

MYELOMA CASE STUDY - The case of the 0.005% survivor.

A special study of a remarkable long term survival in Multiple Myeloma presented with full medical records, and details of orthomolecular and other treatments involved.

The following case-history of a remarkable survivor of Multiple Myeloma is taken from the book *Living Proof* by Michael Gearin-Tosh, published by Simon & Schuster UK Ltd, February 2002, and by Scribner in the US, April 2002, ISBN 0-7432-0677-0, available from Amazon.

FOREWORD

This Case History has been written primarily for interested physicians, oncologists and Myeloma researchers. Well-informed lay readers should be able to understand Michael's protocols from this account, - a glossary is provided, as are tables to which reference is made in the text.

The Case History has been peer-reviewed by Dr Peter Gravett MB MRCS FRCPath of the London Clinic, and Professor Ray Powles MD BSc FRCP FRCPath, Professor of Haematological Oncology, Head of the Leukaemia and Myeloma Units at the Royal Marsden, Sutton, Surrey, and Dr Robert Kyle MD, Professor of Medicine, at the Mayo Clinic. I would like to thank them both for their kind attentiveness, rigorous critique, and generosity with their time.

MULTIPLE MYELOMA - THE CASE OF THE .005% SURVIVOR

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INTRODUCTION

"Multiple myeloma is incurable", the textbooks tell us. (1,2) Median survival depends on the stage at diagnosis and can range from six months to five years. (3) Long term survival is virtually unknown, but not quite. The 1992 survival curve for an unselected series of 156 patients at St Bartholomew's Hospital shows a 2.5% survival at 10 years. (4) A much earlier study at the Mayo Clinic, covering 870 cases, found a not dissimilar total survival rate at 10 years of 2.2%, with a 3% survival for those 597 patients diagnosed in the 1964 onwards, post-chemotherapy, Melphalan era. (5) But among the 273 patients diagnosed in 1960-63, the chemo "virgins", there was only one 10 year survivor, a survival rate of 0.4%. This rare study of long-term survival in Multiple Myeloma observed 19 patients survive beyond 10 years, only 5 of whom were still alive at the conclusion of the study, one of these in his 18th year, and 8 years out from standard chemotherapy treatment, still, miraculously, free of any evidence of Multiple Myeloma. Even the newer treatment approaches of high dose combination chemotherapy with stem cell support, (6) with or without alpha-2-interferon, (7) bisphosphonates (8) or thalidomide, (9) have done little so far to change the outlook for long term survival and cure. In the world of haematological cancers, Multiple Myeloma is both at the most malignant end of the spectrum in relation to other B-cell neoplasms, and still the most elusive in terms of cure, though understanding

of its molecular and genetic basis, (10) pathogenesis and management has vastly increased in the last decade, to a point which may shortly bear fruit, in novel, more targeted approaches. (11) At present however, the rate of attrition in this disease remains grim and undeniable.

Case History

Michael Gearin-Tosh, aged 54 years, was diagnosed with Multiple Myeloma, IgG lambda, in June 1994. He presented with a chest infection, with "signs in his chest indicating he was suffering from bronchitis". (12) His principal symptom, severe night sweating, along with fatigue and some dehydration, led his doctor to investigate things further. Anaemia, (HB 9.4 and mildly macrocytic), an unusually raised Erythrocyte Sedimentation Rate (125), and the presence of paraprotein in the serum (Table 1), prompted a referral to a haematologist. A skeletal X-ray survey, electrophoresis and bone marrow aspirate confirmed a diagnosis of Multiple Myeloma, (Tables 2 and 3), and it was proposed that chemotherapy with Melphalan be instituted immediately. The patient decided to take a little time to thoroughly consider the proposed course of action. At this point the author of this paper suggested to him that he seek a second opinion, partly to ensure that a differential diagnosis of MGUS could be firmly ruled out, and/or to ascertain the exact staging of the disease, since in pre-Stage I Myeloma active treatment can be reasonably deferred, sometimes for years. (13) In the event, in the two months that followed, a total of three bone marrow aspirates were done (Table 3), and no less than four medical opinions were obtained at top institutes. (Fifth and sixth opinions on the basis of the extant medical data were sought in early September 1994 from Dr Bart Barlogie, and Professor Sid Salmon. A seventh opinion was sought in early 1995 from Dr Robert Brouillard at Scripps Memorial Hospital, La Jolla, California.) Whilst the bone marrow aspirates are critical to a diagnosis of Multiple Myeloma, it is both surprising and disappointing that not one of the 3 (or even the 4th done in 1996), should have included a Plasma Cell Labelling Index, let alone any cytogenetic investigation. The Bone Marrow Trepchine Histological report notes the presence of "atypical plasma cells consistent with involvement by Myeloma", but does not go on to elaborate the qualitative abnormalities of these plasma cells. The first Bone Marrow Aspirate (Table 4) did not even specify the percentage of plasmacytosis, and yet, on the basis of this, the patient was, as he has phrased it, "being rushed to treatment." There is a paradox that should be noted here: on the one hand, less than meticulous diagnostic procedures are used to justify possibly life-threatening treatment. On the other, when it comes to the question of proof, as in the demand for proof of unorthodox therapies such as the patient eventually adopted, the medical establishment feels equally no hesitation in demanding Olympian standards of proof. From a scientific viewpoint, there is a certain inconsistency here.

Multiple Myeloma proceeds through a number of phases and stages: MGUS (Monoclonal Gammopathy of Unknown Significance), which is characterised by the presence of monoclonal protein in the serum, without other symptoms, and can last anywhere between 10 to 20 years or more, (14)

corresponding to the latency period now acknowledged to be a feature of most solid tumours; Smouldering Myeloma; Indolent Multiple Myeloma; and Overt Multiple Myeloma, which in turn is divided into 3 stages. (Salmon and Durie). Two haematologists at the John Radcliff, Oxford, and one at the Royal Marsden, Sutton, independently diagnosed the patient as having Stage I Multiple Myeloma. The patient fulfilled one major, and several of the minor, Salmon and Durie criteria (13) for active or overt Multiple Myeloma Stage I. The major criteria fulfilled by the patient was a serum 'M' component of IgG >35g/l: the patient's initially ranged between 37g/l and 31g/l at the 2nd and 3rd opinions. Subsequently over seven years 8 out of 13 readings of his M component have ranged well above >35g/l, up to a high of 45.3g/l, and at the last record 35.4g/l. Salmon and Durie Minor Criteria for Stage I Multiple Myeloma include a bone marrow plasmacytosis of 10-30%: (Depending on site, the patient's ranged from 5-6%, "in keeping with remission", to 22%. This apparent anomaly in such a short space of time is a well-known phenomenon to diagnosticians, and merely the result of sampling at different sites. The higher percentage, from the sternum in this case, is the more meaningful one for diagnosis.) Minor Criteria also includes an immune paresis in suppression of normal IgM and IgA immunoglobulins, which the patient had, (Table 2); anaemia <10.4: the patient's HB was 9.4 one week before diagnosis, at which point it was 10.2 (Table 1); the patient also had diffuse myelomatosis though without apparent lytic lesions (Table 4). According to Salmon and Durie, one major and one minor criteria fulfilment is acceptable for a diagnosis of Overt Multiple Myeloma, as opposed to just Smouldering, Indolent Myeloma, or MGUS. The patient had 1 major and 4 minor criteria fulfilment in total. At diagnosis, the bone loss was such that the patient had the skeleton of a 90 year-old man (Figure 1). Diffuse myelomatosis carries a median survival of 31 months (15) and, in effect, the patient was told he could expect to live about a year and a half, to two years, with treatment. (16)

Nevertheless the patient opted not to have treatment. What was his survival prognosis in this case? In the days before chemotherapy the median survival for Multiple Myeloma was 6 - 9 months. (5) This median survival, in the days before accurate Myeloma classification, may have included a few MGUS and/or Smouldering/Indolent Myeloma patients, so perhaps it erred on the side of generosity. The outlook could not be good. However, a certain stubborn optimism shared by both the patient and his advisor prompted the latter's curiosity on this front. During the two months that followed the initial diagnosis, whilst further opinions were being sought far and wide, - from Barlogie in Arkansas, Salmon in Arizona, to Sherman in Columbia Presbyterian, to Powles at the Marsden, - the question was put again and again: Did any of these clinicians have records or experience of long term survivors, against all the odds? Surprisingly, now and again the answer came back: yes, there were outriders. If the clinician in question had been around long enough, an anomaly could usually be brought to mind. Dr Sherman at Columbia had a patient untreated, and alive and well, with an 'M' spike of 35g/l, for over 15 years. Dr Littlewood at the John Radcliffe, Oxford, could

recall a woman who lived 20 years with Multiple Myeloma, though he had no explanation. The writer of this paper pressed Dr Littlewood further: "What were the chances of anyone, let alone the patient in question, Michael, surviving 20 years or more, untreated?" Dr Littlewood, after some careful thought, gave the answer: "0.005%".

The pair of stubborn optimists looked at this figure unflinchingly. As hope goes, it was a very thin thread. But optimists never need very much to go on. If only one person had survived 20 years with Myeloma, - not MGUS -, untreated, then it must be possible for another patient to repeat this. There is always an outlier in most medical conditions. Dr Littlewood, and others, offered hope: .005% hope, but that was enough. Though he will modestly tell you he is "just marking time", .005% at 20 years became the patient's survival goal. Having thoroughly investigated his options, he elected not to undergo standard conventional, or avant garde medical treatment, in spite of the fact that no less than 4 good, independent oncologists, including Professor Powles at the Royal Marsden, Dr Barlogie at the University of Arkansas, and no less an authority than Sid Salmon himself, the expert in Myeloma staging, on more than one occasion urged treatment as a matter of high priority. He did however adopt an alternative course of action with a strong biochemical rationale. Since the odds were so heavily stacked against him, it must be concluded that if such a course of action led to his continued survival and health, then it was not perhaps an accident, or coincidence, that the patient, who was supposed to have died within 31 months of diagnosis, with treatment, should instead be, nearly 8 years later, in that mysterious "plateau" phase so rarely characteristic of this disease.

The alternative course of treatment is worthy of consideration because it has almost certainly promoted this remarkable remission.

The Treatment

Initially, the patient elected to follow the Max Gerson Cancer Therapy. Inquiries at the Gerson Institute (Bonita, California, U.S.) revealed almost no Gerson experience of Myeloma and certainly no long-term survivors. This did not deter the patient. Myeloma is a relatively rare cancer, (1% of all cancers), though latterly its incidence is on the increase, (17) and cancer sufferers often have recourse to Gerson at too late a stage, or have been pre-treated with chemotherapy, which seems to impair outcomes. There was also a caveat from Gerson himself who clearly viewed blood cancers as more complex and difficult to treat than solid tumours: "*Their metabolisms are much 'deeper' and more differently deranged than we see in other cancer types*". (18) The patient's advisor thought that the Gerson Therapy needed modifying to suit the special needs of Myeloma, - the Gerson Therapy was primarily devised for solid tumours, where its chief successes seem to lie, (19,20) - and that the Therapy also needed updating in terms of the substantial and ever growing current scientific knowledge of the impact of nutrition on the molecular basis of cancer in prevention, treatment and recurrence minimisation. (21) The Gerson Therapy is currently overseen by

Charlotte Gerson, Max Gerson's daughter, who has courageously promoted and maintained the Therapy since the 1950s when her father died. However, she has made only a few changes to it. Max Gerson was a doctor, scientist and empiricist. He would almost certainly have assimilated the explosion of current knowledge on nutrition in cancer and carried on refining and improving the Therapy. (There has been disagreement within the Gerson Institute on this issue. Gar Hildenbrand espouses the latter view).

The Gerson Therapy then was to be modified by the addition of the input of the fathers of "orthomolecular" medicine, one of the greatest scientists of the 20th century, Nobel prize-winner Linus Pauling and his collaborator, Dr Abram Hoffer. (22) As Pauling once said: *"It is not enough for a cancer patient to receive appropriate conventional therapy. To improve quality and quantity of life, a regime of good nutrition is essential."* (23) Also brought to bear was much orthodox scientific work on adjuvant nutritional therapy in cancer, a field which now has its own textbooks, (21,24,25,26,27,28,29) thousands of publications in peer-reviewed journals, and a growing consensus on profitable approaches, largely, but not exclusively, pioneered by North American doctors and scientists at prestigious institutes including Harvard, NIH, the National Cancer Institute, the M.D. Anderson Center, the Linus Pauling Institute, Stanford University Medical Center, UCLA School of Medicine, the Cancer Institute at Edgewater Medical Center, Chicago, clinics such as Cancer Treatment Centers of America, the Center for the Improvement of Human Functioning in Wichita, the Block Medical Center, the Simone Cancer Center, founded by President Regan's oncologist, Dr Charles Simone, to mention but a few. The burgeoning number of professional, scientific conferences on Nutrition and Cancer (30) also attests to the promise and integrity of this "new" field.

To the patient's advisor it was evident that some of the science and medicine behind the Gerson Therapy, as expounded by Gerson himself, (18) was outdated. Thus critiques of Gerson's Therapy based on the original rationale would be largely redundant. (31) More interesting was the empirical fact that some people clearly did survive on the Gerson Therapy. The evidence was in part anecdotal: both the patient and his advisor personally knew of such remarkable cases, some of whom had achieved notoriety in print, (32) and even included a practising doctor. There was also moreover published peer-reviewed evidence which, encouragingly, showed statistically significant survival rates for Gerson versus chemotherapy in two cancers which could rival Myeloma in ferocity and intractability to conventional treatment: ovarian and Melanoma. (19,20) Since the patient was prepared for the rigours and discipline which the Gerson Therapy entails, it seemed a good base on which to devise an orthomolecular medicine programme which might radically improve the patient's general health, and by considerably altering the biochemical environment and micro-environment of the tumour make it difficult for the tumour to thrive. The aim of the programme would, realistically, not necessarily be cure, but control. The patient should be able to enjoy good health and reasonable energy, enough to enable him to

continue to live and work well. It is the same aim that Professor Judah Folkman has envisaged for his developing anti-angiogenesis therapy, (33) and indeed of a spectrum of novel approaches to cancer now in the pharmaceutical pipeline. Since the current kill or cure mind-set has largely produced "kills" (34,35) with both cancer incidence and mortality on the increase (35,36), long-term control seems at the least a more humanitarian option.

Principal Problems Faced in Myeloma

Multiple Myeloma can lead to a number of clinical complications, several of which can be very difficult to deal with and can prove fatal. In August 1994 the patient had all the appearance of a very sick man, and amongst the risks he faced were:

- 1 Hypercalcaemia, due to the heightened osteoclastic activity in Myeloma, which can in turn lead to kidney failure, coma and death;
- 2 Paraplegia/quadruplegia, due to potential vertebral compression fracture, since the patient was already 34.1 mg/cc below the fracture threshold of 110 with a 56% bone density, as a percent of average bone density for a male age-matched control (see Figure 1);
- 3 Serious infections, such as streptococcus, pneumoniae, s. haemophilus, Gram-negative organisms and staphylococcus aureus, which might lead to septicaemia, due to the fact that in Myeloma the humoral arm of the immune system is in effect largely deactivated, so that only cell-mediated immunity is left.

Any of these major problems can considerably shorten life in Myeloma. In addition to running these risks, the patient continued somewhat dehydrated, which suggested some kidney involvement and dysfunction, (his urea and creatinine values were at the high end of normal - Table 1), anaemic and low in energy, - the anaemia in Myeloma is thought to be consequent on bone marrow suppression and possible haemolysis by the tumour (37), - with continued night sweats. Therefore his proposed treatment would have to try and address all the above considerations.

Treatment I: The Gerson Therapy

The patient began the Gerson Therapy in the last week of August 1994. The therapy is composed in part of a diet which is largely vegetarian and low in protein, particularly so in the first two months when no animal or dairy products are allowed. The diet must be fresh - no processed food or additives - high-raw - salads, fresh fruit and juices - with only a small percentage of cooked foods, slow cooked, without water, to minimise nutrient loss. Finally, all ingredients must be organic to minimise stress on the liver, already compromised in cancer, by preventing the introduction of pesticides, preservatives and other toxins which might further promote carcinogenesis. We now know that some phytochemicals, however "natural" and organic, can be liver toxic in varying degrees. Gerson seems to have intuited this and experimented so that the diet tends to avoid such - Gerson issued a list of forbidden fruit and vegetables, pulses, sprouts etc. Instead, the diet

highlights a number of foods in which modern research has identified some key cancer-fighting components: linseed or flax-seed oil - the Omega-3 essential fatty acids in this can interfere with cachexia, (38) being key components of the body's anti-inflammatory response, they oppose the bad eicosanoids which promote the lethal cascade of excess cytokine release in cancer, including Tumour Necrosis Factor and Interleukin-6. Omega-3 fatty acids also appear to interfere with metastasis and promote apoptosis. (39,40) Indeed so impressive is the animal work demonstrating increased long-term survival in cancer with Omega-3 fatty acids, that the National Cancer Institute has already undertaken a trial of Omega-3s in breast cancer. (41,42)

Gerson's key list of fruits includes apples, apricots, bananas, cherries, currants, grapes, grapefruit, mangoes, melons, oranges, peaches, pears, plums, tangerines. Apart from their well-known vitamin and mineral-rich status, many of these fruits are rich in bioflavonoids; black grapes, for instance, contain anthocyanins which have been demonstrated to increase survival in tumour-implanted animals, (43) apples contain flavonoids such as myricetin and quercetin; the white rind in citrus fruit is also rich in quercetin; a star nutrient in the nutrition against cancer field. Dr Patrick Quillin of Cancer Treatment Centers of America, has assembled some interesting data on quercetin in cancer. (24) Quercetin has "the potential to revert a cancerous cell back to a normal healthy cell, called prodifferentiation." (44) Quercetin also induces apoptosis or programmed cell death in otherwise "immortal" cancer cells. (24) It inhibits inflammation by reducing histamine release (24) and reduces tumour cell proliferation. (24) Quillin also refers to new studies which show that quercetin "may be one of the most potent anticarcinogens in nature." (45) Amongst the reasons for this may be the fact that quercetin "competes with oestrogen for binding sites, thus defusing the damaging effects of oestrogen," in breast cancer. Quercetin is also "a potent antioxidant". It "inhibits capillary fragility which protects connective tissue against breakdown by tumours," in angiogenesis and metastasis. Quercetin also interferes with metastasis by reducing cell aggregation or 'stickiness'. It "helps to eliminate toxic metals through chelation." (24)

This is just one component in Gerson's fruit list. When we look at Gerson's chosen vegetables, a similar picture of intuition borne out by current scientific nutritional research emerges. Highlighted Gerson vegetables are cauliflower and radishes, along with cabbage and broccoli members of the cruciferous family. Crucifers are rich sources of isothiocyanates, which can modify carcinogen activation by altering the metabolism of nitrosamines. (46) Garlic and the rest of the allium family also feature high on Gerson's list: a common volatile component of garlic, diallyl sulphide, is a natural detoxifier and has been demonstrated to be a strong inhibitor of cytochrome P450 2E1 (47), an inducible liver isoenzyme, known to be activated in hepatic, colon and head and neck cancers, and which can activate carcinogens, including nitrosamines, hydrazines and carbon tetrachloride. Diallyl sulphide suppresses oxidative demethylation by competitively

inhibiting P450 2E1. (47) Selenium, for which the allium family - onions, leeks, scallions, chives - are also a good source, has been demonstrated to enhance DNA repair mechanisms (48), which apart from cancer chemoprevention may also be essential in switching cancer activity off.

Gerson's fruit and vegetable diet could be subjected to exhaustive analysis in the light of modern nutritional oncology research. One can go on. Resveratrol, a phytochemical in grapes, has been shown to induce phase II enzymes, such as quinone reductase, in the liver. (49) Phase II enzymes are the liver's detoxifiers, and, as Gerson posited, efficient detoxification in the liver is essential in both the prevention and treatment of cancer. To summarize, however, the World Cancer Research Fund's Report for 1997 lists the following compounds under continuing investigation in plant foods as having proven or potential cancer activity: dithiotiones, isothiocyanates, sulfuropanes, terpenoids, isoflavones, protease inhibitors, phytic acid, polyphenols, glucosinolates, indoles, flavonoids, plant sterols, saponins and coumarins. Gerson did not have any of this scientific knowledge, yet, empirically, he devised a method which ensured that a large range of these compounds would be delivered to the cancer patient intact and in pharmacologically active doses: the intensive fresh juicing regime, with 12 juices daily, one every hour. The juices, which are 'whole' juices in that the juicing method ensures virtually nothing is discarded, are also rich sources of Vitamin E, carotenoids and retinoids for which an extensive literature and clinical work have demonstrated differentiating and apoptotic effects in cancer. (26,50,51) Both carotenoids and retinoids regulate gap cell junction communication. (50,52) It is via the cell gap junctions that growth regulatory signals are transmitted. Since cancer cells have poor gap junctions and consequent impaired communication, their growth is deregulated. Carotenoids and retinoids can reverse this and thus interfere with their proliferation and growth.

The juices can be seasoned with a range of herbs but salt is absolutely forbidden. Modern research again suggests that, as Gerson believed, sodium can be a cancer promoter. (53) Gerson's aim was to reduce sodium imbalances by replenishing the body's stores of the Na antagonist, Potassium. The juices are naturally rich in potassium. But since Gerson reasoned that replenishment of the body's potassium stores took time, he added a 10% solution of potassium, with an initial dosage of 10 x 4 teaspoons in each of 10 juices daily gradually reducing over 8 months to a base-line of 6 x 2 teaspoons daily. It is possible that by altering this particular electrolyte imbalance for the better, Gerson was once more enhancing valuable cell to cell communication.

Other prescribed Gerson "medication" which the patient adhered to faithfully, included (Table 5): Lugol's Solution - an iodine supplement; - thyroid extract; niacin - 300 mg daily in 6 split 50 mg doses and sublingually, to avoid the "flush" response -; pancreatin 4 x 3 tablets daily and injections of liver extract and vitamin B12 100 µg daily. Iodine itself has anti-carcinogenic

properties. (54) Allied to the thyroid extract, iodine was intended by Gerson to strengthen and normalise the function of the thyroid gland. We now know that if thyroid function is deficient not only are all aspects of body metabolism altered for the worse, but, critically in cancer, the immune system functions less than optimally. (55) Conventional medical methods of treating cancer - chemo, radiation, - routinely wipe out an already depressed immune system and do little to restore it. Yet, as Gerson realised, it is the immune system which is needed to fight cancer, and therefore building it up should enhance chances of survival.

Niacin has a number of roles in cancer: it improves aerobic metabolism making tumours more accessible and vulnerable to internal destruction by the immune system or external destruction by cytotoxic agents (56); niacin also lowers both cholesterol and insulin-resistance (57), both good things from the point of view of restoring the characteristically deranged metabolism of the cancer patient to normal; niacin also generates ATP energy via the enzyme co-factor NAD (nicotinamide adenine dinucleotide) (57) which is important given that much energy is uselessly lost and expended in cancer patients through the redundant and futile Cori cycle, and the high demands for energy from the tumour itself which often leads to raised basal metabolic rates. (58) Along with niacin, vitamin B12 is the only other artificial vitamin supplement Gerson permitted, at least for the first 6-8 months of treatment. He thought B12 critical because animal data indicated it was "very potent in the restoration of all different tissues, be they damaged by age, chronic illness, operations, degenerative diseases, intoxication or by other means." (18) Once again, modern science has corroborated this view: B12 affiliated enzymes (the B12 molecule structure was only elucidated by Dorothy Hodgkin about the time of Gerson's death), have been described by chemists as "the ultimate radical cages and ultimate radical traps." (59) Moreover, B12 is now known to be involved in DNA synthesis, repair and methylation. (60) (Cancer cells tend to be hypomethylated). As a methyl donor for the enzyme methionine synthase, B12 is also crucial to the bio-availability of folate: without a good store of B12 in the liver folate becomes trapped, and much of the anti-cancer benefits of the intense folate concentration of Gerson's green juices would be lost. (Our patient made these juices greener than green by regularly incorporating in them dandelion leaves, nettles, wild herbs, which he regularly gathers from his native Scottish hills, and Oxford marshes.)

The last and most controversial (30) part of the Gerson Therapy is the use of daily coffee enemas, as many as four a day, to begin with. Coffee enemas, which one might be humourously tempted to dismiss as a Germanic idiosyncrasy, once had medical acceptance and respectability in the Merck Manual, till the 1970s. Their day may yet return, since they are also a key element of Kelley's Metabolic Typing Therapy, as championed by Dr Nicholas Gonzalez and currently in large Phase III trials for pancreatic cancer at Columbia Presbyterian Medical School under the auspices of NIH. (NIH has given Dr Gonzalez significant funding for this trial since he had already

demonstrated remarkable survival numbered in years for this cancer which is so lethal it kills in weeks or months at best). Gerson's rationale for the importance of coffee enemas was simple: as the Therapy began to restore the whole biochemical environment of the tumour in the body, the tumour was liable to be attacked by the newly primed immune system and rapidly broken down to cause what we now know as "tumour lysis syndrome", a dangerous state of affairs which, if unrelieved, can lead to coma and death due to the accumulation of toxic by-products of the breakdown. Coffee enemas effectively avoid this by stimulating the liver's detoxification systems. Once again, Gerson has been proved right in this claim. Coffee enemas appear to stimulate the activation of the glutathione-S-transferase Phase II enzymes which catalyse the conjugation reactions of xenobiotics with glutathione. (61) (Of course, certain fruit and vegetable components such as the isothiocyanates in crucifers and naringenin in grapefruit can also induce GSTs, so that detoxification in Gerson is not exclusive to coffee enemas.) The active ingredients in coffee enemas appear to be kahweol and cafestol, the palmitate constituent of green coffee beans. Recent clinical trials have demonstrated that coffee enemas also make a significant difference to late stage pain control in cancer, reducing the need for opiates. (31) Since pain control in cancer remains an enduring problem, this is of itself remarkable.

The patient anyway had no problem adhering to Gerson's prescription for coffee enemas, and during the first year regularly did 3 to 4 a day. Subsequently he cut down to a maintenance enema of 1 a day, only increasing this in times of stress or minor illness, when he claimed it made him feel physically better. This regime he has followed to the present day. Moreover, though Gerson prescribed an average length of 18 months to two years for the duration of his Therapy, the patient has made only one concession in gradually tapering down the number of juices to 4 a day from 1999 onwards. Otherwise, quite simply, he has never stopped.

Treatment II: Orthomolecular Oncology

"Le terrain: c'est tout," said Pasteur on his deathbed. It is a guiding principle of nutritional oncology that cancer initiates and flourishes primarily in an environment, the body, which is both genetically and biochemically favourable. Moreover, the cancer process has the ability to further change, degrade and adapt the biochemical environment to its advantage. Nutritional, or orthomolecular, oncology proposes that in order to fight cancer successfully it is not enough to treat symptoms with surgery and cytotoxic treatments. Tumour burden should be lowered, ideally, by the least harmful means. Next not only should the general biochemical environment be assessed and supported with the use of diet, supplements, and other biological response modifiers, but the particular metabolic derangements and adaptations caused by cancer should also be addressed. Cancer may then be checkmated. Of course, this principle is largely theoretical and hypothetical, based mostly on substantial in vitro and animal lab work, as well as epidemiology. Yet it is not exclusively so: some clinical evidence is beginning

to emerge, at first anecdotal, but increasingly evidence-based, as in the NCI's "Best-Case Series", in retrospective and prospective studies and NIH funded double-blind trials. There are also scientists newly interested in gathering and assessing systematic data on "Remarkable Recoveries". (62) A number of studies in this field again point to the central role of nutritional approaches. Dr Harold Foster, for example, has found that of 200 such documented cases of "spontaneous" cancer regression, 87% used a vegetarian diet, 55% detoxification, and 65% supplements. (63)

Ideally, with this approach to cancer, treatment should be based on an assessment of biochemical individuality. In North America such testing is relatively easy to access. In Europe it is still not routine; though a movement is afoot as testified by, for example, the existence of the excellent Paracelsus Clinic in St Gallen, Switzerland, or laboratories such as the Medical Biolab in London and Health Interlink, a UK branch of the U.S. led Great Smokies Diagnostics. The Gerson Therapy makes few concessions to biochemical individuality, or indeed to differences amongst cancers, (though serendipitously, its successes with Melanoma may lie in part in the fact that it is a diet low in L-Phenylalanine and L-Tyrosine. (64) Nevertheless, Gerson's is a cookbook approach to cancer. In the beginning, the patient's approach to orthomolecular oncology was also cookbook, the treatment in general being gradually built up, refined and improved over several years, as information, time and resources allowed.

By the end of August 1994 the patient's advisor had conferred with Dr Abram Hoffer and ascertained that of the two Myeloma patients in his retrospective study with Pauling one was still alive. (This study, done with terminal cancer patients, extended survival fourfold compared to controls.) The patient therefore started on the Hoffer-Pauling daily prescription, which was as follows:

- Vitamin C (as Calcium Ascorbate) 12g
- Vitamin B3 (Niacin, niacinamide) 1.5 to 3g
- Vitamin B6 (Pyridoxine) 250mg
- Folic Acid 5 to 10 mg
- Other B Vitamins 25 or 50 times RDAs
- Vitamin E 800 iu
- Beta Carotene 25,000 iu to 50,000 iu
- Selenium 0.2 - 0.5 mg (Patient took 400 µg)
- Zinc Sulphate 220mg (Patient took 50 mg Zinc Citrate, which is more easily digestible).
- Sometimes Calcium, Magnesium or a vitamin tablet.

This prescription was immediately modified by the patient's advisor who pointed out that individual high doses of particular nutrients can be antagonistic to other essential nutrients and thus cause imbalances and deficiencies. Therefore in orthomolecular nutritional treatment a broad base of all essential vitamins and minerals should be used. The American company Solgar's V-2000 (see Table 6) was chosen as meeting this criterion, as well

as because of the realistically high dosages across the spectrum. Anything not supplied in sufficient quantity, such as the Zinc and B3, was then added over and above.

The impressive work of Cameron and Pauling in the Vale of Leven Studies (65) with terminal cancer patients and Vitamin C (10g oral a day), which showed an over fourfold survival time in the treated arm of the study, with a small percentage of unexpected cures, together with two dramatic case histories, one of lung cancer liver metastasis, one of brain tumours, cured in the first instance with 36 grams of oral Vitamin C daily plus radiation, and in the second with 36 grams of oral C daily alone, were all brought to the patient's attention. He was urged to build up to somewhere near 25 grams of oral Vitamin C daily, in split doses. By June 1995 he had managed to build up to 9 grams. In the subsequent year he went on up to 20 grams, which appears to be about his bowel tolerance limit. (As established by Pauling, the bowel tolerance limit seems to be the measure of individual need, and can vary over time, as stress, illness and other factors demand.) The patient has remained on this dose of oral C ever since. Eventually, the patient also switched from calcium ascorbate, magnesium ascorbate, and Ester-C formulations taken in the first 2 years to straight ascorbic acid, since some authorities have suggested this form of the vitamin is more active. (66) (The pH of ascorbic acid is considerably higher than that of the stomach acid HCl.) Vitamin C therapy was intensified in late 1999, without altering dose, through the addition of 200 mg twice daily alpha-lipoic acid, which recycles vitamins E and C in the body. α -Lipoic acid is involved in the generation of ATP, and modulates both antioxidant and redox functions in the body. It is itself a powerful anti-oxidant, chelator and liver detoxifier and helps regulate blood sugar metabolism. (67)

In late 1995 the pioneering educational work in orthomolecular oncology by Dr Patrick Quillin was also brought to the patient's attention. At the time, Dr Quillin, nutritional consultant, writer and organiser of cutting-edge conferences in the field, envisaged an adjuvant nutritional formula for the cancer patient which would contain absolutely everything known to science to impact on cancer prevention and treatment, beyond vitamins and minerals alone. Shortly after this vision became a reality, in 1998, the patient adopted it and continues on it to this day. (Table 7) (The beauty of Immunopower, apart from its all inclusive experimental aspect, is that it dramatically reduces the sheer number of daily pills to be swallowed, as most of it comes in powder form, to be blended with juices.) The Solgar V-2000 was then discontinued as redundant.

Other refinements and biological response modifiers added to the original Hoffer prescription (and now taken in addition to Immunopower), included: Co-Enzyme Q10 (200mg twice daily; currently 50mg once a day); L-glutathione, (500mg daily plus 50mg L-cysteine); Folic Acid (5mg daily); E-Succinate (800 iu daily); Maitake-D-fraction; peppermint oil (2 x 200mg daily) and aspirin. Co-Enzyme Q10 has a role in cellular energy transport and

aerobic metabolism, as well as being an immune stimulant (68) and prostaglandin metabolism improver. Subsequently, Dr Hoffer added Co-Q10 to his regime and noted improved results. L-glutathione is one of the most important and all-pervasive antioxidants in the human body, and it is invariably low in cancer patients. It is a key component of Gerson's favourite detoxifier, Glutathione peroxidase. E-Succinate, a synthetic form of vitamin E, has the ability, unlike natural Vitamin E, the tocopherols, to actually work at the level of the chromosome in switching onco genes off. (50) Maitake-D-fraction is derived from the oriental Maitake mushroom and its anti-cancer properties (69) have been researched and demonstrated to the point where it is used as sole chemotherapy for stomach cancer in Japan. Peppermint oil (200mg twice daily) was added, and is continued with to the present day, because the attention of the patient's advisor was caught by a chance remark in a paper on the molecular biology of Myeloma to the effect that the menthol molecule is a match for the Interleukin-6 receptor. Since Interleukin-6 is overproduced in Myeloma and is the prime promoter of tumour progression, (11) it seemed sensible to try anything that might block IL-6. This was also the rationale for the addition of aspirin: aspirin blocks nuclear factor NF- κ B, which is a key player in the production of IL-6. (70) However, the patient, being drug-averse, ultimately decided not to continue taking aspirin on a daily basis. So this was a short-lived experiment.

Treatment III: Bisphosphonates

The patient's bones were a major source of concern. By February 1995, it was evident that the patient was doing well on his chosen course of treatment. Yet his bones, though stable, were not gaining density and he remained at risk for fractures and compression fractures of the vertebral column. The option of Bisphosphonate Therapy appeared to offer a double benefit, in that bisphosphonates not only interfere with the nesting of Myeloma in bone (15) but can increase bone density over time. (71) Intravenous administration with Pamidronate was discussed, but in the end the patient opted for daily oral Clodronate (Dose 800 mg daily). This was begun in March 1995 but discontinued at the end of May 1995, due to recurrent intestinal upset, which the patient felt might interfere with the optimal absorption of nutrients from the Gerson Therapy.

Almost certainly, this was a short-sighted decision and an alternative route of bisphosphonate administration should have been sought. However the patient continued with the bone-support supplements that had been started concurrently, namely Vitamin D, and Dr Vogel's Bioforce formula, Urticalcin, containing Calcium, Boron, Silica and nettle extract. He also tried Novartis' Meritene for about a year, since this "nutriceutical" formula had been demonstrated in trials with wheelchair-bound elderly to halt bone loss by up to 50%. (72) The patient was told of the importance of exercise to stimulate bone growth, and chose regular walking as a safe compromise. In the circumstances, any more violent load-bearing exercise would have been too risky.

The patient's bones were regularly monitored (Table 8). In December 2000 it became evident that, though there had been no dramatic bone loss since diagnosis - the BMD of the hip remaining pretty constant, - and there was absolutely no evidence of Myeloma activity, the trend for the bone density of the lumbar spine was going in the wrong direction, with a fall of 0.092 since July 1995. The loss could largely have been due to the natural loss of bone in age. But there was a more obvious explanation. A year earlier, in October 1999, a remarkable failure in the patient to absorb some of the key bone-building minerals was identified by Dr Hugh Riordan at the Bio-Laboratory, Wichita, Kansas. In 1994 the patient's advisor had intuitively suspected the patient might suffer from deficient stomach acid production and had urged him to test for this. The test was not done. There was so much else to attend to. By 1999 the patient's continuing stability and good health were a fact. The question however remained: if the patient had had such a remarkable response to his treatment, why was he not continuing to progress? Why were the bones not gaining in density?

More information was needed. If progress were to be possible, the cookbook approach must be discarded. The patient agreed to go and have a state-of-the-art complete biochemical screen at Dr Riordan's Center For the Improvement of Human Functioning (Table 9). The results of this should allow modification and improvement of his chosen treatment.

From the bone-building point of view, this screen revealed not inadequate calcium serum levels of 9.2 mg/dl. Levels of Vitamin D were, by some oversight, unfortunately not measured. Serum phosphorus was off the graph at 5.9 mg/dl, which might suggest some increased osteoclastic activity. (This could also be spurious hyperphosphatemia, for which there are two possible explanations in Myeloma: 1) Occasionally the M-protein may bind phosphate, (73) causing a false increase in serum phosphorus levels; 2) in IgG Myeloma in particular, the M-component can interfere with the phosphate chromogenic assay. (74) Magnesium which, along with phosphorus is essential in bone-building, was extremely low at 3.3 mg/dl, and the trace mineral zinc, also involved in bone-building, was also low, all in spite of supplementation. The latter deficiency might in part be "explained" by the patient's high pyrrole excretion. However, since supplementation of all the minerals was high, it must be surmised that the problem was primarily one of stomach absorption and a related deficiency of acid secretion. The utterly extraordinary thing was that, in spite of an important macro and trace mineral deficiency that had almost certainly existed for years, the patient had done so well on his chosen treatment. The brilliant adaptive powers of the body and its undeniable bent for homeostasis and health are well illustrated here.

The next logical step should have been a Heidelberg test or gastrogram investigation. This was not done till a year and a half had passed and the December 2000 bone scan made manifest the ongoing downward trend. There was now a sense of urgency and a need to gain a margin of safety for the patient on the bone fracture front. In late January 2001 Dr Riordan

prescribed Ipriflavone 600mg a day, though till July 2001 the patient mistakenly took 400mg a day. A non-toxic synthetic analogue of Vitamin D, "Drisdol", which can be safely used in high doses was also prescribed, and the patient takes 50,000 iu once a week. Ipriflavone (chemical structure: 7-isopropoxyisoflavone) is a synthetic isoflavone which has been demonstrated to increase bone density by at least the same percentage as bisphosphonates if not more. Studies have recorded gains of as much as 6% in 2 years. (75) Ipriflavone, like certain bisphosphonates, also interferes with IL-6 activity and production. (75) It is also infinitely better tolerated, as well as having a better safety profile than bisphosphonates as a drug for long term use. Ipriflavone is primarily anti-resorptive but also possesses bone-forming potential. It inhibits parathyroid hormone, Vitamin D, PGE2 and interleukin stimulated bone resorption. (75) The mechanism of action appears to involve inhibition of activation of mature osteoclasts and further osteoclast formation partly through modulation of intra-cellular free calcium, enhancement of osteoblastic differentiation by expression of key bone matrix proteins and mineralization. (75) Ipriflavone does not have oestrogenic effects but nevertheless enhances the bone-building effects of oestrogen. (75) (Even males require oestrogen for bone-building). Endocrinological imbalance in the patient was checked and ruled out in February 2001. Stomach acid levels and pancreatic function were then investigated, and the original suspicions were confirmed. Pancreatic enzyme secretion was slightly depressed, at 70% of normal, and HCl production was well below normal and classified as hypochlorhydria. (See Figure 2). The patient was prescribed between 300-1000mg Betaine HCl before each meal. He elected simply to double at each meal his dose of "Acidol Pepsin", the Gerson supplement, containing pepsin 230mg, raw pancreas 60mg and Betaine HCl 260mg per capsule.

At the end of June 2001, seven years since diagnosis, the patient also commenced bisphosphonate therapy with intravenous Ibandronate. Ibandronate is a 5th generation bisphosphonate with such a powerful dose-efficacy ratio, it need only be given in 2mg doses once every 3 months. The Ipriflavone is being continued indefinitely alongside this treatment, and it is hoped that there will be a synergy between the two which, together with improved mineral absorption, will result in above average bone gain results within the next year. The patient is also fortunate in that this allopathic treatment, Ibandronate, is being administered by an orthomolecularly-oriented physician, Dr Wayne Perry of the Endocrine Centre, London. Dr Perry will therefore monitor and adjust carefully all levels of calcium, magnesium and vitamin D, which can paradoxically be reduced by bisphosphonate treatment even though they are vital for its maximum efficacy. At present the patient has been prescribed "Calcichew D40" which contains 1250mg Calcium Carbonate and 400 iu of cholecalciferol. Dr Perry has also taught the patient a range of special exercises to help strengthen his fragile spine and promote its rebuilding.

Obviously, at this moment in the summer of 2001, the patient has a sense

that he is on a tightrope: Though his Myeloma is inactive and he continues in good health, the Myeloma might yet claim him retrospectively, through the initial damage done to the bones before diagnosis, damage which has as yet not been redressed. However, there are arguments that favour a more optimistic view. In spite of being well below the fracture threshold, the patient has had no fractures in 7 years of active life. Furthermore bone density may not necessarily reflect bone structure. It may be possible to have low bone density but relatively strong tensile structure. Dr Wayne Perry remarks that he has seen far worse cases. There is hope, and the rational course of treatment now embarked on may soon well corroborate this.

Treatment IV: Enzymes

Enzyme therapy in cancer is a controversial topic. There is considerable controversy as to whether enzymes can survive the process of digestion to reach the bloodstream in therapeutically efficacious doses. (76) Still, some intriguing claims are made, including the belief by Donald Kelley that cancer is the end result of a failure to produce sufficient pancreatic and digestive enzymes. Since Kelley's Therapy, which includes the ingestion of vast amounts of such enzymes, is now achieving some unheard of successes with pancreatic, and other, cancers, enzyme therapy may have some basis, and the various hypotheses (76) should be investigated further. One such hypothesis suggests that proteolytic enzymes act locally in the gastrointestinal tract to generate exorphins, and this would be of benefit since opioid agonists have anti-proliferative activity. (76) In animals, enzymes have been shown to slow tumour growth and metastasis. (77) In vitro, enzymes have been shown to both inhibit leukaemia cell growth and promote their differentiation. (78) The problem of enzyme delivery may or may not be a problem. The patient therefore decided to give Enzyme Therapy the benefit of the doubt. Of course, the Gerson Therapy is theoretically a diet rich in enzymes, due to its high raw aspect, and Gerson also prescribes pancreatin. The patient took the Gerson pancreatin till the end of 1998, and then switched to "Megazyme", a formulation containing 325mg pancreatin, protease 81,250 USP, amylase 81,250 USP, lipase 6,500 USP per 2 capsules. The recommended dose of Megazyme is 5 capsules a.m. and 5 capsules p.m. The patient however takes 5 capsules a.m. only.

Treatment V: Metabolic Typing

In early 1999 the patient refined the Gerson Therapy further, influenced by Dr Peter D'Adamo's book, "Eat Right For Your Type". Dr D'Adamo espouses the theory that individual blood groups reflect ancestral provenance. Particular diets would once have been characteristic of the individual blood groups as specific adaptations to the geographical location and environmental conditions of origin of these same individual blood groups. In his view, optimal health is achieved if you eat in harmony with your ancestral blood group diet. The patient is blood group A, for which a largely vegetarian diet with some fish is deemed appropriate, essentially the Mediterranean diet, with olive oil high on the menu, fruit such as plums, figs, grapes, raisins,

berries and pineapple, but in general no tropical fruits, such as coconut, mango, papaya, bananas. Potatoes, which are a staple of Gerson, are also banned altogether. The patient feels no hardship in all this. It seems natural to him. It should be said that Metabolic Typing can sometimes lead to prescriptions for diets high in red meat, and that this does not necessarily militate against successful cancer treatment, as demonstrated by Dr Nicholas Gonzalez and Kelley's Therapy.

Treatment VI: Acupuncture

The British Medical Acupuncture Society makes the following statement about acupuncture: *"Modern research shows that acupuncture can affect most of the body's systems - the nervous system, muscle tone, hormone outputs, circulation, antibody production, and allergic responses, as well as the respiratory, digestive, urinary and reproductive systems."* Research has also firmly established that acupuncture increases the body's release of serotonin, and endorphins, enkephalins, dynorphins and other natural opioids. Acupuncture is also thought to affect enzymatic pathways. Energy and mood can be improved by acupuncture. The corollary of all this is that acupuncture also affects the immune system for the better. No-one claims that acupuncture can cure cancer. But its generalized effects make it a useful tool in treatment strategies that seek to alter the whole biochemical environment in cancer for the better, and optimise the results of other therapies.

This is the rationale behind the patient's use of acupuncture which began in September 1994 and has continued to the present, initially with an intensive regime of weekly, then fortnightly, then monthly sessions, and now at 6 week intervals.

Treatment VII: Mind over Matter; Visualization and Breathing Exercises

Mind over matter, like nutrition, is one of the oldest medicines in the world. As the 4000 year-old Indian Mahabharata (Santi Parva, XVI, 8 & 9), puts it: *"There are two classes of disease - bodily and mental. Each arises from the other, and neither can exist without the other. Thus mental disorders arise from physical ones, and likewise physical disorders arise from mental ones."*

To those who espouse the theological view that matter is mind incarnate, this is uncontroversial. Before the modern technological revolution in medicine, it was also taken for granted. As the great 19th Century physician and researcher, Dr William Osler, said: *"Faith in the gods or saints cures one, faith in little pills another, hypnotic suggestion a third, faith in a plain, common doctor a fourth, the faith with which we work has its limitations but such as we find it, faith is the most precious commodity without which we should be very badly off."* Modern medicine with its stress on technology and allopathic drugs, largely forgot the power of mind over matter. Science, however, did not. The field of "psychoneuroimmunology" began with Hans Selye's studies on the effects of stress, and has gathered momentum and evidence at the end of the 20th Century with the work of George Solomon at Stanford, (79) Robert Ader and David Felten at the University of Rochester,

(80) Candace Pert (81,82) and Solomon Snyder at John Hopkins, (81) the very institute of which Dr Osler had been a founding father. The contribution and connections between the mind, stress and cancer initiation and survival are now well validated. (83)

In devising a treatment that would capitalise on this knowledge, the patient was able to draw on both ancient wisdom, in the meditations and breathing exercises of Chinese Medicine, and the pioneering visualization work of the Simontons. (84) These practices, begun within two months of diagnosis, enabled the patient to survive the trauma and stress of diagnosis, and the stress of life and work in general. The patient has given an eloquent account of these practices and the mind-body connection in health and disease. It is almost certain that, in terms of promoting a healing response, this was and is a critical aspect of his treatment.

Case History Concluded

The patient's blood chemistry and immunology results from diagnosis to the present show a picture of consistent and continuing stability of disease. Some improvements from diagnosis since the start of treatment are noteworthy. The abnormally high ESR rate of 125 mm/hr and 100 mm/hr at the time of diagnosis had fallen to 76 mm/hr by late November 1994 and one year out from diagnosis, in July 1995, was 36 mm/hr. The anaemia, which seemed to show some spontaneous improvement prior to commencing treatment, has persisted but remained relatively stable at higher readings. Albumin, an important index of nutritional status in cancer, which was low at diagnosis (30), has been consistently high in the forty-something range, with an anomaly of 34 in December 2000. Elevated liver enzymes at diagnosis also dropped significantly, and in general liver and kidney function has remained good. Lactate dehydrogenase, another marker for activity in cancer, also dropped from abnormally high levels of 352 at diagnosis and pre-treatment to a recording on the low side of normal, at 119. The blood count has remained normal, apart from a borderline neutropenia.

The results of the October 1999 Complete Biochemical Screen (Table 9) present a picture of a supremely well nourished individual, with the above-mentioned exception of the glaring mineral absorption problem. Levels for all B vitamins are at the top end of normal, with Folate and B12 off the graph and, consequently, enviably low levels of homocysteine. The major antioxidants Vitamins C and E are in the high, above average range, with a strong reading for A. The amino acid profile is very good, with one anomaly in undetectable aspartic acid, but conversely higher than normal L-asparagine, which may reflect low L-asparaginase activity in the patient. (85) (However, aspartic acid is usually only found in trace amounts in serum). The essential fatty acid profile is also very favourable, with exceptionally low arachidonic acid, exceptionally high alpha linoleic, eicosapentanoic and docosahexaenoic acids. The monosaturate oleic acid is also at the top of the high range. C-Reactive Protein was negative. In tandem with this last, it is worth noting that the patient's β 2-microglobulin, like CRP, a major prognostic

factor in Myeloma, has remained low over more than seven years.

So far the threat of serious infection has not materialised. In nearly eight years, the patient has had flu once, three or four colds, the occasional stomach upset, an infected foot which responded well to antibiotics, and recurrent maxillary sinusitis, which is characteristic in Myeloma. This degree of infection is almost better than normal for the average healthy person, let alone a Myeloma patient.

As of July 2001, the patient is currently contemplating the further addition to his treatment of benevolent cytotoxic therapy, as exemplified by Dr Hugh Riordan's experimental use of very high dose (50g - 100g) Intravenous Vitamin C Therapy. (86) Dr Riordan's institute has made a ten year study of the use of intravenous Vitamin C in cancer, and is now conducting Phase II clinical trials. Phase I trials were done at the University of Nebraska Medical School. This approach has produced remarkable remissions in pancreatic cancer, (87) and late-stage lung cancer. The patient's rationale for using this particular therapy is that, as a matter of fact, the Myeloma is still in his marrow, however inactivated. Intravenous Vitamin C can achieve a blood saturation in the order of 200% as opposed to 2% or so by the oral route. In vitro very high doses of Vitamin C have been demonstrated to have an apoptotic effect on cancer cells. A method has now been devised whereby this can be achieved *in vivo*. (86) The hope is that just one final cytotoxic push is needed and the Myeloma will disappear altogether.

Some Hypotheses for the Apparent Success of the Treatments

A few general points may be made on the impact of the above treatments on cancer. Cancer initiation and promotion is known to be favoured by high levels of free radical generation that overwhelm the body's antioxidant defenses. (88) The cancer process itself contributes to this imbalance, which in turn favours the cancer at the host's expense. It makes sense therefore to attempt some redress by supplying ample amounts of antioxidants, and both the Gerson Therapy and Orthomolecular Oncology do this, as amply demonstrated in our case by the patient's 1999 complete biochemical profile. Diets that are low in calories have been demonstrated to slow cancer progression. (89) The Gerson Therapy is based on a calorie restricted diet. This is because it is very low in fats and simple sugars. (Gerson actually encouraged patients to eat as much as possible.) Another factor which can either promote or inhibit the cancer process is the body's acid-alkaline balance or pH. In the serum, pH is very tightly regulated (pH 7.35 - 7.45). Elsewhere, in tissues etc there is more latitude, though in terms of maximal enzymatic efficiency and health there is an ideal balance. Cancer is promoted by extremes of the acid-alkaline balance, but in particular by acidity. Solid tumours produce lactic acid, which makes their immediate environment more acidic. This in turn promotes their growth. It is not known for certain whether in Myeloma plasma cells do this in the micro-environment of the marrow. The patient's initially high Lactate Dehydrogenase levels at diagnosis, a product

perhaps of cellular breakdown in the Myeloma tumour's environment, might suggest this is the case. (About 10% of Myeloma patients at diagnosis have raised LDH of more than 300 u/l). However, the body's acid-alkaline base is important in all cancers. It is noteworthy, once again, that the Gerson diet and juices are naturally alkalising.

Angiogenesis is the means by which solid tumours spread and grow. Without angiogenesis there is no such possibility and cancer would be harmless. It is now known that non-solid tumours also rely on angiogenesis, in the marrow, (90) to increase in malignancy. This is the reason that thalidomide, an anti-angiogenic agent, is believed to be effective in Myeloma. (9) Interestingly enough, the primary impulse for Pauling and Cameron's first experiments with high dose Vitamin C in cancer was the theory that it would act as an anti-angiogenic agent. (65) High doses of C would stimulate production of a substance that inhibits the enzyme hyaluronidase, produced by malignant tumours to attack the hyaluronic acid in inter-cellular cement, weaken their surroundings and allow infiltration. At the same time high dose C would also strengthen the collagen fibrils in this intercellular cement, thus providing a double defense against angiogenesis. One might speculate that the patient's very high doses of Vitamin C may, amongst other things, have played a crucial anti-angiogenic role in the marrow.

The singularly few number of infections experienced by the patient suggests that though in Myeloma the humoral arm of the immune system is deactivated and/or depressed, what remains of the patient's immune system must not only be partially compensating but functioning optimally. In fact, the two arms of the immune system are far from separate and act in "a highly regulated feedback loop", (91) so that some compensation is theoretically possible. For example, CD4 helper T cells are usually involved in the stimulation of antibody production. If these T cells are well primed they may be able to improve antibody response even in pathologically depressed states such as Myeloma. Conversely, it may even be possible that, since T-cells normally regulate antibody secretion through inhibitory lymphokine release, well primed T-cells may also be able to help regulate the abnormal antibody production in Myeloma. The treatments may have general immune system enhancing effects, but there are also some very specific effects. The integrity of lymphocyte function is dependent on good levels of folate. Natural killer cells, a subset of lymphocyte, are thought to be responsible for surveillance and destruction of neoplastic cell clones. This may be just as relevant to cancer remission as to its prevention. Folate, which the patient's therapies supply in abundance, is also critical in DNA repair and stability. (92) In Myeloma remissions, chromosome 13 remains stable, and there are probably no other genetic mutations or karyotypic instability. In order for T-cells, leukocytes, to function effectively they must be saturated with ascorbate. (93) Moreover high doses of ascorbate can result in greatly increased production of lymphocytes in the presence of antigens. (93) Large doses of Vitamin C also boost production of interferons. (93) Some interferons have a known anti-cancer effect, Myelomas included. (94)

Interferons also have anti-viral activity. Since synthetic interferons can be very toxic, Cameron's advice, "*Take more Vitamin C and make your own interferon!*" seems sensible and is exactly what the patient did. Vitamin C is required for the synthesis of the C1-esterase component of complement. Without Vitamin C, complement is not activated. Higher doses of Vitamin C result in higher complement output. (93) As there is some suggestion that complement also does not always function normally in Myeloma, (95) there is a rationale for supporting its optimal production. The Complement Cascade is, like a bridge, a critical part of cell-mediated, as well as humoral, immunity. Improving the function of complement may thus once more help in the compensation process that may have taken place in the patient. Pathogens that cannot be dealt with by complement are routinely dealt with by the widely dispersed macrophages. Macrophages in turn ultimately trigger the release of more complement. Of course, there are microbes that elude the defenses of cell-mediated immunity and which are normally dealt with by humoral immunity. These are the dangerous microbes in Myeloma. Yet though in Myeloma humoral immunity is depressed, this is not the same as non-existent, and therapies which help promote a plausible compensation may well lead to a more efficient, if still depressed, antibody response, and therefore improved survival.

Proliferating Myeloma cells are characterised by an immature phenotype. (96) If Myeloma cells can be induced to differentiate into mature Myeloma cells, paraprotein production goes down, not up. The patient's paraprotein levels have remained more or less the same over 8 years. As noted before, both the Gerson diet and Orthomolecular therapy supply high doses of retinoids and carotenoids, which are used with success clinically, as synthetic drug analogues, to treat both head and neck cancers and certain leukaemias. Latterly, for two years, the patient has been taking a synthetic megadose Vitamin D, for which there is also evidence of differentiation potential in cancer, (97) as well as evidence to show it can promote apoptosis in Myeloma. (98) In particular, Vitamin D is likely to work synergistically with the retinoids and carotenoids.

Overproduction of the cytokine, Interleukin-6, probably in a paracrine fashion in the humoral micro-environment of the bone marrow, has been established as the chief promoter of Myeloma cells' survival and proliferation. 500 to 5,000-fold higher concentrations in vitro and in vivo have been found for IL-6, as opposed to other known Myeloma growth factors: IL-10, OSM, LIF, G-CSF, SCF, IFN- α , TNF- α , IGF-1 and IGF-2. Thus current novel approaches to the treatment and cure of Myeloma are focussing on strategies for the control of IL-6. (11) Small trials of Anti-IL-6 monoclonal antibodies have been undertaken with some promise, (99,100) and refinements in the pipeline include mutated IL-6 (101) and humanized anti-IL-6. (102) But complete inhibition of IL-6 still appears problematic. (11) The test that is currently used to assess IL-6 inhibition is that for C-Reactive Protein, an acute phase protein produced by hepatocytes consequent on gp130 activation by gp130 cytokines, chief of which in Myeloma is IL-6. For this reason, lack of

detectable serum CRP is also now used as an important prognostic factor, along with B2 microglobulin, in Myeloma patients undergoing high-dose chemo and stem cell therapy/bone marrow transplant procedures. Unfortunately, the patient's CRP was not measured at diagnosis. However, in all likelihood it was present and possibly high, as indicated by his abnormally high readings for Lactate Dehydrogenase. However, in October 1999 the test for CRP was done, by Dr Riordan, and the result was negative, exactly what one would expect for Myeloma in remission. This suggests that something in the patient's therapies was doing exactly what currently eludes scientists, and completely blocking IL-6 overproduction and activity.

Induction of IL-6 is mediated by PGE2, a key prostaglandin of the body's inflammatory response cascade. Agents such as indomethacin which oppose PGE2 production also lower IL-6. A crucial aspect of the patient's therapy is the daily ingestion of flax seed oil, a rich source of ω -3 fatty acids. That the patient's resources of ω -3 fatty acids are at the top end of the high range was well established at the October 1999 full biochemical screen (Table 9). ω -3 fatty acids form the basis of the body's anti-inflammatory response. If the anti-inflammatory response is good, production of bad eicosanoids and prostaglandins such as PGE2 is effectively blocked, and levels of circulating cytokines, detrimental in cancer, such as Tumour Necrosis Factor and IL-6, are considerably lower. (A trial of ω -3 fatty acids in Myeloma would certainly be a much simpler and less toxic option than drugs which have still to materialise.)

Other factors in the patient's therapies which may have contributed to IL-6 blocking include Vitamin C as a promoter of interferon production. IFN- α and IFN- β have been shown to affect MM proliferation, at least in part by downmodulation of the IL-6R receptor. (103,104) Consequently, IFN- β reduces IL-6 dependent tyrosine phosphorylation of several signaling proteins which include RAS. (96) IFN- γ is thought to interfere with IL-6 transmembrane signaling, leading to enhanced apoptosis. (99) The patient's high intake of carotenoids and retinoids may also be a relevant factor, since it is known that Retinoic Acid induces apoptosis in Myeloma cell lines by once again downmodulating IL-6R expression. (99) As a general consideration the fact that the therapies appear to have boosted the patient's immunity, as evinced by his relatively low incidence of infection, may also be of relevance here. Infections equal inflammation which means high levels of IL-6 and CRP. Thus protection against infections may itself also protect against promotion and proliferation in Myeloma.

Critical to this discussion also is nuclear factor NF- κ B, a transcription factor which is modified by redox status and regulates gene expression in inflammation and disease response, (67) including cytokines such as IL-6, and cell adhesion molecules. Myeloma cells secrete their own unique cell adhesion molecules which allow them to communicate with the bone marrow micro-environment, (96) and further their lethal effects. Furthermore, activation of NF- κ B is also known to be a key factor in Myeloma angiogenesis

by stimulating the secretion of such pro-angiogenic factors as vascular endothelial growth factors, basic fibroblast growth factors and IL-8. (96) Thus, once again, inhibiting NF- κ B, which is usually dormant in the cytoplasm, may well be doubly beneficial in Myeloma. NF- κ B activation occurs after I κ B phosphorylation and its proteolytic degradation, through extracellular T-cell mediated signals and/or Tumour Necrosis Factor- α , a rogue amongst inflammatory cytokines. Since oxidation is critical to NF- κ B activation, anti-oxidants can play a pivotal role in its suppression, chief amongst these is α -Lipoic acid, which, as we have seen, the patient supplements at high levels, not to mention all the other antioxidants the patient also takes. Aspirin, as already mentioned, also inhibits NF- κ B activation but the patient ultimately declined aspirin. (However a trial of aspirin in Myeloma may be well warranted in this context.)

The above, far from exhaustive analysis, may have begun to suggest some of the ways in which the Gerson and Orthomolecular Oncology therapies may work in Myeloma. The subject merits far more attention and research. Survival in Myeloma is so rare a phenomenon, and the exponential survival cure remains so immutable, that factors impinging upon it deserve to be scrutinised carefully for new clues towards achieving more successful treatment and cure. An open mind is a pre-requisite of such scrutiny.

Conclusion

"Imagination is more important than knowledge." Einstein once said. Imagination is not usually mentioned in medical case histories. Yet it was the patient's imagination which opened up the closed world of a doomed diagnosis, and led to the discovery of other knowledge that has so far saved his life. The hallmark of the patient's survival has been the balanced interplay of imagination and knowledge, the exercise of impressive willpower, discipline and consistency. It is true he has also had tremendous backing from friends, colleagues and doctors. Whether he lives or dies, his is an awe-inspiring achievement. It is a medical achievement as well. By the statistical reckoning behind our representative opening study of long-term survivors, the patient, placed retrospectively in the non-chemo treated arm, for which one can draw up an asymptotic survival curve, would now, in year 8, have reached approximately 0.5% survivorship, bearing in mind that, in the days before chemotherapy, median survival in Myeloma was between 6-9 months. (105) The patient did not undergo chemotherapy, but did follow an alternative, unique and novel form of treatment, which no-one with Myeloma has ever done before. In this study, in his class, he is a 100% survivor. Or 80%, if you take 10 years as the goal. Whimsy aside, the patient's achievement can be put in a more serious context: the best results of medical advances in Myeloma to date.

Bart Barlogie at Arkansas and Ray Powles at the Marsden are two of the pioneers of the new high dose chemotherapy approach to Myeloma with stem cell support and bone marrow transplant, followed by interferon and thalidomide treatment where necessary. Both Barlogie and Powles have

shown immense dedication and enterprise in nearly two decades of this work. The patient investigated what both had to offer thoroughly before declining. This new approach is now well over a decade old. Barlogie and Powles have published numerous papers on results to date. They have been able to identify with some accuracy a defined sub-group of patients who will benefit from the new treatment. For this sub-group Barlogie and Powles have effected some apparent genuine gains: complete remission rates - 50% and 48.4% respectively, and increased overall survival in the order of 4.9 to >5 years. (106,107) These studies follow patients for more than a decade. In summer 2001 Powles appeared in The Times with 2 ten-year survivors and cited a total of 14 ten-year survivors as a result of his work. Powles has treated some 400 patients in this manner over 18 years. In June 2000 the Marsden's prospective database contained 327 living myeloma patients, of whom the 14 were a part. (108) Barlogie certainly has some ten year survivors but they are not mentioned in his studies which focus on improved overall and event-free survival in 1000 patients, in a 10 year span, for the lucky few with the right prognostic factors.

For we are indeed talking about a minority, though the statistics are complex. Both Barlogie and Powles focus on sub-groups. Barlogie starts with 1000 patients and then finds that of 112 with the right prognostic factors, 52% achieve 5 years continuous complete remission. If we put the 112 back into the 1000 patients pool, 5.8% achieve CCR at 5 years. Powles, who has treated 400 patients with the new approaches, has 14 patients alive at the end of 10 years, 2 of these in continued remission at 15 and 16 years, with a median survival age of 11.6+ years. If we turn these 14 into a survivor percentage of the 400 treated, we get 3.5%. As a percentage of the 327 living myeloma patients recruited by the Marsden between April 1979 and May 2000, the 14 equal 4.3%. (108) This is not a very significant difference from the Mayo Clinic's 3% 10 year survival twenty years earlier.

The Mayo Clinic Study cited in our introduction was done in the pre-HDT therapy era. Most of the patients would have been treated with the standard Melphalan and/or radiation. Of these 570 (we have to exclude the 273 pre-chemo era patients) 3% were alive at 10 years. The comparable pre HDT era, Barts 1992 survival curve for 156 unselected patients, already cited, has 4% alive at 10 years. (But, unlike the Mayo study, by the end of the first quarter of year 11 there are 0% survivors on the Barts curve.) Powles himself has noted the baffling phenomenon of relapse in myeloma even after a continuous first remission beyond ten years, not seen in other blood cancers such as acute leukaemia (108), an enigma that remains to be deciphered if cure in myeloma is to become a possibility. One has to conclude that though median survival may have improved with the new approaches, long term survival remains elusive.

Now let us put the patient in a wider historical context: reported long term survival in the standard therapy era, post-1964 and pre-1989, or thereabouts. (Of course, the new approaches were already underway in the

80s, but not yet widely available.) A review of the literature (109) reveals only 50 documented cases of survival beyond 10 years, with one patient reaching a record 31 years, and 12 others exceeding ten years, only two of whom made 20 years. Of these 50 patients, 8 died of other cancers than Myeloma. Melphalan is known to be carcinogenic. Only 4 patients out of the 50 are cited as "untreated". Long term survival in Myeloma begins to look a little equivocal. Moreover it is clearly still a rare phenomenon. These 50 reported survivors are 50 out of literally hundreds of thousands Myeloma cases worldwide in over 30 years.

Our patient has yet to cross the 10 year threshold. The decimal point has still to shift two places, from 0.5% to 0.005%. He is only 8 years out. But he is 8 years out "untreated". This in itself is even more remarkable. As we have seen, most long term survivors to date have been treated, whether with standard chemo or the newer approaches. Not only has the patient achieved a more than comparable survival to the best that modern medicine has to offer, he has done this by following the ancient Hippocratic precept: "Primum non nocere." The same cannot be said of the medical approaches just discussed, which can have a mortality rate of anywhere between 15% up to 41%, if we include allogeneic bone marrow transplants. (110) If you choose to follow such a course of treatment, you risk your life to save your life, and often, the gamble fails. Or perhaps you just risk your life.

Of course, it cannot be said either that there are no risks in the patient's chosen course of treatment. It is, after all, an experiment, still ongoing, and life itself carries the risk of death, particularly for males the wrong side of sixty. But given the risks and difficulties posed by still incurable Myeloma, perhaps this experiment merits some serious attention. The patient's continued survival does not look like chance. The odds at the beginning were too low for that to be the most indubitably obvious explanation. But then again, perhaps it is just luck, a statistical fluke. Is it necessary to wait another 12 years to establish this? The patient, at any rate, is not prepared to abandon any of his therapies just yet.

Only time and further research with Myeloma patients prepared to follow such "eccentric" protocols may finally settle this question. Such research is badly needed. Only perhaps something completely left of field will solve the enigma of Myeloma, and lead to real cures. New ideas are scarce in the clinical world of Myeloma. What conventional medical studies of Myeloma survival have achieved so far is to establish the self-evident fact that chances of survival are improved, 1) if Myeloma is diagnosed at a relatively early stage, with low B2 microglobulin and CRP and absence of chromosome 13 deletion, 2) if patients respond well to treatment. (105) This does not go far enough: it is almost just description after the event. The questions to answer are why do certain patients respond better to treatment than others? What is biochemically different about them? What leads to such difference? Why are CRP, and B2 microglobulin down? What keeps chromosome 13 stable prior to treatment? Case histories such as this may provide real clues. As St

Augustine once said, *“Miracles do not happen in contradiction to Nature, only in opposition to what we know about Nature.”* The miraculous should heighten curiosity and investigation, not be dismissed as just a miracle.

Let me conclude with the biochemist, Dr Jeffrey Bland: *“Nutritional consultation should be a standard for every cancer therapy. In the face of our existing knowledge of the powerful convergenc*

Afterword

Whilst it deals largely with Myeloma, the details of this Case History may be of real interest to all other cancer patients, particularly in the context of the patient’s narrative history and his discussion of the role of temperament, a more scientifically elusive factor in cancer.

I would like to offer this Case History as Case I, in a Best Case Series. By itself this Case History proves nothing. It is only an exalted and well documented anecdote. Anecdotes, however, if attended to, have frequently been the basis of good science. The National Cancer Institute has recently recognised this in the institution of its Best Case Series. Six such anecdotes, equally well documented, are all that is needed by the NCI to form the basis for further trials and investigations. Such a scheme not only recognises that good science is fed by anecdote, it is a major concession to the economic handicaps faced by underfunded and undersupported Complementary and Alternative Medicine, in the struggle to sift unproved from unprovable and gain acceptance by a conservative medical establishment. Thus if there are any Myeloma patients who feel strongly that they do not want to follow the conventional routes of chemotherapy and bone marrow transplants, but wish, on their own responsibility, and with the backing of their physicians, to follow the patient’s protocols, I would advise that you keep full medical records and details of treatment. (It is also possible to combine some or all of the therapies discussed in the Case History with standard medical approaches to Myeloma. This approach may well reduce the risks of medical therapy and further enhance survival.) Survive Cancer, a registered UK and overseas Charity, which is hoping to pioneer a special study of Myeloma, will be very pleased to hear from you.

Our Patient’s Resource Guide should enable you to do most of the things described here. Please note, however, that you should get your doctor/oncologist’s support at all times for any treatment decision. Dr Wheatley and Survive Cancer take no legal responsibility for a patient’s failure to use the considerable best that modern medicine has to offer. Nor do we advise against this.

(Figure 1 - QCT Bone Mineral Densitometry)

(Figure 2 - Gastric Function Test)

(Table 1 - Blood Chemistry)

(Table 2- Immunology)

(Table 3- Haematological Bone Marrow at Diagnosis)

(Table 4 - Bone Marrow Aspirate since Diagnosis)
(Table 5 - Gerson Treatment Plan)
(Table 6 - Solgar's V2000 ingredients)
(Table 7 - Immunopower ingredients)
(Table 8 - Bone Scans)
(Table 9 - Complete Biochemical Profile)

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