasoned questionmarks:

- ‘Why chronic illness is no more an ‘age problem’?’
- ‘Why people are unhappy and depressed in an affluent highly developed society?’
- ‘What went wrong in the provision of healthcare?’
- ‘Is it medical incompetence or political indecisiveness?’

This Part attempts to provide answers to these questions by throwing light to the deeper reasons that led to this situation, through different perspectives, academic, medical, political and public. Literature abounds of criticisms, often self-criticisms, which focus on different areas of the provision of healthcare. The most important of these, which have been further supported by the author’s research in Cyprus, are cited below and include the outdated politics and management of the wider health sector as well as a number of long established practices in the provision of healthcare, such as: the emphasis on an impersonal model of care focussing on particular diseases rather than the whole patient; the narrow conception of the determinants of health, ignoring those falling outside the traditional boundaries of the health sector, such as dietary and lifestyle habits, psychosocial factors, and environmental exposures; the overemphasis on specialisation to the detriment of continuity of care and the family doctor who traditionally used person-centred approaches; and the exclusive use of drug and surgery treatments, largely underplaying the therapeutic power of other factors in the patient’s life, including diet and lifestyle.

Note: In an effort to enhance the objectivity of this critique, the largest part of the review of literature was conducted within work published by medical and pharmaceutical scholars and researchers. A significant part of the evidence was obtained from official reports

CHAPTER I

HEALTH SYSTEMS OUT OF DATE

'Unfortunately, the evidence suggests that the current systems of health care in both developed and developing countries have evolved over the decades on the assumption that the primary need is for a system geared to improving short-term, rapid response to acute illness. This is now considered, in both developed and developing countries, to be increasingly inadequate.'

World Health Organisation 2002iii

There is no doubt that the unprecedented advances in medical science and technology of the last three centuries have resulted in remarkable improvements in several areas of healthcare in the developed societies; however, a volume of criticisms target contemporary health care systems for failing to respond effectively to the global epidemic of chronic disease and to implement an effective chronic disease prevention and treatment model, (Yach et al 2004; Davis & Wagner 1999; WHO [2002ii; 2004i; 2004ii; 2005;2005i; 2008; 2008i]; Mathers & Loncar 2006; Bodane & Brownson 2002; Zimmet 2000; Percy-Smith 2007; Yarnall et al 2003). The World Health Organisation in a report prepared by the Wellcome Trust Meeting of Experts in August 2001, had expressed concerns that modern medicine has 'evolved over the decades on the assumption that primary need is for a system geared to improving short-term rapid response to acute illness', (WHO 2002iii). The Organisation experts criticised the health systems of its Member States at that time as 'based on responding only to acute problems, urgent needs of patients, and pressing concerns', and as not geared to provide for the prevention and successful cure of chronic disease (WHO 2002iii). Seven years later things seem much the same, if not worse, as more recent WHO reports claim that current health systems rarely deal successfully with the long-term needs of people with non-communicable (chronic) diseases, and draw attention to the necessity of 'reorientation of health systems to respond to the need for effective management of diseases of a chronic nature', on the basis of 'new scientific knowledge, available evidence, and a review of international experience', (WHO 2008). In its 2008 World Health Report, the Organisation urges once again for the imperative of renewing primary health care 'now more than ever', criticising health systems of its member states for 'not performing as well', for

being unable to meet 'stated demands and changing needs', and for failing to meet people's expectations and to 'respond better –and faster- to the challenges of a changing world', (*WHO 2008*). The fact, that the nature of health problems has changed at a rate that was not adequately anticipated, is stressed, as well as the 'inadequate and naïve' response of the health sector to these changes. The organisation draws the attention of its member states' to the fact that health systems focus on a 'narrow offer of specialised curative care', to a 'command-and-control approach to disease control' and to an 'unregulated commercialisation of health', (*WHO 2008*).

Similar concerns are expressed at the national level, where researchers criticise the weaknesses and inadequacies of the current Cypriot healthcare system, emphasising specific problems related to prevention and treatment of chronically diseased citizens. Theodora Zachariadou and colleagues, in a study supported financially by the Ministry of Health of Cyprus, view the Cypriot National Health System as inefficient and ineffective and stress the need for the 'introduction of organisational systems to support the management of patients with chronic diseases'. The researchers refer specifically to the absence of national guidelines for cardiovascular disease prevention, despite the fact that Cyprus is included in the high risk regions for this disease, (*Zachariadou et al 2008*). Other researchers claim for 'outdated organization and management', 'badly-managed hospitals', poor-quality clinical services, no-patient-friendly attitudes, and inadequate regulation of private sector providers, (*Antoniadou 2005*); and for a health care system 'inappropriate to modern systems of management' with a 'lack of coordination between the public and private sectors', (*Golna et al. 2004*). Studies demonstrate that private spending for health in Cyprus is disproportionately high compared to the other European countries, due to the absence of an efficient healthcare system that covers the entire population, (*Golna et al 2004, [fig.12+13, p.39-40]; Antoniadou 2005; OECD 2010*). According to official sources the public sector is the main source of health financing in all European countries, apart from Cyprus, (*OECD 2010*). Officials of the Health Insurance Organisation (HIO), which was set up under Law in 2001 with a mission to implement a new National Health System, report that Cyprus spends only 5.8% of its GDP on health –of which 40% on public and 60% on private health-while the EU average spending is 8.3% (*Antoniadou 2005; OECD 2010*) and this information is also confirmed by World Health Organization statistics, (*WHO 2007iii*).

The President of the Board of HIO, replying to questions by the media in November 2010, claimed that ‘the present public health sector has reached its limits’ and that citizens are disappointed by the declining quality of services’ in spite of the fact that the expenses of the public health sector increase at a rate of 11% per year. He characteristically referred to a public demand for modernisation of the National Health System towards more patient-centred approaches, (*Cyprus Health Insurance Organisation 2010*). Similar views were expressed by the Officials of HIO during the interviews with the author for the purpose of this project. In particular, strong support was expressed to a modernised health system, which provides all the prerequisites for citizens to be adequately informed and free to choose their treatment, even if the unions of any profession have a different opinion. The state, they claimed, has the obligation to offer this choice to the patient, “not to direct the patient”. The ultimate aim of the current Board of the Health Insurance Organisation, it was stressed, is to improve and modernise the new Cyprus Health System, on the basis of other European countries’ health systems, in order to be able to offer the European citizen equal level of services wherever they are. These comments were in line with the President’s of HIO statements to the media in November 2010, according to which Cyprus needs to follow the example of other health systems in Europe which develop, modernise, update, and adapt to the changing circumstances of the society in order to offer the level of health citizens expect to have, (*Cyprus Health Insurance Organisation 2010*). In spite of these views, however, the Ministry of Health in its 2007 Annual Report claims that it has managed to offer a ‘high level of health’ to its citizens which is ‘favourably compared with the other developed countries’, (*MOH 2008, p.14*). Similarly, during the first interview with the author, one of the high officials of the Ministry of Health supported the view that the health system of Cyprus is efficient and effective, working perfectly on the basis of a good cooperation between health providers, without major weaknesses and limitations. From a different perspective, another high Official of the same Ministry, during the second interview with the author, acknowledged a number of limitations, (related to the subject of the interview) such as the low emphasis on Nutrition, as well as lack of professionals with adequate scientific knowledge and expertise for therapeutic nutritional interventions. Criticisms against the current establishment in the provision of healthcare were also expressed by the majority of the politicians, during the interviews with the author for low professionalism and bad management, for low emphasis on diet

and lifestyle as means for treatment, and for not adequately providing for citizens to have the right for informed choices for the treatment they wish. Furthermore, the Officials of the Health Insurance Organisation, during the second interview with the author, highlighted the financial constraints preventing the organisation from providing adequate services to the patients.

The low emphasis of the current establishment in the provision of healthcare on scientific nutritional interventions was also evident from the results of the Survey and the analysis of Case Studies from the author's Clinical Practice, both demonstrating that drug and surgery are, as a rule, the first and only options Cypriot patients are offered by the state, in spite of a demonstrated by the research willingness of citizens for other means, such as dietary and food supplements, particularly among citizens with high education and high income. The issue of the gap between patients needs/desires/expectations and the policies of the state is discussed at the end of this chapter with evidence from the present research

An important parameter of the rise of chronic disease is the economic burden on societies, which is estimated by experts to greatly increase with an increasingly ageing population, (*WHO [2002, 2003, 2003iii, 2004i, 2004ii, 2005i, 2007ii, 2008, 2008j]; WHO Europe 2008; EU 2007ii; Zimmet 2000; Elliot & Ong 2002; GRAPH: WHO Europe 2008-Age pyramid 2005, p.12*). By the year 2050, the number of people over 65 is estimated to grow by 70%, and of those over 80 by 170%, skyrocketing demand for healthcare. This will amount to about 25% increase in spending as a share of GDP. Research demonstrates that 70-80% of healthcare expenses in Europe are allocated to chronic conditions, (*WHO Europe, 2006*). The World Health Organisation reports that chronic diseases hinder economic growth and reduce the development potential of countries by directly affecting the quantity and productivity of labour and indirectly savings and investment, (*WHO 2005i WHO 2002ii*). People with diabetes, for example, generate enormous health care costs (*Zimmet 2000*), two to three times those without the condition (*WHO 2002*). The Commission of the European Union in its 2008 White Paper focuses specifically on the annual economic burden of coronary heart disease which amounts to 1% of GDP and of mental disorders to 3-4% of GDP. EU experts claim that if people can remain healthy as they live longer the estimated increase in healthcare spending could be halved, (*EU 2007i*). The Commission draws the attention of policy makers to the Healthy Life Years indicator

(also called Disability-Free Life Expectancy) which puts emphasis on the quality rather than the length of life. This term, which was introduced in 2005 as a Lisbon Structural Indicator, is considered to have important second order effects, such as ‘the opportunity cost (i.e. the benefits forgone) of doing too little to prevent ill-health, resulting in the use of limited health resources for the diagnosis, treatment, and management of preventable illness and injuries’¹ (EU 2007).

Evidently, life expectancies are significantly improving, challenging misguided forecasts which have led to inaccurate calculations of the financial, medical and social needs of the elderly. Research demonstrates that female life expectancy, for example, has risen during the last 160 years at a rate of 3 months per year. According to statistics of the European Union, in the year 1840 Swedish women, who now live 83 years, lived an average of 45 years and were considered as the longest survivors. Forecasts demonstrate that, while in 2002 19% of the EU-25 population were aged 65 and over, this is likely to rise to around 24% by 2025. Increasing age together with more unhealthy life years is translated into more medical needs and higher expenditures (in kind and in cash) for health systems and pensions for the governments². The economic consequences of the diseased population are also stressed by researchers in the case of Cyprus who claim that over the next 25 years, Cyprus will experience a decline in the proportion of the population aged less than 15 years and an increase in that over 65 years. This prospect will, inevitably, be accompanied by reduction in labour force, shrinking of social security revenues and increase of the costs of healthcare. A study published by the Harvard School of Public Health in July 2003, (Hsiao and Jakab, 2003) analysed the financial burden borne by households when they seek health services. It was found that households with chronic illnesses or a severe acute illness may face catastrophic levels of health expenditure, (Golna et al., 2004). Worth noting is the statement of the President of the Cyprus Health Insurance Organisation to the media in November 2010 according to which the expenses of the public health sector increase at a rate of 11% per year, (Cyprus Health Insurance Organisation 2010).

¹ http://ec.europa.eu/health/ph_information/indicators/lifeyears_en.htm

² http://ec.europa.eu/health/ph_information/indicators/lifeyears_en.htm

In acknowledgement of the responsibility of governments in the provision of healthcare, the Commission of the European Union in its 2008 White Paper, urges key actors to formulate new strategies in order to face the growing challenges to health posed by increasingly ageing populations and changing disease patterns. According to the White Paper, in a new era of a more patient-centre and individualised healthcare, the patient is 'becoming an active subject rather than a mere object of healthcare' with a right to participation in decision-making and health literacy. Several researchers and scholars express their concerns for the low level of action taken, and the wrongly directed policies, by key decision makers to reduce the incidence of chronic disease. Drawing from the results of a volume of research which demonstrate the underlying mechanisms of chronic diseases, such as cancer, heart disease, diabetes, and hypertension, and the ways by which these can be prevented, John Weisburger from the Institute for Cancer Prevention of the American Health Foundation in New York, claims that this knowledge has not been used properly by policy makers. In an effort to demonstrate how key players' decisions affect public health, Weisburger claims that, in spite of a high level of awareness among Health Ministry officials of the 185 WHO states for the growing incidence of chronic disease, no comprehensive policies were made and the majority of them had no evidence of integrated approaches to their prevention, surveillance, and control. In particular, the G8 heads of state, while recognising health as the global challenge at their Summit in 2000, agreed to mobilise resources for communicable diseases, such as AIDS, tuberculosis and malaria but made no commitment for chronic diseases. The same appears true for the G77 (heads of state from 130 developing countries) who expressed their concerns that any efforts to reduce sugar consumption might harm their economies, (*Weisburger 2000*).

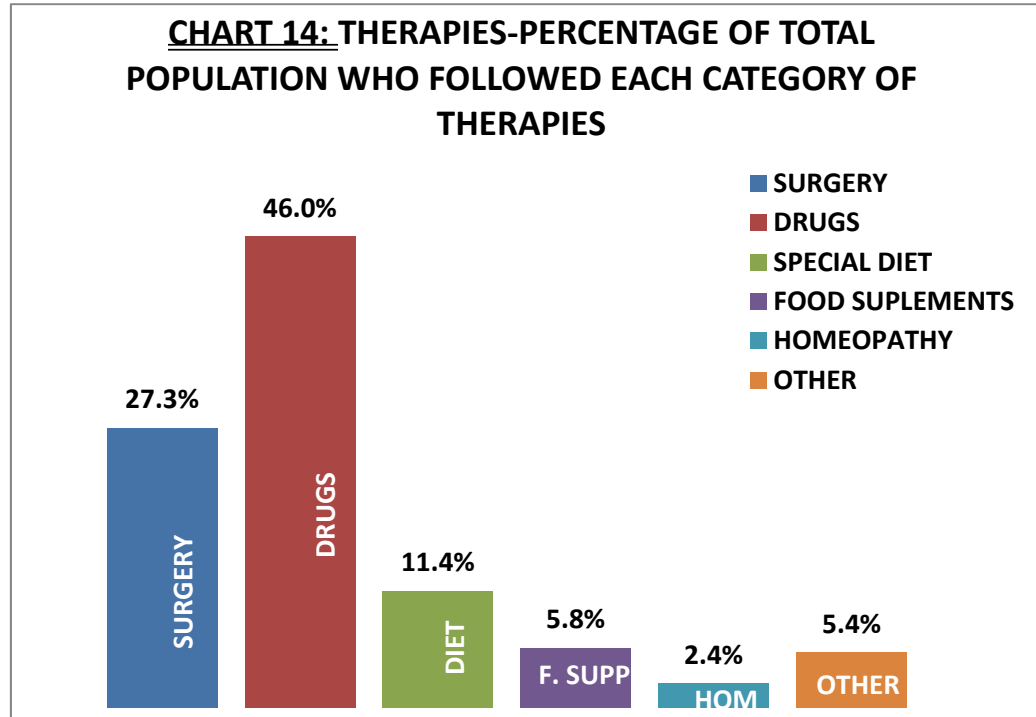
Derek Yach and his colleagues, all medical experts of the World Health Organisation in Geneva, criticise the sole orientation of contemporary health systems towards acute care, arguing that the global response to the problem of chronic disease remains inadequate, 'despite growing evidence of epidemiological and economic impact'. The researchers draw attention to the universal character of the problem, since the stakeholders are the governments, the World Health Organisation and other United Nations bodies, academic and research groups, nongovernmental organisations, as well as the private sector. They express the belief that the reasons for inadequate action lie in wrong perceptions about

the actual causes of chronic disease and the available means for its control, highlighting the fact that 'up-to-date evidence related to the nature of the burden of chronic disease is not in the hands of decision makers', (*Yach et al 2004*). Along the same lines, professor Paul Zimmet from the International Diabetes Institute in Australia, claims that the non-communicable disease epidemic is not possible to be controlled by the traditional medical establishment, as 'it is not in the hands of the medical community' and call the international public health communities to 'lobby and mobilize politicians and other international agencies' to address 'the socio-economic, behavioural, nutritional, and public health issues' related to chronic disease, (*Zimmet 2000*).

Further criticisms refer to the 'dominant modus operandi' of public health policy makers to design and implement generalised, one-size-fits-all programmes, based on a 'narrowly disciplinary worldview', within the context of collective efforts towards enhancing the health of a, wrongly perceived as homogeneous, population, (*Solomons 2009*). Noel Solomons, researcher at the Centre for Studies of Sensory Impairment, Aging, and Metabolism in Guatemala, cites a number of examples, which he calls 'paradoxical findings', and which appear to challenge the generality of one-size-fits-all policies. These include nutritional interventions, usually preventive, having opposite effects on different individuals within a population. The researcher draws the attention of policy makers to the need for 'individualisation of interventions that were once destined to be routine, collective, and universal', especially when implementing large scale preventive programmes, as are the nation-wide fortifications of staple foods, such as flour and breakfast cereals, with folic acid, iron, and other supplements, (*Solomons 2009*).

The responsibility of politicians in the less than optimum health of citizens was clearly evident by the research of the author in Cyprus which demonstrated a gap between the policies of the state and the desires and needs of the citizens further supporting the argument for the outdated health system. The Survey demonstrated that Pharmaceutical and Surgical treatments appear as the first resort to therapy amongst Cypriots. Replying to the question 'If you did more than one treatment for a specific health problem, which order of treatment did you follow?' (*Appendix 1, Question 18*) the replies demonstrated that the order of treatment amongst the population appears as: pharmaceutical (46.2%),

surgery (27.3%), special diet (11.4%), food supplements (5.8%), homeopathy (2.4%) and other (5.4%) (Chart 14:Therapies-Percentage of total population who followed each category of therapies)



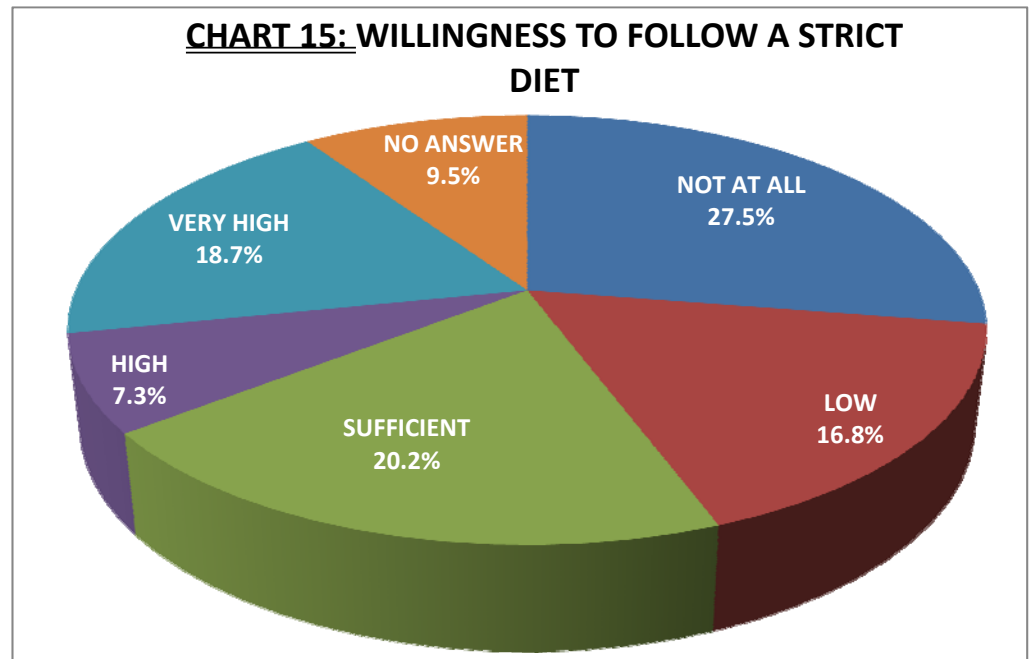
In addition, from the analysis of Case Studies from the author's Clinical practice (Table 9: Nutritional and Drug Prescriptions by Doctors), it appears that the majority of patients (88%) were prescribed pharmaceutical treatments with only 14% of them being offered other than medical prescriptions (mostly consisting of calcium, iron, and multivitamin supplements). Dietary treatment was prescribed to only 2% of them, and was limited to the avoidance of specific foods and always along with their pharmaceutical treatment. Worth noting is that in all cases of other than medical treatments, these were prescribed alongside with drug prescriptions

TABLE 9: NUTRITIONAL AND DRUG PRESCRIPTIONS BY DOCTORS
(50 randomly selected cases from Clinical Practice)

TYPE OF ADVICE	Number of patients	Percentage of total number of patients
No nutritional advice	43	86%
↳ With drug prescription	37	74%
↳ Without drug prescription	6	12%
Calcium supplements	2	4%
↳ With drug prescription	2	4%
↳ Without drug prescription	0	0%
Iron supplements	2	4%
↳ With drug prescription	2	4%
↳ Without drug prescription	0	0%
Calcium and Iron supplements	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%
Multivitamins	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%
Avoidance of foods	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%

The gap between state policies and peoples' desires appears if above finding is contrasted with a number of other findings of the Survey. The first is demonstrated below in Chart 15: Willingness to follow a strict diet,: where a significant percentage of the population appears willing to follow a strict diet, rather than drug therapy, in order to get rid of their

chronic health problems. The question addressed to them was: *'To what extent are you willing, instead of taking drugs, to follow a nutritional therapy which would demand a strict diet excluding your favourite foods, in exchange for your cure?'* (Appendix 1, Question 24). In replying, 26% of the population stated as having 'very high' (18.7%) or 'high' (7.3%) willingness to follow the strict diet for treatment and 20.2% of them expressed 'sufficient' willingness.



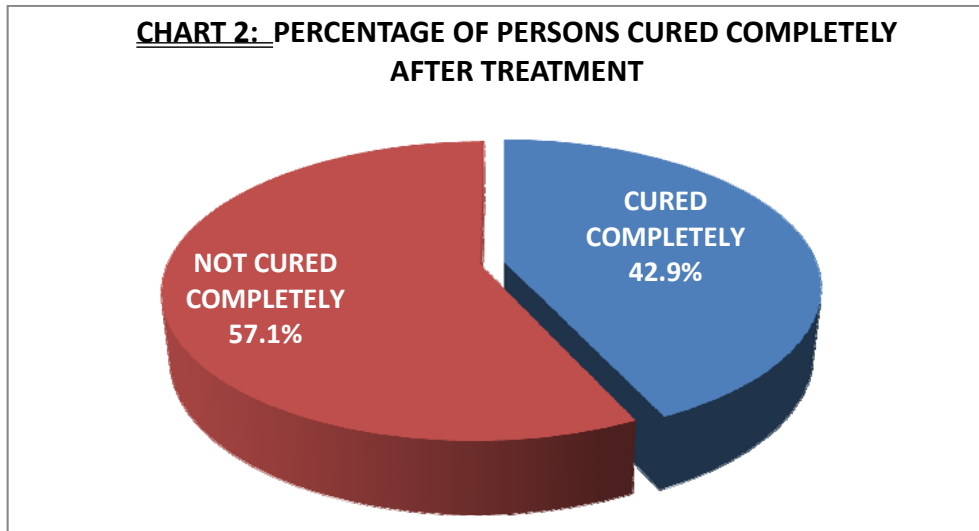
Apparently 46% of the population would accept to follow a strict diet for therapy, *if that was offered to them, or if they could afford it (high income), or if they were informed about it (educated)*. This last conclusion was evident from cross-tabulation of the results of the survey, (Table 5 : Age, Income, Education and Treatment correlations) where education and income were shown to be significantly positively correlated with dietary and nutritional supplement treatments, and education to be significantly negatively correlated with pharmaceutical treatments.

TABLE 5: AGE, INCOME, EDUCATION AND TREATMENT CORRELATIONS

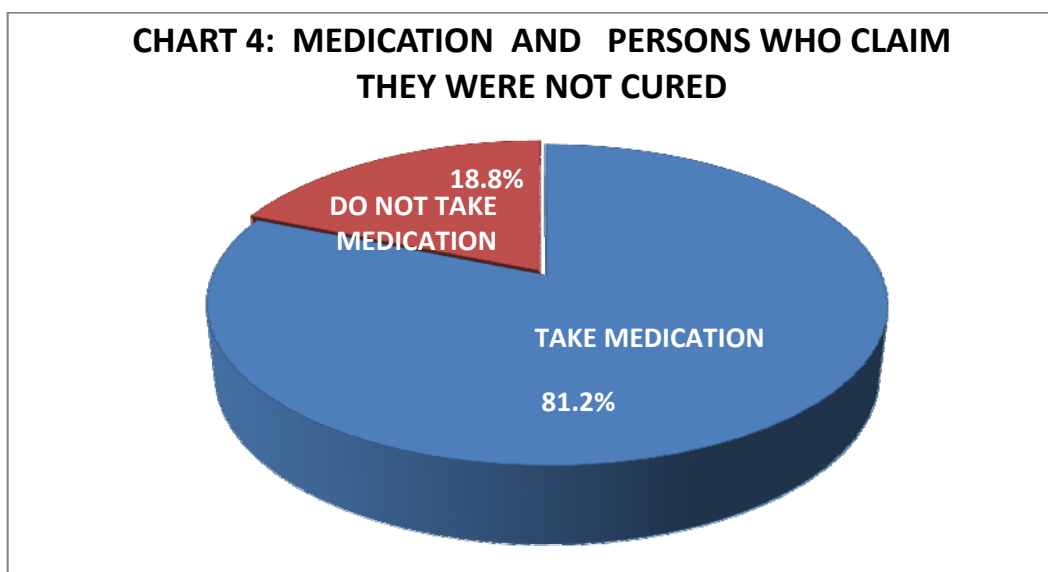
	Age	Education	Monthly family income	What kind of treatment do you usually follow: (drugs)	What kind of treatment do you usually follow: (special diet)	What kind of treatment do you usually follow: (food supplements)	What kind of treatment do you usually follow: (homeopathy)
Education	- 0.493**						
Monthly family income	- 0.237**	0.262**					
What kind of treatment do you usually follow: (drugs)	0.183**	- 0.153**	0.076				
What kind of treatment do you usually follow: (special diet)	0.123**	0.019	0.152**	0.291**			
What kind of treatment do you usually follow: (food supplements)	- 0.020	0.112*	0.152**	0.144**	0.456**		
What kind of treatment do you usually follow: (homeopathy)	0.002	0.036	- 0.004	0.106*	0.157**	0.168**	
What kind of treatment do you usually follow: (other)	0.074	0.002	0.012	0.171**	0.265**	0.181**	0.304**
**Positive Correlation significant at the 0.01 level (2-tailed).							
* Positive Correlation significant at the 0.05 level (2-tailed).							
**Negative Correlation significant at the 0.01 level (2-tailed)							

In addition, dissatisfaction with treatments currently offered (at the order demonstrated above in Chart 14:Therapies-Percentage of total population who followed each category of therapies), was evident from the reply to the question: ‘Do you believe that you were completely cured from your health problem for which you have been treated?’ (Appendix 1,

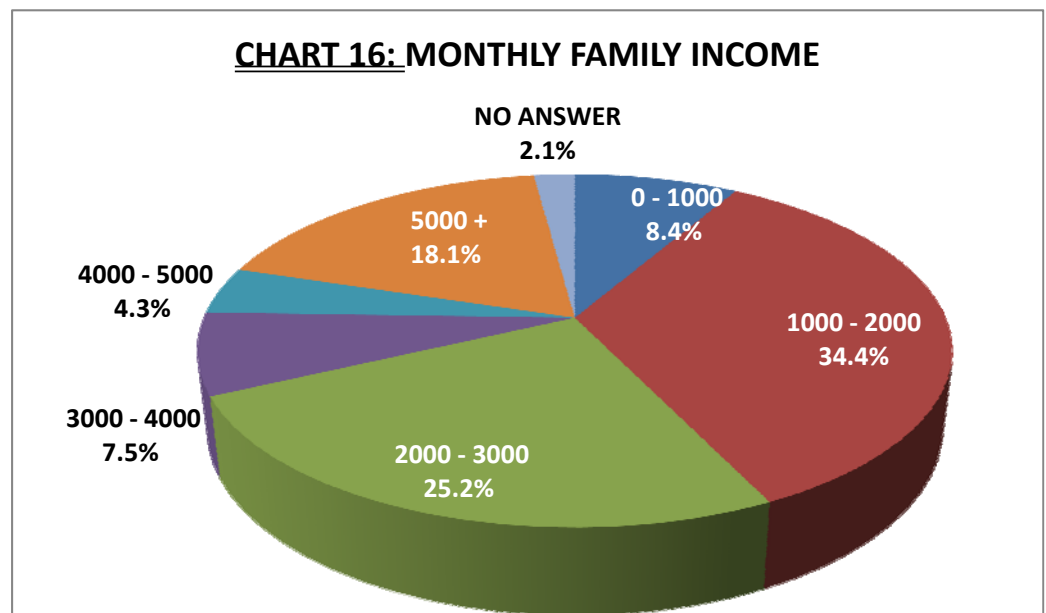
Question 21). In this question 57.1% of persons being treated for a health problem stated as not cured completely, (Chart 2: Percentage of persons cured completely after treatment).



Also from the replies to the question: ‘Do you continue to take medicines for the problem for which you were treated?’ (*Appendix 1, Question 20*), 18.79% of those treated stated that they stopped their medication without being cured, (Chart 4: Medication and persons who claim they were not cured).



A number of factors could be considered as opposing the expressed willingness of Cypriots to follow dietary means: a) high cost of some non-conventional treatments, such as nutritional supplements, which people find them very expensive in the Cypriot market. This particularly affects old age, as age was found (Table 5: Age, Income, Education and Treatment Correlations) to be significantly negatively correlated with income, resulting to a positive correlation between age and the use of drugs, b) non-conventional Medicines are not currently provided by the state: for example Dietary means of treatment according to the Officials of the HIO statements during the interviews with the author, are not subsidised as they are not considered to be part of common medical practice in Cyprus and c) the total family income for 68% of the population is below 3,000 Euros per month as in the Survey (Chart 16: Monthly Family Income)

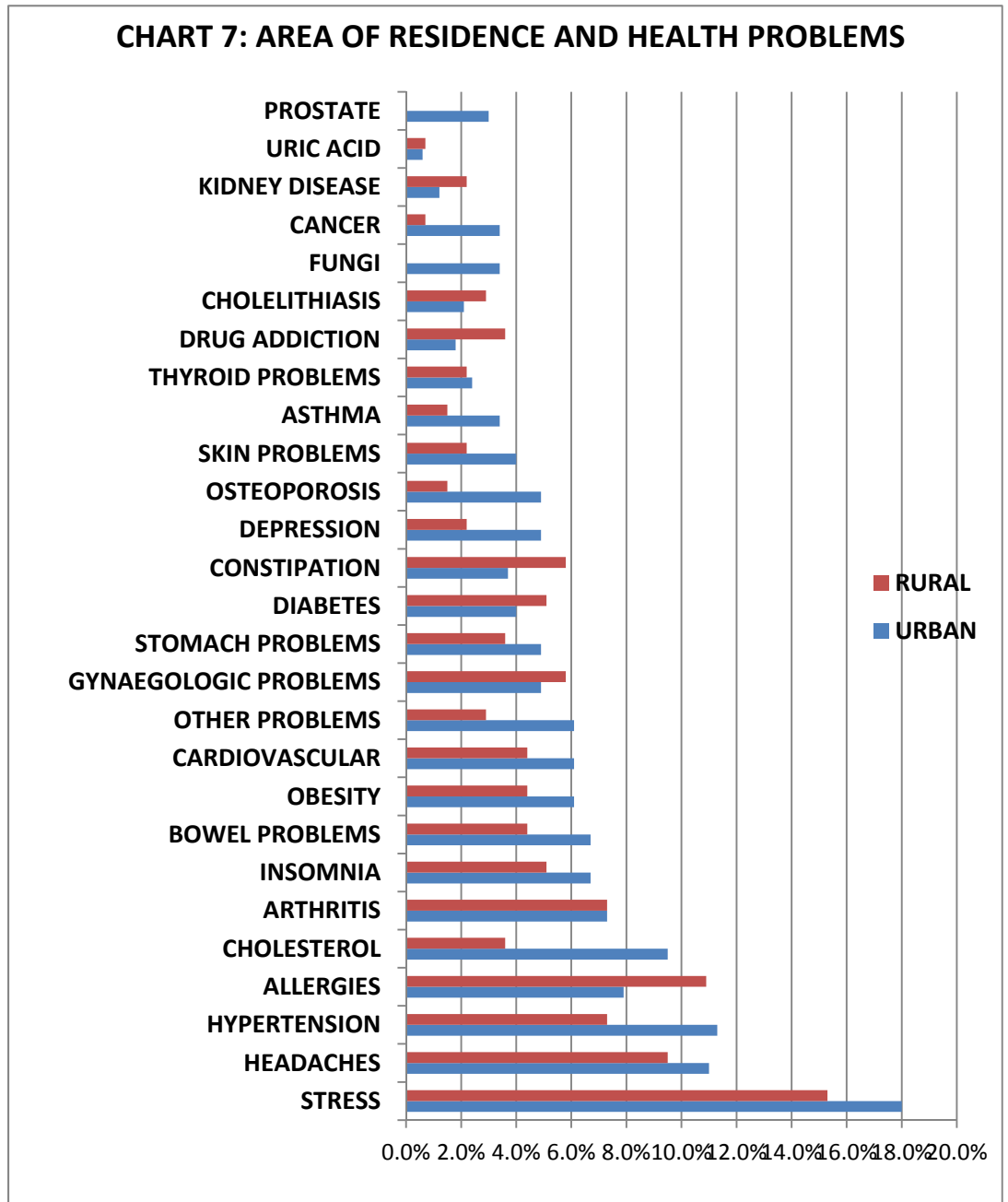


The responsibility of governments is also evident from a volume of evidence demonstrating a strong socioeconomic element in the rising incidence of chronic disease, which occurs more frequently among the most disadvantaged groups of societies. There appears to be a consistent association between socioeconomic status and disease mortality and morbidity, (*WHO [2002iii, 2004ii, 2005i, 2008]; Govil et al. 2009; Rait et al., 2010*). Common, widespread chronic health problems such as cardiovascular disease, dementia, and diabetes are especially prevalent among people with low incomes and low education, (*WHO [2007ix, 2008iv, Govil et al 2009; Drewnowski 2009; Bacon et al., 2009; Rait et al., 2010]*). Greta Rait, senior clinical

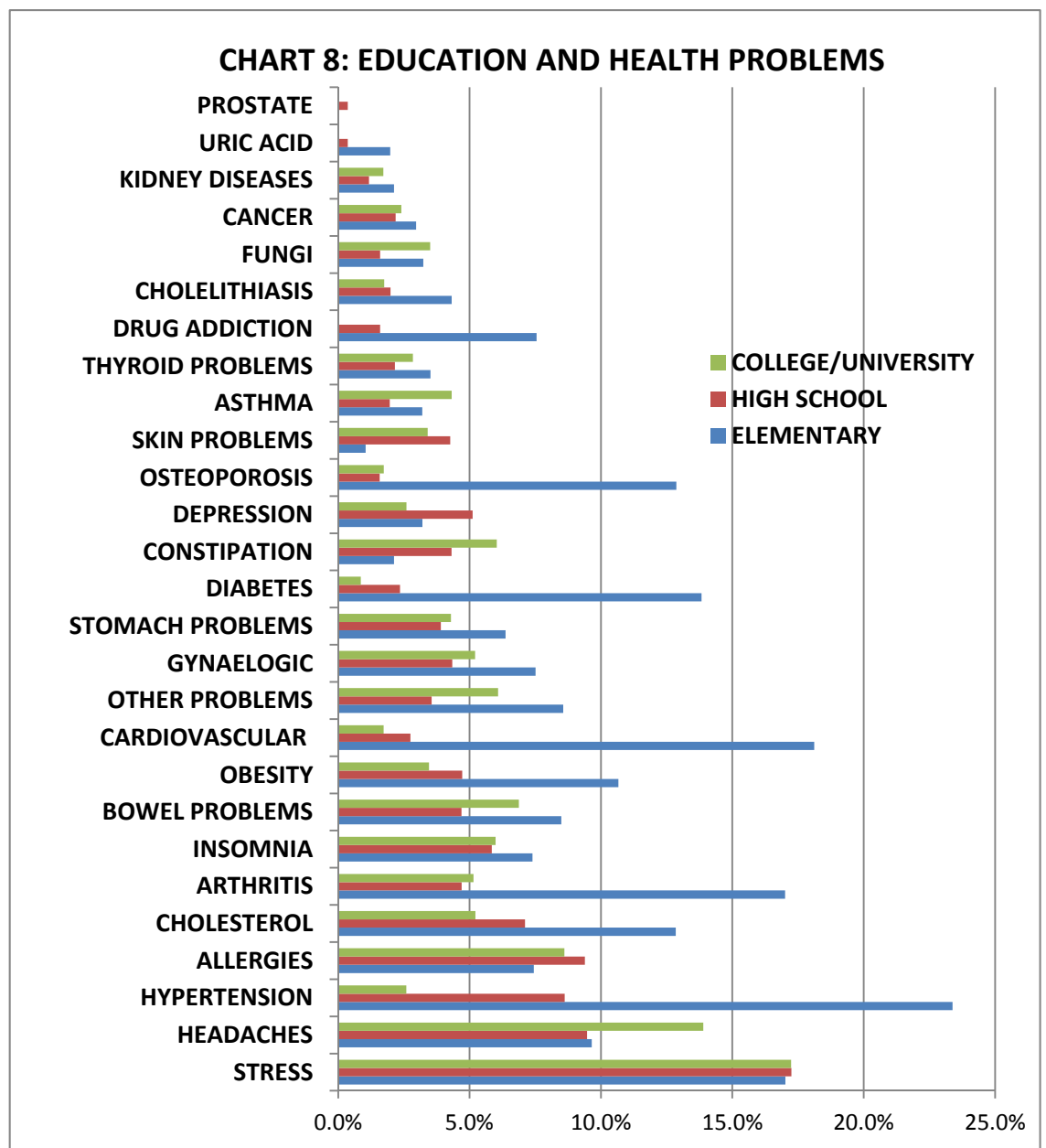
scientist at the General Practice Research Framework in London and her colleagues from the UCL Medical School, in a cohort study in 353 general practices in the United Kingdom, lasting from 1990 to 2007, in which the participants were all adults aged 60 years or over with a first ever code for dementia, found that the incidence of dementia is higher in people aged 60-79 from the most deprived groups compared with those from the least deprived group, (*Rait et al., 2010*). Along the same lines, Sara Govil and colleagues at the Yale School of Nursing, found that chronic disease is promoted by a number of risk factors, highly prevalent among people with low socioeconomic status, such as smoking, obesity, sedentary life, high-fat foods, elevated stress caused by economic hardship, and low social capital to promote health, (*Govil et al 2009*). Alison Goode from the Institute of Applied Economic and Social Research at the University of Melbourne and Kostas Mavromatas of the Institut zur Zukunft der Arbeit, argue that people are forced to resort to cheap and unhealthy food, forced by the circumstances that govern their life, and on the basis of the limited choices they are left with by state policies and imposed economic models, (*Goode & Mavromatas 2008*). Within the same conceptual framework, Adam Drewnowski from the School of Public Health and Community Medicine, of the University of Washington, draws attention to the role of 'social inequalities' and 'inequitable access to healthy foods', claiming that obesity and Diabetes type II 'follow a socioeconomic gradient' with the highest rates being observed among groups with the lowest levels of education and income and in the most deprived areas. The researcher demonstrates the inverse relationship between the energy density (kcal/g) of foods and the energy cost (US\$/1,000kcal), (*Drewnowski 2009-graph: food energy and cost*). Apparently the energy cost of fresh produce is ten times as much as that of vegetable oils and sugars. As indicated by the logarithmic scale, the difference in energy costs between the healthy and unhealthy foods is several thousand percent, (*Drewnowski 2009*).

A significant association between socioeconomic status and chronic disease was also confirmed by the author's research in Cyprus. A number of social and economic factors were found to be significantly correlated to the incidence of chronic disease amongst the Cypriot population. Area of residence was found to be an important factor. As shown in the chart below (Chart 7: Area of residence and Health Problems), cancer, prostate, fungal infections, hypertension, hypercholesterolemia, bowel problems, obesity, cardiovascular disease, depression, osteoporosis, skin problems, and asthma, appear

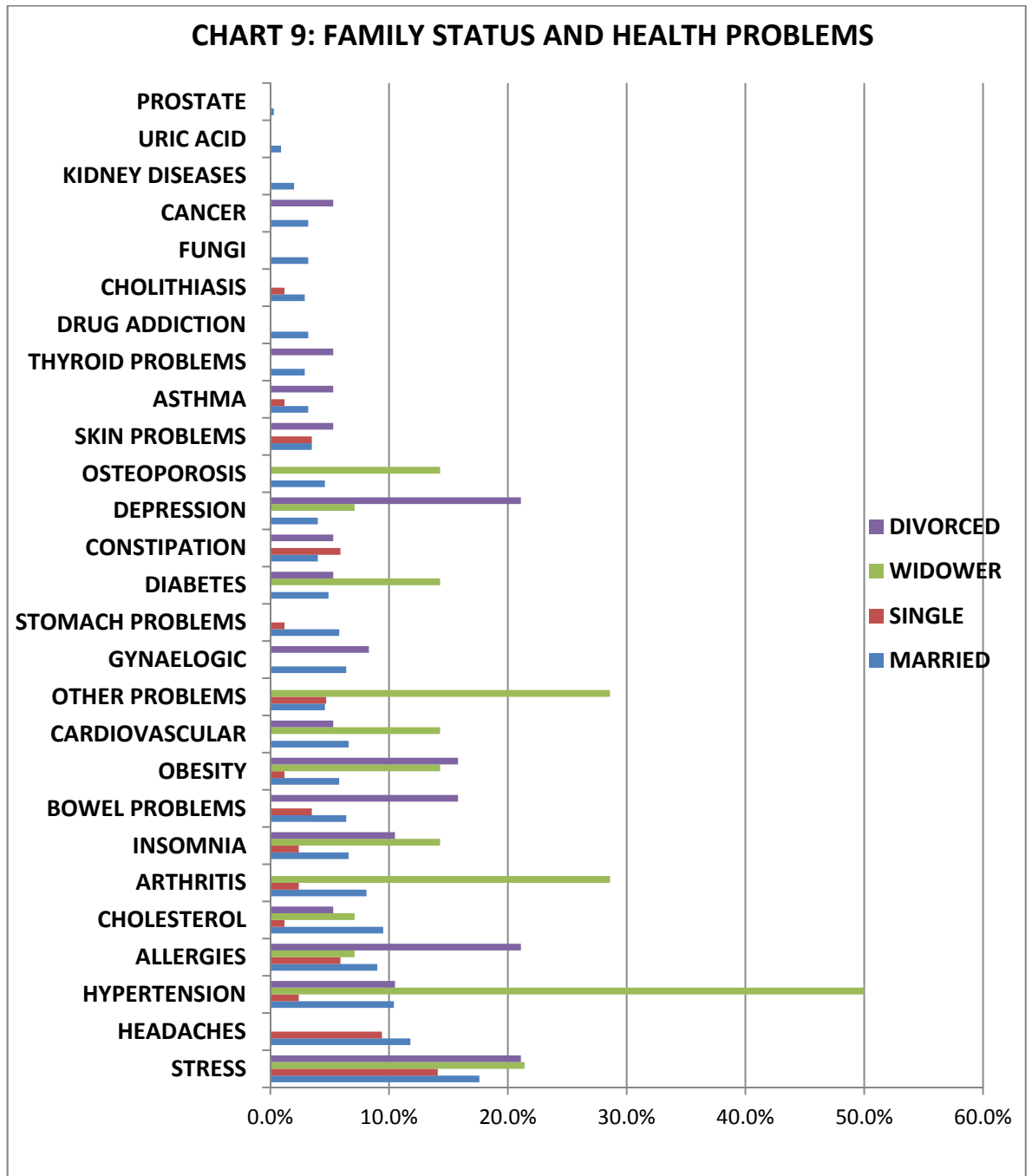
much more frequently in urban areas rather than rural. In contrast, drug addiction, constipation, allergies, and kidney disease are more frequent in rural rather than urban areas. A number of common health problems, occur in both areas with smaller differences, such as arthritis, gynaecological disorders, stomach problems, diabetes, thyroid problems, cholelithiasis and uric acid disorders. Worth noting is that some problems, such as stress, headaches, and insomnia appear in both areas, with small differences, *(further discussion in the following chapters of this Part)*



Education level was found to be strongly negatively related to health problems, which appear to occur more frequently among those with elementary education, falling gradually at high school graduates and further reduced at college/university level (Chart 8: Education and Health Problems). Greater gaps were indentified in diseases, such as cardiovascular disease, hypertension, diabetes, osteoporosis, drug addiction, arthritis, hypercholesterolemia, obesity, cholelithiasis, and uric acid disorders. Stress appears equally at all levels, whilst headaches and constipation are more frequent among college/university graduates. Depression is more frequent in high school graduates (*further discussion in the following chapters of this Part*)



As regards family status, although it was not possible to reach concrete conclusions for all categories, such as the Singles, and Widowers who fall in younger and older ages respectively, a worth noting finding is that the percentage of Divorced suffering from depression is as high as 21.1% compared with only 4% in those married, and 7.1% in widowers. None of the single people interviewed stated to suffer from depression (Chart 9: Family status and Health Problems) (*further discussion in the following chapters of this Part*)



Family income was also found to be negatively related to the incidence of chronic disease demonstrating that the higher the family income, the smaller the incidence of chronic disease, (Table 3: Family Income and Health Problems). Strong negative correlations were found between family income and arthritis, cardiovascular problems, and other problems (*at 1% significance level 2-tailed*); and with stress, skin problems, drug addiction, and cancer (*at 5% significance level 2-tailed*). (*further discussion in the following chapters of this Part*)

TABLE 3: FAMILY INCOME AND HEALTH PROBLEMS

HEALTH ISSUE	PEARSON CORRELATION	SIGNIFICANCE (2-TAILED)	CONCLUSION
NO PROBLEMS	0.201	0	YES AT 0.01 LEVEL
ARTHRITIS	-0.135	0.004	YES AT 0.01 LEVEL
CARDIOVASCULAR PROBL.	-0.13	0.005	YES AT 0.01 LEVEL
OTHER PROBLEMS	-0.145	0.002	YES AT 0.01 LEVEL
STRESS	-0.103	0.028	YES AT 0.05 LEVEL
SKIN PROBLEMS	-0.098	0.037	YES AT 0.05 LEVEL
DRUG ADDICTION	-0.117	0.012	YES AT 0.05 LEVEL
CANCER	-0.106	0.024	YES AT 0.05 LEVEL

CHAPTER II

PATIENT-ORIENTED VS DISEASE-ORIENTED HEALTHCARE

Criticisms against the practice of ‘curing disease and overlooking *illness* -defined as ‘the patient’s experience of disease’, (Fallat *et al.* 2007)- appear frequently in literature very often as self-criticisms emerging from within the medical community. Roberti di Sarsina, medical doctor and expert of the Italian Ministry of Health, refers to the results of numerous surveys in Europe and the USA, which show that *tailoring of the treatment* falls among the first four priorities of patients, (Di Sarsina 2007) while Bruce Barret, medical doctor and researcher at the Department of Family Medicine in the University of Wisconsin Medical School and colleagues, cite evidence demonstrating a ‘collective desire for a kinder and gentler medicine, one that is more caring, patient-oriented, empowering and holistic’, (Barrett *et al.* 2004). Darius Rastegar, medical doctor at the Johns Hopkins Bayview Medical Centre in Baltimore, and colleagues, claim that the modern doctor, in the quest for efficiency in treating individual diseases, becomes more and more expert in specific areas thereby losing contact with the patient as a whole, (Rastegar *et al.* 2004). Professor Sir K.C. Calman of the Department of Health of the United Kingdom, in an article on *The Profession of Medicine*, published in the British Medical Journal, had argued that knowing the name of the ‘disease’ is not enough, stating emphatically that the patient ‘is a person with an illness, not just a label’. He underlined then the role of research and development in medical practice, as well as the crucial implications of a correct diagnostic process, which should be based on a wholistic systematic approach and cannot be fragmented by detaching parts; it should include the consultation with the patient, the accumulation of information, the diagnosis, the prognosis and the possible treatment, as the basic building blocks of health care and resource allocation, without of course failing to acknowledge the key role of the communication of the diagnosis, prognosis, and treatment to the patient or to the community, (Calman 1994). In another article in the Journal of Medical Ethics, a decade later, Professor Calman, in his capacity this time as Vice-Chancellor and Warden at the University of Durham, highlights the importance of the interview of the

patient for making a correct diagnosis -by interview explained as the eliciting information about the patient's present illness, the state of his previous health and that of his family', (*Calman 2004*).

The high significance of the patient-centred approach is also highlighted by a volume of research which demonstrates that every patient is a distinct entity on the a basis of each one's unique biochemical individuality, (*Carlson 1979; Yach et al 2004; WHO [2003; 2005]; Weisburger 2000; Plaskett 2004; EU 2005; Percy-Smith 2007; Schenk et al 2008; Reitman and Schadt 2007; Solomons 2009; Harris 2009; Engel 1977; Bottles 2001; Liska et al., 2004; Hyman et al., 2005*). According to Plaskett, 'each patient is recognised as giving a unique life experience and a unique genetic inheritance', (*Plaskett 2004*). Simon Schenk and his colleagues at the Department of Medicine of the University of California, in a review of studies on the intricacies of insulin sensitivity, discuss the multiplicity of mechanisms and the complexity of factors and aetiologies involved in the development of insulin sensitivity in humans, including nutrient availability, fatty acid metabolism, adipose tissue hypertrophy and inflammatory pathways, (*Schenk et al 2008*). Similarly, Solomons (2009) arguing for the need to 'identify more instances of adaptive response in human biology' claims that the consequences of developmental origins of health and disease in relation to evolutionary biology on public health, challenge the generality of one-size-fits-all solutions in public health policies, (*Solomons 2009*). Noteworthy, even the pharmaceutical companies have come, during the last decade, to realise the imperative of a 'personalised medicine', with Reitman & Schadt, stockholders of Merck & Co, one of the largest pharmaceutical organisations worldwide, providing argumentation for the importance of 'personalised medicine' which will ensure administration of 'the right drug for the right person at the right time', (*Reitman & Schadt 2007*).

Kent Bottles, medical doctor and President of the Genomics Repository of Genomics Collaborative in Cambridge, focussing on the need for genetic approaches to drug therapy to move from one-size-fits-all to a personalised medicine, tailored to the individual patient, claims that for the same disease different genes are implicated in different individuals. For example, at least fifteen different asthma genes were identified by studies that are implicated in some forms of the disease, in some people, at some time, with ten out of eleven gene candidates for susceptibility to asthma found to be unique to only one racial or ethnic group. According to the researcher, the same applies

for most of the common chronic diseases, such as diabetes, rheumatoid arthritis, heart disease, depression, dementia, and cancers, (*Bottles 2001*). John Vogel, medical cardiologist and his colleagues at the American College of Cardiology Foundation Task Force, present a volume of studies demonstrating the mind/body complex interrelationships of each individual patient and their correlations to the development of cardiovascular disease, (*Vogel et al 2005*). It is useful here to recall the old German saying: 'Jederman hat am Ende ein Bischen Tuberculose' ('every man has a touch of tuberculosis'), (*Brock 1916, p.xv*).

The issue of the General Practitioner, as the doctor who uses whole-patient approaches, is recurrently raised, in view of its significance, both for a more patient-centred medicine and as a counterweight to the high specialism of the modern times, (*Gillies et al., 2009; Dirkzwager & Verhaak 2007*). John Gillies Honorary Senior Lecturer at the Department of General Practice in the University of Edinburg, and his colleagues claim that there is a high volume of evidence in support of the fact that well-developed general practice can improve quality of health care, (*Gillies et al., 2009*). Several researchers have demonstrated the positive effects of a good therapeutic relationship between the doctor and the patient, and the importance of the continuity of care to improved health outcomes and reduced hospitalisation, especially for patients with multiple co-existing chronic conditions- (*Saultz & Lochner 2005; Street et al 2008; Starfield 1980; Meryn 1998; Rastegar 2004; Clark et al 1999; Beck et al 2002; Patterson et al 2008; Levinson et al 1999; Hjortdahl 1992; Plaskett 2004; Gillies et al., 2009; Dirkzwager & Verhaak 2007*). Worth noting is the World Health Organisation's, 2008 World Health Report which, focusing on the increasing frequency of multi-morbidity, demonstrates that as many as 25% of 65-69 year olds and 50% of 80-84 year olds are affected by two or more chronic health conditions simultaneously (*WHO 2008ii*). Kurt Stange, medical doctor and Editor of the Annals of Family Medicine, claims that despite the fact that aging patients with 'multi-morbidity' and 'co-morbidity' (co-occurring multiple medical conditions) are the rule rather than the exception among primary care patients, 'most scientific evidence explicitly excludes people with co-morbid conditions' attributing this to 'limitations of the current scientific paradigm' which does not provide for the 'care of whole people with multiple conditions', (*Stange 2009*). John Saultz & Jennifer Lochner (2005), -medical academics and researchers at the Department of Family Medicine of the School of Medicine, in Oregon Health & Science University-, emphasise the importance of 'interpersonal continuity of care' not only to patients but also to family physicians, evoking research which demonstrates a

significant association between interpersonal continuity and improved preventive care and reduced hospitalisation, (*Saultz & Lochner 2005*).

In spite, however, of above evidence, in the publication *Health at a Glance in Europe 2010*, -being the result of the collaboration between the Organisation of Economic Cooperation and Development (OECD) and the European Commission, with the help of national data correspondents from 31 countries¹-, it is demonstrated that in nearly all countries (except Romania and Portugal), the balance between General Practitioners and Specialists has changed over the past decades, with the number of specialists rapidly increasing and generalists decreasing. This is attributed to a reduced attractiveness in the traditional mode of practice of general/family practitioner and in the growing remuneration gap. This evidence raises concerns and many countries are considering ways to improve the attractiveness of general practice as well as developing new roles for other health care providers, such as nurses (*OECD 2010*). Rick Carlson –Juris Doctor and President of the Health Resource Group in San Francisco- used the term ‘compartmentalisation of medicine’ (*Carson 1979*), to emphasise the high specialism in the provision of healthcare, one of the most popular subjects for debate since its inception. Scholars believe that the establishment of the various fields of specialisation in modern medicine, each one of which focuses exclusively upon a particular branch of medicine and the organ system it treats, has its roots in the Cartesian method of analytical thinking, in which complex phenomena are broken into pieces and studied in order to understand the behaviour of the whole, (*Capra, 1996; Goldberg et al., 2002*).

There is no doubt that the benefits of specialisation are well documented, especially in acute diseases, since the specialist doctor is adequately equipped with the necessary training and expertise to investigate deeply and exhaustively specific parts of the body. There is also no doubt that extreme specialisation allowed medical scientists to focus exclusively and exhaustively on specific areas of medical practice and technology and, as a consequence, to contribute greatly to what is universally accepted today as ‘the miracles of medicine’ (discussed in detail in Part II). However, critiques identify also evils in specialisation, particularly in the area of treatment chronic disease, (*Hjordahl 1992; Starfield 1980*;

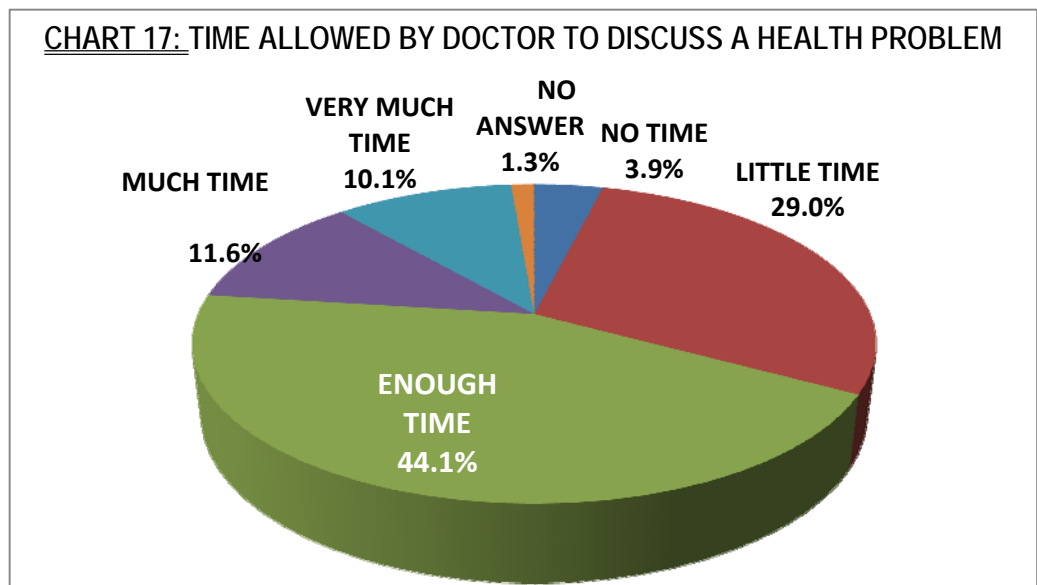
¹ 27 European Union member states +3European Free Trade Association countries (Ireland, Norway and Switzerland), and Turkey

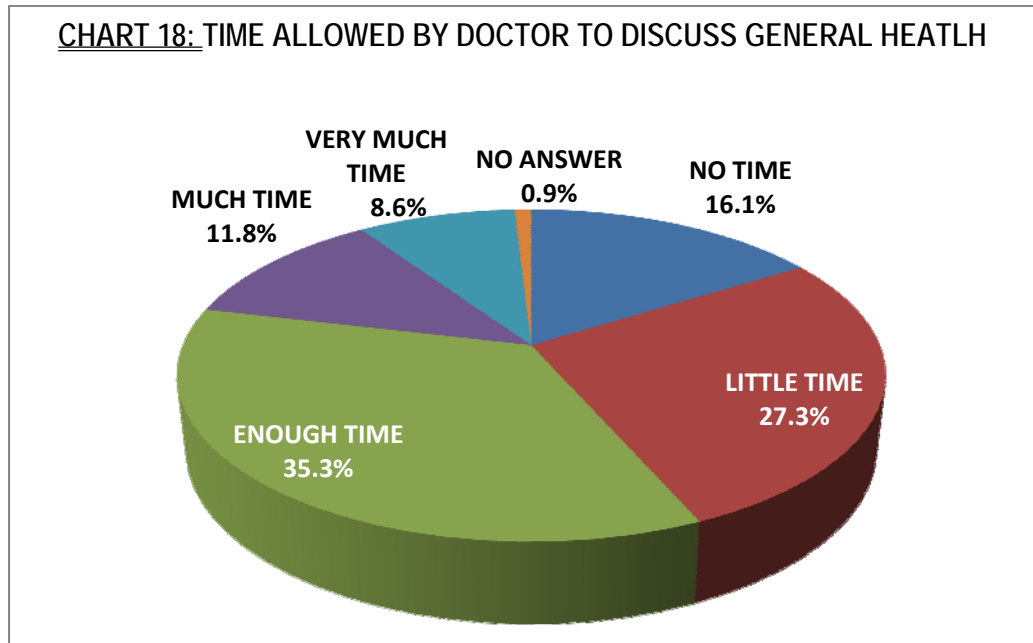
WHO [2002, 2002iii, 2004i; 2008]; Rastegar 2004; Saultz & Lochner 2005). Darius Rastegar (2004) speaks for a 'Taylorisation¹ of healthcare which, as an ever expanding administrative superstructure, emphasises the primacy of the system over the individual. Arguing that specialism is not suitable for patients with multiple chronic health problems, invokes the results from research which demonstrate that specialist care is associated with better outcomes in some conditions but worse in others, such as chronic diseases, and calls decision makers to 'rethink the role of medicine in society', (Rastegar 2004). In a qualitative study investigating adolescents' perceptions, Chris Patterson, Assistant Professor at the School of Nursing of McMaster University of Ontario in Canada, found that 'practice based on holism and partnership was not identified as a common characteristic of a busy, traditional medical practice', (Patterson et al., 2008). William Clark and colleagues, medical doctors and members of the American Academy of Physician and Patient, identify deficiencies in education in 'doctor-patient relationship and psychosocial medicine', claiming that, while 'physician-patient talk of all kinds has been related to highly important outcomes of care', however few physicians interact adequately with the patient (Clark et al 1999). Worth noting is the report of the members of a Working Party set up by the Royal College of Physicians of London in 2005, in which concerns are expressed for the 'don't ask' approaches of some doctors in an effort to avoid a more wholistic view of the patient by 'opening a Pandora's box of potentially difficult issues', (Royal College of Physicians 2005). Mary Fallat, medical doctor and member of the American Committee of Bioethics, and colleagues, identify a degree of 'bureaucratic oversight' and high pressure from modern technology on doctors, which imposes an impersonal model of care, away from 'what called them in the health profession in the first place', which was the desire to care for their patients and their families. According to the researchers, the business medical model imposed prevents the doctor from understanding the health of a child on the basis of different emotional, social, educational, psychological and spiritual factors, (Fallat et al., 2007).

Many of above criticisms were confirmed by the Survey in Cyprus, which demonstrated that citizens expectations and needs for more caring approaches, more person-centred,

¹Taylorisation: A revolutionary innovation in the organisation of work by Frederic Winslow Taylor, which looked at work as something that could be broken down, analysed and standardised to improve efficiency, quality, and productivity, (Rastegar 2005)

and beyond specific diseases, are not met within the current establishment in the provision of healthcare. It was particularly shown that there exists a high degree of dissatisfaction among Cypriots with the time and attention allocated to them by their doctor (Chart 17: Time allowed by doctor to discuss a specific health problem). When replying to the question: *'To what extent do you believe the time allocated to see your Doctor when you are sick, is adequate to discuss exhaustively you specific health problem?'*, (Appendix 1, Question 26), 32.9% of Cypriots stated they were dissatisfied, with only 21.7% stating 'very much' or 'much' satisfied. The percentage of dissatisfaction appears to rise further in the responses to the question: *'To what extent do you believe you are given the opportunity to discuss with your doctor the general state of your health, apart from the specific problem for which you have visited him/her?'* (Appendix 1, Question 27), In this case (Chart 18: Time allocated by doctor to discuss their general health condition), 43.4% of Cypriots stated as 'not given any', or 'given little' time, whilst only 20.4% of the Cypriot population stated as given 'much' or 'very much' time to discuss their general state of health with their doctor.





Furthermore the statistical analysis revealed strong positive correlations between different, often seemingly unrelated health problems, not rarely of both physical and psychological nature, demonstrating the 'multimorbidity case'. As can be seen in the table below (Table 4: Correlations between health problems), *Bowel problems, for example, correlate positively (at the 1% significance level 2-tailed) with stress, allergies, constipation, insomnia, skin problems, drug addiction, depression, fungus infections, obesity, cholelithiasis, headaches, and stomach problems and (at the 0.5% significance level 2-tailed) with kidney disease and cholesterol. Stress correlates positively (at the 1% significance level 2-tailed) with allergies, constipation, insomnia, gynaecological problems, skin problems, bowel problems, drug addiction, depression, fungus infections, kidney disease, obesity, cholelithiasis, headaches, and stomach problems; and (at the 0.5% significance level 2-tailed) with arthritis and cholesterol. Cardiovascular problems, correlate positively (at the 1% significance level 2-tailed) with drug addiction, diabetes, cancer, obesity, stomach problems; and (at the 0.5% significance level 2-tailed) with arthritis, insomnia, depression, and cholesterol. Diabetes correlates positively (at the 1% significance level 2-tailed) with skin problems, drug addiction, cardiovascular problems, kidney disease, osteoporosis, obesity, hypertension, prostate and cholesterol.*

Hypertension was found to correlate positively (*at the 1% significance level 2-tailed*) with insomnia, diabetes, drug addiction, thyroid problems, kidney disease, uric acid disorder, obesity, headaches, prostate, cholesterol and (*at the 0.5% significance level 2-tailed*) with arthritis, and skin problems. *In the below Table 4:Correlations between health problems colours replaced values due to limited space in the document. For more detailed table with values please see Appendix 2).*

TABLE 4: CORRELATIONS BETWEEN HEALTH PROBLEMS

	Stress	Allergies	Arthritis	Asthma	Constipation	Insomnia	Gynaecologic probl.	Skin Problems	Diabetes	Bowel Problems	Drug Addiction	Thyroid Problems	Cardiovascular probl.	Cancer	Depression	Fungi	Kidney diseases	Osteoporosis	Uric Acid	Obesity	Cholelithiasis	Hypertension	Headaches	Prostate	Stomach Problems	Cholesterol	Other problems
Stress		**	*		**	**	**	**		**	**				**	**	**			**	**	**	**	**	**	**	
Allergies	**				**	**	**	**		**		*			**						**	**	**	**	**	**	
Arthritis	*					**	**	**		**			*						**	**		*	*	*	*	*	
Asthma		**			*	*	*	*		*					*						*	*	*	*	*	*	
Constipation	**	**				*	*	*		*					*						*	*	*	*	*	*	
Insomnia	**	*	*		*		*	*		*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Gynaecologic Problems	**				*	*	*	*		*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Skin Problems	**	**			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Diabetes					*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Bowel Problems	**	**			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Drug Addiction	*	*			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Thyroid probl.		*			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Cardiovascular Problems			*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Cancer	**	**			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Depression	**	**		*	*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Fungi	**	*			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Kidney diseases	**				*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Osteoporosis			*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Uric Acid			*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Obesity	**	*			*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Cholelithiasis	**			*	*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Hypertension			*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Headaches	**	**	*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Prostate			*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Stomach Problems	**	*	*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Cholesterol	*		*		*	*	*	*	*	*	*	*	*		*	*	*	*	*	*	*	*	*	*	*	*	*
Other problems												*	*														

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed).

CHAPTER III

A NARROW CONCEPTION OF HEALTH DETERMINANTS

A volume of publications of the last decades demonstrate that important determinants of disease, fall outside the current establishment in the provision of healthcare, (*Carlson 1979; Egeberg 1968; Engel 1977; McCarty 1981; Calman 1994; Zimmet 2000; Yach et al 2004; WHO [2002; 2003i; 2004i; 2005i; 2006; 2007ii; 2007ix; 2008]; Percy-Smith 2007; EU 2005; Vogel et al 2005; Harris 2009; Drewnowski 2009; Fiqueredo 2009*). Several elements are identified as contributing to health and disease, including nutritional deficiencies and excesses, personal and traditional lifestyles, environmental and behavioural factors, and several other psychosocial parameters, such as education, housing, circumstances of work, and other factors, (*Weisburger 2000; Fiqueredo 2009; Yach et al 2004; Percy-Smith 2007*). The World Health Organisation, during the last decade published a series of reports on the importance of addressing the underlying determinants of chronic disease, (*WHO [2004i; 2007ix]*) - 'the causes of the causes'. Similarly, publications by the European Commission demonstrate that up to eighty percent of cases of coronary heart disease, ninety percent of diabetes type II, and one third of cancers can theoretically be avoided through diet and lifestyle changes, (*EU 2005*). Yach et al., (2004), claim that the chronic disease management model is much more complex than that required for acute diseases and that 'it entails multiple causes over a lifetime'. According to the World Health Organisation experts, since all individuals are at risk of chronic disease but differing in the extent of their risk, prevention and treatment should be based on 'a sustained, multisectoral commitment, well beyond the traditional health sector, (*Yach et al 2004*). Percy-Smith, Senior Research Fellow at the SOLAR Action Research Centre at the University of West of England, in Bristol, claims that: 'Being healthy is a little bit about health services and lots more about the whole of your lives, education, where you live, how you live, relationships, employment' and although these issues are well known by academics, this knowledge is not exchanged very effectively within the world of policy and practice, (*Percy-Smith 2007*). Kent Bottles, medical doctor and president of the Genomics Repository of Genomics Collaborative in Cambridge, refers to a study with 44,788 pairs of twins in Scandinavia, which demonstrated that the environment was the principal determinant of

most types of cancers, rather than inheritance, which was found to have only a minor contribution, (*Bottles 2001*).

The importance of a number of factors as determinants of disease was confirmed by the research in Cyprus. As already demonstrated and discussed above in the critique of health systems, much lower incidence of chronic disease was reported by people living in rural areas rather than those in urban areas. In Chart 7: Area of Residence and health problems as well as in Table 10: Urban/Rural and Chronic Health Problems it is clearly demonstrated that cancer, prostate, fungal infections, hypertension, hypercholesterolemia, bowel problems, obesity, cardiovascular disease, depression, osteoporosis, skin problems, and asthma, appear much more frequently in urban areas rather than rural. On the contrary, drug addiction, allergies, and kidney disease were more frequent in rural rather than urban areas. A number of common health problems, occur in both areas with smaller differences, such as arthritis, gynaecological disorders, stomach problems, diabetes, thyroid problems, cholelithiasis and uric acid disorders. Interestingly, a number of common problems of a more psychosocial character, such as stress, headaches, and insomnia appear in both areas, with small differences,

TABLE 10: URBAN/RURAL AND CHRONIC HEALTH PROBLEMS
percentage in each category suffering from a specific health
problem

HEALTH ISSUE	URBAN	RURAL
STRESS	18.0%	15.3%
HEADACHES	11.0%	9.5%
HYPERTENSION	11.3%	7.3%
ALLERGIES	7.9%	10.9%
CHOLESTEROL	9.5%	3.6%
ARTHRITIS	7.3%	7.3%
INSOMNIA	6.7%	5.1%
BOWEL PROBLEMS	6.7%	4.4%
OBESITY	6.1%	4.4%
CARDIOVASCULAR	6.1%	4.4%
OTHER PROBLEMS	6.1%	2.9%
GYNAECOLOGIC PROBLEMS	4.9%	5.8%
STOMACH PROBLEMS	4.9%	3.6%
DIABETES	4.0%	5.1%
CONSTIPATION	3.7%	5.8%
DEPRESSION	4.9%	2.2%
OSTEOPOROSIS	4.9%	1.5%
SKIN PROBLEMS	4.0%	2.2%
ASTHMA	3.4%	1.5%
THYROID PROBLEMS	2.4%	2.2%
DRUG ADDICTION	1.8%	3.6%
CHOLELITHIASIS	2.1%	2.9%
FUNGI	3.4%	0.0%
CANCER	3.4%	0.7%
KIDNEY DISEASE	1.2%	2.2%
URIC ACID	0.6%	0.7%
PROSTATE	3.0%	0.0%

Education was also found to be an important determinant of chronic disease (Table 7: Education and health problems). Apparently, the incidence of chronic disease is much higher among those with elementary education, falling gradually with high school graduates and further reduced at college/university level. Greater gaps were indentified in diseases, such as cardiovascular disease, hypertension, diabetes, osteoporosis, drug addiction, arthritis, hypercholesterolemia, obesity, cholelithiasis, uric acid disorders. Interestingly, stress appears equally at all levels, while headaches and constipation are more frequent among college/university graduates. Depression is more frequent in high school graduates

TABLE 7: EDUCATION AND HEALTH PROBLEMS

HEALTH PROBLEM	ELEMENTARY	HIGH SCHOOL	COLLEGE/ UNIVERSITY
STRESS	17.0%	17.3%	17.2%
HEADACHES	9.6%	9.5%	13.9%
HYPERTENSION	23.4%	8.6%	2.6%
ALLERGIES	7.4%	9.4%	8.6%
HYPERCHOLESTEROLEMIA	12.8%	7.1%	5.2%
ARTHRITIS	17.0%	4.7%	5.2%
INSOMNIA	7.4%	5.8%	6.0%
BOWEL PROBLEMS	8.5%	4.7%	6.9%
OBESITY	10.7%	4.7%	3.5%
CARDIOVASCULAR	18.1%	2.7%	1.7%
OTHER PROBLEMS	8.6%	3.6%	6.1%
GYNAECOLOGICAL	7.5%	4.3%	5.2%
STOMACH PROBLEMS	6.4%	3.9%	4.3%
DIABETES	13.8%	2.4%	0.9%
CONSTIPATION	2.1%	4.3%	6.0%
DEPRESSION	3.2%	5.1%	2.6%
OSTEOPOROSIS	12.9%	1.6%	1.7%
SKIN PROBLEMS	1.0%	4.3%	3.4%
ASTHMA	3.2%	2.0%	4.3%
THYROID PROBLEMS	3.5%	2.2%	2.8%
DRUG ADDICTION	7.6%	1.6%	0.0%
CHOLELITHIASIS	4.3%	2.0%	1.8%
FUNGI	3.2%	1.6%	3.5%
CANCER	3.0%	2.2%	2.4%
KIDNEY DISEASES	2.1%	1.2%	1.7%
URIC ACID	2.0%	0.4%	0.0%
PROSTATE	0.0%	0.4%	0.0%

Family income was also found to be a strong predictor of the incidence of chronic disease (Table 3: Family income and health problems). Significant negative correlations were shown between family income and arthritis, cardiovascular problems, and other problems (at 1% significance level 2-tailed); also negative correlations were shown (at 0.5% significance level 2-tailed) with stress, skin problems, drug addiction, and cancer. The only positive correlation, significant at 1% level 2-tailed, was found between those stating as having 'no-health problems' and family income;

HEALTH ISSUE	PEARSON CORRELATION	SIGNIFICANCE (2-TAILED)	CONCLUSION
NO PROBLEMS	0.201	0	YES AT 0.01 LEVEL
ARTHRITIS	-0.135	0.004	YES AT 0.01 LEVEL
CARDIOVASCULAR PROBL.	-0.130	0.005	YES AT 0.01 LEVEL
OTHER PROBLEMS	-0.145	0.002	YES AT 0.01 LEVEL
STRESS	-0.103	0.028	YES AT 0.05 LEVEL
SKIN PROBLEMS	-0.098	0.037	YES AT 0.05 LEVEL
DRUG ADDICTION	-0.117	0.012	YES AT 0.05 LEVEL

Family status was also demonstrated to be a determinant of disease (Table 11: Family status and health problems). It should be noted that conclusions can mainly be reached for the married and divorced, as singles tend to be mostly young people and widowers mostly old. Divorced people appear to suffer more frequently than other population groups from several common chronic problems, such as stress, allergies, bowel problems, obesity, gynaecological problems, depression, skin problems, asthma, thyroid problems, and cancer. In some diseases the gap is more apparent, as in the case of depression, allergies, obesity, and bowel problems. Some chronic problems appear more frequently amongst married people such as headaches, hypercholesterolemia, stomach problems, drug addiction, and fungus infections

TABLE 11: FAMILY STATUS AND HEALTH PROBLEMS
PERCENTAGE IN EACH CATEGORY SUFFERING FROM A SPECIFIC HEALTH
PROBLEM

HEALTH ISSUE	MARRIED	SINGLE	WIDOWER	DIVORCED
STRESS	17.6%	14.1%	21.4%	21.1%
HEADACHES	11.8%	9.4%	0.0%	0.0%
HYPERTENSION	10.4%	2.4%	50.0%	10.5%
ALLERGIES	9.0%	5.9%	7.1%	21.1%
HYPERCHOLESTEROLEMIA	9.5%	1.2%	7.1%	5.3%
ARTHRITIS	8.1%	2.4%	28.6%	0.0%
INSOMNIA	6.6%	2.4%	14.3%	10.5%
BOWEL PROBLEMS	6.4%	3.5%	0.0%	15.8%
OBESITY	5.8%	1.2%	14.3%	15.8%
CARDIOVASCULAR	6.6%	0.0%	14.3%	5.3%
OTHER PROBLEMS	4.6%	4.7%	28.6%	0.0%
GYNAECOLOGIC	6.4%	0.0%	0.0%	8.3%
STOMACH PROBLEMS	5.8%	1.2%	0.0%	0.0%
DIABETES	4.9%	0.0%	14.3%	5.3%
CONSTIPATION	4.0%	5.9%	0.0%	5.3%
DEPRESSION	4.0%	0.0%	7.1%	21.1%
OSTEOPOROSIS	4.6%	0.0%	14.3%	0.0%
SKIN PROBLEMS	3.5%	3.5%	0.0%	5.3%
ASTHMA	3.2%	1.2%	0.0%	5.3%
THYROID PROBLEMS	2.9%	0.0%	0.0%	5.3%
DRUG ADDICTION	3.2%	0.0%	0.0%	0.0%
CHOLELITHIASIS	2.9%	1.2%	0.0%	0.0%
FUNGI	3.2%	0.0%	0.0%	0.0%
CANCER	3.2%	0.0%	0.0%	5.3%
KIDNEY DISEASES	2.0%	0.0%	0.0%	0.0%
URIC ACID	0.9%	0.0%	0.0%	0.0%
PROSTATE	0.3%	0.0%	0.0%	0.0%

CHAPTER IV

EXCLUSIVE USE OF DRUG AND SURGERY

The over-dependence on drug and surgery approaches largely underplaying the - demonstrated by a volume of scientific research (*in following chapters*)- therapeutic power of food nutrients and lifestyle habits is often highlighted, (*WHO [2002; 2002iii]; Vogel et al 2005; Shai et al 2001; Calman 1994; Nahleh & Tabbara 2003; Fallat et al 2007; Casileth & Deng 2004; Chang et al 2007; Vickers & Zollman 1999; Fairfield & Fletcher 2002; Bodane & Brownson 2002; Shepherd 2009; Zachariadou et al 2008*). Critics claim that most of the time, diet and lifestyle changes are considered effective only as preventive measures or, in the best case, as complementing prescribed drugs, and rarely as means of treatment. This tendency is considered as a limitation of the current establishment of the provision of healthcare and a series of reports published by the World Health Organisation, criticise the exclusive focus on research approaches examining only the effectiveness of drug regimens, (*WHO 2002, 2002iii, 2004i; 2008*). The medical experts of the Organisation have recurrently called Member States to take seriously into consideration the most up-to-date knowledge emerging from new scientific research which supports, both the preventive and the therapeutic power of diet and physical activity, (*WHO 2004ii*).

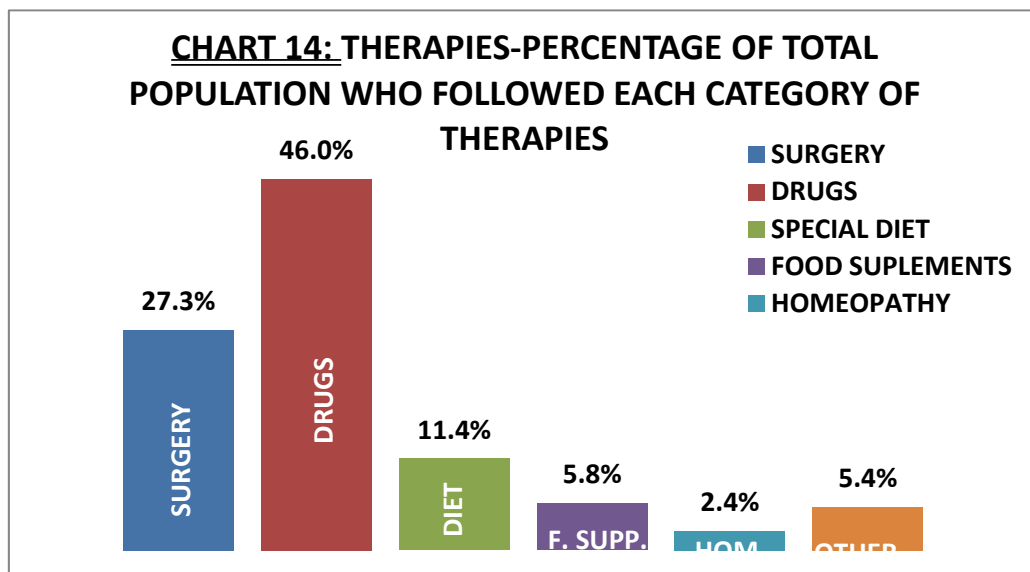
In its 2008 World Health Report, the World Health Organisation, focusing on the increasing frequency of multi-morbidity¹ among patients, criticises twentieth century 'hospital-centrism' -explained as 'health systems built around hospitals and specialists'-, and accuse this practice as carrying 'a considerable cost in terms of unnecessary medicalisation and Iatrogenesis² and as compromising the human and social dimensions of health', (*WHO 2008ii*). According to researchers twenty thousand tonnes of aspirin are consumed per year in the States, accounting for almost two hundred and twenty five tablets per person, whereas in England every tenth night of sleep is induced by a hypnotic drug and nineteen percent of women and nine percent of men take a prescribed tranquillizer during any one year, (*Illich 1995, pp. 72-73*). Other studies demonstrate that

¹ As many as 25% of 65-69 year olds and 50% of 80-84 year olds are affected by two or more chronic health conditions simultaneously (*WHO 2008ii*, http://www.who.int/whr/2008/08_chap1_en.pdf)

² Iatrogenesis: 'induced in a patient by a physicians' activity, manner, or therapy', (*American Heritage Dictionary, 2009*). The term is usually refer to harm induced.

prescribed drugs are the cause of approximately 130,000 deaths annually in America, equating to 365 people daily, (Bodane & Brownson 2002

The over-dependence on drug and surgery approaches, largely underplaying the role of diet and lifestyle, particularly in the area of chronic disease prevention and treatment, was also confirmed by the research in Cyprus. In (Chart 14: Therapies-percentage of total population who followed each category of therapies), it is clearly demonstrated that Drugs and Surgery are the first and second resorts to treatment by Cypriots with large difference from the other, considered non-conventional, treatments. In particular 46.0% of the population resorts to Drugs and 27.3% to Surgery for treatment of specific health problem. Other treatments fall far below, with Special diet used by 11.4%, Food supplements by 5.8%, homeopathy by 2.4% and other therapies by 5.4% of the population



This finding was further supported by the case studies analysis from the author's Clinical Practice (Table 9: Nutritional and Drug Prescriptions by Doctors), as the majority of patients (88%) were prescribed pharmaceutical treatments with only 14% of them being offered other than medical prescriptions, mostly consisting of calcium, iron, and multivitamin supplements. Dietary treatment was prescribed to only 2% of them consisting of avoidance of specific foods and always along with their pharmaceutical treatment. Worth noting is that in all cases of other than medical treatments, these were prescribed alongside with drug prescriptions.

TABLE 9: NUTRITIONAL AND DRUG PRESCRIPTIONS BY DOCTORS
(50 randomly selected cases from Clinical Practice)

TYPE OF ADVICE	Number of patients	Percentage of total number of patients
No nutritional advice	43	86%
↳ With drug prescription	37	74%
↳ Without drug prescription	6	12%
Calcium supplements	2	4%
↳ With drug prescription	2	4%
↳ Without drug prescription	0	0%
Iron supplements	2	4%
↳ With drug prescription	2	4%
↳ Without drug prescription	0	0%
Calcium and Iron supplements	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%
Multivitamins	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%
Avoidance of foods	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%

The fact that this order of treatment is ‘imposed’ by the established system of healthcare and not ‘preferred’ was already discussed in detail in chapter I of this Part, where the gap between state policies and citizens’ needs/desires/expectations was demonstrated (Part III, Chapter I: Health systems out of date)

CHAPTER V

LOW APPLICATION OF THERAPEUTIC, EVIDENCE-BASED, NUTRITIONAL INTERVENTIONS

The scientific justification of the role of diet and lifestyle as major determinants in the prevention and treatment of chronic disease, by a volume of research (*presented in following chapters*), raises concerns as to the extent to which effective therapeutic nutritional interventions are applied within the current establishment of healthcare (*An example of an evidence-based therapeutic intervention from the author's clinical practice is provided in Appendices 3-8*). Taren et al., (2001) drawing from the work carried out by a number of researchers (*Wiesemann 1997, Glanz et al, 1992 and 1995*)¹, claim that physicians offer less than five minutes nutrition counselling to their patients. Other researchers report that modern healthcare providers fail to acknowledge the importance of nutritional treatments for chronic conditions, (*Shai et al 2001*), and only rarely make use of nutritional interventions, allowing the impression that nutritional methods of treatment are part of complementary medicine, (*Vickers & Zollman 1999*). According to Vickers & Zollman (1999), 'doctors are not taught, and therefore do not practice, much in the way of nutritional therapeutics' in spite of the fact that nutrition, as a science, has always been part of conventional medicine. The researchers believe that nutritional medicine has come to be regarded as part of complementary medicine, due to the fact the doctors only rarely make use of nutritional interventions, (*Vickers & Zollman 1999*). In a cross sectional survey carried out by Shai et al., (2001), it was found that doctors fail to take seriously medical treatment protocols which recommend the use of dietary intervention as the primary treatment for several chronic diseases. According to the study, in spite of the fact that physicians seem to agree that dietary treatment is important, almost 50% of them 'reported not using nutritional treatment due to lack of time and awareness of available options', (*Shai et al 2001*). Evidence from most recent studies demonstrate that the prevailing belief today is that little has changed to physicians' nutrition counselling practices during the last fifteen years, in spite of the fact that primary care physicians continue to believe

¹ Quoted in Taren et al 2001

that providing nutrition counselling is within their realm of responsibility, (*Kolasa & Rickett 2010*).

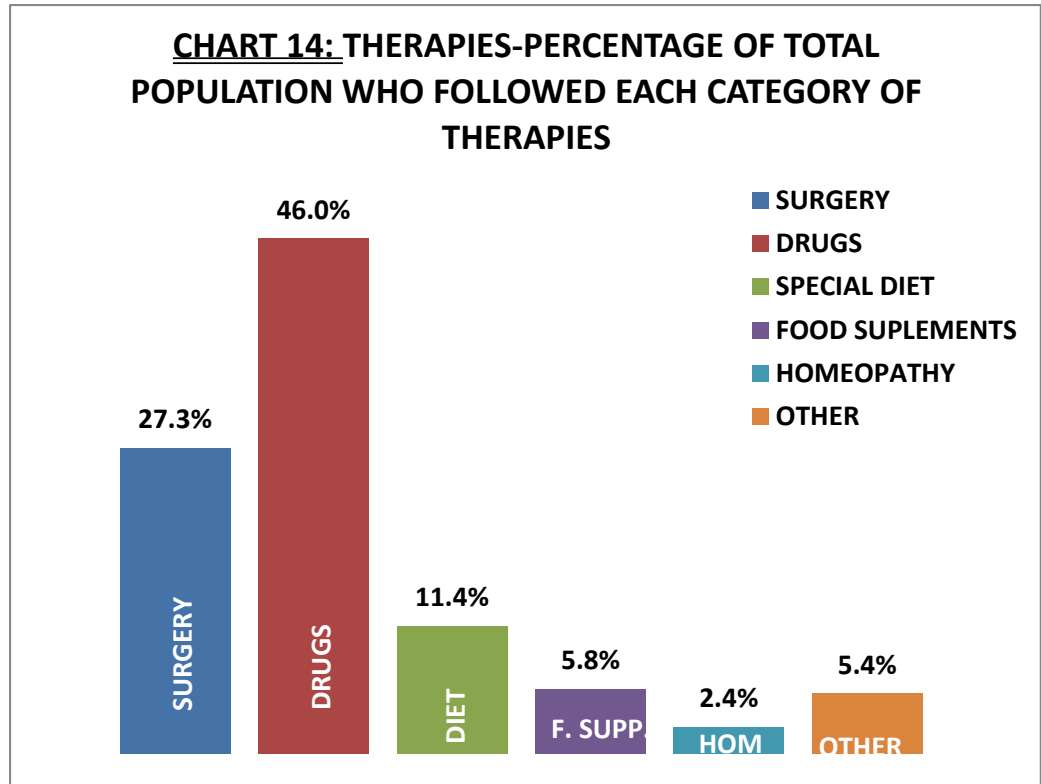
This lack of nutritional counselling competency by most modern doctors is also stressed in a series of reports published by the World Health Organisation, (*WHO [2002; 2002iii; 2004i; 2004ii; 2008]*). According to the experts of the Organisation, modern medicine ‘evolved over the decades on the assumption that the primary need is for a system geared to improving short-term rapid response to acute illness’, (*WHO [2002iii]*). The need for health professionals to acquire more training in healthy diets ‘either within existing programmes or in special workshops, as an essential part of their curricula’ is underlined (*WHO 2004i*). This situation is reported as an international issue and similar concerns about the inadequacy of medical-nutrition education have been raised by European educators. Contrary to past prevailing praxis, focused on knowledge of nutritional deficiencies, new areas of nutrition, including prevention and treatment of chronic diseases, as well as nutrition during pregnancy and lactation, now demand special attention, (*Widhalm et al, 1999*)¹. The European Commission, in its 2005 Green Paper, stresses the need for health professionals to include routine practical nutritional advice to patients and families, during their consultations, (*EU 2005*). The quantity and quality, however, of nutritional education hours offered by the medical school curricula are being challenged by a number of researchers and scholars, who claim that contemporary physicians are not adequately educated to offer effective nutritional advice to their patients, (*Clifford 2000; Hark & Morrison 2000; Jeor et al. 2006; Kolasa 2001; Krebs & Primak 2006; Taren et al. 2001; Vickers & Zollman 1999; Shai et al. 2001; Kolasa & Rickett 2010*). There seems to be a gap between nutrition education and practical application, and a two hour nutrition workshop every seven years, as part of a continuing education programme, does not build adequate confidence for nutritional advice, (*Kolasa 2001; Krebs & Primak 2006*). Taren et al., (2001) have found that, while ninety-eight percent of medical schools present Nutrition as a component of medical education, most of them do not have an identifiable nutrition curriculum and many schools do not even provide the recommended minimum of twenty five hours of nutrition education, (*Taren et al. 2001*). Similar results were also found by other researchers who demonstrated that more than two thirds of medical schools in the United States do not have a specific nutrition course in their curriculum and, even those

¹ Quoted in Taren et al 2001

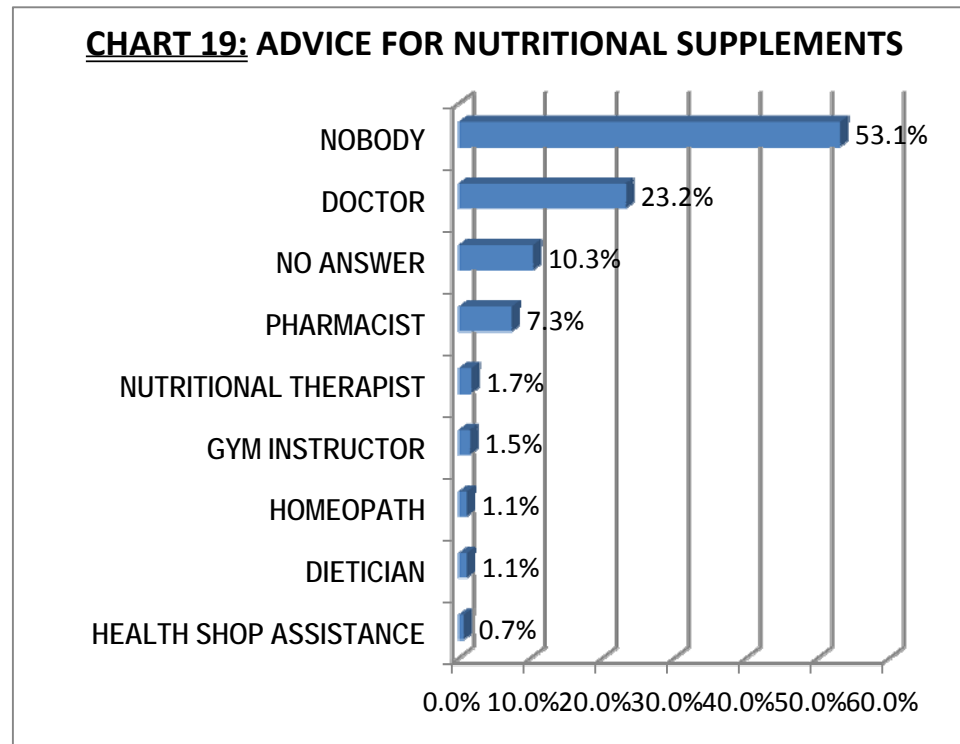
that have, do not deliver the information in a form that can be practically applied, (*Clifford 2000; Jeor et al 2006*). A survey carried out in 2004 by Adams et al., (2006) in all 126 US medical schools accredited at that time, aiming to examine the nutrition knowledge and skills of medical students and physicians, showed that the amount of nutrition education in medical schools remains inadequate, (*Adams et al., 2006*). Worth noting is that nutrition training in medical schools has been identified as an essential component of medical education by a number of organizations in the US, including the American Society for Clinical Nutrition, the American Medical Student Association, the National Academy of Sciences, the American Academy of Family Physicians, the Society for Teachers of Family Medicine, and the US Congress, which passed the National Nutritional Monitoring and Related Research Act of 1990, mandating nutrition as a part of the medical school curriculum, (*Krebs & Primak 2006*).

The research in Cyprus confirmed the two major findings above. The first related to the absence of evidence-based therapeutic nutritional interventions (*as provided in Appendices 3-8*) within the current establishment in the provision of healthcare in Cyprus and the second related to the belief that these nutritional interventions fall within the scope of practice of the medical community. As regards the first finding, it is widely known that the vast majority of Cypriot doctors, study medicine in the medical schools of Europe and the United States where evidence (above) demonstrated inadequate education and training in therapeutic, evidence-based, nutritional interventions. In addition, it was demonstrated in different ways that these interventions do not form part of routine medical practice. During the interviews of the author with the Officials of the Health Insurance Organisation it was clearly stated that there is no provision in the National Health Insurance Scheme to cover dietary therapeutic means, such as nutritional supplements, as they are not currently prescribed by doctors in Cyprus, and they are not generally part of contemporary medical practice. This was also confirmed by the representative of the Doctors' Association who stated that, nutritional supplements are, in general, not part of routine medical practice, because not so many pathological conditions require their use, and doctors do not necessarily need to have special knowledge on these issues as they may not have so many patients who will need them.

Similarly, the Survey of the author demonstrated that only 11.4% of Cypriots followed a special therapeutic diet and 5.8% used nutritional supplements to treat a health problem and it is not clear whether these were prescribed by a doctor, (Chart 14:Therapies-Percentage of total population who followed each category of therapies)

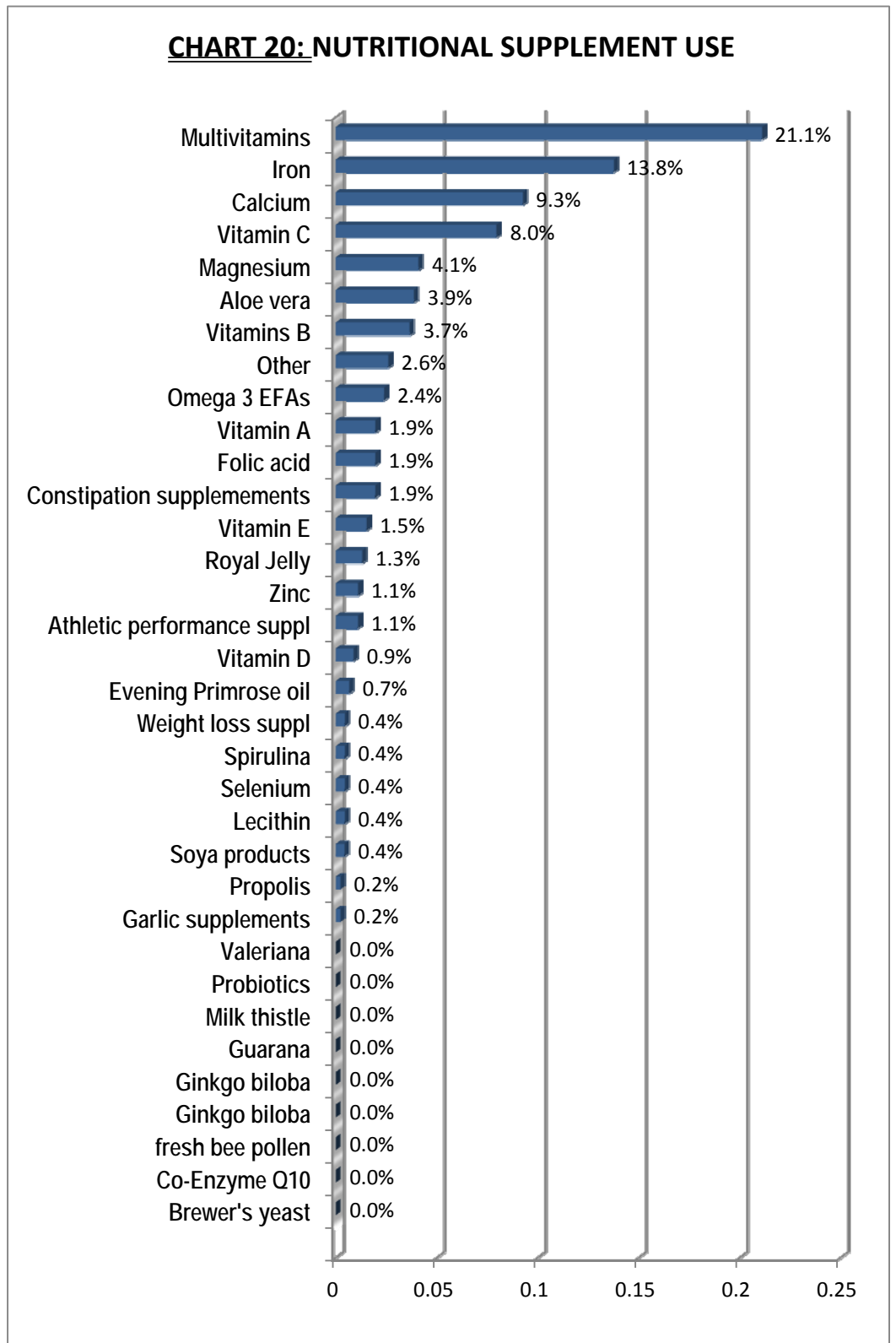


What was clearly deduced from the statistical analysis was that the majority of the population state that nobody advises them for the nutritional supplements they use, while only 23.2% of them get advice from a doctor and 1.7% from a nutritional therapist (Chart 19: Advice for nutritional supplements).

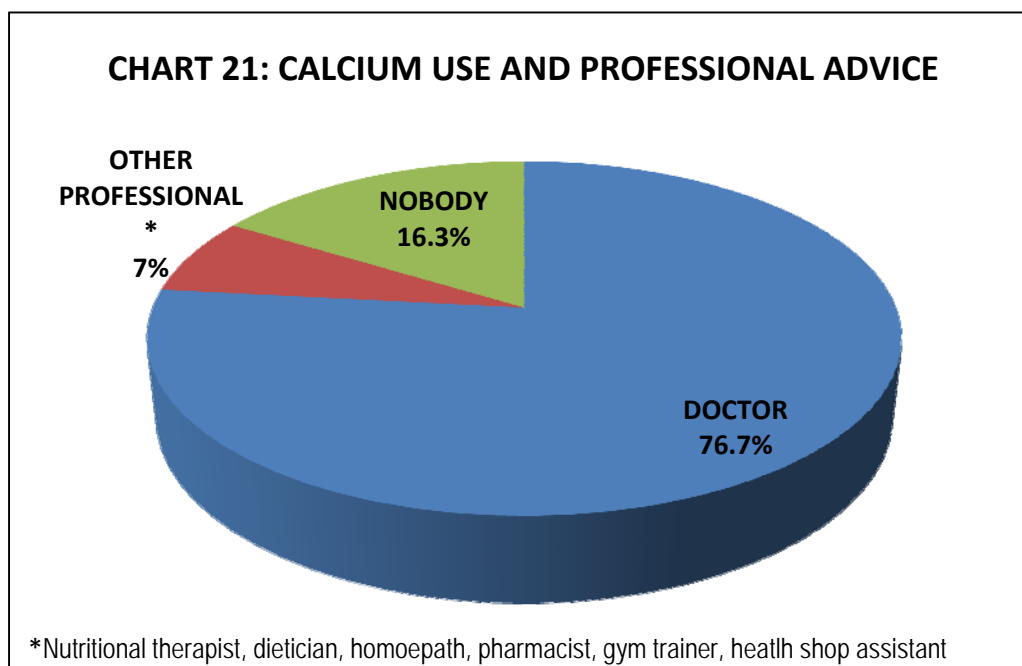


Furthermore, the Survey did not support evidence for a large application of nutritional therapeutic interventions within the Cypriot population. The Chart below (Chart 20: Nutritional Supplement Use) suggests that the most frequently used supplements are Multivitamins which are not usually part of routine Nutritional Therapy practice (although they might be used sometimes in specific cases). As a rule, the nutritional practitioner designs tailor-made prescriptions for each individual patient, using mainly single nutrients (vitamins, minerals, herbs etc), in various therapeutic quantities, according to the particular problems of each patient, (*Appendices 3-8*). Multivitamins usually contain ‘*a little-bit-of-everything*’ and are suitable for most individuals but do not normally contain the levels of nutrients needed for therapeutic interventions. Iron is the second most frequently used supplement followed by Calcium which appears to be the third most frequently used supplement (Chart 20: Nutritional Supplement Use).

CHART 20: NUTRITIONAL SUPPLEMENT USE



Interestingly, doctors appear to be responsible for the use of more than three quarters (76.7%) of this mineral by the Cypriot population (Chart 21: Calcium use and professional advice).



It is worth to note here that Calcium, although important in Nutritional Therapy, it is always used with care, usually in small quantities, on the basis of its particular function in metabolic processes, such as its controlling effect on the intensity of therapy. Most of the time it is used in combination with several other nutrients, including zinc, vitamin D, boron and others, but particularly with adequate magnesium, often in quantities twice as those of calcium, to facilitate its absorption and prevent its deposition in the wrong tissues of the body as calcifications (*discussed in the following chapters*). Worth noting is that Magnesium use in the results of the Survey was generally much lower than Calcium as shown in Chart 20: Nutritional supplement use. A volume of evidence in literature demonstrates the adverse, often fatal, effects of calcium in the body, such as antagonism to both heme and nonheme iron, arterial calcification, nephrolithiasis, and brain lesions, and the need to be always carefully prescribed, only when needed, and always with accompanying nutrients, particularly magnesium, (*discussed in following chapters*). And, of course, after restoring the body's calcium handling capacity, to avoid calcium stored in the wrong tissues (arteries, kidneys etc). This problem is a frequently appearing metabolic

imbalance among western world people and it is often successfully addressed by Nutritional Therapy.

Abovementioned evidence clearly demonstrates the need for more profound education and training in the area of prescribing nutraceuticals, as their action is completely different from medicinal drugs, working synergistically and in different ways, under different conditions, in different individuals.

Further evidence from the author's Clinical Practice, demonstrates the low number of nutritional prescriptions (14%) by doctors (Table 6: Use on Non-Conventional therapies before nutritional treatment)

TABLE 6: USE OF NON CONVENTIONAL THERAPIES BEFORE NUTRITIONAL TREATMENT
(Percentage of 50 randomly selected cases from clinical practice)

TYPE OF NON-CONVENTIONAL THERAPY	percentage
Used supplements for a specific health problem	68%
Used supplements without advice	54%
Used supplements (mainly iron, calcium and multivitamins) with doctor's advice	14%
Had other Non Conventional medicine treatments	24%

Also Table 9: Nutritional and Drug Prescriptions by Doctors, demonstrates that these are mainly for Iron, Calcium, and Multivitamins,

TABLE 9: NUTRITIONAL AND DRUG PRESCRIPTIONS BY DOCTORS
(50 randomly selected cases from Clinical Practice)

TYPE OF ADVICE	Number of patients	Percentage of total number of patients
No nutritional advice	43	86%
↳ With drug prescription	37	74%
↳ Without drug prescription	6	12%
Calcium supplements	2	4%
↳ With drug prescription	2	4%
↳ Without drug prescription	0	0%
Iron supplements	2	4%
↳ With drug prescription	2	4%
↳ Without drug prescription	0	0%
Calcium and Iron supplements	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%
Multivitamins	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%
Avoidance of foods	1	2%
↳ With drug prescription	1	2%
↳ Without drug prescription	0	0%

Further to the above, the research in Cyprus confirmed literature for a general belief amongst a significant proportion of the medical community, and many key actors, that therapeutic nutritional interventions fall within the doctors' realm of responsibility. In the Interviews, replying to the question: '*Who do you think is the right professional to provide nutritional therapeutic diets including nutritional supplements?*' one of the Officials of the

Ministry of Health strongly supported the Cypriot doctors' competency for therapeutic nutritional interventions, adding that any gaps (if any) in this area of practice can be adequately filled by Clinical Dieticians. Oppositely, another official of the Ministry of Health, identified a gap in the area of applying nutritional therapeutic interventions, claiming that these need special education and training which is not currently provided, neither by classical medical education nor by Dietetics. The representative of the Doctors' Association also supported the view that nutritional interventions should be applied by specialists in the field, adding, however, that all these should be prescribed always by doctors. Most key actors, expressed the view that specialists in the field are needed for therapeutic nutritional interventions, however many of them believed that most doctors also have (or they are supposed to have) adequate knowledge for nutritional advice, or that they should have additional education in order to offer nutritional advice, and others that they don't consider it proper to deprive doctors from the right to prescribe nutritional supplements. The opinion that in addition to specialists in the field, also doctors and pharmacists have the knowledge to prescribe supplements if they devote some time to familiarise with them, was also expressed.

CHAPTER VI

REDUCTIONISM AND SCIENTIFIC OBJECTIVITY

'For any conclusion drawn in this way may always turn out to be false: no matter how many instances of white swans we may have observed, this does not justify the conclusion that "ALL swans are white" '

Karl Popper

Another target of criticism is the universal application of oversimplified models within the current establishment of the provision of healthcare. Rick Carlson (1979) , had claimed during the seventies that 'it is not only limiting but impoverishing to assume that health is nothing more than the composite of well-oiled body parts', (Carlson 1979). During the same time, Harold Bursztajn and Robert Hamm Research Fellows in the Division of Primary Care and Family Medicine of the Harvard Medical School, had also criticised the tendency to address human suffering on the basis of oversimplified models of healthcare, which can be practiced 'everywhere from the laboratory bench to the patient's bedside'. The researchers had argued then that causal relations in medical practice are probabilistic, and questioned the possibility of absolute prediction of disease. According to their view, the Probabilistic Paradigm recognises that there is an 'element of irreducible statistical variability in the connections from causes to diseases' and thus, 'the course of the disease cannot be predicted with complete confidence'. They proceeded also to say that the Probabilistic Paradigm of science encourages us to consider the importance of the fact that the clinician is not only an observer but also a participant, (Bursztajn & Hamm 1979), calling to mind the following characteristic words of Claude Bernard¹:

'I acknowledge my inability to understand why results taken from statistics are called laws; for, in my opinion, scientific law can only be based on certainty, on absolute determination, not on probability. What a physician needs to know is whether his patient will recover and only the search for scientific determinism can lead to this knowledge'.

Claude Bernard

(in Bursztajn & Hamm 1979)

¹ French physiologist of the 19th century considered by many as the founder of modern experimental medicine (Capra 1996, p.24; The American Heritage Science Dictionary 2005) and a great medical teacher and investigator (Garrison 1929)

Researchers at the turn of the twentieth century argue that systems theory, complexity theory, models of self-organisation, and quantum physics are concepts of modern science with which seventeenth-century science 'simply does not have a framework for dealing with', (*Cushman & Hoffmann 2004*). Drawing from the statement of Candice Pert, psychoneuroimmunologist and Research Professor in the Department of Physiology and Biophysics at Georgetown University Medical Centre in Washington: 'My research has shown me that the body can and must be healed through the mind, and the mind can and must be healed through the body', (*Pert, 1999, p.274*) they claim: 'since the human body 'is not just a system' but 'a system of systems', we cannot be 'stuck on the biological, disease-oriented model alone' ignoring the contribution of mind and spirit to health and wellness, (*Cushman & Hoffmann 2004*). Capra (1996), drawing from Immanuel Kant's idealistic views of living organisms as 'self-producing, self-organising wholes', in contrast to machines, and Goethe's perception of each creature as 'one great harmonious whole', he claims that the dramatic change in the conception of physics¹ which has occurred during the first three decades of the twentieth century, brought about a shift towards a more wholistic ecological view. The conception of the nature of matter and its relation to the human mind is permeated by new insights which emerge within the wider context of a 'cultural transformation' in which entrenched ideas and values, such as 'human body as a machine', 'life in society as a competitive struggle for existence', and 'female subsumed under the male', are radically revised, (*Capra, 1996, p. 6*). Furthermore, Capra juxtaposes Louis Pasteur's simplistic 'germ theory of disease', -a reductionist view according to which bacteria are the only cause of disease-, with Claude Bernard's theory, which postulates that each organism has an internal environment which remains essentially constant despite external influences by bacteria², (*Capra 1996*).

Francois Gremy, Former Professor of Medical Information Sciences, then of Public Health, in an -awarded for Excellence- 'philosophical promenade' into the technological evolution of medicine, titled: *Hardware, Software, Peopleware, Subjectivity* draws from both the philosophical concepts of scholars such as Aristotle, E. Husserl, M. Henry and J. Searle, and from the most recent advances of neurosciences, to support his claims that

¹ Capra refers to Quantum Physics and Relativity Theory

² The notion of *homoeostasis*, later developed by Cannon (1920),

the deleterious temptation of our civilization since the beginning of “modern times” to eradicate subjectivity is scientifically wrong. The researcher, elaborates on the struggle of the scientific community against subjectivity, questioning the possibility of building objective knowledge solely on the basis of objective facts and ignoring the existence of personal opinions or prejudice in the choice of the thematic of research or in the facts to be investigated. He wonders ‘what should the activity of reason be, without motivation, passion for learning and understanding, and honesty of intelligence’ which are all subjective qualities? Gremy recalls Michel Henry’s statement that ‘every scientist has a twofold life: a part which tends to objectivity when practices research, and a mostly subjective part in his ordinary life, including his relationship with his colleagues’, (*Gremy 2005*). Gremy’s arguments bring to mind another statement made by Heraclitus (mentioned by Garrison): “though reason is accessible to all, most people, it seems, inclined to live according to their own notions”, (*Garrison 1929*)

PART IV

**THE WHOLISTIC
NUTRITIONAL MODEL
OF MEDICINE**

CHAPTER I

NUTRITIONAL MEDICINE DEFINED HISTORICALLY

The use of diet and lifestyle as means for treatment is perhaps as old as humanity. Indian, Chinese, Greek, Egyptians and Native American cultures are only a few of the people worldwide who used –and many of them continue to use as their sole therapeutic agents– food and plant components to treat patients, (*Bodane and Brownson 2002; Thiel 2000; Reid 1996; Chritchley et al., 2000; Vryonis 1989*). However, access to information about nutritional therapeutic applications in the western world was possible only after written texts appeared a few centuries B.C in the eastern part of the Mediterranean, particularly in the writings of Herodotus and Homer, in the Hippocratic Corpus (*Hatzopoulos 1992 [i-xvii]; Lypourlis [2000; 2001]; Goold [1928; 1988i; 1988ii]; Goold & Potter 1994; Goold & Smith 1994*), and later in the writings of Galen, (*Goold 1916; Brock [1916; 1923]*). Herodotus presents the Egyptians as ‘the most learned of all people’ who believed that ‘all illnesses arise from the food they ingest’. The improper digestion of food and ‘particularly the surfeits that remain undigested’, as causes of all diseases of the body were at the basis of Egyptian medicine, (*Vryonis 1989, p.12*). Similarly, Hippocratic medicine attributed great importance to the power of diet in the maintenance of health and the treatment of disease. Hippocrates identified the birth of medicine with the discovery of a variety of methods to make food suitable for people, -which until then only animals could eat. By processing grains to make bread, by cooking and by mixing strong foods with mild foods, adapting it to the human digestive system, people’s health was improved¹. According to Hippocrates, people suffered a lot from pain and deaths from the raw, and unprocessed food, (*Hatzopoulos 1992i, [3], pp.66-68*). One of the basic principles of Hippocratic therapeutics was the liquidizing of food by adding water to reduce its strength to the extent required for the particular patient, (*Lypourlis 2000 [5-6], pp. 64-66; (Hatzopoulos 1992i, [5-6], pp.70-72)*).

It should be noted, however, that Hippocratic medicine was always applied on the basis of the three important principles, being the cornerstones of wholistic medicine: *wholism*,

¹ Τῷ δ’ ἐπιρῆματι τούτῳ και ζητήματι τι ἐν τις οὐνομα δικαότερον ἢ προσῆκον μᾶλλον θεῖη ἢ ἡτρικὴν; ἔτι γε ἐπιρῆται ἐπὶ τῷ τοῦ ἐνθρώπου ἐγίειν τε και τροφῆ και σωτηρίῳ, ἐλλαγμα κείνης τῆς διαίτης, ἐξ ἐς οὐ πόνου και νοῦσοι και θάνατοι ἐγίνοντο.’ (*Hatzopoulos 1992i, [3], p.68*)

functionality and *biochemical individuality*. In the treatise *Ancient Medicine*¹ the doctor is advised to take a wholistic view of the patient before prescribing a treatment, examining all the factors that determine his/her existence² and to investigate deeper than the symptoms³ in search for the underlying causes, (Lypourlis 2000 [20], p. 86; Hatzopoulos 1992i, [20], p.100). Also, in his treatise *Airs Waters Places* he advises the new doctor, when arriving at a new town, to examine thoroughly and carefully the influences exerted on the people by their environment, including seasonal winds, their direction, strength and temperature; the quality of water people use, if it is still, hard or soft, its taste, weight and its source, if it comes from the rocks; the soil and its vegetation; the direction of the town, as regards the rise of the Sun; and the kind of food and drink people prefer, as well as their lifestyle, if they exercise or are sedentary⁴, (Hatzopoulos 1992iii, [1], pp.26-28). Similarly Galen, who espoused and further developed the Hippocratic medicine, placed equal emphasis on the role of diet and lifestyle in health and disease, as well as to the maxims of *functionality*, *wholism* and *biochemical individuality*. He believed to the *creativity* (*techne*)⁵ of the human organism, translated as the ability to produce *active motion* (*drastiki kinisis*) and *qualitative change* (*alliosis*) towards the development of the individual, through a specific feature of every living organism to attract and assimilate from nutrition what is 'appropriate' (*oikeion*) and to reject 'what is foreign (*allogrion*), (Goold 1916). In his treatise *The Natural Faculties*, Galen presents vividly the complicated function of the different organs that take place in the assimilation of food⁶. Several faculties (*dynameis*) of Nature work closely to produce *energies* (*energiae*) which influence the different organs of the body to produce *effects* (*erga*)⁷. At some point in his treatise, Galen refers to the views of Hippocrates and Plato, expounded also by Aristotle and Praxagoras, on the different effects foods might have on the human body in different areas of the world and different seasons of the year, under various circumstances, such as occupation, age, and body

¹ Περί Ἀρχαίας Ἱητρικῆς

² 'Ἐπεὶ τοῦτο γέ μοι δοκεῖ ἀναγκαῖον εἶναι παντὶ Ἱητρῷ περὶ φύσιος εἰδέναι, καὶ πάνυ σπουδάσαι αὐτὸ εἶσεται, εἰπερ τι μελλεὶ τῶν δεόντων ποιήσῃ, καὶ τί τέ ἐστιν ἄνθρωπος πρὸς τὰ ἐσθιόμενα καὶ πινόμενα, καὶ ἄ τι πρὸς τὰ ἄλλα ἐπιτηδεύματα, καὶ ἄ τι ἐφ' ἑκάστου ἐκάστῳ συμβήσεται' (Lypourlis 2000 [20], p. 86; Hatzopoulos 1992i, [20], p.100)

³ 'σκέψασθαι δὲ χρὴ διὰ τίνος προφάσιος ἀπτεῖσθαι ταῦτα ξυνέβη'

⁴ Ἱητρικὴν ὅστι βούλεται ζητεῖν, τάδε χρὴ ποιέειν. Πρῶτον μὲν ἐνθυμέεσθαι τὰς ὥρας τοῦ ἔτους, ὅτι δύναται ἀπεργάζεσθαι ἐκάστη... Ἐπειτα δὲ τὰ πνεύματα τὰ θερμὰ τε καὶ ψυχρὰ.....Δεῖ δὲ καὶ τῶν ὑδάτων ἐνθυμέεσθαι τὰς δυνάμεις, (Hatzopoulos 1992iii, [1], pp.26-28)

⁵ Techne: Greek: τέχνη=art

⁶ 'μη τοῖνον θαύμαζε το πλῆθος τῶν ὀργάνων, ὅσα θρέψεως ἕνεκεν ἡ φύσις ἐδημιούργησε' (Goold, 1916, [X23-24], pp.36-38)

⁷ 'εἴπερ βούλει τὰς δυνάμεις τῆς φύσεως ἀπάσας ἐκμαθεῖν, ὑπὲρ ἐκάστου τούτων ἀν εἴη σοι τῶν ὀργάνων ἐπισκεπτέον. Ἀρχὴ δ' αὐτῶν τῆς διδασκαλίας, ὅσα τοῦ τέλους ἐγγύς ἔργα τε τῆς φύσεως ἐστί καὶ μόρια καὶ δυνάμεις αὐτῶν.', (Goold, 1916, [X23-24], p.38)

temperature¹, (Goold, 1916, [VII, 124-125], pp.192-194). From a functional perspective, Galen attacked the Empiricists for simply identifying the function of an organ but not concerned with the cause of that function, claiming: How are you going to treat the disease successfully if you fail to understand its real essence?², (Goold, 1916, [IX, 127], p.196)

The use of nutritional therapies on the basis of Hippocratic and Galenic principles prevailed for more than two millennia until the nineteenth century when pharmaceuticals were discovered, (King 2001; Seelig 2005; Kemp 1905; Pizzorno & Murray 2007-2011; Garrison 1929; Ligeros 1937; Shai et al., 2001). James (2000) refers to a few examples of nutritional applications before this time, such as the use of lime to treat scurvy and cod liver oil or butter to treat rickets, while at the turn of nineteenth century, accessory food factors such as vitamins and other chemical compounds in food as agents of health and growth, were discovered, (James 2000, pp.3-12). However, even after the advent of the pharmaceutical means, many medical doctors of the beginning of the twentieth century continued to apply nutritional therapies. Lovell Langstroth, medical doctor and educator at the Department of Medicine of the University of California, demonstrates, during the first decades of the twentieth century, several cases of chronic disease from his clinical practice that have been successfully treated with 'dietotherapy', as he called it. In particular, he refers to 100 cases of chronic arthritis seen in private practice which were treated with dietotherapy, (Langstroth 1935). Lloyd Arnold, medical doctor, Professor of Bacteriology, Pathology and Preventive Medicine at the Loyola University School of Medicine in Chicago, lists a series of clinical experiments which substantiate the importance of diet and nutrition in the preservation of the friendly bacteria in the gut, in providing resistance to infection, and even contributing to the reduction of death rates in infants, (Arnold 1927). Theodore Diller, medical doctor, in Pittsburgh, claims that Benjamin Franklin, was a strong advocate of the power of nutrition in medicine. A few quotes by Franklin are cited: 'a full belly makes a dull brain; eat a few suppers and you 'll need few medicines' 'a full belly is the mother of all evils' 'I saw a few die of hunger; of eating, 100,000', 'he that steals the old man's supper does him no wrong', (Diller 1909). Irwin Frasse, medical doctor in Los Angeles, describes how diet and lifestyle affects the vitality

¹ "ενί δε λόγω τοις μεν θερμοίσι σώμασιν ή διά φύσιν ή διά νόσον ή δι' ηλικίαν ή δι' ώραν, ή διά χώραν ή δι' επιτήδευμα χολής γεννητικών, αίματος δε τοις εναντίοις, (Goold, 1916, [VII, 124-125], pp.192-194)

² 'τω γάρ έν έτι τρόπω και των ιαμάτων ευποροίητε την ουσίαν εκάστου των νοσημάτων αγνοούντες; (Goold, 1916, [IX, 127], p.196)

of our organs leading to diseases, including headaches and even certain types of insanities. Frasse believed that lack of tone due to intestinal malabsorption was the deeper cause of many diseases, (Frasse 1907). K. F. Meyer, from the George Williams Hooper Foundation for Medical Research, at the University of Californian Medical School, provides significant evidence from clinical research at the beginning of the twentieth century on the role of nutritional supplementation in 'extraordinary' amounts for the prevention and treatment of 'other than infectious' diseases, (Meyer 1928).

Following the course of time, a large volume of scientific literature appears to support the fact that a significant part of both the medical community and the public continue to be aware of, and apply in practice, the power of nutritional therapy, particularly for the treatment of chronic health problems, (as demonstrated in the following chapters)

CHAPTER II

NUTRITIONAL MEDICINE REDEFINED IN THE TWENTY FIRST CENTURY

In the first decade of the twenty first century different descriptions of Nutritional Medicine or Therapy and its field of action appear in literature using different phraseologies; however all converge on the general underlying meaning that *it is the science that applies drug-free nutritional practices to cure chronic health problems*. According to Mosby's Dictionary, Nutritional Medicine is 'the use of food and nutrition as a medical approach' and 'the supplementation of diet with nutrients, intermediary metabolic products, and probiotics to prevent illness and improve health and healing, (Mosby's 2005). Murray & Pizzorno (2011ii) offer the following description of Nutritional Medicine and of Nutritional Supplements:

'Nutritional Medicine consists of the use of diet and nutritional supplementation as therapeutic modalities. The foundation of nutritional medicine is a health-promoting diet that focuses on the consumption of whole, natural foods. Nutritional supplements are used in the overall context of Nutritional Medicine as complementary agents, not as sole primary medicines. Diet is always primary, and supplementation secondary.'

'Nutritional supplementation -the use of vitamins, minerals, and other food factors to support good health as well as preventing or treating illness -is an important component of nutritional medicine. The key functions of nutrients like vitamins and minerals in the human body revolve around their role as essential components in enzymes and coenzymes'

*Michael T. Murray
Joseph E. Pizzorno
Chapter 44, Textbook of Nutritional Medicine, 2011*

In the United Kingdom, the Complementary and Natural Healthcare Council (CNHC) –the Government-sponsored, voluntary registration body for Complementary Healthcare Practitioners- (Kmietowicz 2010; NHS 2011i; Crispin et al., 2010; DH 2010i; www.cnhc.org.uk), defines the work of Nutritional Therapy Practitioners as follows:

Nutritional Therapy Practitioners work in preventive medicine, the optimization of physical and mental health, and in the treatment of chronic diseases, often with complex multiple causes. Nutritional Therapy encompasses personalised dietary therapy and nutraceutical prescription, and lifestyle advice within a Functional Medicine framework', (CNH8 2010)

The public appears often confused by the different types of nutritional advisors and particularly by what 'optimum nutrition' means. To assist people in making informed choices, the Nutrition Society of the United Kingdom published a report, in 2004, funded by the Department of Health, on 'Understanding the differences between nutrition health professionals' (BANT 2006). On the basis of this report, the work of a Nutritional Therapist is defined as the preparation of :

'...individual prescriptions for diet and lifestyle, in order to alleviate or prevent ailments and promote optimal gene expression through all life stages. Recommendations may include guidance on natural detoxification, procedures to promote colon health, methods to support digestion and absorption, the avoidance of toxins or allergens and the appropriate use of supplementary nutrients, including phytonutrients. Nutritional therapists advise on each person's unique dietary and nutritional needs for metabolic and hormonal homeostasis, using a variety of biochemical and functional tests to inform recommended protocols and programmes', (BANT 2006)

A further report, published in August 2009 by the British Association of Applied Nutritional and Nutritional Therapy (BANT), underlines the differences between Nutritional Therapists and other nutritionists in key areas of nutritional practice, as is the *Detoxification process* which is the biotransformation and excretion of harmful molecules from the body. BANT's arguments are supported by evidence from scientific research, cited in the report, (BANT 2009). An extract of this report defines the detoxification process as an important component of Nutritional Therapy:

'Detoxification, which is the biotransformation of harmful molecules, is a core determinant of physical and mental health and is dependent on nutritional status. Poor conjugation and poor excretion of exo- and endo-toxins, combined with elevated toxic load, results in insidious and cumulative damage to metabolic processes and increasing susceptibility to disorders such as inflammatory joint disease, neurological impairment, atherosclerosis, allergies, chronic fatigue, and cancer. The primary mechanism of biotransformation involves activation of cytochrome P450 enzymes for Phase I

oxidative metabolism followed by Phase II conjugation to facilitate excretion. Phase I metabolism can either directly neutralise some compounds or transform them to highly reactive metabolites ready for Phase II conjugation. Balanced Phase I and Phase II activity is important to avoid increased production of intermediary metabolites, which without sufficient antioxidant protection, are damaging to DNA. Common variants (including deletions) in genes encoding for Phases I and II enzymes increase genome events which mediate aging (mitochondrial decay) and the disease process. Poor nutritional status leading to inefficient biotransformation contributes to long-term adverse health outcomes', (BANT 2009)

Drawing from above descriptions, and after reviewing a volume of relevant literature, it appears that the epistemological framework, on which Nutritional Medicine bases its methods of practice, is firmly supported by the maxims of *wholism, functionality, and biochemical individuality*. On the basis of this paradigm, the nutritional therapist approaches the individual as a unique entity, with distinct biochemical qualities and behaviour but, at the same time, as an inseparable functional unit of a larger highly complex system, with which constantly interacts and inter-associates receiving and transmitting influences at different levels and intensities. The therapist's ultimate aim is to identify and eliminate the deeper causes of the patient's symptoms, usually located in cellular biochemical imbalances, and disorders in metabolic pathways -which in turn can be attributed to various factors, including genetic, nutritional, environmental, and emotional-, and uses nutritional and lifestyle programmes for treatment. The interpretation of the individual's health symptoms is based on the idea that the body works as a functional systemic whole, within a dynamic complex environment, (Plaskett 2004 (i-xv); Jensen 1978; Balch & Balch 2000; Pizzorno & Murray 2006; Werbach & Moss 1999; Goldberg et al., 2002; Werbach [1996, 1997, 1999]; Garrow et al. 2000; Kumar 2007; Jones et al., 2005; Glenville 2001; Micozzi 2001; Ballentine 1978; Bland 2002; Brody 1999; Lessel 2001; Liska et al., 2004; Yarnell 2000; Capra 1977).

CHAPTER III

THE EPISTEMOLOGICAL BASIS OF NUTRITIONAL MEDICINE

Functionalism, Wholism, and Biochemical Individuality

The importance of the function an entity fulfils, or the purpose for which it is designed or exists, rather than its static matter, is a basic principle of wholistic philosophy, as inherited by our ancient ancestors. As already discussed in Part II, Aristotle view the human body as a functional whole, -not as a sum of its constituent parts-, existing and functioning in an intelligently organised mode for the sake of the whole, (*Peck 1961, [546a35,p.100; Hatzopoulos 1992xxii, p.136]*). The functional view of the organism represents the cornerstone of the patient-centred approach to treatment. Intracellular and intercellular communication, bioenergetics (transformation of food, air, and water into energy), replication, repair, and maintenance of structural integrity from the cellular to the whole-body level, elimination of waste, protection and defence, transport and circulation are the fundamental physiological processes to be addressed by a functional approach (*Jones et al., 2005, p.8*). Levin et al., (2011) describe in an apposite way the functional perspective of the relationship of the 'part' to the 'whole'. A non-functional approach is resembled to a view of a shattered china teacup, which can be reassembled or glued back together to re-establish the 'whole' from which it came. From a functional perspective, however, Levin et al., propose a view of a shattered hologram¹, which when it breaks it does not shatter into discrete pieces with different sizes and shapes since each piece 'visibly contains the complete and original hologram'. The importance of treating the patient not as made of anatomically distinct body parts or systems, but as made of parts visibly containing the original hologram, described as the 'whole body capability' is stressed, (*Levin et al., 2011*)

Within the same conceptual framework, Jones et al., (2005) identifies the functional approach with the restoration of the following systemic imbalances that arise from

¹ Hologram: a three-dimensional representation in photographic form, recorded on film by a reflected laser beam of a subject illuminated by part of the same laser beam (*The Gale Group, 2008*). If a hologram is cut into pieces, each piece projects the entire image, but as it viewed from a smaller subset of angles (*The American Heritage Science Dictionary 2005*)

disturbances in the fundamental physiological processes and which are the precursors of symptoms and signs, commonly known as 'diseases'.

1. Hormonal and neurotransmitter imbalances
2. Oxidation-reduction imbalances and mitochondriopathy
3. Detoxification and biotransformational imbalances
4. Immune and inflammatory imbalances
5. Digestive, absorptive, and microbiological imbalances
6. Structural imbalances from cellular membrane function to the musculoskeletal system (*Jones et al., 2005*)

From a similar perspective, Plaskett (2004) highlights the importance of a holistic functional patient-centred view for formulating a correct diagnosis, which will in turn guide to an effective treatment. The need to take into consideration all parameters that contribute to the *particular* life processes of the *particular* individual, as a biochemically distinct functional entity, is stressed. Tracing the patient's pathway of disease, several factors are considered including: family history (sometimes extending to past generations), past and present medical history, recurrent symptom patterns, eliminatory events, dietary and lifestyle habits, and environmental exposures. The case history is followed by interpretation and diagnosis on the basis of careful study, including research for most recent scientific evidence, which leads the way to the identification of constitutional weaknesses, weak organs/systems, metabolic imbalances, and nutrient deficiencies. Four major functional metabolic imbalances occurring at intracellular level are considered by Plaskett to be at the basis of most chronic health problems, both physical and psychological:

1. Sodium/potassium imbalance
2. Calcium mishandling
3. Poor fat handling
4. Blood sugar instability, (*Plaskett 2004viii*)

(see the example of a patient's case study in appendices 3-8)

Werbach & Moss, in their account of the deeper causes of chronic disease highlight the importance of a functional approach, by demonstrating the complexity of internal and external functions of the individual organism and the multitude of ways by which health is maintained, (*Werbach & Moss 1999, pp.3-26*):

1. Neuroendocrine imbalance. This imbalance -considered as the most important because it is the one most often ignored by both clinicians and researchers when investigating the causes of chronic illness- emerges largely from the malfunctioning of the *stress response mechanisms* of the human body. These are composed of two interrelated systems: The **Catecholamine-mediated system** (commonly known as the 'fight or flight' system) which prepares the body to act and it is controlled primarily by the hormones *epinephrine* and *norepinephrine*, and the **hypothalamic-pituitary-adrenal axis** which mobilises energy and it is primarily mediated by *cortisol*
2. Improper Nutrition: this involves qualitative and quantitative *macronutrient* imbalances, (proteins, fats, carbohydrate) and *micronutrient* deficiencies/excesses including antioxidants, essential fatty acids and homocysteine accumulation.
3. Chemical and/or heavy metal toxicity: attributed to different sources of toxicity (environmental, industrial, poisons in foods) but most importantly to the malfunctioning *endogenous detoxification mechanisms* of the human body. According to Werbach & Moss the human body exhibits a dynamic relationship between toxic load and its endogenous detoxification capacity which determines whether the patient will present symptoms of illness. Detoxification, although involving various overlapping metabolic pathways, it primarily depends on a two-stage process that takes place in the liver: *The Phase I (Cytochrome P-450)*, consisting of several cytochrome P-450 enzymes, each being specific for certain families of fat-soluble toxic substances and the *Phase II (conjugation)* consisting of a small group of enzymes which convert the metabolites of Phase I to substances that can be easily eliminated by the kidneys or bile.

4. Compromised mucosal barriers: this involves the condition of the intestinal mucosa and its relationship with the intestinal microflora population. The deterioration of the intestinal mucosa, which may occur from poor diet, stress and other factors, prevents proper absorption of nutrients necessary for the functioning of the metabolic pathways of the body leading to chronic illness. In addition, the imbalance in the billions of microorganisms that reside in the gastrointestinal system, result in the development and domination of hostile flora that produces by-products which promote illness. Werbach & Moss highlight the instrumental role of gut microflora on determining toxic load and hormonal status of the body through their effect on the *enterohepatic circulation* which is responsible for reabsorption and recirculation of hormones and xenobiotic agents.

5. Genetics: In spite of the long held belief that nothing can be done to alter genetic make-up, most recent research demonstrates that genes are responsive to environmental, nutritional and lifestyle factors. While from the negative side several so-called *xenobiotics* have been shown to have mutagenic effects on genes, from the positive side evidence suggests that supplementation with specific nutrients can enhance DNA repair mechanisms. Similarly, stress has been shown to affect gene expression, whereas some heavy metals can be poisonous for some individuals and harmless for others depending on the genetic profile of each which determines the production of the liver Phase I and Phase II detoxification enzymes, (*Werbach & Moss 1999, pp.3-26*)

The functional approach is further supported by a volume of medical research which demonstrates the existence of common underlying causal factors of, often seemingly unrelated, chronic health problems, substantiating the case for intracellular functional disorders underlying superficial symptoms. A few characteristic examples include; the finding that Rheumatoid Arthritis and Cardiovascular Disease emerge from deeper common causes, such as tissue inflammation and small HDL particles, (*Chung et al., 2010; Solomon et al., 2010*); metabolic syndrome was found to be highly prevalent among individuals with psoriasis, (*Love et al., 2010*); psoriasis was also shown to be an independent risk factor for cardiovascular disease, (*Gelfand et al., 2006; Malebra et al., 2007; Besgen et al., 2010; Tobin et al., 2010; Mehta et al.,*

2010 Chen et al., 2008) -through oxidative stress, endothelial dysfunction, hyperchomosysteinemia, and platelet adhesion, (Malebra et al., 2007) - with diabetes mellitus, (Solomon et al., 2010), and with psychological morbidity, particularly depression, anxiety and suicidality, (Alevizos et al., 2007; Kurd et al 2010). Researchers claim that the common pathogenesis is located in functional gene interaction with environmental factors, (Besgen et al., 2010; Tobin et al., 2010).

The intricacies of biochemical individuality

The importance of individualisation of nutritional interventions is increasingly raised by medical and other academic researchers, as well as by official reports, during the last decade. The proponents of this view claim that non-homogeneity among populations is evident by research, but it is also a fact that each person is biochemically different, with distinct response to dietary components on the basis inter-individual variations in genetic, epigenetic, and metabolic status, (Ballentine 1978; McCarthy 1981; Go et al., 2005; Kaput 2007; Davis & Milner 2004; Kumar 2007; Jones et al., 2005; Ansell et al., 2003; Highton 2003; Ginsburg & Willard 2009; EU 2005; WHO [2003; 2005]; Bottles 2001; Elliot & Ong 2002; Grossman et al., 2010; Bottles 2001; Yach et al., 2004; Miggiano & De Sanctis 2006; Newell-McGloughlin 2008; Fairweather-Tait, 2003; Corthesy-Theulaz et al., 2005; Lovegrove & Gitau 2008; German et al., 2004; Junyent et al., 2009 ; Solomons 2009; Schenk et al., 2008). In a report published in December 2009, the British Association of Applied Nutrition and Nutritional Therapy (BANT) underlines the emphasis placed by Nutritional Therapy Practitioners on *biochemical individuality* and on the *unique* nutritional needs of each person, as well as the 'potential flaws in transferring population guidelines to recommendations for optimising individual health'. Evidence from research is cited in support of these arguments, with reference to statements by medical and nutrition experts from national and international organisations: Artemis Simopoulos from the Centre for Genetics, Nutrition and Health in Washington, in 2002 questioned the existence of 'such thing as a "normal population" with respect to nutrient requirements, as was assumed when dietary reference values were established', claiming that populations should not copy each other's dietary recommendations for the prevention of any chronic disease. Along the same lines in 2006, Fineberg, the President of the US Institute of Medicine, draws attention to the need for a public health paradigm of universal education to be adapted to the new scientific reality and scientific knowledge

which demonstrates that nutrients may affect different population groups in different ways, and these differences should be taken into account when setting public health guidelines. Similarly, experts from the European Food Safety Authority, in 2007 stressed the need of considering the differences, not only between nations but also between special groups within a nation, when establishing food-based dietary guidelines, (*BANT 2009*).

According to Murray & Pizzorno (2011ii), the concept of 'biochemical individuality' was coined in the 1970s by the nutritional biochemist Roger Williams, in recognition of the wide range in enzymatic activity and nutritional needs of humans (*Murray & Pizzorno 2011ii*). A decade later, McCarthy (1981) focused on the individual differences in absorption, tissue uptake, activation or enzyme affinity, resulting in different persons to require larger intakes of a given nutrient than others. To support this theory, Mc Carthy referred to the so-called *vitamin-dependency syndromes*, such as *homocystinuria*, *pyridoxine-dependend anaemia*, and *cystathionuria*, in which a decreased affinity of an enzyme for a cofactor (usually *pyridoxal phosphate*), owing to a genetically-determined defect of enzyme structure, may have dramatic and not rarely life-threatening effects, (*McCarthy 1981*).

A volume of research of the last decade further substantiates the case for a unique biochemical profile of each individual and for the need to take this into consideration in all therapeutic interventions. Solomons (2009) refers to a number of studies which demonstrate that the intake of commonly supplemented, often nationwide, nutrients, such as iron or folic acid, may have beneficial effects to some individuals but serious adverse effects to others. In particular, supplementation with 12.5mg of iron and 50mg of folic acid in preschool children in Zanzibar produced mixed results, including increased hospitalisation and death. Especially, folic acid is increasingly used in maternity to prevent neural tube defects while, in some nations, fortification of flour and breakfast cereals with folic acid (*pteroylglutamic acid*) is recommended, despite accumulating evidence that oral intake of folic acid from fortification and nutrient supplements can accelerate the progression of incipient colorectal tumours, (*Solomons 2009*).

Ballentine (1978) claims that there exist several reasons for which our body does not supply itself with the necessary minerals it needs, either through poor *selection*, incomplete *absorption*, or failure of *biological transmutation*. In the chapter titled 'Entropy versus life', of his book *Diet and Nutrition*, he claims that there is much more to the chemistry of biological systems than the Newtonian views of isolated atoms 'sidling up' one to another to establish a chemical bond. Atoms, he argues, are not isolated and do not move singly, either. They, instead, form parts of complex molecules, arranged together with hundreds of others surrounding it, with important relationships between them. Elaborating on the enzymatic activities called *biological transmutations*, refers to the results of several studies, conducted and repeated over a long period, demonstrating the inherent, highly complex processes underlying the power of the individual human body 'to create itself', by using the nutrients from nutritional, environmental, or other sources in an extremely intelligent manner. In this case our enzymes perform a critical role in intricately manipulating the atoms of the minerals to effect changes at low temperatures, which under other conditions would require the extremely high temperatures present in an atomic reactor. In particular, hens fed with food without any calcium and living on soil derived from granite, could lay eggs with completely calcified eggs. The researchers found that calcium was derived from the biological transmutation of potassium contained in the mica¹ hens were fed. Similarly, researchers found much higher amounts of calcium in sprouted seeds than that contained in the seeds before sprouting, although double-distilled, mineral-free water was used to feed them. Studies were repeated by other researchers with high scientific rigour, and the results were the same: Hens, through enzymatic activity, transformed potassium to calcium with addition of one proton (hydrogen ion) to the nucleus of a potassium ion. Similarly, plant enzymes performed the biological transmutation from potassium to calcium. Interestingly, when mica (which contained the potassium), was removed from the hens diet, and they had access only to clayey soil, their eggs became soft and pliable after a few days. When mica was added eggs were calcified again. Similar experiments were conducted with fish and bird eggs which contained no calcium but hatched to produce tiny fishes and birds with complete and well-calcified skeletons, which they developed while inside the egg. The most interesting, however, finding was that which provided significant insights of human

¹ Rock-forming mineral consisting of hydrous silicates of aluminium, potassium etc

physiology interacting with intense heat. In a study with a team of oil workers in Sahara desert, who stayed and worked under the broiling sun for long periods, it was found, after measuring the temperature inputs and outputs and their perspiration every day, that the workers retained an amount of 1800 calories daily, which meant that death should ultimately result from overheating. After studying the mineral metabolism the researchers found that the workers ate tremendous amounts of salt (*sodium chloride*) which, apart from small quantities lost in perspiration and the faces, simply 'disappeared'. At the same time huge amounts of potassium were excreted through their sweat glands, although their diet was very low in potassium. Similarly, much more magnesium than that ingested was excreted. Later experiments demonstrated that sodium is converted to potassium and some of it to magnesium using heat. Ballentine explains that these *biological transmutations*, which are chemical reactions that result in the change of the nuclei of atoms and not merely the altering of the shells of the electrons, require tremendously high levels of temperature, such as those found in a reactor designed for atomic fusion; however inside the body, they take place with lower temperatures assisted by our intelligent enzymes, (*Ballentine 1978, pp.563-570*).

Apparently, living systems possess an ability to completely change one form of matter to another. As a consequence human bodies have the potential to create, at least some of, the vital for life minerals missing from their diet. However, Ballentine claims, it is clear that not everybody has this potential and this is an important factor underlying the need for individual interventions. Bland (2002), referring to Linus Pauling's¹ theory of the genetic uniqueness of disease and the complex interrelationships between genes, metabolism and environment underlying its genesis, he claims that the new model of the genotype/environment/phenotype connection challenges the view that 'nothing can be done for the individual who carries the genes for heart disease, cancer, diabetes, or any other major age-related disorder', (*Bland 2002, p.23*). Worth noting is a paragraph from Lewontin's *Triple Helix*, quoted in Bland (2002):

'of course it is true that lions look different from lambs, and chimps from humans, because they have different genes, and a satisfactory explanation for the

¹ Linus Pauling: chemist and biologist, the only individual ever to win two unshared Nobel Prizes', pioneer in the application of quantum-mechanical principles to the structure of molecules, ' (Higdon 2003)

differences between lions, lambs, chimps, and us need no involve other causal factors. But if we want to know why two lambs are different from one another, a description of their genetic differences is insufficient and for some of their characteristics may be irrelevant. ...There exists, and has existed for a long time, a large body of evidence that demonstrates that the ontogeny of an organism is the consequence of a unique interaction between the genes it carries, the temporal sequence of external environments through which it passes during its life, and random events of molecular interactions within individual cells,' Lewontin 2000, pp.17-18¹

¹ Quoted in Bland 2002, p.23

CHAPTER IV

NUTRIGENOMICS/NUTRIGENETICS

As discussed in the previous chapter, the case for a unique biochemical profile of each individual and for the need to take this into consideration in all therapeutic interventions, is substantiated by a volume of medical research. Ruan Elliot, Nutritional Genomics Programme Leader of the Institute of Food Research in Norwich and his colleague Teng Jin Ong, speak of ‘inter-individual genetic variation as a critical determinant of differences in nutrient requirements’, emphasising the importance of evaluating all the possible effects of specific food components in a genetically heterogeneous population, in order to determine unintended risks as well as intended benefits, (Elliot & Ong 2002). According to Vay Liang Go and colleagues, from the Department of Medicine of the David Geffen School of Medicine at UCLA, Los Angeles, at the heart of biochemical individuality lies the genetic and genomic profile of each individual, which represents the highly complex organisational structure of the human body into organ systems, tissues, cells, and cell elements, further reduced to genetic and atomic components. An individual’s overall health phenotype is a function of both the sum of metabolic activities, taking place under different circumstances within the life cycle, and the complex interactions among genotype, metabolic phenotype, diet, lifestyle, and the environment. (Go et al., 2004).

Terms such as *genomics*, *genetics*, *genomic medicine*, *nutrigenomics*, *haplotypes*¹, *disease phenotype*², *proteomics*³, *metabolomics*⁴, and *molecular basis of disease* are increasingly used by medical researchers in the last decade in their explanations of the deeper causes of disease, (Kumar 2007; Jones et al., 2005; Ansell et al., 2003; Ginsburg & Willard 2009; Bottles 2001; Grossman et al., 2010; Go et al., 2005; Miggiano & De Sanctis 2006). According to definitions, Genomics, which

¹ **Haplotype**: the antigenic phenotype determined by closely linked genes inherited as a unit from one parent (*The American Heritage Medical Dictionary 2007*); A set of alleles (an alternative form of a gene that can occupy a particular place on a chromosome) of a group of closely linked genes which are usually inherited as a unit, (*Gale Encyclopedia of Medicine 2008*)

² **Phenotype**: the physical and biochemical characteristics of an organism as determined by the interaction of its genetic constitution and the environment (*Collins English Dictionary, 2003*); the physical appearance of an organism as distinguished from its genetic makeup. The phenotype of an organism depends on which genes are dominant and on the interaction between genes and environment (*The American Heritage Science Dictionary 2005*); what an organism looks like as a consequence of the interaction of its genotype and the environment (*Farlex 2011*)

³ **Proteomics**: The branch of biochemistry concerned with the structure and analysis of the proteins occurring in living organisms (*Collins English Dictionary, 2003*)

⁴ **Metabolomics**: the study of all the metabolites present in cells, tissues, and organs, (*Collins English Dictionary, 2003*)

provides the blueprint, encompasses the entire genomes of organisms -including all genes, nucleotide sequences, regulatory sequences and noncoding DNA segments, in the chromosomes of an organism-, and the application of this knowledge in medicine, pharmacy, etc, while Genetics refers to the genetic constitution of an individual, group or class, to specific genes, their different traits and characteristics, and the mechanisms of hereditary transmission, (*The American Heritage Dictionary 2000; Kumar 2007; Collins English Dictionary, 2003; Miggiano & De Sanctis 2006; German et al., 2004*). Proteomics is the study of the structure, occurrence, and catalytic activities of all expressed proteins in a cell, tissue or organism, (*German et al., 2004; Davis & Milner 2004*). The human body is almost entirely composed of proteins, produced on the basis of instructions from the genes, which are replicated and translated by messenger RNA. Proteins, called *enzymes* and *hormones* are responsible for the biochemical reactions in the body and for 'turning genes on and off', (*Bottles 2001*). Metabolomics refer to the study which measures, by quantitative metabolic phenotyping, all the dynamic metabolic activities of the organism, carried out by the small-molecular-weight molecules and compounds, acting within the entire spectrum of biochemical pathways in a cell, tissue or organism, (*German et al., 2004; Davis & Milner 2004*).

Nutrigenomics, investigates how different nutrients interact with humans and the ways they regulate and/or modify gene expression, and it is linked to Nutrigenetics, which studies the genetic variations and gene polymorphisms among individuals and their different responses to the same nutritional stimulus leading to different outcomes in respect to health and disease, (*Newell-McGloughlin 2008; Desiere 2004; The American Heritage Dictionary 2000; Kumar 2007; Collins English Dictionary, 2003; Miggiano & De Sanctis 2006*). Miggiano & De Sanctis (2006) define *Nutrigenomics* as a multidisciplinary science that applies 'high-throughput genomics tools to the study of diet-gene interactions in order to identify dietetic components having beneficial or detrimental health effects'. The important contribution of *nutrigenomics* in understanding the etiologic aspects of chronic diseases, such as cancer, diabetes, obesity, cardiovascular disease and metabolic syndrome is stressed, (*Miggiano & De Sanctis 2006*). Jim Kaput from the Laboratory of Nutrigenomic Medicine, Department of Surgery, of the University of Illinois, Chicago, identifies *Nutrigenomics* as the science that studies how constituents of diet interact with genes to alter *phenotypes* and then the determinant role of these *phenotypes* on how the body metabolises the constituents of diet into

nutrients, anti-nutrients and bioactive compounds. The researcher acknowledging the challenges posed to the investigator of gene-nutrient interactions due to the chemical complexity of food, the genetic heterogeneity of humans, and the complexity of biological processes and physiological responses to nutrient intakes in conditions of health and disease, stresses the need for the development of high throughput *omic* technologies, improved experimental designs, and research collaborations, (Kaput 2007). The cumulative effects of food components on genetic expression profiles and the individual responses to these effects are named *Nutrigenetic effects* and are classified into two categories: the *nutritional transcriptomics* and *nutritional epigenomics*, (Davis & Milner 2004).

The idea that the underlying mechanisms of disease rest at the intracellular level, and are strongly related to the distinct genetic and genomic profile of each individual and its complex interactions with the environment, gains ground on the basis of increasingly accumulating evidence of the last decade, (Kumar 2007; Jones et al., 2005; Ansell et al., 2003; Ginsburg & Willard 2009; Bottles 2001; Grossman et al., 2010; Go et al., 2005; Miggiano & De Sanctis 2006; Newell-McGloughlin 2008). Researchers claim that Genomic medicine -which is informed by each person's unique clinical, genetic, genomic, and environmental information- allows the best clinical practice of 'personalised medicine', since it can expedite our understanding of the molecular basis of disease, guide medical decision making, and assist prognostication and prediction of treatment outcomes, (Ansell et al., 2003; Ginsburg & Willard 2009). According to Miggiano & De Sanctis (2006), a really personalised diet would be the one that considers the *genotype* of the individual, amongst other parameters, -such the nutritional status, the nutritional needs, work and physical activities- and would integrate all information, including *genomic*, *proteomic* and *metabolomics* analyses, to define the individual's '*nutritional phenotype*', (Miggiano & De Sanctis 2006). Go et al., (2005), drawing from a volume of studies, claim that an individual's overall *phenotype of health* is maintained 'by the sum of metabolic activities functioning under differing circumstances within the life cycle and the complex interactions among *genotype*, *metabolic phenotype*, and the environment'. The researchers argue that humans exhibit different responses to diet due to their inter-individual variations in their genetic, epigenetic, and metabolic phenotype status, and therefore specific tools and knowledge should be developed for the investigation of the molecular basis of genetic variation, and the transformation of current population-based

dietary guidelines into more personalised dietary recommendations, (Go et al., 2005). Along the same lines, Jones et al., 2005 focus on the importance of nutrients in modulating physiological processes at the biomolecular level, arguing for a new age in medicine heralded by the idea that the origins of disease are related to 'intricacies of interaction between the environment and genes and their expression', (Jones et al., 2005, pp.20-21).

Researchers claim that the sequencing of the human genome has opened the door to a new era in nutritional science. Optimal health can be promoted through individual tailored made food programmes, and possibly tailored food products, on the basis of individual genotype, (Fairweather-Tait, 2003). According to Kumar (2007), the distinct genetic makeup of each individual constantly interacts in various ways with dietary, environmental and other factors. In nutrigenomics a specific nutrient interferes with the expression of certain genes and proteins by influencing the intracellular metabolic pathways at particular points. The prevention, progression and treatment of cancer, for example, are now considered to depend on the genomic profile of the individual which is affected in many stages by different nutritional and metabolic factors. This is called the 'cancer phenotype', which is the complex interaction of both genetic and environmental factors, and it is confirmed by numerous studies. The researcher draws attention to the multitude of combinations and interrelationships between metabolic activities and the complex interactions among genotype, metabolic phenotype, and the environment, occurring 'under different circumstances, at different stages of the life cycle', (Kumar 2007). Corthesy-Theulaz et al., 2005 speak of a new nutrition research concept, that of *nutritional systems biology*, which centres on the extreme complexity of interactions between the human body and nutrition, involving mechanisms at various levels of molecular function –genes, gene expression, proteins and metabolites. The gene expression modulation by the different classes of foods, such as carbohydrates and fatty acids is discussed with special reference to gene polymorphisms which highlight the different ways by which each individual organisation utilises nutrients, resulting in different susceptibilities to develop obesity and disease, (Corthesy-Theulaz et al., 2005). On the same issue Milner (2006), focusing on the *nutrigenetic effect* according to which genetic polymorphisms can alter the response to dietary components by influencing the absorption, metabolism or site of action, claim that some of the inconsistencies in the

response to foods can be explained by fluctuations in the nutritional transcriptomic effect, that is the ability of food components to increase or depress gene expression, (Milner 2006).

A volume of research of the last decade has produced extremely useful insights on the underlying gene-diet-interaction-based causes of particular chronic diseases which are considered common killers worldwide. Lovegrove & Gitau (2008) focus on the ineffectiveness of population-based prescribed recommendations for reducing the risk of cardiovascular disease, attributing this to the extreme variability between individuals in their response to dietary manipulations and in the interactions between diet and the individual's genetic background, defined as *nutrigenetics*. The researchers stress the need for a shift towards more personalised nutritional advice, tailored to the individual's particular genotype, (Lovegrove & Gitau 2008). Grossman et al., (2010), claim that evidence is amassing to support the hypothesis that defective mitochondrial metabolism and function are the deeper causes for pathological changes that result to Alzheimer's disease, a common neurological disorder affecting over 10% of people over the age of 71 years and demonstrating high rates of increase, (Grossman et al., 2010). Kaput et al., (2007) claim that inherited gene variations, such as single nucleotide polymorphisms produce differences in height and weight potentials, food metabolism, food-gene interactions and susceptibilities to chronic disease such as Diabetes Mellitus type II. The researchers stress the importance of indentifying genes contributing to chronic disease, that are regulated by diet, in order to develop personalised interventions for prevention and treatment of specific diseases, such as Diabetes, (Kaput et al., 2007). Similarly, cancer is now considered as a chronic disease of the genome and, as that, nutritional, genetic, environmental, and metabolic factors play a significant role for its prevention, progression, and treatment, (Go et al., 2005; Kumar 2007). Diet and associated lifestyle are considered as the strongest factors in carcinogenesis, with 80% of the cancers of the colon, breast and prostate, attributed to these, (Kumar 2007). Diet contains significant nutrients –but also non-nutrient compounds, such as phytochemicals- with anti-carcinogenic and antimutagenic properties, (Go et al., 2005; Kumar 2007). It is estimated that 25,000 chemical compounds exist in plants consumed by humans, which include carotenoids, flavonoids, organosulfur compounds, isothiocyanates, indoles, monoterpenes, phenolic acids and chlorophyll, and most of

which can influence gene expression through the genotype-phenotype relation, (*Davis and Milner 2004*). Kumar (2007) claims that the strongest evidence for environmental factors in carcinogenesis is that of dietary factors, 'estimated that 80% of colon, breast, and prostate cancer cases and approximately of one third of all other types of cancer may be caused by dietary and life-style associated factors', (*Kumar 2007*) while Go et al., (2005) identify the genomic-nutrient and metabolic-phenotype interactions as major factors underlying the dietary effects in cancer risk, (*Go et al., 2005*). According to Milner (2006), to understand the relationship between dietary interventions, proteome changes, and cancer, it is important to consider functional proteomic studies which capture the totality of proteins a species produces and link them to physiological significance within the cell, (*Milner 2006*).

German et al., (2004), claimed that there no such thing as 'a better diet'. A diet that is optimal for one individual may predispose another to disease on the basis of the wide genetic and phenotypic variation among humans (*German et al., 2004*). This fact is further confirmed by evidence from *haplotyping* studies which demonstrate that gender and ethnicity-specific gene polymorphisms are implicated in susceptibilities to chronic disorders such as diabetes, cardiovascular disease and some cancers, (*Newell-McGloughlin 2008; Corthésy-Theulaz et al., 2005*). A characteristic example relates to the risks posed to certain *haplotypes* from the high intake of well-done meat, through acetylation of *heterocyclic aromatic amines* produced in the meat from the reaction of its amino acids with creatine under high temperatures. Apparently, only individuals possessing the *fast acetylator haplotypes* can perform this acetylation, and these are the ones found to be more susceptible to some cancers such as colon cancers, if they consume large quantities of red meat, (*Newell-McGloughlin 2008*). The effects of the common food ingredient, fructose, are also mentioned, on the molecular and biochemical mechanisms underlying the development of insulin resistance, hepatic steatosis (fatty liver), and the metabolic syndrome. Studies have recently shown that fructose can alter gene expression patterns (such as peroxisome proliferator-activated receptor- γ coactivator-1 α/β in the liver), alter satiety factors in the brain, increase inflammation, reactive oxygen species and portal endotoxin concentrations, and induce leptin resistance, all related to above mentioned chronic health problems, (*Dekker et al., 2010*). An interesting finding by Junyent et al., 2009

demonstrated a synergistic relationship between genes and diet which appears to support the '*thrifty genotype hypothesis*', (*Speakman 2006*), according to which genes that were originally beneficial for energy storage became harmful through a process of evolution under conditions of over nutrition. The study showed that in obese individuals, consumption of high PUFAs and carbohydrates triggers the deleterious effect of the PDZK1 genetic variant leading to the development of metabolic syndrome, whereas a protective effect was observed in non-obese individuals consuming the same quantities of PUFAs and carbohydrates, (*Junyent et al., 2009*).

CHAPTER V

NUTRACEUTICALS AND FUNCTIONAL FOODS IN NUTRITIONAL THERAPY

An increasingly rising volume of research exists to demonstrate the effects of nutrients in health and disease. Worth noting is that a significant part of this research is conducted by medical researchers who have come to acknowledge the importance of therapeutic dietary interventions,

(Ames 2006; Ames 2010; Balch & Balch 2000; Baldewicz et al., 1998; Ballentine, 1978; Barbagallo et al., 2007; Beckett & Arthur 2005; Benton & Donohoe 1999; Benyon 1998; Bereswill et al., 2010; Bland [2002 and 2004]; Bland 2004; Bodane & Brownson 2002; Bohager 2008; Bolland et al., 2010; Calvaresi & Bryan 2001; Carlsen et al., 2010; Cattaneo et al., 2001; Chakraborti et al., 2002; Chen et al., 2009; De Lau et al., 2006; De Roos et al., 2009; Duda et al., 2009; Elmali et al., 2007; Erasmus, 1993; Kris-Etherton et al., 2002; Fairfield & Fletcher 2002; Fenech 2001; Ferguson 2009; Ford 2001; Forestier et al., 2008; Frederickson et al., 2005; Garland et al., 2007; Garrison 1982; Garrow et al., 2000; Gawande et al., 2008; Glenville [1997; 2001; 2005]; Goldberg et al., 2002; Gonzalez-Gross et al., 2001; Gorelik et al., 2003; Green & Miller 1999; Guarner 2007; Guerrero-Romero & Rodriguez-Moran 2005; Gurusamy et al., 2008; Hanaway 2005; Harper & Jacobson 2001; Hasler et al., 2000; He et al., 2011; Hennen 1999; Herbert 2000; Higdon 2003; Holmquist et al., 2007; Hudson & Murray 2011; Jensen 1978; Jha et al., 2010; Jia et al., 2010; John et al., 2010; Jones et al., 2005; Kale et al., 2010; Karunakaran et al., 2007; Kelloff et al., 2000; Kidd 1996; Kim et al., 2004; Knekt et al., 2002; Lakhan & Kirchgessner 2010; Lamson & Plaza 2002; Lassi et al., 2010; Leader & Leader 2006; Levin et al., 2006; Ley 1998; Libby 2005; Linde et al., 1996; Lipton et al., 1979; Liska & Bland 2005; Looijer-van Langen & Dieleman 2009; Lyon et al., 2005; Ma et al., 2005; Maczurek et al., 2008; Maes et al., 2009; Mandel et al., 2004; McCann & Ames 2009; Mancuso et al., 2007; McCarty [1981; 2000, 2000ii]; McKay et al., 2000; McKenna et al., 2001; Meplan et al., 2007; Meydani 2001; Michaud et al., 2000; Molloy & Scott 2001; Muecke et al., 2010; Murray & Lyon 2003; Murray & Pizzorno [2011; 2011i; 2011ii]; Murray [1994i; 1994ii; 1996; 2002]; Murray, et al., 2005i; Natural Medicines Comprehensive Database [1995-2011]; NIH et al., 2004; Obeid et al., 2007; Pan et al., 2009; Panayiotakos et al., [2007i 2007ii, 2009]; Papathanasopoulos & Camilleri 2010; Parkes et al., 2008; Pfeiffer [1975; 1972; 1987]; Pittler & Ernst 1998; Pizzorno & Murray 2006; Pizzorno et al., 2002; Plaskett 2004 [i-xv]; Polychronopoulos et al., 2008; Proby 1975; Puchau et al., 2009; Quillin & Quillin 2005; Radhika et al., 2002; Rayburn & Friedman 2010; Reckeweg 1991; Reid et al., 2003; Reznichenko et al., 2010; Rideout et al., 2008; Robinson et al., 1998; Romieu & Trenga 2001; Sahley & Birkner 2001; Salinthon et al., 2008; Schauss 2011; Scholle et al., 2009; Schurgers et al., 2007; Sharma et al., 2007; Showell et al., 2011; Silva et al., 2010; Simopoulos 2002; Singh & Das 2011; Singh & Jialal 2008; Smith et al., 1996; Song et al., 2006; Song et al., 2009; Song et al., 2010ii; Soo et al., 2008; Steinbrecher et al., 2010; Stoll 1998; Taylor et al., 2002; Tenenbaum et al., 2008; Tunon et al., 2009; Vauzour et al., 2008; Verhaar 2002; Vogel et al., 2005; Vosper 2009; Wang et al., 2001; Wang et al., 2010; Watts 1995; Weber et al., 1996; Wei et al., 2009; Weisburger 2000; Werbach & Moss 1999; Werbach & Murray 2000; Werbach [1996, 1997, 1999 2002]; Wilner 2005; Wilt et al., 1998; Witte et al., 2001; Yamori et al., 1992; Yamori et al., 2010; Yarnell 2000; Zhou et al., 2009; Zoccollella et al 2007).

Nutritional supplementation represents a major tool for Nutritional Practitioners and it used always along with tailored-made dietary programmes and lifestyle changes for the treatment of many chronic health problems (see: *Appendices 3-8: A case study from the*

authors clinical practice). A number of terms appearing in literature, such as, 'nutraceuticals', 'functional foods', 'food supplements', and 'phytochemicals', denote foods or specific nutrients that are used as medicines. They are all isolated from foods and they were found by scientific studies to have the power to support good health and prevent or treat illness by influencing the expression of both structural genes and transcription factors in human cells, (Newell-McGloughlin 2008; Go et al., 2005; Pizzorno & Murray 2007-2011; BANT 2006). A particular definition for the nutraceutical is 'any substance that may be considered a food or part of a food that provides health benefits, including the prevention and treatment of disease', (Goldberg 1994¹; Newell-McGloughlin 2008). The term, *anti-nutrients* is also used to denote substances from foods or other sources related to the individual's environmental exposure -but also produced by the body during metabolism of food- that can limit the bioavailability of nutrients, (Newell-McGloughlin 2008).

It is estimated that plants produce about 200,000 phytochemicals from which 25,000 represent different metabolites, (Go et al., 2005; Newell-McGloughlin 2008; Davis and Milner 2004). Food components of dietary interest are classified into four categories (Newell-McGloughlin 2008):

1. Macronutrients: proteins, carbohydrates, fats, and fibre
2. Micronutrients: vitamins, mineral, and functional metabolites
3. Anti-nutrients: substances that block the bioavailability of nutrients e.g. phytates
4. Allergens: toxins and intolerances,

As explained by Newell-McGloughlin (2008), the first two categories represent the beneficial nutrients, whose *metabolomics* signals must compete with myriad *anti-nutrient* and *allergens* signals, such as the *free radicals* -poisons from different sources, external and internal. The latter includes toxic substances occurring from the natural process of cellular metabolism of food, which have the potential to harm the cells by altering molecules of protein and fat and by damaging DNA. Counteracting or neutralising free radicals is a vitally important task undertaken by the different antioxidants, such as phytochemicals, vitamins and microminerals, (Newell-McGloughlin 2008).

Several studies emphasise the function of nutrients like vitamins and minerals in the human body as essential co-factors for the function of enzymes and co-enzymes at

¹ Quoted by Newell-McGloughlin 2008

optimum levels, (*Murray 1996; Pizzorno & Murray 2011; Werbach [1996; 1997; 1999; 2002]; Werbach & Moss 1999; Werbach & Murray 2000; Plaskett 2004 [i-xv]; Natural Medicines Comprehensive Database [1995-2011]*). Enzymes are explained as those molecules involved in speeding up chemical reactions necessary for human bodily function, while coenzymes assist enzymes in their function, (*Murray 1996; Ballentine 1978*). According to Pizzorno & Murray, nutrients at supraphysiologic levels can induce the manufacture of enzymes, induce enzyme to become more active, or even inhibit enzyme action. The researchers refer to the example of Niacin or Nicotinic acid, a vitamin from the B-group, which has been shown to be a lipid-lowering agent when given at high dosages (2-6g /day). Its mechanism of action appears to occur via inhibition of the activity of enzymes which manufacture the Low Density Lipoprotein (LDL) in the liver (*Pizzorno & Murray 2011*).

NOTE: A more detailed account on the importance of nutraceuticals in health and disease is offered in the following chapters

PART V

PUSHING FORWARD THE BOUNDARIES OF HEALTHCARE

CHAPTER I

A NEW PHILOSOPHY IN THE PROVISION OF HEALTHCARE

The first decade of the twenty first century coincides with a number of developments, occurring in response to a worldwide awareness for the increasingly rising numbers of chronically ill people with multiple co-existing health problems, (*as discussed in previous chapters*). Agitation at different levels, academic, political, medical and social, demonstrates that the time is ripe for a new philosophy in the provision of healthcare, more capable of coping with the challenges facing the health systems of the twenty first century, and providing solutions to the problems created by the rising incidence of chronic disease. There is no doubt that this era represents a critical moment in the history of the health systems of the western world, a turning point at which important decisions need to be taken at all levels –political, social and medical. At present, adequate evidence exists to demonstrate that a new paradigm in healthcare is already widely discussed within academic and medical forums, appearing in increasing frequency as an item in the agenda of national and international conventions, (*Carlson 1979; Cooper et al 1998; Mahady 2001; Bodane & Brownson 2002; Nahleh & Tabbara 2003; Sampson et al. 2003; WHO 2003ii; Barrett et al 2004; Cushman & Hoffman 2004; Go et al., 2004; Mann et al. 2004; Vogel et al 2005; Hakobyan et al. 2006; Kaboru et al. 2006; Baer 2007; Chang et al. 2007; Di Sarsina 2007; Chen 2008; Patterson et al 2008; Tang et al. 2008; Joos et al. 2009; Stange 2009*). New wholistic, functional and biopsychosocial models of healthcare are proposed, which acknowledge the strengths of the current paradigm and at the same time offer solutions to tackle its limitations, placing the benefit of the patient at the heart of all actions. (*Engel [1977; 1980]; Guzman et al., 2002; Bland [2002; 2004]; Leichsenring 2004; Mann et al., 2004; Liska et al., 2004; Cushman & Hoffmann 2004; Jones et al., 2005; Jones & Quinn 2005; Liska 2005; Galland 2005; Hyman et al., 2005; Lamb 2005; Sudak 2005; Sult 2005; Levin et al., 2006; Di Sarsina 2007; Stange 2009; Maes & Twisk 2010; Harding et al., 2010*);

George Engel, Professor of Psychiatry and Medicine, at the University of Rochester School of Medicine, New York, -considered by scholars as the Father of the Biopsychosocial model of healthcare, (*Travakoli 2009; Barett et al., 2004*)- had already argued in 1977 that, 'all of medicine is in crisis', (*Engel 1977*). A few years later, drawing from his belief that the conceptual models around which the physicians knowledge is organised influence the way they approach their patients, he compared and contrasted the implications of the

use of *biopsychosocial* versus *biomedical* models, (Engel 1980). Within the same conceptual framework about a decade earlier, in a scientific symposium convened in the Austrian Alps in summer 1968, a number of scientists from a variety of fields, -biologists, biochemists, developmental psychologists, psychopharmacologists, humanist psychiatrists, evolutionary biologists, and systems theory experts- expressed their concerns for ‘the insufficient emancipation of the life sciences from the mechanistic concepts of nineteenth century physics and the resulting crudely reductionist philosophy’. The participants used different ways to describe life, such as observations, scientific experiments, and mathematical formulae, however the common thread was that, both biological and social phenomena, ‘are best understood as both parts and wholes’ –which wholes are also parts of other wholes- and, like molecular and physical occurrences, they evolve as events with many degrees of freedom, but with their expression restrained by the integral activity of ‘the whole in its patterned systems dynamics’, (Stange 2009ii). it is worth to remind here Jamshid Gharajedaghi’s attempt to describe the futility of trying to understand the whole by knowing only one part of it, using the parable of an elephant: A number of blind men trying to identify an elephant are positioned at a different part of the elephant and each one of them reports his findings from his perspective position, as “it is a snake”, ‘it is a pillar”, “it’s a fan”, “it’s a spear”, (Gharajedaghi 2004)

Several decades later, during the sixteenth Nobel laureate meeting in July 2010 in Germany, concerns were also expressed for the increasing dependence of modern medicine on drugs generated through chemistry and diagnostics that rely on physics. Aaron Ciechanover, who won the 2004 Nobel Prize for Chemistry for elucidating the role of *ubiquitin*¹ in degrading cellular proteins, claimed at the meeting that the boundaries of biology, chemistry and physics are artificial, ‘concepts developed from our need to teach’, (Roehr 2010). Researchers and scholars now speak: for a ‘diversification’ of the conceptual frameworks of healthcare, (Ernst et al., 2004); for wholistic ‘biopsychosocial interventions’, such as the biopsychosocial model of management of pain, (Guzman et al., 2002; Harding et al., 2010); for a transition to Genomic Medicine, (Go et al., 2004; Guttmacher & Collins 2003); and for ‘non-linear interactions’ between physiological systems and the environment, which pose a challenge to conventional bio-statistical assessments and standard reductionist models, (Patil & Giordano

¹ a small regulatory protein found in almost all tissues

2010). Paolo Roberti di Sarsina, medical doctor and expert in non conventional medicines of the Italian Ministry of Health, identifies a 'trend reversal' and a shift in emphasis from the symptom to a more general and comprehensive psychophysical well-being of the patient, (*Di Sarsina 2007*). Vay Liang Go and colleagues, from the Department of Medicine of the David Geffen School of Medicine at UCLA, Los Angeles, view the practice of medicine of the twenty first century 'on the verge of being revolutionized once again' to a new model where the role for patient responsibility grows significantly and the role of the physician 'merges into one of a healthcare team', (*Go et al., 2004*). Alan Guttmacher and Francis Collins, also medical doctors, drawing information from the National Human Genome Research Institute, National Institutes of Health, Bethesda, speak of a change in the practice of medicine under the pressure of the new knowledge of the biology of health, (*Guttmacher & Collins 2003*), while Kurt Stange, medical doctor and Editor of the Annals of Family Medicine, claiming that healthcare has not kept up with the most recent advances in biology, physics, human organisation, and systems theories, proposes 'a generalist solution', that of 'reducing fragmentation and fostering integration', (*Stange 2009*).

The political arena

'People-centeredness is not a luxury, it is a necessity'

World Health Organisation 2008

A number of policies and other forms of action within the political realm further support the fact that a new paradigm in the provision of healthcare is imminent. The World Health Organisation, acknowledging the limitations of the current paradigm in the area of treatment of chronic disease, (*WHO 2002iii*), invites Member States to formulate and implement policies and national regulations on Non-Conventional Medicines (NCMs)¹; to establish registration and licensing of NCMs practitioners; to recognise the role of Traditional Medicine (TM) providers; and to strengthen cooperation between Conventional Medicine and NCMs/TM providers, (*Di Sarsina 2007*). In Europe, a major New Health Strategy under the title *Health in All Policies* is promoted. In the European

¹ The term NCMs (Non-Conventional Medicines) is used as a preferred term to denote all Complementary and Alternative Medicines (CAM). The term CAM is only used when is included in quoted texts by other authors

Commission's 2008 *White Paper*, reference is made to a number of policies already implemented, and other programmed to be applied soon, under the pressure of increasingly emerging new challenges in the area of healthcare. These include strategies: to promote prevention, rather than treatment of illness; to promote health throughout lifespan by tackling social, economic, and environmental determinants; and to revolutionise the way health is promoted and illness is predicted, prevented, and treated, using innovative technologies in genomics, biotechnology and nanotechnology. A core value in all EU policies is *Citizen's Empowerment*, where healthcare is becoming increasingly patient-centred and individualised, with the patient becoming an active subject rather than a mere object of healthcare, with a right to 'decision-making' and 'health literacy', (EU 2007). In addition, a number of public health programmes, aiming at enhancing prevention of chronic disease by addressing the health determinants falling outside the narrow boundaries of the traditional health sector, are also promoted in collaboration with the Organisation for Economic Development and Cooperation (OECD), (OECD 2010). In April 2010 leading researchers from across Europe were invited by the European Commission to participate in the first of a series of *EU Joint Programming Initiatives* designed to address the "grand challenges" in health, which cannot be tackled by any one Member state acting alone. The aims of the *Joint Programming Initiatives* is to promote joint research programmes among member states in order to tackle the health-related, social, technological, and environmental "grand challenges" which face all European citizens. As the European Commissioner for Health stated during the first *Programming Initiative* on neurodegenerative diseases, 'existing treatments for neurodegenerative diseases are limited and mainly treat the symptoms, rather than addressing the cause', (EU 2010iii).

Furthermore various projects are designed to promote the EU policy, *Towards personalised medicine*, on the basis of the, increasingly gaining recognition, concept of *biochemical individuality*. Two recent EU workshops in Brussels with experts from a variety of academic and political fields were convened to discuss the visions and bottlenecks for the materialisation of the EU's policy for a more 'personalised medicine'. The first workshop focused on the need for radical changes in healthcare, on the basis of a new model which will prioritise prevention by determining predispositions to disease and will use therapeutic strategies 'for the right person at the right time'. The role of

genomics as an important contributor in the materialisation of *personalised medicine* was stressed by the EU experts, who expressed their high awareness of the multiple challenges facing the health sector in Europe, including ageing population, failures of blockbuster approaches, and limited knowledge of the mechanisms of disease, (EU 2010i). The second workshop's major task was the clarification of the scope for *stratification biomarkers* and the identification of bottlenecks in the process from the discovery of *biomarkers* to their use in medical practice. *Biomarkers* were defined as specific biological characteristics, which can be molecular, anatomic, physiologic, or biochemical and which allow the early diagnosis of disease and the identification of risks, as well as responses to specific therapeutic interventions, while *stratification* is the identification of groups of patients sharing similar 'biological' characteristics (biomarkers). *Biomarkers* are identified through *genomics*, by genotyping and gene expression analysis, and form an important component of personalised medicine. The experts emphasised the need for stronger cooperation between the industry and academia in obtaining a better understanding of the mechanisms of disease, avoiding the exclusive support of stratified medicine on pharmaceutical industry and the diagnostic manufacturers, (EU 2010ii)

A number of steps towards opening the boundaries of healthcare to include Non-Conventional Medicines (NCMs), that have proved effective in dealing with chronic disease, have already been taken by the European Commission. Resolution No 1206 , of Nov 4, 1999 on NCMs of the Council of Europe, states that it is possible for various forms of medicine to co-exist side by side and complement one another. The different forms of complementary and alternative therapies can be practiced by doctors of conventional medicine as well as by well-trained practitioners on non-conventional medicines, (Di Sarsina 2007). Noteworthy, some NCMs are currently legally recognised in some European countries. These include Chiropractic (Belgium, Cyprus, Denmark, Finland, Hungary, Italy, Malta, Portugal, Sweden, United Kingdom), Osteopathy (Belgium, Finland, France [MDs only], Hungary, Malta, Portugal, United Kingdom), Acupuncture (Belgium, Hungary [MDs only], Malta, Portugal), and Homeopathy (Belgium, Bulgaria [MDs only], Hungary [MDs only], Portugal). In addition, a number of Regulatory Actions for NCMs Practitioners have been promoted in Belgium (2003), Catalonia-Spain (2007), Denmark (2006), Ireland (2006-07), Netherlands (1993), Norway (2006), Portugal (2006), Sweden (2006), and United Kingdom (1993, 2000, 2007) (Di Sarsina 2007).

In the United Kingdom, the Princes Foundation for Integrated Health (PFIH), following the House of Lords Science and Technology Report on CAM¹, invited in 2000 applications from complementary healthcare groups to enter a regulation programme. The programme was supported by the King's Fund and Department of Health of the country. The result of a series of actions that followed was the establishment of a separate and independent regulatory body, in January 2008, which became known as The Complementary and Natural Healthcare Council (CNHC). A year later, in January 2009, the CNHC opened its registry for complementary healthcare practitioners. The ultimate aim of CNHC is to enhance public protection, achieved by working with the professions to maintain and improve standards. Special reference is made, in the CNHC website, to the differences between Regulatory bodies and Professional bodies, the most important being that the former 'acts in the interest of the public' whereas the latter 'acts in the interest of the profession', (CNHC 2011). In 2011 the Department of Health expresses continued support for CNHC in the following press release:

'Over the last two years the CNHC has clearly done a lot to set standards for a range of complementary healthcare disciplines and the Department of Health welcomes its continued good work. The CNHC is sponsored by the Department of Health and we recommend that where people are looking for complementary healthcare practitioners, they use someone who is CNHC-registered.'

(CNHC 2011)

In Cyprus, as it was already demonstrated, (Part III, Chapter I: Health Systems out of date), the Health Sector needs urgent modernisation since at its present state is unable to cope with the challenges posed by the ageing population, the rising incidence of chronic disease, and the increasing numbers of patients with multimorbidity (as discussed in Part I: Identifying the problem). During the interviews of the author with politicians and other key actors it was revealed that, although not major developments have yet occurred in the area of healthcare, on the basis of International and European guidelines, there exists an awareness for the imperative of a more pluralistic system of healthcare in which new

¹ According to the U.S National Library of Medicine the terms 'complementary' and 'alternative' are used interchangeably. Furthermore, Mosby's Medical, Nursing & Allied Health Dictionary defines alternative medicine as "any of the systems of medical diagnosis and treatment differing in technique from that of the allopathic practitioner's use of drugs and surgery to treat disease and injury" (Bodane & Brownson 2002). Hence in this book the term NCMs (Non-Conventional Medicines) is used as a preferred term to denote all Complementary and Alternative Medicines (CAM). The term CAM is only used when is included in quoted text but other authors

therapeutic modalities are included to complement the current system. It was generally accepted by almost all key actors that citizens should be free to exert their right to choose the treatment they prefer for their chronic health problems and to have access to more natural methods of treatment if they wish, as long as they are evidence-based and practiced by approved-by-the-government practitioners. The role of the government in safeguarding, with adequate laws and regulations, the right of citizens to make informed choices and their protection from unauthorised so-called 'therapists' was stressed. The officials of the Ministry of Health admitted that the issue of inclusion of some non-conventional therapies is recurrently brought to the table for discussion for quite some time now. However, it was made clear that any new policies should be formulated and implemented at the European Union level first. The representative of the Cypriot Doctors' Association revealed that a number of non-conventional modalities are already being examined for inclusion in the national health system, under the pressure of public demand. The Officials of the Health Insurance Organisation stated that they are aware of the worldwide trends for a new philosophy in healthcare, and seriously consider to investigate in the near future the possibility of including non-conventional medicines in the new system, provided they are practiced by practitioners adequately educated and trained to conform to European Union accepted scientific standards. However, they currently concentrate on conventional forms of healthcare only, such as offering incentives to medical doctors for further clinical examinations related to the prevention of disease at its onset. They also revealed the existence of a number of bottlenecks to the inclusion of NCMs related to the current establishment.

In the educational domain

A new paradigm of healthcare would unavoidably impose major pressures on medical education, since the physician of the twenty first century should be adequately educated and trained to deliver healthcare, focussing on prevention of disease, maintenance of wellness, and treatment, within the context of a multidisciplinary approach and the realities of the postgenomic era. The new philosophy of healthcare demands from doctors to be able to determine the risks each individual patient runs to develop specific diseases, and prevent or intervene early enough to provide maximum benefit, (*Snyderman &*

Williams 2003; Go et al., 2004). Literature abounds of academic publications and official reports which stress the need to push forward the boundaries of healthcare in order to incorporate, the so-called 'non-conventional' therapeutic modalities, into biomedical education and practice, (*Carlson 1979; Cooper et al 1998; Mahady 2001; Bodane & Brownson 2002; Sampson et al. 2003; Nahleh & Tabbara 2003; ; WHO 2003ii; Barrett et al 2004; Mann et al. 2004; Cushman & Hoffman 2004; Vogel et al 2005; Hakobyan et al. 2006; Kaboru et al. 2006; Di Sarsina 2007; Baer 2007; Chang et al. 2007; Chen 2008; DeSylvia et al., 2008; Patterson et al 2008; Tang et al. 2008; Joos et al. 2009; Ben-Arye 2010; Theodosopoulou 2010*). Adequate evidence exists that this tendency is materialising in practice. There appears a shift of focus of medical education towards more integrative multidisciplinary approaches. In particular, studies conducted in several countries, such as the United States, the United Kingdom, and Israel, demonstrate enthusiasm among students for being educated in Integrative Medicine, (*Theodosopoulou 2010; Cushman & Hoffman 2004*). In the United States, the White House advocates the inclusion of NCMs in the curriculum of medical practitioners' education as a means of improving communication and collaboration, while the majority of medical schools now offer courses on NCMs, within the context of Integrated and Biopsychosocial paradigms of healthcare (*Eisenberg et al 1998; Cushman & Hoffman 2004; Theodosopoulou 2010*). The National Centre for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (NIH), together with its recommendations for the teaching of Integrative Medicine in medical schools, focuses on specific guidelines regarding the content and approaches to such education, (*DeSylvia et al., 2008*). Researchers report that seventy five Universities, mainly through their medical schools, offer undergraduate and postgraduate courses in NCMs, including the universities of Columbia, Albert Einstein, Duke, Mount Sinai, Stanford, Arizona, Harvard, Maryland, Pennsylvania and others, (*Theodosopoulou 2010; Cushman & Hoffman 2004*). According to Eleni Theodosopoulou, Ass. Professor at the Nursing school of the University of Athens, several hospitals in the US educate doctors in NCMs, through a two-year fellowship programme within the context of their speciality, while in the hospitals of Harvard, Baltimore and the Boston hospital for children, doctors are involved in special educational and research projects on NCMs, (*Theodosopoulou 2010*).

Evidence from research outside the United States suggests that NCMs are popular throughout the whole industrialised world, (*Eisenberg et al 1998*). In response to the rising demand, already a number of universities in the European region have established NCM chairs: in Germany (*University of Witten/Herdecke, University of Duisburg/Essen,*

Technical University of Munich). In the United Kingdom a number of universities offer undergraduate and postgraduate courses in NCMs, (*University of Exeter, Middlesex University and University of Southampton*), some in combination with Conventional medicine, (*Di Sarsina 2007; Theodosopoulou 2010*). Also in the UK the Thames Valley University (University of West London) offers degrees in wholistic Nutritional Therapy as an evidence-based complementary medicine, (*TVU 2011*). Middlesex University offers Wholistic medicine (*Western Conventional medicine together with Traditional Chinese Medicine*) and postgraduate degree in Ayurveda, in cooperation with the Beijing University of China. Furthermore, the Middlesex validates the undergraduate and post-graduate courses in Nutritional Therapy of the Northern College of Acupuncture (*NCA 2011*) and of the Centre for Nutrition Education and Lifestyle Management, (*CNELM, 2011*). Herfordshire also offers postgraduate degrees in Acupuncture, (*Theodosopoulou 2010*). Researchers claim that an increasingly rising number of medical students and physicians worldwide express their interest in studying NCMs. In some EU countries doctors can obtain specific additional qualifications in NCM issued by their national medical associations (*Austria, Germany, Latvia, Romania*). In Germany 10% of all working medical doctors hold an additional NCMs qualification, (*number increased by 125% in 8 years*), with 5000 hospital doctors having NCM qualifications, (*mainly chiropractic and naturopathy*), (*Di Sarsina 2007*). Theodosopoulou refers to a study by Strange et al., (2008) which demonstrates that 51% of doctors apply NCMs in Germany, (*Theodosopoulou 2010*). Reference is also made to a British survey which demonstrated that 32% of 2875 members and fellows of the UK Royal College of Physicians practice NCMs, while 41% of them refer patients to NCMs, (*Ben-Arye 2010*). According to Theodosopoulou (2010), 80% of doctors and pharmacists in the UK participate in special educational programmes in NCMs offered by several UK hospitals. These include programmes in nutrition and herbal supplements, (*Theodosopoulou 2010*). In total, more than 130,000 doctors in the European Union have taken training courses in a particular NCM therapy; (*Di Sarsina 2007*). Worth noting is that in some countries the national medical associations are in favour of statutory regulation of NCM for physicians (*France, United Kingdom, Greece, Italy, Spain*), (*Di Sarsina 2007; Crispin et al., 2010*). In Greece the National Centre for CAM, member of the National Institute for Health, in recognition of the need for further education on NCMs subsidises a five-year programme of education of health professionals, (*Theodosopoulou 2010*).

The public response

It appears that Non-Conventional Medicines (NCMs) continue to gain popularity, 'even as Biomedicine continues to break frontiers of treatment, through advances in technology, physiology, and genetics', (*Cushman & Hoffman 2004*). A volume of research shows that at the same time with the widespread problematisation on the imperative of radical changes in the provision of healthcare, there appears an unprecedented burgeoning of Non-Conventional Medicines (NCMs) in the western world, revealing that the public is already applying in practice a paradigm shift in medicine. Literature demonstrates a high prevalence of NCMs use by the public, (*Carlson 1979; Eisenberg et al., 1998; Vickers & Zollman 1999; Cooper et al. 1998; Risberg et al. 1999; Mahady 2001; Bodane & Brownson 2002; Nahleh & Tabbara 2003; Casileth & Deng 2004; Mann et al. 2004; Barret et al. 2004; Hakobyan et al. 2006; Kaboru et al. 2006; Chang et al. 2007; Baer 2007; Di Sarsina 2007; Kennedy et al., 2007; Patterson et al. 2008; ; Avogo et al. 2008; Joos et al. 2009; Theodosopoulou 2010*). According to Bodane & Brownson (2002), mounting evidence shows that Conventional medicine does not offer all the answers to preventing illness and curing disease and consumers increasingly demand alternative options. This has led to the rapid increase of the use of NCMs in the United States, (*Bodane & Brownson 2002*). David Eisenberg, medical doctor and researcher in Beth Israel Deaconess Medical Centre and his colleagues from the Harvard Medical School, in Boston, in a follow-up National Survey which was conducted in the United States in 1991 and 1997, with a total of 1539 and 2055 adults respectively, observed a 380% increase in the use of herbal remedies and a 130% increase in high-dose vitamin use, while 1 in 5 individuals taking prescription medications also was taking herbs and high-dose vitamin supplements. Most interestingly, the researchers found that 96% of 1997 respondents, who saw a practitioner of alternative therapy for a principal condition, also saw a medical doctor during the prior 12 months, (*Eisenberg et al 1998*). Bruce Barret, medical doctor and researcher at the Department of Family Medicine in the University of Wisconsin Medical School, drawing from Eisenberg et al (1993), refers to 425 million yearly reported visits to NCMs practitioners compared to 388million visits to primary care physicians, (*Barrett et al., 2004*).

Researchers demonstrate that 63%-83% of breast cancer patients in the United States use at least one type of NCMs, (*Di Gianni et al., 2002*), while a high proportion use dietary supplements, (*Di Gianni et al., 2002; Nahleh & Tabbara 2003*). Reasons reported are, boosting the

immune system (63%), increase quality of life (53%), prevent metastasis (42%), provide a feeling of control over life (38%), and aid conventional medical treatment (38%), (*Di Gianni et al., 2002*). In fact, several studies demonstrate favourable results from NCMs use including, improved survival, better pain control, reduced anxiety, improvement in coping strategies, and significant efficacy in treating nausea and vomiting in serious chronic disease, (*Nahleh & Tabbara 2003*). Most recent reports present 30-50% of Americans utilizing some form of NCM for a variety of clinical conditions, such as chronic pain, cancers survivors, functional bowel disorders, stroke, and depression, (*DeSylvia et al., 2008; Vogel et al., 2005*). Chang et al., (2007) in a review of eighteen studies conducted—most of them within conventional hospitals- in nine countries from different parts of the world, during the period 2000 and 2006, found that nearly half (45.53%) of people with diabetes have used some form of NCMs in conjunction with conventional medicines, (*Chang et al., 2007*). Brenda Mears medical academic, from the Department of Paediatrics of the University of Texas at South-western Medical School, Dallas, refers to the 2007 National Health Interview Survey conducted by the Centres for Disease Control and Prevention's National Centre for Health Statistics, which demonstrates 38.2% of adults and 11.8% of children, used some type of NCM in the preceding 12 months. The researcher claims that in some groups the rates of NCMs use range as high as 70% and surveys show also that 87% of paediatricians were asked by their patients or parents about NCM. Interestingly, about 66% of patients do not tell their physicians that they use NCMS, with a significant percentage of the cost for this undertaken by the family, (*Mears 2010*).

In Europe, public opinion polls and consumers' association surveys demonstrate high prevalence rates of NCMs use, (*Eisenberg et al 1998; Risberg et al., 1999; Di Sarsina 2007*). In a survey of 172 physicians, 374 nurses and 96 clerks in northern Norway hospitals, 56% demonstrated a positive attitude towards NCMs, while 12% of physicians, 32% of nurses and 46% of the clerks reported as being using NCMs, (*Risberg et al., 1999*). According to Di Sarsina (2007), 40-70% of the European population has used some form of NCM; in the United Kingdom 83% of doctors refer for NCM treatments, 66% have significant interest in NCMs, and 20-40% provide NCM treatment (chiropractic, acupuncture, homeopathy); in Germany 70% of GPs support NCMs (*Di Sarsina 2007*). Educational level and socioeconomic status appear to be strong predictors of the use of NCMs. Research demonstrates a

higher prevalence of NCM use among college and university graduates, (*Chang et al. 2007; Kennedy et al. 2007; Lee et al. 2002; Eisenberg et al. 1998; Avogo et al. 2008*).

In Cyprus the results of the research by the author verified the worldwide awareness for a more pluralistic health system and demonstrated that patients with multiple chronic health problems occurring simultaneously are the rule rather than the exception (see Part III, Chapter II: Patient-oriented vs disease-oriented healthcare). This finding appears to be related with other findings of the research which showed that Cypriots follow the worldwide trend towards the materialisation of a paradigm shift in the provision of healthcare. It was particularly demonstrated that the Cypriot public frequently resorts to non-conventional therapies, often in conjunction with their medical treatments, in an effort to find solutions to their multiple chronic health problems. In Table 5: Age, Income, Education, and Treatment Correlations below, pharmaceutical treatment was shown to be significantly positively correlated at the 0.01 level(2-tailed) with: special dietary treatment (0.291**), nutritional supplement treatment (0.144**), and other NCMs (0.171**) and at the 0.05(2-tailed) with homoeopathy (0.106*),

TABLE 5: AGE, INCOME, EDUCATION AND TREATMENT CORRELATIONS

	Age	Education	Monthly family income	What kind of treatment do you usually follow: (drugs)	What kind of treatment do you usually follow: (special diet)	What kind of treatment do you usually follow: (food supplements)	What kind of treatment do you usually follow: (homeopathy)
Education	- 0.493**						
Monthly family income	- 0.237**	0.262**					
What kind of treatment do you usually follow: (drugs)	0.183**	- 0.153**	0.076				
What kind of treatment do you usually follow: (special diet)	0.123**	0.019	0.152**	0.291**			
What kind of treatment do you usually follow: (food supplements)	- 0.020	0.112*	0.152**	0.144**	0.456**		
What kind of treatment do you usually follow: (homeopathy)	0.002	0.036	- 0.004	0.106*	0.157**	0.168**	
What kind of treatment do you usually follow: (other)	0.074	0.002	0.012	0.171**	0.265**	0.181**	0.304**
** Positive Correlation significant at the 0.01 level (2-tailed).							
* Positive Correlation significant at the 0.05 level (2-tailed).							
** Negative Correlation significant at the 0.01 level (2-tailed)							

In the analysis of Case Studies from the author's Clinical Practice, in Table 6: Use of Non-Conventional therapies before Nutritional Treatment: 24% of the randomly selected cases stated that they had a non-conventional treatment in the past, and 68% used in the past, or use now, nutritional supplements (vitamins, minerals, herbs, etc) for a specific health

problem; and 54% used some kind of nutritional supplements without specialist advice, while 14% stated that their doctor prescribed nutritional supplements (mainly iron, calcium and multivitamins

TABLE 6: USE OF NON CONVENTIONAL THERAPIES BEFORE NUTRITIONAL TREATMENT
(Percentage of 50 randomly selected cases from clinical practice)

TYPE OF NON-CONVENTIONAL THERAPY	percentage
Used supplements for a specific health problem	68%
Used supplements without advice	54%
Used supplements (mainly iron, calcium and multivitamins) with doctor's advice	14%
Had other Non Conventional medicine treatments	24%

An important finding was the identification of the level of socioeconomic status as a strong predictor of the use of Non-Conventional Medicine use, confirming literature. Cypriots with high education and high income appear more likely to use complementary and alternative, rather than conventional, therapies for treatment. A significant negative correlation between level of education and use of pharmaceutical means (-0.153^{**}) at the 0.01 level (2-tailed) was found, as well as a significant positive correlation ($+0.112^*$) at the 0.05 level (2-tailed) between educational level and use of nutritional supplements, for treatment of a specific health problem (see previous page: Table 5: Age, Income, Education, and Treatment Correlations). In addition a significant positive correlation was evident between the level of income of one's family and the extent of use of special dietary treatment ($+0.152^{**}$) at the 0.01 level (2-tailed), and/or nutritional supplements ($+0.152^{**}$) at the 0.01 level (2-tailed), for treatment of a health problem (Table 5: Age, Income, Education, and Treatment Correlations). Drug addiction is also very high at low educational levels, gradually decreasing and approaching zero at the college and university levels of education, as demonstrated (Table 7: Education and Health Problems).

TABLE 7: EDUCATION AND HEALTH PROBLEMS

HEALTH PROBLEM	ELEMENTARY	HIGH SCHOOL	COLLEGE/ UNIVERSITY
STRESS	17.0%	17.3%	17.2%
HEADACHES	9.6%	9.5%	13.9%
HYPERTENSION	23.4%	8.6%	2.6%
ALLERGIES	7.4%	9.4%	8.6%
CHOLESTEROL	12.8%	7.1%	5.2%
ARTHRITIS	17.0%	4.7%	5.2%
INSOMNIA	7.4%	5.8%	6.0%
BOWEL PROBLEMS	8.5%	4.7%	6.9%
OBESITY	10.7%	4.7%	3.5%
CARDIOVASCULAR	18.1%	2.7%	1.7%
OTHER PROBLEMS	8.6%	3.6%	6.1%
GYNAECOLOGICAL	7.5%	4.3%	5.2%
STOMACH PROBLEMS	6.4%	3.9%	4.3%
DIABETES	13.8%	2.4%	0.9%
CONSTIPATION	2.1%	4.3%	6.0%
DEPRESSION	3.2%	5.1%	2.6%
OSTEOPOROSIS	12.9%	1.6%	1.7%
SKIN PROBLEMS	1.0%	4.3%	3.4%
ASTHMA	3.2%	2.0%	4.3%
THYROID PROBLEMS	3.5%	2.2%	2.8%
DRUG ADDICTION	7.6%	1.6%	0.0%
CHOLELITHIASIS	4.3%	2.0%	1.8%
FUNGI	3.2%	1.6%	3.5%
CANCER	3.0%	2.2%	2.4%
KIDNEY DISEASES	2.1%	1.2%	1.7%
URIC ACID	2.0%	0.4%	0.0%
PROSTATE	0.0%	0.4%	0.0%

The analysis of Case Studies from the author's Clinical Practice also supported the socioeconomic element of NCMs use. As shown in Table 8: Educational level of patients from Clinical Practice compared to Survey population sample, the majority of those who visited the clinic for a nutritional treatment belong to the higher educational groups. Analytically, 56.7% of the 350 patients who visited the clinic between the years 2005 and 2008 and had at least one consultation after receiving their treatment, were college or university graduates, 40.1% have secondary education, and only a 3.2% were of primary

education. Taking into consideration the distribution of the whole adult population of Cyprus into different educational levels as established by the Survey, -university/college 24.9%, high school 54.8%, and elementary 20.2%-, it is obvious that the proportion of persons with higher education who visited the clinic for a nutritional treatment was in fact more than double compared to their proportion in the whole population,

TABLE 8: EDUCATIONAL LEVEL OF PATIENTS FROM CLINICAL PRACTICE COMPARED TO SURVEY POPULATION SAMPLE

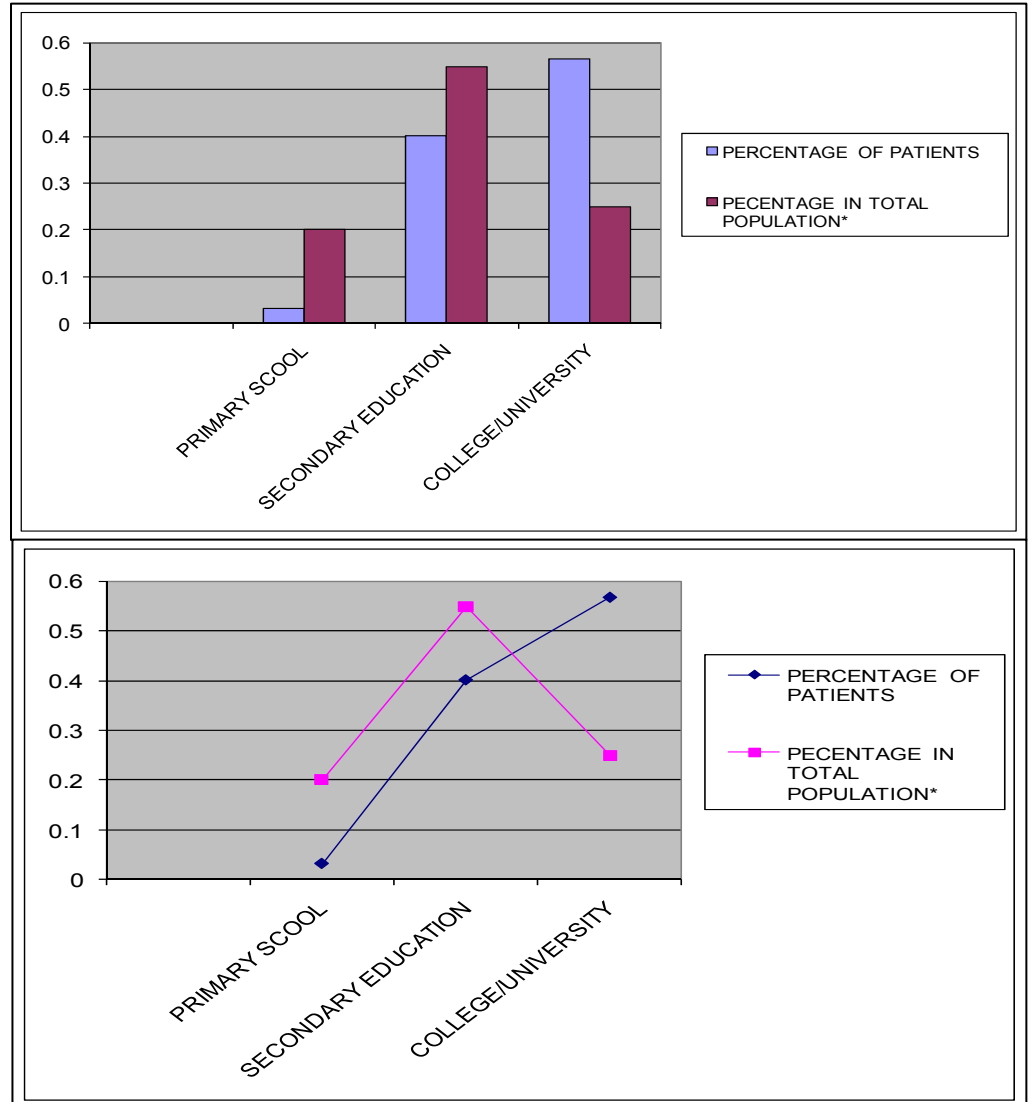
EDUCATIONAL LEVEL	PATIENTS WHO VISITED THE CLINIC FOR NUTRITIONAL THERAPY*	PERCENTAGE IN TOTAL POPULATION**
Primary school	3.2%	20.2%
Secondary education	40.1%	54.8%
College/university	56.7%	24.9%
TOTAL	100.0%	100.0%

***Based on 350 cases who came back for at least one consultation after receiving their prescription**

**** Based on the survey**

It is worth noting that in most cases, the appointment for a consultation at the clinic for those that belong to the lower educational levels was arranged by a close relative (offspring, brother, etc) with higher education. This strengthens further the case for the education-alternative medicine positive correlation.(A graphical representation of the table above as shown in Chart 13: Educational level of patients from Clinical Practice compared to Survey population sample)

**CHART 13: EDUCATIONAL LEVEL OF PATIENTS FROM
CLINICAL PRACTICE COMPARED TO THE SURVEY
POPULATION SAMPLE**



CHAPTER II

NEW MODELS OF HEALTHCARE PROPOSED

A significant part of the scientific community of the twenty first century appears adequately prepared to adopt and promote the principles of the new paradigm. A volume of scientific publications present the views of medical and other academic scholars and researchers on how the new model of healthcare should be, using terms such as 'Integrated', 'Biopsychosocial', 'Nutrigenomic', 'Functional', and 'Wholistic', (Engel [1977; 1980]; Guzman et al., 2002; Bland 2002; Leichsenring 2004; Mann et al., 2004; Bland 2004; Liska et al., 2004; Cushman & Hoffmann 2004; Jones et al., 2005; Jones & Quinn 2005; Liska 2005; Galland 2005; Hyman et al., 2005; Lamb 2005; Sudak 2005; Sult 2005; Levin et al., 2006; Di Sarsina 2007; Stange 2009; Maes & Twisk 2010; Harding et al., 2010;). A closer look at these models allows no doubt that they all share the same philosophy of healthcare: approaching the patient, through various multidisciplinary approaches as a whole, biochemically distinct, functional entity, in constant interaction with his/her environment. In fact, they are all integrated models, since they all advocate some form of integration between conventional and non-conventional approaches to healthcare with Biomedicine remaining a basic component in all.

Integrated medicine

The Consortium of Academic Health Centres for Integrative Medicine (CAHCIM), which gathers more than thirty universities, has formulated the following definition of Integrative Medicine:

'Integrative Medicine is the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to achieve optimal health and healing'

Quoted in:

The social demand for a medicine focused on the person

*By Paolo Roberti Di Sarsina MD
Expert in Non Conventional Medicines
of the Italian Ministry of Health*

According to Eran Ben-Arye, from the Complementary and Traditional Medicine Unit of the Department of Family Medicine, Faculty of Medicine, at the Technion-Israel Institute of Technology in Haifa, a paradigm shift in the provision of healthcare is already occurring during the last three decades, from a disease-centred to a more wholistic patient-centred approach and, at the same time a shift of the terminology and concept of non-conventional medicines towards mainstream medicine. The term integrative medicine is used both to describe the merging of non-conventional medicines within Biomedicine and to identify 'a higher-order system, or systems, of care that emphasizes wellness and healing of the entire person', (Ben-Arye 2010). Grone & Carcia-Barbero (2001), officials of the World Health Organisation, in a paper outlining the need of Integrated Care from a European perspective, provide a theoretical meaning of Integrated Care and its strategies and summarise the programmes of WHO, which aim to support European countries to improve their health services. The officials, drawing from evidence for an increasing demand for healthcare reforms, in view of the fact that *expansion of life expectancy* goes hand in hand with *expansion of morbidity*, they stress the imperative of integrated forms of healthcare, capable of handling the proliferation of multiple disorders with functional, psychological and social dimensions. New patterns of chronic morbidity require more complex forms of treatment than those currently provided in acute hospitals, which among other things, should involve multi-professional teams and institutions. The experts identify several definitions of Integrated Care, however the one more applicable to the context of European health systems, is based on the conception of Integration as a *unity for health*, which is 'the act of making a whole out of parts; the co-ordination of different activities to ensure harmonious functioning' and it is offered as follows:

'Integrated Care is a concept bringing together inputs, delivery, management and organisation of services related to diagnosis, treatment, care, rehabilitation and health promotion. Integration is a means to improve the services in relation to access, quality, user satisfaction and efficiency'

Quoted in:

*Integrated Care: a position paper of the
WHO European office for Integrated health care services*

By Oliver Grone, Public Health, Research Assistant
& Mila Garcia-Barbero MD, Head of Office
Barcelona

Ralf Snyderman, Chairman of the Association of American Medical Colleges in Washington and Sanders Williams from the Department of Medicine of the Duke University Medical Centre in Durham (2003), claim that the transformation of medicine already materialises on the breakthroughs in science and know-how occurring a century after its last transformation, when science was introduced into the practice of medicine in the early 20th century. The new models will be based on prospective health care which will have the potential to determine the risk of individuals to develop specific diseases, to detect the disease's earliest onset, and to prevent and intervene early enough to provide maximum benefit, (*Snyderman & Williams 2003*). Along the same lines, Golda Ginsburg & Hutington Willard from the Duke Institute for Genome Sciences and Policy, at Duke University in Durham, North Carolina, claim that the advances in genomic medicine of the last decade provide the tools that enable more informed and effective approach to patient care, with precise prediction and treatment of disease and medical decision making, on the basis of detailed information on each person's unique clinical, genetic, genomic and environmental information. The researchers draw the attention of policy makers in the health care sector for the need to develop, standardise and integrate several important tools, such as health risk assessment, family health history, and clinical decision support for complex risk and predictive information, into health systems and clinical workflows (*Ginsburg & Willard 2009*). Douglas Mann, medical academic at the Department of Neurology of the University of North Carolina School of Medicine, and colleagues, speak of 'new trends of the twenty first century' towards more pluralistic health care systems, based on different conceptual frameworks, which are coming to challenge the current system in the provision of healthcare that dominated the twentieth century. The researchers use the terms 'integrated' or 'integrative' to describe approaches which, 'while retaining many of the characteristics and strengths of Biomedicine, also embrace the more wholistic concepts and methods of complementary and alternative practices' (*Mann et al. 2004*).

Within the same conceptual framework, Cushman and Hoffman (2004) argue that there is a need and room for both conventional medicine and non-conventional medicines in addressing contemporary health issues, a concept gaining recognition among healthcare practitioners, (*Cushman & Hoffman 2004*). E. Ernst, medical doctor and Professor at the

Department of Complementary Medicine of the Postgraduate Medical School at the University of Exeter in the UK, provide a 'positive', as they call it, definition of the totality of non-conventional medicines, which is now been adopted by the Cochrane Collaboration's 'field' in complementary and alternative medicine (CAM): 'CAM is diagnosis, treatment, and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual frameworks of medicine' (*Ernst et al 2004*). Di Sarsina (2007) suggests that modern medicine should take advantage of the educational and therapeutic potential of complementary medicines, replacing the old outdated conception of health as 'absence of illness', for the new World Health Organisation definition of health as 'the psychophysical well-being'. According to the medical expert, while the Conventional Medical Doctrine led to great undeniable medical progresses in the end of the nineteenth century, Non-Conventional Medicines (NCM) represent a development of medical knowledge and practice, useful to meet the twenty first century requirements, (*di Sarsina 2007*). Similarly, Stange (2009i) proposes a new medicine which, together with focused laboratory research, necessary to understand the behaviour of discrete treatments for discrete diseases, will consider the behaviour of multiple interacting factors which will 'advance the health of whole people within communities'. According to the psychiatrist, the new model of healthcare will put an end to the underlying, critical, and underappreciated problem of the current paradigm: fragmentation' or 'brokenness' which he explains as 'the focusing and acting on the parts without adequately appreciating their relation to the evolving whole, (*Stange 2009i*).

Biopsychosocial medicine

The incorporation of a psychosocial element into traditional biomedical approaches to the prevention and treatment of chronic disease is frequently now proposed by researchers and healthcare practitioners, (*Engel [1977;1980]; Guzman et al., 2002; Jones et al., 2002; Borrell-Carrio et al., 2004; Lane et al., 2005; Aujoulat et al., 2007; Quirke & Quadilliere 2008; Weiner 2008; Travakoli 2009; Harding et al., 2010; Van Weel & Rosser 2010*). Chris van Weel & Walter Rosser, medical academics at the Departments of Family Medicine, the former of the University Medical Centre Nijmegen

in Netherlands and the latter at the Department of Family Medicine of the Queens University in Kingston, Ontario, Canada, emphasise on the need to include a mixture of methods and approaches in order to handle the complexity of family medicine research. Considering the biopsychosocial reality of patients and their families with their values and expectations, as well as their socioeconomic and cultural determinants of health, will greatly improve the problem solving capacity of the family physician, (*Van Weel & Rosser 2004*). A study carried out by William Clark and colleagues, medical doctors and researchers, on the importance of physician-patient talk on outcomes of care, provided adequate evidence to support criticisms for deficient education in psychosocial medicine and ineffective doctor-patient interaction. The researchers particularly highlight the significance of medical interviewing and the role of interview-related variables as determinants of improved biomedical and disease outcomes, (*Clark et al., 1999*). According to Francesc Borrell-Carrio, medical academic at the Department of Medicine of the University of Barcelona in Spain, and colleagues, the Biopsychosocial model is not a new paradigm in the sense of a new set of scientific laws, as the term 'paradigm' would suggest; it is both 'a philosophy of clinical care', related to the understanding how suffering, disease, and illness are influenced by multiple levels of organisation, from the societal to the molecular, and 'a practical clinical guide' which is used to understand the patient's subjective experience in order to formulate an accurate diagnosis and prescribe the necessary treatment, (*Borrell-Carrio et al., 2004*). Jean-Pierre Unger, medical academic and researcher at the Department of Public Health of the Prince Leopold Institute of Tropical Medicine in Antwerp, Belgium and colleagues, emphasise the need for a biopsychosocial, patient-centred care, on the basis of the Hippocratic ideals, where patients are viewed as 'persons' rather than as 'cases' and family and community healthcare are at the core of services. The researchers stress also the importance of medical educational programmes to go beyond the biomedical paradigm and include psychosocial care in the training of health professionals, (*Unger et al., 2006*). Common health problems, as is pain, are increasingly being treated as biopsychosocial phenomena through integrated, multidisciplinary approaches, rather than through bio-medical intervention considered historically as having an organic basis, (*Harding et al., 2010; Guzman et al., 2002*). According to Geoffrey Harding from the Peninsula Medical School (Primary Care), in Exeter, UK, and colleagues, chronic pain is approached as being caused by the 'dynamic interaction between patient's

physical, psychological and social influences shaping their responses to pain'. Key elements of the Biopsychosocial model include elements of cognitive/behavioural principles and physical approaches, such as exercise, and other lifestyle parameters, (Harding et al., 2010).

The United States Institute of Medicine, in a 2008 Report on how to improve medical education through enhancement of the behavioural and social science content of medical school curricula, highlights the fact that about half of all deaths in the United States are linked to behavioural and social factors. Acknowledging that these factors can be changed, and the fact that there are methods available to facilitate these changes, physicians will be able to provide appropriate interventions to improve the health of their patients if, of course, have already been equipped with the knowledge and skills for these methods. In view of this imperative, the Institute convened the Committee on Behavioural and Social Sciences in Medical School Curricula to provide the National Institutes of Health and the Robert Wood Johnson Foundation with a critical analysis of the behavioural and social sciences in medical schools at present. The Committee, based on the unavailability of adequate information on the issue, recommended the development of a new national behavioural and social sciences database and proposed an integrated behavioural and social science curriculum for medical students, that extends throughout the four years of medical school. The six domains identified for inclusion were: mind-body interactions in health and disease, patient behaviour, physician role and behaviour, physician-patient interactions, social and cultural issues in health care, and health policy and economics, (IOM 2008).

Medical scholars credit the genesis of the Biopsychosocial model to Professor of Psychiatry and Medicine George Engel, who wrote in 1977 *'The Need for a New Medical Model: A challenge for Biomedicine'*, as a counterpoint to the increasing focus of medical schools on molecular biology, (Travakoli 2009; Barrett et al., 2004). During the seventies, Engel had criticised Biomedicine for leaving no room within its framework for the social, psychological, and behavioural dimensions of illness, claiming that the biomedical model of disease which dominates medical practice, is based exclusively on molecular biology which assumes disease to be 'fully accounted for by deviations from the norm of

measurable biological (somatic) variables'. Engel described the conventional medical model as a model of illness in which taxonomy of diseases progresses from symptoms to clusters of symptoms, to syndromes, and finally to diseases with specific pathogenesis and pathology. Recognition and palliation of symptoms leads to characterisation of a specific disease with known aetiology and pathogenesis and for which a rational and specific treatment is given. Engel's biopsychosocial model was proposed as 'a blueprint for research, a framework for teaching, and a design for action in the real world of healthcare'. Citing evidence of a tendency to improve the communication across scientific disciplines and to mitigate the wholist-reductionist dichotomy, he claimed that there are ways to make wholistic approaches more amenable to the scientific inquiry and conceptualisation through general systems theory and suggested that it should become part of the education of physicians and medical scientists, (*Engel 1977*). A few decades later, in another article in the *American Journal of Psychiatry*, Engel presented his findings on the implications of the use of a Biopsychosocial model for the study and care of a patient with acute myocardial infarction, (*Engel 1980*).

A volume of studies are coming in the last decade to confirm the theory supporting the Biopsychosocial model of medicine. Jorge Guzman medical academic and colleagues from the Faculty of Medicine of the University of Manitoba, in Canada, aiming to assess the effect of multidisciplinary biopsychosocial rehabilitation on pain, function, employment, quality of life, and global assessment outcomes in subjects of chronic disabling low back pain, as compared with a non-multidisciplinary control intervention, they reviewed a volume of randomised controlled trials with a total of 1964 patients, using the comprehensive search strategy recommended by the Back Review Group of the Cochrane Collaboration. The results demonstrated that intensive multidisciplinary bio-psychosocial rehabilitation with a functional restoration approach improved function and pain when compared with inpatient or outpatient non-multidisciplinary treatments, (*Guzman et al., 2002*). Richard Lane, medical academic and researcher, from the Department of Psychiatry of the University of Arizona, Tucson, Arizona and colleagues, in an attempt to verify previous studies demonstrating that emotional stress is a trigger of sudden death amongst patients with Coronary Heart Disease, they conducted a study in which 25 patients, survivors of idiopathic ventricular fibrillation, were compared with 25 patients with documented

coronary heart disease who had sustained myocardial infarction or unstable angina requiring angioplasty without cardiac arrest. The study found that severe or moderate psychological stress was more frequently reported, both in the 6 months and in the 24 hours preceding cardiac events in survivors of Idiopathic Ventricular Fibrillation than among survivors of an acute coronary event. The researchers believe that their findings support the importance of biopsychosocial approaches in patients with cardiovascular disease, (*Lane et al., 2005*). John Vogel, medical cardiologist and his colleagues at the American College of Cardiology Foundation Task Force, in a document commissioned by the American College of Cardiology Foundation (ACCF) and reviewed by a number of medical associations, provide a perspective on the current state of Non-Conventional Medicines (NCMs), specifically related to cardiovascular diseases, and inform and guide clinical practice on potential utilisation of NCMs by cardiovascular practitioners. The researchers claim that compassion enhanced by science must be the guiding principles for integrated NCMs into conventional medicine taking into consideration the latter's commitment to caring for patients on a physical, mental, and spiritual level. The medical experts acknowledge the fact that NCMs are widely used by patients, including those with cardiovascular problems, (*Vogel et al., 2005*)

Within the context of a biopsychosocial approach, Aujoulat et al., (2007), aiming to examine how the term 'empowerment' has been used in relation to the care and education of patients with chronic conditions over the past decade, they analysed fifty-five articles, using a qualitative method of thematic analysis. Their findings supported a personalised approach where, the goals and outcomes of patient empowerment should neither be predefined by health-care professionals, nor restricted to particular disease and treatment-related outcomes, but they should be discussed and negotiated with every patient on the basis of their own particular situation and life realities, (*Aujoulat et al., 2007*). According to B. K. Weiner from the Weill Cornell Medical College, Department of Orthopaedics, The Methodist Hospital, in Houston, Texas, the Biopsychosocial model has afforded significant advances by 'placing the disease back into the patient' and by approaching illness as experienced within the patient's unique biological, psychological, social, and economic environment. The findings of Weiner's evaluation of the general theory of the Biopsychosocial model and literature as the model is applied to spine care,

demonstrate an important strength of the Biopsychosocial model: that it reminds that different clinical decisions have to be taken for patients with similar medical health problems, according to their complex social conditions, (*Weiner 2008*).

Functional Medicine

Jeffrey Bland, founder and Board Chair of the Institute for Functional Medicine, referring to a 2005 article in the *New England Journal of Medicine*, which points out that, in spite that the United States spends twice as much capita for health as any other country children being born today may be the first generation in the history of the United States with a lower life expectancy than their parents, presents Functional Medicine as the most effective response for a new model of care. According to Bland, Functional Medicine was born out of collaborations among clinicians of many different disciplines and specialties, including clinical laboratory scientists, health sciences researchers, health educators, health policy professionals, and healthcare administrators to address the rising incidence and cost of chronic disease, (*Bland 2005*). Functional medicine integrates Biomedicine with the complementary and alternative medicines, creating a focus on prevention through: nutrition, diet, and exercise; use of the latest laboratory testing and other diagnostic techniques; and prescribed combinations of drugs and/or botanical medicines, supplements, therapeutic diets, detoxifications programmes, or stress-management techniques, (*IMF 2008*). The Functional Medicine's medical model views disease as arising out of dysfunction, rather than from infectious organisms or inborn errors of metabolism, (*Bland 2005, p.iv*). A major target of Functional Medicine is to identify, using a patient-centred approach, the biomarkers of function that can be used as indicators of the onset of disease, and also as markers of the success of interventions. It attributes great importance to environmental insults for the development of chronic conditions and to the implications from the mind-body interaction, as approached by psychoneuroimmunology. Bland locates the origin of the concept of function in Dr. Hans Selye's pioneering work on the functional endocrinology of stress and its relation to various chronic diseases, such as peptic ulcer, hypertension and heart disease. Selye's functional model focused on dysfunction, rather than invading infectious organisms or

inborn errors of metabolism, based on the concept that 'it is more important to know what kind of person has the disease, than what disease the person has', (Bland 2005).

Along the same lines, Jones et al., (2005) define Functional Medicine as a dynamic approach to assessing, preventing, and treating complex chronic disease, through identification and amelioration of the dysfunctions in the physiology and biochemistry of the human body. According to the functional theory, chronic disease is almost always preceded by a lengthy period of declining function in one or more of the body's systems. Lifelong interactions among our environment, lifestyle, and our genetic predispositions are key factors that result in these dysfunctions which include:

- Hormonal and neurotransmitter imbalances
- Oxidation-reduction imbalances and mitochondriopathy
- Detoxification and biotransformation imbalances
- Immune imbalances
- Inflammatory imbalances
- Digestive, absorptive, and microbiological imbalances
- Structural imbalances from cellular membrane function to the musculoskeletal system

(IMF 2008: Jones et al., 2005)

Each patient, for Functional Medicine, is a unique, complex, and interwoven set of influences on intrinsic functionality which set the stage for the development of disease or the maintenance of health, (Jones et al., 2005, pp.5-6). Jones sums up the functional theory into six fundamental principles:

1. Biochemical individuality related to the individual variations in metabolic function that derive from genetic and environmental differences among individuals
2. Patient-centred medicine which emphasises patient-care rather than disease care
3. Dynamic balance among internal and external factors in a patient's body, mind, and spirit
4. Web-like interconnections of internal physiological factors rather than individual systems functioning autonomously
5. Health as a positive vitality -not merely the absence of disease
6. Promotion of organ reserve explained as enhancing health span, not just life span,

(Jones 2005, p.6).

According to Liska (2005), Functional medicine relies on science and requires an active interaction with the scientific literature, requiring from the clinician to keep up with new findings in human physiology and biochemistry. Within the context of an analytical and integrative model it incorporates scientific findings into a patient-centred approach, (Liska 2005). *Homeodynamics*, a basic principle of Functional Medicine, describes a range of continuously occurring metabolic and physiologic activities that enable an individual to adapt to changing circumstances, stresses and experiences. This is in contrast to the universally accepted *Homeostasis*, which describes the balance of interconnected components that keep all physical and chemical parameters of the body relatively constant, (Levin et al., 2006). According to Levin et al (2006) the strength of the Functional model of medicine lies in that it does not require a change in basic clinical orientation of the healthcare practitioner. It can be incorporated into the everyday practice of all healthcare practitioners regardless of training and specialty, as it capitalizes not only on the accomplishments of basic and applied science but also on the strengths of specialty fields and specialized approaches to clinical practice. Medical doctors, chiropractors, naturopaths, nutritionists, dieticians, homeopaths, acupuncturists, Ayurvedic physicians are included in the long list of diversely trained practitioners that can enhance their practice by incorporating the principles of Functional medicine, (Levin et al., 2006).

PART VI

NUTRITIONAL MEDICINE

PRACTICE

IN THE

NEW PARADIGM

CHAPTER I

NUTRITIONAL SCIENCE: A science without borders

The application of Nutritional Science as a therapeutic modality, titled Nutritional Medicine, or Nutritional Therapy, occurs within the context of the revolutionary developments in the science of medicine and biology, and particularly in genetic science. The unprecedented advances in genomics of the last two decades have verified and further strengthened the principles of *biochemical individuality, functionalism and wholism*, which provided the epistemological basis of Wholistic Nutritional Medicine at its inception. The volume of evidence presented in the previous Parts on the rising incidence of chronic disease, and the imperative for more integrated, biopsychosocial and functional approaches to the provision of healthcare attest to an upgraded and enhanced role of Nutritional Medicine as a vital partner of the emerging twenty first century paradigm.

Apparently, the time is ripe for what was appositely defined by Zeisel and colleagues from the Long Range Planning Committee of the American Society for Nutritional Sciences, as 'scientific integrationism', where the Science of Nutrition can act as a 'cross-disciplinary, integrationist life science'. An increasingly rising volume of evidence testifies to the fact that the science of nutrition has the potential to integrate scientific knowledge from various disciplines, and promote it at the different levels of life interaction, from cell and molecule to whole body and then to populations, on the basis of its potential as a cross-disciplinary, integrationist life science, (*Zeisel et al., 2001*). According to the researchers, while the sciences of Physiology, Pharmacology, and metabolic and nutritional Biochemistry, focusing exclusively on molecular events and using reductionist scientific approaches and new molecular techniques, have managed to generate incredible knowledge into human Biology, Nutritional Science offers the skills required to enhance and transmit this knowledge to the whole body metabolism and metabolic regulation and recently to epidemiology and behaviour, (*Zeisel et al., 2001*). Within the same conceptual framework, Gretel Pelto and Hedley Freake, from the same committee of the American Society for Nutritional Sciences, elaborate on the role of nutritional science at the different levels of

organisational complexity from individual organisations to societies and from molecules through metabolism to populations, and discuss the social determinants, social mechanisms and social consequences of food and nutrition at both population and individual levels (where 'social' encompasses a variety of concepts such as economics, anthropology, psychology, sociology, political science, demography and epidemiology). Evidently, nutritional science finds application in wholistic models that address all determinants with their consequences and overlapping interactions. A characteristic example mentioned is that of obesity which, despite the advances in our knowledge about metabolic and molecular pathways which govern energy metabolism and food intake, continues to rise to epidemic proportions. The researchers highlight the added complexity from the recognition of the fact that undernutrition exists side by side with obesity, (*Pelto & Freake 2003*). According German et al., (2003), metabolic disturbances are a function of undernutrition and are related to much more nutritional issues than nutrient deficiencies, extending beyond essential nutrients to macronutrient fuels and nonessential nutrients and, furthermore, to several aspects of lifestyle and environmental exposure, where 'environment' is explained as the sum of all external variables, including diet, lifestyle, and coexisting organisms, (*German et al., 2003*).

CHAPTER II

THE HUMAN BODY: A NUTRITIONAL REALITY

The science on which Nutritional Medicine bases its prescriptions, -which include dietary and lifestyle guidelines and often nutritional supplements-, represents an extremely complicated, continuously revised and upgraded, system of knowledge, focusing on the functions of the human body and its complex endogenous and exogenous interactions. It is a highly scientific discipline, profoundly extending into all domains of life and environmental sciences, including biology, anatomy, physiology, and cellular biochemistry, and cannot be possibly reduced to the calculating simplicity of recommendations aiming to address population-wide deficiencies. The incredible intelligence of the workings of the human body in relation to nutrients is revealed by a volume of scientific studies which demonstrate how cleverly a ‘higher intellect’, governs all functions and organises, selects, allocates, and discards nutrients, in different ways, at different times, under different conditions. The utilisation of nutrients is a function of a multitude of parameters, including gastrointestinal health status, individual metabolic phenotype, endocrine and nervous system function, bioavailability of nutrients, synergism/antagonism between nutrients, toxins (exogenous and endogenous), and psychological and emotional status. The ‘higher intellect’ guides, in an amazingly prudent and sensible manner, all the highly complicated, and to a large extent remaining to be explored, biochemical functions occurring every moment at the cellular level. The human body is composed of hundreds thousands million cells each one being a chemical factory of its own in which a multitude of raw materials are continuously processed through numerous functions and interactions to produce energy which is the basis of life. Knowledge of the basic structures and functions of the human cell is essential for understanding the vital role of nutrients and why these often need to be supplemented. A very brief overview from Brody’s *Nutritional Biochemistry* is offered below:

Each human cell consists of the following structures: a *plasma membrane* being the outer border of the cell and synthesised by the cell itself, which contains phospholipids and proteins used to facilitate the transport of nutrients in and out of the cell; the *cytoplasm*,

the fluid contained within the membrane, with a gel-like consistency due to the high concentration of proteins, in which most chemical reactions occur; and the *organelles* which include the *nucleus*, the *endoplasmic reticulum*, the *sarcoplasmic reticulum*, *secretory vesicles*, *lysosomes*, and the *mitochondria*. Energy in the form of *adenosine triphosphate* (ATP) is produced in the mitochondria and is used by thousands of different reactions in the cell. Brody (1996) parallels ATP as a portable battery that can be used anywhere in the cell for a chemical reaction. Its utilisation results in its conversion to *adenosine diphosphate* (ADP) plus *inorganic phosphate*. ADP is recharged to be converted to new ATP molecule again in the mitochondria a process which represents the main purpose of the mitochondria. The *ribosomes* are structures floating in the *cytoplasm*, on which all proteins are synthesised. The *endoplasmic reticulum* is a network of interconnected tubules on which *ribosomes* bind. The *sarcoplasmic reticulum* is a network-like organelle used for the rapid release and uptake of calcium ions (Ca^{+2}) which are responsible for muscle contraction through their cytosolic changes. *Lysosomes* are large vesicles which receive material entering the cell via endocytic vesicles, digest (hydrolyze) it into small molecules and release the end products into the *cytoplasm*. The *nucleus* contains the genetic material of the cell which is used, through a process called *transcription*, for synthesis of the messengers *Ribonucleic Acid* (mRNA) molecules, which in turn enter the *cytoplasm* to be used for the synthesis of *polypeptides*. The central molecule of the genetic material is the *Deoxyribonucleic Acid* (DNA) which contains the information needed to formulate the sequence of *ribonucleotides* in the RNA. The DNA is divided into 46 pieces, the *chromosomes* which consist of 22 numbered *chromosomes* occurring in duplicates and 2 sex *chromosomes*. DNA is used for storage of genetic information while mRNA for its transfer. Brody uses the characteristic phrase to denote this relation: '*DNA makes RNA makes protein*'. *Translation* is the process of polymerisation of amino acids into *polypeptides* using mRNA as a template, which is used several times, until eventually degraded. The specific order by which the various *amino acids* are synthesized into a *polypeptide* is determined by the mRNA that encoded its synthesis and predetermined their destination and function. *Proteins* then are synthesised as *polypeptide chains*, containing the necessary information to perform specific functions. Some of the *proteins* are used as *cell membrane proteins* to be used as *transport proteins*, *hormone receptors*, *ion pumps*, and *proteins* that transmit impulses

along nerves or muscle fibres. *Proteins* secreted into the extracellular fluid include *albumin*, hormones such as *insulin*, blood clotting proteins, as *thrombin* and *fibrinogen*, *lipoproteins* and *antibodies* or *immunoglobulins* (Brody 1996, pp.31-54).

Proteins are the building blocks of the body making up the framework of its more rigid structures, such as the cell walls, skin, bones, solid organs, blood vessels etc. Defects in any of these proteins can cause different health problems such as cardiovascular disease, cystic fibrosis, diabetes etc. *Enzymes* are proteins used as *catalysts* of specific biochemical reactions, through their action on specific *substrates*. *Catalysing* means, greatly accelerating the rate of a particular reaction without the *catalyst* being used up or altered, though in theory only, because in the real world all *enzymes* are eventually degraded or converted back into their constituent *amino acids*, often as a result of *oxidation* or other types of damage. Each cell of the body contains several thousand different types of *enzymes*. Examples of important enzymes include the *enzyme chymotrypsin* which catalyses the digestion of dietary proteins and *dihydrofolate reductase* which catalyzes a step in vitamin metabolism. Another important enzyme is *hexokinase* which is the enzyme required for the first step in the body's utilisation of glucose. Glucose is transported through the wall of the gut, through the bloodstream into the cells where it is broken down to *acetate groups* and then to *carbon dioxide*. This process releases heat, part of it is captured as chemical energy ATP, which is in turn used by the body for a multiple of functions, such as muscle contraction, nervous system activities, growth and reproduction (Brody 1996)

CHAPTER III

NUTRIENTS AT WORK

The pathway a molecule of food follows, from the mouth to the cell, represents a very long journey with several stopovers. The major stages/functions of this process are the *digestion*, *absorption* and *metabolism* of food, each one being an intricately complex operation, involving a plethora of nutrients in different forms, (*enzymes*, *coenzymes*, *vitamins*, *electrolytes*, *hormones*, etc) and in different roles, (*catalysts*, *substrates*, *fuels*, *transporters*, *chemical messengers*, *building blocks*, etc). The basic components in food ingested are the, so called, *bulk nutrients* -carbohydrates, fats, and proteins- which are needed in comparatively larger quantities than *vitamins* and *minerals* – described by Ballentine as ‘the screws and bolts necessary for the construction and operation of the body’ (Ballentine 1978). *Vitamins (vital amines)* are organic compounds, essential for the preservation of life and the avoidance of metabolic disorders; however they cannot be biochemically produced by the human cell, so they should be provided through food, mainly plant food. *Minerals* consist of two major classes the *macrominerals*, such as sodium, potassium, calcium, phosphorus and magnesium, and the *microminerals* which are tiny or trace amounts of minerals, including zinc, manganese, iodine, copper, chromium, selenium, etc. (Plaskett 2004; Wrong 2000; Fairfield & Fletcher 2002). *Micronutrients* is a term used to denote nutrients that are required in only trace amounts by the body, in spite of the fact that their physiological action is extremely important and vital for life. The term covers the *vitamins*, the *microminerals*, *amino acids*, *essential fatty acids*, and a number of trace elements scientifically demonstrated to have vital role in the biochemical processes of the body, including *organic acids*, *flavonoids*, and *phospholipids*.

The correct amount of nutrients, especially minerals as *ions* carrying electrical potential, and the balance between them is crucial for the proper functioning of the body. The *monovalent electrolytes*, *sodium* (Na^+), *potassium* (K^+) and *chloride* (Cl^-), for example, are responsible for almost the entire *osmolality* of body fluids, and the mode in which they are disposed within the body determines the volume of intracellular and extracellular fluids. *Potassium ions* are found mainly inside the cell together with *magnesium*,

phosphate and *proteinate anion*, whereas *sodium* and *chloride* are mainly located in the extracellular fluid. The enzyme *Na⁺/K⁺ linked ATPase* (known also as the *sodium pump*) is responsible for the maintenance of ionic composition of intracellular and extracellular fluids. Asymmetric distribution of diffusible ions between extracellular and intracellular fluids produces a *negative electric charge* of about 80mV across the cell membrane. This *electrical potential* is extremely important for the normal function of the cell, and consequently for the normal excitable behaviour of muscles and nerves. The *sodium pump* is also responsible for amino acid and glucose transport into the cell, (*Plaskett 2004; Wrong 2000, pp.149-150*). *Vitamins* and *minerals* perform a vital function in the human body, through their role as essential *cofactors* in *enzymes* and *coenzymes*. Most *enzymes* are composed of a protein along with an *essential mineral* and possibly a *vitamin*. Many enzymes require additional support to perform their functions and this task is undertaken by a *coenzyme*, a molecule composed of *vitamins* and/or *minerals*, which acts along with the *enzyme*. Vitamin C, for example, is an essential coenzyme of the enzyme *proline Hydroxylase* which catalyses the synthesis of *collagen*. Apart from vitamins and minerals a number of other nutrients have been demonstrated by scientific research to have important effects on the biochemical workings of the body. These include *essential fatty acids, flavonoids, probiotics, carnitine, coenzyme Q10, Ginkgo Biloba, Aloe Vera, Bromelain* and many others, (*Ballentine 1978; . Elia 2000; Plaskett 2004*).

Several studies both *in vitro* and *in vivo* demonstrate the effects of deficiency or excess of dietary nutrients, in health and disease. Watts (1995) describes the synergistic and cooperative workings of nutrients at the metabolic level as an 'interlocking gear system', demonstrating that effect in one mineral induces effects on at least two other minerals, which in turn affect two others and so on. A multitude of synergistic and antagonistic relationships between nutrients are discussed in detail demonstrating, for example, that: *iron* cannot be incorporated in *haemoglobin* without *copper* support; *vitamin C* prevents accumulation of *copper* to poisonous levels and assists intestinal absorption of *iron*; *magnesium* corrects *potassium* deficiency and too much *magnesium* can contribute to *calcium* deficiency and vice versa; *calcium, magnesium* and *phosphorus* work together to maintain bone health; *vitamin D* enhances *calcium* absorption but too much of it can cause *potassium* depletion; *zinc* is required for *vitamin A* to be mobilised from storage areas in the body; *vitamin E* excess causes *vitamin A* deficiency and vice versa, (*Watts 1995*).

CHAPTER IV

PRACTISING NUTRITIONAL MEDICINE IN THE NEW PARADIGM

NOTE: Please read this chapter with reference to appendices 3-8 where an example from the author's Nutritional Therapy clinical practice is provided

A fundamental principle of Nutritional Medicine is that disease is most of the time, if not always, the manifestation of a *deeper cause, or causes*, associated with malfunctioning in one or more of the systems of the body and it is usually the outcome of a long degenerative process, its onset often identified long before manifested, non infrequently, generations back. Serious damage in vital organs or systems can occur years before symptoms appear and, even then, the actual source of the damage might not be adequately identified, (as is fatigue, unexplained pain, inflammation, autoimmune reaction, panic attacks etc). A second fundamental principle is that the human body is a *highly complex network* of organs and systems, participating every moment in extremely complicated, interrelated and overlapping processes, not all of them clearly understood yet. A multitude of inputs are used simultaneously for the proper functioning of the human organism, including endogenously produced or exogenously ingested nutrients, environmental elements, and social and psychological stimulants. This biochemical complexity provides poses the imperative of a third fundamental principle, that of *biochemical individuality*, according to which each human is unique and should be approached in an equally unique way. These three principles set the basis of all nutritional clinical practice.

The major steps followed for each individual patient, as formulated by Plaskett (2004), are the following:

- i. The first consultation for primary and secondary data collection
- ii. Analysis and synthesis of data
- iii. Interpretation and diagnosis
- iv. Preparation of treatment

- v. Second consultation to offer and explain the treatment to the patient
- vi. Follow-up consultations with further observational data collected, analysed and synthesised
- vii. Subsequent amendments to treatment.
- viii. Maintenance dietary programmes

A major objective of the first consultation is to *elicit the right information* from the patient, or those responses that stimulate reasoning and understanding of hidden facts, necessary for the treatment to be prescribed. A second equally important aim is the establishment of a good *therapeutic relationship* with the patient, considered crucial for the steps to follow, (Plaskett, 2004^{viii}). The consultation process requires knowledge, skills and expertise and cannot be delegated to any secretary or other assistant of the clinic. It has often been the case, patients not to reveal important information because they don't consider it necessary as not related to their present problems¹. A characteristic example is the surgical removal of a gallbladder due to cholelithiasis which, from a biomedical perspective, is considered a cure and nothing to worry, apart from avoiding fatty food. However, for the nutritional practitioner, cholelithiasis reveals a serious systemic deeper cause related to the wrong mishandling of calcium by the body, usually emerging from mineral imbalances/deficiencies. Hence, removal of the gallbladder, simply eliminates one of the many potential sites of calcium dumping, it does not eliminate the deeper mineral imbalances. Tracing, therefore, the pathway of disease of the patient in order to formulate a correct diagnosis, which will in turn guide a successful treatment, requires eliciting all possible important information about the patient. This should include: 1) the patient's present history, present health problems, recurrent symptoms and medical events of the past year, waterworks and bowel habits, psychology, treatments already followed, any available medical or other diagnoses, biochemical tests and medical reports, medicinal drugs or supplements prescribed, etc; 2) the patient's past history, childhood diseases, maternal exposures, maternal nutrition and lifestyle, breastfeeding, birth events, medical events, pregnancies, stressful psychoemotional traumas, nutritional stresses, health status of other members of the family etc; 3) diet: daily menu, eating preferences, dislikes and intolerances, vegetarianism, veganism, childhood and teenage diet, etc; and 4) lifestyle practices: smoking, alcohol, exercise, sleep, working hours,

¹ This issue was discussed in Part I, Chapter II: Perceptions of Health

family and socioeconomic conditions, environmental and work exposures etc. An important issue is to find out what the patient expects from the treatment. Plaskett highlights the importance of not losing sight of mental and emotional aspects by concentrating only on the physiology and chemistry of the body, (*Plaskett 2004 viii, p.A49*)

The establishment of a therapeutic relationship with the patient has been shown by a volume of studies to have much more importance in the overall outcome of the treatment than it has been traditionally considered by healthcare practitioners, (*Saultz & Lochner 2005; Patterson et al., 2008; Plaskett 2004viii; Bennett 2011; Rao et al., 2000; Clark et al., 1999; Goldberg et al., 2002; Starfield 1980; Meryn 1998; Rastegar 2005*). Bennett (2011), referring to current research documenting the doctor-patient relationship as an important factor contributing to the genesis of the 'placebo effect', claims that 'the history of medicine is as much a history of the relationship between doctor and patient as the evolution of medical technology and techniques', (*Bennett 2011*). Spending adequate time with the patient and listening to them, how they feel and how they perceive their health problems, allows the practitioner to attune to their problems, needs and fears. Plaskett draws attention to the fact that the consultation process is a live and dynamic process, not a 'dry repetitive work' of data collection, and as such it is unique for each individual patient (*Plaskett 2004viii, p.B3*). Adequate time should be allocated to the patient (usually one to one and a half hour for the first consultation) in a comfortable and relaxing environment that will encourage them to express their deeper feelings and how they perceive their own problems. In addition, the patient should be adequately informed about what nutritional therapy means and for the possibility of radical dietary and lifestyle changes. After all, in nutritional therapy, the patient is not a mere observer of the healing process but an active participant and it is important that s/he is adequately prepared for this.

Formulating the diagnosis might take several hours of evaluating the patient's case history, in an effort to identify constitutional strengths and inherited weaknesses, weak organs, nutrient deficiencies and metabolic imbalances. Scientific research is often undertaken to identify the most recent developments and new evidence regarding the therapeutic power of nutrients in disease. The nutritional treatment prescribed to the patient represents a tailor-made programme which includes dietary and lifestyle guidelines and often supplementation, designed to individual needs, to enhance the

therapeutic process in different ways. The nutritional therapy process follows a number of stages according to the case with stepping up intensities of detoxification and organ/system stimulation. Each stage of the therapy is decided after reviewing the patient's progress in each follow-up consultation and discussing possible unforeseen complications. A fundamental rule of Nutritional medicine is that the patient is an active participant to his/her therapy therefore *educating the patient* is one of the major tasks of the nutritional practitioner. The patient needs to know that the nutritional therapy is a wholistic process and all elements of the therapy work synergistically, including dietary and lifestyle changes and often in conjunction with other treatments, medical or natural. When nutraceuticals are used it is explained to the patient that these do not work the same way as pharmaceuticals, which are universally considered to act as sole agents, but they form part of the process to support the whole effort towards restoring metabolic imbalances and nutrient deficiencies, stimulating weak organs and systems, and generally enhancing the body's self healing powers. The nutritional therapy process should not be anticipated as a short-term dietary programme, to be abandoned as soon as the symptoms are relieved. What the patients need to know is that to reverse the pathway of disease and prevent further deterioration of their health they must permanently abandon past wrong dietary and lifestyle practices and make effort to embark on a 'new life' which means permanently adapting to new healthier habits of eating, cooking, and living (Plaskett 2004). It has been recurrently reported that lifestyle practices are equally important for preventing and treating disease, (WHO [2000iii; 2003i; WHO 2004i; 2004ii; 2007i; 2008]; Panayiotakos et al., 2007; Tyrovolas 2009; Plaskett 2004; Goldberg et al., 2002; Hays 2005; Murray & Pizorno 2011i; Campbell & McTiernan 2007; Bernstein et al., 1994) , as for example is the strong relation between exercise and osteoporosis, (EU [2005; 2007ij; WHO 2003iii; Moynihan et al., 2002; Musnick 2005]). Apparently, there are no 'magic pills' or otherwise called, 'magic bullets', to solve all problems overnight.

If the patient is under medication prescribed by a doctor or other means of treatment by another healthcare provider, possible interactions between medicines and dietary components are evaluated before including specific nutrients or nutritional supplements. It is often the case, dietary components only, even without supplements, to interact with medicines, such as *turmeric*¹ and *linseed oil*² (especially in combination) with

¹ Turmeric: a spice usually found in curry dishes but used often in nutritional therapy for its beneficial action in the liver

² Linseed oil: used in salads as an excellent source of omega-3 essential fatty acids, as an alternative to fish oil

anticoagulants (eg Warfarin), and they should not be included. Within the context of teamwork and in respect of the work of other healthcare professionals, adequate communication with the patient's attendant doctor(s) should be established and any supplementation to be added to the diet should be in agreement with them. Often the doctor should be adequately informed even if the treatment does not contain any nutraceuticals. If, for example, the patient is prescribed an anti-hypertensive or hypoglycaemic diet only without supplements, and s/he is under blood pressure lowering or diabetic medication, the doctor should be aware in order to monitor the patient for the need at some point to reduce medication accordingly. Placing the patient's benefit at the centre of all actions, it is important for the nutritional therapist –as it should have been for all healthcare practitioners- to know the limitations of their approach, and refer the patient to other specialists when needed. In cases of cancer, for example, the patient is advised to consult their doctor for the possibility of removing the tumour through surgery, if the doctor considers necessary, and the patient to be referred back to the nutritional therapist to work on preventing metastasis. In addition it is also important to avoid nutritional therapy when the patient is under chemotherapy, since the two therapies have opposite targets, the former stimulating the immune system and the latter suppressing it. A further example is that of anorexia. There is a common fallacy among the public that this is a nutritional problem and often resort to a nutritional practitioner. It is the nutritional practitioner's obligation to refer these cases, immediately to a doctor, specialising in this area and request from the doctor to refer the patient back for supplementing the medical treatment with a nutritional programme. All these considerations highlight the imperative for teamwork and harmonious cooperation between healthcare providers for better outcomes. It is worth noting evidence which demonstrates that the majority of patients do not inform their doctors about non-conventional treatments they follow and this may have serious adverse effects on their health, (*Chang et al., 2007; Eisenberg et al., 1998; Kennedy et al., 2007*).

CHAPTER V

THE RATIONALE FOR NUTRITIONAL SUPPLEMENTATION

Obviously, the very term ‘supplementation’ denotes the ‘**supplementing**’ of diet with specific nutraceuticals and not the ‘**substituting**’ of diet. This means that supplements are not supposed to act independently of dietary practices (and lifestyle) and they should not be used to compensate for poor dietary habits, a negative attitude, or lack of exercise. Recalling from Murray & Pizzorno (2011ii):

‘Nutritional Medicine consists of the use of diet and nutritional supplementation as therapeutic modalities. The foundation of Nutritional Medicine is a health-promoting diet that focuses on the consumption of whole, natural foods. Nutritional supplements are used in the overall context of Nutritional Medicine as complementary agents, not as sole primary medicines. Diet is always primary, and supplementation secondary.

Nutritional supplementation -the use of vitamins, minerals, and other food factors to support good health as well as preventing or treating illness –is an important component of Nutritional Medicine. The key functions of nutrients like vitamins and minerals in the human body revolve around their role as essential components in enzymes and coenzymes’

Murray & Pizzorno 2011ii
Online Textbook of Natural Medicine (e-edition)

In addition, it is essential for any healthcare practitioner to bear in mind that nutraceuticals are highly different from pharmaceuticals and do not work, -and therefore should not be prescribed- on the same basis as pharmaceuticals (a pill for a specific labelled-disease). A volume of research demonstrates the biological action of nutrients as both preventive and therapeutic agents, with their effects varying between different individuals, under different circumstances, acting individually or through synergies and antagonisms with other nutraceuticals and/or pharmaceuticals. Profound knowledge of Nutritional Biochemistry, and particularly of the pharmacological effects of nutrients in the body, is essential for practicing Nutritional Medicine, and this knowledge is not adequately available through current biomedical studies. Basic knowledge of nutrition, as currently offered in medical schools of the western world, does not offer the knowledge

and expertise for evaluating deficiencies and using supplements as therapeutic agents and this fact is confirmed by a volume of research, (*Kolasa 2001; Taren et al. 2001; Clifford 2000; Hark & Morrison 2000; Jeor et al. 2006; Vickers & Zollman 1999; Krebs & Primak 2006; Adams et al., 2006; Kolasa & Rickett 2010; WHO [2002; 2002iii; 2004i; 2004ii; 2008]*)

Biological action of nutrients

The significant pharmacological action of nutrients, especially of minerals in their micronutrient ionised form, has been shown by several studies. According to Finney & O' Halloran from the Departments of Chemistry and Biochemistry, Molecular Biology and Cell Biology, of Northwestern University, Evanston, USA, *metalloproteins*, (proteins carrying *metal ion cofactors*), are as abundant as metals in the cell, acting as *cytosolic partners* for the membrane transporters of cellular *metal ions*, and correspond to about one third of all structurally characterised proteins, (*Finney & O'Halloran 2003*). **Zinc** (Zn^{2+}), for example, a critical micromineral for cell growth, development and differentiation, for DNA synthesis, RNA transcription, cell division and cell activation, is an essential cofactor of many proteins, including 300 signalling molecules and transcription factors, (*John et al., 2010*). A major contribution of minerals in body health is through their role as scavengers of *reactive oxygen species* (ROS), chemically reactive molecules containing oxygen (such as peroxides), which are implicated in a variety of inflammatory responses, (such as ischaemic injury) as well as promoting the aging process. The major endogenous enzymatic antioxidant defence systems of the body are both *enzymatic* and *non-enzymatic*. The *enzymatic defence* includes 1) the *Superoxide Dismutase* (SOD), which degrades *superoxide anion* (O_2^-) and *Catalase*; 2) the *Glutathione Redox System*, which inactivates *hydrogen peroxide* (H_2O_2), one of the most powerful oxidisers, (commonly known as *bleach*); and 3) the *Catalase*, (*Romieu & Trenga 2001¹; Song et al., 2010²*). *Non-enzymatic defence* includes vitamins and other antioxidants (flavonoids, phenolic compounds, carotenes, etc). Under normal circumstances the body's defence system offers adequate protection, as it happens with the inactivation of *Hydrogen peroxide* (a by-product of the

¹ Isabelle Romieu from the Pan American Health Organisation and National Institute of Public Health, Center for Population Studies, Mexico & Carol Trenga from the Department of Environmental Health at the University of Washington, Seattle

² Department of Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles;

cell's normal biochemical processes) and the *Superoxide Radical* (which develops from natural substances and is retained in the body). However in pathological conditions, such as diabetes, deregulation and imbalances between the systems allow the accumulation of toxicity, (Song et al., 2010)

According to Erica John and colleagues from the Departments of Surgery, Occupational Health, Immunology and Medicine of the University of Pittsburgh, USA, another major area of action of *mineral ions* is their regulatory role in *apoptosis*, a mechanism of cell function which enables the removal of excess, mutant, or damaged cells. *Apoptosis* which, in contrast to *necrosis*, deletes cells without releasing their contents causing damage and inflammation to neighbouring cells, is a major function of the mitochondrion with the assistance of mineral free ions, such as Zn^{2+} . In their anti-apoptotic role minerals offer protection to the cells against oxidative damage by preventing protein oxidations by reactive oxygen species (ROS) and inhibiting important ROS-protective enzymes. Dysregulation of *apoptosis* is at the centre of pathogenesis of many diseases, being increased in neurodegenerative diseases, AIDS, and diabetes mellitus, and decreased in autoimmune diseases and cancer, (John et al., 2010). Equally important is the role of minerals in *signalling pathways*. **Zinc** has an extracellular signalling role, (as in *neurotransmitters*), and an intracellular one, (as in *calcium second-messenger systems*), (John et al., 2010) and copper has been shown to have a role in protecting neurons from oxidative stress through its participation in the antioxidant protein *Atox 1*, (Prohaska & Gybina 2004). **Selenium** is a mineral with also important antioxidant activity, incorporated into the antioxidant enzyme *glutathione peroxidase*, in the prevention of lipid peroxidation and cell membrane instability, (Romieu & Trenga 2001). The multiple roles of selenium, in the form of *selenoproteins*, are evident in *cell signalling systems* and in modifying the immune response, cell growth and cell survival, (many of them, especially in the area of endocrine malignancies, remain to be discovered), (Becket & Arthur 2005).

Mineral ions, such as Zn^{2+} are critically involved in immune function, including gene expression for the *cytokines*, *DNA repair enzymes*, and in maintaining the *neuroendocrine-immune axis* function. Under suboptimal levels of zinc, cells adapt by changes in the expression of genes in *cytokines*, *DNA repair enzymes*, *zinc transporters*, and *signalling*

molecules, (John et al., 2010). Zinc acts as neuromodulator at excitatory synapses and has a considerable role in the *stress response* mechanism and in the functionality of zinc-dependent enzymes contributing to maintenance of brain compensatory capacity, (Mocchegiani et al., 2005¹). The complexity and importance of Zinc homeostasis is reflected by the large number of proteins, potentially dedicated to Zn^{2+} transport and buffering -even though the action of most of them still remains unknown, (Sekler et al., 2007; John et al., 2010). Dyshomeostasis in zinc-binding metalloproteins, such as *metallothioneins* –proteins which mediate zinc turnover and regulate the intracellular free zinc ions- has been associated with decline in brain functions in aging. These proteins, whereas serving as a protection in young and adult age, turn into being harmful in aging, (Mocchegiani & Malavolta 2007). Alterations in zinc homeostasis have been reported in Parkinson's and Alzheimer's disease as well as in transient forebrain ischemia, seizures and traumatic brain injury, (Mocchegiani et al., 2005). A number of dietary or environmental factors may alter the set point of steady-state cell ion activity in regulating a number of functions, such as insulin sensitivity, vascular tone, and blood pressure homeostasis. For example, high sugar content in the diet or high levels of antagonistic minerals either ingested or absorbed from environmental sources, may cause deficiency of **magnesium** which has been shown to be a common feature of diabetes, hypertension, cardiovascular and metabolic disease and aging, (Barbagallo et al., 2007²). **Copper**, although an essential cofactor of several enzymes, such as in *tyrosinase* for the production of *melanin*, and a vital mineral in the production of energy (Krebs Cycle), in its free ion form reacts readily with *hydrogen peroxide* to yield deleterious *hydroxyl radicals*. The same is true for several other minerals, such as cobalt, iron, manganese and molybdenum, (Prohaska & Gybina 2004).

The high presence of total metal ion concentrations inspires wonder of how the cell allocates the correct metals to specific protein sites while avoiding toxic reactions. This brings up again the issue of the high intelligence of the human body, and how wrong dietary and lifestyle practices can upset and deregulate the body's inherent mechanisms, rendering these metal toxic to cells. For example, the role of **calcium** (Ca^{2+}) in excitotoxic injury is evident in large volume of studies. Similarly, mutations or malfunctioning in the

¹ Immunology Center (Laboratory of Nutrigenomic and Immunosenescence), Research Department, INRCA, Ancona,

² Institute of Internal Medicine and Geriatrics, University of Palermo,

copper-transporting ATPases, allows accumulation of **copper** in the liver (as in the case of Wilson's disease) instead of being transformed to *ceruloplasmin* or excreted in the bile. *Hypopigmentation* is considered a consequence of copper deficiency through limiting *tyrosinase*, (Prohaska & Gybina 2004). A number of adverse effects of **zinc** are reported, which in its 'free' or loosely bound form of the ion appears to be profoundly toxic to cells, (Bozym *et al.*, 2010¹; Sekler *et al.*, 2007). Studies demonstrate that a 20-fold rise in cellular Zn²⁺ contributes to cardiac myocytes and neuron death, (Bozym *et al.*, 2010), following seizure or an ischemic episode. Also many studies confirm the contribution of zinc (Zn²⁺) in neurodegeneration through its accumulation, under specific conditions, in postsynaptic neurons. This appears to occur together with a decrease in extracellular zinc *chelators*. A malfunction of the mitochondria is associated with this dysregulation, which has been shown in conditions of epilepsy and ischemia, (Ziang *et al.*, 2001). Similarly, dysregulation of free zinc has also been implicated in the formation of *beta-amyloid* plaques associated with Alzheimer's disease and permeation of zinc that is co-released with *insulin* from pancreatic beta-cells is emerging as an important factor in the degeneration of these cells, (Sekler *et al.*, 2007²). Abnormally low levels of zinc have also been demonstrated by several studies in patients with cancers of the breast, gallbladder, lung, colon, head and neck and bronchus and colon cancer, (John *et al.*, 2010). The synergies or antagonisms between metals may also have both beneficial and adverse effects, under certain conditions, (Watts 1995; Ziang *et al.*, 2001). Both **zinc** (Zn²⁺) or **calcium** (Ca²⁺) were individually shown to cause mitochondrial damage with their rapid entry into mitochondria; however the effect was worse, when both of them enter together, (Ziang *et al.*, 2001). It is worth noting that whereas low zinc levels are demonstrated by studies in most cancer cases, this is not the case for tumour tissue in breast and lung cancer in which elevated zinc levels are present. Furthermore, higher zinc content appears in the peripheral tissue surrounding liver, kidney, and lung metastasis in which zinc was low. Researchers believe that this paradox supports that theory of *upregulation* of cellular zinc *importers* in most cancers.

Apart from minerals, antioxidant properties have been shown by several other micronutrients. Examples include **vitamin C and E**. The former is the most abundant

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² Department of Physiology, Faculty of Health Science, and The Zlotowski Center for Neuroscience, Ben Gurion University of the Negev, POB 653, Beer-Sheva, Israel;

antioxidant in the extracellular fluid lining the lung, a scavenger of the *superoxide radical* O_2 , and affects *arachidonic acid* metabolites, particularly *prostaglandins*. **Vitamin E**, a lipid-soluble vitamin is the body's principal defence against oxidant-induced membrane injury in human tissue, via its role in breaking the lipid peroxidation chain reaction. Other nutrients, such as **quercetin** and other flavonoids, are also shown to be scavengers of superoxide anions, (*Romieu & Trenga 2001*). Carlsen et al., (2010), from a study that lasted a period of eight years (2000-2008), produced the 'most comprehensive Antioxidant Food Database published' which shows that plant-based foods introduce significantly more antioxidants into human diet than non-plant foods. In particular from plant-based foods the highest antioxidant content was found in vitamin and dietary supplements, herbal/traditional plant medicine, berries and berry products, chocolate with high cocoa content, nuts and seeds, and fruit and fruit juices. Dairy products were found to have low antioxidant content except those with added chocolate or berries, (*Carlsen et al., 2010, table 1*). **Spices**, have also been shown by several studies to exert potent antioxidant effects and therapeutic power through scavenging of excessive amount of *Nitric Oxide (NO)* and regulation of pathological conditions caused by *peroxynitrate* (oxidation product of Nitric Oxide), (*Baliga et al., 2003*).

Exogenous oxidative stress: Food chain and environmental inputs

Nutrition is often defined as the process by which living organisms obtain food and use it for growth, metabolism and repair, (*The American Heritage Science Dictionary*). *Good nutrition* is crucial for *good health*, and the term *good nutrition* is explained often as a 'good' balanced diet including a wide variety of the right foods containing nutrients and other food substances, that can promote health through maintenance of metabolic homeostasis and fulfilment of our energy requirements. However, during the last few decades eating the right foods no longer ensures good health due to the multitude of hazardous human interventions on different stages of food production and preparation. Hence, speaking of diet what matters is not only what food we eat but what pathway this food followed from planting and growing to the table for consumption and, of course,

good *health* is only established with lifelong healthy nutritional and lifestyle habits and regular intakes of nutritious, clean, whole foods containing nutrients capable of counteracting daily endogenously produced and exogenously ingested, and otherwise acquired, toxins. The same applies for those foods termed *functional foods* which are thought to significantly contribute to the prevention and treatment of chronic diseases, however these should be consumed in adequately balanced amounts and on a consistent basis for very long time to effect significant changes in health, (*Hasler et al., 2000*); and without, underestimating the risk of often overloading the body with huge quantities of protecting or curing fatty foods, such as those containing the essential fatty acids, (*Kris-Etherton et al., 2002*) in an effort to treat a specific health problem.

A healthy human body produces every moment an amount of toxins during the normal biochemical processes of its metabolic functions. These toxins are, under normal conditions, processed and excreted through the inherent detoxification mechanisms of the organism (*as discussed above*). However, a volume of toxins are also ingested, inhaled or absorbed from the environment, the intake of food, and several other sources which the body has not always the capacity to expel. In spite of the fact that authorities, responsible for licensing chemical substances to be used in various stages of the food industry or for being released in the environment, undersign the safety of each one of them separately, a volume of research demonstrates the hazards on health from the accumulation and combination of recurrent long-term low-level exposures to these poisons. The case is worse in conditions of essential nutrient/antioxidant deficiencies which occur, among other factors, from wrong farming and manufacturing practices. Adequate evidence exists to demonstrate the depletion of soil from vital nutrients from over-farming the land; the excessive use of chemical fertilizers, pesticides, growth hormones and herbicides; the genetic engineering of food for human and animal consumption; the excessive food processing with overuse of additives and chemicals; the irradiation of several foods; and the contamination of the food supply with environmental and other toxins. In particular, over 400 pesticides are licensed for use in America's food and no calculation is made by the licensing authorities for the potential risks of multiple exposures to the same pesticide, or the synergistic risks from the cocktail of chemicals ingested in a meal, (*Goldberg et al., 2002*).

Alarming facts on how stuff promoted for human consumption is grown and processed are provided by researchers: About 2000 *food additives* are permitted, including artificial colours and flavours, stabilizing agent, texturizers, sweeteners, antimicrobials, and synthetic antioxidants. Aiming to increase animal milk production, a significant part of the cows are injected twice per month with *Recombinant bovine growth hormone*, a genetically engineered synthetic version of a hormone. *Irradiation*, a process which exposes food to radioactive materials, such as *cesium-137*, and *cobalt-60*, is used in many foods (such as spices) to kill insects, bacteria, moulds, and fungi, to prevent sprouting and increase shelf life, leading to the formation of the toxic substances *benzene* and *formaldehyde* in foods, which also lose much of their nutritional value, such as their vitamins. While irradiated foods are supposed to be labelled, several foods such as sauces that may contain irradiated foods are not labelled. Fishing in polluted by industrial and agricultural residues rivers, lakes, and seas, brings to the table of the consumer fish overloaded with chemicals such as *PCBs (polychlorinated biphenyls)* and *methyl mercury*, (Goldberg et al., 2002,pp181-7). A volume of research demonstrates the immunotoxic effects of *organochlorine compounds*, such as *pesticides, fungicides, and chlorinated solvents* (used in dry cleaning and elsewhere), *polycyclic aromatic hydrocarbons (PAHs)*, and *organophosphate pesticides (OPs)*. Studies with thousands of patients at the Environmental Health Centre in Dallas have shown that persons with two or more *organochlorine compounds* present in their serum have some form of immunotoxicity and development of autoimmunity, linked to exposure to industrial chemicals such as *formaldehyde* and other volatile compounds. Similarly multiple studies have shown elevated levels of different *organochlorine compounds* in the adipose tissue of breast cancer patients, in particular a chlorinated pesticide used in shampoos to treat lice infestations. Childhood brain cancer was linked to exposure to *no-pest strips*, termite treatment, and *anti-lice* shampoo, flea collars on pets, *diazinon* used in the garden, household insecticides and herbicides in the garden, (Crinnion 2011).

Other studies with children demonstrated associations between household and garden pesticides and insecticides with leukaemia, no-pest strips with leukaemia, and home insecticides with brain tumours in younger than 20 years of age. A compound sprayed in

roadways by municipalities and states, to keep weeds at the sides of the road down, was strongly associated with lung cancer, stomach cancer, leukaemia, Hodgkin's lymphoma, non-Hodgkin's lymphomas, and soft tissue sarcoma. Elevated levels of several *phthalates* (*plasticisers*) were found in the serum of child-girls (aged 6 months to 8 years) who have premature breast development; the metals *cadmium*, *cobalt*, *lead*, *mercury* and *thallium* were present in all samples taken from people considered 'generally healthy', who had no known exposure to these chemicals; out of 210 *xenobiotic compounds* tested in a group of people, 167 were present in their serum. Apparently all these chemicals have been accumulating for several decades of chemical exposure to contaminated air, food, and water. The chemicals *p-xylene*, *tetrachloroethylene*, *ethylbenzene*, *benzene 1,1,1-trichloroethane*, and *o-Xylene*, have been found to be 'ubiquitous' in the air we breathe, while *chloroform*, *carbon tetrachloride*, *styrene*, and *p-Dichlorobenzene* are listed as 'often present'; indoor air pollution over a 24-hour period was higher than outdoor air, (*Crinnion 2011*). A volume of studies in different areas of the world, testing chemical residues on food, found no food sources free of contamination. On the contrary contaminants were present in multiple forms. The Total Diet Survey conducted by the FDA, looking for the presence of many different chemicals, found *DDE*¹, a chemical formed by partial dechlorination of *DDT*², a powerful insect poison, in more than 63% of food samples tested, in spite of the fact that this chemical was banned in the United States. Foods with the highest concentrations of DDE were fresh or frozen spinach, butter, collards, pork sausage, lamb chops, and canned spinach. *DDT*¹⁸⁷ was also found in raisins, spinach, chilli con carne, beef, cheese, hamburger, hot dogs, chicken, turkey, ice cream, lamb chops, butter, sauces etc, (*Crinnion 2011*). *Monosodium Glutamate (MSG)*, a common flavour enhancer, present in various canned food and sauces, and particularly used in Chinese restaurants to enhance sauces, was shown to mediate neuronal injury during ischemia, (*Greenwood et al., 2007*), and to induce a dose-dependent swelling and death of mature neurons in 12-14 days of use. Boiling did not reduce its toxicity, (*Xiong et al., 2009*).

¹ DDE is formed by a partial dechlorination of DDT. This can occur in the human body within 6 mo of exposure to DDT. On degradation the DDT becomes DDE or DDD, (*Crinnion 2011*).

² Dichlorodiphenyltrichloroethane; a colourless contact insecticide, toxic to humans and animals when swallowed or absorbed through the skin, that has been banned in the United States for most uses since 1972, (*The American Heritage Medical Dictionary 2007*)

Acrylamide a highly suspected carcinogen is shown by an increasingly rising number of scientific studies to develop from cooking at high temperatures, in the most common processed foods, particularly those with high starchy content, such as breads, cereals, chips, nuts etc (Muttucumaru et al., 2006; Hansen et al., 2009; Elmore et al., 2008; Rayburn & Friedman 2010). The presence of *acrylamide* in heat treated food products was first reported, around the end of April 2002, by the Swedish Food Administration. *Acrylamide* has been shown to be toxic and carcinogenic in animals and has been classified by the World Health Organisation IARC¹ as 'probably carcinogenic for humans'. Konings et al., (2003) in their study within the Dutch population found the highest *acrylamide* amounts in potato crisps, chips, cocktail snacks and gingerbread, and a non-negligible risk of cancer from exposure to *acrylamide*, (Konings et al., 2003). More recent studies found that when wheat is grown under conditions of severe sulphate depletion, free *asparagine* concentration in the grains raises dramatically, up to 30 times more compared to samples receiving normal sulphate fertilizer levels. *Asparagine*, a nonessential² amino acid, has been shown to be the precursor of *acrylamide* in baked cereal products. The study demonstrated that when flours from the sulphate-deprived wheat are cooked at 160 °C for 20min, levels of *acrylamide* rise between 2600 and 5200 mcg/kg compared to 600-900 mcg/kg in wheat grown with normal levels of sulphate fertilisation, (Muttucumaru et al., 2006). Similar results were found by other researchers, who demonstrated the teratogenic potential of *acrylamide*, (Rayburn & Friedman 2010), and the toxic effects of *glycidamide*, a metabolite of *acrylamide* in the reproductive systems of both, humans and animals, (Hansen et al., 2009). Several studies have been conducted in different countries to examine the content of *acrylamide* in daily meals. A survey in Belgium among university students and staff members found biscuits, French fries, bread and chocolate in the canteen food and drink to be major sources of *acrylamide*, (Mestdagh et al., 2007). Similarly, an investigation of the *acrylamide* content in Polish foods, demonstrated bread, French fries, potato crisps and roasted coffee to be major sources of dietary *acrylamide*, (Mojska et al., 2010).

¹ WHO's International Agency for Research on Cancer

² Nonessential denotes that it is produced by the body

Evaluating nutrient deficiencies

The evidence presented in the previous paragraphs on the multiple properties of nutrients and their numerous sites of action, their synergistic and antagonistic effects, as well as the specific circumstances of the host under which action takes place, allow no doubt that each individual has unique nutritional requirements and a nutrient sufficient for one person may be inadequate or often in excess, and even harmful, for another. Characteristic examples were mentioned above, as for example the vital for life nutrients zinc and copper which have been shown to have serious adverse, and often fatal, effects when not properly used by the body. Another example is that of **calcium**, a crucially important mineral for bone health and for proper muscle function, but highly detrimental to health when wrongly absorbed and deposited, as is the case of osteoporosis, osteoarthritis, calcification of the arteries, gallstones and many others (*Plaskett 2004; Smith 2000*). Also, vitamin B6, 2mg/day of which is adequate for good health, whereas for individuals with inherited defects in B6 metabolism, 30 to 100 times this amount is needed, (*Zimmerman 2000*). Several factors, apart from genetic differences, profoundly influence nutritional requirements, including age, gender, dietary habits, lifestyle practices, state of health, psychological and emotional states, environmental exposures, digestive health, and many others. Hudson & Murray (2011) refer to studies demonstrating the impaired calcification of growing bones in children consuming soft drinks regularly. In particular, a significant inverse correlation between serum calcium level and the number of bottles of phosphate-containing soft drinks consumed each week was found in children aged 18 months to 14 years, (*Hudson & Murray 2011*). Fairfield & Fletcher (2002) in a review of large number of studies published from 1966 until 2002, investigating the relation of vitamins to chronic disease, found that vitamin requirements are not the same for all groups of people. In particular, elderly people, vegans, alcoholics, and patients with malabsorption have higher requirements of several vitamins; and women during early pregnancy should avoid excessive doses of some vitamins especially some fat soluble vitamins. The researchers emphasise the need for physicians to shift from classical vitamin deficiencies, being at the basis of clinical syndromes not common any more in western societies, and focus on the pressing problem of suboptimal vitamin status and its association with abnormal metabolism and consequently with many chronic

diseases such as cardiovascular disease, cancer, and osteoporosis. The importance of tailoring the contents of multivitamins to specific characteristics of patients in order to avoid both suboptimal levels as well as excesses, which can both lead to disease, is stressed, (*Fairfield & Fletcher 2002; Fletcher & Fairfield 2002*) and this is where **the science of nutritional supplementation** comes to play a vital role.

It is important to consider, when evaluating nutrient requirements, the gastrointestinal factor, since the conditions within the human intestine vary considerably between different individuals, even in health, and this extra dimension should be added in the case of illness, (*Plaskett 2004ii, p.A30-32*) . According to Liska & Bland (2005), a proper diet is only the beginning of the process and in order for the nutrients to be properly absorbed, they must be first properly digested. Furthermore, the nature of food ingested influences the digestive process and the utilisation of nutrients. For example, a diet high in sugar induces the rapid release of high levels of insulin which in turn poses increased demands on the regulatory systems and enzymes which need specific nutrients as cofactors for proper function, (*Liska & Bland 2005, p.190*). Yarnell (2000), provide evidence of how nutritional deficiencies associated with gastrointestinal malabsorption, seemingly minor and unimportant, can lead to serious systemic toxicity problems. A number of endogenously produced toxins are listed, many of which occur during normal metabolism of food, which demand ingested nutrients for their detoxification. Examples include: *Homocysteine* an endogenous toxin produced normally by all nucleated cells in the body, which under normal conditions is detoxified by enzymes heavily dependent on folic acid, cobalamin (B12), and pyridoxine (B6). Malabsorption of these nutrients influenced by the conditions of the gut represents an important risk for atherosclerosis. Also a high-meat diet generates high levels of *ammonia*, produced from the degradation of amino acids. Detoxification of *ammonia* represents an extra demand on enzymes and nutrients needed by the liver for its transformation into urea for excretion, (*Yarnell et al., 2000; Plaskett 2004*).

Lawrence Plaskett cites several major factors affecting digestion and absorption of nutrients including: the ability of some nutrients to be absorbed more efficiently than others; the vitality of the 'feedback mechanism', a normal physiological control system which informs promotion of inhibition of absorption depending on the nutritional status

of the individual; the chemical form in which the mineral was ingested; other components in the diet acting as binding agents, either rendering minerals unavailable, such as *oxalic* and *phytic acids* or, oppositely, assisting their absorption through binding such as *ligands* and *amino acids*; the overall physical and chemical nature of the gut contents, such coating of the intestinal wall with mucus-producing foods, as are dairy products, thereby inhibiting absorption; the presence of specific *carrier substances* (proteins on cell membranes) which 'passively' or 'actively' facilitate the entrance of nutrients across cell membranes, such as the *sodium pump* (K^+/Na^+); antagonism among minerals for the same carriers thereby the absorption of one mineral depressed in favour of another; the physical nature of the diet, as is the presence or absence of fibres affecting the rate of passage of food through the intestine; the sugar content of the ingested food which adversely affects absorption; the use of drugs, such as purgatives or laxatives which precipitate evacuation thereby allowing insufficient time of food in the gut to be properly absorbed. As a consequence administration of supplements without seriously considering these factors may render it useless for therapeutic purposes, (*Plaskett 2004ii, p.A30-32*). Another important factor affecting the absorption of nutrients is the frequent use of *antacids* and *proton pump inhibitors* to address common complains, such as indigestion, heartburn and bloating. These class of drugs, often prescribed by medical practitioners, but more often used regularly and long term by patients without prescription, raise gastric pH¹ above 3.5, (*hypochlorhydria*) thereby effectively inhibiting the action of *pepsin*, the enzyme involved in protein digestion and mineral dissociation. Furthermore, *hypochlorhydria* creates a hostile environment for the beneficial bacteria of the gut and at the same time promotes the overgrowth of putrefactive bacteria thereby rendering the malabsorption a permanent condition, (*Murray & Pizzorno 2011; Plaskett 2004*).

McCann & Ames (2009) claim that micronutrient deficiencies are widespread, but not severe enough to cause overt clinical symptoms, especially in the poor, children, adolescents, the obese, and the elderly, in part because of the high consumption of calorie-rich, micronutrient-poor, unbalanced diets. These deficiencies induce insidious changes which occur gradually with aging leading to an increased risk of disease at a later

¹ pH: the symbol relating the hydrogen ion (H⁺) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H⁺ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases, (*Dorland's Medical Dictionary 2007*)

age. In an attempt to provide an explanation for this, refer to the *triage theory*¹ which postulates that, when a micronutrient is inadequate in the body, nature ensures that micro-nutrient dependent functions required for short-term survival are protected, at the expense of those functions whose lack has only long-term consequences. The researchers parallel the *triage theory* to the *disposable soma theory* according to which, as a result of *natural selection*, metabolic resources are preferentially allocated to functions necessary for reproductive survival at the expense of those required for survival beyond reproductive age. *Natural selection* favours short-term survival at the expense of long-term health and, on the basis of the *triage theory*, micronutrient deficiencies that trigger the *triage response* would accelerate cancer, aging, and neural decay, but will not affect critical metabolic functions such as ATP production, (Ames 2006). McCann & Ames attempted to prove the *triage theory*, using vitamin K1 and the potential effects of its deficiency on age-associated diseases. The results of their study provided adequate evidence to support the *triage theory*, demonstrating that a system exists, which in vitamin K scarcity prioritises the protection of vitamin-K-dependent functions according to their essentiality for short term survival, at the expense of functions required to maintain long-term health. The study revealed the existence of a number of *homeostatic mechanisms*, as described by the *triage theory*, accomplishing this prioritization through the preferential distribution of ingested vitamin K1. These included: *tissue redistribution* in response to deficiency; normal *micronutrient tissue distribution* patterns that favour some tissues or cells over others; activation of *stress responses* leading to protective metabolic changes in essential processes; *up-regulation* of transporters; and different *cofactor binding constants* for isoenzymes, as observed for polymorphic variants of many enzymes that bind micronutrient cofactors with different affinities. According to the researchers, their study developed adequate evidence to support the major predictions of the *triage theory*, though with some weaknesses which however do not affect their main results. The two major predictions are: 1) micronutrient-dependent functions required for short-term survival will be more resistant to micronutrient inadequacy than less essential functions; 2) decreased functionality of vitamin K-dependent proteins, not required for short-term survival can increase the risk of diseases associated with aging.

¹ Dictionary definition of 'triage': A process for sorting injured people into groups based on their need for or likely benefit from immediate medical treatment. Triage is used on the battlefield, at disaster sites, and in hospital emergency rooms when limited medical resources must be allocated (*The American Heritage Medical Dictionary 2007*)

The three factors that modify vitamin K function were: genetic loss, dietary availability of K, and chronic anticoagulant therapy, (McCann & Ames 2009). In a most recent review of their previous research on this issue, Ames (2010) reconfirms the various lines of evidence, suggesting that healthier lives can be achieved by optimising our metabolism. Apparently, current recommendations fail to take into account the insidious biochemical damage of the *metabolic triage*, occurring gradually and at modest levels of deficiency without any overt pathological changes, until later in age when particular age-related diseases, such as cardiovascular disease, cognitive dysfunction and cancer make their appearance. Bringing *micronutrient-dependent proteins* into the picture will make possible preventing deleterious genetic alterations by nutritional interventions. The *triage theory* appears to explain why modest micronutrient deficiencies may cause age-related diseases such as osteoporosis, cardiovascular disease, and cancer; and if additional mechanisms are used by the body to allocate scarce resources, a necessity is raised for optimising intakes of micronutrients according to the needs of the most dispensable organ or cells. If this theory is correct it may provide the framework for the identification of sensitive and specific *biomarkers* of micronutrient deficiencies that can be used to optimise metabolism both at a personal and population level, (Ames 2010)

Lee Hooper from the School of Medicine, Health Policy and Practice at the University of East Anglia, Norwich and colleagues, also emphasise on the need of reliable *biomarkers* for the assessment of, both individual- and population-based, micronutrient status in order to provide updated, micronutrient recommendations, across Europe. A *biomarker* is defined by the National Institutes of Health as ‘a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, or pharmacologic responses to a therapeutic intervention’. *Biomarkers* that reflect changes in micronutrient status can be used to facilitate the understanding of relationships between intakes and status and between status and health. In this way, the effects of micronutrient status on a range of health outcomes can be determined. The fact that often the results of epidemiological studies show no substantial relation between micronutrient status and a specific health outcome, it may be due to the *biomarker* being an inadequate measure of status or the absence of any relation between status and the specific health outcome. In many cases the micronutrient may not have a direct effect of a health outcome because

the *biomarker* used in the study may be a *surrogate variable*, meaning that is responding to another factor, (e.g. obesity which has a direct effect on health). The researchers, focussing on the imperative of identifying the right *biomarkers*, truly reflecting nutrient status (whether deficiency, adequacy, or excess) as well as other factors driving *biomarker* changes, attempted to develop a generic, systematic review, methodology for use in the assessment of the status of a number of micronutrients. The nutrients, *selenium, iodine, copper, zinc, riboflavin, vitamin B12, vitamin D, and omega 3 essential fatty acids* were selected for studying, on the basis of their importance for European public health. Their generic methodology developed a solid base on which to establish: which *biomarkers* truly appear to respond to changes in nutritional status; in which populations; and under what circumstances; thereby providing firm grounds for basing epidemiological research that relates nutritional status to health status. Studies reviewed were sub-grouped according to baseline micronutrient status, sex, population group, supplementation type, dose, duration, and analytic method. The researchers claim that there are still large gaps in our understanding of the usefulness of many potential *biomarkers* in particular populations groups, or in people with different baseline micronutrient status, (Hooper et al., 2009).

Other researchers suggest *kinetic studies* to determine the process of action, the metabolite concentrations under defined circumstances, and the sites where micronutrients interact with other nutrients –vitamins, minerals and trace elements- as well as the degree of interaction, in order to predict nutrient requirements, (Wastney et al., 2000; German et al., 2004). According to Wastney et al., (2000), kinetic studies are used to investigate the differences in metabolic processes as determined by conditions modified by diet, environment, genetics or disease. Kinetic studies for zinc, for example, have shown that there are multiple pools of zinc that turnover from minutes to years and that processes, such as zinc absorption and excretion are regulated to maintain tissue levels when zinc intake varies, (Wastney et al., 2000). Erica John and colleagues from the Departments of Surgery, Occupational Health, Immunology and Medicine of the University of Pittsburgh, USA, referring to the role of zinc as an important nutrient for the biochemical processes of the body, claim that targeting zinc-dependent cellular processes needs much stronger approaches than just adding supplements to diet. The need to use drugs and

treatments capable of targeting zinc levels of specific pools within the cell or inhibiting zinc binding to a restricted class of protein, is stressed. At the moment there are some critical limitations preventing adequate understanding of the role of zinc, such as quantitative zinc sensors;, improved analytical tools to approach the zinc proteome; inadequate progress in evaluating the biomarkers of zinc deficiency; incomplete information on polymorphisms in various zinc transporters, importers and binding proteins; and methods of targeting specific subcellular pools of zinc, (*John et al., 2010*). In addition zinc concentrations in tissues were found by studies to be influenced by age, gender, diet, and genetic background (*Wastney et House 2008*). Although supplementation of specific nutrients have been shown to reverse several diseases identified as associated with nutrient deficiencies, quantifying nutrients in the human body to identify and prevent deficiencies but also toxicity from excess supplementation are considered an ongoing challenge, (*John et al., 2010*). Zinc ions, despite their beneficial effects in elevated concentrations are known to kill cells in vitro. Studies demonstrate that, while 5 nmol/L of free zinc produced apparently healthy cells in cultures of cardiac myocytes and neurons in vitro, 20-fold higher ions were harmful, (*Bozym et al., 2010*)

CHAPTER VI

NUTRITIONAL MEDICINE: EVIDENCE-BASED PARTNER

The following paragraphs focus on evidence from scientific research to support the essential role of Nutritional Medicine as a vital partner of the of the Twenty First Century Medicine. The health-deteriorating effects of a number of factors related to diet, lifestyle, environmental exposure and psychosocial stresses, with which Nutritional Medicine deals, are further demonstrated in addition to all mentioned above, and the means and methods employed in each case as therapeutic agents are presented. All evidence presented below is obtained from the results of scientific research, mainly of the last decade, which demonstrates the most recently updated knowledge on the power of nutrients either individually or in combination with pharmacological agents in the prevention, or the reversal of the progression, or treatment of a number of the most common diseases rising at alarming rates during the last decades. It should be repeated once again that nutraceuticals are not considered as replacement of a healthy diet and lifestyle otherwise their effect is usually valid as long as they are used. There exists adequate evidence to support the theory that the body's endogenous defence mechanisms can be manipulated with elimination of the sources of oxidative stress, such as those related to diet, lifestyle and various social, emotional, and environmental exposures. A combination of: a healthy diet containing as much as possible clean, unprocessed, and free from added chemicals food, as well as specific functional foods proved by scientific evidence for their antioxidant properties; a prudent lifestyle with adequate sleep, exercise, and avoidance of stress, minimum environmental exposure to toxins; and occasional intake of antioxidant nutritional supplements, when necessary (as in cases of deficiencies or known exposure to toxicity), may have tremendous beneficial effects on prevention of disease and maintenance of health and may often reverse the progression of specific diseases, (*Plaskett 2004; Jones 2005; Goldberg et al., 2002; Pizzorno & Murray 2011; Liska et al 2004; Balch & Balch 2000*). In cases of serious illness, as are neurodegenerative diseases, cardiovascular disease, autoimmune diseases, and cancer, multidisciplinary approaches combining biomedical, nutritional, psychosocial and other interventions within the context of a harmonious teamwork, and placing the benefit of the patient at the heart of

all actions, are considered as the best therapeutic intervention by a rising number of scholars, (*IMF 2008; Jones et al., 2005; Calabrese et al., 2005; Mandel et al., 2004; Reznichenko et al., 2010*)

The synergistic action of nutrients

The list of studies in support of the preventive and therapeutic power of nutrients, in conjunction with a health promoting diet and lifestyle and often within the context of a functional biopsychosocial approach, is already very long and new evidence emerges every moment, (*Ames [2006; 2010]; Balch & Balch 2000; Baldewicz et al., 1998; Ballentine, 1978; Barbagallo et al., 2007; Beckett & Arthur 2005; Benton & Donohoe 1999; Benyon 1998; Bereswill et al., 2010; Bland [2002 and 2004]; Bodane & Brownson 2002; Bohager 2008; Bolland et al., 2010; Calvaresi & Bryan 2001; Carlsen et al., 2010; Cattaneo et al., 2001; Chakraborti et al., 2002; Chen et al., 2009; De Lau et al., 2006; De Roos et al., 2009; Duda et al., 2009; Elmali et al., 2007; Erasmus, 1993; Kris-Etherton et al., 2002; Fairfield & Fletcher 2002; Fenech 2001; Ferguson 2009; Ford 2001; Forestier et al., 2008; Frederickson et al., 2005; Garland et al., 2007; Garrison 1982; Garrow et al., 2000; Gawande et al., 2008; Glenville [1997; 2001; 2005]; Goldberg et al., 2002; Gonzalez-Gross et al., 2001; Gorelik et al., 2003; Green & Miller 1999; Guarner 2007; Guerrero-Romero & Rodriguez-Moran 2005; Gurusamy et al., 2008; Hanaway 2005; Harper & Jacobson 2001; Hasler et al., 2000; He et al., 2011; Hennen 1999; Herbert 2000; Higdon 2003; Holmquist et al., 2007; Hudson & Murray 2011; Jensen 1978; Jia et al., 2010; John et al., 2010; Jones et al., 2005; Kale et al., 2010; Karunakaran et al., 2007; Kellof et al., 2000; Kidd 1996; Kim et al., 2004; Knekt et al., 2002; Lakhan & Kirchgessner 2010; Lamson & Plaza 2002; Lassi et al., 2010; Leader & Leader 2006; Levin et al., 2006; Lewontin 2000; Ley 1998; Libby 2005; Linde et al., 1996; Lipton et al., 1979; Liska & Bland 2005; Looijer-van Langen & Dieleman 2009; Lyon et al., 2005; Ma et al., 2005; Maczurek et al., 2008; Maes et al., 2009; Mandel et al., 2004; McCann & Ames 2009; Mancuso et al., 2007; McCarty [1981; 2000, 2000i]; McKay et al., 2000; McKenna et al., 2001; Meplan et al., 2007; Meydani 2001; Michaud et al., 2000; Molloy & Scott 2001; Muecke et al., 2010; Murray & Lyon 2003; Murray & Pizzorno [2002; 2011; 2011i; 2011ii]; Murray [1994i; 1994ii; 1996; 2002]; Murray et al., 2005; *Natural Medicines Comprehensive Database [1995-2011]; NIH et al., 2004; Obeid et al., 2007; Pan et al., 2009; Panayiotakos et al., [2007i; 2007ii, 2009]; Papathanasopoulos & Camilleri 2010; Parkes et al., 2008; Pfeiffer [1975; 1972; 1987]; Pittler & Ernst 1998; Pizzorno et al., 2002; Plaskett 2004 [i-xv]; Polychronopoulos et al., 2008; Proby 1975; Puchau et al., 2009; Quillin & Quillin 2005; Radhika et al., 2002; Rayburn & Friedman 2010; Reckeweg 1991; Reid et al., 2003; Reznichenko et al., 2010; Rideout et al., 2008; Robinson et al., 1998; Romieu & Trenga 2001; Sahley & Birkner 2001; Salinthon et al., 2008; Schauss 2011; Scholle et al., 2009; Schurgers et al., 2007; Sharma et al., 2007; Showell et al., 2011; Silva et al., 2010; Simopoulos 2002; Singh & Das 2011; Singh & Jialal 2008; Smith et al., 1996; Song et al., 2006; Song et al., 2009; Song et al., 2010ii; Soo et al., 2008; Steinbrecher et al., 2010; Stoll 1998; Taylor et al., 2002; Tenenbaum et al., 2008; Tunon et al., 2009; Vauzour et al., 2008; Verhaar 2002; Vogel et al., 2005; Vosper 2009; Wang et al., 2001; Wang et al., 2010; Watts 1995; Weber et al., 1996; Wei et al., 2009; Weisburger 2000; Werbach & Moss 1999; Werbach & Murray 2000; Werbach [1996, 1997, 1999 2002]; Wilner 2005; Wilt et al., 1998; Witte et al., 2001; Yamori et al., 1992; Yamori et al., 2010; Yarnell 2000; Zhou et al., 2009; Zoccolella et al 2007).**

Several nutrients appear to exert pharmacologic effects in more than one areas of body health. Zinc, which was found to be generally low in obesity, if supplemented with Cyclo-(His-Pro) increases the synthesis of brain tissue *insulin degrading enzyme* by 30%, which

in obese individuals is inhibited by the action of elevated free fatty acids, (Song et al. 2009; Franz et al., 2002). Zinc, as a *metalloenzyme activator* was also found to have lipid lowering effects and to support immune function, (Franz et al., 2002). Lassi et al., 2010, in a review of six trials with 7850 children participants, age 2-59 months, found that zinc supplementation reduced the incidence of pneumonia by 13% and the prevalence of pneumonia by 41% (Lassi et al., 2010). Furthermore, in a most recent Cochrane systematic review of 13 therapeutic trials with 966 participants and two preventive trials with 394 participants, it was found that intake of zinc is associated with a significant reduction in the duration and severity of common cold symptoms. When supplemented for at least five months, it reduces cold incidence, school absenteeism and prescription of antibiotics in children (Singh & Das 2011). *Magnesium* is shown by several studies to have a significant role in the development, and treatment of Diabetes mellitus, (Song et al., 2006; Afridi et al., 2008; Balon et al., 1995), as well as in the prevention of diabetic complications, (Guerrero-Romero & Rodriguez-Moran 2005) while combined supplementation with magnesium and calcium was found to be inversely associated with Diabetes type II, in humans (Villegas et al., 2009; Song et al., 2006). As regards *calcium*, however, several studies demonstrate the need for a more prudent use of calcium supplements. In particular, a meta-analysis of 15 placebo controlled trials with 20,072 patients receiving calcium supplements ≥ 500 mg/day demonstrated an increased risk of myocardial infarction from calcium use. The study draws attention to the need for health practitioners to reassess the role of calcium supplements in the management of osteoporosis, (Bolland et al., 2010). Similarly, calcium with vitamin D supplementation among healthy post-menopausal women resulted in a small but significant improvement in hip bone density; however did not significantly reduce hip fracture and increased the risk of kidney stones, (Jackson et al., 2006).

The effectiveness of personalised approaches with combined pharmacological/nutraceutical therapies is evident by a volume of studies which demonstrate the deeper causes located in the gene expression of common health problems, such as arterial calcification. *Warfarin*, for example, is a common anticoagulant prescribed often by doctors for patients with cardiovascular problems and prothrombotic disposition. However studies demonstrate a pro-calcification effect of Warfarin which can be mitigated with the use of *vitamin K* supplementation. Yao et al., (2008) have shown that

the calcium binding, vitamin K-dependent *Matrix-Gla Protein (MGP)* and *bone morphogenetic protein (BMP)* are independent but functionally intertwined processes and BMP binding is essential for prevention of vascular calcification. *Warfarin* renders the *matrix-Gla protein*, which binds/inhibits the action of *BMP-4*, non-functional through the effect of *vitamin K* activity, thereby promoting calcification. *Proline* and *phenylalanine* have been shown to be critical for *BMP-4* binding by *MGP* to prevent calcification (Yao et al., 2008). Similar results relating the role of *matrix-Gla protein*, as a member of the vitamin K-dependent protein family, as an inhibitor of arterial wall and cartilage calcification, and the calcification-promoting role of the anticoagulant *Warfarin* via its vitamin K-antagonism, were showed by other studies, (Zebboudj et al., 2001; Tyson et al., 2003; Wajih et al., 2004; Schurgers et al., 2007). Schurgers et al., (2007) found a vitamin K deficiency in the sites of calcification and by adding a vitamin K-rich diet they induced 50% decrease in the arterial calcium content and restoration of arterial distensibility, (Schurgers et al., 2007). Similar results were found by Price et al., (1998), demonstrating that high doses of *Warfarin* cause focal calcification of the elastic lamellae in the media of major arteries and in aortic valves in the rat. Aortic calcification was evident after 2 weeks of *Warfarin* treatment. Concurrent administration of *Warfarin* with vitamin K represented an improved treatment protocol, (Price et al., 1998). Vitamin K has, in total, 16 (known at the moment) vitamin K-dependent proteins required for coagulation. Health problems have been shown to emerge from: genetic loss of any of these proteins; dietary vitamin K deficiency; or human polymorphisms or mutations; and vitamin K deficiency induced by chronic anticoagulant therapy (e.g. *Warfarin*, *Coumadin* etc), (McCann & Ames 2009). McCann & Ames refer to a volume of studies demonstrating that Vitamin K deficiency is associated by studies to loss of bone mineral density, increased fracture risk, arterial calcification, cardiovascular disease, cancer, insulin resistance, osteoarthritis, chronic kidney disease (frequently accompanied by vascular calcification), and inflammation. In the case of cancer, pharmacologic doses of vitamin K appear to inhibit cancer cells and also to have a therapeutic effect on cancer progression though modulation of gene transcription, (McCann & Ames 2009).

Chang et al., 2007 demonstrate the results of the effects of different nutritional supplements in the treatment of Diabetes, extracted from a review of studies conducted—

most of them within conventional hospitals- in nine countries from different parts of the world during the period 2000 and 2006. These include hypoglycaemic agents such as *Bitter Melon (Momordica charantia)*, *Fenugreek (Trigonella foenum graecum)* which has also lipid lowering effects and increases HDL cholesterol, and *Ginseng (Panax ginseng)* which has immune stimulant effects and improves psycho-physiological performance; antioxidants with protective effects on the nervous and cerebrovascular systems, such as *Ginkgo Biloba*, (Shane-McWhorter 2001); mineral supplements with effects on insulin sensitivity, and lipid-lowering effects, such as *Chromium*, essential in glucose metabolism and preventing diabetic complications, such as *Magnesium*, (Guerrero-Romero & Rodriguez-Moran 2005), and metalloenzyme activators with lipid-lowering effects and supporters of immune function, improved insulin levels and weight loss, such as *Zinc*, (Franz et al., 2002). A volume of studies demonstrate that beneficial effects of nutrition also exist in the area of psychological and emotional disorders. Ernst (2000), claims that there is adequate scientific evidence on the effective use of nutrients in treatment of disease and refers to a number of studies, systematic reviews and meta-analyses of randomised clinical trials on the efficacy of herbal supplements. *St John's wort*, for example, a herbal antidepressant – the sales of which increased by 2800% in one year in the US-, was found after a meta-analysis of 23 randomised trials with 1757 patients, to be more effective than placebo and as effective as conventional antidepressants –and with half the incidence of their adverse effects- in alleviating the symptoms of mild to moderate depression. Chronic Fatigue Syndrome, a disease characterised by neuropsychological disturbances such as headaches, myalgia, arthralgia, and post-exertional malaise, cognitive difficulties with impaired memory and concentration, and mood changes such as depression and anxiety, is found to emerge from disturbances in deeper pathophysiological mechanisms not confined to one organ but involving interactions between physical, psychological and mental processes. The role of the gut *microflora* in Chronic Fatigue, through their influence on the central nervous system and emotional behaviours such as anxiety and depression is also confirmed by studies. As a consequence *probiotics* supplementation was found to have the potential to normalise the cytokine profile, reduce oxidative stress, and ultimately contribute to improvement of the Chronic Fatigue pathogenesis. (Lakhan & Kirchgessner 2010).

A number of studies focus on the benefits on nutritional supplementation in hospitalised patients. Pneumonia, for example is an important cause of mortality in intensive care units, ranging between 7-40%. The crude mortality from ventilator associated pneumonia may exceed 50% and the use of systemic prophylactic antibiotics was found essential to prevent mortality, (*Liberati et al., 2006*). Forestier et al., (2008), in a prospective, randomised, double-blind, placebo-controlled pilot study found that the occurrence of ventilator-associated pneumonia due to *pseudomonas aeruginosa* in intensive care unit patients was significantly delayed in patients receiving *probiotics* consisting of *Lactobacillus casei rhamnosus*, (*Forestier et al., 2008*). *Probiotics* together with *prebiotics* were also found to significantly lower urinary infections and to reduce hospital stay, as well as the intensive unit stay, of patients undergone liver transplantation, (*Gurusamy et al., 2008*). Researchers report several factors, now urging physicians to examine the use of nutritional means in clinical settings. These include: the surging levels of multidrug resistance among pathogenic organisms, particularly in hospitals; the increasing demands by consumers for natural substitutes for drugs; and emerging clinical and scientific evidence on the efficacy on nutrients, such as *probiotics*. According to Reid et al., (2003), many studies have demonstrated the benefits of *probiotic* supplementation, such as improving the outcome of intestinal infections and reducing the recurrence of urogenital infections. The Food and Agriculture Organisation of the United Nations (FAO) and the World Health Organisation have already supported the potential of *probiotic* foods on the basis of adequate scientific evidence, (*Reid et al., 2003*). It is worth noting, however, that supplementing probiotics without providing for their survival will not produce the effects expected, or at least to the extent expected. This applies to all nutrients. The importance of a Wholistic Nutritional Therapy with the addition of adequate enzymes and possibly minerals or vitamins, together with a properly designed dietary programme and a healthy lifestyle, minimising toxic environmental exposures, and eliminating any emotional, social and psychological stressors, should be seriously considered. For more detailed discussion, four major disease classes were selected as among the most common health disorders causing most of the morbidity and mortality in the western world, and particularly in Cyprus

It is important to note that there are diseases, such as cancer or many autoimmune diseases, in which Nutritional Therapy is usually more effective in the prevention rather

than treatment, but also in the after-surgery cure of the patient and the prevention of metastasis. Cancer and autoimmune-disease patients, for example, are among those sufferers that benefit much from multidisciplinary approaches particularly a good cooperation between medical and nutritional approaches. The removal of the tumour by the specialist surgeon (if s/he considers necessary and applicable) followed by an intense Nutritional Therapy, and close monitoring by the patient's doctor throughout, is the among the best treatments that can be offered to the cancer patient. The author, absolutely disagrees with therapists claiming to treat cancers and advising their patients to abandon their medical treatments. This last remark, which relates to professional ethics, applies of course to all cases of patients who resort to other therapists in conjunction with their medical treatment

Neurodegenerative diseases

The generation of *Reactive Oxygen Species (ROS)* and/or *Reactive Nitrogen Species (RNS)*, and its association with mitochondrial dysfunction (without underestimating the genetic element), is shown by significant scientific evidence to be involved in the pathogenesis of several neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, Friedreich's ataxia, Multiple Sclerosis, Huntington's disease, and Amyotrophic Lateral Sclerosis, (*Calabrese et al., 2005*). Studies demonstrate that neurodegeneration is triggered by multifactorial events such as neuroinflammation, glutamatergic excitotoxicity, increases in free iron, and/or depletion of endogenous antioxidants, (*Vauzour et al., 2008*). The mitochondria genome appears to be the primary site of damage, where various stresses, such as oxidative stress occurring from oxidant/antioxidant imbalance, induce a defect synthesis of the *heat shock response* defence mechanisms of the cell. Under normal conditions, *heat shock proteins* are synthesised, in response to various forms of stress, including oxidative stress and various environmental stressful exposures, to serve as molecular chaperones to protect cells. Finney & O' Halloran (2003), elaborating on the metal ion trafficking and on how intracellular speciation of metal ions is regulated, claim that normal healthy cells concentrate significant amounts of many transition metals, and different physical and chemical stresses, and disease can disrupt the normal trafficking of

these metals leading to deleterious reactions and to neurodegenerative diseases such as Alzheimer's, Parkinson's, and Creutzfeldt-Jacob Disease, (Finney & O' Halloran 2003). Willner (2005) provides a detailed account of the uniqueness of the nervous system and the challenges it faces every moment in fine-tuning the functions of *awareness* (perception) and *performance*, within the context of its general *sense of communication* between all organs and systems, often at great distances from the origins of signals. Willner lists a number of factors posing high demands on the nervous system, including: high energy requirements and consistent access to oxygen and glucose to keep the levels of electrical potentials necessary for the maintenance of electrochemical gradients, which allow the generation of action potentials and the proper functioning of receptors; continuous recycling of neurotransmitters and their receptors for the proper functioning of communication at synapses; maintenance of the membrane structure and myelin insulation, in which the high lipid content of polyunsaturated fatty acids places the brain at significant risk of lipid peroxidation, secondary to free radical damage; and the high concentration of iron in certain regions of the brain (*substantia nigra* and the *striatum*), which increases the risk of peroxidation (Willner 2005, pp. 258-9). Abnormal iron accumulation in the *substantia nigra pars compacta*, in the *reactive microglia*, and -in association with *neuromelanin*- within the melanin containing dopamine neurons, has been shown by studies to be one of the prominent pathological features of Parkinson's disease, Alzheimer's disease, and other neurodegenerative disorders. Free iron promotes generation of toxic reactive oxygen radicals and induces inert *α -synuclein* to toxic aggregates, playing a critical role in iron oxidative stress-induced pathogenesis of dopamine neuron degeneration, (Mandel et al., 2004; Mandel et al., 2006). According to Wang et al., (2010), over expression and abnormal accumulation of aggregated *α -synuclein* results from both genetic mutations and chronic exposures to neurotoxins leading to mitochondrial dysfunction, (Wang et al., 2010). Crinnion (2011) provides a number of biochemical reasons which render the nervous system highly susceptible to toxins. These include: the adult neuron does not divide and so toxin-killed nerve cells cannot regenerate; the blood-brain barrier does not block non-polar substances or those actively transported; due to the network-based function of the brain, damage to even a small portion has marked effects to the whole system; because of the high lipid content in

myelin of nerves, lipophilic xenobiotics easily accumulate; neurons have high surface areas and therefore increased exposure to toxins. (Crinnion 2011).

In addition to endogenously produced oxidative stress, several sources of exogenous oxidative stress have been associated by epidemiological and experimental studies with neurodegeneration, and this is an area where Nutritional Medicine can significantly contribute through carefully designed, tailor-made, programmes. As discussed above, a major source of oxidative stress is the chronic exposure to *insecticides, herbicides* and *pesticides*, (Sherer et al., 2002; Peng et al., 2004; Thiruchelvam, et al., 2005; Callio et al., 2005; Siddiqui et al., 2010; Song et al., 2010; Crinnion 2011). According to Crinnion, (2011), most of the major classes of pesticides contain *neurotoxins* which disrupt the ion flow along the neuron axon. *Organophosphate pesticides* (which came out of nerve gas research) affect the enzyme *acetylcholinesterase* resulting in excessive acetylcholine levels in the synapses. Other sources include: *Solvents* (some of which originally used as anaesthetics) dampen the propagation and transmission of electrical impulses along nerve axons. *Methylmercury* preferentially damages the granule cells of layer 4 in the visual cortex, the granular layer of the cerebellum, and the sensory neurons of the dorsal root ganglia, bringing about neuronal degeneration and demyelination. *Aluminium* causes fatal dialysis encephalopathy following 3-7 years of intermittent dialysis, (Crinnion 2011). According to Goldberg et al., (2002), studies have shown that *aluminium* and *mercury* are linked to the onset of Alzheimer's and senile dementia. In addition, research demonstrated that *mercury fillings* contribute to Alzheimer's and, even minute amounts of mercury in the brain, can seriously damage brain tissue related to Alzheimer's disease, (Goldberg et al., 2000, p.525). *Monosodium Glutamate*, contained in many common foods (discussed above) was shown to induce a dose-dependent damage to nerve cells, (Greenwood et al., 2007; Xiong et al., 2009). *Acrylamide*, a polymerising agent used to strengthen paper, clarifying drinking water and in other industrial applications, but also produced during high-temperature cooking (as is frying) of many daily consumed foods (chips, biscuits, breakfast cereals), is demonstrated by scientific evidence to have neurotoxic effects -by primarily affecting sensory fibres- in humans and genotoxic and carcinogenic effects in animals, (Bolger et al., 2010; Crinnion 2011). *Carbon disulphide* (solvent for fats and lacquers and for extraction of oil from oil-bearing fruits such as olives and palmstones) produces distal axonopathy to both sensory and motor fibres and decreases

norepinephrine levels. *Organotins* (used in plastic, wood, textiles, and silicone) cause myelinopathies. *Hexachlorophene* (added to soaps for antimicrobial action) is readily absorbed through skin and mucous membranes and causes damage to myelin, with the optic nerve particularly susceptible to it. *Solvents* in dry cleaning fluid also cause myelinopathies, (*Crinnion, 2011*)

According to Vauzour et al., (2008), most of the currently used drugs, as is *Ibuprofen*¹, although shown to delay the onset of neurodegenerative disorders, as in Parkinson's disease, the majority of them have failed to prevent the underlying degeneration of neurons, (*Vauzour et al., 2008*). A number of dietary components (in supplement form and pharmacological doses), such as botanical antioxidants and dietary polyphenols were found by studies, either independently or in combination with other pharmacological agents, (and always as part of a healthy diet and lifestyle) to delay the onset or retard the progression of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease. A major class are the *flavonoids*, constituents of fruit, vegetables, and beverages such as wine, tea, cocoa, and fruit juices, which appear to exert multiple neuroprotective effects against neurotoxins, suppress neuroinflammation, and enhance memory, learning and cognitive function. Examples include, *blueberry extracts, quercetin, wogonin, bacalein, catechins, and epigallocatechin gallate*, as well as the isoflavone *genistein*, which have all been shown by studies to attenuate inflammation, (*Vauzour et al., 2008*). The common spice *curcumin*, otherwise known as *turmeric* (extensively used in Asian curry dishes), combined with supplemented *vitamin E*, has been shown to forestall the development of Alzheimer's disease, (*Calabrese et al., 2003*). More recent studies demonstrate *curcumin*, as well as *ferulic acid* (a major constituent of fruit and vegetables) as strong inducers of the *heat shock response* in the brain, (*Calabrese et al., 2006; Mancuso et al., 2007*). *Curcumin*, which can cross the blood brain barrier, can alleviate aggregated α -*synuclein*-induced toxicity, reduce Reactive Oxygen Species levels and protect cells against *apoptosis*, (*Wang et al., 2010*).

A volume of research demonstrates the beneficial effects of *catechins*, polyphenols in green tea, particularly effective in delaying the onset or retarding the progression of Alzheimer's Disease, by inhibiting Reactive Oxygen Species and protecting neurons from

¹ Ibuprofen: a Non Steroidal Anti-inflammatory Drug

amyloid-β peptide-induced inhibition of *N-methyl-D-aspartate*-stimulated free calcium ions (Ca^{+2}) influx and mitochondrial dysfunction, (He et al., 2011). *Catechins* appear in studies to possess divalent metal chelating, antioxidant and anti-inflammatory properties. They penetrate the brain barrier to prevent neuronal death, (Mandel et al., 2006) and are particularly beneficial in Parkinson's disease, (Vauzour et al., 2008). Mandel et al., (2006) demonstrated the multipharmacological neuroprotective activities of green tea *catechins*, especially their brain-permeable, nontoxic, transitional metal (iron and copper) chelatable/radical scavenger properties, (Mandel et al., 2006). Reznichenko et al., (2010) have shown a significant effect of the use of *catechins* in patients with Parkinson's disease treated with *rasagiline* (an anti-Parkinson medicine). In particular a beneficial synergistic action was shown between *rasagiline* and green tea *epigallocatechin-3-gallate* (the main antioxidant/iron chelator polyphenolic constituent of green tea), in protecting the dopamine neurons in the *substantia nigra* and replenishing *striatum* dopamine, (Reznichenko et al., 2010). A nutrient mixture of green tea extract with *quercetin* and red onions was found to increase the bioavailability of *epigallocatechin gallate*, (Kale et al., 2010). The use of radical scavengers, such as *R-apomorphine* in combination with antioxidants, such as the green tea *catechins*, as well as *iron chelators*, have been shown to prevent the accumulation of free iron and its neurodegenerative effects, (Mandel et al., 2004).

Other nutrients with beneficial pharmacological action against neurodegeneration include: *Ginkgo Biloba*:¹ Its therapeutic activity, which lies in its ability to enhance peripheral and cerebral circulation (McKenna et al., 2001) and to protect hippocampal neurons from *Nitric Oxide* and *beta-amyloid*-induced neurotoxicity, (Vauzour et al., 2008), has been demonstrated in a variety of disorders including dementia, Parkinson' disease, failing memory, and poor cerebral and ocular flow, (McKenna et al, 2001; Vauzour et al., 2008; Ahlemeyer & Kriegelstein 2003). Studies demonstrated neuroprotective properties of *Ginkgo biloba*, against ischaemia-induced neuronal death in vivo and glutamate-induced neuronal death in vitro by synergistic mechanisms involving excitotoxicity, inhibition of free radical generation, scavenging of *Reactive Oxygen Species* and *Nitric Oxide*, and regulation of mitochondrial gene expression, (Chandrasekaran et al., 2003; Bastianetto et al., 2000; Smith et al., 1996). In particular Ginkgo

¹ Ginkgo leaf and its extracts contain several active constituents including flavonoids, terpenoids, and organic acids. Many ginkgo leaf extracts are standardized to contain 24% to 25% flavonoid glycosides and 6% terpenoids, (Natural Medicines Comprehensive Database, 2011).

was shown in all nine placebo controlled, double blind randomised trials covering 1497 patients, reviewed by Ernst (2000), to be more effective than placebo in delaying the clinical course of dementia, (Ernst 2000). Although Ginkgo's constituents have been shown to have more potent pharmacological effects working synergistically rather than each one individually, intrinsic effects have been shown also for each of its constituent flavonoids, terpenoids, and organic acids, (Natural Medicines Comprehensive Database, 2011). *Alpha-lipoic acid*¹: A naturally occurring antioxidant cofactor to the mitochondrial enzymes *pyruvate dehydrogenase* and *alpha-ketoglutarate dehydrogenase*, as well as a cofactor in the production of *acetyl-CoA*², is shown by evidence to interfere with the pathogenesis or progression of Alzheimer's disease, (Maczurek et al., 2008; Holmquist et al., 2007) by protecting against the activation of *apoptosis signalling pathway* and mitochondrial dysfunction. It was also shown to attenuate dopaminergic cell loss in mice (Karanukaran et al., 2007); to reduce and recycle cellular antioxidants such as glutathione; to chelate zinc, copper and other transition metal ions and heavy metals; and several other properties that support its utilisation as a therapeutic agent for Multiple Sclerosis and Alzheimer's disease, (Salinthonne et al., 2008; Singh & Jialal 2008). Other nutrients include the amino acids, *N-acetyl-l-cysteine (NAC)* and *reduced glutathione*, found to protect from the teratogenic potential of *acrylamide*, (Rayburn & Friedman 2010); and *vitamin C* which has been shown to offer significant protection against *monosodium glutamate toxicity*, (Xiong et al., 2009)

The preventing and therapeutic role of high doses of *B vitamins* -as precursors of mitochondrial enzyme cofactors- on mitochondrial dysfunction, oxidative stress, and neurodegenerative disorders, are demonstrated by both epidemiological and experimental studies. Jia et al., (2010) found that administration of high doses of a complex of *B-vitamins* in *rotenone*³-treatment-induced cellular models of Parkinson's disease elevates mitochondrial enzyme cofactors, working in the prevention of oxidative stress and improving mitochondrial function. Individual *B vitamins* at the same doses did not show a similar effect suggesting that *B vitamins* work synergistically, (Jia et al., 2010).

¹ Alpha Lipoic acid was classified as a vitamin 50 years ago, but was reclassified upon the finding that it is synthesised in humans and animal. Dietary sources include red meat, organ meats, spinach, broccoli, potatoes, yams, carrots, beets, and yeast, (Natural Medicines Comprehensive Database, 2011)

² Acetyl-coA: a coenzyme derivative in the metabolism of glucose and fatty acids that contributes substrates to the Krebs cycle. It plays a central role in the synthesis, catabolism, and use of nutrients for energy production and growth, (McGraw-Hill Concise Dictionary of Modern Medicine 2002)

³ chemical insecticide

Similarly, De Lau et al., (2006) in a prospective, population-based cohort study lasting for 9.7 years, with 5289 participants aged 55 years and older, free of dementia and parkinsonism, found that higher intake of *vitamin B6* was associated with a significantly decreased risk of Parkinson's disease (association restricted to smokers), (De Lau et al., 2006). *B-vitamins* have been also positively associated with beneficial effects on neurodegenerative diseases through their influence on *homocysteine* plasma concentration, (Obeid et al., 2007). *Homocysteine* is a sulphur-containing amino acid occurring naturally in all humans, as a product of the metabolism of the essential amino acid *methionine* in all cells, through the normal methylation process, and its blood levels are influenced by the presence of *folic acid* and the *vitamins B6* and *B12*, (Stanger et al., 2003; Hamzaoui et al., 2010). Epidemiological studies show a positive, dose-dependent relationship between plasma total *homocysteine* concentration and neurodegenerative disease risk. Chacon et al., (2009), in a study with 2100 individuals 55 years and older found that elevated total *homocysteine* levels posed a fourfold increase in the risk of dementia (Chacon et al., 2009). *Homocysteine* is a marker of *B-vitamin (folate, B12, B6)* status. *Hypomethylation* caused by low B-vitamin status and *hyperhomocysteinemia*, is linked to key pathomechanisms of dementia. In retrospective studies, the association between total plasma *homocysteine* and cognition is impressive and evidence demonstrates that increased *hyperhomocysteinemia* and low serum *folate* occur in patients with Parkinson's disease, especially those receiving *L-dopa*, (Obeid et al., 2007). The causative relation between *L-dopa* treatment and *hyperhomocysteinemia* is based on the *O-methylation* of the drug catalyzed by the enzyme *catechol-O-methyltransferase*, and it is confirmed by research, (Zoccolella et al 2007; Belcastro 2009). Belcastro et al., (2009) found that one-month intake of 5mg/day of *folate* normalizes plasma total homocysteine levels in all hyperhomocysteinemic Parkinson's disease patients. However, *hyperhomocysteinemia* recurs within 4 months of discontinuation of folic acid, (Belcastro et al., 2009) confirming fact that supplementation per se may be beneficial but more radical changes in the patient's overall diet and lifestyle practices, as promoted by Nutritional Medicine, are required to address the deeper causes of disease (as discussed in previous chapters). A similar association between *hyperhomocysteinemia* and Multiple Sclerosis was found by Obeid et al., (2007), who also demonstrated evidence for a causal role of total plasma *homocysteine* in Epilepsy. The researchers found also that certain anti-epileptic medicine enhances

hyperhomocysteinemia and stress the need to use *folic acid*¹, *B12*, and *B6* in elderly patients with this disorder, (Obeid et al., 2007).

In addition to above, adequate evidence exists to support a major role of the gastrointestinal bacterial population against toxicity. In the small intestine and the liver, *flavonoids* act as substrates for *Phase I* (hydrolysing and oxidising) and *Phase II* (conjugating and detoxifying), (Vauzour et al., 2008). Singh et al., (2004) found with kinetic analyses that *CueO* (*copper oxide*), an essential component of the copper regulatory mechanism of *Escherichia coli*², has robust *oxidase* activity, severalfold higher than any homologue, suggesting a functional role of *CueO* in protecting against copper toxicity. *Copper* serves as a cofactor for numerous enzymes; however, as a redox-active transition metal is also cytotoxic through generation of *Reactive Oxygen Species (ROS)* in aerobic cells. Studies demonstrate that disturbances in copper homeostasis leads to several diseases, such as Menkes disease, Wilson disease, Parkinson's disease, Alzheimer's disease and related aging disorders. *Escherichia coli* has a two-component copper regulatory system enabling it to survive high concentrations of copper that may be generated through proteolytic and acidic degradation of food in the gut. Based on their findings, Singh et al., believe that *CueO* can convert the extremely toxic form of *copper Cu(I)* to *Cu(II)* which is less toxic, (Singh et al., 2004). Restoring the bowel population is among the primary targets of Nutritional Therapy, as part of its 'addressing the deeper causes' principle, including specific dietary guidelines with addition of nutritional supplements, in particular mega doses of *probiotics* and *enzymes*. The extremely important role of the gastrointestinal population, in most diseases is confirmed by a volume of studies, (Plaskett 2004; Goldberg et al., 2002; Murray & Pizzorno 2011; Sult 2005; Hanaway 2005). According to Hanaway (2005), over the course of a lifetime, we ingest an average of 30-60 tonnes of food, including huge amounts of macro- and micronutrients, chemicals, and toxins, (Hanaway 2005, p.444). The human stomach contains about one hundred bacteria per gram of contents, whereas the large intestine contains about one billion bacteria per gram, (Brody, 1999, p.148). An increasingly rising number of diseases are associated with gut malfunction which is largely based on its microorganism population, including cancer and autoimmune disorders, such

¹ Folic acid is a vitamin of the B family

² *Escherichia coli* or E-coli, a bacterium part of the normal bowel flora of the gastrointestinal system, it aids digestion and produces small amounts of vitamins B12 and K (Columbia Encyclopaedia 2007)

as rheumatoid arthritis, diabetes type I, and Hashimoto' thyroiditis, (*Hanaway 2005, pp.444-5*). Studies now also link autism spectrum disorders with gastrointestinal dysfunction (*Hanaway 2005, pp.444-5; Nicholson 2011*). Nutritional biochemistry demonstrates that clusters of cells belonging to the immune system occur in the small intestine. These include the Peyer's patches which interact with the bowel bacteria and synthesise antibodies against components of the bacterial cells, (*Brody, p.135*).

Cardiovascular disease

A significant amount of scientific evidence supports the association of nutritional and lifestyle factors with the pathogenesis of cardiovascular disorders, including, coronary heart disease, stroke, atherosclerosis, congestive heart failure, dyslipidaemia, and hypertension. Yamori et al., (1992), in a review of experimental studies with rats, demonstrated the gene/environment interaction in the humoral, neural, vascular and nutritional mechanisms of hypertension and cardiovascular disease. In particular, salt intake was found to accelerate cholesterol absorption from the intestine, to induce arterial fat deposition and active platelet aggregation promoting the pathogenesis of atherosclerosis at the cellular level of vascular smooth cells, (*Yamori et al., 1992*). About two decades later, these findings were reconfirmed in humans, by the WHO-coordinated Cardiovascular Diseases and Alimentary Comparison (CARDIAC) Study, a multi-centre epidemiological survey on diets and cardiovascular risks and mortalities in 61 populations, conducted over a period of 25 years (*Yamori et al., 2010*). Several lines of evidence link dietary factors as a cause of hypertension and subsequent Left Ventricular Hypertrophy, which occurs when protein synthesis exceeds protein breakdown resulting in a net accumulation of protein and expansion in cell size. Insulin was found to stimulate protein synthesis and inhibit protein breakdown in the heart, (*Brownsey et al., 1997; Young et al., 1992; Sharma et al., 2007*). It was also shown that insulin exposure of the heart after consumption of high carbohydrate meals activates the mechanisms of increased protein synthesis, (*Sharma et al., 2007*), associated with Left Ventricular Hypertrophy (*Shigenmatsu et al., 2005; Ceravolo et al., 2003; Sharma et al., 2007*). Increased levels of plasma *homocysteine* -occurring often due to vitamin B12 or folate deficiency or secondary to treatment with methotrexate- were also found to

increase risk for cardiovascular disease and venous thrombosis, through lipid peroxidation, impaired vasomotor regulation, vascular endothelial injury, and atherothrombogenesis, (Hamzaoui et al., [2009; 2010]). According to Stanger (2003), mild *hyperhomocysteinemia* has been consistently shown by numerous studies to be independently related to cardiovascular disease (CVD) or all-cause mortality, and it is thought to be responsible for about 10% of total CVD risk. It is also found to be present in 5-10% of the general population and in up to 40% of patients with vascular disease. The metabolism of *homocysteine*, which induces a pro-coagulant environment, appears to be influenced by numerous agents, drugs, diseases and lifestyle factors. A common factor is *folic acid* deficiency. Intracellular increased levels of *homocysteine* also occur with reduced enzyme activities inhibiting its breakdown, (Stanger et al., 2003). The relationship between high levels of *homocysteine* and vascular disease was also demonstrated by Chacon et al., (2010) in a study with 2100 individuals 55 years and older, (Chacon et al., 2010). Stanger et al., (2003) claim that, reduction of elevated plasma *homocysteine* levels may theoretically prevent up to 25% of cardiovascular events, (Stanger et al., 2003).

In addition, several, so-called 'functional foods', such as *soybeans, oats, psyllium, garlic, tea, fish, grapes* and *nuts* are thought to have a significant contribution in the prevention and treatment of cardiovascular disease, including reducing blood lipid levels, improving arterial compliance, reducing cholesterol oxidation, decreasing plaque formation, scavenging free radicals, and inhibiting platelet aggregation, as long as they are consumed in adequate amounts and on a consistent long-term basis, (Hasler et al., 2000). Nutritional supplements, such as *magnesium, calcium, dietary fibres, protein, some amino acids* and *essential fatty acids*, have been shown by extensive experimental research, to counteract directly or indirectly the atherogenic effects of excess salt intake in rats, being therefore effective in preventing stroke, the typical complication of hypertension, (Yamori et al., 1992). Gorelik et al., (2003) based on their findings showing that patients with congestive heart failure have lower than recommended levels of *magnesium, calcium, zinc, copper, manganese, thiamine, riboflavin, and folate*, advice supplementation especially for those patients treated with *furosemide*, (Gorelik et al., 2003). *Magnesium*, in particular, was found in a meta-analysis of nine randomised double-blind controlled trials, to significantly increase high density lipoprotein (HDL), (Song et al., 2006). Other researchers provide evidence from a

large volume of studies demonstrating the hypolipidaemic effects and cardioprotective benefits of dietary soluble *fibre* (Rideout et al., 2008), such as the dose- and time-dependent lipid lowering effects of *psyllium* supplementation, (Wei et al., 2009; Anderson et al., 2000) and *flaxseed* and its derivatives, (Pan et al., 2009)

Vogel et al., 2005 after reviewing several studies, stress the importance of dietary modification for the primary and secondary prevention of coronary heart disease and hypertension, listing specific nutrients and nutritional supplements that can either accelerate or retard the development of cardiovascular disease. Nutrients mentioned include bioactive components in foods such as *plant sterols*, *soluble fibre (psyllium, guar gum and oat bran)*, *omega-3 essential fatty acids* and *garlic*. Supplements include *vitamins, mineral, herbs, amino acids, enzymes, organ tissues, glandular and metabolites*. The researchers refer to studies demonstrating the power of antioxidant vitamins to prevent both atherosclerosis and its complications by retarding LDL oxidation and by inhibiting the proliferation of smooth muscle cells, platelet adhesion and aggregations, the expression and function of adhesion molecules and the synthesis of leukotrienes. They also believe to improve endothelial function, reduce ischemia, and stabilize atherosclerotic plaques to prevent plaque rupture, (Vogel et al., 2005). In particular the following nutrients were found to exert beneficial effects, with or without the synergistic effect of biomedical treatments, on cardiovascular disease: *Vitamin C* in high dosages over 360mg per day was associated with 27% lower risk for coronary heart disease and 28% of nonfatal myocardial infarction, compared with no supplemental intake. *Vitamin C in combination with_vitamin E* was found to decrease the rate of atherosclerosis, especially in men, as measured by carotid artery intima-media thickness. *Magnesium*, at doses of 176 to 423 mg/day, significantly lowered blood pressure. Also intake of *magnesium* 365mg twice daily for 6 months led to 14% improvement in exercise duration and a decrease in exercise-induced chest pain, compared to no change in the placebo group. In addition *magnesium* was found to decrease the frequency of ventricular arrhythmias in patients with congestive heart failure. *CoEnzyme Q10*, being a free radical scavenger and membrane stabiliser and involved in oxidative phosphorylation and the generation of *ATP (adenosine triphosphate)*, has been shown by over 40 controlled trials and several reviews to be beneficial in subjective (quality of life, decrease in

hospitalisations) and objective (increased left ventricular ejection fraction, stroke index) parameters. One of the largest trials with 651 New York Heart Association functional class III or IV congestive heart failure found a significant decrease (38%-61%) in the number of hospitalisations, incidences of pulmonary oedema, and episodes of cardiac asthma with the use of CoEnzyme Q10. *L-carnitine*, which is involved in the transport of free fatty acids across mitochondrial membrane for energy production, was shown by studies to significantly improve maximum exercise times and ejection fractions, in the New York Heart Association functional class II or III congestive heart failure. Also in patients with claudication significant improvement in exercise treadmill performance (54% increased walking time) and functional status was achieved with *L-carnitine* 2g/day for 6 months. *L-arginine* has been shown to improve coronary and brachial artery endothelial function and reduce monocyte/endothelial cell adhesion and platelet aggregability. Improvements were also shown in patients with recurrent chest pain, and in coronary blood flow in response to acetylcholine. *Hawthorn* was found to have positive inotropic¹ effects, antiarrhythmic properties and to be a peripheral vasodilator. It has been used for congestive heart failure, cor pulmonale², ischemic heart disease, arrhythmias, blood pressure reduction, atherosclerosis, and cerebral insufficiency. The researchers claim that in Germany *hawthorn* is prescribed by doctors for mild cardiac insufficiency. Several studies using bicycle ergometry or spiroergometry on patients with heart failure have shown significant improvement in cardiac performance after 6-8 weeks of *hawthorn* use at a minimum dose of 300mg daily. Similarly, improvement was shown in patients with congestive heart failure. No adverse effects were reported. *Hawthorn* has been found to have a wider therapeutic range, lower risk of toxicity, safer to use in renal impairment, and can be safely used with diuretics and laxatives, compared to digitalis. *Ginkgo Biloba* was found by a meta-analysis of eight randomised, placebo-controlled, double-blind studies to significantly increase pain-free walking distance by 34m in patients with claudication. *Horsechestnut* (*Aesculus hippocastanum*) was found to be effective in the treatment of chronic venous insufficiency. In particular, in a systematic review of eight placebo controlled and five comparative randomised trials with a total of 1083 patients *Horsechestnut* was found to have equivalent effect with other active therapies. These

¹ Affecting heart muscle contraction

² Acute strain or hypertrophy of the right ventricle caused by a disorder of the lungs or of the pulmonary blood vessels, (The American Heritage Dictionary of the English Language (2000)

included reduction in leg volume and leg circumference as well as reduction of leg pain, pruritus, and feeling of fatigue and tenseness, (Ernst 2000; Vogel et al., 2005). The use of *Horsechestnut* was approved by the German Commission E to be used for chronic venous insufficiency, (Vogel et al., 2005).

Other researchers highlight the beneficial effects of combination therapies, within the context of integrative approaches to the treatment of cardiovascular disease. In particular it is argued that statin¹ monotherapy commonly used by doctors, may be highly effective for lowering Low Density Lipoprotein (LDL) levels, however, the high doses needed for the prevention of nonfatal cardiovascular events, have been associated with hepatotoxicity, myopathy, and non-cardiovascular death. In fact, statins do not completely eliminate cardiovascular risk, such as coronary events, particularly in patients with metabolic syndrome, or with other independent risk factors such as high triglycerides, atherogenic dyslipidaemia, and low High Density Lipoprotein (HDL). They therefore advise combination therapies using statins together with a number of nutrients proved for their effectiveness. Suggestions include, *plant sterols/stanols, fibrates, niacin* and *omega-3 essential fatty acids*. *Niacin* (vitamin B3 or nicotinic acid) has been shown, as the best mean to achieve normal lipid values in several high risk populations, (Scholle et al., 2009; Cziraky et al., 2008; Tenenbaum et al., 2008:). Vosper (2009) refers to several studies that demonstrate *niacin* as the most effective treatment currently available for increasing High Density Lipoprotein (HDL) an effect accompanied by a reduction in total cholesterol, Low Density Lipoprotein (LDL), Triglycerides and Very Low density lipoproteins (VLDLs). Its use is particularly useful for patients who, despite *statin* therapy, still have low HDL levels. In addition, researchers believe that *niacin* may directly influence events in the development of cardiovascular disorders, through its antithrombotic effect and its ability to increase intracellular *nicotinamide adenine dinucleotide (NAD⁺)* and to inhibit *reactive oxygen species (ROS)* production in endothelial cells. Co-administering *niacin* with *statins* has been shown to have very good effects, (Vosper 2009)

Supplementation with *essential fatty acids*, especially as part of combination approaches, in patients with cardiovascular problems under medical therapy has been shown to have

¹ Statins: 3-hydrox-3-methylglutaryl coenzyme A reductase inhibitors

significant beneficial effects. Duda et al., (2009) in an overview of meta-analyses of a large number of randomised trials, found growing evidence that supplementation with *omega-3 EFAs* has potential therapeutic effects for patients with heart failure. These include: lowering serum triglycerides (*a meta-analysis of 72 placebo-controlled trials demonstrated reductions of 25-35% in serum triglycerides*); inducing transcription of genes encoding proteins involved in cardiac lipid metabolism thereby protecting mitochondria from deterioration and improving their function in ATP production; reducing production of pro-inflammatory cytokines, and increasing production of anti-inflammatory prostaglandins and cardioprotective hormones through effects on gene expression; lowering blood pressure (*meta-analysis of 36 randomised trials: systolic pressure reduced by 2.1mm/Hg and diastolic by 1.6mm/Hg*); and reducing heart rate by 2.5 bpm (*meta-analysis of 30 randomised trials*), (Duda et al., 2009). A report published by a working group established by the National Institutes of Health, the Office of Dietary Supplements and the National Heart, Lung, and Blood Institute of the U.S. Department of Health and Human Services after reviewing the evidence-based reports on *omega-3 fatty acids* and their relation to cardiovascular disease risk factors, concluded that the body of evidence is consistent that *omega-3 fatty acid* consumption reduces 20%-45% cardiovascular events through beneficial effects on risk factors and biomarkers of cardiovascular disease: Lowering triglycerides by 10-30%, decrease in systolic and diastolic pressure by about 2mm/Hg, preventing coronary artery restenosis after angioplasty, and increasing exercise capacity in patients with atherosclerosis, (NIH et al., 2004)

A number of other supplements have also demonstrated preventive and therapeutic properties in cardiovascular disease. *Taurine* was found by experimental studies with animals to contribute to the prevention of stroke and cardiovascular disease, (Yamori et al., 1992), and these effects were also confirmed in human studies. The CARDIAC epidemiological study, conducted within 61 populations over a period of 25 years, found *taurine* supplementation to be inversely related significantly with lower coronary heart disease mortality, body mass index, systolic and diastolic blood pressure, total cholesterol, and atherogenic index (total cholesterol/HDL). A particularly beneficial effect of *taurine* was observed in salt-sensitive blood pressure rise individuals, (Yamori et al., 2010). *Naringin*, a citrus bioflavonoid, in supplement form, was shown to significantly increase

the concentration of plasma vitamin E, (Jeon *et al.*, 2001) and to lower plasma cholesterol via inhibition of hepatic *HMG-CoA reductase* activity, (Kim *et al.*, 2004). In addition, it was found to have an important role in regulating the antioxidative capacities of the body by increasing the *SOD* (*superoxide dismutase*) and *catalase* activities, up-regulating the gene expressions of *SOD*, *catalase*, and *GSH-Px* (*glutathione peroxidase*), and protecting the plasma vitamin E, (Jeon *et al.*, 2001). The crucial role of the gastrointestinal system is also stressed in cardiovascular health. Papathanasopoulos & Camilieri (2010), in a review conducted from a gastroenterological perspective, they demonstrated the multiple benefits from the dietary incorporation of fibre supplements and natural foods and grains on cardiovascular risk, especially focusing on the vital contribution of gastrointestinal function for obtaining maximum benefit from foods supplements through the fibre modulation of gastric and small intestine motility, intestinal absorption, hormonal milieu, colonic microflora, and fermentation. The researchers advise the integrating of knowledge on dietary supplements, such as *fibre*, in medical practice, (Papathanasopoulos & Camilieri 2010).

Cancer

A series of reports of the last few decades, by national and international organisations provide evidence of a global consensus among experts that most major chronic diseases such as cancer are influenced, and can be prevented, by dietary and lifestyle patterns. These include the report *Diet, Nutrition, and Cancer*, published in 1982 by the National Cancer Institute Cancer Commission of the National Academy of Sciences and the Committee on Diet, Nutrition, and Cancer; the 1997 report of the American Institute for Cancer Research and the World Cancer Research Fund; and a series of handbooks on cancer prevention in relation to dietary factors published by the World Health Organisation International Agency for Research Cancer, (Go *et al.*, 2004). Campbell & McTiernan (2007) refer to estimates by the International Agency for Research on Cancer according to which 25% of cancer cases worldwide are caused by overweight or obesity and a sedentary lifestyle. Effects of unhealthy lifestyle patterns include: increased *estrogens* and *testosterone*, leading to increased risk of breast and endometrial cancers;

hyperinsulinaemia and *insulin resistance*, leading to increased risks of colon, breast, and pancreatic cancers; and increased *inflammation*, and *depressed immune* function leading to several cancers. The researchers refer to a volume of randomized clinical trials which have shown that diet and lifestyle interventions can alter biomarkers of cancer risk. In a controlled physical activity trial they found that serum *oestrogen*, *testosterone*, and *insulin* in overweight, sedentary, postmenopausal women, were reduced after a year of 45 minutes per day moderate aerobic exercising five days a week. In another controlled trial with middle-aged to older persons, colon *crypt cell* proliferation was reduced in men who exercised 60 minutes daily, 6 days per week for one year (*Campbell & McTiernan 2007*). Similarly, Bernstein et al., 1994, found that amount of hours spent in physical exercise activities per week was a significant predictor of reduced breast cancer risk, (*Bernstein et al., 1994*)

A number of deficiencies and/or excesses in vital micronutrients, as well as environmental exposures have been also associated with cancer through their effect on immune system function. Reynolds et al., (2010)¹, in a review of current evidence pertaining to dietary factors and cancer, found that specific dietary constituents may influence the mechanisms of tumorigenesis. These include *glucosinolates*, *organosulphur compounds*, *genistein*, *curcumin*, *catechins*, *resveratrol* and *lycopene* (*Reynolds et al., 2010*). In particular, *resveratrol* (in grapes, mulberries, red wine, and other plants) was found to exert unique biological actions, such as life prolongation and protection against early development of cancer. Its action is associated with induction of a strong but reversible *S-phase*² delay and a mild *DNA synthesis* inhibition, yet without the induction of *apoptotic* or *necrotic* cell death, (*Zhou et al., 2009*). *Saw Palmetto*, an extract derived from the deep purple berries of the saw palmetto fan palm *serenoa repens*, was found by a meta-analysis of 18 randomised controlled trials with 2939 patients to be significantly more effective than placebo and as effective as *finasteride*³ –and with fewer adverse effects- in improving urological symptoms and flow measures in patients with Benign Prostate Hyperplasia, (*Ernst 2000*). Several other nutrients were found by scientific evidence to have anti-carcinogenic effects. *Epigallocatechin gallate* from green tea has been prescribed to

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² S-phase: the phase of the cell cycle in which DNA is synthesised before mitosis (*Mosby's Medical Dictionary 2009*)

³ Finasteride: drug used for treatment of Prostate Benign Hypertrophy (*Mosby's Medical Dictionary 2009*)

cancer patients, in a mixture (for enhancing bioavailability) containing also *ascorbic acid* (vitamin C), *selenium*, *N-acetyl cysteine* and other nutrients in different formulations resulted in an increase in the systemic bioavailability of *epigallocatechin gallate* by 27% (Gawande et al., 2008). *Red pepper seeds* were shown to have antimutagenic effects against the *aflatoxin B1* and *MNNG*, and anticarcinogenic effects in human cancer cells. In addition ethanol extract or *red pepper seed* reduces the accumulation of reactive oxygen species, (Song et al., 2010). *Zinc*, also appears to be a crucial micromineral for immune function. *Free zinc* is regulated by 14 distinct *zinc importers* and *transporters* in immune cells and its depletion induces cell death via *apoptosis* (or *necrosis* if the pathways for *apoptosis* are blocked). The same is true for cancer cells which have been shown to upregulate *zinc importers*, and frequently increase zinc levels, for their survival. Therefore approaches are recommended which locally regulate zinc levels to promote survival of immune cells and/or induce *apoptosis* of tumour cells, (John et al., 2010). *Selenium* is also a very important mineral and its status is frequently associated with cancer risk. *Selenium* is a crucial cofactor in the most important endogenous antioxidative systems and *sodium selenite* supplementation, in women undergoing radiation therapy for gynaecological cancer, was shown to have significant beneficial effects, without protecting tumour cells (as often suspected by oncologists), (Muecke et al., 2010). Studies demonstrate a role for *selenium* in prostate cancer aetiology and development, through polymorphisms in *selenoenzymes*, (Steinbrecher et al., 2010). The therapeutic power of *selenium* has been shown in malignancies responsive to endocrine manipulation, such as prostate cancer. Its role is associated with inhibiting tumour cell growth via down-regulation of androgen receptor expression, (Beckett & Arthur 2005).

The gastrointestinal system appears to have an enhanced and upgraded role in the prevention but also the inhibition of cancer. Studies demonstrate the significant contribution of *probiotic* therapy in restoring the bowel microflora and their activity as anti-inflammatory and anti-carcinogenic agents. In particular, *probiotics* were found to upregulate both ileal and colonic mucosal levels of *alkaline sphingomyelinase*, an enzyme which correlates positively with increases in levels of *caspase-3* and *IL-1 beta-converting enzyme*. *Alkaline sphingomyelinase* was found to have the capacity to induce *apoptosis* in adenocarcinoma cells and inhibit the process of carcinogenesis (Soo et al., 2008). Reduced

activity of *alkaline sphingomyelinase* and the resulting accumulation with *sphingomyelin* were found in human colon cancers and colonic adenomatous tissue. High fat diets and beef with fat diets were found to reduce intestinal *alkaline sphingomyelinase* by 80% and 84% respectively, *ceramidase* enzymatic activity by 60% and 92% respectively and *caspace-3* activity by 80% and 84% respectively. These effects have been implicated in colonic carcinogenesis, (Yang et al., 2002). Similar effects of high fat diet on *alkaline sphingomyelinase* were found by other studies with patients with colorectal cancer but also in patients with chronic colitis. It was also shown that a decrease in *alkaline sphingomyelinase* activity associated with age is a general phenomenon of premature aging of the mucosa in chronic colitis, (Cheng et al., 2004; Sjoqvist et al., 2002). A number of nutrients demonstrated by studies for their anticarcinogenic effects are often not readily absorbed by the small intestine, depending on several factors, such as molecular size, lipophilicity, solubility, gastric and intestinal transit time, alkalinity, membrane permeability etc and *Probiotics* play an important role in many of these factors.

Autoimmune and inflammatory diseases

The aetiology of autoimmune diseases and very often of inflammatory disease is still largely unknown. Hamzaoui et al., (2010) found that plasma *homocysteine* levels are increased in psoriasis, systemic inflammatory vasculitis (Behçet's Disease¹), and inflammatory bowel disease, (Hamzaoui et al., 2010). Maes et al., (2009), found that *Coenzyme Q10*, a mitochondrial nutrient which acts as an essential cofactor for the production of ATP in mitochondria and which displays significant antioxidant activities, plays a role in the pathophysiology of *Myalgic Encephalomyelitis* or otherwise known as *Chronic Fatigue Syndrome (ME/CFS)* a medical illness characterised by disorders in inflammatory, oxidative and nitrosative pathways. The study demonstrated that patients with ME/CFS would benefit from *Coenzyme Q10* supplementation. The researchers comparing their findings with other findings showing that *Coenzyme Q10* is an independent predictor of chronic heart failure, and that *statins* significantly reduce plasma *CoQ10*, they

¹ Behçet's Disease: a systemic inflammatory disease with vascular damage, deep vein thrombosis, arterial obstruction, aneurysms, etc (Hamzaoui et al., 2009)

recommend *statin/CoQ10* co-supplementation in patients with ME/CFS, (Maes et al., 2009). Several other nutrients were found to have highly beneficial effects in ameliorating inflammation and inhibiting its degenerative effects. Studies demonstrated that *resveratrol* (grapes, mulberries, red wine, and other plants) reduces the severity of Severe Acute Pancreatitis through its anti-inflammatory effects by inhibition of the inflammatory response and a decreased expression of *Tumour Necrosis Alpha*, *interleukin* and *nitric oxide* in peritoneal macrophages, (Ma et al., 2005); intra-articular injection of *resveratrol* may protect cartilage against the development of experimentally induced inflammatory arthritis, (Elmali et al., 2007); and oral treatment with *resveratrol*, *curcumin* or *simvastatin* ameliorates acute small intestinal inflammation, by down-regulating *Th1-type* immune responses, and prevents bacterial inflammation by maintaining gut barrier function, (Bereswill et al., 2010). Therefore this treatment can be an effective intervention strategy for inflammatory bowel diseases such as *Crohn's disease (ileitis terminalis)* and *ulcerative colitis* (Bereswill et al., 2010). Tunon et al., (2009) in a review summarising recent research data on the modulation of the expression of different inflammatory mediators by *flavonoids* and the effects on cell signalling pathways responsible for their anti-inflammatory activity, found a clear potential utility of dietary *flavonoids* or new *flavonoids-based agents* for the possible treatment of inflammatory diseases, (Tunon et al., 2009)

The importance of intestinal integrity and function is again highlighted by several studies which demonstrate that *dysbiosis*¹ in *commensal enteric microbes* plays an important role in the pathogenesis of *inflammatory bowel diseases*, *Crohn's disease*, and *ulcerative colitis*. A host-bacterial metabolite, *hippurate* was found to be at significantly lower quantities in the urine of sufferers of above diseases, than in healthy individuals. The production of *hippurate* involves a process which begins with the degradation of dietary compounds in the intestine by the bowel bacteria leading to the production of *benzoate* which conjugated with *glycine* promotes the production of *hippurate*. The researchers demonstrated that the low excretion of *hippurate* among sufferers despite intake of foods high in *benzoate* or supplementation of *benzoate* is due to insufficient intestinal microbial metabolism, (Williams et al., 2010). Other studies have shown altered composition in

¹ Dysbiosis: from the Greek words δυς (bad) + βίωσις (life)

the *gut ecosystem* (Guarner 2007), such as a consistent reduction of *Clostridium leptum* subgroup in patients with *Irritable bowel disease* and particularly *Crohn's disease*, (Sokol et al., 2008). Studies indicate that the intestinal surface barrier is one of the most important parts of the immune system and bowel microorganisms are not 'innocent bystanders in humans' but they actively interfere in the shaping of the immunological network of the host. The synergism between gastrointestinal *microflora*, a 'leaky' intestinal mucosal barrier and altered mucosal immunity is shown by evidence; therefore potential targets for intervention should include maintenance of *microflora* and tightening in interepithelial junctions. In addition prevention of propagation of inflammation and autoimmunity could be effected by nutritional or pharmacologic means, (Vaarala et al., 2008). There appears to exist strong experimental evidence to support the use of supplemented *probiotics* and *prebiotic* nutrients that promote intestinal health, such as *inulin* and *oligofructose* can prevent or mitigate intestinal inflammatory lesions, (Guarner 2007; Loojjer-van Langen & Dieleman 2009).

PART VII

NUTRITIONAL

RESEARCH

A CRITIQUE

CHAPTER I

NUTRITIONAL RESEARCH-THE LIMITATIONS

In spite of the fact that a volume of clinical research already exists in support of the power of nutrients in the prevention and treatment of disease, it is believed that the most rigorous and transparent approach to synthesise this evidence, minimise biases, and formulate scientific consensus statements, is the *Systematic review*, (Lichtenstein et al., 2008). *Systematic reviews* critically appraise research, relevant to clearly formulated questions, utilising explicit methodology to identify, select, and analyse data from studies, included in the review, on the basis of predetermined inclusion criteria. They are considered as a vital link in 'the chain of evidence that stretches from the laboratory bench to the bedside' and are defined as 'the application of scientific strategies that limit bias by the systematic assembly, clinical appraisal, and synthesis of all relevant studies on a specific topic', (Manchikanti et al., 2009) *Meta-analysis* is often the final step in a systematic review, but it can be also performed with a systematic review. It generates a summary of estimates of effects demonstrated by the statistically pooled results across several studies, (Manchikanti et al., 2009). Scholars focus on a number of important strengths of systematic reviews, some of them especially relevant to nutritional research. These include: the transparent, objective, and rigorous nature of the process; the ability to combine small studies with meta-analyses, thereby increasing the statistical power available to address specific questions, a characteristic particularly useful for systematic reviews of nutrition topics, in view of the limited number of large trials in this area; its flexibility in addressing wide variations in the nature of questions, a particularly challenging issue for the nutrition community, which has moved beyond the traditional population-based recommendations for preventing deficiencies, to the prevention of chronic disease and nutrient excesses; its ability to identify gaps of available data especially useful in the formulation of policy and programme decisions; and its ability to identify where improvements in the quality and nature of reporting are needed, (Lichtenstein et al., 2008).

However, a number of limitations are also presented, being especially evident when applying systematic reviews in the field of nutrition, together with recommendations for how they can be minimised, and possibly eliminated. These include: incomplete reporting of basic study design and conduct; and poor characterisations of baseline, placebo, and intervention characteristics, even for topics for which there are a number of published trials, which limits the ability to make definitive conclusions about the outcome of interest, (*Lichtenstein et al., 2008*). Balk et al., (2007) focus on the weaknesses in interpretation, emerging from a number of factors which pose much more challenges in interpreting human studies in the area of nutrition, than interpreting drug trials. Examples are: the individual's *energy balance*, where changes in body weight can perplex resulting values, such as LDL cholesterol, therefore if one food is subtracted from the diet, another one must be added to compensate; *the individual's background diet*, if it is already rich in foods (e.g. fish) which contain the nutrient under study (e.g. fish oil) or poor in other foods such as meat; *food preparation methods* (e.g. frying); *other compounds or contaminants* possibly contained in different food supplements; and *balance between different EFAs* (omega 6, omega 3, EPA, DHA, ALA¹). The researchers found that, whereas diets and nutritional supplements contain many nutrients that may interact, only rarely were taken into consideration, probably due to added complexity to their evaluation, (*Balk et al., 2007*).

To support their claims they provide an example of a critical examination of a large series of systematic reviews of the relationship between omega-3 essential fatty acid (EFAs) consumption (from both marine and plant sources) and many clinical conditions, and discuss the lessons learned from this review and the limitations identified in the conducted studies, which they consider responsible for the inconclusive results regarding the health benefits of omega-3 EFAs. These included:

- **Limitations common to health sciences research:** inadequate study design (eg, no control group); inadequate analysis (*e.g. no direct comparison between interventions*), poor reporting of studies (*e.g. missing data and inconsistencies between abstract, text and tables*); inadequate descriptions of the interventions,

¹ Alpha-linolenic acid

controls, and outcomes; use of intermediate outcomes, not directly associated with condition of interest or not been validated; small size of study; inclusion of only highly narrow populations, thereby limiting applicability; short-term follow-up; inadequate analysis or report of results of crossover studies (no reporting of outcomes at all stages of the study, improper analytic techniques, no analysis of the comparison between intervention and control); Inadequate reporting of safety data

- **Limitations specific to the omega-3 EFAs (and other nutrition research):** large variety of dietary components (*3 types of omega-3 EFAs*), doses, and fish oil sources; lack of evaluation of potential cofounders (*consumption of other fats, antioxidant vitamins, pro-oxidant nutrients, weight changes, and other risk factors for disease outcomes*); possible effects of other bioactive food components (e.g. sterols or mercury in fish oils); failure to describe baseline consumption of omega-3 EFAs or of background diet; failure to evaluate changes in omega-6/omega-3 ratio; failure to evaluate changes in EPA/DHA ratios and consumption of α -linolenic acid; failure to use validated measures of dietary intake or biomarkers of omega-3 fatty acid exposure; estimation of omega-3 fatty acid exposure only from single measures of dietary consumption; failure to validate omega-3 EFAs consumption with tissue concentrations; few direct comparisons of different sources, doses, and ratios of EFAs; inadequate information on treatment products (e.g. purity, composition, presence other bioactive compounds, or effective masking of taste or smell characteristics); inadequate description and characteristics of placebo products and carrier substances, (*Balk et al., 2007*).

Along the same lines, Chung et al., (2009) in an examination of the reporting quality of 141 Systematic Reviews (105 with and 36 without meta-analyses) linking nutrient supplementation, such as vitamins, minerals and antioxidants, with health outcomes they concluded that, although the reporting quality of Systematic Reviews has improved since publication of the reporting standards, the reporting of nutrition or diet variables has not. The analysis documented the lack of consistent standards in conducting and reporting

Systematic Reviews of nutrition-related topics. The researchers emphasise the need to report: the source -brand names, components, formulation etc- of nutrient supplements or foods; the dose and intervention regimens –e.g. number of times per day; the baseline nutrient exposures or the background diet, (because this could be a source of heterogeneity, that is differential effects of nutrient supplementations on health outcomes); the methods or instruments for assessing intakes of nutrient exposures. In the case of nutrition epidemiological studies, the researchers stressed the importance of reporting the methods or instruments for assessing intakes of nutrient exposures, ranges or distributions of the nutrient exposures, measurement errors of the diet or nutrient variables, and the potential impact of the errors from assessing the nutrient exposures on the nutrient-outcome association. The result identified by the researchers was the limiting of the potential value of a volume of studies in helping to formulate nutrition related guidelines, recommendations, or research agendas, (*Chung et al., 2009*).

Researchers believe that improvements are necessary, and possible, in the area of nutritional research. They offer a number of recommendations suggesting different ways for conducting and reviewing nutrition research, not only of additional studies. These include substantial methodological improvements in the quality of study rationale, design, conduct, and documentation, in order to provide robust evidence on the health effects of nutrients; developing improved models of disease interactions; and testing hypotheses in persons both with and without a history of the conditions of interest. Furthermore, for many clinical conditions, such as dementia and cancer, dietary interventions should begin at a relatively young age with very long-term follow-up and therefore in order to evaluate primary prevention, they recommend converting randomised trials or dietary or supplement interventions into long-term observational studies. The importance of the collaboration of research groups on multicentre trials in enhancing the applicability and strength of studies and allowing consideration of confounding factors is also stressed, (*Balk et al., 2007*). *Manchikanti et al., (2009)* claim that, in spite of the fact that most medical research is observational, randomized controlled trials have been considered as the primary method of research to support evidence-based medicine. A number of reasons are offered for this, such as insufficient quality and poor reporting of observational studies which prevents the generalizability of the mixed

results. The researchers, question the ability of randomised controlled trials to effectively determine the efficacy of an intervention, claiming that evidence-based medicine based only on randomized control trials represents a shift in medical paradigm, since it rejects intuition, unsystematic clinical experience and pathophysiological rationale as sufficient grounds for clinical decision making. They claim that pragmatic non-randomised studies are a necessary part of the evidence base for medicine, both because they are able to provide information about a larger and more diverse population of patients, and because they are more likely to follow patients at outcome over a long period of time. The effectiveness of an intervention in a community can be identified through observation only and not through a special setting of a controlled trial. Observational studies include aetiological or effectiveness studies, cross-sectional studies, case studies, case-control designs, designs with historical controls or cohort designs. The quality of randomised and non-randomised studies depends in part on whether potentially confounding factors, such as age, gender, or the presence of co-morbid conditions, occur in roughly the same proportions in the treatment and the control groups'. The researchers highlight the need of acknowledgement of the fact that clean and pragmatic studies provide equally important kinds of evidence to inform clinical decision-making; therefore, to eliminate dangerous discrepancy between the experts and the evidence, they suggest the conduct of systematic reviews of observational studies, which represent an important complementary source of information, in conjunction with randomised controlled trials, provided that the data will be analysed and interpreted within the context of confounding bias to which observational studies are prone, (*Manchikanti et al., 2009*)

Along the same lines, Lichtenstein et al., (2008) draw attention to the unique characteristics of the area of nutrition (e.g. essentiality and habitual exposure) which necessitate the development of a more complex set of research questions and approaches, than those used in other fields. The researchers express the view that the Systematic Review process is adequately flexible and can accommodate the unique challenges posed by questions related to nutrition, if the necessary steps are taken to minimise bias, indentify the areas unique to the discipline of nutrition and set recommendations and guidelines to ensure integrity of the reviews. A number of issues, particular to nutrition-related topics, that do not normally arise in systematic reviews of

pharmaceuticals, are discussed and suggestions for handling them are offered. These include:

- **The Baseline Exposure** where, in contrast to pharmaceutical trials, in nutrition-related studies all persons have some level of background dietary exposure to the nutrient of interest, either through diet or supplementation, or in some cases from endogenous synthesis (e.g. Vitamin D, vitamin K);
- **Nutrient Status** of an individual or population, is not easy to evaluate, since it is unique to each nutrient and depends on nutrient-specific tissue availability for sampling and on homeostatic mechanisms regulating plasma concentrations;
- **Bioequivalence** of nutrients poses a challenge in determining accurate conversion factors for the calculation of nutrient equivalents (such as vitamin K as phylloquinone and menaquinone);
- **Bioavailability** of different chemical forms of nutrients, being a function of various interactions with other nutrients, foods, drugs, of the biological response to single compared with multiple daily doses and of the habitual intake effect on efficiency of absorption and excretion, of food processing;
- **Multiple and interrelated biological functions of a nutrient**, where the biological function of a nutrient may be dependent on its interaction with multiple nutrients (eg. Folate with vitamin B12 and B6 or vitamin D with calcium);
- **Undefined nature of nutrient intervention** where food-based nutrient interventions, in contrast to nutrient supplement-based interventions, pose unique challenges in accurately quantifying the absolute intake of the specific nutrient (as is the EPA¹ and DHA² levels in different fish, or different species of fish, or the time of year the fish was caught, and animal husbandry practices for farm-raised fish);
- **Uncertainties in assessing dose-response relationships** where measurement and assay procedures can alter apparent dose-response relationships between nutrient intake or dietary pattern and health outcomes, an issue particularly important for systematic reviews where absolute intake/response relationships, rather than relative intake response relationships are needed to assess the importance of a particular intervention, and establish recommendations, for public health (Lichtenstein *et al.*, 2008).

¹ Eicosapentaenoic acid in fish oil

² Docosahexaenoic acid in fish oil

Becker & van Binsbergen from the Department of Family Medicine of SUNY Upstate Medical University of Syracuse, USA and the Department of General Practice of The University Medical Centre Nijmegen in the Netherlands, respectively, provide a number of arguments to support their view that randomised controlled trials, from which the majority of Cochrane reviews retrieve evidence, are insufficient to prove the significance of individual nutritional interventions. Reference is made to how difficult and often unfeasible to contact randomise trials in this area, for a number of reasons such as: the difficulty of recruiting individuals willing to make major changes to their diets on a randomized basis, and stick to their prescribed intervention which might need years to produce effects; and the requirement of a variety of tailor-made nutritional interventions, on the basis of the complexity of evidence related to the individual patient's pathophysiological background and their cultural and psychosocial conditions. The researchers criticise the Cochrane Collaboration for while aiming to be the 'best single source of reliable evidence about the effects of health care' and, in fact 'is well on the way to doing so', this does not apply for topics beyond the traditional medical boundaries, such as is Nutrition. Claiming that the editorial functions of the Cochrane Collaboration are arranged along disease-specific lines in Collaborative Review Groups and no group or 'entity' (in Cochrane terms) exists in the area of diet and nutrition, they bring up the example of the Department of General Practice/Family Medicine of the University Medical Centre Nijmegen, The Netherlands, which in cooperation with the Dutch Cochrane Centre and Heelsumworkshop (*a collaboration between nutritionists and family physicians*), is in the process of establishing a Cochrane Diet and Nutrition Field, either as a separate entity or as a subgroup of the existing Primary Health Care Field. Becker & van Binsbergen believe that this new entity, perhaps acting initially as a subgroup, would deal with Nutrition issues within the Collaboration and promote the translation of evidence from nutritional interventions to the consulting room of the primary care clinician, (*Becker & van Binsbergen 2005*)

EPILOGUE

The volume of evidence presented in this book provides solid grounds to support the fact that the Science of Nutrition, in its applied form as Nutritional Medicine, or Nutritional Therapy, has a vital role to perform along the spectrum of medical practice of the twenty first century. This fact has been acknowledged and promoted by the worldwide academic community and it is gradually gaining the respect of the medical community, as demonstrated in the previous chapters. However, the largest proportion of the power to design and implement transformative policies into the wider area of the provision of healthcare rests with the politicians who, apart from their political power, they need the *scientific potential est*¹, essential to support decision-making. The experiential learning gained from a number of professional and political activities in which the author was involved for several years, together with the insights extracted from the analysis of the interviews with a representative number of Cypriot key actors, demonstrated that, in spite of a general consensus on the importance of diet and lifestyle in the prevention of disease, there exists a significant knowledge deficit, on the actual role of Nutrition as a scientific, evidence-based, therapeutic agent. This gap in knowledge appears to be one of the major impediments to transformation and change in the provision of healthcare in Cyprus and this is what this book was prepared for: to fill this gap by providing adequate evidence-based information about the vital role of applied Nutritional Science not only in prevention but also in treatment of disease.

The research has demonstrated that a consensus exists among Cypriot politicians for the need of modernisation and transformation of the health sector to conform to European new policies and directives, following the example of other European countries. In particular, the high officials of the Cyprus Health Insurance Organisation demonstrated awareness of the ‘disappointment of citizens for the declining quality of services’, and of their demand for a more person-centred, National Health System which would provide the prerequisites for informed choices, in line with other health systems in Europe. The imperative of transformation of the Cyprus Health Sector is firmly supported by the evidence contained in this book, which was accumulated from this research. An important finding is that the health of Cypriots, in spite of government statements that it

¹ Knowledge is power

'favourable compares with the health of other European citizens', it actually deteriorates. According to official reports, whereas Cypriots have high Life Expectancies, they, however, have the second lowest Healthy Life Expectancy among all European countries, an indicator which shows that Cypriots lose an average of 10 years of their lives to illness. Some chronic health problems, such as cardiovascular disease, and diabetes have reached epidemic levels and one in two Cypriots are overweight or obese, with obesity being strongly correlated by scientific evidence with several common chronic diseases.

During the Survey more than half of the population stated as 'suffering, or suffered in the past' from at least one or more chronic health problems, and the majority of the rest - who stated as 'not suffering, or suffered in the past' from any health problem- take some form of medication, demonstrating that successful 'management' of a disease with medication equals to 'no disease'. Furthermore, the majority of those who stated as 'suffering, or suffered in the past' from a health problem and had a treatment for this, claim as 'not completely cured' from their treatments, while 15% from those stating as 'cured completely after treatment' continue to take medication. In other words only just over one third of those treated for one or more health problems state as 'completely cured without continuing to take medication'. This confirms that almost two thirds of people treated for their chronic health problems were not cured completely, or believe they were cured but still take medication, demonstrating that their health is not at optimum levels. Worth noting is the very unhealthy lifestyle habits amongst the Cypriot population. About one third of Cypriots are active smokers and almost half of the population state passive smokers. More than two thirds of Cypriots never exercise with only about one sixth of the population stating as exercising at least three times weekly. This evidence together with another finding demonstrating that obesity has reached epidemic levels, with almost half of the population being overweight or obese, cannot possibly support the government's optimism for a 'high level of health of Cypriots'. The research has also demonstrated that chronic disease appears increasingly at lower ages with some common chronic health problems, such as asthma, depression, bowel problems, headaches, stress, constipation and allergies showing no significant correlation with age.

The responsibility of the politicians and other key actors, rather than the medical community's, for the low health status of Cypriots was evident in a number of findings from the research. A number of social and economic factors were found to be strong predictors of chronic disease demonstrating the importance of state policies in public health. In particular, education, income, area of residence, and family status were significantly positively or negatively correlated with some common chronic diseases such as cancer, hypertension, diabetes, cardiovascular disease, and hypercholesterolemia, as well as with psychological problems such as depression, insomnia and stress. The gap between state policies and citizens needs/desires/expectations was evident from a number of other findings. It was particularly demonstrated that Pharmaceutical and Surgical treatments are the first resort to therapy among Cypriots appearing highly up in the order of treatment, while Dietary means, and other Non-Conventional treatments appear very low. This however, does not appear to be a 'citizen preference', since the research has demonstrated a willingness for a strict dietary therapy instead of drugs by almost half of the Cypriot population, if that was offered to them or could afford it, or knew about it. This last conclusion is derived from the finding of a socioeconomic element in the willingness for dietary means, further highlighting the state's responsibility. In particular, education and income were shown to be major determinants of dietary and food supplement use for treatment, while education was also shown to be negatively correlated with pharmaceutical treatments. In other words, Cypriot citizens, if they can afford (high income), they use dietary means for treatment, often in conjunction with their medicines, and if they 'know' (educated) they opt for dietary rather than pharmaceutical means of treatment. A number of factors could be considered as opposing the expressed willingness of Cypriots to follow dietary means. One of these is the high cost of non-conventional treatments, such as nutritional supplements, specifically in view of the finding of the research that total family income for the majority of the population is below 3,000 Euros per month. This particularly affects old age, as age was found to be significantly negatively correlated with income, resulting to the finding of a positive correlation between age and the use of drugs. Another factor is the fact that Non-Conventional Medicines are not currently provided by the state. This was evident during the interviews with the Officials of the HIO, who stated that subsidisation of nutritional supplements is not in their plans as they are not considered as part of

common medical practice in Cyprus. A similar statement was expressed by the representative of the Doctors' Association.

The fact that patients' expectations are not met was also evident from the high degree of dissatisfaction among Cypriots for the time allocated to them to see their doctor and discuss with him/her not only their specific health problem but also their general state of health. Only about one fifth of the population stated as 'much' or 'very much' satisfied with the time allocated to discuss their specific health problem, while a significant percentage (43%) stated as 'not given any', or 'given little' time to discuss their general state of health, apart from the specific problem for which they have visited their doctor. This last finding is further supported by another finding which demonstrated significant correlations between chronic health problems, of both physical and psychological nature supporting worldwide evidence that patients with multiple, coexisting problems are the rule rather than the exception. For example, bowel problems co-exist with stress, allergies, insomnia, skin problems, cholelithiasis, kidney disease, cholelithiasis, and depression; stress co-exists with allergies, constipation, insomnia, gynaecological problems, skin problems, depression, headaches and stomach problems; and cardiovascular disease coexists with diabetes, cancer, stomach problems, arthritis, insomnia and depression.

Apparently, Cypriots expect, desire, and most importantly, need, more caring approaches, more person-centred, beyond specific diseases, and these expectations/ needs/ desires are not met by the current establishment in the provision of healthcare in Cyprus. The Cyprus public appears ready and eager for a modernised health sector, in which they can have access to more wholistic, person-centred approaches and to nutritional means of treatment without spending a fortune on it. A significant proportion of the Cypriot population resorts to alternative methods of treatment, particularly dietary, in an effort to find more effective solutions for their chronic health problems, often in conjunction with their medical treatments. This tendency underlines the importance of a more pluralistic health system in which Nutritional Medicine can significantly contribute as a vital partner along the spectrum of 21st century medical practice. The Health Insurance Organisation should seriously consider the results of this research which demonstrate

that prevention of a large number of common chronic diseases is possible and attainable, through application of the principles of Nutritional Medicine, with a consequent significant reduction of the expenses of lifelong medical treatments, which are estimated to greatly increase with the rising proportion of aged population with multiple chronic health problems. Those elected by the citizens to serve the public common good have the obligation to provide them the highest possible quality of healthcare which will offer them the possibility to live healthily and die in old age without morbidity and disability.

BIBLIOGRAPHY

- Aasland, G.O., & Forde, R. (2005). 'Impact of feeling responsible for adverse events on doctors' personal and professional lives: the importance of being open to criticism from colleagues'. Quality and Safety of Healthcare, 14, pp.13-17,
- Abercrombie, N., Hill, S., & Turner, S.B. (1994). *The Penguin Dictionary of Sociology* (3rd ed.). Penguin Books.
- Adams, E.W. (1904). 'Founders of modern medicine. III: James Benignus Winslow. (A.D. 1669-1760). With a note on Theophilus Bonetus and the 'Sepulchretum''. Medical Library and Historical Journal, 2(1), pp. 28-34. NCBI,US NLM
- Adams, M.K., Lindell, C.K. Kohlmeier, M. & Zeisel, H.S. (2006). 'Status of nutrition education in medical schools'. American Journal of Clinical Nutrition, 83(4), pp.941S-944S. American Society for Nutrition
- Afridi, H.I., Kazi, T.G., Kazi, N., Jamali, M.K., Arain, M.B., Jalbani, N., Sarfaraz, R.A., Shah, A., Kandhro, G.A., Shah, A.Q., & Baig, J.A. (2008). 'Potassium, calcium, magnesium, and sodium levels in biological samples of hypertensive and non-hypertensive diabetes mellitus patients'. Biol Trace Elem Res, 124(3), pp.206-224.
- Ahlemeyer, B., & Krieglstein, J. (2003). 'Pharmacological studies supporting the therapeutic use of Ginkgo biloba extract for Alzheimer's disease'. Pharmacopsychiatry, 36(supp1), pp. S8-S14. Thieme Journals.
- Aihara, H. (1986). Acid & Alkaline. (5th ed.). California: George Ohsawa Macrobiotic Foundation
- Akbaraly, T.N., Kivimaki, M., Brunner, E.J., Chandola, T., Marmot, M.G., Singh-Manoux A., & Ferrie, J.E. (2009). 'Association between metabolic syndrome and depressive symptoms in middle-aged adults: results from the Whitehall II study'. Diabetes Care, 32(3), pp. 499-504.
- Alberts, B., Bray, D., Johnson, A., Lewis, J., Raff, M., Roberts, K. & Walter. P. (1999). Βασικές Αρχές Κυτταρικής Βιολογίας. Α μέρος. Σταματόπουλος, Κ. (Μετάφραση) Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Alberts, B., Bray, D., Johnson, A., Lewis, J., Raff, M., Roberts, K. & Walter. P. (2000). Βασικές Αρχές Κυτταρικής Βιολογίας. Β μέρος. Σταματόπουλος, Κ. (Μετάφραση) Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Alevizos, A., Larios, G., & Mariolis, A. (2007). 'Psoriasis and risk of myocardial infarction'. Journal of the American Medical Association, 297(4), p.361. The American Medical Association
- Alvesson, M. & Karreman, D. (2000). 'Varieties of discourse: on the study of organisations through discourse analysis'. Human Relations, 53(9), pp.1125-1149. The Tavistock Institute, SAGE publications
- Ameerally, P. (1998). Anatomy. London: Mosby International Ltd
- Ames, N.B. (2006). 'Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage'. PNAS, 103(47), pp. 17589-17594. The National Academy of Sciences of the USA
- Ames, N.B. (2010). 'Prevention of mutation, cancer, and other age-associated diseases by optimising micronutrient intake'. Journal of Nucleic Acids, 2010Anderson, D. M., Keith, J., Novak, P. D. & Elliot, M. A. (2002) Mosby's Medical, Nursing and Allied Health Dictionary. (6th ed.). UK: Mosby Inc. (A Harcourt Health Sciences Company

- Anderson, J.W., Allgood, L.D., Lawrence, A., Altringer, L.A., Jerdack, G.R., Hengehold, D.A., & Morel, J.G. (2000). 'Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: meta-analysis of 8 controlled trials'. American Journal of Clinical Nutrition, 71(2), pp.472-479
- Andreazza, A.C., Kapczinski, F., Kauer-Sant'Anna, M., Walz, J.C., Bond, D.J., Goncalves, C.A., Young, L.T., & Yatham, L.N. (2009). '3-Nitrotyrosine and glutathione antioxidant system in patients in the early and late stages of bipolar disorder'. Journal of Psychiatry and Neuroscience, 34(4), pp. 263-271
- Angell, Y.S., Silver, D.L., Goldstein, P.G., Johnson, M.C., Deitcher, R.D., Frieden, R.T., & Bassett, T.M. (2009). 'Cholesterol control beyond the clinic: New York City's trans fat restriction'. Annals of Internal Medicine, 151(2), pp.129-134,
- Ansell, M.S. Acherman, J.M., Black, L.J., Roberts, R.L., & Tefferi, A. (2003). 'Primer on medical genomics-Part VI: genomics and molecular genetics in clinical practice'. Mayo Clinic Proceedings, 78(3), pp.307-317. Mayo Foundation for Medical Education and Research
- Antoniadou, M. (2005). 'Can Cyprus overcome its health-care challenges?-World Report'. The Lancet. vol.365, pp.1017-1020, March 19, 2005
- Arieti, J. A. (2005). Philosophy in the Ancient World. USA: Rowman & Littlefield Publishers
- Arif, A.I., & Khan, A.H. (2010). 'Environmental toxins and Parkinson's disease: putative roles of impaired electron transport chain and oxidative stress'. Toxicology and Industrial Health, 26(2), pp.121-128. SAGE publications
- Armstrong, C. G. (1935i). Translation and Comments on Aristotle-Oeconomica-Books I-III. London: Harvard University Press (Loeb classical library)
- Armstrong, C. G. (1935ii). Translation and Comments on Aristotle-The Magna Moralia-Books I-II. London: Harvard University Press (Loeb classical library)
- Armstrong D. (1977). 'Clinical sense and clinical science'. Soc. Sci. & Med., 11, pp. 599-601. Pergamon Press
- Arnold, L. (1927). 'Influence of food upon the bacterial flora of the small intestine'. California and Western Medicine, 17(9), pp.918-921
- Arnold, S.V., Spectus, J.A., Ciechanowski, P.S., Soine, L.A., Jordan-Keith, K., Caldwell, J.H., & Sullivan M.D. (2009). 'Psychosocial modulators of angina response to myocardial ischemia'. Circulation, 120(2), pp. 126-133. NCBI,US NLM
- Aro, P., Talley, N.J., Ronkainen, J., Storskrubb, T., Vieth, M., Johansson, S.E., Boling-Sternevald, E., & Agreus, L. (2009). 'Anxiety is associated with uninvestigated and functional dyspepsia (Rome III criteria) in a Swedish population-based study'. Gastroenterology, 137(1), pp. 94-100
- Aujoulat, I., d'Hoore, W., & Deccache, A. (2007). 'Patient empowerment in theory and practice: polysemy or cacophony?'. Patient Educ Couns., 66(1), pp.13-20. NCBI,US NLM
- Avogo, W., Frimpong, A.J., Rivers, A.P. & Kim, S.S (2008). 'The effects of health status on the utilization of complementary and alternative medicine'. Health Education Journal, 67(4), pp.258-275
- Bachmann, M.L., Puhan, A.M. ter Riet, G., Bossuyt, M.P. (2006). 'Sample sizes of studies on diagnostic accuracy: literature survey'. British Medical Journal, 332(7550), pp.1127-1129. BMJ Publishing Group Ltd.
- Bacon, L.S., Bouchard, A., Loucks, B.E., & Lavoie, L.K. (2009). 'Individual-level socioeconomic status is associated with worse asthma morbidity in patients with asthma'. Respiratory Research, 10(1), p.125, BioMed Central

- Baer, A.H. (2007). 'Why is the Australian government interested in complementary medicine? A case study of economic rationalism'. Complementary Health Practice Review, 12(3), pp. 167-178. Sage Publications
- Baggaley, A. (Ed). (2001). Human Body. London: Dorling Kindersley Ltd
- Balch, P. A. & Balch, J. F. (2000). Prescription for Nutritional Healing. (3rd ed.). Avery (a member of Penguin Putnam Inc.)
- Baldewicz, T., Goodkin, K., Feaster, D.J., Blaney, N.T., Kumar, M., Kumar, M. Kumar A., Short-Posmer, G., & Baum, M. (1998). 'Plasma pyridoxine deficiency is related to increased psychological distress in recently bereaved homosexual men'. Psychosom Med, 60(3), pp.297-308 . NCBI,US NLM
- Baliga, M.S., Jagetia, G.C., Rao, S.K., & Babu, K. (2003). 'Evaluation of nitric oxide scavenging activity of certain spices in vitro: a preliminary study'. Nahrung, 47(4), pp.261-4.
- Balk, E.M., Horsley, T.A., Newberry, S.J., Lichtenstein, A.H., Yetley, E.A., Schachter, H.M., Moher, D., MacLean, C.H., & Lau, J. (2007). 'A collaborative effort to apply the evidence-based review process to the field of nutrition: challenges, benefits, and lessons learned'. American Journal of Clinical Nutrition, 85(6), pp.1448-1456.
- Ballentine, R. (1978). Diet and Nutrition – A Holistic Approach. USA: Himalayan International Institute
- Balme, D. M. (1991). Translation and Comments on Aristotle-History of animals-Books VII-X. London: Harvard University Press (Loeb Classical Library)
- Balon, T.W., Gu, J.L., Tokuyama, Y., Jasman, A.P. & Nadler, J.L. (1995). 'Magnesium supplementation reduces development of diabetes in a rat model of spontaneous NIDDM). American Journal of Physiology, 269(4Pt1), pp.E745-753
- BANT. (2006). 'Understanding the differences between nutrition health professionals "optimum nutrition". British Association for Applied Nutrition and Nutritional Therapy available at http://www.bant.org.uk/bant/pdf/Optimum_Nutrition_Boundaries.pdf accessed 25/3/2010
- BANT. (2009). 'Detoxification: understanding the differences between Dieticians and Nutritional Therapists'. British Association for Applied Nutrition and Nutritional Therapy available at <http://www.bant.org.uk/bant/pdf/DETOXIFICATION.pdf> accessed 25/3/2010
- BANT. (2009i). 'Evidence-based practice: understanding the differences between dieticians and nutritional therapists'. British Association for Applied Nutrition and Nutritional Therapy available at http://www.bant.org.uk/bant/pdf/Bant_briefing_EVIDENCE_BASED_PRACTICE.pdf accessed 25/3/2010
- BANT. (2011). 'Nutrition Titles'. British Association for Applied Nutrition and Nutritional Therapy, available at <http://www.bant.org.uk/bant/jsp/nutritionTitles.faces> (accessed 18 /3/ 2011)
- Banting, F.G., Best, C.H., Collip, J.B., Campell, W.R., & Fletcher, A.A. (2007). 'Pancreatic extracts in the treatment of diabetes mellitus'. Indian J Med Res, 125(3), pp.141-6. NCBI,US NLM
- Barbagallo, M., Dominquez, L.J., & Resnick, L.M. (2007). 'Magnesium metabolism in hypertension and type 2 diabetes mellitus'. Am J Ther., 14(4), pp.375-385
- Barret, B., Marchand, L., Scheder, J. Appelbaum, D., Plane, B.M. Blustein, J., Maberry, R., & Capperino, C. (2004). 'What complementary and alternative medicine practitioners say about health and healthcare'. Annals of Family Medicine, inc, 2, pp.253-259.

- Bastianetto, S., Zheng, W.H., & Quirion, R., (2000). 'The Ginkgo biloba extract (EGb 761) protects and rescues hippocampal cells against nitric oxide-induced toxicity: involvement of its flavonoids constituents and protein kinase C.' J Neurochem., 74(6), pp. 2268-2277
- Bean, D., Cundy, T., & Petrie, J.K. (2007). 'Ethnic differences in illness perceptions, self-efficacy and diabetes self-care'. Psychology & Health, 22(7), pp. 787-811
- Beattie, B.L., (2007). 'Consent in Alzheimer's disease research: risk/benefit factors'. Can J Neurol Sci. 34 (Suppl 1), pp.S27-31. PubMed NCBI,US NLM
- Beaujouan, G. (1963). Article on Salerno's origins in Taton, R. (Ed) (1963). History of Science Ancient and Medieval, English translation, quoted in Geanakoplos, D. (1966). Byzantine East & Latin West: Two Worlds in Middle Ages and Renaissance. Harper Torch Books
- Beck, S.R., Daughtridge, R., & Sloane, D.P. (2002). 'Physician-patient communication in the primary care office: A systematic review', J Am Board Fam Pract 15, pp.25-38.
- Becker, L.A. & van Binsbergen, J.J. (2005). 'How can a proposed Cochrane diet and nutrition field work effectively?'. European Journal of Clinical Nutrition, 59(1), pp.S167-S171. doi:10.1038/sj.ejcn.1602192,
- Beckett, J.G., & Arthur, R.J. (2005). 'Selenium and endocrine systems'. Journal of Endocrinology, 184, pp.455-465. Society for Endocrinology.
- Beckett, S.W., Jacobs, R.D., Yu, X., Iribarren, C., & Williams, D.O. (2001). 'Asthma is associated with weight gain in females but not in males, independent of physical activity'. American Journal of Respiratory and Critical Care Medicine, 164(11), pp. 2045-2050
- Beers, H. M. & Berkow, R. (Ed) (1999). The Merck Manual of Diagnosis and Therapy. (17th ed.). USA: Merck Research Laboratories (Division of Merck & CO., Inc)
- Bekelman, E.J., Li, Y., & Gross, P.C. (2003). 'Scope and impact of financial conflicts of interest in biomedical research'. The Journal of the American Medical Association, 289(4), pp.454-465.
- Bekyarova, E., Ni, Y., Malarkey, B.E., Montana, V., McWilliams, L.J. Haddon, C.R., & Parpura, V. (2009). 'Applications of carbon nanotubes in biotechnology and Biomedicine'. Journal of Biomedicine and Biotechnology, 1(1), pp.3-17
- Belcastro, V., Pierguidi, L., Castrioto, A., Menichetti, C., Gorgone, G., Lintile, R., Pisani, F., Rossi, A., Calabresi, P. & Tambasco N. (2009). 'Hyperhomocysteinemia recurrence in levodopa-treated Parkinson's disease patients'. European Journal of Neurology,17(5),pp.661-665. The Author(s). Journal compilation The European Federation of Neurological Societies.
- Bell, J. (2005). Doing your Research Project. (4th ed.). England: Open University Press
- Bellavite, P. & Signorini, A. (1995). The Emerging Science of Homeopathy : Complexity, Biodynamics, and Nanopharmacology. (Reversed Ed.). USA: North Atlantic Books
- Ben Arye, E. (2010). 'The role of dual-trained conventional/complementary physicians as mediators of integration in primary care'. Oxford Journals-Evidence based Complementary and Alternative Medicine-eCAM, 2010 7(4), pp. 487-491, 2008 The Author(s)
- Bender, A. E. & Bender D. A. (1995). A Dictionary of Food and Nutrition. Oxford University Press
- Bennett, J. (2001). Learning from Six Philosophers. Oxford University Press
- Bennett, P. (2011). 'Placebo and the power to heal'. In Pizzorno, J. & Murray, M. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc

- Benton, D. & Donohoe, R.T. (1999). 'The effects of nutrients of mood'. Public Health Nutrition, 2(3A), pp. 403-9, available at <http://www.ncbi.nlm.nih.gov> (accessed 18/4/2010)
- Benyon, S. (1998). Metabolism and Nutrition. London: Mosby International Ltd
- Bereswill, S., Munoz, M., Fischer, A., Plickert, R., Haag, L., Kuhl, A.A., Loddenkemper, C., Gobel, B.U., & Heimesaat, M.M. (2010). 'Anti-inflammatory effects of resveratrol, curcumin and simvastatin in acute small intestinal inflammation'. PLoS One,5(12), e15099
- Bergvall-Kareborn, B., Mirijamdotter, A., & Basden, A. (2005). 'Basic principles of SSM modelling: and examination of CATWOE from a soft perspective'. Systemic Practice and Action Research, 17(2), pp.55-73.
- Bergvall-Kareborn. (2001). 'Enriching the model-building phase of soft systems methodology'. Research paper published online 10.1002/sres.416. 2001 John Wiley & Sons, Ltd. (accessed 20/11/2008)
- Berlivet, L. (2008). 'Between expertise and Biomedicine: public health research in France after the Second World War'. Medical History, 52(4), pp.471-492. The Wellcome Trust Centre for the History of Medicine at UCL
- Bernier, F.N., & Clavier, C. (2011). Public health policy research: making the case for a political science approach'. Health Promotion International, 26(1), pp. 109-116. Oxford Journals
- Bernstam, V.E., Hersh, R.W., Johnson, B.S. et al. (2009). 'Synergies and distinctions between computational disciplines in biomedical research: perspective from the clinical and translational science award programs'. Academic Medicine, 84(7), pp.964-970. National Institute of Health
- Berry, S.L., Coffrey, D.S., Walsh P.C., & Ewing L.L. (1984). 'The development of human benign prostatic hyperplasia with age'. J Urol. 132, pp.474-479, quoted in Wilt et al. 1998.
- Bernstam, V.E. Hersh, R.W., Johnson, B.S., Chute, G.C., Nguyen, H., Sim, I., Nahm, M., Weiner, M., Miller, P. DiLaura, P.R. Overcash, M., Lehmann, P.H., Eichman, D., Athey, D.B., Scheuerm, H.R., Anderson, N., Starren, B.J., Harris, P.A., Smith, W.J., Barbour, E., Silverstein, C.J., Krusch, D.A., Nagarajan, R., & Becich, J.M., (2009). 'Synergies and distinctions between computational disciplines in biomedical research: perspective from the clinical and translational science award programs'. Acad Med., 84(7), pp.964-970. PubMed Central, NCBI,NLM
- Berstein, L., Henderson, E.B., Hanisch, R., Sullivan-Halley, J., & Ross, K.R. (1994). 'Physical exercise and reduced risk of breast cancer in young women'. Journal of the National Cancer Institute, 86(18), pp.1403-1408. Oxford Journals
- Besgen, P., Trommler, P., Vollmer, S., & Prinz, C.J. (2010). 'Ezrin, Maspin, Peroxiredoxin 2, and heat shock protein 27: potential targets of a streptococcal-induced autoimmune response in psoriasis'. The Journal of Immunology,184(9), pp.5392-5402.
- Bianchi, I. (1989). Principles of Homotoxicology-Vol.1. (1st English ed.). Germany: Aurelia-Verlag GmbH
- Bitsori, M., & Galanakis, E. (2004). 'Epicurus' death'. World J Urol, 22(6), pp.499-469. Epub 2004 Sep 15.
- Bixquert, J.M. (2009). 'Treatment of irritable bowel syndrome with probiotics. An aetiopathogenic approach a last?'. Rev Esp Enferm Dig., 101(8), pp.553-564
- Bjelke, E. (1975). 'Dietary vitamin A and lung cancer.' Int J Ca, 15, p. 561. Quoted in McCarthy 1981

- Blackburn, P., Lemieux, I., Almeras, N., Bergeron, J., Cote, M., Tremblay, A., Lamarche, B., & Despres, J.P. (2009). 'The hypertriglyceridemic waist phenotype versus the national cholesterol education programme-adult treatment panel III and International Diabetes Federation clinical criteria to identify high-risk men with an altered cardiometabolic risk profile'. Metabolism, 58(8), pp.1123-1130. Elsevier
- Blackburn, S., (1996). The Oxford Dictionary of Philosophy. (2nd ed.) Oxford University Press
- Blackburn, S. (2005). The Oxford Dictionary of Philosophy. (2nd ed.). Oxford University Press
- Bland, J. S. (2002). Nutritional Endocrinology- Breakthrough Approaches for Improving Adrenal and Thyroid Function. WA: The Institute For Functional Medicine
- Bland, J. S. (2004). Nutrigenomic Modulation of Inflammatory Disorders: Arthralgias, Coronary Heart Disease, PMS-and Menopause-Associated Inflammation. WA: The Institute For Functional Medicine
- Bland, J.S. (2005). 'Preface', in Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Bloom, S. R. (Ed) (1995). Toohy's Medicine. (15th ed.). UK: Churchill Livingstone (Elsevier Science Ltd.)
- Blun, K., Chen, J.H.T., Blun, H.S., Downs, W.B., Braverman, R.E., Mengucci, F.J., & Meshkin, B. (2006). 'Nutrigenomics and pharmacogenomics: a scientific wonderland'. Social Science Information, 45(1), pp.35-52
- BNF (British National Formulary) 49. (2005). UK: British Medical Association & Royal Pharmaceutical Society of Great Britain
- Boccia, S., Torre., G., Persiani, T., D'Ugo, D., van Duijn, C., Ricciardi, G. (2007), 'A critical appraisal of epidemiological studies comes from basic knowledge: a reader's guide to assess potential for biases', World Journal of Emergency Surgery doi:10.1186/1/1749-7922-2-7, BioMed Central Ltd.
- Bodane, C., & Brownson, K. (2002). 'The growing acceptance of complementary and alternative medicine'. Health Care Manager, 20(3), pp.11-21. Aspen Publishers, Inc.
- Bodenreider, O., & Burgun, A. (2008). 'Accessing and integrating data and knowledge for biomedical research'. Yearb Med Infor., pp.91-101. National Institutes of Health
- Bohager, T. (2008). Everything You Need to Know About Enzymes. USA: Greenleaf Book Group Press
- Bolen, J. S. (2004). The Tao of Psychology Synchronicity and the Self. (2nd ed.). HarperSanFrancisco (HarperCollins Publishers)
- Bolger, P.M., Leblanc, J.C., Woodrow, S.R. (2010). 'Application of the margin exposure (MoE) approach to substances in food that are genotoxic and carcinogenic: example: acrylamide (CAS No. 79-06-1)'. Food Chem Toxicol., 48(Suppl 1), pp.S25-S33
- Bolland, J.M., Avenell, A., Baron, A.J., Grey, A., MacLennan, S.G., Gamble, D.G. & Reid, R.I. (2010). 'Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis'. British Medical Journal, 341, c.3691. BMJ Publishing Group Ltd
- Bolsin, S., Faunce, T., & Oakley, J. (2005). 'Practical virtue ethics: healthcare whistleblowing and portable digital technology. Journal of Medical Ethics, 31, pp612-618
- Borg, M.A., Scicluna, E., De Kraker, M., Van de Sande-Bruinsma, N., Tiemersma, E., Gur, D., Ben Redjeb, D., et al. (2006). 'Antibiotic resistance in the southeastern Mediterranean-preliminary results from the ARMed project'. Euro Surveillance: Bulletin

- Européen Sur Les Maladies. Transmissibles=European Communicable Disease Bulletin 11(7), pp.164-167
- Borrell-Carrio, F., Suchman, A.L., & Epstein, R.M. (2004). 'The biopsychosocial model 25 years later: principles, practice, and scientific inquiry'. Annals of Family Medicine, 2(6), pp.576-582. NCBI,US NLM
- Bosch, P.R., Traustadottir, T., Howard, P., & Matt, K.S. (2009). 'Functional and physiological effects of yoga in women with rheumatoid arthritis: a pilot study'. Alternative Therapies in Health & Medicine, 15(4), pp. 24-31
- Bottles, K., (2001). 'A revolution in genetics: changing medicine, changing lives'. Physician Executive, 27(2), pp. 58-63
- Bovet, P., Romain, S., Shamlaye, C., Mendis, S., Darioli, R., Riesen, W., Tappy, L., and Paccaud, F. (2009). Cardiovascular Diabetology, 8(34). BioMed Central Ltd
- Boyles, M.C., Bailey, H.P., & Mossey, S. (2008). 'Representations of disability in nursing and healthcare literature: and integrative view.' Journal of Advanced Nursing. 62(4), pp.428-437. The Authors. Journal compilation. Blackwell Publishing Ltd.
- Bozym, A.R., Chimienti, F., Giblin, J.L., Gross, W.G., Korichneva, I., Li, Y., Libert, S., Maret, W., Parviz, M., Frederickson, J.C., & Thompson, B.R. (2010). 'Free zinc ions outside a narrow concentration range are toxic to a variety of cells in vitro'. Experimental Biology and Medicine, 235, pp.741-750. Society for Experimental Biology and Medicine. London: The Royal Society of Medicine Press
- Bradley, M.S. (1871). 'Description of the brain of an idiot'. Journal of Anatomy and Physiology, 6(Pt 1), pp. [65] -75, 512-519. NCBI,US NLM
- Brand-Miller, J., Powell-Foster, K. & Holt, S. (2004). The New Glucose Revolution. UK: Hodder & Stoughton Ltd (A division of Hodder Headline)
- Brock, A. J. (1916). Translator of Galen-On the Natural Faculties-Books I-III. London: Harvard University Press (Loeb Classical Library)
- Brock, A.J. (1923). 'Galen', British Medical Journal, 1(3241), p.258. BMJ Publishing Group Ltd
- Brody, T. (1999). Nutritional Biochemistry. (2nd ed.). UK: Academic Press
- Brook, G. D. C. & Marshall N. J. (2001). Endocrinology. (4th ed.). London: Blackwell Science Ltd
- Brown, P.K. (1917). 'The patent medicine evil'. California State Journal of Medicine, 15(9), pp. 371-374. NCBI,US NLM
- Brown, R. (1929). 'The menace to medicine'. California and Western Medicine, 30(2), pp. 73-77. NCBI,US NLM
- Brownsey, R.W., Boone, A.N., & Allard, M.F. (1997). 'Actions of insulin on the mammalian heart: metabolism, pathology and biochemical mechanisms'. Cardiovascular Research, 34(1), pp.3-24. Oxford Journals, National Institutes of Health, U.S. National Library of Medicine
- Bryce, P.H. (1912). 'Ontology in relation to preventive medicine'. American Journal of Public Health (NY), 2(1), pp. 32-33. NCBI,US NLM
- Buchholz, A.C. & Bugaresti, J.M. (2005). 'A review of body mass index and waist circumference as markers of obesity and coronary heart disease risk in persons with chronic spinal injury'. Spinal Cord, 43(9), pp. 513-518.
- Buddeberg-Fischer, B., Dietz, C., Klaghofer, R., & Buddeberg, C. (2006). 'Swiss residents' arguments for and against a career in medicine'. BMC Health Services Research, 6(98) BioMed Central

- Buklijas, R., & Lafferton, E. (2007). 'Science, medicine and nationalism in the Habsburg Empire from the 1840s to 1918'. Studies in History and Philosophy of Biological and Biomedical Sciences, 38(4), pp.679-686
- Bullock, A., Stallybrass, G., & Trombley, S. (Eds). (1988). The Fontana Dictionary of Modern Thought (2nd edition). London: Fontana Paperbacks
- Bunker, P.J., (1999). 'James Le Fanu: The rise and fall of modern medicine'. Review, British Medical Journal, 319, p.1276. BMJ Publishing Group Ltd
- Bursztajn, B.H., & Hamm, M.R. (1979). 'Medical maxims: two views of science'. The Yale Journal of Biology and Medicine, 52, pp. 483-6. NCBI,US NLM
- Bushe, R.G., & Kassam, F.A. (2005). 'When is Appreciative Inquiry transformational? A meta-case analysis'. The Journal of Applied Behavioural Science, 41(2), pp.161-181
- Cagnon, M.P., Legare, F., Fortin, J.P., Lamothe, L., Labrescque, M., & Duplantie, J., (2008). 'An integrated strategy of knowledge application for optimal e-health implementation: A multi-method study protocol'. BMC Medical Informatics and Decision Making 2008. 8:17 . BioMed Central Ltd
- Cain, K.C., Jarrett, M.E., Burr, R.L., Rosen, S., Hertig, V.L., & Heitkember, M.M. (2009). 'Gender differences in gastrointestinal, psychological, and somatic symptoms in irritable bowel syndrome'. Digestive Diseases and Sciences, 54(7), pp. 1542-1549
- Calabrese, V., Butterfield, D.A., & Stella, A.M. (2003). 'Nutritional antioxidants and the heme oxygenase pathway of stress tolerance: novel targets for neuroprotection in Alzheimer's disease' Ital J Biochem, 52(4), pp.177-181
- Calabrese, V., Lodi, R., Tonon, C., D'Agata, V., Sapienza, M., Scapagnini, G., Mangiameli, A., Pennisi, G., Stella, A.M., Butterfield, D.A. (2005). 'Oxidative stress, mitochondrial dysfunction and cellular stress response in Friedreich's ataxia'. J. Neurol Sci., 233(1-2), pp.145-162
- Callio, J., Oury, D.T., & Chu, T.C. (2005). 'Manganese superoxide dismutase protects against 6-hydroxydopamine injury in mouse brains'. The Journal of Biological Chemistry, 280, pp.18536-18542. The American Society for Biochemistry and Molecular Biology
- Calman, K. C. (1994). 'The profession of medicine'. British Medical Journal, 309, p1140. BMJ Publishing Group Ltd
- Calman, K.C. (2004). 'Evolutionary ethics: can values change'. Journal of Medical Ethics, 30, pp.366-370. BMJ Publishing Group Ltd
- Calvaresi, E., & Bryan, J. (2001). 'B vitamins, cognition, and aging'. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 56, pp.327-339. The Gerontological Society of America
- Camilieri, M. (2010). 'Serotonin in the gastrointestinal tract'. Curr Opin Endocrinol Diabetes Obes., 16(1), pp.53-59
- Campbell, C. T. & Campbell T. M. (2006). The China Study. USA: BenBella Books, Inc.
- Campbell, L.K., & McTiernan, A. (2007). 'Exercise and biomarkers for cancer prevention studies'. The Journal of Nutrition, 137(1), pp.161S-169S. The American Society for Nutrition
- Capra, F. (1982). The Tao of Physics. (3rd ed.). London: Flamingo (HarperCollins Publishers)
- Capra, F. (1996). The Web Of Life. London: Flamingo (HarperCollins Publishers)
- Carlsen, H.M., Halvorsen, L.B., Holte, K., Bohn, K.S., Dragland, S., Sampson, L., Wiley, C., Senoo, H. Yuko, U., Sanada, C., Barikmo, I., Berhe, N., Willet, C.W., Phillips, M.K., Jacobs, R.D., Jr, & Blomhoff, R. (2010). 'The total antioxidant content of more than 3100 foods,

- beverages, spices, herbs, and supplements used worldwide'. Nutrition Journal, 9(3). BioMed Central Ltd
- Carlson, J.R. (1979). 'Holism and reductionism as perspectives in medicine and patient care, in Orthodox medicine, humanistic medicine and holistic health care-a forum. The Western Journal of Medicine, 131, pp.466-70. NCBI,US NLM
- Carpenter, J.K. (2003). 'A short history of nutritional science: Part 3(1912-1944). The Journal of Nutrition, 133(10), pp.3023-3032. The American Society for Nutritional Sciences.
- Carpenter, J.K. (2003i). 'A short history of nutritional science: Part 1(1785-1885). The Journal of Nutrition, 133(3), pp.638-645. The American Society for Nutritional Sciences
- Carpenter, J.K. (2003ii). 'A short history of nutritional science: Part 2(1885-1912). The Journal of Nutrition, 133(4), pp.975-984. The American Society for Nutritional Sciences
- Carper, J. (2000). Food- Your Miracle Medicine. (2nd ed.). UK: Pocket Books (A Viacom Company)
- Carr, I. (1920). 'Introduction' to Harington, J. (1920). The Salerno Book of Health, The University of Manitoba Libraries
- Carriero, N. Osier, V.M., Cheung, K., Miller, L.P., Gerstein, M., Zhao, H. Wu, B., Rifkin, S., Chang, J., Zhang, H., White, K., Williams, K., & Schultz, M. (2005). 'A high productivity/low maintenance approach to high-performance computation for Biomedicine: four case studies'. Journal of the American Medical Informatics Association, 12(1), pp. 90-98. American Medical Informatics Association
- Carroll, R.T. (2007). 'Experimenter Effect'. The Skeptic's Dictionary <http://skepdic.com/experimentereffect.html> (accessed 6/5/2007)
- Casileth, R.B. & Deng, G. (2004). 'Complementary and alternative therapies for cancer'. The Oncologist, 9, pp. 80-89
- Cassels, P. Hughes, A.M. Cole, C., Mintzes, B., Lexchin, J. & McCormack, P.J. (2003). 'Drugs in the news: an analysis of Canadian newspaper coverage of new prescription drugs'. Canadian Medical Association Journal, 168(9), p.1133. Canadian Medical Association
- Cattaneo, M., Lombardi, R., Lecchi, A., Brucciarelli, P., & Mannucci, P.M. (2001). 'Low plasma levels of vitamin B6 are independently associated with a heightened risk of deep-in thrombosis'. Circulation, 104, p.2442
- Ceravolo, R., Maio, R., Cuda, G., Scozzafava, A., Sciacqua, A., Vatrano, M., Bellieni, G., D'Angelo, G., Schipani, F.A., Sesti, G., & Perticone, F. (2003). 'Relation of fasting insulin related to insertion/deletion polymorphism of angiotensin-converting enzyme-gene and cardiac mass in never-treated patients with systemic hypertension'. American Journal of Cardiology, 92(10), pp.1234-1237. National Institutes of Health, U.S. National Library of Medicine
- Chacon, J.I., Molero, E.A., Pino-Ramirez, G., Luchsinger, A.J., Lee, H.J., & Maestre, E.G. (2009). 'Risk of dementia associated with elevated plasma homocysteine in a Latin American Population'. International Journal of Alzheimer's Disease, 2009 (2009), Article ID 632489, 6 pages
- Chakraborti, S., Chakraborti, T., Mandal, M., Mandal, A., Das, S., & Chosh, S. (2002). 'Protective role of magnesium in cardiovascular diseases: a review'. Mol Cell Biochem, 238(1-2), pp. 163-79. NCBI,US NLM
- Chandrasekaran, K., Mehrabian, Z., Spinnewyn, B., Chinopoulos, C., Drieu, K., & Fiskum, G. (2003). 'Neuroprotective effects of bilobalide, a component of Ginkgo biloba extract (EGb 761) in global brain ischaemia and in excitotoxicity-induced neuronal death'. Pharmacopsychiatry, 36(suppl1), pp. S89-S94. Thieme Journals

- Chang, H., Wallis, M., & Tiralongo, E. (2007). 'Use of complementary and alternative medicine among people living with diabetes: literature review'. Review paper, The Authors. Journal compilation, pp. 307-319 Blackwell Publishing Ltd
- Charalambous, A., Pantelas, G., & Pouloukas, S. (2007). 'Preregistration programme for medical practice: a survey of Cypriot trainees (2000 & 2002). Eastern Mediterranean Health Journal, 13(1)
- Checkland, P. & Tsouvalis, C. (1996). 'Reflecting on SSM: the link between Root Definitions and Conceptual Models'. Research Paper, published online. 1997 John Wiley & Sons, Ltd. (accessed 20/11/2008)
- Chen, O.G., Zeng, Y.S., Qu, Z.Q., Tang, J.Y., Qin, Y.J., Chung, P., Wong, R., & Hagg U. (2009). 'The effects of Rhodiola rosea extract on 5-HT level, cell proliferation and quantity of neurons at cerebral hippocampus of depressive rats'. Phytomedicine, 16(9), pp. 830-838. EBSCO Industries, Inc
- Chen, Y. (2001). 'Chinese values, health and nursing'. Journal of Advanced Nursing, 36(2), pp. 270-273. Blackwell Science Ltd
- Chen, Y.J., Wu, C.Y., Shen, J.L., Chu, S.Y., Chen C.K., Chang, Y.T., & Chen, C.M. (2008). 'Psoriasis independently associated with hyperleptinemia contributing to metabolic syndrome'. Archives of Dermatology, 144(12), pp.1571-1575. American Medical Association
- Chen, Z. (2008). 'Biomedical science and technology in China'. The Lancet available at <http://www.thelancet.com> (accessed 22October 2008)
- Cheng, Y., Ohlsson, L., & Duan, R.D. (2004). 'Psyllium and fat in diets differentially affect the activities and expressions of colonic sphingomyelinases and caspase in mice'. British Journal of Nutrition, 91(5), pp.715-723
- Chinese Medicine history. (2010). TheFreeDictionary.com. Farlex, Inc. 11 Jun. 2010, available at <http://encyclopedia.thefreedictionary.com/Chinese+Medicine+history> (accessed 20/9/2010)
- Cho-Chung, Y.S., & Pitot, H.C. (1968). 'Regulatory effects of nicotinamide on tryptophan pyrrolase syntheses in rat liver in vivo'. Eur J Biochem, 3, p.401. Quoted in McCarthy (1981)
- Chow, D., Nunalee, L.M., Lim, W.D., Simnick, J.A. & Chilkoti, A. (2008). 'Peptide-based biopolymers in Biomedicine and biotechnology'. Mater Sci Eng R Rep., 62(4), pp.125-155
- Chrispin, E., Brannan, S., Davies, M., English, V., Mussell, R., Sheather, J. & Sommerville, A. (2010). 'Complementary and Alternative therapies'. Ethics briefings. Journal of Medical Ethics doi: 10.1136/jme.2010.036392. BMJ Publishing Group Ltd
- Christodoulou, N. (2007). 'Continuing medical education and continuing professional development in the Mediterranean countries'. Europa Medicophysica, 43(2), pp. 95-202, The British Library
- Chung, M., Balk, E.M., Ip, S., Raman, G., Yu, W.W., Trikalinos, T.A., Lichtenstein, A.H., Yetley, E.A. & Lau, J. (2009). 'Reporting of systematic reviews of micronutrients and health: a critical appraisal'. Am J Clin Nutr, 89(4), pp.1099-1113. National Center for Biotechnology Information, U.S., National Library of Medicine
- Chung, P.C., Oeser, A., Raggi, P., Sokka, T., Pincus, T., Solus, F.J., Linton, F.M., Fazio, S., & Stein, M.C. (2010). 'Lipoprotein subclasses determined by nuclear magnetic resonance spectroscopy and coronary atherosclerosis in patients with Rheumatoid arthritis'. Journal of Rheumatology, 37(8), pp.1633-1638.
- Clark, R.L.S. (2000). 'Ancient Philosophy', in Kenny, A. (Ed) (2000). The Oxford History of Western Philosophy. Oxford University Press Inc.

- Clark, W., Lipkin, M., Graman, H., & Shorey, J. (1999). 'Improving physician's relationships with patients'. Journal of General Internal Medicine, 14(1), pp.S45-S50. American Academy of Physician and Patient
- Clayton, P. (2000). Health Defence. (2nd ed.). UK: Accelerated Learning Systems Ltd
- Cleghorn, A.R. (1965). 'Psychosomatic principles'. Le Journal de L'Association Medicale Canadienne, 92(9), pp.441-7. NCBI,US NLM
- Clifford, L. (2000). 'Integrating nutrition as a theme throughout the medical school curriculum'. American Journal of Clinical Nutrition, 72(suppl), pp. 882S-9S. American Society for Clinical Nutrition
- CNELM. (2011), available at <http://www.cnelm.co.uk/> (accessed 30 /3/ 2011)
- CNH8. (2010). Provide Nutritional Therapy to clients. Final version approved June 2010. Skills for Health, available at <https://tools.skillsforhealth.org.uk/competence/show?code=CNH8> (accessed 16/3/2011)
- CNH9. (2010). Prescribe nutraceuticals to clients. Final version approved June 2010. Skills for Health, <https://tools.skillsforhealth.org.uk/competence/show?code=CNH89> (accessed 16/3/2010)
- CNHC. (2008). Code of Conduct, Performance and Ethics for Registrants. Complementary and Natural Healthcare Council, available at <http://www.cnhc.org.uk/assets/1-006.pdf> (accessed 16/3/ 2011)
- CNHC. (2011). 'Key Characteristics of Regulatory Bodies and Professional Bodies'. Complementary and Natural Healthcare Council, available at <http://www.cnhc.org.uk/assets/2-001.pdf> accessed 10/3/ 2011
- CNHC. (2011i). 'Department of Health expresses continued support for CNHC'. Added to CNHC news page on 7/01/11. Available at http://www.cnhc.org.uk/pages/newsManager.cfm?page_id=2&news_id=76 accessed 12/3/ 2011
- Cody, Wm. G. (2010). 'A brief history of early American Medicine with an emphasis on natural healing' in chapter 4 'The History of Naturopathic Medicine, Part I: The Emergence of an American School of Healing, in in Pizzorno, J. & Murray, M. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc. www.naturalmedtext.com
- Cogo, E., Sampson, M., Ajiferuke, I., Manheimer, E., Campbell, K., Daniel, R., & Moher, D. (2009). 'Searching for controlled trials of complementary and alternative medicine: A comparison of 15 Databases. Oxford Journals. eCam Advance Access published online May 25, 2009. Oxford University Press.
- Cohen, L., Manion, L. & Morrison, K. (2000). Research Methods in Education. (5th ed.). London: RoutledgeFalmer (Taylor & Francis Group)
- Collins Concise Dictionary. (1999). (4th ed.). Glasgow: HarperCollins Publishers
- Collins English Dictionary, (online) (2003). Complete and Unabridged. HarperCollins Publishers
- Connelly, D. M. (1994). Traditional Acupuncture: The Law of the Five Elements. (2nd ed.) Maryland: Tai Sophia institute
- Constantinou, C., Papas, A., & Constantinou, A.I. (2008). 'Vitamin E and cancer : an insight into the anticancer activities of vitamin E isomers and analogs'. International Journal of cancer. Journal International Du Cancer, 123(4), pp.739-752

- Coogan, F.P., Palmer, R.J., O'Connor, T.G., & Rosenberg, L. (2009). 'Body mass index and asthma incidence in the Black Women's Health Study'. The Journal of Allergy and Clinical Immunology, 123(1), pp.89-95
- Cooper, R.A., Laud, P., Craig, L., Dietrich, B.S. (1998). 'Current and projected workforce of non-physician clinicians'. JAMA, Sep 2, 280 (9), pp.788-794. American Medical Association. NCBI,US NLM
- Cooperrider, D.L., & Whitney, D. (2001). 'A positive revolution in change'. In Cooperrider, D.L., Sorenson, P., Whitney, D. & Yeager, T. (eds). Appreciative Inquiry: An emerging direction for organisation development (9-29). Campaign, IL:Stripes
- Cordell, F.E. (1904). 'The importance of the study of the history of medicine'. Medical Library and Historical Journal, 2(4), pp. 268-282. NCBI,US NLM
- Corthesy-Theulaz, I., den Dunnen, J.T., Ferre, P., Geurts, J.M., Muller, M., van Belzen, N., & van Ommen, B. (2005). 'Nutrigenomics: the impact of biomics technology on nutrition research'. Ann Nutr Metab., 49(6), pp.355-365. National Centre for Biotechnology Information, U.S. National Library of Medicine
- Couprie, D., Goodbrand, A., Li, B., & Zhu, D. (2006). 'Soft Systems Methodology: A report', Department of Computer Science, University of Calgary, available online at <http://sern.ucalgary.ca/courses/seng/613/F97/grp4/ssmfinal.html> (accessed 17/3/2008)
- Cozzens, E.Z. (2010). 'Quality of life returns from basic research.' Health Research Policy and Systems, 8(18),
- Craik, M. E. (2009). 'Hippocratic bodily "channels" and oriental parallels'. Medical History, 53(1), pp.105-116. The Wellcome Trust Centre For The History of Medicine at UCL
- Creswell, W.J., Fetters, D.M., & Ivankova, V.N. (2004). 'Designing a mixed methods study in primary care'. Anal of Family Medicine. 2 (1) pp.7-12
- Crinnion, J.W. (2005). 'Systemic in-office detoxification'. Ch. 31, pp.554-556, In Jones, D. S. (Ed). (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Crinnion, J.W. (2011). 'Environmental Medicine'. Chapter 36 in Pizzorno, J. & Murray, M. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc. www.naturalmedtext.com (accessed 12/2/2011)
- Crispin, E., Brannan, S., Davies, M., et al., (2010). 'Ethics briefings-Complementary and alternative therapies'. Journal of Medical Ethics, 36, pp.375-377
- Critchley, J.A., Zhang, Y., Suthisisang, C.C., Chan, T.Y., & Tomlinson, B. (2000). 'Alternative therapies and medical science: designing clinical trials of alternative/complementary medicines-is evidence-based traditional Chinese medicine attainable?'. The Journal of Clinical Pharmacology, 40, pp.462-467. American College of Clinical Pharmacology, Sage Publications
- Crombie, A. (1959). Medieval and Early Modern Science, I, pp.232-236. quoted in Geanakoplos, D. (1966). Byzantine East & Latin West: Two Worlds in Middle Ages and Renaissance. Harper Torch Books
- Crowell, D.M. (2004). 'Role of serotonin in the pathophysiology of the irritable bowel syndrome'. British Journal of Pharmacology,141(8), pp.1285-1293. Nature Publishing Group
- Cushman J.M., & Hoffman J.M., (2004). 'Complementary and Alternative health care and the home care population'. Home Health Care Management &Practice, Aug 2004. 16 (5) pp. 360-373. SAGE Publications

- Cutts, T.F., Waldman, J.R., & Zoffman, M.H. (1993). 'Surveillance for the expanded programme on Immunization'. Bulletin of the World Health Organisation, 71(5), pp.633-639. PubMed NCBI ,US NLM
- Cyprus Dietetic Association (2009). 'Duties: Dietician –Clinical Dietician' Definitions. Cydadiet.org, available at <http://www.cydadiet.org/main/111,0,0,0-ΟρισμοίDefinitions.aspx> (accessed 18 /3/ 2011)
- Cyprus Health Insurance Organisation. (2008). Annual Report 2008, available at <http://www.hio.org.cy/en/roadmap.html> (accessed 16 /3/ 2009)
- Cyprus Health Insurance Organisation. (2008i). 'Vision & Goals'. Our organisation, available at <http://www.hio.org.cy/en/roadmap.html> (accessed 16 /3/ 2009)
- Cyprus Health Insurance Organisation. (2008ii). 'Strategy'. National Health System, available at <http://www.hio.org.cy/en/roadmap.html> (accessed 16 /3/ 2009)
- Cyprus Health Insurance Organisation. (2008iii). 'President's message'. Our Organisation, available at <http://www.hio.org.cy/en/roadmap.html> (accessed 16 /3/ 2009)
- Cyprus Health Insurance Organisation. (2008iv). Roadmap, available at <http://www.hio.org.cy/en/roadmap.html> (accessed 16 /3/ 2009)
- Cyprus Health Insurance Organisation. (2009). Annual Report 2009, available at <http://www.hio.org.cy/en/roadmap.html> (accessed 16 /3/ 2009)
- Cyprus Health Insurance Organisation. (2010). 'Interviewing the President of HIO. ΑΛΛΗΛΕΓΓΥΗ Magazine of ΔΕΟΚ, November 2010. Cyprus Health Insurance Organisation website , available at <http://www.hio.org.cy/en/roadmap.html> (accessed 18 /3/ 2011)
- Cyprus Statistical Service. (2003). 'Health Survey 2003'. Health Statistics, Series II, Report No.6. Republic of Cyprus
- Cyprus Statistical Service. (2006). 'Έρευνα για άτομα με μακροχρόνια προβλήματα υγείας ή ανικανότητας'. Στατιστικές Υγείας, Σειρά II, Αρ. Έκθεσης 7. Κυπριακή Δημοκρατία
- Cyprus Statistical Service. (2006i). 'Economic statistics on health 2006'. Statistics on Services, Series II, Report No. 1. Republic of Cyprus
- Cziraky, M.J., Watson, K.E., Talbert, R.L. (2008). 'Targeting low HDL-cholesterol to decrease residual cardiovascular risk in the managed care setting'. Journal of Managed Care Pharmacy, 14(8 Suppl), pp.S3-28; quiz S30-31. The Academy of Managed Care Pharmacy.
- D' Arms, J.D. (1998). 'Empathy and Evaluative Inquiry'. Chicago-Kent Law Review, 74, pp.1467-1500. HeinOnline, <http://www.lawreview.kentlaw.edu> (accessed 9/5/2007)
- Damjanov, I. (2000). Pathology for the Health-Related Professions. (2nd ed.). USA: W.B. Saunders Company (A Division of Harcourt Brace & Company)
- Darer, J.D., Hwang, W., Pham. H.H., Bass, E.B. & Anderson, G. (2004). 'More training needed in chronic care: a survey of US physicians'. Academy of Medicine, 79(6), pp.541-548. National Institutes of Health. U.S National Library of Medicine
- Daugherty, C.K., (1999). 'Ethical issues in the development of new agents'. Invest New Drugs, 17(2), pp.145-53. PubMed NCBI. ,US NLM
- Davis C.D. & Milner, J. (2004). 'Frontiers in nutrigenomics, proteomics, metabolomics and cancer prevention'. Muta Res., 551(1-2), pp.51-64
- Davis, M.R. & Wagner, H.E. (1999). 'Managing chronic disease'. British Medical Journal Apr. 1999, 318, pp. 1090-1. BMJ Publishing Group Ltd
- Davis, M.R., Edoute, Y., Stock, S., & Halperin M.L., (2002). 'Severe degree of hyperglycaemia: insights from integrative physiology'. Q J Med 2002, 95, pp.113-124. Association of Physicians

- Dawson, J. S., Taylor, M. & Reide, P. (2002). Pharmacology. (2nd ed.) London: Mosby (Elsevier Science Ltd)
- De Lau, L.M.L., Koudstaal, J.P., Witteman, C.M.J. Hofman, A., & Breteler, B.M.M. (2006). 'Dietary folate, vitamin B12, and vitamin B6, and the risk of Parkinsons disease'. Neurology, 67(2), pp.315-318. American Academy of Neurology. AAN Enterprises, Lippincott Williams & Wilkins HighWire
- De Roos, B., Mavrommatis, Y., & Brouwer, A.I. (2009). 'Long-chain n-3 polyunsaturated fatty acids: new insights into mechanisms relating to inflammation and coronary heart disease'. Themed Section: Advances in Nutritional Pharmacology-Review, The British Journal of Pharmacology, 158, pp. 413-428. The British Pharmacological Society. Wiley InterScience
- Debernardi, A., Sala, E., D'Aliberti, G., Talamonti, G., Franchini, A.F., & Collice, M. (2010). 'Alcmaeon of Croton'. Neurosurgery, 66(2), pp.247-252. National Institute of Health
- Dekker, J.M., Su, Q., Baker, C., Rutledge, C.A., & Adeli, K. (2010). 'Fructose: a highly lipogenic nutrient implicated in insulin resistance, hepatic steatosis, and the metabolic syndrome'. American Journal of Physiology, Endocrinology, and Metabolism, 299(5), pp.E685-E694. American Physiological Society
- Desiere, F. (2004). 'Towards a systems biology understanding of human health: interplay between genotype, environment and nutrition'. Biotechnol Annu Rev., 10, pp.51-84
- DeSylvia, D., Stuber, M., Chi Fung, C., Bazargan-Hejazi, S., & Cooper, E. (2008). 'The Knowledge, attitudes and usage of complementary and alternative medicine of medical students'. Evidence Based Complementary and Alternative Medicine, pp.1-5 doi:10.1093/ecam/nen075. The Author(s)
- DH. (2010). 'Next steps for complementary therapy'. Statements by Health Secretary Andy Burnham. Department of Health Newsdesk, available at <http://www.dh.gov.uk/MediaCentre/Statements/index.htm> (accessed 20 /3/ 2011). Crown Copyright
- DH. (2010i). 'Complementary healthcare regulation'. GP and Practice Team Bulletin, October 2010, UK Department of Health. Crown copyright 2011 available at http://www.dh.gov.uk/en/Publicationsandstatistics/Bulletins/GPbulletin/DH_120728#_11 (accessed on 2 /1/ 2011). Crown Copyright
- DH. (2010ii). 'New voluntary register for complementary healthcare'. Policy news. The Week, 16-22 Jan2009, 79, p.4. NHS Leadership Team. UK Department of Health. Crown Copyright http://collections.europarchive.org/tna/20100509080731/http://www.dh.gov.uk/en/Publicationsandstatistics/Bulletins/theweek/DH_093681 (accessed on 2 /1/2011)
- DH. (2011i). 'NHS modernisation'. Statements by the Health Minister Simon Burns. Press releases. Department of Health Media centre. Available at http://www.dh.gov.uk/en/MediaCentre/Statements/DH_124892(accessed on 2 /1/2011). Crown copyright
- DH. (2011ii). 'Millions of patients set to benefit from a modern NHS'. Press releases, 14 March 2011. Department of Health Media centre. Available at http://www.dh.gov.uk/en/MediaCentre/Pressreleases/DH_125042 (accessed on 2 /1/2011). Crown Copyright
- Di Sarsina, P. (2007). 'The social demand for a medicine focused on the person: the contribution of CAM to healthcare and healthgenesis'. Evidence-based Complementary and Alternative Medicine: eCAM, 4(suppl 1), pp.45-51. The Authors. Oxford University Press

- Dick, B., & Swepson, P. (1994). 'Appropriate validity and its attainment within action research: an illustration using soft systems methodology'. Available at <http://www.scu.edu.au/schools/gcm/ar/arp/sofsys2.html> (accessed 5/12/ 2008)
- Dickinson, A., Boyon, N., & Shao, A. (2009). 'Physicians and nurses use and recommend dietary supplements: report of a survey'. *Nutrition Journal*, 8(29). BioMed Central Ltd
- DiGianni, M.L., Garber, E.J., & Winer, P.E. (2002). 'Complementary and Alternative medicine use among women with breast cancer'. *Journal of Clinical Oncology*, 20(18s), pp. 34s-38s. American Society of Clinical Oncology
- Diller, T. (1909). 'The writings of Benjamin Franklin pertaining to medicine and the medical profession'. *Aesculapian*, 1(2), pp. 65-84. NCBI,US NLM
- Diller, T. (1909i). 'The writings of Benjamin Franklin pertaining to medicine and the medical profession'. *Aesculapian*, 1(3-4), pp. 156-197. NCBI,US NLM
- Dirkzwager, J.E.A. & Verhaak, F.M.P. (2007). 'Patients with persistent medically unexplained symptoms in general practice: characteristics and quality of care'. *BMC Family Practice*, 8(33). NCBI,US NLM
- Dock, W. (1928). 'The lure of medical history'. *California and Western Medicine*, 29(3), pp. 182-184. NCBI,US NLM
- Dong, S., & Phillips, R.M. (2008). 'Evolution of China's health-care system', *The Lancet*, available at www.thelancet.com (accessed on 22 /10/2008).
- Donnet, A., Lanteri-Milnet, M., Aucoin, F., & Allaf B., (2009). 'Use and oversue of antimigraine drugs by pharmacy personnel in France: COTA survey'. *Headache: The Journal of Head and Face Pain*, 49(7), pp.1014-1021. Wiley & Sons, Inc
- Dorland's - Ιατρικό Λεξικό – Αγγλοελληνικό & Ελληνοαγγλικό. (1997). Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Doyle, P.R. (). 'How medical facts are developed: why some are more potent than others'. Posted online on <http://www.quackwatch.org/06ResearchProjects/doyle.html>, October 2, 2004. Quackwatch (accessed 7/12/2008)
- Drennan, J., (2003), 'Cognitive interviewing: verbal data in the design and pretesting of questionnaires', *J Adv Nurs*. 42(1), pp. 57-63 PubMed NCBI,US NLM
- Drewnowski, A. (2009). 'Obesity, diets, and social inequalities'. *Nutrition Reviews*, 67(1), pp.S36-S39. International Life Sciences Institute
- Drummen, P.C.G. (2010). 'Quantum dots-from synthesis to applications in Biomedicine and Life Sciences'. *International Journal of Molecular Sciences*, 11(1), pp.154-163. Molecular Diversity Preservation International, Basel, Switzerland
- Duda, K.M., O'Shea, M.K., & Stanley, C.W. (2009). 'ω-3 polyunsaturated fatty acid supplementation for the treatment of heart failure: mechanisms and clinical potential'. *Cardiovascular Research*, 84(1), pp.33-41. Oxford Journals. The European Society of Cardiology
- Dunbar, J.A., Reddy, P., Davis-Lameloise, N., Philpot, B., Laatikainen, T., Kikkinen, A., Bunker, S.J., Best, J.D., Vartiainen, E., Lo, S.K., & Janus, E.D. (2008). 'Depression: an important comorbidity with metabolic syndrome in a general population'. *Diabetes Care*, 31(12), pp.2368-2373(25 ref)
- EBCTCG (Early Breast Cancer Trialists' Collaborative Group). (2000). 'Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials'. *The Lancet*, 355(9217), pp.1757-1770
- EFDA (2011). 'Definition of a dietician'. European Federation of the Associations of Dieticians, available at <http://www.efad.org/everyone/1273/7/0/32> (accessed 14 /3/2011)

- Egeberg, O.R. (1968). 'The scope and responsibility of medicine'. California Medicine, 109(4), pp. 332-333.
- Egger, M., & Smith, D.G. (1995). 'Misleading meta-analysis'. British Medical Journal, 310(6982), pp.752-754. BMJ Publishing Group Ltd
- Einstein A. & Infeld L. (1938). Η εξέλιξη των ιδεών στην Φυσική. Translated by Ευτ. Μπιτσάκης (1978). Εκδόσεις Δωδώνη, Αθήνα
- Eisenberg, M.D., Davis, B.R., Etnner, L.S., et al. (1998). 'Trends in Alternative Medicine use in the United States, 1990-1997 : Results of a follow-up national survey'. JAMA, 280(18), pp.1569-1575,
- Elia, M., (2000). "Fuels of the tissues". ch4, in Garrow J.S., James W.P.T., Ralph, A., (eds) (2000), Human Nutrition and Dietetics, (10th ed). Churchill Livingstone
- Elliott, R., & Ong, J.T., (2002). 'Science, medicine, and the future: Nutritional genomics- Clinical Review'. British Medical Journal, 2002, 324, pp.1438-1442. BMJ Publishing Group Ltd
- Elmali, N., Baysal, O., Harma, A. Esenkaya, A., & Mizrak, B. (2007). 'Effects of resveratrol in inflammatory arthritis'. Inflammation, 30(1-2), pp.1-6
- Elmariah, S., Delaney, A.C.J., Budoff, J.M., Fuster, V., Kronmal, A.R. & Halperin, L.J. (2010). Journal of the Americal College of Cardiology, 56, pp.1752-1759. The American College of Cardiology Foundation
- Elmore, J.S., Parker, J.K., Halford, N.G. Muttucumaru, N., & Mottram, D.S. (2008). 'Effects of plant sulphur nutrition on acrylamide and aroma compounds in cooked wheat'. J Agric Food Chem., 56(15), pp.6173-6179
- Elsayed, F.E., Tighiouart, H., Weiner, E.D., Griffith, J., Salem, D., Levey, S.A., & Sarnak, J.M. (2008). 'Waist hip ratio and body mass index as risk factors for cardiovascular events in chronic kidney disease'. American Journal of Kidney Disease, 52(1), pp. 49-57
- Ely, W.J., Osheroff, A.J., Chambliss, L.M., & Ebell, H.M. (2006). 'Approach to leg oedema of unclear aetiology'. The Journal of the American Board of Family Medicine, 19(2), p.p.148-160
- Engel, L.G. (1977). 'The need for a new medical model: a challenge for Biomedicine'. Science, 196(4286), pp. 129-136. The American Association for the Advancement of Science (AAAS),
- Engel, L.G. (1980). 'The clinical application of the biopsychosocial model'. The American Journal of Psychiatry, 137, pp.535-544. American Psychiatric Association
- Englyst. N. H. & Hudson. J. G., (2000). "Carbohydrates", ch5. in Garrow J.S., James W.P.T. & Ralph, A., (eds) (2000), Human Nutrition and Dietetics. 10th edition, Churchill Livingstone
- Erasmus, U. (1993). Fats that Heal Fats that Kill. Canada: Alive Books
- Ernst, E. (Ed) (2001). The Desktop Guide to Complementary and Alternative Medicine-An evidence Based Approach. London: Mosby (Harcourt Publishers Ltd)
- Ernst, E., Cohen, M.H., & Stone, J. (2004). 'Ethical problems arising in evidence based complementary and alternative medicine'. Journal of Medical Ethics, 30(2), pp. 156-159. NCBI,US NLM
- EU. (2005). 'Promoting healthy diets and physical activity: a European dimension for the prevention of overweight, obesity and chronic diseases'. Green Paper COM(2005) 637 final. Brussels, 08.12.2005
- EU. (2007i). White Paper-Together for Health; a strategic approach for the EU 2008-2013, COM(2007) 630 final. Brussels: European Commission

- EU. (2007ii). 'EU Platform on diet, physical activity and health'. Annual Report 2007, Synopsis commitments, [version 13 Mar 2007, 09.00h]. The Netherlands: RIVM, National Institute for Pupil Health and the Environment.
- EU. (2009i). 'Perceived general health'. EUPHIX-European Union Public Health Information System, version 1.11, 17 Dec 2009. RIVM, Bilthoven.
- EU. (2009ii). 'Perceived and function health'. Eurostat Statistical Database of the European Union, version 1.9, 28 May 2009.
- EU. (2009iii). 'Perceived general health'. Eurostat Statistical Database of the European Union, version 1.9, 28 May 2009.
- EU. (2010i). '-omics in personalized medicine'. Workshop to explore the role of -omics in the development of personalized medicine. Summary report. Brussels 29-30 April 2010: European Commission, Health Research Directorate
- EU. (2010ii). 'Stratification biomarkers in personalized medicine'. Workshop to clarify the scope for Stratification biomarkers and to identify bottlenecks in the discovery and the use of such biomarkers. Summary report-Biomarkers for Patient Stratification. Brussels: European Commission, Health Research Directorate
- EU. (2010iii). 'The European Commission welcomes the first EU 'Joint Programming Initiative' to boost research on Alzheimer's and other neurodegenerative diseases'. Press release IP/10/431, 15 April 2010. Brussels, European Commission, available at <http://europa.eu/rapid/pressReleasesAction.do?reference=IP/10/431&format=HTML&aged=0&language=EN&guiLanguage=en> (accessed 20 /11/2010)
- EU. (2010iv). 'Health in the EU: Nutrition deemed a growing challenge for health in the EU and beyond'. Public Health Report IP/10/1674. Brussels: European Commission
- Evans, B.D., Tandon, A., Murray, L.J.C., & Lauer, A.J. (2001). 'Comparative efficiency of national health systems: cross national econometric analysis'. British Medical Journal, 323, pp.307-310. BMJ Publishing Group Ltd
- Ewald, F. (1999). 'Foucault and the contemporary scene'. Philosophy & Social Criticism, 25(3), pp. 81-91. SAGE Publications
- Fahy, N., McKee, M., Busse, R., & Grundy, E. (2011). 'How to meet the challenge of ageing populations'. British Medical Journal, 2011;342:d3815 doi: 10.1136/bmj.d3815. BMJ Publishing Group Ltd
- Fairclough, N. (1992). 'Discourse and Text: Linguistic and Intertextual-Analysis within Discourse Analysis'. Discourse & Society, 3(2), pp.193-217. Lancaster University
- Fairclough, N. (2000). 'Language and Neo-Liberalism'. Discourse & Society, 11(2), pp.147-148. SAGE publications
- Fairclough, N. (2005). 'Critical Discourse Analysis'. Merges Linguistics, 9, pp.76-94
- Fairclough, N. (2005i). 'Discourse analysis in organisational studies: the case for critical realism'. Organisational Studies, 26, pp. 915-939
- Fairfield, M.K. & Fletcher H.R. (2002). 'Vitamins for chronic disease prevention in adults'. Scientific Review in JAMA, Jun 2002, 287(23), pp. 3116-26. American Medical Association
- Fallat, E.M., Glover, J., & The committee of bioethics'. (2007). 'Professionalism in paediatrics'. Pediatrics, 120, pp.e1123-e1133. American Academy of Pediatrics
- Faunce, T., Bolsin, S., & Chan, W.P. (2004). 'Supporting whistleblowers in academic medicine: training and respecting the courage of professional conscience'. Journal of Medical Ethics 30, pp.40-43. . BMJ Publishing Group Ltd
- Fenech, M. (2001). 'Recommended dietary allowances for genomic stability'. Mutat Res, 1(480-481), pp. 51-54. NCBI,US NLM

- Ferguson, L.R. (2009). 'Nutrigenomics approaches to functional foods'. Journal of American Dieticians Association, 109(3), pp.452-458
- Fessler, A. (1950). 'A medical contract from the eighteenth century'. British Medical Journal, 2(4688), pp. 1112-1113. BMJ Publishing Group Ltd
- Fetrow, W. C. & Avila, R.J. (2004). Professional's Handbook of Complementary & Alternative Medicines. (3rd ed.). USA: Lippincott Williams & Wilkins (A Wolters Kluwer Company)
- Finney, A.L., & O'Halloran, V.T. (2003). 'Transition metal speciation in the cell: insights from the chemistry of metal ion receptors'. Science Magazine, 300(5261), pp.931-936.
- Figueroa, V.M. (2009). 'The time has come for physicians to take notice: the impact of psychosocial stressors on the heart'. The American Journal of Medicine, 122(8), pp. 704-712
- Fisher, C.P. (1905). 'Proposed regulation of the practice of medicine and surgery in Pennsylvania in the eighteenth century'. Medical Library and Historical Journal, 3(2), pp. 113-117. NCBI,US NLM
- Fisher, L. (1993). The Clinical Science of Mineral Therapy. (2nd ed.). Australia: The Maurice Blackmore Research Foundation
- Fisk, J.D. (2007). 'Ethical considerations for the conduct of antidementia trials in Canada', Can J Neurol Sci. 34 Suppl 1, pp. S32-6, PubMed NCBI ,US NLM
- Fletcher, B.L., & Tappel, A.L. (1973). 'Protective effects of dietary a-tocopherol in rats exposed to toxic levels of ozone and nitrogen dioxide.' Environ Res, 6, pp.165. Quoted in McCarthy (1981)
- Fletcher, H.R. & Fairfield, M.K. (2002). 'Vitamins for chronic disease prevention in adults' Clinical applications in JAMA, Jun 2002, 287(23), pp. 3127-29. American Medical Association
- Flood, G.D. (1996). An Introduction to Hinduism. Cambridge University Press, Cambridge, UK
- Forbes, C., Shirran, L., Bagnall, A.M., Duffy, S., & ter Riet, G. (2001). 'A rapid and systematic review of the clinical effectiveness and cost-effectiveness of topotecan for ovarian cancer'. Health Technol Assess, 5(28), pp. 1-110. NCBI,US NLM.
- Ford, E.S. (2001). 'Vitamin supplement use and diabetes mellitus incidence among adults in the United States.' Am Epidemiol
- Forestier, C., Guelon, D., Cluytens, V., Gillart, T., Sirot, J., & De Champs, C. (2008). 'Oral probiotic and prevention of Pseudomonas aeruginosa infections: a randomised, double-blind, placebo-controlled pilot study in intensive care unit patients'. Cri Care., 12(3), R69. BioMed Central Ltd
- Forster, E. S. (1961i). Translation and Comments on Aristotle-Movement of Animals. (3rd ed.). London: Harvard University Press (Loeb Classical Library)
- Forster, E. S. (1961ii). Translation and Comments on Aristotle-Progression of Animals. (3rd ed.). London: Harvard University Press (Loeb Classical Library)
- Foster, C.M., Hwang, J.S., Larson, G.M., Lichtman, H.J., Parikh, I.N., Vasan, S.R., Levy, D., & Fox, S.C. (2008). 'Overweight, obesity, and the development of stage 3 chronic kidney disease-The Framingham Heart Study'. American Journal of Kidney Disease, 52(1), pp. 39-48
- Fox, B. A. & Cameron A. G. (1995). Food, Science-Nutrition & Health. (6th ed.).London: Edward Arnold (A member of the Hodder Headline Group)
- Franke, S., Grass, G., & Nies, H.D. (2001). 'the product of the *ybdE* gene of the Escherichia coli chromosome is involved in detoxification of silver ions'. Microbiology, 147(2001), pp. 965-972. The Society of General Microbiology.

- Fraser, M.D. (1997). 'Ethical Dilemmas and practical problems for the Practitioner Researcher'. Educational Action Research, 5(1), pp.161-171. Taylor and Francis 2007
- Fraser, I.N. (1907). 'Some important and practical points in medicine'. California State Journal of Medicine, 5(2), pp. 22-25. NCBI,US NLM
- Frederickson, C.J., Koh, J.Y. & Bush, A.L. (2005). 'The neurobiology of zinc in health and disease'. Nat Rev Neurosci. 6(6), pp.449-462
- Friedman, M. (2005). Fundamentals of Naturopathic Endocrinology. Toronto: CCNM Press Inc.
- Gaby, A. R. (1994). Preventing & Reversing Osteoporosis. USA: Prima publishing (Random House, Inc.)
- Gale Encyclopedia of Medicine (online) (2008). The Gale Group, Inc
- Galland L., (2005). 'Patient-centered care: Antecedents, triggers and mediators'. Ch.8, in Jones, D. S. (Ed) (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Galli, U., Gaab, J., Ettlin, D.A., Ruggia, F., Ehlert, U. & Palla, S. (2009). 'Enhanced negative feedback sensitivity of the hypothalamus-pituitary-adrenal axis in chronic myogenous facial pain'. European Journal of Pain (London, England), 13(6), pp. 600-605
- Garcia-Berthou, E., & Alcaraz, C. (2004). 'Incongruence between test statistics and P values in medical papers'. BMC Medical Research Methodology,4(13). BioMed Central
- Garcia-Puig, J., Ruilope, L.M. Lague, M., Fernandez, J., Ortega, R., & Dal-Re, R. (2006). 'Glucose metabolism in patients with essential hypertension'. The American Journal of Medicine, 119(4), pp. 318-326. Elsevier Inc.
- Gardner, A., Howell, R. T. & Davies T. (2000). Human Genetics. London: Arnold (a member of the Hodder Headline Group)
- Garland, L.H. (1928). 'The lure of medical history: IMHOTER: Patron of physicians and deity of medicine in ancient Egypt'. California and Western Medicine, 29(2), pp. 96-69. NCBI,US NLM
- Garland, M.R., Hallahan, B., McNamara, M., Carney, P.A., Grimes, H., Hibbeln, J.R., Harkin, A., & Conroy, R.M. (2007). 'Lipids and essential fatty acids in patients presenting with self-harm'. The British Journal of Psychiatry: The Journal of Mental Science [Br J Psychiatry], 190, pp. 112-117
- Garrison, F.H. (1929). 'Medicine as an agency in the advancement of science, art and civilisation'. Bulletin of the New York Academy of Medicine, 5(4), pp. 305-327. NCBI,US NLM
- Garrison, R. (1982). Lysine, Tryptophan and Other Amino Acids. USA: Keats Publishing, Inc.
- Garrow, J. S., James, W. P. T. & Ralph, A. (Eds) (2000). Human Nutrition and Dietetics. (10th ed.). UK: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Garrow, J.S. (2000). 'Composition of the body'. Chapter 2 in Garrow, J. S., James, W. P. T. & Ralph, A. (Eds) (2000). Human Nutrition and Dietetics. (10th ed.). UK: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Gates, E.P., Tanaka, H., Hiatt, R.W., & Seals, R.D. (2004). 'Dietary sodium restriction rapidly improves large elastic artery compliance in older adults with systolic hypertension'. Hypertension, 44(1), pp.35-41. The American Heart Association, Inc
- Gawande, S., Kale, A., & Kotwal, S., (2008). 'Effect of nutrient mixture and black grapes on the pharmacokinetics of orally administered epigallocatechin gallate from green tea extract: a human study'. Phytother Res., 22(6), pp.802-808

- Geanakoplos, D. (1966). Byzantine East & Latin West: Two Worlds in Middle Ages and Renaissance. Harper Torch Books
- Gelfand, M.J., Neimann, L.A., Shin, B.D., Wang, X., Margolis, J.D., & Troxel. B.A. (2006). 'Risk of myocardial infarction in patients with psoriasis'. The Journal of the American Medical Association, 296(14), pp. 1735-1741. The American Medical Association
- German, B.J., Bauman, E.D., Burrin, G.D., Failla, L.M., Freake, C.H., King, C.J., Klein, S., Milner, A.J., Pelto, H.G., Rasmussen, M.K., & Zeisel, H.S. (2004). 'Metabolomics in the opening decade of the 21st century: building the roads to individualised health'. The Journal of Nutrition, 134(10), pp.2279-2732. The American Society for Nutritional Sciences
- German, B.J., Roberts, M.A. & Watkins, S.M. (2003). 'Personal metabolomics as a next generation nutritional assessment'. The Journal of Nutrition, 133(12), pp.4260-4266. The American Societies for Nutritional Sciences.
- Gerson, M. (1999). A Cancer Therapy: Results of Fifty Cases. (6th ed.). USA: The Gerson Institute
- Gey, K.F. (1993). 'Prospects for the prevention of free radical disease, regarding cancer and cardiovascular disease.' British Medical Bulletin, 49, pp. 679-99. NCBI,US NLM.
- Gharajedaghi J. (2004). 'A Holistic Language of Interaction and Design- Seeing through Chaos and Understanding Complexities', Systems Methodology, pp. 1-15,
- Ghosh, D., Skinner, M.A., & Laing, W.A. (2007). 'Pharmacogenomics and nutrigenomics: synergies and differences'. European Journal of Clinical Nutrition, 61(5), pp.567-574. NCBI,US NLM
- Giljevic, Z. & Vlask, T. (2006). 'Treatment of osteoporosis by risedronate-speed, efficacy and safety'. Reumatizam, 53(2), pp. 66-71 . NCBI,US NLM
- Gillies, C.M.J., Mercer, W.S., Lyon, A., Scott, M., Watt, & C.M.G. (2009). 'Distilling the essence of general practice : a learning journey in progress'. British Journal of General Practice, 59(562), pp.e167-e176
- Ginsburg, G.S. & Willard, H.F. (2009). 'Genomic and personalised medicine : foundations and applications. Translational Research, 154(6), pp.277-287
- Glenville, M. (2001). The Nutritional Health Handbook for Women. London: Judy Piatkus (Publishers) Limited
- Glenville, M. (2005). Osteoporosis – The silent epidemic. London: Kyle Cathie Limited
- Glenville, M. (1997). Natural Alternatives to HRT. London: Kyle Cathie Limited
- Go, V.L., Higginbotham, S., & Vucenic, I., (2007). 'Review of the international research conference on food, nutrition and cancer, 2006. Journal of Nutrition, 137(1), pp.159S-160S. The American Society for Nutrition
- Go, V.L., Nguyen, H.T., Harris, M.D., & Lee, P.W. (2005). 'Nutrient-Gene Interaction: metabolic genotype-phenotype relationship'. Journal of Nutrition, 135(12), pp.3016S-3020S. The American Society for Nutrition
- Go, V.L., Wong, D.A., Wang, Y., Butrum, R.R., Norman, H.A., & Wilkerson, L. (2004). 'Diet and cancer prevention: evidence-based medicine to genomic medicine'. The Journal of Nutrition, 134(12 Suppl) pp.3513S-3516S. The American Society for Nutritional Sciences
- Godlee, F. (2010). 'Dreaming of a fairer world'. British Medical Journal, 341:c3658. BMJ Publishing Group Ltd.
- Godlee, F. (2010i). 'Vested interests'. British Medical Journal, 340 (c1922) . BMJ Publishing Group Ltd
- Goffman, E. (1981). Forms of Talk. Philadelphia, Pennsylvania: University of Pennsylvania Press

- Goldberg, B., Trivieri, L., & Andreson, J. (2002). Alternative Medicine The Definitive Guide. (2nd ed.). USA: Celestial Arts
- Goldberg, B. & Triviery, L. (2004). Chronic Fatigue, Fibromyalgia & Lyme Disease. (2nd ed.). Berkeley: Celestial Arts
- Golna, C., Pashardes, P., Allin, S., Theodorou, M., Merkur, S., & Mossialos, E. (2004). Health systems in transition: Cyprus. ISSN 1020-9077, 6(5). Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies, 2004.
- Gonzalez-Gross, M., Marcos, A., & Pietrzik, K. (2001). 'Nutrition and cognitive impairment in the Elderly'. British Journal of Nutrition, 86(3), pp.313-21. NCBI,US NLM
- Goode, A. & Mavromaras, K. (2008). 'Obesity as a multidisciplinary research topic: Editors' Introduction'. The Australian Economic Review, 41(1), pp.67-71. Melbourne Institute of Applied Economic and Social Research, The University of Melbourne. Blackwell Publishing Asia Pty Ltd
- Goold, P.G. & Balme, D. M. (Eds). (1991). Aristotle-History of animals-Books VII-X. London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. & Potter, P. (Eds) (1995). Hippocrates-Volume VIII. London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. & Smith, W. D. (Eds). (1994). Hippocrates-Volume VII. London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. (ed). (1916). 'Book I-III', Galen-On the Natural Faculties. With an English translation by Brock, J.A. London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. (Ed). (1928). Hippocrates-Volume III. London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. (Ed). (1961i). Aristotle-Parts of Animals. (3rd ed.). London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. (Ed). (1961ii). Aristotle-Movement of Animals. (3rd ed.). London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. (Ed). (1961iii). Aristotle-Progression of Animals. (3rd ed.). London: Harvard University Press (Loeb Classical Library)
- Goold, P.G. (Ed). (1988i). Hippocrates-Volume V. London: Harvard University Press & W. Heinemann Ltd (Loeb Classical Library)
- Goold, P.G. (Ed). (1988ii). Hippocrates-Volume VI. London: Harvard University Press & W. Heinemann Ltd (Loeb Classical Library)
- Gorelik, O., Almozno-Sarafian, D., Feder, I., Wachsman, O., Alon, I., Kitvinjuk, V., Rshovsky, M., Modai, M., & Cohen, N. (2003). 'Dietary intake of various nutrients in older patients with congestive heart failure'. Cardiology, 99(4), pp.177-181. Karger AG,
- Gorell, M.J., Peterson, L.E., Rybicki, A.B., & Johnson, C.C. (2003). 'Multiple risk factors for Parkinson's disease'. Journal of the Neurological Sciences. 217(2), pp.169-174. The World Federation of Neurology.
- Gotzsche, C.P. & Olsen, O. (2000). 'Is screening for breast cancer with mammography justifiable?'. The Lancet, 355(9198), pp.129-134.
- Govil, S.R., Weidner, G., Merritt-Worden, T., & Ornish, D. (2009). 'Socioeconomic status and improvements in lifestyle, coronary risk factors, and quality of life: the Multisite Cardiac Lifestyle Intervention programme'. American Journal of Public Health, 99(7), pp. 1263-1270
- Graedon, J. & Graedon, T. (1995). Deadly Drug Interactions. St. Martin's Griffin (Graedon Enterprises, Inc.)

- Green, R., & Miller, J.W. (1999). 'Folate deficiency beyond megaloblastic anemia: hyperhomocysteinemia and other manifestations of dysfunctional folate status'. Semin Hematol, 36(1), pp. 47-64. NCBI,US NLM.
- Greenhalgh, T. (1997). 'How to read a paper: Papers that summarise other papers (systematic reviews and meta-analyses)'. British Medical Journal, 315(7109), pp.672-675. BMJ Publishing Group Ltd
- Greenstein, B. (1994). Endocrinology at a Glance. (2nd ed.). London: Blackwell Science Ltd
- Greenwood, M.S., Mizielinska, M.S., Frenguelli, G.B., Harvey, J., & Connolly, N.C. (2007). 'Mitochondrial dysfunction and dendritic beading during neuronal toxicity'. The Journal of Biological Chemistry, 282(36), pp.26235-26244. The American Society for Biochemistry and Molecular Biology Inc. JBC Papers in Press.
- Gremy, F. (1984). 'Will our health system fall apart? The need for a new paradigm'. Eff Health Care. 1(5). Pp.239-47
- Grossberg, G. T. & Fox, B. (2007). The Essential Herb-Drug-Vitamin Interaction Guide: The Safe Way to Use Medications and Supplements Together. Broadway Books (The Doubleday Broadway Publishing Group)
- Grossman, I., Lutz, W.M., Crenshaw, G.D., Saunders, M.A. Burns, K.D., & Roses, D.A. (2010). 'Alzheimer's disease: diagnostics, prognostics and the road to prevention'. The Epma Journal, 1(2), pp.293-303
- Guaner, F. (2007). 'Prebiotics in inflammatory bowel disease'. British Journal of Nutrition, 98(suppl 1), pp.S85-S89
- Guerrero-Romero, F., & Rodriquez-Moran, M. (2005). 'Complementary therapies for diabetes: the case for chromium, magnesium, and antioxidants'. Arch Med Res, 36(3), pp.250-7. PubMed. NCBI ,US NLM
- Gump, B.B., Reihman, J., Stewart, P., Lonky, E., Darvill, T., Granger, D.A., & Matthews, K.A. (2009). 'Trajectories of maternal depressive symptoms over her child's life span: relation to adrenocortical, cardiovascular, and emotional functioning of children'. Development and Psychopathology [Dev Psychopathol], 21(1), pp. 207-225
- Gurpinar, E., Musal, B., Aksakoglu, G., & Ucku, R., (2005). 'Comparison of knowledge scores of medical students in problem-based learning and traditional curriculum on public health topics'. BMC Medical Education, 5(7)
- Gurusamy, K.S., Kumar, Y., & Davidson, B.R. (2008). 'Methods of preventing bacterial sepsis and wound complications for liver transplantation'. Cochrane Database Syst Rev., 8(4), CK0066600
- Guttmacher, E.A., & Collins, S.F. (2003). 'Welcome to the genomic era'. The New England Journal of Medicine, 349, pp.996-998. NEJM.org. Massachusetts Medical Society
- Guzman, J., Esmail, R., Karjalainen, K., Malmivaara, A., Irvin, E., & Bombardier, C. (2002). 'Multidisciplinary bio-psycho-social rehabilitation for chronic low back pain'. Cohrane Database Systematic Reviews, 1, CD000963
- Hackenberg, D.T. (2009). 'Realism without truth: a review of Giere's science without laws and scientific perspectivism'. Journal of Experimental Analysis of Behavior. 91(3), pp.391-402. Society for the Experimental Analysis of Behavior
- Hakobyan, T., Nazaretyan, M., Makarona, T., Aristakeshyan, M., Margaryants, H., & Nolte, E. (2006). 'Armenia-Health system review'. Health systems in transition, 8(6), pp. 1-180. The European Observatory on Health Systems and Policies, WHO Regional Office for Europe.

- Hammer R.H., & Jonas B.W. (2004). 'Managing social conflict in Complementary and Alternative Medicine research: Antineoplastons'. Integrative Cancer Therapies, 3(1) pp.59-65. SAGE
- Hammersley, M. & Atkinson, P. (1995). Ethnography. (2nd ed.). London: Routledge (Taylor & Francis Group)
- Hampton, J.R. (1997). 'Evidence-based medicine, practice variations and clinical freedom'. J Eval Clin Pract, 3(2), pp. 123-131,
- Hamzaoui, A., Harzallah, O., Klii, R., & Mahjoub, S. (2010). 'Hyperhomocysteinaemia in Behcet's disease'. Biochemistry Research International, 2010(2010), ID 361387, 5 pages. Hindawi Publishing Corporation
- Hanaway, P. (2005). 'Balance of flora, GALT, and mucosal integrity', in Jones, D. S. (Ed) (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Hansen, S.H., Olsen, A.K., Soderlund, E.J., & Runborg, G. (2009). 'In vitro investigations of glycidamide-induced DNA lesions in mouse male germ cells and in mouse and human lymphocytes'. Mutat Res [Epub ahead of print] Elsevier B.V.
- Hanssen, M. & Marsden J., (1988). E for Additives, (2nd ed). UK: Thornsons (Harper Collins Publishers) UK.
- Hanzlik, J.P. (1927). 'Progress in medicine on the pacific coast during 1926-27'. California and Western Medicine, 27(2), pp. 196-199. NCBI,US NLM
- Harbers, M.M, (2008). 'Percentage of adults with good or very good self-perceived health, for men, women and total, in the EU-27, Iceland, Norway and Switzerland'. EUPHIX, EUphact. Bilthoven: RIVM, available at [http://www.euphix.org/EUphact/Health Status/Perceived and functional health/Perceived general health](http://www.euphix.org/EUphact/Health%20Status/Perceived%20and%20functional%20health/Perceived%20general%20health) (accessed 28 /2/ 2008)
- Harding, G., Campbell, J., Parsons, S., Rahman, A., & Underwood, M. (2010). 'British pain clinic practitioners' recognition and use of the bio-psychosocial pain management model for patients when physical interventions are ineffective or inappropriate: results of a qualitative study'. BMC Musculoskeletal Disorders, 11(51). BioMed Central Ltd
- Hark, A.L. & Morrison, G. (2000). 'Development of a case-based integrated nutrition curriculum for medical students'. American Journal of Clinical Nutrition, 72(suppl) 890S-7S. American Society for Clinical Nutrition
- Harper, C.R. & Jacobson, T.A. (2001). 'The facts of life: the role of omega-3 fatty acids in the prevention of coronary heart disease'. Arc Intern Med, 161(18), pp.2185-92. NCBI,US NLM.
- Harris, C.J. (2009). 'Toward a restorative medicine-the science of care'. Summary of the original article and commentary on [Peabody, F. (1927). 'The care of patient'. JAMA, 88(12), pp. 877-882]. JAMA, 301(16), pp. 1710-1712, American Medical Association. NCBI,US NLM
- Harris, J.T. (1927). 'Colonial medicine of the doctor of our forefathers'. California and Western Medicine, 3(12), pp. 707-721. NCBI,US NLM
- Harris, J.T. (1929). 'History of post-graduate medicine in New York City'. Bulletin of the New York Academy of Medicine, 5(8), pp. 789-801. NCBI,US NLM
- Harisson (2001). 'Research: the rigors of reciprocity'. Qualitative Inquiry, 7(3). 323-345. Sage Publications
- Hartmut H., (2000). Homotoxicology and Ground Regulation System (GRS), (1st English ed.). Germany: Aurelia-Verlag GmbH
- Hasler, C.M., Kundrat, S., & Wool, D. (2000). 'Functional foods and cardiovascular disease'. Curr Atheroscler Rep. 2(6), pp.467-475

- Hatch, D., (2001). 'Professionally led regulation in medicine'. British Journal of Ophthalmology, 85, pp.512-515. British Medical Association
- Hatzopoulos, O., (Ed). (1992i). Ιπποκράτης-Άπαντα 1, Γενική Ιατρική. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992ii). Ιπποκράτης-Άπαντα 2, Προληπτική Ιατρική. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992iii). Ιπποκράτης-Άπαντα 3, Παθολογία-Οφθαλμολογία. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992iv). Ιπποκράτης-Άπαντα 4, Ανατομία-Φυσιολογία. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992v). Ιπποκράτης-Άπαντα 5, Διαιτητική-Θεραπευτική 1. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992vi). Ιπποκράτης-Άπαντα 6, Διαιτητική-Θεραπευτική 2. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992vii). Ιπποκράτης-Άπαντα 7, Γυναικολογία 1. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992viii). Ιπποκράτης-Άπαντα 8, Γυναικολογία 2. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992ix). Ιπποκράτης-Άπαντα 9, Γυναικολογία 3. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992x). Ιπποκράτης-Άπαντα 10, Μαιευτική-Εμβρυολογία. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xi). Ιπποκράτης-Άπαντα 11, Χειρουργική. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xii). Ιπποκράτης-Άπαντα 12, Ορθοπαιδική. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xiii). Ιπποκράτης-Άπαντα 13, Επιδημίες 1. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xiv). Ιπποκράτης-Άπαντα 14, Επιδημίες 2. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xv). Ιπποκράτης-Άπαντα 16, Παθήσεις-Επιληψία. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xvii). Ιπποκράτης-Άπαντα 17, Επιστολές. Athens: Kaktos
- Hatzopoulos, O., (Ed). (1992xix). 'Περί φύσεως', Πλάτων-Τίμαιος, Athens: Kaktos
- Hatzopoulos, O., (Ed) (1992xx). 'Ατλαντικός', Πλάτων-Κριτίας. Athens: Kaktos
- Hatzopoulos, O., (Ed) (1992xxi). 'Μετά τα φυσικά 1, βιβλία [Α-Δ]', Αριστοτέλης-Άπαντα, Τόμος 10. Athens: Kaktos
- Hatzopoulos, O., (Ed) (1992xxii). 'Μετά τα φυσικά 2, βιβλίο [Ε-Ι]', Αριστοτέλης-Άπαντα, Τόμος 11. Athens: Kaktos
- Hays, B. (2005). 'Hormonal imbalances'. In Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- He, Y., Cui, J., Lee, J.C., Ding, S., Chalimoniuk, M., Simonyi, A., Sun, A.Y., Gu, Z., Weisman, W.G., Wood, W.G., & Sun, G.Y. (2011). 'Prolonged exposure of cortical neurons to oligomeric amyloid-beta impairs NMDA receptor function via NADPH oxidase-mediated ROS production: protective effect of green tea (-)-epigallocatechin-3-gallate'. ASN Neuro., 3(1), e00050. The Author(s)
- Heine, H. (2000). Homotoxicology and Ground Regulation System (GRS). Germany: Aurelia-Verlag GmbH
- Heisenberg, W. (1963). Physics and philosophy. Allen & Unwin, London, quoted in Capra, F. (1982). The Tao of Physics. (3rd ed.). London: Flamingo (HarperCollins Publishers)
- Heller, A.M., & Eisengerg, S.R. (Can patents deter innovation? The anticommens in biomedical research'. Science, 280,(698). The American Association for the Advancement of Science.
- Hemmeter, J.C. (1906). 'German-American influence in medicine and surgery'. Medical Library and Historical Journal, 4(3), pp. 287-292. NCBI,US NLM

- Henderson J., & Goold, P.G. (Eds). (1942). Aristotle-Generation of animals. London: Harvard University Press (Loeb Classical Library)
- Henderson, J. (Ed). (1970). Aristotle-History of animals- Books IV-VI. London: Harvard University Press (Loeb Classical Library)
- Henderson, J. (Ed). (1923i). Hippocrates-Volume I. London: Harvard University Press (Loeb Classical Library)
- Henderson, J. (Ed). (1923ii). Hippocrates-Volume II. London: Harvard University Press(Loeb Classical Library)
- Henderson, J. (Ed). (1931). Hippocrates-Volume IV. London: Harvard University Press (Loeb Classical Library)
- Henderson, J. (Ed). (1933). Aristotle-Metaphysics-Books I-IX. London: Harvard University Press (Loeb Classical Library)
- Henderson, J. (Ed). (1935i). Aristotle- Metaphysics-Books X-XIV. London: Harvard University Press (Loeb Classical Library)
- Henderson, J. (Ed). (1935ii). Aristotle-Oeconomica-Books I-III. London: Harvard University Press (Loeb classical library)
- Henderson, J. (Ed). (1935iii). Aristotle-The Magna Moralia-Books I-II. London: Harvard University Press (Loeb classical library)
- Henderson, J., & Goold, P.G. (Eds). (1965). Aristotle-History of animals-Books I-III. London: Harvard University Press (Loeb Classical Library)
- Hennen, W. (1999). Fibromyalgia-A Nutritional Approach. Utah: Woodland Publishing, Inc.
- Henry, J. A. (Ed) (2002). The British Medical Association-New Guide to Medicines and Drugs. (5th revised ed.). London: Dorling Kindersley Ltd
- Herbert, V. (2000). 'Preventing early morbidity and mortality in millions of elderly and saving billions: new evidence that 100mcg free vitamin B12 (cobalamin) orally daily from age 50 will prevent gastric atrophy of the elderly from producing subtly progressive B12 deficiency, neuropsychiatric dementia & stumbling and later anemia'. FASEB J, 14(4), p. A292 (abstract 226.1)
- Herzberger, G. (2003). The Fundamentals of Homotoxicology-Diagnosis and Therapy of Homotoxicoses. (2nd English ed.). Germany: Aurelia-Verlag GmbH
- Heyland, K.D., Heyland, D.R., Jones, E.N., Khaliwal, R., Day, G.A., Jiang, X., Morrison, S., & Davies, R.A. (2008). 'Creating a culture of clinical excellence in critical care nutrition: The 2008 'Best of the Best' Award'. JPEN Journal of Parenteral and Enteral Nutrition .
- Higdon, J. (2003). An Evidence-Based Approach to Vitamins and Minerals-Health Benefits and Intake Recommendations. Thieme Medical Publishes, Inc.
- Hjortdahl, P. (1992). 'Continuity of care: general practitioners' knowledge about, and sense of responsibility toward their patients'. Family Practice, 9,(1), pp.3-8. Oxford University Press.
- Hodges, J.G., Gros, R., Hegele, A.R., Van Uum, S., Shoemaker, K.J. & Feldman, D.R. (2010). 'Increased blood pressure and hyperdynamic cardiovascular responses in carriers of a common hyperfunctional variant of Adenylyl Cyclase 6'. The Journal of Pharmacology, 335(2), pp.451-457. The American Society for Pharmacology and Experimental Therapeutics
- Hodges, S., Ferreira, K., Israel, N., & Mazza, J. (2006). 'Strategies for system of care development: making change in complex systems'. Research and Training Center Study 2. Case Studies of System Implementation, pp.1-14. University of South Florida

- Holmquist, L., Stuchbury, G., Berbaum, K., Muscat, S., Young, S., Hager, K., Engel, J., & Munch G. (2007). 'Lipoic acid as a novel treatment for Alzheimer's disease and related dementias'.
- Holum, J. R. (1998). Fundamentals of General, Organic, and Biological Chemistry. (6th ed.). USA: John Wiley & Sons, Inc.
- Hooper, L., Ashton, K., Harvey, J.L., Desci, T., & Fairweather-Tait, J.S. (2009). 'Assessing potential biomarkers of micronutrient status by using a systematic review methodology: methods'. American Journal of Clinical Nutrition, 89(6), pp.19535-19595. American Society for Nutrition
- Hope, W.C., Dalton, C., Machlin, L.J., Filipski, R.J., & Vane, F.M. (1975). Influence of dietary vitamin E on prostaglandin biosynthesis in rat blood'. Prostaglandins, 10, p.557. Quoted in McCarthy (1981)
- Hopkins, S. J. (1999). Drugs and Pharmacology for Nurses. (13th ed.). UK: Churchill Livingstone (Elsevier Limited)
- Horrobin, D.F. (1980). 'The regulation of prostaglandin biosynthesis: negative feedback mechanisms and the selective control of formation of 1 and 2 series prostaglandins: relevance to inflammation and immunity'. Medical Hypotheses, 6, p.687. Quoted in McCarthy (1981)
- Houghton, L., & Ledington, P.W.J. (2002). 'The evolution of confusion: Soft Systems Methodology and Social Theory revisited'. AJIS, 9(2), pp.75-83
- Hudson, T. & Murray, T.M. (2011). 'Osteoporosis'. Chapter 196, in Pizzorno, J. & Murray, M. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc
- Hughes, B.B., Kuhn, R., Peterson, M.C., Rothman, S.D., Solorzano, R.J., Mathers, D.C., & Dickson, R.J. (2011). 'Projections of global health outcomes from 2005 to 2060 using the International Futures integrated forecasting model'. Bulletin of the World Health Organisation, April 2011. World Health Organisation
- Hulswit, M. (2002). 'A short history of "causation" ', an abridged version of the first chapter of From Cause to Causation, A Peircean Perspective, Dordrecht, Kluwer Publishers,
- Hyman M., MacDonald B., & Jones S.D. (2005). 'Biochemical individuality and genetic uniqueness'. Ch. 7, in Jones, D. S. (Ed) (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- IFM (2008). *What is Functional Medicine* The Institute for Functional Medicine, available at www.functionalmedicine.org (accessed 25/11/ 2010)
- Illich, I. (1974). 'Medical nemesis'. Lancet, i, pp.918-921, , reprinted in Journal of Epidemiology and Community Health, 57, pp.919-922,
- Illich, I. (1995). Limits to Medicine-Medical Nemesis: The Expropriation of Health. (2nd enlarged edition with a new introduction by the author). UK & US: Marion Boyars Publishers Ltd.
- Ingham, S.D. (1929). 'Psychology in medicine'. California and Western Medicine, 31(3), pp. 173-177. NCBI,US NLM
- IOM, (2008). 'Institute of Medicine Report: Improving medical education-enhancing the behavioural and social science content of medical school curricula'. Academy Emergency Medicine, 13(2), pp.230-231. Institute of Medicine. Wiley Online Library
- Irvine, D. (1997). 'The performance of doctors I: professionalism and self regulation in a changing world'. British Medical Journal, 314, p.1540. BMJ Publishing Group Ltd
- Izzo, A.A., Piscitelli, F., Capasso, R., Aviello, G., Romano, B., Borelli, F., Petrosino, S., & Di Marzo V. (2009). 'Peripheral endocannabinoid dysregulation in obesity : relation to

- intestinal motility and energy processing induced by food deprivation and re-feeding'. Themed Section: Advances in nutritional pharmacology, British Journal of Pharmacology, 158(2), pp. 451-461. The British Pharmacological Society. Wiley InterScience.
- Jackson, D.R. LaCroix, Z.A., Gass, M., Wallace, R., et al (2006). 'Calcium and vitamin D supplementation and the risk of fractures'. New England Journal of Medicine, 354, pp.669-683. NEJM.org, Massachusetts Medical Society
- Jackson, P.V. (2002). 'Screening mammography: controversies and headlines'. Radiology, 225, pp.323-326, RSNA
- Jacobson, S.J., Grann R.V., Gnatt, A.M., Hibshoosh H., Austin H.M.J., Millar S. & Neugut I.A. (2005). Cancer outcomes at the Hufeland (Complementary/Alternative medicine) Klinik: A best-case series Review. Integrative Cancer Therapies, 4(2), pp.156-167. SAGE Publications
- James, W.P.T. (2000). 'Historical Perspective', chapter 1, in Garrow, J. S., James, W. P. T. & Ralph, A. (Eds) (2000). Human Nutrition and Dietetics. (10th ed.). UK: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Jamison, J. R. (1999). Differential Diagnosis for Primary Practice. London: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Janks, H. (1997). 'Critical Discourse Analysis as a Research Tool'. University of the Witwatersrand, Johannesburg, South Africa, Discourse Queensland available at <http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.133.1971&rep=rep1&type=pdf>(accessed 24/5/2009)
- Jarvis, C. (2007). 'BOLA: CATWOE and Soft Systems Methodology', Business Open Learning Archive, available at <http://www.bola.biz/research/ssm.html> (accessed 5/12/2008)
- Jary D., & Jary J. (Eds). (1995). Collins Dictionary of Sociology (2nd ed.). HarperCollinsPublishers.
- JECH (Journal of Epidemiology and Community Health). (2003). 'Ivan Illich- Obituary'. The Times, reprinted in the Journal of Epidemiology and Community Health, 57, pp.923-924.
- Jeng, M. (2006). 'Error in statistical tests of error in statistical tests'. BMC Med Res Methodol., 6(45). BioMed Central
- Jensen, B. (1978). Nature Has A Remedy. California: Bernard Jensen International
- Jensen, B. (1982). Iridology- The Science and Practice in the Healing Arts- Volume II. USA: Bernard Jensen International
- Jeor, S.T.S, Krenkel, A.J. Plodkowski, A.R., Veach, L.T., Tolles, L.R., & Kimmel, H.J. (2006). 'Medical nutrition: a comprehensive, school-wide curriculum review'. American Journal of Clinical Nutrition, 83(suppl), pp. 963S-7S. American Society for Nutrition,
- Jeste, V.D. & Vahia, V.I. (2008). 'Comparison of the conceptualisation of wisdom in ancient Indian literature with modern views'. Psychiatry, 71(3), pp.197-209
- Jha, R.K., Ma, P., Sha, H., & Palikhe, M. (2010). 'Emerging role of resveratrol in the treatment of severe acute pancreatitis'. Front Biosci (Schol Ed)., 2, pp.168-175
- Jia, H., Liu, Z., Li X., Feng, Z., Hao, J., Li, X., Shen, W., Zhang, H., & Liu, J. (2010). 'Synergistic anti-Parkinsonism activity of high doses of B vitamins in a chronic cellular model'. Neurobiolo Aging, 31(4), pp.636-646
- Jiang, D., Sullivan, G.P. Sensi, L.S. Steward, O., & Weiss, H.J. (2001). 'Zn²⁺ induces permeability transition pore opening and release of pro-apoptotic peptides from neuronal mitochondria'. Journal of Biological Chemistry, 275, pp.47524-47529.
- Job, D.E., Whalley, H.C., McConnell, S., Glabus, M., Johnstone, E.C., & Lawrie, S.M. (2002). 'Structural grey matter differences between first-episode schizophrenics and normal

- controls using voxel-based morphometry'. Neuroimage, 17(2), pp.880-889. PubMed NCBI, US NLM
- John, E., Laskow, C.T., Buchser, J.W., Pitt, R.B., Basse, H.P. Butterfield, H.L., Kalinski, P., & Lotze, T.M. (2010). 'Zinc in innate and adaptive tumor immunity'. Journal of Translational Medicine, 8, 118. BioMed Central Ltd
- Jones, B. (1999). Pathology. London: Mosby (Mosby International Ltd)
- Jones, D. S. (Ed). (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Jones, M., Edwards, I., & Gifford, L. (2002). 'Conceptual models for implementing biopsychosocial theory in clinical practice'. Manual Therapy, 7(1), pp.2-9. NCBI, US NLM
- Jones, S.J., Bland S.J., & Quinn S. (2005). 'What is Functional Medicine?'. Chapter 2, in Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Jones, S.J., & Quinn S., (2005). 'Why Functional Medicine ?'. Ch.3, in Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Jones, W. H. S. (1923i). Translation and Comments on Hippocrates-Volume I. London: Harvard University Press (Loeb Classical Library)
- Jones, W. H. S. (1923ii). Translation and Comments on Hippocrates-Volume II. London: Harvard University Press (Loeb Classical Library)
- Jones, W. H. S. (1931). Translation and Comments on Hippocrates-Volume IV. London: Harvard University Press (Loeb Classical Library)
- Joos, S., Musselmann, B., & Szecsenyi, J. (2009). 'Integration of Complementary and Alternative Medicine into family practices in Germany: Results of a National Survey'. Evidence Based Complementary and Alternative Medicine, Mar 17 nep019v1.
- Juntunen, A., Nikkonen, M. & Janhonen, S. (2000). 'Utilizing the concept of protection in health maintenance among the Bena in Tanzania'. Journal of Transcultural Nursing, 11(3), pp. 174-181. Transcultural Nursing Society, Sage Publications
- Junyent, M., Arnett, K.D., Tsai, Y.M., Kabagambe, K.E., Straka, J.R., Province, M., An, P., Lai, Q.C., Parnell, D.L., Shen, J., Lee, Y.C., Borecki, I., & Ordovaw, M.J. (2009). 'Genetic variants at the PDZ-interacting domain of the scavenger receptor class B Type I interact with diet to influence the risk of Metabolic Syndrome in obese men and women'. The Journal of Nutrition, 139(5), pp.842-848. The American Institute of Nutrition
- Kaboru, B.B., Falkenberg, T., Ndubani, P., Hojer, B., Vongo, R., Brugha, R., & Faxelid, E. (2006). 'Can biomedical and traditional health care providers work together? Zambina practitioners' experiences and attitudes towards collaboration in relation to STIs and HIV/AIDS care: a cross-sectional study'. Human Resources for Health, 4(16). BioMed Central Ltd
- Kal, V. (1988). Philosophia Antiqua – On Intuition and Discursive Reasoning in Aristotle. The Netherlands: E. J. Brill
- Kale, A., Gawande, S., Ktawal, S., Netke, S., Roomi, W., Ivanov, V., Niedzwiecki, A. & Rath, M. (2010). 'Studies of the effects of oral administration of nutrient mixture, quercetin and red onion on the bioavailability of epigallocatechin gallate from green tea extract'. Phytother Res, 24(supp 1), pp.S48-55
- Kant, I. (2004). Metaphysical Foundations of Natural Science. England: University Press Cambridge
- Kaplan, L. A. & Pesce, A. J. & Kazmierczak S. C. (2003). Clinical Chemistry: Theory, Analysis, Correlation. (4th ed.). Usa: Mosby

- Kaput, J. (2007). 'Developing the promise of nutrigenomics through complete science and international collaborations'. Forum Nutr., 60, pp.209-223
- Kaput, J., Noble, J., Hatipoglu, B., Kohrs, K., Dawson, K., & Bartholomew, A. (2007). 'Application of nutrigenomics concepts to type 2 diabetes mellitus'. Nutr Metab Cardiovasc Dis., 17(2), pp.89-103
- Karekla, M., Symeou, A., Kapsou, M., & Anderson, D. (2007). 'Prevalence and psychosocial parameters of smoking in Cypriot college students'. Health Psychology Review, 1(1), pp.9-309. European Health Psychology Society. Abingdon:Taylor & Francis (accessed 23/11/2010)
- Kartakoullis, N.L., Phellas, C., Pouloukas, S., Petrou, M., & Loizou, C. (2008). 'The use of anabolic steroids and other prohibited substances by Gym enthusiasts in Cyprus.' International Review for the Sociology of Sport, 43(3), pp.271-287
- Karunakaran, S., Diwakar, L., Saeed, U, Agarwal, V., Ramakrishnan, S., Iyengar, S., & Ravindranath, V. (2007). 'Activation of apoptosis signal regulating kinase 1(ASK1) and translocation of death-associated protein, Daxx, in substantia nigra pars compacta in a mouse model of Parkinson's disease: protection by α -lipoic acid'. The FASEB Journal, 21(9), pp.2226-2236.
- Kassirer, P.J. (1995). 'Doctor discontent'. Editorial, The New England Journal of Medicine, 339(21), pp.1543-1545
- Kassirer, P.J. (1998). 'Managed care and the morality of the marketplace'. Editorial, The New England Journal of Medicine, 333(1), pp.50-52
- Kaufman, R.S. (2010). 'Time, clinic technologies, and the making of reflexive longevity: the cultural work of 'time left' in an aging society'. Social Health Illn. 32(2technogenarians), pp.225-237. National Institute of Health
- Keji, C. (Ed) (1994). Clinical Case Studies. China: Foreign Languages Press and New World Press
- Kelloff, J.G., Crowell, A.J., Steele, E.V., Lubet, A.R., Malone, A.W., Boone, W.C., Kopelovich, L., Hawk, T.E., Lieberman, R., Lawrence, A.J., Iqbal, A., Viner, L.J., & Sigman, C.C. (2000). 'Progress in cancer chemoprevention: development of diet-derived chemoprotective agents'. The Journal of Nutrition, 130, pp.467S-471S
- Kellog, H.W. (1928). 'Problems in preventive medicine'. California and Western Medicine, 29(3), pp. 177-182. NCBI,US NLM
- Kempf, J.E. (1905). 'European Medicine-a resume of medical progress during the eighteenth and nineteenth centuries'. Medical Library and Historical Journal, 3(4), pp. 231-248
- Kennedy, J., Wang C.C., & Wu H.C. (2007). 'Patient disclosure about herb and supplement use among adults in the US'. The Authors, eCam, 5(4), 451-456. Advance Access Publication
- Kenny V., & Gardner G. (1988). 'Constructions of Self-Organising Systems'. The Irish Journal of Psychotherapy, 9(1) 1-24.
- Kenny, A. (Ed) (2000). The Oxford History of Western Philosophy. Oxford University Press
- Kenny, P.N. (1997). 'Does good science make good medicine? Incorporating evidence into practice is complicated by the fact that clinical practice is as much art as science'. Journal of the American Medical Association, 157(1), pp. 33-36
- Kerr, W.K., Barkin, K., & Levers, P.E. (1979). 'The effect of cigarette smoking on bladder carcinogens in man'. J Canad Med Assoc, 93, p.1. Quoted in McCarthy 1981
- Kidd, P. M. (1996). Phosphatidylserine – A Remarkable Brain Nutrient. U.K:Biomedical Information Services Ltd

- Kilpatrick, S.I., Johns, S.S., Millar, P., Le, Q., & Routley, G. (2006). 'Shortages in health: innovative solutions using vocational education and training'. The International Electronic Journal of Rural and Remote Health, 2007: 623, available at <http://www.rrh.org.au> (accessed on 19 /11/2010)
- Kim, H.J. Oh, G.T., Park, Y.B., Lee, M.K., Seo, H.J., & Choi, M.S. (2004). 'Naringin alters the cholesterol biosynthesis and antioxidant enzyme activities in LDL receptor-knockout mice under cholesterol fed condition'. Life Sciences, 74(13), pp. 1621-1634
- Kim, J.M., Stewart, R., Kim, S.W., Yang, S.J., Shin, I.S., & Yoon, J.S. (2006). 'Vascular risk factors and incident late-life depression in a Korean population'. The British Journal of Psychiatry: The Journal of Mental Science [Br J Psychiatry], 189, pp. 26-30
- King D.C. (1945). 'The meaning of normal'. Yale Journal of Biology and Medicine, 17(3) pp. 493-501. NCBI,US NLM
- King, H. (2001). Greek and Roman Medicine. London: Bristol Classical Press
- Kmietowicz, Z. (2010). 'Registering herbalists will improve patients' safety, says health secretary'. British Medical Journal, 340, p.c1897. BMJ Publishing Group Ltd
- Knekt, P., Kumpulainen, J., Jarvinen, R., Rissanen, H., Heliovaara, M. Reunamen, A., Hakulinen, T., & Aromaa, A. (2002). 'Flavonoid intake and risk of chronic diseases'. American Journal of Clinical Nutrition, 76(3), pp.560-8 . NCBI,US NLM
- Kolasa, M.K. (2001). ' "Images" of nutrition in medical education and primary care'. American Journal of Clinical Nutrition, 73, pp. 1006-9. American Society for Clinical Nutrition. NCBI,US NLM
- Kolasa, M.K. & Rickett, K. (2010). Barriers to providing nutrition counselling cited by physicians-a survey of primary care practitioners'. Nutrition in Clinical Practice,25(5), pp.502-509. Sage Journals
- Kolovou, G. & Giannakopoulou, V. (2010). 'The influence of gene polymorphisms on coronary artery disease'. Angiology, 62(1), pp.5-6. Sage
- Konings, E.J., Baars, A.J. van Klaveren, J.D., Spanjer, M.C., Rensen, P.M., Hiemstra, M., van Kooij, J.A., & Peters, P.W. (2003). 'Acrylamide exposure from foods of the Dutch population and an assessment of the consequent risks'. Food Chem Toxicol., 41(11), pp.1569-1579
- Krebs F.N., & Primak, E.L. (2006). 'Comprehensive integration of nutrition into medical training'. American Journal of Clinical Nutrition, 83(suppl), pp. 945S-50S. American Society for Nutrition
- Kress, G.H. (1917). 'Organised medicine-a consideration of some of its California problems'. California State Journal of Medicine, 15(6), pp. 186-192. NCBI,US NLM
- Kreuter, W.M., Lezin, A.N., & Young, A.L. (2000). 'Evaluating community-based collaborative mechanisms: implications for practitioners'. Health Promotion Practice, 1(1), pp. 49-63. Society for Public Health Education, Sage Publications
- Kris-Etherton-, P.M., Etherton, T.D., Carlson, J. & Gardner, C. (2002). 'Recent discoveries in inclusive food-based approaches and dietary patterns for reduction in risk for cardiovascular disease'. Curr Opin Lipidol., 13(4), pp.397-407
- Krishnan, M.K. (2010). 'Biomedical nanomagnetism: a spin through possibilities in imaging, diagnostics and therapy'. IEEE Trans Magn., 46(7), pp. 2523-2558
- Kristensen, E., Nielsen, B.D., Jensen, N.L., Vaarst, M. & Enevoldsen, C. (2008). 'A mixed inquiry into the validity of data'. Acta Veterinaria Scandinavica, 50(30). doi:10.1186/1751-0147-50-30. BioMed Central (accessed 9/4/2009)
- Kumar, D. (2007). 'From evidence-based medicine to genomic medicine'. Genomic Medicine, 1(3-4), pp.95-104. Springer Science+Business Media B.V. 2007

- Kurd, K.S., Troxel, B.A., Crits-Cristoph, P., & Gelfand, M.J. (2010). 'The risk of depression, anxiety, and suicidality in patients with psoriasis'. Archives of Dermatology, 146(8), pp.891-895. The American Medical Association
- Kuriyama, S. (2002). The Expressiveness of the Body and the Divergence of Greek and Chinese Medicine. Zone Books
- Labaree, V.R. (2002). 'The risk of 'going observationalist': negotiating the hidden dilemmas of being an insider participant observer'. Qualitative Research, 2(1), pp. 97-122. SAGE Publications
- Lackie, J. M. & Dow J. A. (2002). Ερμηνευτικό Λεξικό Κυτταρικής & Μοριακής Βιολογίας. Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Lacy, B., Loew, B., & Crowell, M. (2009). 'Prucalopride for chronic constipation'. Drugs of Today (Barcelona, Spain:1998), 45(12), pp. 843-853
- Lakhan, E.S, & Kirchgessner, A. (2010). 'Gut inflammation in chronic fatigue syndrome'. Nutrition & Metabolism (Lond), 7, p.79
- Lamb J.J. (2005). 'Homeostasis: A dynamic balance'. Ch. 9, in Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Lamson, D.S. & Plaza, S.M. (2002). 'The safety and efficacy of high-dose chromium'. Alternative Medical Review, 7(3), pp.218-35. NCBI,US NLM
- Lane, R.D., Laukes, C., Marcus, F.I., Chesney, M.A., Sechrest, L., Gear, K., Fort, C.L., Priori, C.L., Schwartz, P.J., & Steptoe, A. (2005). 'Psychological stress preceding idiopathic ventricular fibrillation'. Pshychosomatic Medicine-Journal of Biobehavioural medicine, 67(3), pp.359-365. American Psychosomatic Society. NCBI,US NLM
- Langstroth, L. (1924). 'Disturbed metabolism as a background for disease'. California and Western Medicine, 22(9), pp. 453-456. NCBI,US NLM
- Langstroth, L. (1928). 'A new emphasis in medicine'. California and Western Medicine, 29(3), pp. 165-168. NCBI,US NLM
- Langstroth, L. (1935). 'The treatment of chronic arthritis by diet and sunlight'. California and Western Medicine, 42(3), pp. 145-149. NCBI,US NLM
- Lardos, A. (2006). 'The botanical material medica of the Iatrosophikon-a collection of prescriptions from a monastery in Cyprus'. Journal of Ethnopharmacology, 104(3), p.387. Elsevier Ireland Ltd.
- Lassi, S.Z., Haider, A.B., & Bhutta, A.Z. (2010). 'Zinc supplementation for the prevention of pneumonia in children aged 2 months to 59 months'. Cochrane Database of Systematic Reviews, Issue 12. Art. No.: CD005978. DOI: 10.1002/14651858.CD005978.pub2. The Cochrane Collaboration, John Wiley & Sons, Ltd.
- Lazarides, L. (2002). The Amino Acid Report. London: Waterfall 2000
- Lazarou, C., Panayiotakos, D.B., Panayiotou, G., & Matalas, A.L., (2008). 'Overweight and obesity in preadolescent children and their parents in Cyprus: prevalence and associated socio-demographic factors-the CYKIDSstudy.' Obesity Reviews: An official Journal of the International Association for the Study of Obesity, 9(3), pp.185-193
- Leader, G. & Leader, L. (2006). Parkinson's Disease – Reducing Symptoms with Nutrition Drugs. London: Denor Press Ltd
- Lee, D, (1997). Osteoporosis. USA: Woodland Publishing
- Lee, M.M., Chang, S.J., Jacobs, B., & Wrensch, R.M. (2002). 'Alternative medicine use among men with prostate cancer in 4 ethnic populations'. American Journal of Public Health, 92(10), pp. 1606-1609. Peer reviewed, Research and Practice.
- Leibovici, L., & Lievre, M. (2002). 'Medicalisation: peering from inside medicine'. Editorial in British Medical Journal, 324(7342), pp. 866. BMJ Publishing Group Ltd

- Leichsenring, K. (2004). 'Developing integrated health and social care services for older persons in Europe'. International Journal of Integrated Care, 4(e10)
- Lemieux, I., Poirier, P., Bergeron, J., Almeras, N., Lamarche, B., Cantin, B., Dagenais, G.R., & Despres J.P. (2007). 'Hypertriglyceridemic waist : a useful screening phenotype in preventive cardiology ?'. Canadian Journal of Cardiology, 25(3), pp140-149
- Lessel, B.C. (2001). The Complementary Formulary-A guide for prescribers. Reed Educational and Professional Publishing Ltd (a member of the Reed Elsevier plc group)
- Levin, B., Bland, J., & Schmidt, M. (2006). 'Functional Medicine in Natural Medicine'. Ch.2 in Pizzorno, E. J., & Murray, T.M., (eds). (2006) Textbook of Natural Medicine, Vol. 2, 3rd ed. Churchill Livingstone Elsevier.
- Levin, B., Bland, J., & Schmidt, M. (2011). 'Functional Medicine in Natural Medicine'. Chapter 2, in Pizzorno, Jr. & Murray, M. T. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc, available at www.naturalmedtext.com (accessed 12/2/ 2011)
- Levin, L. (2003). 'Ivan Illich'. Commentary in Journal of Epidemiology and Community Health, 57, pp.925
- Levinson, W., Gorawara-Bhat, R., Dueck, R., Egener, B., Kao, A., Kerr, C., Lo, B., Perry, D., Pollitz, K., Reifsteck, S., Stein, T., Santa, J., & Kemp-White, M. (1999). 'Resolving disagreements in the patient-physician relationship'. JAMA, 282(15), pp.1477-1483.
- Lewontin, R.C. (2000). The Triple Helix, pp.17-18. Boston, MA: Harvard College, quoted in Bland, J. S. (2002). Nutritional Endocrinology- Breakthrough Approaches for Improving Adrenal and Thyroid Function. WA: The Institute For Functional Medicine
- Ley, B. M. (1998). MSM: On Our Way Back To Health With Sulfur. USA: BL Publications'
- Libby, P., (2005). 'Clinical approaches to immune balance and inflammation'. Ch.27, in Jones, D. S. (Ed) (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Liberati, A., D'Amico, R., Pifferi, S., Torri, V., Brazzi, L., Gensini, G.F., & Gusinu, R. (2006). 'Antibiotic prophylaxis to prevent nosocomial infections in patients in intensive care units: evidence that struggle to convince practising clinicians'. Intern Emerg Med., 1(2), pp.160-162
- Lichtenstein, H.A., Yetley, A.E. & Lau, J. (2008). 'Application of systematic review methodology to the field of nutrition'. Journal of Nutrition, 138(12), pp.2297-2306. American Society for Nutrition.
- Ligeros. K. A. (1937). How Ancient Healing Governs Modern Therapeutics. London: G. P. Putnam's Sons
- Lima, K.C.N., Abbassi, F., Lamendola, C., & Reaven, M.G. (2009). 'Prevalence of insulin resistance and related risk factors for cardiovascular disease in patients with essential hypertension'. American Journal of Hypertension, 22(1), pp.106-111
- Lin, H.R. & Bauer-Wu, M.S. (2003). 'Psycho-spiritual well-being in patients with advanced cancer: an integrative review of literature'. Journal of Advanced Nursing, 44(1), pp. 69-80. Blackwell Publishing Ltd
- Linde, K., & Willich, N.S. (2003). 'How objective are systematic reviews? Differences between reviews on complementary medicine'. Journal of the Royal Society of Medicine, 96(1), pp.17-22. The Royal Society of Medicine. PubMed NCBI ,US NLM
- Linde, K., Ramirez, G., Mulrow, D.C., Pauls, A., Wedenhammer, W., & Melchart, D. (1996). 'St John's wort for depression-an overview and meta-analysis of randomised clinical trials'. British Medical Journal, 3 Aug 1996, 313, 253-258. BMJ Publishing Group Ltd

- Linz, J.A., Haas, F.P., Fallon, F.L., & Metz, J.R. (2005). 'Impact of concierge care on healthcare and clinical practice'. The Journal of the American Osteopathic Association, 105(11), pp.515-520
- Lipton, M.A., Mailman, R.B., & Nemeroff, C.B. (1979). 'Vitamins, megavitamin therapy and the nervous system.' Nutrition and the Brain, 3, p.183. Wurtman, R.J., Wurtman, J.J. (eds). Raven Press, New York, Quoted in McCarthy (1981)
- Liska D. (2005). 'Functional Medicine is science-based'. Ch.6, in Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Liska, D., Quinn, S., Lukaczer, D., Jones, S. D., & Lerman, H. R. (2004). Clinical nutrition – A Functional Approach, 2nd Edition, The Institute for Functional Medicine, USA.
- Lockwood, D.C. (1928). Discussion on Langstroth, L. (1928). 'A new emphasis in medicine'. California and Western Medicine, 29(3), pp. 165-168. NCBI,US NLM
- Looijer-van Langen M.A., & Dieleman, L.A., (2009). 'Prebiotics in chronic intestinal inflammation'. Inflammatory Bowel Disease, 15(3), pp.454-462
- Lopez, D.A., Mathers, D.C. Ezzati, M., Jamison, T.D., & Murray, J.L.C. (2006). Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data'. Lancet, 367, pp.1747-1757.
- Lovegrove, J.A. & Gitau, R. (2008). 'Nutrigenetics and CVD: what does the future hold?'.
- Lund, B.F. (1929). 'Allusions to medicine in classical literature'. Bulletin of the New York Academy of Medicine, 5(9), pp. 845-859. NCBI,US NLM
- Lyon, M., Bland, J., & Jones, S.D. (2005). 'Clinical approaches to detoxification and biotransformation'. Chapter 31 in Jones, D. S. (Ed). (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Lypourlis, D. (Ed). (2000). Ιπποκράτης-Ιατρική θεωρία και πράξη. Thessaloniki: Zitros
- Lypourlis, D. (Ed). (2001). Ιπποκράτης-Γυναικολογία-Μαιευτική. Thessaloniki: Zitros
- Ma, Z.H., Ma, Q.Y., Wang, L.C., Sha, H.C., Wu, S.L., & Zhang, M. (2005). 'Effect of resveratrol on peritoneal macrophages in rats with severe acute pancreatitis'. Inflammatory Res., 54(12), pp.522-527
- Macfarlane, P. S., Reid, R., & Callander R. (2000). Pathology Illustrated. (5th ed.). London: Churchill Livingstone (Harcourt Publishers Ltd)
- MacKinney, L. (1955). 'Tenth century Medicine'. In 'Symposium in the Tenth Century'. Medivalia et Humanistica, IX, pp.10-13. Quoted in Geanakoplos, D. (1966). Byzantine East & Latin West: Two Worlds in Middle Ages and Renaissance. Harper Torch Books.
- Maczurek, A., Hager, K., Kenklies, M., Sharman, M., Martins, R., Engel, J., Carlson, D.A., & Munch, G. (2008). 'Lipoic acid as an anti-inflammatory and neuroprotective treatment for Alzheimer's disease'. Adv Drug Deliv Rev., 60(13-14), pp.1463-1470
- Maes, M. & Twisk, N.M.F. (2010). 'Chronic fatigue syndrome: Harvey and Wessely's (bio)psychosocial model versus a bio(psychosocial) model based on inflammatory and oxidative and nitrosative stress pathways'. BMC Medicine, 8(35), pp.1-13
- Maes, M. (2009). "'Functional" or "psychosomatic" symptoms, e.g. a flu-like malaise, aches and pain and fatigue, are major features of major and in particular of melancholic depression'. Neuro Endocrinol Lett. 30(5), pp.564-73
- Maes, M. (2010). 'An intriguing and hitherto unexplained co-occurrence: depression and chronic fatigue syndrome are manifestations of shared inflammatory, oxidative and nitrosative (IO&NS) pathways'. Prog Neuropsychopharmacol Biol Psychiatry
- Maes, M., Mihaylova, I., Kubera, M., Uytterhoeven, M., Vrydags, N., & Bosmans, E. (2009). 'Lower plasma Coenzyme Q10 in depression: a marker for treatment resistance and

- chronic fatigue in depression and a risk factor to cardiovascular disorder in that illness'. Neuro Endocrinol Lett. 30(4), pp.462-9
- Magee, B. (2005). Η περιπέτεια της Φιλοσοφίας. Αθήνα: Εκδόσεις Σαββάλας
- Mahady, B.G. (2001). 'Global harmonisation of herbal health claims'. The Journal of Nutrition, 131, pp.1120S-1123S, , The American Society for Nutritional Sciences
- Mahan, K. L. & Escott-Stump S. (2008). Krause's Food & Nutrition Therapy. (12th ed.).USA: Saunders (Elsevier Inc.)
- Malebra, M., Gosondi, P., Radaeli, A., & Girolomoni, G. (2007). 'Psoriasis and risk of myocardial infarction'. The Journal of the American Medical Association,297(4), pp.361-362. The American Medical Association
- Mallinger, J. (1998). Τα Εσωτερικά Μυστικά των Πυθαγορείων. (Μετάφραση: Γράβιγγερ, Π.) Αθήνα: Ιδεοθέατρων & Δίμελη
- Maloy, S., & Schaechter, M. (2006). 'The era of microbiology: a golden phoenix'. International Microbiology, 9(1), pp. 1-7
- Manchikanti, L. (2008). 'Evidence-based medicine, systematic reviews, and guidelines in interventional pain management, part I: introduction and general considerations'. Pain Physician, 11(2), pp.161-186
- Manchikanti, L., Datta, S., Smith, S.H., & Hirsch, A.J. (2009). 'Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: part 6. Systematic reviews and meta-analyses of observational studies'. Pain Physician, 12(5), pp.819-850. The American Society of Interventional Pain Physicians
- Mancuso, C., Scapagini, G., Curro, D., Giuffrida, S.A.M. De Marco, C., Butterfield, D.A. & Calabrese, V. (2007). 'Mitochondrial dysfunction, free radical generation and cellular stress response in neurodegenerative disorders'. Fron Biosci. 12, pp.1107-1123
- Mandel, S., Amit, T., Reznichenko, L., Weinreb, O., & Youdim, M.B. (2006). 'Green tea catechins as brain-permeable, natural iron chelators-antioxidants for the treatment of neurodegenerative disorders'. Mol Nutr Food Res, 50(2), pp.229-234
- Mandel, S., Maor, G., & Youdim, M.B. (2004). 'Iron and α -synuclein in the substantia nigra of MPTP-treated mice: effect of neuroprotective drugs R-apomorphine and green tea polyphenol (-)-epigallocatechin-3-gallate'. Journal of Molecular Neuroscience, 24(3), pp.401-416
- Manini, M.L, Camilleri, M., Goldberg, M., Sweetser, S., McKinzie, S., Burton, D., Wong, S., Kitt, M.M., Li, Y.P., and Zinsmeister, A.R. (2009). 'Effects of Velusetrag (TD-5108) on gastrointestinal transit and bowel function in health and pharmacokinetics in health and constipation'. Neurogastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society, 22(1), p. 42
- Mann, D., Gaylord, S., & Norton, S. (2004). 'Moving toward integrative care: Rationales, models, and steps for conventional-care providers'. Complementary Health Practice Review, 9(3), pp. 155-172. Sage Publications
- Mann, J. & Truswell, S. (2002). Essentials of Human Nutrition. (2nd ed.). Oxford University Press Inc.
- Mannian, A. F. (1999). 'Whither continuity of care?' The New England Journal of Medicine, 340, pp.1362-1363. Massachusetts Medical Society
- Mapother, E. (1934). 'Tough or tender. A plea for nominalism in psychiatry'. Proceedings of the Royal Society of Medicine, Section of Psychiatry 27(12), pp. 1687-1712
- Martin, E. (1998). Concise Medical Dictionary. (5th ed.). Oxford University Press
- Martin, E. & Hine, R. (2000). A Dictionary of Biology. (4th ed.). Oxford University Press.

- Martinez-Gonzalez, A.M., Bes-Rastrollo M., Serra-Majem L., Lairon D., Estruch, R., & Trichopoulou, A. (2009). 'Mediterranean food pattern and the primary prevention of chronic disease: recent developments'. Nutrition Reviews, 67(1), pp.S111-S116. International Life Sciences Institute
- Martyn, Ch. (2004). 'What price better health? Hazards of the research imperative'. Review of Daniel Callahan's book in British Medical Journal, 328(7448), p.1140. BMJ Publishing Group Ltd
- Mathers, D.C., & Loncar D. (2006). Updated projections of global mortality and burden of disease, 2002-2030: data sources, methods and results. World Health Organisation
- Maxwell, A.J. (2004). 'Reemergent scientism, postmodernism, and dialogue across differences'. Qualitative Inquiry, 10(1), pp. 35-41. Sage Publications
- Mayou, R., & Farmer, A., (2002). 'ABC of psychological medicine: functional somatic symptoms and syndromes'. British Medical Journal, (Clinical Research Ed.), 325(7358), pp. 265-268. BMJ Publishing Group Ltd
- Mbambiniotis, G. (2002). Λεξικό της Νέας Ελληνικής Γλώσσας. (2nd ed.). Athens: Kentro Lexicologias E.Π.Ε.
- Mbitsakis, E. (1978). Translated and Revised Einstein A. & Infeld L., (1938) Η εξέλιξη των ιδεών στην Φυσική. Athens: Dodoni
- McArthur, W.T. (1927). 'The evolution of organised medicine'. California and Western Medicine, 26(5), pp.625-628 . NCBI,US NLM
- Food Standards Agency. (2002). McCance and Widdowson's The Composition of Foods, Sixty summary edition. Cambridge: Royal Society of Chemistry
- McCann, C.J., & Ames, N.B. (2009). 'Vitamin K, and example of triage theory: is micronutrient inadequacy linked to diseases of aging?' American Journal of Clinical Nutrition, 90(4), pp.889-907. The American Society for Nutrition
- McCarty, M.F. (1980). 'The therapeutic potential of glucose tolerance factor'. Med Hypoth, 6. Quoted in McCarty (1981)
- McCarty, M.F. (1981). 'Point of view-a role for "nutritional insurance" supplementation in preventive medicine'. Medical hypotheses, 7(2), pp.171-185. Eden press.
- McCarty, M.F. (2000). 'Toward a wholly nutritional therapy for type 2 diabetes'. Medical Hypotheses, 54(3), pp. 483-7. Harcourt publishers
- McCarty, M.F. (2000i). 'Toward practical prevention of type 2 diabetes'. Medical Hypotheses, 54(5), pp. 786-93. Harcourt publishers
- McClave, S.A., Mechanick, I.J., Bistran, B., Graham, T., Hegazi, R., Lensen, L.G. Kusher, F. R. & Merritt, R. (2010). 'What is the significance of a physician shortage in Nutrition Medicine?' JPEN Journal of Parenteral and Enteral Nutrition, 34(6 suppl), pp.7S-20S
- McGraw-Hill Concise Dictionary of Modern Medicine. (2002). The McGraw-Hill Companies, Inc.
- Mciness, A., & Lawson-Brown, V. (2007). ' "God" and other "Do-gooders"- A comparison of the regulation of services provided by general practitioners and social workers in England'. Journal of Social Work, 7(3), pp.341-354, Sage Publications
- McKay, D., Perrone, G., Rasmussen, H., Dallas, G., Hartman, W., Cao, G., Prior, R., Roubenoff, R., & Blumberg, J. (2000). 'The effects of a multivitamin/mineral supplement on micronutrient status, antioxidant capacity and cytokine production in healthy older adults consuming a fortified diet'. Journal of the American College of Nutrition, 19(5), pp. 613-621
- McKenna, D.J., Jones, K., & Hughes, K. (2001). 'Efficacy, safety and use of ginkgo biloba in clinical and preclinical applications'. Altern Ther Health Med. 7(5), pp. 88-90

- McNeill G.,(2000). 'Energy intake and expenditure'. (ch3). in Garrow J.S., James W.P.T. & Ralph, A., (eds) (2000). Human Nutrition and Dietetics. (10th ed.) Churchill Livingstone
- McNeill, P. (Ed) (1990). Research Methods. (2nd ed.). London: by Routledge
- McNiff, J., Lomax, P., & Whitehead, J. (2003). You and your Action Research Project. (2nd ed.). London: RoutledgeFalmer (Taylor & Francis Group)
- Mears, J.B. (2010). 'Ethics for the paediatrician-the ethics of complementary and alternative medicine'. Pediatrics in Review, 31, pp.e49-351. American Academy of Pediatrics.
- Mechanic, D. (1996). 'Changing medical organisation and the erosion of trust'. Milbank Q., 74(2), pp.171-89
- Mechanic, D., McAlpine, D.D., & Rosenthal, M. (2001). 'Are patients' office visits with physicians getting shorter?'. The New England Journal of Medicine, 344(3), pp.198-204. Massachusetts Medical Society
- Mehta, N.N., Azfar, S.R., Shin, B.D., Neimann, L.A., Troxel, B.A., & Gelfand, M.J. (2010). 'Patients with severe psoriasis are at increased risk of cardiovascular mortality: cohort study using the General Practice Research Database'. European Heart Journal, 31(8), pp.1000-1006. Oxford Journals
- Meir, A. & Rubinsky, B. (2009). 'Distributed network, wireless and cloud computing enabled 3-D ultrasound; a new medical technology paradigm'. PLOS One, 4(11): e7974
- Meland, O.N. (1927). 'Physical therapy: the trend in modern medicine'. California and Western Medicine, 27(6), pp. 815-816. NCBI, US NLM
- Melnick, I., Landes, R.R., Hoffman, A.A., & Burch, J.F. (1971). 'Magnesium therapy of recurrent calcium oxalate urinary calculi'. J Urol, 105, p.119. (Quoted in McCarthy 1981)
- Menninger, A.K. (1938). 'Emotional factors in hypertension'. Bull N Y Acad Med, 14(4), pp.198-211. NCBI, US NLM
- Meplan, C., Crosley, K.L., Nicol, F., Beckett, J.G., Howie, F.A., Hill, E.K., Horgan, G., Mathers, C.J., Arthur, R.J., & Hesketh, E.J. (2007). 'Genetic polymorphisms in the human selenoprotein P gene determine the response of selenoprotein markers to selenium supplementation in a gender-specific manner (the SELGEN study). The FASEB Journal, 21, pp.3063-3074. FASEB
- Meryn, S. (1998). 'Improving doctor-patient communication-not an option, but a necessity'. British Medical Journal, 316, p.1922. BMJ Publishing Group Ltd
- Mestdagh, F., Lachat, C., Baert, K., Moons, E., Kolsteren, P., Van Peteghem, C., & De Meulenaer, B. (2007). 'Importance of a canteen lunch on the dietary intake of acrylamide'. Nol Nutr Food Res. 51(5), pp.509-516
- Mettlin, C., & Graham, S. (1979). 'Dietary risk factors in human bladder cancer'. American Journal of Epidemiology, 110, p. 255. Quoted in McCarthy 1981
- Mettlin, C., Graham, S., & Swanson, M. (1979). 'Vitamin A and lung cancer'. J Nat Ca Inst, 62, p.1435. Quoted in McCarthy 1981
- Meydani, M. (2001). 'Nutrition interventions in aging and age-associated disease'. Ann N Y Acad Sci, 928, pp.226-236. NCBI, US NLM
- Meyer, F.K. (1928). 'Research in medicine on the pacific coast during 1927-1928'. California and Western Medicine, 29(3), pp. 145-152. NCBI, US NLM
- Michaud, D.S., Spiegelman, D., Clinton, S.K., Rimm, E.B., Willet, W.C., & Giovannucci, E. (2000). 'Prospective study of dietary supplements, micronutrients, and risk of bladder cancer in US men'. American Journal of Epidemiology, 152(12), pp. 1145-53. NCBI, US NLM

- Micozzi, M. S. (2001). Fundamentals of Complementary and Alternative Medicine. (2nd ed.). USA: Churchill Livingstone
- Middleton, N., Yiallourous, P., Kleanthous, S., Kolokotroni, O., Schwartz, J., Dockery W.D., Demokritou, P., & Koutrakis, P. (2008). 'A 10-year time-series analysis of respiratory and cardiovascular morbidity in Nicosia, Cyprus: the effect of short-term changes in air pollution and dust storms'. *Environmental Health* 2008, 7(39), available at <http://www.ehjournal.net/content/7/1/39> (accessed 7/6/ 2009)
- Miggiano, G.A. & De Sanctis, R. (2006). 'Nutritional genomics: toward a personalized diet'. Clin Ter., 157(4), pp.355-361
- Miller, J.M., Kinnally, E.L., Ogden, R.T., Oquendo, M.A., Mann, J.J., & Parsey, R.V. (2009). 'Reported childhood abuse is associated with low serotonin transporter binding in vivo in major depressive disorder'. Synapse, 63(7), pp. 565-573
- Milner, J.A. (2006). 'Diet and cancer: facts and controversies'. Nutr Cancer, 56(2), pp.216-224
- Mitchell, A. & Cormack, M. (1998). The Therapeutic Relationship in Complementary Health Care. London: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Mizutani, Y. & Seishima, M. (2009). 'Autoerythrocyte sensitization syndrome with vertigo and hemilateral auditory impairment'. Clinical and Experimental Dermatology, 34(5), pp. e134-136
- Mocchegiani E., & Malavolta, M. (2007). 'Zinc homeostasis, ageing and neurodegeneration: implications of A2M and inflammatory gen polymorphisms'. Journal of Alzheimer's Disease, 12(1), pp.101-109
- Mocchegiani, E., Bertoni-Freddari, C., Marcellini, F., & Malavolta, M. (2005). 'Brain, aging and neurodegeneration: role of zinc ion availability'. Prog Neurobiol 75(6), pp.367-390
- Mogg, K., Bradley, P.B., Hyare, H. & Lee, S. (1998). Selective attention to food-related stimuli in hunger: are attentional biases specific to emotional and psychopathological states, or are they also found in normal drive states?. Behaviour Research and Therapy, 36(2), pp.227-237. Elsevier Science Ltd
- MOH (2008). Annual Report 2007. Nicosia: Cyprus Ministry of Health
- MOH (2011i). 'Non-communicable diseases'. Health Promotion and Disease Prevention. Website of the Republic of Cyprus, Ministry of Health, available at <http://www.moh.gov.cy/MOH/moh.nsf/All/03536A3966C53E1EC2256D4900401810?OpenDocument> (accessed 14/3/ 2011)
- MOH (2011ii). 'Cardiovascular disease'. Health Promotion and Disease Prevention. Website of the Republic of Cyprus, Ministry of Health, <http://www.moh.gov.cy/MOH/moh.nsf/All/3406AADB69CEBA71C2256E220039CB92?OpenDocument> (accessed 14/3/ 2011)
- MOH (2011iii). 'Diabetes'. Health Promotion and Disease Prevention. Website of the Republic of Cyprus, Ministry of Health, available at <http://www.moh.gov.cy/MOH/moh.nsf/All/E4A7F1DDF1AB6C37C2256E22003ACF77?OpenDocument> (accessed 14/3/ 2011)
- MOH (2011iv). 'Νομοσχέδιο με τίτλο 'Ο περί Εγγραφής Επιστημόνων Τροφίμων και Διαιτολόγων (Τροποποιητικός) Νόμος του 2010'. Ministry of Health
- Mohteshamzadeh, M., Wilkinson, R., & Thomas, H.L.S. (2005). 'Insulin resistance in men with treated hypertension at increased risk for cardiovascular disease: results of a 3-year study'. American Journal of Hypertension, 18, pp.452-456. Nature publishing group

- Mojska, H., Gielecinska, I., Szponar, L., & attarzewski, M. (2010). 'estimation of the dietary acrylamide exposure of the Polish population'. Food Chem Toxicol. 48(8-9), pp.2090-2096. Elsevier Ltd
- Molloy, A.M., & Scott, J.M. (2001). 'Folates and prevention of disease'. Public Health Nutrition, 4(2B), pp. 601-9
- Moon, R.O. (1923). 'The post Hippocratic schools of medicine'. The British Medical Journal. 1(3240), pp.187-189. BMJ Publishing Group Ltd
- Moore, R. D. (2001). The High Blood Pressure Solution. (2nd ed.). USA: Healing Arts Press (Inner Traditional International)
- Morgagni, G.B. (1903). 'Founders of modern medicine: Giovanni Battista Morgagni. (1682-1771)'. Medical Library and Historical Journal, 1(4), pp. 270-277
- Morrison, I. (2000). 'The future of physician's time'. Annals of Internal Medicine, 132(1), pp.80-84.
- Mosby's (2005). Dictionary of Complementary and Alternative Medicine. Elsevier
- Mosby's Medical Dictionary. (2009). 8th edition. Elsevier
- Mosby's Medical, Nursing and Allied Health Dictionary. (2002). (6th ed.). UK: Mosby Inc. (A Harcourt Health Sciences Company)
- Moss, G.A. (2000). 'Historical perspectives on health-Medicine 2000 years ago: the case of Qumran and other biblical sites'. The Journal of The Royal Society for the Promotion of Health, 120(4), pp.255-261
- Mount, J. L. (1979). The food and Health of Western Man. Precision Press
- Moynihan, R. (2010). 'Rosiglitazone, marketing, and medical science'. British Medical Journal, 340(c1848). BMJ Publishing Group Ltd
- Moynihan, R. & Smith, R. (2002). 'Too much medicine? Almost certainly.' British Medical Journal, 324(7342) pp.859-860. BMJ Publishing Group Ltd
- Moynihan, R., Heath, I., & Henry, D. (2002). 'Selling sickness: the pharmaceutical industry and disease mongering'. Education and Debate in British Medical Journal, 324(7342), pp.886-891. BMJ Publishing Group Ltd
- Mozaffarian, D., & Stampfer, J. (2010). 'Removing industrial trans fats from foods'. British Medical Journal, 340, p.c1826. BMJ Publishing Group Ltd
- Muecke, R., Schomburg, L., Buentzel, J., Kisters, K., Micke, O., et al., (2010). 'Selenium or no selenium-that is the question in tumor patients: a new controversy'. Integrative Cancer Therapies, 9(2), pp.136-141. Sage Journals
- Muhtz, C., Zyriax, B.C., Klann, T., Windler, E., & Otte, C. (2009). 'Depressive symptoms and metabolic risk: effects of cortisol and gender'. Psychoneuroendocrinology, 34(7), pp. 1004-1011
- Murray, M. (2002). The Pill Book Guide to Natural Medicines. UK: Bantam Books
- Murray, M. T. (1994i). Diabetes & Hypoglycemia. Three Rivers Press (Random House, Inc.)
- Murray, M. T. (1994ii). Natural Alternatives to Over-the-Counter and Prescription Drugs. Quill William Morrow
- Murray, M. T. (1996). Encyclopedia of Nutritional Supplements: The Essential Guide for Improving Your Health Naturally. USA: Prima Health (A Division of Prima Publishing)
- Murray, M. T. & Lyon, M. R. (2003). How to Prevent and Treat Diabetes with Natural Medicine. Riverhead Books (The Berkley Publishing Group)
- Murray, M., Pizzorno, J., & Pizzorno, L. (2005i). The Encyclopedia of Healing Food. New York: Atria Books

- Murray, M.T. & Pizzorno, Jr. (2011). 'Maldigestion'. Chapter 59 in Pizzorno, Jr. & Murray, M. T. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc, available at www.naturalmedtext.com (accessed 12 /2/ 2011)
- Murray, M.T. & Pizzorno, J. (2011i). 'Immune support'. Chapter 57 in Pizzorno, Jr. & Murray, M. T. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.) Elsevier Inc, available at www.naturalmedtext.com (accessed 10 /1/ 2011)
- Murray M.T. & Pizzorno, E.J. (2011ii). 'Nutritional Medicine'. Chapter 44, in in Pizzorno, Jr. & Murray, M. T. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition). Elsevier Inc, available at www.naturalmedtext.com (accessed 20 /3/ 2011)
- Murray, W.M. (1867). 'The physical and physiological action of medicines'. Journal of Anatomy and Physiology, 1(2), pp. 319-322 . NCBI, US NLM
- Murray. M., Birdsall, T., Pizzorno, J., & Reilly, P. (2005ii). Καρκίνος Πρόληψη-Θεραπεία με Φυσικά Μέσα. Αθήνα: Εκδόσεις ΔΙΟΠΤΡΑ
- Musnick, D. (2005). 'Clinical approaches to structural imbalance'. in Jones, D. S. (Ed). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Muttucumaru, N., Halford, N.G., Elmore, J.S., Dodson, A.T., Parry, M., Sewry, P.R., & Mottram, D.S. (2006). 'Formation of high levels of acrylamide during the processing of flour derived from sulphat-deprived wheat'. J Agric Food Chem., 54(23), pp. 8951-8955
- Nagase, Y. Uchiyama, M., Kaneita, Y., Li, L., Kaji, T., Takahashi, S., Konno, M., Mishima, K., Nishikawa, T., & Ohida, T. (2009). 'Coping strategies and their correlates with depression in the Japanese general population'. Psychiatry Research, 168(1), pp. 57-66
- Nahleh, Z., & Tabbara, A.I. (2003). 'Complementary and alternative medicine in breast cancer patients'. Palliative and Supportive Care, 1, pp. 267-273. Cambridge University Press
- Natural Medicines Comprehensive Database. (1995-2011). Therapeutic Research Faculty available at <http://www.naturaldatabase.com> accessed on a daily basis in the last 4 years
- Naurath, H.J., Joosten, E., Riezler, R., Stabler, S.P. Allen, R.H., & Lindenbaum, J. (1995). 'Effects of vitamin B12, folate and vitamin B6 supplements in elderly people with normal serum vitamin concentrations'. Lancet, 346(8697), pp.85-9. NCBI, US NLM
- NCA. (2011). 'Nutritional Therapy prospectus'. Northern College of Acupuncture. Available at http://www.chinese-medicine.co.uk/downloads/nutritional_prospectus_2011_12.pdf accessed 10 /3/ 2011
- Neiner, A. J., Howze, H.E., & Greaney, L.M. (2004). 'Using scenario planning in public health: anticipating alternative futures'. Health Promot Pract, 2004, 5(1), pp. 69-79. Society for Public Health Education, Sage Publications .
- Newell-McGloughlin, M., (2008). 'Nutritional improved agricultural crops'. Plant Physiology, 147, pp.939-953. The American Society of Plant Biologists
- Ng, M.L., & Hargreaves, J.A. (1984). 'Status of nutrition education in Canadian dental and medical schools'. Canadian Medical Association Journal, 130(7), pp.851-853,
- Nguyen, T.X., Lane, J., Smith, R.B., & Nguyen, T.N. (2009). 'Changes in inflammatory biomarkers across weight classes in a representative US population: a link between obesity and inflammation'. Journal of Gastrointestinal Surgery, 13(7), pp.1205-1212
- NHS. (2011). 'Dietary and Nutritional Therapies'. NHS Evidence-complementary and alternative medicine. Available at <http://www.library.nhs.uk/CAM/ViewResource.aspx?resID=333780&tabID=288&catID=10839#Definition> (accessed 15/3/2011).

- NHS. (2011i). 'Introduction to Dietary and Nutritional Therapies'. NHS Evidence- Complementary and Alternative Medicine, available at <http://www.library.nhs.uk/cam/ViewResource.aspx?resID=333780&tabID=290> (accessed 15 /3/ 2011)
- Nicholson J. (2011). 'The human microbiome and its impact on gene expression'. Presentation at the BANT AGM Conference, Feb 5, 2011, The Brewery, Chiswell str. London EC1Y 4SD
- NIH et al., (2004) (National Institutes of Health, Office of Dietary Supplements and National Heart, Lung, and Blood Institute). Working group report on future clinical research directions on omega-3 fatty acids and cardiovascular disease. U.S. Department of Health and Human Services
- Nikolakakis, K., Skowronski, E.M, Coreno, J.A., West, E., Nader, Z.N., Smith, L.R., & McFadden, R.E. (2008). 'Observations on the physiological interaction between obesity and asthma'. Journal of Applied Physiology, 105(5), pp.1533-1542
- NLM (National Library of Medicine Online) (2010). 'Andreas Vesalius's De Humani Corporis Fabrica'. In Turning the Pages Online. United States: National Institutes of Health, available at <http://archive.nlm.nih.gov/proj/ttp/books.htm> (accessed 12 /2/ 2011)
- Nottingham, C. & Dougall, R. (2007). 'A close and practical association with the medical profession: Scottish medical social workers and social medicine, 1940-1975'. Medical History, 51(3), pp.309-336
- Nowak, T. J. & Handford, G. A. (2004). Pathophysiology: Concepts and Applications for Health Care Professionals. (3rd ed.). McGraw-Hill New York
- Noyes, D.H. (1865). 'Specialties in medicine'. Transactions of the American Ophthalmological Society, 1(2), pp.57-74 . NCBI, US NLM
- Obeid, R., McCaddon, A., & Herrmann, W. (2007). 'The role of hyperhomocysteinemia and B-vitamin deficiency in neurological and psychiatric diseases'. Clinical Chemistry and Laboratory Medicine, 45(12), pp.1590-1606. Walter de Gruyter
- OECD (2010). Health at a Glance: Europe 2010. OECD Publishing.
- Ong, C.K., Bodeker, G., Grundy, C., Burford, G., & Shein, K. (2005). WHO global atlas of traditional, complementary, and alternative medicine. The WHO Centre for Health Development, World Health Organisation
- Ordovas, J.M. & Mooser, V. (2004). 'Nutrigenomics and nutrigenetics'. Curr Opin Lipidol., 15(2), pp.101-108
- Orthoefer, F. (1998). Lecithin and Health. USA: Vital Health Publishing
- Ostbye, T., Yarnall, S.H.K., Krause, M.K., Pollak, I.K., Gradison, M., & Michener, J.L. (2005). 'Is there time for management of patients with chronic diseases in primary care?'. Annals of Family Medicine, 3(3), pp. 209-214
- Owen, M.J., (2007). 'Focusing Evaluative Inquiry: evaluation forms and approaches'. Programme Evaluation: Forms and Approaches, 3rd edition, Guilford Publications
- Pagana, K. D. & Pagana T. J. (2002). Mosby's- Manual of Diagnostic and Laboratory Tests. (2nd ed.). USA: Mosby
- Paice, E., Heard, S., & Moss, F. (2002). 'How important are role models in making good doctors?' British Medical Journal, 325, pp.707-710. BMJ Publishing Group Ltd
- Pan, A., Yu, D., Demark-Wahnefried, W., Franco, H.O., & Lin, X. (2009). 'Meta-analysis of the effects of flaxseed interventions on blood lipids'. The American Journal of Clinical Nutrition, 90(2), pp. 288-297. American Society for Nutrition.

- Panayiotakos, D.B., Lionis, C., Zeimbekis, A., Gelastopoulou, K. Papairakleous, N., Das, U.N., & Polychronopoulos, E. (2009). 'Long-term tea intake is associated with reduced prevalence of type 2 diabetes mellitus among elderly people from Mediterranean islands: MEDIS epidemiological study.' Yonsei Medical Journal 50(1), pp.31-38
- Panayiotakos, D.B., Lionis, C., Zeimbekis, A., Makri, K. Bountziouka, V., Economou, M., Vlachou, I., Micheli, M., Tsakountakis, N., Metallinos, G., & Polychronopoulos, E. (2007i). 'Long-term, moderate coffee consumption is associated with lower prevalence of diabetes mellitus among elderly non-tea drinkers from the Mediterranean islands (MEDIS study).' The Review of Diabetic Studies, 4(2), pp.105-112
- Panayiotakos, D.B., Polystiopi, A., & Polychronopoulos, E. (2007ii). 'Prevalence of type 2 diabetes and physical activity status in elderly men and women from Cyprus (the MEDIS study). Asia-Pacific Journal of Public Health / Asia-Pacific Academic Consortium for Public Health, 19(3), pp.22-28
- Panayiotakos, D.B., Zeimbekis, A., Boutziouka, V., Economou, M., Kourlaba, G., Toutouzas, P., & Polychronopoulos, E., (2007). 'Long-term fish intake is associated with better lipid profile, arterial blood pressure, and blood glucose levels in elderly people from Mediterranean islands (MEDIS epidemiological study)'. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research 13(7), pp.307-12
- Papadimitriou, D.J., Skiadas, P., Mavrantonis, S.C., Polimeropoulos, V., Papadimitriou, J.D., & Papacostas, J.K. (2007). 'Euthanasia and suicide in antiquity: viewpoint of the dramatists and philosophers'. Journal of the Royal Society of Medicine, 100(1), pp.25-28
- Papanastasiou, K. & Papanastasiou, E. (2005). Μεθοδολογία Εκπαιδευτικής Έρευνας. Nicosia: Papanastasiou & Papanastasiou
- Papathanasopoulos, A., & Camilleri M. (2010). 'Dietary fiber supplements: effects in obesity and metabolic syndrome and relationship to gastrointestinal functions'. Gastroenterology, 138(1), pp.65-72 e1-2
- Parkes, G.C., Brostoff, J., Whelan, K., & Sanderson, J.D. (2008). 'Gastrointestinal microbiota in irritable bowel syndrome: their role in its pathogenesis and treatment'. Am J Gastroenterol., 103(6), pp. 1557-1567
- Parsons, J.K., Samma, A.V., Mcvary, K., & Wei, J.T. (2009). 'Obesity and benign prostatic hyperplasia: clinical connections, emerging etiological paradigms and future directions'. Journal of Urology, 182(6Suppl), pp.S27-31
- Pasamanick, B. (1957). 'Future explorations in mental health and disease'. Am J Public Health Nations Health. 47(10), pp. 1242-1249 . NCBI, US NLM
- Patil, R. & Giordano, J. (2010). 'On the ontological assumptions of the medical model of psychiatry: philosophical considerations and pragmatic tasks'. Philosophy, Ethics, and Humanities in Medicine, 5(3)
- Patterson, C., Arthur, H., Noesgaard, C., Caldwell, P., Vohra, J., Francoeur, C., & Swinton M. (2008). 'Exploring adolescent complementary/alternative medicine (CAM) use in Canada'. Journal of Interprofessional Care, 22(1), pp.45-55. Informa Healthcare
- Payne, E.M., Anderson, J.B. & Steffens, C.D. (2008). 'Calcium and vitamin D intakes may be positively associated with brain lesions in depressed and non-depressed elders'. Nutr. Res. 28(5), pp.285-292. PubMed Central NCBI, US NLM
- Peart, H.F. (1938). 'Legal right of a corporation to practice medicine'. California and Western Medicine, 49(6), p. 497 . NCBI, US NLM
- Peck, A. L. (1942). Translation and Comments on Aristotle-Generation of animals. London: Harvard University Press (Loeb Classical Library)

- Peck, A. L. (1961). Translation and Comments on Aristotle-Parts of Animals. (3rd ed.). London: Harvard University Press (Loeb Classical Library)
- Peck, A. L. (1965). Translation and Comments on Aristotle-History of animals- Books I-III. London: Harvard University Press (Loeb Classical Library)
- Peck, A. L. (1970). Translation and Comments on Aristotle-History of animals -Books IV-VI. London: Harvard University Press (Loeb Classical Library)
- Pedziwiatr, J.M. (1999). 'Role of history and philosophy of medicine in the professional formation of a physician: writings of Polish school of philosophy of medicine'. Croatian Medical Journal, 40(1), pp. 14-19
- Pelto, H.G., & Freake, C.H. (2003). 'Social research in an integrated science of nutrition: future directions'. The Journal of Nutrition, 133(4), pp.1231-1234. The American Society for Nutritional Sciences.
- Pelton, R. & LaValle, J. B. (2000). The Nutritional Cost of Prescription Drugs. USA: Morton Publishing Company
- Peng, J., Mao, O.X., Stevenson, F.F., Hsu, M., & Andersen, K.J. (2004). 'The herbicide paraquat induces dopaminergic nigral apoptosis through sustained activation of the JNK pathway'. The Journal of Biological Chemistry, 279, pp.32626-32632.
- Pentzopoulou-Valala, T. & Petrou, A.A. (2001). 'Ιάμβλιχος- Περί του Πυθαγορικού βίου. Θεσσαλονίκη: Εκδόσεις Ζήτρος
- Percy-Smith, B. (2007). 'You think you know?...You have no idea': youth participation in health policy development'. The Author, 22(6), pp.879-894. Oxford University Press.
- Perlmutter, D. (2000). BrainRecovery.com – Powerful Therapy for Challenging Brain Disorders. USA: The Perlmutter Health Center
- Pert, C. B. (1999). Molecules of Emotion-Why you feel the way you feel. (2nd ed.). UK: Pocket Books (An imprint of Simon & Schuster UK Ltd)
- Understanding the Placebo Effect in Complementary Medicine. UK: Churchill Livingstone (Harcourt Publishers Limited)
- Pfeiffer, C. C. (1975). Mental and Elemental Nutrients. USA: Keats Publishing Inc.
- Pfeiffer, C. C. (1987). Nutrition and Mental Illness- an Orthomolecular Approach to Balancing Body Chemistry. USA: Healing Arts Press (A division of Inner Traditions International)
- Pfeiffer, C.C. (1972). 'On mechanisms of nullification of CNS effects of l-dopa by pyridoxine in Parkinsonian patients.' J Neurochem, 19, p.2175. Quoted in McCarthy (1981)
- Pimlott, N. (2009). 'Pride and prejudice'. Can Fam Physician, 54(11), p1507. The College of Family Physicians of Canada
- Pittler, H.M., & Ernst, E. (1998). 'Horsechestnut seed extract for chronic venous insufficiency'. A criteria based systematic review. Archives of Dermatology, Nov 1998, 134(11), pp.1356-1360.
- Pizzorno, J. & Murray, M. (Eds). (1999). Textbook of Natural Medicine, Volumes I and II (2nd ed.). USA: Churchill Livingstone, Elsevier.
- Pizzorno E. J., & Michael T. M. (eds), (2006), Textbook of Natural Medicine, Volumes 1 and 2, 3rd edition, Churchill Livingstone Elsevier.
- Pizzorno, J. & Murray, M. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc. available at <http://www.naturalmedtext.com/content/default.cfm> accessed on a daily basis
- Pizzorno, J. E. Murray, T.M., & Joiner-Bey, H. (2002). The Clinician's Handbook of Natural Medicine. London: Churchill Livingstone (Harcourt Publishers Ltd)

- Pizzorno, M.A. (2005). The Encyclopedia of Healing Foods. Atria Books.
- Plaskett L., (2004). 'Course in Nutrition-Folders 1-15'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004i). 'Folder One-The Wholistic Model of Healthcare'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004ii). 'Folder Two-Minerals at work in Nutrition-Part I'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004iii). 'Folder Three-The Bulk Nutrients'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004iv). 'Folder Four-Food and Food Classes'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004v). 'Folder Five-Minerals at Work in Nutrition, Part II'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004vi). 'Folder Six-The Vitamins'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004vii). 'Folder Seven-Bowel Flora and the Maintenance of Health'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004viii). 'Folder Eight-Diagnosis'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004ix). 'Folder Nine-Treatment'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004x). 'Folder Ten-Gerson Therapy'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004xi). 'Folder Eleven-Herbs and Special Nutrients'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004xii). 'Folder Twelve-The Pathology and Treatment of Named Medical Conditions-Part One'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004xiii). 'Folder Thirteen-The Pathology and Treatment of Named Medical Conditions-Part Two'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004xiv). 'Folder Fourteen-Preclinical Studies and Therapeutic Relationships'. Thames Valley University Course Texts, Thames Valley University UK
- Plaskett L., (2004xv). 'Folder Fifteen-Cancer'. Thames Valley University Course Texts, Thames Valley University UK
- Polychronopoulos, E., Zeimbekis, A., Kastorini, C., Papairakleous, N., Vlachou, I., Bountziouka, V., & Panayiotakos, D.B. (2008). 'Effects of black and green tea consumption on blood glucose levels in non-obese elderly men and women from Mediterranean islands (MEDIS epidemiological study)'. European Journal of Nutrition. 47(1), pp.10-16
- Popkin, M.B. (2009). 'What can public health nutritionists do to curb the epidemic of nutrition-related noncommunicable disease?'. Nutrition Reviews, 67(1), pp. S79-S82. International Life Sciences Institute
- Potter, P. (1988i). Translation and Comments on Hippocrates-Volume V. London: Harvard University Press & W. Heinemann Ltd (Loeb Classical Library)
- Potter, P. (1988ii). Translation and Comments on Hippocrates-Volume VI. London: Harvard University Press & W. Heinemann Ltd (Loeb Classical Library)

- Pratter, R.M. Brightling, E., Boulet, L.P. & Irwin, S.R. (2006). 'An empiric integrative approach to the management of cough'. Chest, 129 (1Suppl), pp.222S-231S. The American College of Chest Physicians
- Prescott, C.A., Kuhn, J.W., & Pedersen, N.L., (2007). 'Twin Pair Resemblance for Psychiatric Hospitalisation in the Swedish Twin Registry: a 32-year Follow-up Study of 29,602 twin Pairs'. Behav Genet. (Epub ahead of printing) Published on www.pubmed.gov (Accessed 9/5/07)
- Price, A.P., Faus, A.S., & Williamson, K.M. (1998). 'Warfarin causes rapid calcification of the elastic lamellae in rat arteries and heart valves'. Arteriosclerosis, Thrombosis, and Vascular Biology, 18, pp.1400-1407. The American Heart Association
- Price, W. A. (2004). Nutrition and Physical Degeneration. (6th ed.). California: The Price-Pottenger Nutrition Foundation, Inc.
- Proby, J. (ed). (1975). Lindlahr, H. (1862-1924). Philosophy of Natural Therapeutics. UK: The C.W. Daniel Company Ltd
- Prohaska, R.J., & Gybina, A.A. (2004). 'Intracellular copper transport in mammals'. The Journal of Nutrition, 134(5), pp.1003-1006. The American Society for Nutritional Sciences.
- Pronsky, Z. M. (2006). Food Medication Interactions. (14th ed.). USA: Food-Medication Interactions
- PSC (Prospective Studies Collaboration). (2009). 'Body-mass index and cause-specific mortality in 900,000 adults: collaborative analyses of 57 prospective studies. Lancet, 373(9669), pp.1083-1096. Elsevier Ltd
- Puchau, B., Zulet, A.M., Gonzalez de Echavarri, A., Navarro-Blasco, I., & Martinez, J. (2009). 'Selenium intake reduces serum C3, an early marker of metabolic syndrome manifestations, in health young adults'. European Journal of Clinical Nutrition, 63, pp. 858-864. Nature publishing group
- Quillin, P. & Quillin, N. (2005). Beating Cancer With Nutrition. (3rd ed.). USA: Nutrition Time Press, Inc.
- Quinn S., & Jones S.D., (2005). 'Training clinicians in new approaches to care'. Ch.4, in Jones, D. S. (Ed). (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Quirke, V. & Gaudilliere, J.P. (2008). 'The era of Biomedicine: science, medicine, and public health in Britain and France after the Second World War'. Medical History, 52(4), pp. 441-452. The Wellcome Trust Centre for the History of Medicine at UCL Central
- Radhika, M.S., Bhaskaram, P., Balakrishna, N., Ramalakshmi, B.A., Deve, S., & Kumar, B.S. (2002). 'Effects of vitamin A deficiency during pregnancy on maternal and child health'. BJOG, 109(6), pp. 689-93 . NCBI, US NLM
- Rae, A. (1986). Κβαντομηχανική: πλάνη ή πραγματικότητα; Cambridge University Press. Translated by Tsoukalakis Th. Athens: Katoptro publishers
- Rait, G., Walters, K., Bottomley, C., Petersen, I., Iliffe, S., and Nazareth I. (2010). 'Survival of people with clinical diagnosis of dementia in primary care: cohort study'. British Medical Journal, 341(52), pp.c3584. BMJ Publishing Group Ltd
- Ramsey, F., Ussery-Hall, A., Garcia, D., McDonald, G., Easton, A., Kambon, M., Balluz, L., Garvin, W., & Vigeant, J. (2008). 'Prevalence of selected risk behaviours and chronic diseases-behavioural risk factor surveillance system (BRFSS), 39 states communities, United States, 2005', Morbidity and Mortality Weekly Report, 57(SS11), pp. 1-20, Centers for Disease Control and Prevention
- Randall, J.L. (1996). 'Evolution of the new paradigm'. Primary Care, 23(1), pp. 183-198

- Rao, K.J., Weinberger, M., & Kroenke, K. (2000). 'Visit-specific expectations and patient-centered outcomes-A literature review'. Archives of Family Medicine, 9(10), pp.1148-1155.
- Rapgay, L. (1996). The Tibetan Book of Healing. USA: Passage Press
- Rastegar, A.D. (2005). 'Health care becomes an Industry'. Annals of Family Medicine, 2(1), pp.79-83.
- Ravnskov, U. (2000). The Cholesterol Myths. Washington: New Trends Publishing
- Rayburn, J.R., & Friedman, M., (2010). 'L-Cysteine, N-Acetyl-L-Cystein and glutathione protect xenopus laevis embryos against acrylamide-induced malformations and mortality in the frog embryo teratogenesis assay'. J Agric Food Chem
- Real, G.F., Svanes, C., Bjornsson, H.E., Franklin, K., Gislason, D., Gislason, T., Gulsvik, A., Janson, C., Jogi, R., Kiserud, T., Norback, D., Nystrom, L., Toren, K., Wentzel-Larsen, T., & Omenaas, E. (2006). 'Hormone replacement therapy, body mass index and asthma in perimenopausal women: a cross sectional survey'. British Medical Journal, 61(1), pp. 34-40. BMJ Publishing Group and British Thoracic Society
- Reckeweg, H. H. (1991). Homotoxicology- Illness and Healing through Anti-homotoxic Therapy. (3rd ed.). USA: Menaco Publishing Company, Inc.
- Reid, D. (1996). The Shambhala Guide to Traditional Chinese Medicine.(2nd ed.). USA: Shambhala Publications
- Reid, G., Jass, J., Sebulsky, T.M. & McCormick, K.J. (2003). 'Potential uses of probiotics in clinical practice'. Clinical Microbiology Reviews, 16(4), pp. 658-672. The American Society for Microbiology
- Reitman, L.M. & Schadt, E.E. (2007). 'Pharmacogenetics of metformin response: a step in the path toward personalised medicine'. The Journal of Clinical Investigation, 115(5), pp.1226-1229
- Reoch, J. (1874). 'The acidity of gastric juice'. Journal of Anatomy and Physiology, 8(Pt 2), pp. 274-284
- Reynolds, V.J., Donohoe, L.C., & Doyle, L.S. (2010). 'Diet, obesity and cancer'. Ir J Med Sci. Royal Academy of Medicine in Ireland
- Reznichenko, L., Kalfon, L., Amit, T., Youdim, M.B., Mandel, S.A. (2010). 'Low dosage of rasagiline and epigallocatechin gallate synergistically restored the nigrostriatal axis in MPTP-induced parkinsonim'. Neurodegener Dis, 7(4), pp.219-231
- Rideout, C.T., Harding, V.S., Jones, J.H.P. & Fan, Z.M. (2008). 'Guar gum and similar soluble fibers in the regulation of cholesterol metabolism: current understandings and future research priorities'. Vascular Health and Risk Management, 4(5), pp. 1023-1033. Dove Medical Press Ltd
- Risberg, T., Kolstad, A., Johansen, A., & Vingerhagen, K. (1999). 'Opinions on and use of althalternative medicine among physicians, nurses and clerks in northen Norway'. In Vivo, 13(6), pp. 493-498.
- Roberts, H. A. (1995). The Principles and Art of Cure by Homeopathy. UK: Homeopathic Book Service
- Robinson, K., Arheart, K., Refsum, H., Brattstrom, L., Boers, G., Ueland, P., Rubba, P., Palma-Reis, R., Meleady, R., Daly, L., Witteman, J., & Graham, I. (1998). 'Low circulating folate and vitamin B6 concentrations: risk factors for stroke, peripheral vascular disease, and coronary artery disease'. Circulation, 97, pp.437-43. American Heart Association,
- Robson, C. (2002). Real World Research. (2nd ed.). UK: Blackwell Publishing
- Rodondi, P.Y., Maillefer, J., Suardi, F., Rodondi, N., Cornuz, J. & Vannotti, M. (2009). 'Physician response to 'by-the-way' syndrome in primary care'. Journal of General Internal Medicine, 24(6), pp.739-741

- Roehr, B. (2010). 'Future of medicine lies in integration of disciplines, say Nobel laureates'. British Medical Journal, 2010, 341:c3647. BMJ Publishing Group Ltd.
- Romieu, I., & Trenga, C. (2001). 'Diet and obstructive lung diseases'. Epidemiologic Reviews, 23(2), pp.268-287. The Johns Hopkins University Bloomberg School of Public Health.
- Ronald, J., Rajagopalan, R., Cerrato, F., Nord, S.A. Hatsukami, T., Kohler, T., Marcovina, S., Heagerty, P., & Jarvik, P.G. (2010). 'Genetic variation in LPAL2, LPA, and PLG predicts plasma lipoprotein (a) level and carotid artery risk'. Stroke, 42, pp.2-9. The American Heart Association
- Rose, J., & Haynes, M. (1999). 'A Soft Systems approach to the evaluation of complex interventions in the public sector'. Journal of Applied Management Studies, 8(2), pp.199-216.
- Rose, M.R. & Oakley, T.H. (2007). 'The new biology: beyond the Modern Synthesis'. Biology Direct, 2(30)
- Rose, S. (1999). The Chemistry of Life. (4th ed.). London: Penguin Books Ltd
- Ross & Wilson (Eds) (2001). Anatomy and Physiology in Health and Illness. (9th ed.). London: Churchill Livingstone (of Harcourt Publishers Ltd)
- Ross, F., O'Tuathail, C., & Stubberfield, D. (2005). 'Towards multidisciplinary assessment of older people: exploring the change process'. Journal of Clinical Nursing, 14(4), pp.518-529. 1999-2011 John Wiley & Sons, Inc
- Roy, M. (1999). The Principles of Homoeopathic Philosophy. UK: Winter Press
- Royal College of Physicians-Working Party. (2005). 'Doctors in society. Medical professionalism in a changing world'. Clinical Medicine, 5(6), Supp. 1, pp. S5-40. Ingenta connect
- Roys, C.K. (1913). 'Chinese medicine in America'. California State Journal of Medicine, 11(3), pp. 114-118 . NCBI, US NLM
- Rubin, E. (Ed) (2002i). Βασική Παθολογική Ανατομική. Τόμος Ι. (3rd ed.). Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Rubin, E. (Ed) (2002ii). Βασική Παθολογική Ανατομική. Τόμος ΙΙ. (3rd ed.). Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Russ, R. (1915). 'After medicine, what?' California State Journal of Medicine, 13(3), pp. 110-113 . NCBI, US NLM
- Rutherford, W. (1867). 'Report on the progress of physiology: from 1st January to 1st July 1866'. Journal of Anatomy and Physiology, 1(1), pp. 154-167 . NCBI, US NLM
- Sackett, D.,L (1979). 'Bias in analytic research'. J Chron Dis 32,pp.51-63, quoted in Boccia et al, (2007)Sahley, B. J. & Birkner K. M. (2001). Heal with Amino Acids and Nutrients. USA: Pain & Stress Publications
- Salant, P. & Dillman, D. A. (1994). How to Conduct your Own Survey. John Wiley & Sons, Inc
- Salinthon, S., Yadav, V., Bourdette, D.N., & Carr, D.W. (2008). 'Lipoic acid: a novel therapeutic approach for multiple sclerosis and other chronic inflammatory diseases of the CNS'. Endocr Metab Immune Disord Drug Targets, 8(2), pp.132-142
- Saltman, B.R., & Figueras, J. (1998). 'Analysing the evidence on European health care reforms'. Health Affairs, 17(2), pp.85-108, European Reforms, The People-to-people Health Foundation,
- Salway, J. G. (1999). Metabolism at a Glance. (2nd ed.).London: Blackwell Science
- Sampson, M., Campbell, K., Ajijeruke, I., & Moher, D. (2003). 'Randomised controlled trials in pediatric complementary and alternative medicine: Where can they be found?'. BMC Pediatrics 2003, 3(1). BioMed Central Ltd

- Sanger, G.J. (2009). 'Translating 5-HTP receptor pharmacology'. Neurogastroenterology and Motility: The Official Journal of the European Gastrointestinal Motility Society, 21(12), pp. 1235-1238
- Saultz, J.W., & Lochner, J. (2005). 'Interpersonal continuity of care and care outcomes : A critical review'. Annals of Family Medicine, 3, pp. 159-166.
- Savva, S.C., Chadjoannou, M., & Tornaritis, M.J. (2007). 'Policy options for responding to the growing challenge of obesity: Cyprus national findings.' Obesity Reviews: An Official Journal of the International Association for the Study of Obesity, 8(2), pp.37-45
- Savva, S.C., Tornaritis, M., Chadjigeorgiou, C., Kourides, YA., Savva, M.E., Panagi, A., Christodoulou, E., & Kafatos, A. (2005). 'Prevalence and socio-demographic associations of undernutrition and obesity among preschool children in Cyprus.' European Journal of Clinical Nutrition, 59(11), pp.1259-1265
- Scahill et al., (2001). 'A Placebo-controlled study of Guanfacine in the treatment of children with Tic Disorders and Attention Deficit', American Journal of Psychiatry, 158, pp.1067-1074m. PubMed NCBI ,US NLM
- Scarborough, J. (Ed). (1985). Symposium on Byzantine Medicine. Dumbarton Oaks Papers 38.
- Schauss, A.G. (2011). 'Suggested optimum nutrient intake of vitamins, minerals, and trace elements'. Chapter 127 in Section 5 'Pharmacology of Natural Medicines' in Pizzorno, J. & Murray, M. (Eds). (2007-2011). Online Textbook of Natural Medicine, (e-edition.). Elsevier Inc (accessed 12/2/2011)
- Schenk, S., Saberi, M., & Olefsky, M.J. (2008). 'Insulin sensitivity: modulation by nutrients and inflammation. The Journal of Clinical Investigation, 118(9), pp. 2992-3002.
- Schmid, F. (1991). Biological Medicine – Scientific Position, Medication and Therapeutic Techniques. (1st English ed.). Germany: Aurelia-Verlag
- Scholle, J.M., Baker, W.L., Talati, R., & Coleman, C.I. (2009). 'the effect of adding plant sterols or stanols to statin therapy in hypercholesterolemic patients: systematic review and meta-analyses.' J Am Coll Nutr 28(5), pp.517-524
- Schulze, E., Laudenslager, M., & Coussons-Read, M. (2009). 'An exploration of the relationship between depressive symptoms and cortisol rhythms in Colorado ranchers'. The Journal of Rural Health: Official Journal of the American Rural Health Association and the national Rural Health Care Association, 25(1), pp. 109-113
- Schurgers, L.J., Spronk, M.H.H. Soute, M.A.B., Schiffrs, M.P., DeMey, R.G.J. & Vermeer, C. (2007). 'Regression of Warfarin-induced medial elastocalcinosis by high intake of vitamin K in rats'. Blood, 109(7), pp.2823-2831. The American Society of Hematology
- Schwartz, S.M., Marshall, L.M., & Barid, D.D. (2000). 'Epidemiologic contributions to understanding the etiology of uterine leiomyomata'. Ep, 108(suppl 5), pp.821-827
- Schwitzer, G. (2003). 'How the media left the evidence out in the cold'. British Medical Journal, 326, pp.1403-1404. BMJ Publishing Group Ltd
- Scott, P. (1906). 'On union in medicine: with some reflections on the present state of homeopathy and homoeopathic literature'. Medical Library and Historical Journal, 4(2), pp. 189-197 . NCBI, US NLM
- Seale, C., Gobo, G., Gubrium, F. J., & Silverman, D. (Eds) (2007). Qualitative Research Practice. London: Sage Publications Ltd
- Seelig, M.G. (1905). 'Superstition in medicine'. Medical Library and Historical Journal, 3(3), pp. 174-184 . NCBI, US NLM
- Seelig, M.G. (1908). 'Geography and medicine'. Aesculapian, 1(1), pp. 9-18

- Sekler, I., Sensi, L.S., Hershinkel, M., & Silverman, F.W. (2007). 'Mechanism and regulation of cellular zinc transport'. Molecular Medicine, 13(7-8), pp.337-343. The Feinstein Institute for Medical Research
- Shai, I., Shahar, D., & Fraser, D. (2001). 'Attitudes of physicians and medical students toward nutrition's place in patient care and education at Ben-Gurion university.' Education for Health, 14(3), pp.405-415. Taylor & Francis Ltd.
- Sharma, N., Okere, C.I., Duda, K.M., Chess, J.D., O'Shea, M.K. & Stanley, C.W. (2007). 'Potential impact of carbohydrate and fat intake on pathological left ventricular hypertrophy'. Cardiovascular Research, 73(2), pp. 257-268. National Institutes of Health
- Shaw, B.E. (1968). 'The scope and responsibility of medicine-a forum with a purpose'. California Medicine, 109(4), pp. 332-334 . NCBI, US NLM
- Sheenan, E.H., & Hussain, J.S. (2002). 'Unani Tibb: history, theory, and contemporary practice in South Asia'. The Annals of the American Academy of Political and Social Science, 583(1), pp. 122-135. Sage Publications on behalf of the American Academy of Political and Social Science.
- Shen, S., Szameitat, A.J., & Sterr, A. (2007). 'VBM lesion detection depends on the normalization template: a study using simulated atrophy', Magnetic Resonance Imaging, 2007 Apr 27; (Epub ahead of print) Published on www.pubmed.gov (Accessed 9/5/07)
- Shepherd, A. (2009). 'Nutrition through the life span. Part 3: adults aged 65 years and over.' British Journal of Nursing, 18(5), pp.301-307
- Sherer, B.T., Betarbet, R., Stout, K.A., Lund, S., Baptista, M., Panov, V.A., Cookson, R.M., & greenamyre, J.T. (2002). 'An in vitro model of Parkinson's disease: linking mitochondrial impairment to altered alpha-synuclein metabolism and oxidative damage'. The Journal of Neuroscience, 22(16), pp.7006-7015.
- Shigenmatsu, Y., Hara, Y., Ohtsuka, T., Ohgimoto, A., Inoue, K., & Higaki, J. (2005). 'Relation of genetic predisposition and insulin resistance to left ventricular hypertrophy in hypertension'. American Journal of Hypertension, 18(4 Pt 1), pp.457-463. National Institutes of Health, U.S. National Library of Medicine
- Showell, G.M., Brown, J., Yazdani, A., Stankiewicz, T.M., & Hart, J.R. (2011). 'Antioxidants for male subfertility'. Cochrane Database of Systematic Reviews, Issue 1. Art. No.: CD007411. DOI: 10.1002/14651858.CD007411.pub2. The Cochrane Collaboration, John Wiley & Sons, Ltd.
- Siddiqui, M.A., Kashyap, M.P., Khanna, V.K., Yadav, S., Al-Khedhairi, A.A., Musarrat, J., Pant, A.B. (2010). 'Association of dopamine DA-D2 receptor in rotenone-induced cytotoxicity in PC12 cells'. Toxicology and Industrial Health, 26(8), pp.533-542. SAGE journals online
- Siden H., Steele, R., Brant, R., Cadell, S., Davies, B., Straatman, L., Widger, K., & Andrews, S.G. (2010). 'Designing and implementing a longitudinal study of children with neurological, genetic or metabolic conditions: charting the territory'. BMC Pediatrics, 10(67)
- Siegel, B. (1974). 'Enhanced interferon response to murine leukaemia virus by ascorbic acid.' Infect Immun, 10, p.409. Quoted in McCarthy 1981
- Silva, A.L., Silveira, C.L.P. Ronsani, M.M., Souza, S.P. Scheffer, D., Vieira, C.L., Benetti, M., de Souza, T.C., & Pinho, A.R. (2010). 'Taurine supplementation decreases oxidative stress in skeletal muscle after eccentric exercise'. Cell Biochemistry and Function, 29(1), pp.43-49. John Wiley & Sons, Ltd.
- Silverman, D. (2006). Interpreting Qualitative Data. (3rd ed.). London: Sage Publications.

- Simopoulos A.P. (1999). 'Essential fatty acids in health and chronic disease'. American Journal of Clinical Nutrition, 70(3), pp.560S-569S. American Society for Clinical Nutrition.
- Simopoulos, A.P. (2002). 'The importance of the ratio of omega6/omega3 essential fatty acids'. Biomed Pharmacother, 56(8), pp. 365-79 . NCBI, US NLM
- Singh, K.S., Grass, G., Rensing, C., & Montfort, R.W. (2004). 'Cuprous oxidase activity of CueO from Escherichia coli'. Journal of Bacteriology, 186(22), pp.7815-7817. American Society for Microbiology
- Singh, M., & Das, R.R. (2011). 'Zinc for the common cold'. Cochrane Database of Systematic Reviews, 2 Art. No.: CD001364. DOI: 10.1002/14651858.CD001364.pub3. The Cochrane Collaboration. John Wiley & Sons, Ltd
- Singh, U. & Jialal, I. (2008). 'Alpha-lipoic acid supplementation and diabetes'. Nutr Rev., 66(11), pp.646-657
- Sivaramakrishnan, K. (2006). 'Constructing boundaries, contesting identities: the politics of Ayurved in Punjab (1930-40)'. Studies in History,22(2), pp. 253-283. Sage publications
- Sjoqvist, U., Hertervig, E., Nilsson, A., Duan, R.D., Ost, A., Tribukait, B., & Lofberg, R. (2002). Inflamm Bowel Dis., 8(4), pp. 258-263
- Skills for Health. (2010i). 'CNH8 Provide Nutritional Therapy to Clients' available at <https://tools.skillsforhealth.org.uk/competence/show/html/code/CNH8/> (accessed 18 /3/ 2011)
- Skills for Health. (2010ii). 'CNH9 Provide Nutritional Therapy to Clients' available at <https://tools.skillsforhealth.org.uk/competence/show/html/code/CNH9/> (accessed 18 /3/ 2011)
- Slembrouck, S. (2001). 'Explanation, interpretation and critique in the analysis of discourse'. Critique of Anthropology, 21(1), pp.33-57. SAGE Publications.
- Slembrouck, S. (2006)). 'What is meant by "discourse analysis"'. Published online on www.bank.rug.ac.be/da/da.htm, accessed on 2/11/2007
- Smart, N. (2000). World Philosophies. (2nd ed.). Routledge (Taylor & Francis Group)
- Smith, B.H. & Taylor, R.J. (1996). 'Medicine-a healing or a dying art?' The British Journal of General Practice, 46(405), pp. 249-251 . NCBI, US NLM
- Smith, D.G, Sterne, J., Fraser, A., Tynelius, P. Lawlor, A.D., & Rasmussen, F. (2009). 'The association between BMI and mortality using offspring BMI as an indicator of own BMI: large intergenerational mortality study'. British Medical Journal, 339(b5043) . BMJ Publishing Group Ltd
- Smith, D.W. (2009). 'Phenomenology'. In Zalta, N.E. (ed.), The Stanford Encyclopedia of Philosophy, (Summer 2009 edition), URL
- Smith, J.D., O'Dea, K., McDermott, R., Schmidt, B., & Connors, C. (2006). 'Educating to improve population health outcomes in chronic disease: an innovative workforce initiative across remote, rural and indigenous communities in northern Australia'. The International Electronic Journal of Rural and Remote Health Research, Education, Practice and Policy, 2006: 606
- Smith, P.F., Maclennan, K., Darlington, C.L. (1996). 'The neuroprotective properties of the Ginkgo biloba leaf: a review of the possible relationship to platelet-activating factor (PAF). J Ethnopharmacol, 50(3), pp.131-139
- Smith, R. (1998). 'Regulation of doctors and the Bristol inquiry'. Editorials. British Medical Journal, 5 Dec, 1998, 317, pp1539-1540. BMJ Publishing Group Ltd
- Smith, R. (1998i). 'All changed, changed utterly'. British Medical Journal, 316, pp. 1917-1918. BMJ Publishing Group Ltd

- Smith, R. (2000). 'Bone mineral'. Chapter 11, In Garrow, J. S., James, W. P. T. & Ralph, A. (Eds) (2000). Human Nutrition and Dietetics. (10th ed.). UK: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Smith, R. (2002). Review of Illich, I., book: 'Limits to Medicine. Medical Nemesis: the Expropriation of Health', in British Medical Journal, 324, p.923. BMJ Publishing Group Ltd
- Smith, R. (2002i). 'In search of "non-disease"'. Clinical Review in British Medical Journal, 324 (7342), pp. 883-885. BMJ Publishing Group Ltd
- Smith, W. D. (1994). Translation and Comments on Hippocrates-Volume VII. London: Harvard University Press (Loeb Classical Library)
- Smith, W.H. (1947). 'Plato and Clementine'. The Bulletin N Y Acad Med, 23(6)pp.352-377. NCBI, US NLM
- Smyth, D.S., & Checkland, P.B. (1976). 'Using a Systems Approach: The Structure of Root Definitions'. J. Appl. Sys. Anal., 1, pp.75-83.
- Snyderman, R. & Williams, R.S. (2003). 'Prospective medicine: the next health care transformation'. Acad Med, 78(11), pp.1079-1084. National Center for Biotechnology Information, U.S. National Library of Medicine
- Sokol, H., Lay, C., Seksik, P., Gerald, W., & Tannock. (2008). 'Analysis of bacterila bowel communities of IBD patients: What has it revealed?'. Inflammatory Bowel Diseases, 14(6), pp.858-867. PubMed NCBI ,US NLM
- Sole, M.J., & Jeejeebhoy, K.N. (2002). 'Conditional nutritional requirements: therapeutic relevance to heart failure'. Herz 27(2), pp. 174-8. NCBI, US NLM
- Solomon, H.D., Kremer, J., Curtis, R.J., Hochberg, C.M., Reed, G., Tsao, P., Farkouh, E.M. Setoguchi, S., & Greenberg, D.J. (2010). 'Explaining the cardiovascular risk associated with rheumatoid arthritis: traditional risk factors versus markers of rheumatoid arthritis severity'. Annals of the Rheumatic Diseases-The EULAR Journal, 69, pp.1920-1925.
- Solomon, H.D., Love, J.T., Canning, C., & Schneeweiss, S., (2010i). 'Risk of diabetes among patients with rheumatoid arthritis, psoriatic arthritis and psoriasis'. Annals of the Rheumatic Diseases-The EULAR Journal, 69, pp.2114-2117. BMJ Publishing Group & European League Against Rheumatism.
- Solomons W.N. (2009). 'Developmental origins of health and disease: concepts, caveats, and consequences for public health nutrition'. Nutrition Reviews, 67(1), pp.S12-S16. International Life Sciences Institute
- Song, C., Kanthasamy, A., Anantharam, V., Sun, F., & Kanthasamy, A.G. (2010). 'Environmental neurotoxic pesticide increases histone acetylation to promote apoptosis in dopaminergic neuronal cells: relevance to epigenetic mechanisms of neurodegeneration'. Molecular Pharmacology, 77(4), pp.621-632. The Americal Society for Pharmacology and Experimental Therapeutics
- Song, F., Parekh, S., Hooper, L., Loke, Y.K., Ryder, J., Sutton, A.J., Hing, C., Kwok, C.S., Pang, C., & Harvey, I. (2010i). 'Dissemination and publication of research findings: an updated review of related bias'. Health Technol Assess., 14(8):iii, ix-xi, pp.1-193. National Center for Biotechnology Information, U.S. National Library of Medicine
- Song, M.K., Rosenthal, M.J., Song, A.M., Uyemura, K., Yang, H., Ament, M.E., Yamaguchi, D.T., & Cornford, E. (2009). 'Body weight reduction in rats by oral treatment with zinc plus cyclo-(His-Pro)'. Themed Section: Advances in nutritional pharmacology. British Journal of Pharmacology, 158(2), pp. 442-250. The British Pharmacological Society. Wiley InterScience

- Song, W-Y., Ku, K-H., & Choi, J-H. (2010ii). 'Effect of ethanol extracts from red pepper seeds on antioxidative defense system and oxidative stress in rats fed high-fat, high-cholesterol diet'. Nutr Res Pract., 4(1), pp.11-15. The Korean Nutrition Society and the Korean Society of Community Nutrition
- Song, Y., He, K., Levitan, E.B., Manson, J.E., & Liu, S. (2006). 'Effects of oral magnesium supplementation on glycaemic control in type 2 diabetes: a meta-analysis of randomized double-blind controlled trials'. Diabet Med. 23(10), pp.1050-1056
- Soo, I., Mardsen, L.K., Rejpar, Q., Sydora, C.B., Sherbaniuk, R., Cinque, B., Di Marzio, L., Cifone, M.G., Desimone, C., & Fedorak, N.R. (2008). 'VSL#3 probiotic upregulates intestinal mucosal alkaline spingomyelinase and reduces inflammation'. The Canadian Journal of Gastroenterology, 22(3), pp.237-242. Pulsus Group Inc
- Spallholz, J.E., Martin, J.L., Gerlach, M.L., & Heinzerling, R.H. (1973). 'Immunologic responses of mice fed diets supplemented with selenite selenium'. Proc Soc Exp Biol Med. 143, p.685. Quoted in McCarthy (1981)
- Speakman, R.J. (2006). 'Thrifty genes for obesity and the metabolic syndrome-time to call off the search?'. Diabetes and Vascular Disease Research, 3(1), pp.7-11. SAGE,
- Spiller, R. (2007). 'Recent advances in understanding the role of serotonin in gastrointestinal motility in functional bowel disorders: alterations in 5-HTP signalling and metabolism in human disease'. Neurogastroenterology And Motility: The Official Journal Of The European Gastrointestinal Motility Society 19(2), pp. 25-31
- Stange, C.K. (2009i). 'The problem of fragmentation and the need for integrative solutions'. Annals of Family Medicine, 7(2), pp. 100-103
- Stange, C.K. (2009ii). 'A science of connectedness'. Editorial in Annals of Family Medicine, 7(5), pp.387-395),
- Stanger, O., Herrmann, W., Pietrzik, K., Fowler, B. Geisel, J., Dierkes, J., & Weger, M. (2003). 'DACH-LIGA Homocysteine (German, Austrian and Swiss Homocysteine Society): Consensus paper on the rational clinical use of homocysteine, folic acid and B vitamins in cardiovascular and thrombotic diseases: guidelines and recommendations'. Clinical Chemistry and Laboratory Medicine, 41(11), pp. 1392-1403. De Gruyter Reference Global
- Starfield, B. (1980). 'Continuous confusion?'. American Journal of Public Health, 70(2), pp. 117-118.
- Starr, J.M. & Marsden, L. (2008). 'Characterisation of user-defined health status in older adults with intellectual disabilities'. Journal of Intellectual Disability Research, 52(6), pp. 483-489
- Steinbrecher, A., Meplan, C., Hesketh, J., Schomburg, L., Endermann, T., Jansen, E., Akesson, B., Rohrmann, S. & Linseisen, J. (2010). 'Effects of selenium status and polymorphisms in selenoprotein genes on prostate cancer risk in a prospective study of European men'. Cancer Epidemiology Biomarkers & Prevention, 19, 2958
- Stimler, C. (1997). 'Buddha'. Chest, 111 (2), pp. 524-525. Official publication of the American College of Chest Physicians
- Stoeckert, C.J. & Parkinson, H. (2003). 'The MGED ontology: a framework for describing functional genomics experiments'. Comparative and Functional Genomics, 4(1), pp. 127-132 . NCBI, US NLM
- Stoll, B.A. (1998). 'Essential fatty acids, insulin resistance, and breast cancer risk'. Nutr Cancer, 31(1), pp.72-7 . NCBI, US NLM

- Strandberg, L.E., Ovhed, I., Borgquist, L. & Wilhelmsson, S. (2007). 'The perceived meaning of a (w)holistic view among general practitioners and district nurses in Swedish primary care: a qualitative study'. BMC Family Practice, 8(8)
- Street, L.R., O'Malley, J.K., Cooper, A.L., & Haidet, P. (2008). 'Understanding concordance in patient-physician relationships: personal and ethnic dimensions of shared identity'. Annals of Family Medicine, 6(3), pp. 198-205
- Stroud, L.R., Foster, E., Papandonatos, G.D., Handwerger, K., Granger, D.A., Kivlighan, K.T., & Niaura, R. (2009). 'Stress response and the adolescent transition: performance versus peer rejection stressors'. Development and Psychopathology (Dev Psychopathol), 21(1), pp. 47-68
- Suda (2002). Byzantine Lexicon of 10th century AD. Thessaloniki: Thyrathen
- Sudak N., (2005). 'The goal of health is more than the absence of frank disease'. Ch.11, in Jones, D. S. (Ed) (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Sult, T., (2005). 'Clinical approaches to gastrointestinal imbalance'. Ch.28, in Jones, D. S. (Ed) (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Suzuki, T.D. (1968). The essence of Huddhism. Hozokan, Kyoto, Japan. Quoted in Capra, F. (1982). The Tao of Physics. (3rd ed.). London: Flamingo (HarperCollins Publishers)
- Synderman, R., Williams, R.S. (2003). 'Prospective medicine: the next health care transformation'. Acad Med, 78(11), pp.1079-1084. National Center for Biotechnology Information, U.S. National Library of Medicine
- Szopa, M., Wybranska, I., Malczewska-Malec, M., & Dembinska-Kiec, A. (2005). 'Nutrigenomics-about genetics and nutrition'. Przegl Lek., 62(4), pp.245-252
- Tait, C.W. (1904). 'The legal definition of the practice of medicine'. California State Journal of Medicine, 2(4), pp. 119-121 . NCBI, US NLM
- Tan, O.A.J., & Koelch, M. (2008). 'The ethics of psycholarmacological research in legal minors'. Child and Adolescent Psychiatry and Mental Health, 2(39). BioMed Central Ltd
- Tang, J.L., Liu, B.Y., & Ma W.K. (2008). 'Traditional Chinese Medicine', available at www.thelancet.com (accessed 22 /10/ 2008)
- Taren, L.D., Thomson, A.C., Koff, A.N., Gordon R.P., Marian, J.M., Brassford, L.T., Fulginiti, V.J., & Ritenbaugh, K.C. (2001). 'Effect of an integrated nutrition curriculum on medical education, student clinical performance, and student perception of medical-nutrition-training'. American Journal of Clinical Nutrition, 73, pp.1107-12
- Tavakoli, R.H. (2009). 'A closer evaluation of current methods in psychiatric assessments'. Psychiatry (Edgmont.), 6(2), pp,25-30 . NCBI, US NLM
- Taylor, A., Jacques, F.P., Chylack, T.L., Hankinson, E.S., Khu, M.P., Rogers, G., Friend, J., Tung, W., Wolfe, K.J., Padhye, N., & Willet, C.W. (2002). 'Long-term intake of vitamins and carotenoids and odds of early age-related cortical and posterior subcapsular lens opacities'. American Journal of Clinical Nutrition, 75(3), pp.540-9. American Society of Clinical Nutrition
- Temkin, O. (1962). 'Byzantine Meidcine and Empiricism'. Dumbarton Oaks Papers, 16, pp.97-115
- Tenenbaum, A., Fisman, E.Z., Motro, M., & Adler, Y. (2008). 'Optimal management of combined dyslipidemia: what have we behind statins monotherpay?' Adv Cardiol, 45, pp.127-153
- Thain, M. & Hickman, M. (2000). The Penguin Dictionary of Biology. (10th ed.)London: Penguin Books

- Thayer, W.S. (1929) 'Individualism in medicine'. California and Western Medicine, XXXI(6), pp. 377-381
- The American Heritage Dictionary of the English Language (The) (2000). 4th edition (online). Houghton Mifflin Company . NCBI, US NLM
- The British Dietetic Association. (2011). Delivering nutritional care through food and beverage services-A toolkit for Dieticians. Produced by: The Food Counts Specialist group. Commissioned by: The British Dietetic Association Professional Development Committee, available at http://www.bda.uk.com/publications/Delivering_Nutritional_Care_through_Food_Beverage_Services.pdf (accessed 18 /3/ 2011)
- The Rector and Visitors of the University of Virginia (2009). Byzantine Medicine. Claude moor Health Sciences Library
- Theodorou, M., Tsiantou, V., Pavlakis, A., Maniadakis N., Fragoulakis, V., Pavi, E., and Kyriopoulos, J. (2009). 'Factors influencing prescribing behaviour of physicians in Greece and Cyprus: results from a questionnaire based survey'. BMC Health Services Research, 9 (150), doi: 10.1186/1472-6963-9-150. BioMed Central
- Theodosopoulou, E. (2010). Alternative Therapies and Education. Presentation at the Athens World Iridology Conference.
- Thiel, R. J. (2000). Combining Old and New: Naturopathy for the 21st Century. Warsaw: Whitman Publications.
- Thiruchelvam, M., Prokopenko, O., Cory-Slkechta, A.D., Richfield, K.E., Buckley, B., & Mirochnitchenko, O. (2005). 'Overexpression of superoxide dismutase or glutathione peroxidase protects against the paraquat+maneb-induced Parkinson disease phenotype'. The Journal of Biological Chemistry, 280, pp.22530-22539.
- Thoma, G., Pearson, G., & Chung, M. (2003) 'Andreas Vesalius's De Humani Corporis Fabrica'. Turning the Pages-U.S. National Library of Medicine, site visited 21/11/10
- Tobin, A., Veale, J.D., Gizgerald, O., Rogers, S., Collins, P., O'Shea, D., & Kirby, B. (2010). 'Cardiovascular disease and risk factors in patients with psoriasis and psoriatic arthritis'. The Journal of Rheumatology, 37(7), pp.1386-1394.
- Tomamichel, M., Sessa, C., Herzig, S., De Jong, J., Pagani, O., Willems, Y., & Cavalli, F. (1995). 'Informed consent for phase I studies: evaluation of quantity and quality of information provided to patients', Ann Oncol, 6(4):363-369. PubMed NCBI, US NLM
- Toms, J. (2009). 'So what? A reply to Roger Cooter's 'after death/after-"life": the social history of medicine in Post-modernity'. Oxford Journals-Social History of Medicine, 22(3), pp.609-815. Oxford University Press on behalf of the Society for the Social History of Medicine
- Tortora, G. & Grabowski, S. (2003). Principles Of Anatomy & Physiology. (10th ed.) USA: John Wiley & Sons
- Tovey, P., Chatwin, J., & Ahmad, S. (2005). 'Toward an understanding of decision making on complementary and alternative medicine use in poorer countries: the case of cancer care in Pakistan'. Integrative Cancer Therapies, 4(3), pp.236-241, Sage Publications
- Tredennick, H. (1933). Translation and Comments on Aristotle-Metaphysics-Books I-IX. London: Harvard University Press (Loeb Classical Library)
- Tredennick, H. (1935). Aristotle- Metaphysics-Books X-XIV. London: Harvard University Press (Loeb Classical Library)
- Trivieri, L. & Andreson, J. (Ed) (2002). Alternative Medicine The Definitive Guide. (2nd ed.). USA: Celestial Arts
- Trochim W. (2006) 'Research Methods Knowledge based' Published online on <http://www.socialresearchmethods.net/kb> (accessed 9/5/2007)

- Troskie, R. (1997). 'The importance of traditional midwives in the delivery of health care in the Republic of South Africa'. Curationis, 20(1), pp.15-20. PubMed NCBI
- Tunon, J.M. Garcia-Mediavilla, V.M., Sanchez-Campos, S., & Gonzalez-Gallego, J. (2009). 'Potential of flavonoids as anti-inflammatory agents: modulation of pro-inflammatory gene expression and signal transduction pathways'. Curr Drug Metab., 10(3), pp.256-271. Bentham Direct
- Tversky, A. & Kahneman, D. (1974). 'Judgment under uncertainty: Heuristics and biases'. Science, 185(4157), pp.1124-1131. The American Association for the Advancement of Science
- TVU. (2011). 'Course details'. University of West London available at <http://courses.uwl.ac.uk/CourseDetails.aspx?CourseInstanceID=30164> accessed 20 /3/ 2011
- Tyrovolas, S., Lionis, C., Zeimbekis, A., Bountziouka, V., Micheli, M., Katsarou, A., Papairakleous, N., Metallinos, G., Makri, K., Polychronopoulos, E., & Panayiotakos, D.B. (2009). 'Increased body mass and depressive symptomatology are associated with hypercholesterolemia, among elderly individuals; results from the MEDIS study'. Lipids in Health and Disease, 8(10). BioMed Central Ltd
- Tyson, L.K., Reynolds, L.J., McNair, R., Zhang, Q., Weissberg, L.P. & Shanahan, M.C. (2003). 'Osteo/chondrocytic transcription factors and their target genes exhibit distinct patterns of expression in human arterial calcification'. Arteriosclerosis, Thrombosis, and Vascular Biology, 23, pp.489-494. American Heart Association, Inc.
- UMDL (University of Michigan Digital Library). (2005) Dictionary of Greek and Roman Biography and Mythology. By various writers. Ed. By Smith, W. (1849). Ann Arbor, Michigan: University of Michigan Library 2005,
- Unger, J.P., DePaepe, P. Ghilbert, P., Soors, W., & Green, A. (2006). 'Integrated care: a fresh perspective for international health policies in low and midde-income countries'. International Journal of Integrated Care, 6(e15)
- Vaarala, O, Atkinson, A.M. & Neu, J. (2008). 'The perfect storm for type 1 Diabetes : the complex interplay between intestinal microbiota, gut permeability, and mucosal immunity'. Diabetes, 57(10), pp.2555-2562, American Diabetes Association
- Valentine, G.W. & Sanacora, G. (2009). 'Targeting glial physiology and glutamate cycling in the treatment of depression'. Biochemical Pharmacology, 78(5), pp. 431-439
- Valier, H., & Timmermann, C. (2008). 'Clinical trials and the reorganization of medical research in post-second world war Britain'. Medical History, 52(4), pp.493-510. The Wellcome Trust Centre for the History of Medicine at UCL
- Vallance, J. T. (1990). The Lost Theory of Asclepiades of Bithynia. Clarendon press (Oxford)
- Van Dijk, A.T. (1993). 'Principles of Critical Discourse Analysis'. Discourse & Society, 4(2), pp.249-283. SAGE publications
- Van Dijk, A.T. (1998). 'Critical discourse analysis'. Second draft: to appear in Tannen, D., Schiffrin, D., & Hamilton, H. (Eds). Handbook of Discourse Analysis (in preparation). Available at <http://www.hum.uva.nl/~teun/cda.htm>
- Van Kreijl C.F. (RIVM). (2009). 'Latest developments and insights-Judging the evidence-. In EUPHIX, EUphocus. Biltboven: RIVM, available at <http://www.euphix.org.EUphocus/Food, Nutrition, Physical activity and Cancer>, (accessed 11 /5/ 2009)

- Van Weel, C. & Rosser, W.W. (2004). 'Improving health care globally: a critical review of the necessity of family medicine research and recommendations to build research capacity'. Annals of Family Medicine, 2(suppl 2), pp.s5-s16
- Vardavas, C.I., Yiannopoulos, S., Kiriakakis, M., Poulli, E., & Kafatos, A. (2006). 'Fatty acid and salt contents of snacks in the Cretan and Cypriot market: a child and adolescent dietary hazard'. Food Chemistry, 101(2007), pp.924-931. Elsevier Ltd
- Vauzour, D., Vafeiadou, K., Rodriguez-Mateos, A., Rendeiro, C., & Spencer, P.E.J. (2008). 'The neuroprotective potential of flavonoids: a multiplicity of effects'. Genes & Nutrition, 3(3-4), pp.115-126. Springer-Verlag
- Verhaar, M.C., Stroes, E., & Rabelink, T.J. (2002). 'Folates and cardiovascular disease'. Arteriosclerosis, Thrombosis, and Vascular Biology, 22(6). American Heart Association
- Vesey, G., & Foulkes, P. (1990). Collins Dictionary of Philosophy. British Library Cataloguing in Publication Data
- Vickers, A., & Zollman, C. (1999). 'Unconventional approaches to nutritional medicine'. Clinical Review. British Medical Journal, 27 Nov1999, 319, pp. 1419-1422. BMJ Publishing Group Ltd
- Villegas, R., Gao, Y.T., Dai, Q., Yang, G., Cai, H., Li, H., Zheng, W., & Shu, X.O. (2009). 'Dietary calcium and magnesium intakes and the risk of type 2 diabetes: the Shanghai Women's Health Study'. The American Journal of Clinical Nutrition, 89(4), pp.1059-1067. American Society for Nutrition.
- Vithoulkas, G. (1980). The Science of Homeopathy. Grove Press NY
- Vogel, H.K.J., Bolling, F.S., Costello B.R., Guarneri, M.E., Krucoff, W.M., Longhurst, C.J., Olshansky, B., Pelletier, R.K., Tracy, M.C., & Vogel, A.R. (2005). 'Integrating complementary medicine into cardiovascular medicine: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (Writing Committee to develop an expert consensus document on complementary and integrative medicine)'. Journal of the American College of Cardiology, 46(1), pp. 184-221. The American College of Cardiology Foundation. Elsevier Inc.
- Vorning, A. (1997). Μια σύντομη ιστορία του Ελληνικού Πολιτισμού' Athens: Kastaniotis A.E.
- Vosper, H. (2009). 'Niacin: a re-emerging pharmaceutical for the treatment of dyslipidaemia'. Themed Section: Advances in Nutritional Pharmacology British Journal of Pharmacology, 158(2), pp. 429-441. The British Pharmacological Society. Wiley InterScience
- Vryonis, S. (1989). The Medical Unity of the Mediterranean World in Antiquity and the Middle Ages. Lecture delivered at the first Mediterranean medical meeting, Herakleion – Crete: Crete University Press
- Wadhwa, S. & Kapila, S. (2008). 'TMJ Disorders: future innovations in diagnostics and therapeutics'. J Den Educ., 72(8), pp. 930-947
- Wajih, N., Borrás, T., Xue, W., Hutson, M.S., & Wallin, R. (2004). 'Processing and transport of matrix gamma-carboxyglutamic acid protein and bone morphogenetic protein-2 in cultured human vascular smooth muscle cells-evidence for an uptake mechanism for serum fetuin'. The Journal of Biological Chemistry, 279, p.43052-43060. The American Society for Biochemistry and Molecular Biology, Inc
- Wallin, R., Wajih, N., Greenwood, G.T. & Sane, D.C. (2001). 'Arterial calcification: a review of mechanisms, animal models, and the prospects for therapy'. Med Res Rev., 21(4), pp.273-301

- Wang, H.X., Wahlin, A., Basun, H., Fastbom, J., Winblad, B., & Fratiglioni, L. (2001). 'Vitamin B12 and folate in relation to the development of Alzheimer's disease'. Neurology 56(9), pp.1188-94 . NCBI, US NLM
- Wang, S.M., Boddapati, S., Emadi, S, & Sierks, R.M. (2010). 'Curcumin reduces a-synuclein induced cytotoxicity in Parkinson's disease cell model'. BMC Neuroscience,11(57). BioMed Central Ltd
- Wann, S. (2005). 'Determination of professional competency in a rapidly changing environment'. Journal of American College of Cardiology, 46, pp.1996-1998.
- Warbasse, P.J. (1904). 'Medicine and its relation to human progress'. Address delivered before the Long Island Alumni Association of the Medical Department of Columbia University, Nov 23, 1904, Medical Library and Historical Journal, 2(1), pp. 28-34 . NCBI, US NLM
- Warnecke, R.B., Johnson, T.P., Chavez, N., Sudman, S., O'Rourke, D.P., Lacey, L., & Horm, J., (1997), 'Improving question wording in surveys of culturally diverse populations'. Ann Epidemiol, 7(5), pp.334-42
- Warshafsky, S., Kamer, S.R., & Sivak, L.S. (1993). 'Effect of Garlic on Total Serum Cholesterol' A Meta-Analysis, Annals of Internal Medicine, 119 (7) Part 1, pp599-605.
- Wastney, M.E. & House, A.W. (2008). 'Development of a compartmental model of zinc kinetics in mice'. Journal of Nutrition, 138(11), pp. 2148-2155. American Society for Nutrition
- Wastney, M.E., House, W.A., Barnes, R.M., Subramanian, K.N. (2000). 'Kinetics of Zinc metabolism: variation with diet, genetics and disease'. Journal of Nutrition, 130(5S Suppl) pp. 135S-9S. The American Society for Nutrition
- Waterman, H., Marshall, M., Noble, J., Davies, H., Walshe, K., Sheaff, R., & Elwyn, G. (2007). 'The role of action research in the investigation and diffusion of innovations in health care: The Pride project'. Qualitative Health Research, 17(3), pp.373-381. Sage Publications
- Watts, D. L. (1999). Trace Elements and Other Essential Nutrients. USA: 3rd Writer's B-L-O-C-K- edition
- Weber, P., Bendich, A., & Scharch, W. (1996). 'Vitamin C and human health-a review of recent data relevant to human requirements'. Int J Vitam Nutr Res, 66(1)
- Weeks, B.W., & Wallace, E.A. (2003). 'Time and money-A retrospective evaluation of the inputs, outputs, efficiency and incomes of physicians'. Archives of Internal Medicine, 163(8), pp.944-948.
- Wei, Z.H., Wang, H., Chen, X.Y., Wang, B.S., Rong, Z.X., Wang, B.S., Su, B.H., & Chen. H.Z. (2009). 'Time- and dose-dependent effect of psyllium o serum lipids in mild-to-moderate hypercholesterolemia: a meta-analysis of controlled clinical trials'. European Journal of Clinical Nutrition, 63(7), pp.821-827
- Weijer, C., Dickens B., & Meslin, E.M., (1997), 'Bioethics for Clinicians: 10. Research ethics'. Canadian Medical Association J 156(8)
- Weiner, B.K. (2008). 'Spine update: the biopsychosocial model and spine care'. Spine (Phila Pa 1976), 33(2), pp.219-223 . NCBI, US NLM
- Weisburger H.J. (2000). 'Approaches for chronic disease prevention based on current understanding of underlying mechanisms'. American Journal of Clinical Nutrition, 2000, 71(suppl):1710S-4S. American Society for Clinical Nutrition
- Weissmann, G. (2008). 'Back to basic science: time for another Flexner Report'. The FASEB Journal, 22, pp. 3097-3100.

- Welschhoff, A. (2006). 'Community participation and primary health care in India'. Dissertation der Fakultät für Geowissenschaften der Ludwig-Maximilians-Universität München. Tag der mündlichen Prüfung
- Werbach, M. R. (1996). Nutritional Influences on Illness. (2nd ed.). USA: Third Line Press
- Werbach, M. R. (1999). Nutritional Influences on Mental Illness- A sourcebook of clinical research. (2nd ed.). USA: Third Line Press, Inc.
- Werbach, M. R. & Murray, M. T. (2000). Botanical Influences on Illness- A Sourcebook of Clinical Research. (2nd ed.). USA: Third Line Press Inc. Tarzana
- Werbach, M. R. (Ed) (2002). Case Studies In Natural Medicine. USA: Third Line Press Inc.
- Werbach, M.R. & Moss, J. (1999). Textbook of Nutritional Medicine, Third Line Press, INC- Tarzana, California.
- Werbach, R.M.(1997). Foundations of Nutritional Medicine-A Sourcebook of clinical research. Third Line Press, INC- Tarzana, California.
- Whitney, L.J. (1928). Discussion on Langstroth, L. (1928). 'A new emphasis in medicine'. California and Western Medicine, 29(3), pp. 165-168 . NCBI, US NLM
- WHO (1997). 50 facts-population and life expectancy. World Health Organisation
- WHO (2000). 'Traditional and Modern Medicine-Harmonizing the two approaches' Report of the meeting held in Beijing China 22-26 Nov 1999. World Health Organisation.
- WHO (2002). Integrating prevention into health care. Fact sheet No 172. World Health Organisation.
- WHO (2002i). Diet, physical activity, and health. Agenda item 13.11. Fifty-fifth world health assembly, WHA55.23. World Health Organisation.
- WHO (2002ii). Keep fit for life-Meeting the nutritional needs of older persons. World Health Organisation / School of Nutrition and Policy, Tufts University
- WHO (2002iii). Secondary prevention of non-communicable diseases. Report of WHO- Wellcome Trust Meeting of Experts 1-3 Aug 2001, Hinxton, Cambridge, UK. World Health Organisation
- WHO (2003). 'Chronic disease-key risk factors include high cholesterol, high blood pressure, low fruit and vegetable intake'. Global Strategy on diet, physical activity and health. World Health Organisation
- WHO (2003i). 'Surveillance of noncommunicable disease risk factors'. Fact sheet No273, March 2003. World Health Organisation
- WHO (2003ii). 'Traditional medicine'. Fact sheet No134, revised May 2003. World Health Organisation.
- WHO (2003iii). 'Global burden of musculoskeletal disease revealed in new WHO report'. Bulletin of the World Health Organisation 81(11), pp. 853-4. World Health Organisation
- WHO (2004i). Global strategy on diet, physical activity, and health. World Health Organisation.
- WHO (2004ii). Global strategy on diet –Report by the Secretariat. Fifty-seventh World Health Assembly 17 April 2004. World Health Organisation
- WHO (2005). The impact of chronic disease in the Eastern Mediterranean. World Health Organisation
- WHO (2005i). Preventing chronic diseases: a vital investment: Who global report. World Health Organisation
- WHO (2006). 'Working together for health'. World Health Report 2006. World Health Organisation
- WHO (2006i). 'Basic Indicators'. World Health Report. World Health Organisation

- WHO (2006ii). 'Statistical annex-Explanatory notes'. World Health Report 2006. World Health Organisation
- WHO (2006iii). 'Cyprus'. Mortality country fact sheet 2006. World Health Organisation
- WHO (2006iv). 'Highlights on health in Cyprus-2005'. World Health Organisation
- WHO (2007). World Health Statistics 2007. World Health Organisation
- WHO (2007i). 'A safer future'. The World Health Report 2007. World Health Organisation
- WHO (2007ii). 'Ten statistical highlights in global public health' Part 1. World Health Statistics 2007. World Health Organisation
- WHO (2007iii). 'Health Systems-Health Expenditure'. World Health Statistics 2007. World Health Organisation
- WHO (2007iv). 'Demographic and socioeconomic statistics'. World Health Statistics 2007. World Health Organisation
- WHO (2007v). 'Health systems-Human resources for health'. World Health Statistics 2007. World Health Organisation
- WHO (2007vi). 'Inequities in health'. World Health Statistics 2007. World Health Organisation
- WHO (2007vii). 'Risk factors'. World Health Statistics 2007. World Health Organisation
- WHO (2007viii). 'Health status-morbidity'. World Health Statistics 2007. World Health Organisation
- WHO (2007ix). 'Cardiovascular diseases'. Fact sheet N^o317 Feb 2007. World Health Organisation.
- WHO (2007x). 'Health status-mortality'. World Health Statistics 2007. World Health Organisation
- WHO (2007xi). 'Cyprus-The impact of cancer'. Reports, Cancer Review WHO Global InfoBase Online. World Health Organisation.
- WHO (2007xii). 'Health systems-everybody's business-a framework for action'. Draft 2007-07-04. World Health Organisation
- WHO (2008). Action Plan 2008-2013 for the global strategy for the prevention and control of noncommunicable diseases. World Health Organisation
- WHO (2008i). 'Diabetes'. Fact sheet No312, Nov 2008. World Health Organisation
- WHO (2008ii). 'The challenges of a changing world'. The World Health Report 2008. World Health Organisation
- WHO-Europe (2006). Gaining health-The European strategy for the prevention and control of noncommunicable diseases. World Health Organisation_Regional Office for Europe
- WHO-Europe (2008). Atlas of Health in Europe. (2nd ed.). World Health Organisation Regional Office for Europe
- WHO-Europe. (2008i). 'Policies and practices for mental health in Europe-meeting the challenges'. Fact Sheet 10 Oct. 2008. World Health Organisation-Regional Office for Europe
- WHO-Europe. (2008ii). 'Mental health: facing the challenges, building solutions'. Report from the WHO European Ministerial Conference. World Health Organisation-Regional Office for Europe
- Wickramasinghe, S.N. (1999). 'the wide spectrum and unresolved issues of megaloblastic anemia'. Semin Hematol, 36(1), pp.3-18 . NCBI, US NLM
- Widdowson, H.G. (1995). 'Discourse analysis: a critical view'. Language and Literature, 4(3),pp.157-172, Longman Group Limited

- Williams, R. J. (1998). Biochemical Individuality: The Basis for the Genetotropic Concept. (2nd ed.). USA: Keats Publishing, Inc.
- Williams, R.T. H., Cox, J., Walker, G.D., Cobbold, F.L.J., Taylor-Robinson, D.S., Marshall, E.S., & Orchard, R.T. (2010). 'Differences in gut microbial metabolism are responsible for reduced hippurate synthesis in Crohn's disease'. BMC Gastroenterol., 10, p.108. BioMed Central Ltd
- Wilner, C. (2000). 'Neurological imbalances'. Chapter 20 in Jones, D. S. (Ed). (2005). Textbook of Functional Medicine. Gig Harbor: Institute for Functional Medicine
- Wilson, J. L. (2001). Adrenal Fatigue-The 21st Century Stress Syndrome. USA: Smart Publications
- Wilson, L. (2005). Nutritional balancing and hair mineral analysis. (3rd Revised ed.). UK: L.D. Wilson Consultants, Inc.
- Wilt, J.T., Ishani, A., Stark, G., et al. (1998). 'Saw Palmetto extracts for treatment of Benign Prostatic Hyperplasia: A systematic review'. JAMA, Nov 11, 280(18), pp. 1604-9
- Wise, A.L., Palmer, R.J., Spiegelman, D., Harlow, L.B., Stewart, A.E., Adms-Campbell, L.L., & Rosenberg, L. (2005). 'Influence of body size and body fat distribution on risk of uterine leiomyomata in US black women'. Epidemiology, 16(3), pp.346-354
- Withington, E. T. (1928). Translation and Comments on Hippocrates-Volume III. London: Harvard University Press (Loeb Classical Library)
- Witte, K.K., Clark, A.L., & Gleland, J.C. (2001). 'Chronic heart failure and micronutrients'. Journal of the American College of Cardiology, 37(7), pp. 1765-74 . NCBI, US NLM
- Woese, R.C., & Goldenfeld, N. (2009). 'How the microbial world saved evolution from the Scylla of Molecular biology and the Charybdis of the Modern Synthesis'. Microbiology and Molecular Biology Reviews, 73(1), pp.14-21. The American Society of Microbiology
- Woodfin, R. & Groves, J. (2001). Aristotle. United Kingdom: Icon Books
- Woodham, A. (1994). HEA Guide to Complementary Medicine and Therapies. London: Health Education Authority
- Woolf, D.A. & Akesson, C. (2001). 'Understanding the burden of musculoskeletal conditions-The burden is huge and not reflected in national health priorities'. British Medical Journal, 322(7294), pp.1079-1080. BMJ Publishing Group Ltd
- Wrong, O. (2000). 'Water and monovalent electrolytes'. Chapter 10 in Garrow, J. S., James, W. P. T. & Ralph, A. (Eds) (2000). Human Nutrition and Dietetics. (10th ed.). UK: Churchill Livingstone (An imprint of Harcourt Publishers Limited)
- Wu, H., Pan, A., Yu, Z., Qi, Q., Lu, L., Zhang, G., Yu, D., Zong, G., Zhou, Y., Chen, X., Tang, L., Feng, Y., Zhou, H., Chen, X., Li, H., Demark-Wahnefried, W., Hu, B.F., & Lin, X. (2010). 'Lifestyle counselling and supplementation with flaxseed or walnuts influence the management of metabolic syndrome'. The Journal of Nutrition, 140(11), pp.1937-1942. American Society for Nutrition
- Wu, S.H., Ho, S.C., & Zhong, L., (2010i). 'Effects of vitamin D supplementation on blood pressure'. South Med J, 103(8), pp. 729-737. NCBI, US NLM
- Xiong, S.J., Branigan, D., & Li, M. (2009). 'Deciphering the MSG controversy'. Int J Clin Exp Med, 2, pp.329-336.
- Yach, D., Hawkes, C., Gould, L.C., & Hofman, J.K. (2004). 'The global burden of chronic diseases-Overcoming impediments to prevention and control'. JAMA, 291(21), pp.2616-2622, American Medical Association.
- Yamori, Y., Nara, Y., Mizushima, S., Murakami, S., Ikeda, K., Sawamura, M., Nabika, T., Horie, R. (1992). 'Gene-environment interaction in hypertension, stroke and atherosclerosis in experimental models and supportive findings from a world-wide cross-

- sectional epidemiological survey: a WHO-cardiac study'. Clin Exp Pharmacol Physiol Suppl., 20, pp.43-52. WHO Collaborating Center for Research on Primary Prevention of Cardiovascular Diseases, Izumo, Japan
- Yamori, Y., Taguchi, T., Hamada, A., Kunimasa, K., Mori, H., & Mori, M. (2010). 'Taurine in health and disease: consistent evidence from experimental and epidemiological studies'. Journal of Biomedical Science, 17(suppl1), S6 . NCBI, US NLM
- Yang, L., Mutanen, M., Cheng, Y. & Duan, R.D. (2002). 'Effects of fat, beef and fibre in diets on activities of sphingomyelinase, ceramidase and caspase-3 in rat colonic mucosa'. Med Princ Pract., 11(3), pp. 150-156
- Yanik, B. Ayrim, A., Ozol, D., Koktener, A., & Gokmen, D. (2009). 'Influence of obesity on bone mineral density in postmenopausal asthma patients undergoing treatment with inhaled corticosteroids'. Clinics (Sao Paulo), 64(4), pp. 313-318. Hospital das Clinicas da FMUSP
- Yao, Y., Shahbazian, A., & Bostrom, I.K. (2008). 'Proline and gamma-carboxylated glutamate residues in matrix Gla protein are critical for binding of bone morphogenetic protein-4'. Circulation Research, 102(9), pp.1065-1074. American Heart Association, Inc
- Yarnall K.S.H., Pollak, K.I., Ostbye, T., Krause, M.K. & Michener, L.J. (2003). 'Primary care: is there enough time for prevention?'. Peer Reviewed, Research and Practice, American Journal of Public Health, 93(4), pp. 635-641. American Public Health Association.
- Yarnell, E. (2000). Naturopathic Gastroenterology. USA: Naturopathic Medical Press
- Yearman et al, (2004), 'Susceptibility to Thrombin-Induced Platelet Microbicidal Protein is associated with increased Fluconazole Efficacy against experimental endocarditis due to Candida Albicans', Antimicrobial agents and Chemotherapy, 48(8),pp.3051-3056. PubMed NCBI,US NLM
- Yin, R. K. (2003). Case Study Research. (3rd ed.). UK: Sage Publications
- Young, L.H., Dahl, D.M., Rauner, D., & Barrett, E.J. (1992). 'Physiological hyperinsulinaemia inhibits myocardial protein degradation in vivo in the canine heart'. Circ Res. 71(2), pp.393-400. National Institutes of Health, U.S. National Library of Medicine
- Yu – Lan, F. (1976). A Short History of Chinese Philosophy. USA: The Free Press
- Zachariadou, T., Stoffers, E.J.H., Christofi, A.C., Philalithis, A., & Lionis, C. (2008). 'Implementing the European guidelines for cardiovascular disease prevention in the primary care setting in Cyprus: Lessons learned from a health care services study'. BMC Health Services Research, 8(148) . NCBI, US NLM
- Zaracostas, J. (2010). 'Global cancer cases and deaths are set to rise by 70% in next 20years'. British Medical Journal, 340, p.3041. BMJ Publishing Group Ltd
- Zarcone, T. (2003). 'View from Islam, view from the West'. Diogenes, 50(4), pp.49-59, ICPHS, Sage Publications
- Zatouroff, M. (2005). Τα Κλινικά σημεία στην Παθολογία. (2^η έκδοση). Αθήνα: Ιατρικές Εκδόσεις Π.Χ. Πασχαλίδης
- Zeboudj, F.A., Imura, M., & Bostrom, K. (2001). 'Matrix GLA Protein, a regulatory protein for bone morphogenetic protein-2'. The Journal of Biological Chemistry, 277, pp.4388-4394.
- Zeisel, H.S., Allen, H.L., Coburn, P.S., Erdman, W.J., Failla, L.M., Freake, C.H., King, C.J., & Storch, J. (2001). 'Nutrition: A reservoir for integrative science'. Journal of Nutrition, 131(4), pp.1319-1321. The American Society for Nutritional Sciences

- Zhao, L.J., Liu, Y.J., Liu, Y.P., Hamilton, J., Recker, R.R., & Deng, H.W. (2007). 'Relationship of obesity with osteoporosis'. The Journal of Clinical Endocrinology and Metabolism, 92(5), pp.1640-1646
- Zhou, R., Fukui, M., Choi, J.H., & Zhu, T.B. (2009). 'Induction of a reversible, no-cytotoxic S-phase delay by resveratrol: implications for a mechanism of lifespan prolongation and cancer protection'. Themed Section: advances in nutritional pharmacology-Research paper, British Journal of Pharmacology, 158(2), pp.462-474. The British Society of Pharmacology, Wiley InterScience
- Zieman, J.S., Melenovsky, V., & Kass, A.D. (2005). 'Mechanisms, pathophysiology, and therapy of arterial stiffness'. Arteriosclerosis, Thrombosis, and Vascular Biology, 25, pp.932-943. The American Heart Association Inc
- Zimmermann, M. (2001i). Burgerstein's Handbook of Nutrition. Germany: Georg Thieme Verlag
- Zimmermann, M. (2001ii). Pocket Guide to Micronutrients in Health and Disease. Germany: Georg Thieme Verlag
- Zimmet, P. (2000). 'Globalization, coco-colonisation and the chronic disease epidemic: can the Doomsday scenario be averted?'. Journal of Internal Medicine, 247, pp.301-310. Blackwell Science Ltd
- Zoccollella, S., Iliceto, G., DeMari, M., Livrea, P., & Lamberti, P. (2007). 'Management of L-Dopa related hyperhomocysteinemia: catechol-O-methyltransferase inhibitors or B vitamins? Results from a review.' Clinical Chemical Laboratory Medicine, 45(2), pp.1607-1613. De Gruyter ReferenceGlobal
- Zunin D.I. & Wong M., (2006), 'Easter Origins of Integrative Medicine and Modern Applications', ch1, in Pizzorno E. J., & Michael T. M. (eds), (2006), Textbook of Natural Medicine, Volume 2, 3rd edition, Churchill Livingstone Elsevier.

SURVEY QUESTIONNAIRE

ΜΕΡΟΣ Α: ΔΗΜΟΓΡΑΦΙΚΑ ΣΤΟΙΧΕΙΑ

1. Έτος γέννησης

2. Φύλο:

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

Ανδρας	<input type="checkbox"/>
Γυναίκα	<input type="checkbox"/>

3. Ύψος εκατοστά

4. Βάρος κιλά

5. Πίεση

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

Πιο χαμηλή από την κανονική	<input type="checkbox"/>
Κανονική	<input type="checkbox"/>
Πιο ψηλή από την κανονική	<input type="checkbox"/>

6. Οικογενειακή κατάσταση

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

Έγγαμος/ η	<input type="checkbox"/>
Άγαμος/ η	<input type="checkbox"/>
Χήρος/α	<input type="checkbox"/>
Χωρισμένος/η	<input type="checkbox"/>

7. Αριθμός τέκνων

8. Σπουδές

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

Μέχρι Δημοτικό	<input type="checkbox"/>
Γυμνάσιο/Λύκειο	<input type="checkbox"/>
Κολλέγιο/Πανεπιστήμιο	<input type="checkbox"/>

9. Διαμονή

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

	Αστική	Αγροτική
Λευκωσία		
Λεμεσός		
Λάρνακα		
Πάφος		
Αμμόχωστος		

10. Επάγγελμα

.....

11. Πόσες ώρες εργάζεστε καθημερινά; ώρες

12. Είστε καπνιστής;

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

ΝΑΙ	
ΟΧΙ	

13. Είστε παθητικός καπνιστής; (κάποιος καπνίζει στον σπίτι, ή στο χώρο εργασίας)

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

ΝΑΙ	
ΟΧΙ	

14. Πόσο συχνά γυμνάζεστε το μήνα;

Σημειώστε Χ στο τετραγωνάκι που ισχύει στην περίπτωση σας

Καθόλου	
Αραιά (μερικές φορές τον μήνα)	
Ελαφρά άσκηση (1-2 φορές την εβδομάδα)	
Μέτρια (3-4 φορές την εβδομάδα)	
Συστηματικά (καθημερινά: πχ γυμναστήριο ή ποδήλατο ή κολύμπι ή γοργό περπάτημα ή άλλη εντατική άσκηση)	

15. Σημειώστε ποια από τα παρακάτω γεύματα τρώτε κάθε μέρα;

Σημειώστε Χ στα τετραγωνάκια που ισχύουν στην περίπτωση σας

Πρόγευμα	
Γεύμα	
Δείπνο	
Ενδιάμεσα σνακς	

ΜΕΡΟΣ Β: ΤΡΟΠΟΙ ΠΡΟΛΗΨΗΣ ΚΑΙ ΘΕΡΑΠΕΙΑΣ ΧΡΟΝΙΩΝ ΑΣΘΕΝΕΙΩΝ

16. Σημειώστε αν υποφέρετε ή υποφέρατε στο παρελθόν από κάποιο από τα πιο κάτω προβλήματα υγείας.

Σημειώστε Χ στο τετραγωνάκι (ή τετραγωνάκια) που ισχύει στην περίπτωση σας

Δεν υποφέρω ούτε υπέφερα στο παρελθόν από κανένα πρόβλημα υγείας	
Άγχος	
Αλλεργίες	
Αρθριτικά	
Άσθμα	
Δυσκοιλιότητα	
Αϋπνία	
Γυναικολογικά	
Δερματικά	
Διαβήτης	
Εντερικά (Φουσκώματα, ευερέθιστο έντερο, σπαστική κολίτιδα, διάρροιες, κλπ)	
Εξάρτηση από φάρμακα	
Θυρεοειδής	
Καρδιά	
Καρκίνος	
Κατάθλιψη	
Μύκητες	
Νεφροπάθεια	
Οστεοπόρωση ή οστεοπενία	
Ουρικό οξύ	
Παχυσαρκία	
Πέτρες στην χολή	
Πίεση	
Πονοκέφαλοι	
Προστάτης	
Στομάχι (φουσκώματα, έλκος, γαστρίτιδα, δυσπεψία, κλπ)	
Χοληστερόλη	
Άλλο πρόβλημα υγείας που δεν περιλαμβάνεται πιο πάνω	

ΠΡΟΛΗΨΗ ΚΑΙ ΘΕΡΑΠΕΙΑ ΧΡΟΝΙΩΝ ΝΟΣΗΜΑΤΩΝ ΣΤΗΝ ΚΥΠΡΟ

17. Σημειώστε αν κάνατε κάποιες από τις πιο κάτω θεραπείες για το πρόβλημα (ή τα προβλήματα σας)

Σημειώστε Χ στο τετραγωνάκι (ή τετραγωνάκια) που ισχύει στην περίπτωση σας

Εγχείρηση	
Με φάρμακα	
Με ειδική διαίτα	
Με διατροφικά συμπληρώματα (βιταμίνες, βότανα, κλπ)	
Ομοιοπαθητική	
Άλλη εναλλακτική θεραπεία (βελονισμός, χειροπρακτική, οστεοπαθητική, φυσιοθεραπεία, φυσικοπαθητική, βοτανοθεραπεία, μασάζ κλπ)	

18. Αν κάνατε περισσότερες από ένα είδος θεραπείας για το ίδιο πρόβλημα, με ποια σειρά τις κάνατε;

Σημειώστε στο τετραγωνάκι δίπλα από την κάθε θεραπεία την σειρά προτεραιότητας που την κάνατε με αριθμούς: 1, για την πρώτη θεραπεία, 2 για την δεύτερη κλπ

	Αριθμός
Εγχείρηση	
Με φάρμακα	
Με ειδική διαίτα	
Με διατροφικά συμπληρώματα (βιταμίνες, βότανα, κλπ)	
Ομοιοπαθητική	
Άλλη εναλλακτική θεραπεία (βελονισμός, χειροπρακτική, οστεοπαθητική, φυσιοθεραπεία, φυσικοπαθητική, βοτανοθεραπεία, μασάζ κλπ)	

19. Ποια θεραπεία πιστεύετε ότι ήταν η περισσότερο αποτελεσματική για το πρόβλημα σας;

Σημειώστε με αριθμούς τον βαθμό αποτελεσματικότητας (πχ 1:για την περισσότερο αποτελεσματική θεραπεία, 2:για την δεύτερη πιο αποτελεσματική κλπ.

	Αριθμός
Εγχείρηση	
Με φάρμακα	
Με ειδική διαίτα	
Με διατροφικά συμπληρώματα (βιταμίνες, βότανα, κλπ)	
Ομοιοπαθητική	
Άλλη εναλλακτική θεραπεία (βελονισμός, χειροπρακτική, οστεοπαθητική, φυσιοθεραπεία, φυσικοπαθητική, βοτανοθεραπεία, μασάζ κλπ)	

20. Συνεχίζετε να παίρνετε φάρμακα για το πρόβλημα υγείας για το οποίο κάνατε την θεραπεία (ή τις θεραπείες);

ΝΑΙ	
ΟΧΙ	

21. Πιστεύετε ότι έχετε θεραπευθεί εντελώς από το πρόβλημα για το οποίο κάνατε θεραπεία;

ΝΑΙ	
ΟΧΙ	

22. Σημειώστε ποια από τα παρακάτω διατροφικά συμπληρώματα χρησιμοποιείτε ή χρησιμοποιήσατε στο παρελθόν?

Σημειώστε Χ στα τετραγωνάκια που ισχύουν στην περίπτωση σας

Πολυβιταμίνες διάφορες	
Βιταμίνη Α	
Βιταμίνες Β	
Βιταμίνη Γ (Vitamin C)	
Βιταμίνη Δ (Vitamin D)	
Βιταμίνη Ε	
Φολικό οξύ (Folic acid)	
Ασβέστιο (Calcium)	
Μαγνήσιο	
Ψευδάργυρος (Zinc)	
Σίδηρος	
Σελήνιο (Selenium)	
Λάδι νυχτολούλουδου (Evening primrose oil)	
Αλόη Βέρα (Aloe Vera)	
Εχινάκια (Echinacea)	
Ginkgo Biloba	
Βασιλικός πολτός (Royal jelly)	
Ginseng	
Propolis	
Γύρις (fresh pollen)	
Γκουαράνα (Guarana)	
Σπιρουλίνα	
Συμπληρώματα σκόρδου	
Valeriana	
Μαγιά μύρας (brewer's yeast)	
Λεκιθίνη	
Milk Thistle	
Co Enzyme Q10	
Συμπληρώματα για χάσιμο βάρους (χρωμίου, καφεΐνης, πράσινου τσαγιού, Carnitine, Kelp κλπ)	
Συμπληρώματα για αθλητική απόδοση (Creatinine, Whey Protein, Glutamine, Arginine, Ornithine, CLA, BLAA, ισοτονικά ποτά κλπ)	
Παράγωγα σόγιας (γάλα σόγιας, ισοφλαιβόνες, τοφού κλπ)	
Ωμέγα 3 (Fish oil, Λάδι λιναρόσπορου, Linseed oil, Flaxseed oil, EPA/DHA, κλπ)	
Βότανα για δυσκοιλιότητα (Σέννα, φύλλα Αιγύπτου, τσάι με διάφορα βότανα, Psyllium κλπ)	
Probiotics (Acidophilus, Lactobacillus, κεφίρ, Inulac κλπ)	
Άλλα συμπληρώματα (αναφέρατε ονομαστικά πιο κάτω)	

23. Ποιος ειδικός σας συμβουλεύει για να πάρετε διατροφικά συμπληρώματα;

Σημειώστε X στα τετραγωνάκια που ισχύουν στην περίπτωση σας

Κανείς	
Ιατρός	
Ειδικός θεραπευτικής διατροφολογίας	
Διαιτολόγος	
Ομοιοπαθητικός	
Φαρμακοποιός	
Γυμναστής	
Πωλητής καταστήματος υγιεινής διατροφής	

24. Σε ποιο βαθμό είστε διατεθειμένοι, αντί να πάρετε φάρμακα, να ακολουθήσετε μια διατροφική θεραπεία η οποία θα απαιτούσε αυστηρή δίαιτα με αποχή από αγαπημένα σας φαγητά με αντάλλαγμα την πλήρη αποθεραπεία σας;

Σημειώστε X στο τετραγωνάκι που ισχύει στην περίπτωση σας

Καθόλου	
Λίγο	
Αρκετά	
Πολύ	
Πάρα πολύ	

25. Πόσο συχνά ακολουθείτε τις πιο κάτω θεραπείες όταν έχετε κάποιο πρόβλημα υγείας; *Σημειώστε X στο τετραγωνάκι που ισχύει στην κάθε περίπτωση πιο κάτω*

ΘΕΡΑΠΕΙΑ	ΠΟΤΕ	ΑΡΑΙΑ	ΣΥΧΝΑ	ΠΟΛΥ ΣΥΧΝΑ	ΠΑΝΤΟΤΕ
Με φάρμακα					
Με ειδική δίαιτα					
Με διατροφικά συμπληρώματα (βιταμίνες, βότανα, κλπ)					
Ομοιοπαθητική					
Άλλη εναλλακτική θεραπεία (βελονισμός, χειροπρακτική, οστεοπαθητική, φυσιοθεραπεία, φυσικοπαθητική, βοτανοθεραπεία, μασάζ κλπ)					

26. Σε ποιο βαθμό πιστεύετε ότι ο χρόνος που σας παρέχεται για να δείτε τον παθολόγο σας όταν είστε άρρωστοι, είναι αρκετός για να συζητήσετε διεξοδικά το πρόβλημα υγείας σας;

Σημειώστε X στο τετραγωνάκι που ισχύει στην περίπτωση σας

Καθόλου	
Λίγο	
Αρκετά	
Πολύ	
Πάρα πολύ	

27. Σε ποιο βαθμό πιστεύετε ότι σας δίνεται η ευκαιρία να συζητήσετε με τον γιατρό σας τα γενικότερα προβλήματα υγείας σας εκτός από το συγκεκριμένο πρόβλημα για το οποίο τον επισκεφθήκατε;

Σημειώστε X στο τετραγωνάκι (ή τετραγωνάκια) που ισχύει στην περίπτωση σας

Καθόλου	
Λίγο	
Αρκετά	
Πολύ	
Πάρα πολύ	

28. Σε ποια από τις πιο κάτω κατηγορίες εμπίπτει το καθαρό μηνιαίο εισόδημα της οικογένειας (συμπεριλαμβανομένου του εισοδήματος του/της συζύγου σας)

Σημειώστε X στο τετραγωνάκι που ισχύει στην περίπτωση σας

€0 – €1000	
€1001 – €2000	
€2001 – €3000	
€3001 – €4000	
€4001– €5000	
€5001 και άνω	

APPENDIX 2: CORRELATIONS BETWEEN HEALTH PROBLEMS

	Stress	Allergies	Arthritis	Asthma	Constipation	Insomnia	Gynaecologic Problems	Skin Problems	Diabetes	Bowel Problems	Drug Addiction	Thyroid Problems	Cardiovascular Problems	Cancer	Depression	Fungi	Kidney diseases	Osteoporosis	Uric Acid	Obesity	Cholelithiasis	Hypertension	Headaches	Prostate	Stomach Problems	Cholesterol	Other problems
Stress		0.140**	0.113*	0.061	0.184**	0.377**	0.177**	0.258**	0.044	0.220**	0.229**	0.004	0.063	-0.002	0.280**	0.154**	0.178**	-0.003	-0.037	0.162**	0.191**	0.055	0.345**	-0.021	0.203**	0.102*	-0.003
Allergies	0.140**		-0.029	0.177**	0.196**	0.171**	0.065	0.149**	-0.029	0.208**	-0.048	0.101*	-0.076	-0.051	0.127**	0.051	0.024	-0.023	-0.025	0.056	-0.048	-0.029	0.165**	-0.014	0.005	0.052	-0.038
Arthritis	0.113*	-0.029		0.053	0.022	0.201**	0.009	0.038	0.022	0.033	0.065	0.065	0.111*	-0.046	0.067	0.065	0.033	0.158**	0.184**	0.075	0.065	0.098*	0.092*	-0.013	0.098*	0.104*	0.009
Asthma	0.061	0.177**	0.053		0.093*	0.118*	0.078	-0.032	-0.036	0.012	-0.026	0.059	-0.041	-0.028	0.097*	0.059	-0.021	0.034	-0.014	0.072	0.059	-0.014	0.027	-0.008	0.089	0	-0.04
Constipation	0.184**	0.196**	0.022	0.093*		0.121**	0.046	0.076	0.06	0.125**	0.037	0.037	-0.052	-0.035	0.117*	0.037	-0.026	0.012	-0.017	-0.005	0.106*	0	0.169**	-0.01	0.056	0.018	
Insomnia	0.377**	0.171**	0.201**	0.118*	0.121**		0.101*	0.195**	0.033	0.159**	0.135**	0.194**	0.092*	0.07	0.396**	0.252**	0.114*	0.04	0.09	0.169**	0.252**	0.150**	0.346**	-0.012	0.287**	0.158**	0.02
Gynaecologic Problems	0.177**	0.065	0.009	0.078	0.046	0.101*		0.009	-0.049	0.023	-0.036	0.028	-0.014	0.023	0.148**	0.156**	0.131**	-0.047	-0.019	0.07	-0.036	0.019	0.173**	-0.011	0.09	0.078	0.033
Skin Problems	0.258**	0.149**	0.038	-0.032	0.076	0.195**	0.009		0.134**	0.151**	0.204**	0.126**	-0.046	-0.031	0.199**	0.204**	0.170**	0.023	0.132**	0.211**	0.204**	0.093*	0.243**	-0.009	0.129**	0.210**	0.063
Diabetes	0.044	-0.029	0.022	-0.036	0.06	0.033	-0.049	0.134**		-0.009	0.316**	0.037	0.133**	0.032	0.01	-0.033	0.148**	0.122**	-0.017	0.179**	0.106*	0.140**	0.065	0.219**	0.005	0.137**	0.046
Bowel Problems	0.220**	0.208**	0.033	0.012	0.125**	0.159**	0.023	0.151**	-0.009		0.139**	0.02	0.017	0.073	0.222**	0.139**	0.117*	-0.051	0.093*	0.135**	0.139**	0.005	0.149**	-0.012	0.250**	0.096*	0.023
Drug Addiction	0.229**	-0.048	0.065	-0.026	0.037	0.135**	-0.036	0.204**	0.316**	0.139**		0.069	0.208**	0.242**	0.254**	0.162**	0.213**	-0.031	0.164**	0.393**	0.348**	0.276**	0.269**	0.298**	0.102*	0.326**	-0.036
Thyroid Problems	0.004	0.101*	0.065	0.059	0.037	0.194**	0.028	0.126**	0.037	0.02	0.069		-0.038	-0.025	0.111*	-0.024	-0.019	0.042	-0.013	0.085	-0.024	0.136**	0.223**	-0.007	0.034	0.114*	-0.036
Cardiovascular Problems	0.063	-0.076	0.111*	-0.041	-0.052	0.092*	-0.014	-0.046	0.133**	0.017	0.208**	-0.038		0.137**	0.092*	0.085	-0.03	0.048	-0.02	0.144**	0.085	0.012	0.038	-0.011	0.127**	0.105*	0.112*
Cancer	-0.002	-0.051	-0.046	-0.028	-0.035	0.07	0.023	-0.031	0.032	0.073	0.242**	-0.025	0.137**		0.103*	0.153**	-0.02	0.108*	-0.013	0.137**	0.153**	-0.01	0.032	0.285**	0.095*	0.105*	-0.038
Depression	0.280**	0.127**	0.067	0.097*	0.117*	0.396**	0.148**	0.199**	0.01	0.222**	0.254**	0.111*	0.092*	0.103*		0.182**	-0.026	0.015	-0.017	0.281**	0.111*	-0.033	0.141**	-0.01	0.06	0.184**	0.001
Fungi	0.154**	0.051	0.065	0.059	0.037	0.252**	0.156**	0.204**	-0.033	0.139**	0.162**	-0.024	0.085	0.153**	0.182**		0.097*	-0.031	-0.013	0.208**	0.255**	0.042	0.223**	-0.007	0.375**	0.167**	-0.036
Kidney diseases	0.178**	0.024	0.033	-0.021	-0.026	0.114*	0.131**	0.170**	0.148**	0.117*	0.213**	-0.019	-0.03	-0.02	-0.026	0.097*		-0.025	-0.01	0.124**	0.213**	0.134**	0.188**	-0.006	0.058	0.162**	0.051
Osteoporosis	-0.003	-0.023	0.158**	0.034	0.012	0.04	-0.047	0.023	0.122**	-0.051	-0.031	0.042	0.048	0.108*	0.015	-0.031	-0.025		-0.016	0	-0.031	0.044	0.04	-0.009	0.01	0.067	0.054
Uric Acid	-0.037	-0.025	0.184**	-0.014	-0.017	0.09	-0.019	0.132**	-0.017	0.093*	0.164**	-0.013	-0.02	-0.013	-0.017	-0.013	-0.01	-0.016		-0.02	0.164**	0.151**	-0.028	-0.004	0.112*	0.077	-0.019
Obesity	0.162**	0.056	0.075	0.072	-0.005	0.169**	0.07	0.211**	0.179**	0.135**	0.393**	0.085	0.144**	0.137**	0.281**	0.208**	0.124**	0	-0.02		0.270**	0.198**	0.191**	0.191**	0.127**	0.210**	-0.057
Cholelithiasis	0.191**	-0.048	0.065	0.059	0.106*	0.252**	-0.036	0.204**	0.106*	0.139**	0.348**	-0.024	0.085	0.153**	0.111*	0.255**	0.213**	-0.031	0.164**	0.270**		0.089	0.177**	-0.007	0.307**	0.220**	-0.036
Hypertension	0.055	-0.029	0.098*	-0.014	0	0.150**	0.019	0.093*	0.140**	0.005	0.276**	0.136**	0.012	-0.01	-0.033	0.042	0.134**	0.044	0.151**	0.198**	0.089	0.164**	0.138**	0.099*	0.303**	0.014	
Headaches	0.345**	0.165**	0.092*	0.027	0.169**	0.346**	0.173**	0.243**	0.065	0.149**	0.269**	0.223**	0.038	0.032	0.141**	0.223**	0.188**	0.04	-0.028	0.191**	0.177**	0.164**		-0.016	0.195**	0.267**	-0.08
Prostate	-0.021	-0.014	-0.013	-0.008	-0.01	-0.012	-0.011	-0.009	0.219**	-0.012	0.298**	-0.007	-0.011	0.285**	-0.01	-0.007	-0.006	-0.009	-0.004	0.191**	-0.007	0.138**	-0.016		-0.01	0.160**	-0.011
Stomach Problems	0.203**	0.005	0.098*	0.089	0.056	0.287**	0.09	0.129**	0.005	0.250**	0.102*	0.034	0.127**	0.095*	0.06	0.375**	0.058	0.01	0.112*	0.127**	0.307**	0.099*	0.195**	-0.01	0.170**	0.170**	-0.051
Cholesterol	0.102*	0.052	0.104*	0	0.018	0.158**	0.078	0.210**	0.137**	0.096*	0.326**	0.114*	0.105*	0.105*	0.184**	0.167**	0.162**	0.067	0.077	0.210**	0.220**	0.303**	0.267**	0.160**	0.170**	0.170**	-0.068
Other problems	-0.003	-0.038	0.009	-0.04	-0.049	0.02	0.033	0.063	0.046	0.023	-0.036	-0.036	0.112*	-0.038	0.001	-0.036	0.051	0.054	-0.019	-0.057	-0.036	-0.014	-0.08	-0.011	-0.051	-0.068	

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed).

CASE STUDY 1 (X)**1. ASSESSING THE CLIENT'S NEEDS AND THE APPROPRIATENESS OF NUTRITIONAL THERAPY****a. SYNOPSIS OF CURRENT PRESENTING SYMPTOMS****DATA COLLECTION / METHODS**

A Patient Informed Consent Form was read and signed by the client before entering the consultation room

i. Requested before hand and provided by X at the 1st consultation

- Family medical questionnaire: X's babyhood and early childhood, family medical and lifestyle details, medication/supplements.
- Available biochemical, diagnostic and other laboratory tests and reports
- Doctors' previous diagnoses/reports
- Pharmaceutical drugs (Active ingredients, leaflets etc)

ii. Recorded in handwriting during the first consultation

- X's present and past medical history, lifestyle, and dietary habits

PORTRAIT OF THE CLIENT (*Appendix 4, Initial Consultation Worksheet*)

X visited the clinic with a number of serious problems. She complained that she felt toxic, painful and tired. Her hair was dull and oily and her skin had brown spots. Her psychology was very bad due to long-lasting family problems, and poor sleep due to pain. Her complaints included:

- Chronic gastrointestinal problems including, constipation (since childhood) with occasional bouts of diarrhoea, pain and bleeding, painful and bloated stomach difficult to digest meat. She had a medical diagnosis for ulcerative colitis for which she was prescribed Sulphasalazine tablets. Both a kinesiologist and a homeopath diagnosed Candidiasis. She used Begunis tea for constipation and caprylic acid for Candida. She was operated in the past to remove precancerous polyps in the colon. At that same time she was diagnosed with Irritable Bowel Syndrome.
- Chronic joint pains, stiffness and cramps, since her early 30s. She had medical diagnoses for severe osteoporosis, osteoarthritis and degenerative bone and cartilage changes. She was prescribed Joint Ace (glucosamine/chondroitin) and Voltaren. She had a cartilage operation in the past.
- High cholesterol and triglycerides
- Large volumes of urine daily but she felt she had water retention because her fingers were 'puffy' often.
- Circulatory: A lot of small thread veins and one medium size on her thighs
- Strong headaches, getting more frequent recently. Used aspirin
- Chesty cough and heavy catarrh. Sinus problem with green mucus all her life. Used a lot of antibiotics in the past for this
- Heavy periods since young age. Last summer had hormonal treatment to shrink an ovarian cyst. Took the Pill for many years in younger age. Period late onset (at her 14)

- X's life has been full of stress and unhappiness. Her father abandoned her mother while pregnant, and late in her life got married to a very demanding husband, who pushed her to have an abortion on the 5th month on her pregnancy (which she denied). Not long after her baby's birth he forced her to sterilisation to avoid future pregnancies. Her key-hole surgery was infected leading to septicaemia and emergency operation to save her life.

b. RATIONALE**INHERITANCE**

X's has a heavy inheritance of accumulated toxicity (cancer) and weakness of important organs and systems (digestive, circulatory, liver, immune) from the maternal side. Both grandparents died at early age from cardiovascular weakness. Mother, a heavy smoker and daily alcohol consumer, presents a strong liver picture and a seriously compromised immune as a result of severe bowel flora imbalances (chronic diarrhoea) and malabsorption leading to deficiencies of essential nutrients and mineral imbalances (poor arteries, fatigue, cancer, frequent infections, chronic headaches, hypertension, chronic joint pains), most importantly zinc (mouth ulcers, hypertension, poor memory, frequent infections) and calcium/magnesium imbalance (joint and muscle pains and stiffness, poor arteries).

PATHWAY OF DISEASE

Not surprisingly, interpretation and evaluation of X's data revealed severe gastrointestinal dysbiosis, evident from her chronic constipation, pain, bleeding, bloating and indigestion. Apparently, this condition was both inherited and acquired. Her digestive system had an environment with disturbed acidity and seriously imbalanced bowel flora, since birth (constipated), and this condition had worsened from the volume of antibiotics (for life-long sinus problems) and steroids (birth pills for 17 years in young age) together with an overloaded with meat, cheese and alcohol, acid-forming diet. This condition had led to malabsorption of nutrients from the small intestine, which in turn created:

- Mineral deficiencies/imbalances: particularly zinc (frequent infections, precancerous polyp, late menstruation and irregularities, abnormal birth delivery) and magnesium (cramps, poor musculoskeletal function, puffy fingers). The case of heavy metal (mercury) toxicity could not be ruled out, since X had too many mercury fillings until her mid 30s, allowing the reasonable suspicion of mercury leaking and accumulating for years in her body.
- Metabolic imbalances: such as poor fat handling (high cholesterol), sodium/potassium imbalance (joint pains, heavy periods, oily hair, sinus, headaches), and calcium mishandling (osteoporosis, osteoarthritis, shoulder calcification, joint and muscle stiffness and cramps). In addition, X's acid forming diet with lots of protein, starch and fats was an important stimulator of bone resorption through triggering parathormone secretion to restore blood pH.

WEAK AND COMPROMISED ORGANS/SYSTEMS IDENTIFIED:

- Compromised immunity, (septicaemia, precancerous polyps). Immune cells also participate in bone manufacturing process which is also malfunctioning.
- Weak circulatory system: (varicose veins, oedema)
- Lymphatic system: congested (mucus in chest, and sinus)
- Enterohepatic route: X, similarly to her mother, presents a strong liver picture, with a suppressed function of the enterohepatic route. Her liver is seriously compromised and malfunctioning, not properly handling and eliminating fats (high cholesterol), and toxic material (heavy catarrh) from the body leading to internal deposition of toxins (ovary cyst, colon polyps).

EVALUATION OF THE LIFE FORCE

Apparently, X's Life Force is seriously compromised. She is deeply chronic however her Life Force still demonstrates signs of a low degree of vitality, in the attempts to overthrow a volume of toxins through heavy periods and frequent colds with heavy catarrh. There is hope that a well designed deep constitutional therapy, with radical changes in her diet and lifestyle and adequate nutrient supplementation could significantly enhance her self healing mechanisms to throw out as much as possible of the inherited and acquired toxicity and support the efforts towards regression of the pathway of disease. It is important that the treatment is so designed as to promote simultaneous enhancement of the function of the body's eliminatory organs, which appear compromised especially the liver, bowel, and lymphatic, to avoid recirculation of toxins and self-poisoning.

c. RESOURCES, OPTIONS and RISKS

Before designing the treatment an evaluation of available resources and options as well as potential risks to the patient were taken into consideration as follows:

- X 's financial situation was not very good and therefore the cost of the therapy was kept to the minimum possible, using only those supplements considered essential for the wholistic therapy, and for some pain relief. This matter was discussed with the patient before preparation of the treatment.
- X was under medical treatment for her ulcerative colitis with Sulfasalazine tablets. Some other drugs and supplements mentioned were taken in the past, mostly for symptomatic relief, not regularly and at the time of the consultation she was not taking any on them. Therefore, careful investigation of possible interactions between sulfasalazine and prescribed dietary supplements was undertaken. No supplements with strong anticoagulant effect were included, in view of evidence demonstrating the possibility of Sulfasalazine to increase the effects of anticoagulants.
- X was diagnosed as highly toxic and in a state of chronicity, however due to the fact that her life force was demonstrating a degree of vitality, a smaller intensity of treatment was decided to avoid aggravations, especially taking into account her pains and ulcerations and the fact that she was under medication.

2. EDUCATING THE CLIENT

a. EXPLAIN THE SELECTION OF ASSESSMENT METHODS USED TO DETERMINE CLIENT TREATMENT

The first stage of the treatment was designed on the basis of the interpretation above (1b) and the attendant considerations (1c). The programme consisted of dietary guidelines and a list of nutritional supplements, (*Appendix 5*). The purpose of the first prescription (as outlined in the second page of the patient's treatment booklet (*Appendix 5, p.2*)) was to:

- i. Promote active elimination of the body's toxic load
- ii. Enhance liver function
- iii. Restore any possible nutrient deficiencies and mineral imbalances
- iv. Address the calcium dumping syndrome and osteoporosis
- v. Enhance immune system function
- vi. Restore bowel flora balance
- vii. Control blood sugar fluctuations

b. DIETARY ADVICE

(*Appendix 5, pp. 4-8*)

Special attention was taken, when constructing this diet, to remove all sources of toxins, to reduce protein intake in order to reduce liver workload, and to increase the ratio of omega3/omega6 essential fatty acids. Omega 3 EFAs perform several functions, relative to her health condition, such as: production of anti-inflammatory prostaglandins; inhibition of the arachidonic acid pathway which leads towards the production of pro-inflammatory prostaglandins, and promotion of the health of heart and the circulatory system. The importance of the intake of three meals and two snacks daily was highlighted at the first page of the diet to help stabilise blood sugar levels, essential for the patient's physical and psychological wellbeing.

Meats were not allowed in order to keep the protein content of the diet low; to discourage the putrefactive bacteria from thriving in the intestines; and to reduce the production of arachidonic acid in the body which promotes the production of pro-inflammatory prostaglandins. Fish was included for directional purposes, towards raising the omega3/omega6 ratio and the production of good prostaglandins and for contributing to the control of the intensity of the treatment. Dairy products were entirely excluded because, among their other adverse effects, they suppress liver function, leave hard residues on the bowel walls blocking the absorption of nutrients, make bowel flora alkaline encouraging zinc deficiency and encourage sodium entry into the cells leading to massive potassium loss. Nuts were included for their highly beneficial effect on health generally, but at limited quantities due to their high protein and fat content. Wheat products were also entirely excluded because among other things, they are highly acidic to the cells, suppress liver and intestinal function and block the production of prostaglandins series 1 which are important for immune function. Rye was excluded for being also acidic to the cells. Salt was eliminated to help restore sodium/potassium imbalance and promote de-sodiumisation and re-mineralisation of the cells. Increased sodium in the cells displaces potassium thereby suppressing cell energy production and the patients' life force. Sodium is

also a known zinc antagonist. Linseeds and pumpkin seeds were included for directional purposes, towards increasing the intake of omega 3 fatty acids. Linseeds were particularly included because they can improve digestion and prevent and reverse constipation, since they are an excellent natural laxative due to their mucilage content. They also, improve cardiovascular health by treating fatty degeneration in cardiovascular disease. Olive oil was included for its numerous beneficial effects on health, among which it decreases the synthesis of Leukotrienes B4 which are involved in the pain, redness and swelling that occurs in acute inflammation. Linseed oil was also included for its exceptionally high content of omega 3 essential fatty acids. All other oils were strictly excluded in order to maintain the desirable level of omega3/omega6 ratio and also to keep the fat content of the diet low. Nuts were allowed for their high nutritional value, but only sparingly, in order to keep in check their negative influence on the omega3/omega6 ratio. Walnuts were proposed as a first choice due to their higher omega 3 content compared to other nuts. Brown, short grain rice was a compulsory item in the diet due to its importance in facilitating second stage elimination. The use of potatoes and other grains was limited in order to allow the use of higher amounts of rice. Fruit were eliminated for the first two weeks to keep aggravations under control. This concern was related to the patient's ulcerative colitis which was active when she came for the consultation and her strong joint pains. All food containing yeast and other forms of fermentation (bread, vinegar, mushrooms) were also excluded within the context of the attempt to restore bowel bacterial balance. The need of daily consumption of specific vegetables (such as garlic and ginger) was stressed for their antibacterial effect in the bowel, as well as a list of vegetables and spices with known anti-oxidant properties. No dried fruit, honey or molasses were allowed for their sugar content which encourages the putrefactive bacteria. The importance of drinking and cooking with filtered, non chlorinated water was stressed

c. INITIAL SUPPLEMENT PROTOCOL WITH RATIONALE

(Appendix 5, p. 11)

The first stage of the treatment was designed to provide adequate supplementation for a rather low intensity of therapy, taking into consideration the patient's low financial resources and the condition of her health (*as described above*). The major concern was to embark on a degree of detoxification but at the same time include a directional element towards opening the routes of elimination (liver, bowel), in order to avoid serious aggravations, and to provide a degree of pain relief and mood enhancement to the patient. Choice of supplements was limited in the Cyprus market. From the therapeutic formulae, only Archturus were available.

The Archturus Basic Formula One was prescribed as the basic vitamin/ mineral formula which contained adequate magnesium for effective first stage (cell level) detoxification on one hand, but supplemented together with calcium in order to keep the intensity under some control. Patient was guided to start with very low dosage for the first week and then to double the dosage the following week. Inulac, a good probiotic available in the Cyprus market, together with Betaine/Pepsin HCl and Pancreatin were included as a good combination of the beneficial bacteria supplied together with the essential enzymes, required to provide the acidic environment for their survival and enhancement. In addition,

Glucosamine (combined with MSM as a painkiller) was included for its effect on gradually restoring degenerated cartilage. Increased dosage was prescribed initially to eliminate pain. In addition DL-Phenylalanine (DLPA complex) was included, to be taken only when needed, for pain, as well as for its mood enhancing, effects. To keep the prescription cost low, pantothenic acid, although considered important for its general action upon the well-being of the cells, was planned for the following stage when intensity would have been increased.

d. LIFESTYLE ADVICE

A significant part of the patient's handout was devoted to general lifestyle guidelines which included advice for healthy cooking, exercise, quality of food consumed, relaxation, and caution of environmental and other sources of toxins, (*Appendix 5, p. 9*).

In addition guidelines were given to help stabilise blood sugar levels, in order to avoid the effects of hypoglycaemia on the physical and emotional parts of the body, (*Appendix 5, p. 10*).

The last three pages (*Appendix 5, pp.12-14*) included a general guide-food plan and simple recipes specifically designed for the client.

e. SUMMARY

At the end of the first consultation, it was explained to the client that the nutritional therapy would be a multi stage process and the length and number of stages would depend on the intensity of the treatment and the progress of the patient. Any new stage would be decided after reviewing the progress of the patient during the previous stage and any symptoms, complaints, or other comments she might have. It was made clear to her that she would be an active participant to her treatment and that the nutritional therapy is not a diet with an expiry date but a new way of diet and lifestyle, a 'new page' in her life, and that the target is to get rid of, as much as possible, the old bad habits

3. EVALUATING AND REVIEWING EFFECTIVENESS OF NUTRITIONAL THERAPY

Due to the fact that the initial prescription was of a very low intensity, with a rather preliminary character, and in an attempt to monitor this specific patient more closely, she was asked to come for a second consultation earlier than usually.

2nd Consultation: (Duration of treatment: two weeks)

Client returned with the following comments

- Fells better overall and more active
- Bad headaches during the first day: alleviated with DLPA. After that she had them only twice in two weeks
- Ulcerative colitis: no symptoms
- At some point she had bad pain all over her body
- Developed mouth ulcers and her haemorrhoids were aggravated
- Constipation: very much improved, she has daily bowel movements, sometimes twice
- Weight: lost 2 kg
- Bloating: mild 1-2 hours after lunch time

2nd prescription: (*Appendix 6*)

In view of the patient's progress it was decided that the intensity of the treatment could be moderately increased at the second stage.

The Basic Formula One (containing the calcium to control the detoxifying effect of magnesium) was kept in the prescription but dosage increased. Calcium Pantothenate was added at a dosage of 2000mg daily to support adrenal function and handle aggravations. Attention was drawn to avoid taking this supplement in the evening due to its stimulating effect that might affect sleep. The rest of the supplements were left as the first prescription. Dietary changes included only the addition of one apple daily.

3rd Consultation: (Duration of treatment: four weeks)

Clients comments

- Feels 'much much better' very energetic!
- GI track: no pain, no bloating no vomiting, no constipation!
- Musculoskeletal pains and stiffness very much improved, she can walk for 40 minutes without pain
- Headaches: she had only one severe headache when she increased her formula
- Coughing: gone!
- Period: the lightest and least painful period she ever had!
- Urinate: reduced
- Water retention: improved

3rd prescription (*Appendix 7*)

In view of above progress, the patient was considered ready for a higher intensity, this time focusing on liver stimulation and support. Choline and Inositol Formula One –higher magnesium content but still calcium included- was added in full dosage (4 caps 3X daily), to substitute Basic Formula One. Calcium Pantothenate dose was reduced to 1000mg daily, since the patient had no significant aggravations to warrant the increased dosage and cost of this supplement. The rest of the supplements remained as previous prescription. Dietary changes included the addition of another fruit, increasing choices with pear and banana, and barley bread, (*barley is being extensively used for therapeutic purposes in the Mediterranean diet, and can be traced in the ancient treatises of Hippocrates, the Father of Medicine*)

4th Consultation: (Duration of treatment: 6 weeks)

Clients comments

- Lost 5kg in total
- Some dizziness at commencement of Choline & Inositol Formula one
- A vagina boil which lasted for 3 days
- Haemorrhoids also aggravated for 3 days
- Pains: almost gone!
- Ulcerative colitis: no more symptoms, no stomach pain, no vomiting even though she had gone through serious financial stress
- No more headaches
- Some constipation

4th prescription (*Appendix 8*)

The patient has made a great improvement in her health with many of her problems solved. However I had to make clear once again to her that health is not achieved with a two or three month nutritional programme and that she needs to follow the basic principles of healthy diet and lifestyle, as much as possible, for the rest of her life. I also advised her to have a consultation with her GP to review the state of her ulcerative colitis.

Consequently I proceeded to decrease her supplements gradually, while at the same time increased the intensity of treatment with Choline & Inositol Formula Two, which contains no calcium. Calcium Pantothenate reduced to 500mg daily and Pancreatin to two tablets daily. The plan was to further decrease supplementation at the next stage but the patient did not appear again. During the 4th consultation the patient stated that she had to move abroad where her husband was employed recently and she promised to continue her prescription and come back for the next appointment. However she did not appear again although she sent frequent regards and her gratitude for being pain-free and healthy.

Note: If X had entirely completed her treatment she would have received a final maintenance booklet with diet and lifestyle guidelines for the rest of her life as it happens with all patients who complete their treatments.

INITIAL CONSULTATION WORKSHEET

Name of the Patient: X

Date of Consultation: 24 January 2006

IRIDOLOGY EXAMINATION: 15 minutes
CASE HISTORY: 90 minutes

Time: 1 hour and 45 minutes

THE CASE HISTORY

1. PRELIMINARY DETAILS

i. Personal details

Name: X
Gender: Female
Age: 44 (27/6/61)
Height: 1.68m
Weight: 72 kg
Marital status: married with one daughter

Address:
Tel: home: mob:
Email:
Blood pressure: 120/70 mmHg

ii. Studies

iii. Occupation

Present: unemployed
Past: office manager

iv. Physical appearance

Skin: open pores, brown spots
Hair: dull and oily
Teeth: too many mercury fillings but removed them 10 years ago (age 34)
Nails: strong, but white spots occasionally
Eyes: she had radial keratotomy on right eye and laser treatment to improve her left eye short sight (12.75 degrees) (50% improvement)
Varicose veins: a lot of thread veins and one medium size on her thighs

2. MEDICAL LIFE HISTORY

i. The present condition focusing upon the past year

Rhesus negative

Musculoskeletal system:

- Osteoporosis: Diagnosed last month on the spine. The symptoms are pains on the neck, shoulder, arm, ribs. She saw a chiropractor but had no improvement. She was told that her bone density is of a 70 years old woman.
- Hip pain: she has it for the last 3 years. An x-ray showed nothing. She takes Joint ace for treatment and on and off and Voltaren for pain.
- Osteoarthritis: she was diagnosed last month with a neck disc worn away
- Cramps: she used to have frequent calf cramps but they stopped when her colitis started.
- Joint stiffness: Recently she has morning thumb joint stiffness

Bowels: She has chronic constipation. She has a bowel movement every 3 days and she actually never feels her bowel empty. She has frequent bouts of pain, and bleeding with bowel movements. Diagnosed with ulcerative colitis 3 months ago. When she is nervous or excited about something she gets some diarrhoea but not often. She uses Begunis tea for the constipation. She was prescribed Sulphasalazine tablets for her colitis which she takes for a month but she has not seen much improvement yet. Both a kinesiologist and a homoeopath told her that she has Candida.

Headaches: less often in the past but now she has them about twice weekly and takes aspirin.

Cravings: she has a lot of cravings for sweets. She took caprylic acid for some time.

Thrush: she had it three times in her life

Colds: she has chesty cough with heavy catarrh. She had sinus problems always with green mucus. She used to take a lot of antibiotics but not any more for quite a few years.

Stomach: she has pain with bloating. She noticed she gets indigestion with meat.

Sleep: she used to sleep well. Now her sleep is disturbed by pain (last 4 months)

Waterworks: she urinates quite a lot

Ovaries: Last summer she was diagnosed with an ovarian cyst. She was prescribed the Pill for one month and the cyst shrank

Menstruation: she always had, and still has, heavy bleeding, PMS: she feels irritated

Fatigue: she feels tired

Water retention: she feels her fingers puffy

ii. **Babyhood and pre-school years**

X's mother was 21 years old and healthy. However due to the fact that the father disappeared when he found out about her pregnancy she was very unhappy and anxious. After birth baby X had jaundice and she was given blood transfusion.

At 4 years old she had a hernia operation

Childhood diseases: Chickenpox

Other problems: Constipated all her life.

iii. **School years up to age 18**

At age 13-14: she had her first period

At age 17: she took the Pill for about 18 years up to age 35

iv. **Adult life up to a year ago**

At age 30: She had a cartilage operation on the knee and used steroidal creams

At age 39: she got married and had her baby

At age 40: she had her first pregnancy. During this period she had a lot of problems with her marriage. She had to have a Caesarean section because she was over her due date. She did not feel the baby. The doctor said the baby's heart was in distress. After the delivery, at 41 years old, she was sterilised because her husband did not want to take precautions.

At 41 years: she had an infection from the key-hole surgery (laparoscopy) for the sterilisation and had septicaemia. She went through an emergency operation to save her life.

At age 42: after a colonoscopy, she had precancerous polyps removed. She was then diagnosed with IBS.

3. DRUGS AND SUPPLEMENTS

For colitis: 112 Sulazine EC (Sulphasalazine)enteric coated tablets)

For hip pain: Joint Ace (glucosamine / chondroitin

For Candida: caprylic acid

For sinus: Sudafed

For eyes: Various eye creams

For osteoporosis: calcium 600mg twice daily

Wellwoman Multivitamins

4. MEDICAL TESTS/REPORTS/DOCTOR'S DIAGNOSES

Degenerative changes in joints

Reduction of the space between spine vertebrae

Loss of normal spine arc

Shoulder calcification

Cholesterol: 248 mg/dl High

Triglycerides: 229 High (normal 150)

LDL cholesterol: 143: high (normal 130)

Tests for liver, gallbladder and pancreas: normal

5. PSYCHOLOGY

X had an unhappy life. Her father disappeared when he found out about her mother's pregnancy. She was brought up by her grandparents.

X's husband is Lebanese. He is a very demanding man and during some time he had also financial problems that made him worse. When she was 5 months pregnant he asked her to have an abortion. He is better now.

6. LIFESTYLE

Alcohol: 1-2 glasses of red wine twice weekly

Smoking: used to be a social smoker (5 daily) and stopped last Christmas)

Exercises: not much due to back problems

7. FAMILY HISTORY

i. FATHER'S FAMILY

a. Father

X never met her father so she has no information of any of his family

b. Paternal grand father

c. Paternal grandmother

ii. **MOTHER'S FAMILY**

a. **Mother**

She is 65 years with one brother, two sisters and one cot death. She was the first child. She has wine daily. She was a heavy smoker all her life.

- Cervix cancer
- Chronic diarrhoea
- Frequent colds/infections
- Chronic headaches
- Hypertension
- Chronic joint pains
- Morning joint stiffness
- Frequent mouth ulcers
- Fatigue and muscle weakness
- Poor memory
- Skin brown stains
- Artery bypass

b. **Maternal grandfather**

He died from heart attack at age 59. He was the first of two children. He smoked about 20 cigarettes daily for many years

c. **Maternal grandmother**

She died at 62 from stroke. She was the third of 4 children

iii. **OFFSPRING**

iv. **BROTHERS AND SISTERS**

No brothers or sisters

v. **OTHER RELATIVES**

8. **DIET**

Recently she gave up dairy products. She takes soya, fish

i. **A TYPICAL DAY'S MENU during the last 3 months**

a. **Breakfast 6.00 am**

Aloe vera juice first thing

After 15 min: Jordan muesli with soya milk or porridge, pitta bread with halloumi or yoghurt and honey

b. **11.00 a.m**

A fruit or a bar of chocolate

c. **Lunch (2.30 pm)**

Brown and wild rice with noodles or

Meatballs (soya) (twice weekly soya) or

Fish (1-2 times weekly) or
beans with rice and boiled veg or
pasta twice weekly

She has no raw salads due to colitis. She eats only boiled vegetables
after lunch she wants something sweet

d. Dinner

Halloumi cheese with cucumber and tomatoes and brown pitta bread
Boiled egg

e. Snacks

Sugary things, chocolates and biscuits

f. Beverages

Herbal tea
One coffee daily

ii. A TYPICAL DAYS MENU before 3 months

More red meat, more wine, more chicken, a lot of cheese, and lot of yoghurt, olive
and lots of milk (she always drank a lot of milk since she was brought up in a farm)

NUTRITIONAL TREATMENT

For

X

Date of consultation: 24 January 2006



Duration

Two weeks

Date given to the patient

6 February 2006

Next consultation

2 weeks after commencing the treatment

This prescription was designed exclusively for X

THE PRESCRIPTION

This treatment is designed on the basis of the following the conclusions derived after rigorous examination and interpretation of the facts obtained from your case history, including your medical and family histories

The purpose of this prescription is to:

1. Promote active elimination of the body's toxic load
2. Enhance liver function
3. Restore, wherever possible, nutrient deficiencies and mineral imbalances
4. Address the calcium dumping syndrome and osteoporosis
5. Enhance immune system function
6. Restore bowel flora balance
7. Control blood sugar level fluctuations

This prescription represents the first stage of your treatment. It should be followed for a period of two weeks, so long as no adverse reactions occur in the meantime. Subsequent stages and changes to the prescribed diet and supplements will be decided after reviewing your progress and position during the next consultation. Due to the fact that the treatment aims to release toxins from the liver and other parts of the body, I must draw your attention to the possibility of inconvenient or troublesome symptoms that may occur upon the application of this prescription. It is possible that your present symptoms may actually be aggravated. In order that your condition is monitored carefully, you should report immediately back to me any significant alterations or adverse reactions that may occur. Further steps may have to be taken in order to ameliorate the symptoms, or perhaps some changes may need to be made to the diet or supplementation accordingly. Please use the private telephone number **XXXXXXXX** in case anything more sudden occurs. Minor changes and mild symptoms are signs that elimination is occurring successfully and they should be reported during the next consultation.

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THE DIET

Please note that you should take 3 meals daily at regular intervals and two snacks in between meals

- ✓ **Breakfast:** this should be the largest meal of your day
- ✓ **Lunch:** Normal size meal
- ✓ **Dinner:** This should be the lightest meal.
- ✓ **Snacks:** Two snacks daily in between meals consisting of rice cakes, fruits or vegetables (carrots, celery, etc)

MEAT

No meats are used in this diet.

FISH

Fish may be included at **three meals per week**, consisting of fresh or frozen fish but **not packaged frozen fish or canned or packaged fish products**. **Avoid** fish that has been **salted, cured or smoked**. Include some, at least, of the following: Fresh or frozen herring, eel, mackerel, salmon, sardines, tuna or cod roe. Shellfish or crustaceans (crab or lobster) may be taken once monthly, if fresh.

Caution! Avoid farmed fish.

EGGS

Two per week may be used.

Notes:

- **Eggs should be organic.** If you cannot find organic eggs it is better not to use any.
- **Please leave at least two days weekly without any animal food.**

FATS AND OILS

Use only olive oil in any heated dishes. In addition use edible **linseed oil** (one tablespoonful per day) as a salad dressing.

Caution!

- Linseed oil should be eaten raw (never heated) and should be kept refrigerated.
- Always buy oils (olive oil also) in **small dark, tightly closed, glass bottles** for maximum protection from light and oxygen. According to Dr Erasmus (1993) deterioration of oils by light starts from the minute they are exposed on supermarket shelves in light-coloured bottles. The best protection is **'no exposure to light and oxygen'**.

FRIED FOOD

Fried food is excluded, except for ***stir-fry vegetables***, if desired, using only quick cooking in a small amount of olive oil, avoiding any excessively high cooking temperatures. Use this method of cooking only 2-3 times per week.

DAIRY PRODUCE

NO DAIRY PRODUCE OF ANY KIND is used in this diet, so all forms of ***milk***, whether Pasteurised or not and from whatever animal, are excluded. Similarly are all kinds of ***cheese and yoghurt*** are excluded.

Beware of: packaged foods that contain 'hidden' milk in the form of ***milk powder, skimmed milk powder, sodium caseinate, lactalbumen*** or ***whey***.

Remember that dairy produce can occur in such diverse items as ***bakery products, meat products, desserts*** and ***margarines***.

OAT / RICE MILK

This may be used in moderation ie up to 150ml per day in place of other forms of milk.

SOYA BEAN MILK

This may be ***used in moderation***, for example, on porridge, on muesli, or in drinks, in place of ordinary milk. It is the heaviest form of vegetable protein to digest, so ***the quantity used should not be allowed to greatly expand***. It is not a very good idea, for example, to make rice puddings with it, because this employs too much soya milk.

Note: ***Buy only organic soya products made from whole soya beans.***

NUTS

Nuts can be sprinkled onto salads, used as the basis of main meals (e.g. nut roast, nut rissoles etc.) or turned into 'milk'. For the main-meal applications refer again to VEGAN cookery books, but use their recipes ***without the use of salt*** or salty condiments that they may recommend. Note the order of preference (in descending order): ***(1)Walnuts (2)Almonds (3) Cashews***, Only these three should ever be used as the main base of a meal, or for milks or spreads. Other nuts, e.g. Brazils/walnuts, are acceptable in small amounts in cakes (if any of these are included in the Diet) or in small amounts to chew as kernels. ***Chestnuts are fully acceptable***, but their protein content is negligible.

Caution! Never eat any nuts that smell or taste tangy. Keep all nuts in the fridge especially in summertime. Always buy walnuts in their shells and consume them immediately after taken off their shells. These guidelines are important in order to reduce to the minimum any possible oxidative damage.

SEEDS

Sunflower, sesame or pumpkin seeds may be used. These seeds may be added to muesli, sprinkled onto salads or used on or in cooked dishes. **Tahini**, from ground-up sesame seeds, is very good for spreading onto bread or toast (if the Diet contains them) or onto non-wheat bread or rice-cakes. **Make sure the tahini does not contain any extra vegetable oil** because this is usually hydrogenated vegetable fat. Please read the label before buying it. Furthermore take every day **one tablespoon of linseeds, freshly ground** (in a coffee grinder) and added to breakfast cereal or salads. Alternatively add to a large glass of water and drink immediately after grinding.

Caution! Grinding of the seeds is an advantage to digestion, but they should be **consumed immediately after grinding in order to avoid oxidative damage** to the essential fatty acids. All seeds should be consumed **fresh and unsalted**. They should be best **stored in the fridge in dark containers**, especially during summer time.

PULSES

Pulses are included because they are a protein concentrate, and hence can be used to replace meat, dairy produce etc. **Their full use is of great importance in cooking** for the Nutritional Therapy patient so please, make very full use of recipes which highlight these items. They can form the main item in a dish (such as lentil roast, bean casserole etc.) They can also enrich the homemade soup (lentils are a good thickener when liquidized}. Refer for this purpose to VEGAN cookery books and VEGAN recipes, but use them **without the additions of salt or salty condiments like soy sauce**, which they so often employ

GRAINS

WHEAT and RYE: This Diet contains **no wheat or rye**, so all bakery goods - bread, cakes, biscuits, pastry and pasta are excluded. Guard against getting '**hidden**' wheat in the form of flour included in formulated packaged products.

RICE (brown, organic, shortgrain) or millet, may be used **without limit**. Aim to consume **not less than 100g of RICE or MILLET per day** (with rice being the greater part). The weight given is the weight of the grain before cooking; it gathers 2-3 times its own weight in water, during cooking. Some of the rice may be taken in the form of **salt-free rice-cakes**. Please note that rice is a compulsory item in the diet since it will help elimination of toxins.

OATS may be used in porridge or homemade muesli, **once per day**.

Note: Soak oats for several hours before consuming them (from the previous night if they are to be consumed at breakfast). Oats need to be soaked in order to break down the phytates they contain which interfere with the absorption of nutrients from the gut.

Buckwheat, barley and sweetcorn may be used as occasional variations.

BREAD

No bread is allowed at this stage of the diet

POTATOES

Potatoes may be used subject to the condition that the rice or millet intake should not be compromised as a result. Discard any potatoes with sprouts or green areas.

VEGETABLES

It is very important that vegetable intake should be high (about **40%** of all food consumed).

Aim to take each day:

- a) Two cloves of **garlic** daily
- b) **Ginger root** (1-2cm square)
- c) One large bowl of home made **vegetable soup** slightly thickened with lentils, if desired. Bone stock from chicken or lamb may be used by non-vegetarians, if desired.
- d) One large **fresh salad**, imaginatively prepared using multiple salad vegetables along with grated carrots, red or white cabbage etc.
- e) **Cooked vegetables** with the main meal (boiled with minimum water, steamed or stir-fried as above).

Items a) to c) should be as plentiful and varied as possible

Items a) & b) each comprising a wide variety within each serving

The following vegetables have known anti-oxidant properties so give them preference:

Garlic, Cabbage, Red Cabbage, Red-Leaved Lettuce, Carrots, Celery, Parsley, Parsnips, Onions (especially red), Onions (green), Tomatoes, Aubergines, Broccoli (Broccoli helps the body get rid of the harmful type of oestrogen that promotes cancer), Cucumber, Kale, Cauliflower, Sweet Potatoes, Radishes, Brussels sprouts, Endives, Watercress, Pepper (capsicum). **Mushrooms are not included at this stage in your diet**

Caution!

Pepper, aubergines and **tomatoes** belong to the Nightshade family and contain natural **toxins** (Rudolph Steiner). Nonetheless, these vegetables are wholesome. Please place a limit on the use of these (taken together) of **150g/day**. **Spinach**, and **Swiss chard** (λάχανα Κυπριακά) do not belong to the same family but also contain other natural toxins. Please limit the amount of these (taken together) to **100g/day**.

SPICES AND HERBS

Herbs and **mild spices** are included wherever desired, so as to produce interesting flavours, and wherever corn has been included, **corn flour** may also be used occasionally, on a small scale, **as a thickener**. It not then **arrowroot** can almost always be permitted.

Caution! If possible buy organic spices

FRUIT

No fruit are allowed at this stage of your diet.

DRIED FRUIT

No dried fruit are allowed at this stage of your diet

HONEY AND MOLASSES

No honey or molasses are allowed at this stage of you diet

BEVERAGES

This diet includes **NO COFFEE, NO BLACK or GREEN TEA**

Use only the following:

- **Herb teas:** Use fresh infusions of Nettle, Ginger, Fennel, Lemon Verbena, Chamomile etc. Use blends of different herbs or vary the type you buy.
- **Grain-based coffee substitutes** such as, Barley Cup, Caro, Caro Extra or Yannah. Rooibosch tea. Dandelion coffee.
- **Water**

Nettle tea: Aim to drink 2-3 cups of good quality organic nettle tea every day in order to build up serotonin levels and strengthen kidney/adrenal function

WATER

Aim to drink, and cook with, filtered water. The best solution is to install an under sink reverse osmosis plant which will remove any pesticides, nitrates and nitrites, heavy metals, chlorine, PCBs, fluoride aluminium etc. It is essential that you drink at least **2 litres of good quality bottled water daily**. This is best drunk **at room temperature**, as iced water is not well absorbed by the body. Try to develop the habit of drinking the water gradually throughout the day (**sipping**), rather than too much at one time. The easiest way to do this is to have a bottle with you throughout the day and keep sipping from it. This is very important in order to help the body re-hydrate and rebalance. If you drink too much at a time, the water goes through you.

Note: Avoid drinking during meal times as gastric juices are diluted and digestion is impaired. Try to drink by the method of sipping, either 15 minutes before or 30 minutes after meals.

EXCLUDE

In addition to the items already mentioned, exclude the following:

- ▶ **Salt.** Alternatively you can use any **salt substitute** based wholly upon **potassium**, such as **Hipposal** (it is sold in local health shops)
- ▶ **Sugar** of all kinds,
- ▶ **Frozen or canned fruit or vegetables,**
- ▶ **Texturized soya,**
- ▶ **Confectionery, ice-cream, chocolate,**

Nitsa Kiliari

Nutritional Medicine Practitioner

- ▶ **Carbonated beverages, sodas and squashes,**
- ▶ **Alcohol,**
- ▶ **Vinegar**
- ▶ **Yeast or yeast extract, Oxo, Marmite, Bovril, Vecon** and related products whether as **cubes** or as **pastes, soy sauce, miso, tamari,**
- ▶ **Made-up meat products** such as sausages, burgers, faggots, luncheon meat and
- ▶ **All canned products.**

GENERAL GUIDELINES

COOKING

- ◆ Food must never come in contact with direct heat. Always cook food covered in **glass or stainless steel containers** and try, as much as possible, to cook slowly under **low fire**. Very high temperatures produce cancerous substances in our food. The safest and more nutritious food is that cooked in water (**boiled**) or **steamed**. Water can never reach temperatures higher than its steaming point. So, contrary to conventional beliefs, the healthier part of bread is the soft inner part, which is actually steamed, not the crunchy outer part.
- ◆ Never use aluminium utensils or **aluminium foil** when cooking. Rapidly accumulating scientific evidence demonstrates high aluminium content in the brains of **Alzheimer's patients**.
- ◆ Wherever possible, **add the olive oil at the end of cooking**, a few minutes after removing food from fire. By this way you significantly reduce the risk of creating **free radicals** in the food.

EXERCISE

Take any form of exercise which you enjoy and which you can sustain for a minimum of 45 minutes at least 4 times per week. Perform a relaxation exercise (deep breathing, meditation, prayer, etc) 10-15 minutes daily.

The slant board: use it daily for about 5-10 minutes to improve blood and oxygen circulation to the head and brain area. The regular use of the slant board reverses the long-term bad effects of gravity on the brain and the spine.

QUALITY OF FOOD

Consume a diet that focuses on whole, unprocessed foods (whole grains, legumes, vegetables, fruits, nuts and seeds). Try to **eat organic produce** wherever possible, in order to eliminate the intake of more toxins and to ensure adequate supply of nutrients.

OVEREATING

Do not overeat. The body uses high amounts of energy to digest and process food. Energy is much needed for the body's detoxification processes and should not be wasted. Aim to feel light and comfortable after a meal.

RELAXATION

Relax during meals and eat slowly, chewing your food well. Do not eat if you are upset or stressed, as your digestion will be affected. Please note that food eaten under stress turns into bad energy into your body.

ENVIRONMENTAL TOXINS

Reduce chemical exposure from environment by avoiding the use of household chemical products (aerosols, insect sprays etc), gardening sprays and chemicals, cosmetics and hairsprays and oil and petrol fumes.

GENERAL GUIDELINES TO STABILIZE BLOOD SUGAR LEVELS

- ◆ Never eat carbohydrates alone. Eat them with protein or fatty food.
- ◆ Eat fewer carbohydrates if you are sedentary and/or overweight; eat more if you are active.
- ◆ Eat three small meals and two snacks daily.
- ◆ Strictly avoid any products containing sucrose, fructose, maltose, dextrose, polydextrose, corn syrup, maple syrup, molasses, sorbitol, maltodextrin. Always check the labels. Food products containing sugar and chemicals include barbecue sauces, fish sauces, ketchup, relishes, sweet pickles, Worcestershire.
- ◆ Strictly avoid smoked or cured meats which contain N-nitro-compounds. This substance is similar in structure and function to a compound (streptozotocin) that is used to induce diabetes in studies with animals (Pizzorno et al, 2002, p100)
- ◆ Strictly avoid salt and any hidden sources of it such as, soda bicarbonate (the common baking powder), and salted packaged food. The entry of insulin inside the cells in order to burn the glucose depends on salt which acts as a carrier. Excess of salt upsets this process and insulin cannot burn the sugar. (*this is an oversimplified prescription of the sodium pump function, to make it easily understood*)

SUPPLEMENTATION

→ **Archturus Basic Formula One (180Caps)**

Take one capsule with each of three meals (total 3 capsules daily) for one week and then increase to 2 capsules with each of three meals (total 6 capsules daily)

Note: This is the main mineral/vitamin formula

→ **Archturus Glucosamine & MSM**

Take 3 capsules with each of three meals (total 9 capsules daily). When pain recedes reduce to 2 capsules with each of three meals (total 6 capsules daily)

→ **Inulac Tablets**

Chew one tablet followed with a large glass of water half hour before breakfast. After one week add another tablet in the evening before sleep (total 2 tablets daily)

Note: Probiotics may initially increase flatulence and bloating and may cause mild diarrhoea. If discomfort continues, reduce intake and increase the dosage gradually.

→ **Nature's Plus Pancreatin tablets 1000mg**

Take one tablet just 10 minutes before each of three meals (total 3 tablets daily)

→ **Archturus Betaine/Pepsin HCl tablets**

Take 2 tablets 10 minutes before each meal.

→ **Organic Linseed (Flaxseed) oil**

Take one tablespoon daily. Linseed oil should not be heated. It should be eaten raw.

Note: If you cannot take linseed oil order the linseed capsules and take 6 capsules daily with meals

Please keep linseed oil always tightly closed and refrigerated.

→ **Organic Flaxseed Meal**

Take two tablespoonfuls daily in a large glass of water or add it to your muesli.

Please keep linseeds always tightly closed and refrigerated.

TAKE THE FOLLOWING ONLY WHEN NEEDED
FOR HEADACHES MIGRAINES OR OTHER PAIN

→ **Archturus DLPA Complex**

1 to 2 capsules 15 - 30 minutes before each meal (up to a maximum of 5 capsules daily). This supplement is most effective when taken half an hour before any meal or at bedtime

Caution

DLPA Complex must not be taken by Phenylketonuria sufferers (PKU). DLPA Complex should not be used with MAO inhibitors (a type of anti-depressant medicine). Not recommended for pregnant or lactating women.

FOOD PLAN - GENERAL GUIDE

The following recipes represent only some general guidelines to a healthier way of eating. Use your imagination to create your own recipes with the ingredients you prefer, as long as they are contained in your dietary programme.

BREAKFAST

Muesli with soya milk

Fill a breakfast bowl with:

- 2-3 tablespoonfuls oat flakes (soaked overnight) . You may use a mixture of pre-soaked oat, barley and rice flakes (3 tablespoons in total)
- one tablespoon pumpkin seeds (raw unsalted)
- one tablespoon sunflower seeds (raw unsalted)
- 1 tablespoonful freshly ground linseeds (grind them just before use)
- A glass of organic soya milk (Alternatively you can use rice milk or oat milk or water)

MID-MORNING OPTIONS

- Herb tea
- 2 rice or oat cakes spread with a little home made Houmous or tahini
- Vegetables (celery, carrots, cucumbers etc.)

How to cook brown rice

We need 2 ½ glasses of water (sometimes a bit more) for one glass of rice. Measure the water and boil it. Pour the rice (which you have washed well) stir it once and cover it. Lower the heat to 1/3 of the maximum. Make sure steam does not escape from the pot. Leave to cook for about 40 minutes, **WITHOUT OPENING IT OR STIRRING IT AGAIN.** With small portions cooking might take a little less, perhaps 35 minutes.

LUNCH or DINNER OPTIONS

Please try to eat your dinner before 8.00 pm and eat smaller portions for dinner compared to lunch. Do not eat anything after dinner except for relaxing herbal teas. Do not drink water with you meals. Allow about half an hour after meal and drink water by sipping.

1ST OPTION

Fish ,(preferably prepared by steaming, poaching or even baking in a covered glass or stainless steel container. This minimises damage or oxidation to the natural fish oils/essential fatty acids). Tinned tuna may also be used occasionally, though the brine water should be

rinsed off). Serve with boiled short grain **brown rice**, steamed **vegetables** and fresh **salad**. Use some **olive oil** and **lemon** for dressing. Add freshly ground **black pepper** or other **spices** of your choice.

2nd OPTION

Beans (haricot, chickpeas etc) with boiled or fresh vegetables served with olive oil and lemon. Alternatively beans can be cooked with fresh tomatoes, onions and spices. Serve with **rice cakes**

3rd OPTION

Lentils with **brown rice**, onions, olive oil and spices. Serve with steamed **carrots, broccoli or cabbage**.

4th OPTION

Freshly prepared **vegetable soup**. Steam the vegetables and put them all in the liquidiser with a little **tahini, garlic, lemon, black pepper** and any spices or herbs of your choice. Serve with **rice cakes**

5th OPTION

Brown rice boiled. Stir in a little turmeric and serve with **fresh salad** or steamed **vegetables**. Add some **pumpkin seeds** and half an **avocado** to the salad. Use olive oil and lemon for dressing.

6th OPTION

Beetroot salad made with **beetroots, potatoes**, fresh **onions**, one organic **egg**, and fresh **vegetables** of your choice (coriander, parsley etc). Add olive oil and lemon

7th OPTION

Rice or corn pasta made with home made **pesto sauce** or home made **tomato sauce** or **stir-fry vegetables** and **spices**. Serve with **fresh salad**

The Pesto Sauce

Put in a small mixer fresh or dried basil leaves, olive oil, pumpkin seeds, garlic, black pepper and add some of the water in which you have boiled the pasta. Make a delicious green paste and mix it with the pasta.

8th OPTION

Stuffed vine leaves, courgettes, onions and eggplants. Serve them with **fresh salad**.

Instructions:

Mixed brown rice with chopped **onions, leeks, mushrooms, tomatoes, pine** or blanched **almond** nuts, olive oil, lemon, herbs, spices and any vegetables you like (artichokes cut in very small pieces make a good stuffing). Mix them all together and stuff the vine leaves and any vegetables available (courgettes, aubergines, onions etc). Cook them in the oven in a covered glass or stainless steel container. Always cook your food at low temperatures (not higher than 190). Serve them with **fresh salad**.

9th OPTION

A large fresh salad made with any vegetables of your choice plus **walnuts, pumpkin seeds, ground linseeds** and **avocado**. Use olive oil and lemon for dressing. Alternatively, you may use a tablespoonful of **tahini** for dressing. Serve with **rice cakes**.

10th OPTION

Boil brown rice with a little turmeric. Keep it aside and prepare your vegetables.

Put in a pan a little olive oil and different vegetables such as, onions, peppers, courgettes, carrots, cabbage, peas or any other vegetables you like. Add herbs, such as oregano, thyme, cumin, as well as spices of your choice. If you like black pepper use it freely. You can add some carry powder if you like it.. Stir fry keeping low heat all the time. When the vegetables are slightly soft, add the rice into the pan and stir it in for a few minutes.

AFTERNOON OPTIONS

- Herbal tea
- Two rice cakes
- One fruit

EVENING

Relaxing herbal teas only.

X
23/2/06
Second prescription

- **Archturus Healthlink Basic Formula 1 (180Caps)**
Start increasing your daily dose gradually until you get up to 4 capsules with each of three meals (total 12 capsules daily)
Note: This is the main mineral/vitamin formula

- **Archturus Calcium Pantothenate (500) mg**
Take two capsules with your breakfast and two capsules with your lunch (total of 4 capsules daily) for two weeks. Avoid taking in the evening

- **Archturus Glucosamine & MSM**
Take 3 capsules with each of three meals (total 9 capsules daily). When pain recedes reduce to 2 capsules with each of three meals (total 6 capsules daily)

- **Inulac Tablets**
Chew one tablet followed by a large glass of water half hour before breakfast and one in the evening before sleep (total 2 tablets daily)

- **Nature's Plus Pancreatin tablets 1000mg**
Take one tablet just 10 minutes before each of three meals (total 3 tablets daily)

- **Archturus Betaine/Pepsin HCl tablets**
Take 2 tablets 10 minutes before each meal.

- **Organic Linseed (Flaxseed) oil**
Take one tablespoon daily. Linseed oil should not be heated. It should be eaten raw. Please keep linseed oil always tightly closed and refrigerated.

- **Organic Flaxseed Meal**
Take two tablespoons daily in a large glass of water or add it to your muesli. Please keep linseeds always tightly closed and refrigerated.

TAKE THE FOLLOWING ONLY WHEN NEEDED
FOR HEADACHES, MIGRAINES OR OTHER PAIN

- **Archturus DLPA Complex**
1 to 2 capsules 15 - 30 minutes before each meal (up to a maximum of 5 capsules daily). This supplement is most effective when taken half an hour before any meal or at bedtime
Caution
DLPA Complex must not be taken by Phenylketonuria sufferers (PKU). DLPA Complex should not be used with MAO inhibitors (a type of anti-depressant medicine). Not recommended for pregnant or lactating women.

DIET CHANGES/ADDITIONS

Fruit: add one green apple daily in your diet. Please do not eat apples with brown spots indicating the presence of yeast

X
9/3/06
Third prescription

- **Archturus Choline & Inositol Formula One (180 caps)**
Take 4 capsules three times daily with meals (total of 12 capsules)

- **Archturus Calcium Pantothenate (500) mg**
*Take one capsule with your breakfast and one with your lunch (total of 2 capsules daily).
Avoid taking in the evening*

- **Archturus Glucosamine & MSM**
*Take 2 capsules with each of three meals (total 6 capsules daily). When pain recedes
reduce to 4 capsules daily*

- **Inulac Tablets**
*Chew one tablet followed by a large glass of water half hour before breakfast and one in
the evening before sleep (total 2 tablets daily)*

- **Nature's Plus Pancreatin tablets 1000mg**
Take one tablet just 10 minutes before each of three meals (total 3 tablets daily)

- **Archturus Betaine/Pepsin HCl tablets**
Take 2 tablets 10 minutes before each meal.

- **Organic Linseed (Flaxseed) oil**
*Take one tablespoon daily. Linseed oil should not be heated. It should be eaten raw.
Note: If you cannot take linseed oil order the linseed capsules and take 6 capsules daily
with meals
Please keep linseed oil always tightly closed and refrigerated.*

- **Organic Flaxseed Meal**
*Take two tablespoonfuls daily in a large glass of water or add it to your muesli.
Please keep linseeds always tightly closed and refrigerated.*

TAKE THE FOLLOWING ONLY WHEN NEEDED
FOR HEADACHES MIGRAINES OR OTHER PAIN

- **Archturus DLPA Complex**
*1 to 2 capsules 15 - 30 minutes before each meal (up to a maximum of 5 capsules daily).
This supplement is most effective when taken half an hour before any meal or at
bedtime*
Caution
*DLPA Complex must not be taken by Phenylketonuria sufferers (PKU). DLPA Complex
should not be used with MAO inhibitors (a type of anti-depressant medicine). Not
recommended for pregnant or lactating women.*

DIET CHANGES/ADDITIONS

FRUIT

Limited to ***apple, pear or banana***, no more than ***two fruits per day***. No fruit juice or tomato juice. Citrus fruits are not allowed at this stage.

BREAD

Barley bread may be used at one meal per day, made with wholemeal barley and sour dough. Alternatively barley rusks, made with sour dough, can be used for meals in the office. Please ***make sure they don't contain wheat or rye***. Always read the labels.

X
23/3/06
Fourth prescription

- **Archturus Choline & Inositol Formula Two (180 caps)**
Take 4 capsules three times daily with meals (total of 12 capsules)

- **Archturus Calcium Pantothenate (500) mg**
Take one capsule with your breakfast

- **Archturus Glucosamine & MSM**
Take 2 capsules with each of three meals (total 6 capsules daily). When pain recedes reduce to 4 capsules daily

- **Inulac Tablets**
Chew one tablet followed by a large glass of water half hour before breakfast and one in the evening before sleep (total 2 tablets daily)

- **Nature's Plus Pancreatin tablets 1000mg**
Take one tablet 10 minutes before each of two main meals (total 2 capsules daily)

- **Archturus Betaine/Pepsin HCl tablets**
Take 2 tablets 10 minutes before each meal.

- **Organic Linseed (Flaxseed) oil**
Take one tablespoon daily. Linseed oil should not be heated. It should be eaten raw.
Note: *If you cannot take linseed oil order the linseed capsules and take 6 capsules daily with meals*
Please keep linseed oil always tightly closed and refrigerated.

- **Organic Flaxseed Meal**
Take two tablespoonfuls daily in a large glass of water or add it to your muesli.
Please keep linseeds always tightly closed and refrigerated.

TAKE THE FOLLOWING ONLY WHEN NEEDED
FOR HEADACHES MIGRAINES OR OTHER PAIN

- **Archturus DLPA Complex**
1 to 2 capsules 15 - 30 minutes before each meal (up to a maximum of 5 capsules daily). This supplement is most effective when taken half an hour before any meal or at bedtime
Caution
DLPA Complex must not be taken by Phenylketonuria sufferers (PKU). DLPA Complex should not be used with MAO inhibitors (a type of anti-depressant medicine). Not recommended for pregnant or lactating women.