Changes in direction of cancer research over the 20th century:

What prompted change -

research results, economics, philosophy

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Master of Science (Honours)

A thesis submitted to the
University of Western Sydney

April 2007

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Dedication

This research is dedicated to the cancer patients who have so willingly shared their stories with me over the last two decades, and to future patients who will hopefully fare better.

I also dedicate this work to my darling grand-daughter, Sophia, and to her generation in the hope that, by her adulthood, cancer will be prevented rather than treated. If in the future treatment for cancer is necessary, my wish is that such treatment will be humane and patient focused.
Acknowledgements

I wish to thank my supervisor, Stuart Hill, for his patience, support, good cheer and assistance in all facets of this work. I am indebted to my brother, Michael Howe, for his support, critiques and his wealth of knowledge of the legal system in Australia.

My thanks and appreciation must go to Dr. Karen Bridgman and Professor Andras Szasz for their support, wisdom and scholarly advice. My friends who are medical practitioners have cheerfully spent long hours in discussion relating to this study, and I thank them for their patience and clear-sightedness. Thank you to Megan Mathews and Giselle Cooke.

During the writing of this thesis, I have been privileged in having the support of two exceptional scientists. Firstly, Dr Horace Drew III, a molecular biologist of world renown, has provided advice on matters of science. I am convinced that his open-mindedness, intelligence and curiosity, if shared by the majority of scientists, would improve all areas of science. Dr Maxine McCall has shown amazing patience in spending time with me in discussion and in listening to my airing of concepts. I thank you both.

My daughters, Kerri and Moya, have offered support and encouragement in this endeavour and have never doubted my ability to finish this work. The staff at my laboratory have also given help and support in large quantities. Jane Howard, Linda Tutty and all the staff have worked harder to compensate for the time I have taken off while writing. Their help has been most appreciated.

I would like to express my sincere appreciation for the time given in proof reading by both Robert Gammal and Sharon Millyard. Without Sharon’s assistance, in particular, this paper would not have been finished in a timely manner.

I thank you all very much for your assistance in bringing this thesis to reality.
Statement of Authentication

The work presented in this research is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part, for a degree at this or any other institution.
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Abstract

This research examines the changes in cancer research and treatment over the 20th century through to the present date. The aim of the research is to consider which of three factors—research results, economics or philosophy—was most likely to have induced change.

Although it is not an in-depth assessment of the current state of knowledge of cancer research, the thesis does provide an outline of critical changes in knowledge of both cancer cause and treatment. Treatments that are used routinely by conventional medicine are examined. Also investigated are areas of research that aroused interest in the earlier parts of the last century but were then ignored, only now being revisited.

I examine whether economic factors guided research and whether that guidance was directed towards specific ends. The influence and extent of infiltration, if any, by the pharmaceutical industry into the sphere of medicine was also investigated.

The philosophy of medicine is discussed, with particular emphasis on the differences between ethics and philosophy. The philosophy of the profession itself (or lack thereof) may have contributed to decisions on whether to adopt or discard particular research studies and treatments.

I postulate that the medical system, with oncology as one sub-set, may be viewed using the Maturana and Varella (1980) concept of an autopoietic system. Using this analogy, the structural coupling of medicine with industry shows the change that this autopoietic system has undergone to survive. Whether the changes required for survival by the system then produce benefit for the greater environment—the public in general and cancer patients as a specific instance—is examined.

Introduction

Research into cancer has changed significantly during the 20th century. The aim of this study was to investigate the reasons for this change in direction. Three likely parameters for change are:

- Research findings,
- Economics, and
- Philosophy.

Each of these parameters was examined for its effect on cancer research.

The Origin of This Study

All my working life has been centred around laboratories, in both hospital pathology and private laboratories. Over the last 20 years I have seen great changes in the type of work and in the nature of laboratories themselves.

Training in routine pathology predisposes laboratory scientists towards rigid belief patterns that support orthodox scientific views. Our science would not work at all if our beliefs did not form a strong foundation for our actions. It is commonly assumed that the fundamentals of our laboratory training are indisputable.

As Thomas Kuhn (1962) states in *The Structure of Scientific Revolutions*:

> Normal science often suppresses fundamental novelties because they are necessarily subversive of its basic commitments.¹

Investigating Links Between Bacteria and Cancer

For the past 20 years I have been passionately interested in bacterial pleomorphism, the phenomenon whereby, under certain conditions, bacteria can change their form into a different cell type. I have worked with several groups overseas investigating both pleomorphism and the links between bacteria and cancer.

In my current laboratory, Australian Biologics, we perform Polymerase Chain Reaction (PCR) testing for the presence of certain species of bacteria that may be

present in the blood of patients with a variety of conditions. In 2002, we conducted a research project with a small number of women with breast cancer and found that almost 50% of these women tested positive for *Mycoplasma* species. This figure correlated with a larger study on multiple cancer types—also examined by PCR for *Mycoplasma*—where 39 out of 63 women with breast cancer were positive for *Mycoplasma*².

I became intrigued that there was a long history of investigations into bacterial induction of cancer, and found it most puzzling that this field of research had appeared to have been abandoned without earlier studies having been refuted.

One particularly interesting experiment, carried out in 1925, described a gram positive micrococcus that was cultured from a human breast tumour. This organism, considered to be possibly one of the streptococcus group, was then inoculated into mice and dogs, inducing the growth of pre-cancerous lesions in many of the subjects and, in some cases, resulting in breast cancer. Control mice, inoculated with cultures of (non-cancerous) streptococcus and staphylococcus, did not develop any lesions.³

Further investigation of the literature led me to many interesting studies that are discussed further in the History of Cancer Research.

**Challenging Scientific Tenets**

The presence of bacteria in the blood is considered to be indicative of septicaemia, which generally causes mortality if untreated. For most scientists working in routine laboratories, this is such a basic tenet that it is unquestioned. Consequently, research that has questioned this tenet has generally been ignored.

Mass screening for the presence of bacteria that may be involved in the cancer process has not occurred, and there has been no systematic testing of cancer patients for the presence of bacteria. I have not been able to find reports of any study that tested—and treated—cancer patients for such microbes. Therefore we have no developed knowledge in oncology of the effect that anti-microbial treatment may have on the prognosis of such patients.
The belief that bacteria have no involvement in the cancer process was not held in the earlier part of the 20th century, but interest in this possibility lost popularity by the middle of the century. Now, 50 to 60 years later, research is being done and papers are being published, postulating that at least some cancers are of viral or bacterial origin. A search of PubMed⁴, using the terms ‘bacteria’ and ‘cancer’, yielded the following:

<table>
<thead>
<tr>
<th>Years</th>
<th>Number of Publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960 – 1970</td>
<td>7</td>
</tr>
<tr>
<td>1970 – 1980</td>
<td>127</td>
</tr>
<tr>
<td>1980 – 1990</td>
<td>414</td>
</tr>
<tr>
<td>1990 – 2000</td>
<td>1222</td>
</tr>
<tr>
<td>2000 – 2001</td>
<td>334</td>
</tr>
<tr>
<td>2005 – 2006</td>
<td>2252</td>
</tr>
</tbody>
</table>

The loss of so many years of potentially productive research on bacterial involvement in cancer has led me to question why such interesting fields of cancer research have been abandoned and taken so long to reappear? Why do particular lines of research flourish whereas others are neglected?

I felt there was a need to examine the paths research has taken over the last century and to identify the factors that influence and determine which lines of research are followed. Was any hierarchical structure involved that contributed to such decisions? Was it a question of finance, of who would fund such studies or whether a profit margin might contribute to a decision to follow a particular line of thought?

**Questioning Medical Doctrines**

The medical science paradigm has patriarchal grounding, which emphasises control through objective rationality and separation between observer and observed.⁵

During medical school, students are expected to memorise a massive amount of detailed information, all provided by lecturers, professors and textbooks and regurgitated in exams. Critical examination of this information and questioning of the validity of these so-called facts is not encouraged. This is possibly because of
time constraints, but is more likely a result of the assumption that these ‘facts’ are immutable truths. Teaching methods in medicine tend to encourage the ‘subservience’ of students. A medical practitioner (M.M.) told me in an interview, “We were expected to stand with head bowed, and hands clasped either in front of or behind the body”.

This conditioning of the ‘acolytes’ at the beginning of their careers does not promote critical thinking or questioning of any of the tenets of the medical profession. Instead, it promotes a devotion to the medical doctrine espoused. As Griffin stated in 1995:

By a linear process of mind that cannot ultimately be separated from the desire for domination by both church and state, a nearly invisible idea of hierarchy in science has determined both its epistemology and its methodology. What was once divine authorship has been replaced by the myth of objectivity, an imagined position which, like the Christian idea of the divine, is not embedded in nature, and from which truth alone can be perceived. The absolute truth of religion has been replaced by the abstract principles of science, as if the numbers or statistics were intrinsically beyond doubt, even by quantification. And just as religious doctrine placed the sacred above the profane, scientific theory has been placed above experience itself, while socially the scientific establishment has come to occupy the same position of authority once held by the church.6

Addressing the Medical Paradigm

The antagonism of the orthodox medical world to any criticism of medicine was discussed in an article by Dr Eveleen Richards of the Department of Science and Technology Studies at the University of Wollongong and quoted by Carter in Racketeering in Medicine7:

“According to the revised view, these conflicts must be treated as essentially political issues where there are no impartial experts. The medical expert must be seen as a necessarily ‘partisan participant’ in a political debate, not as an apolitical arbiter of medical truth, and this implies a radical review of the expert’s role in therapeutic evaluation…. The difficulties of the enterprise, however, are not to be underestimated. The institution of medicine has a great deal invested in the perpetuation of the myth of objective evaluation. It underpins the cognitive and social authority of its practitioners and legitimate powerful vested interests, not only in medicine, but in society at large.”
In 1998, when invited to address a Rotary Club, I suggested that I call my talk “The Politics of Cancer”. The audience included three medical practitioners. As I discussed the monetary interests involved in medicine and the extent to which these interests may decide the range of research conducted, these doctors became more and more agitated. Towards the end of my talk, one doctor leapt to his feet, pointed his finger at me and announced, “You would be the type of person who, if your child had leukaemia, wouldn’t allow them to have chemotherapy!” I found it extraordinary that a discussion of possible corruption in the ‘system’ of their profession would be regarded as a threat, and would provoke such an astonishing personal attack.

Another experience that caused me to question the objectivity of medical doctors occurred when, in 1988, a friend (P.S.) organised a talk for medical students at the medical school of an Australian University. The talk was given by the head of a holistic cancer clinic based in Mexico.

In the early 1980s, while in her late twenties, P.S. was diagnosed with malignant melanoma. She underwent surgical removal of the tumour and was told that a clear margin had been taken and she would be ‘fine’.

Within six months, she had developed a secondary tumour in the lymph node at the groin. She visited three local oncologists, who all agreed that the melanoma had metastasised and that she had only around half a year to live. She declined palliative treatment in her home city and travelled to Mexico, where she underwent several months of treatment at a hospital headed by Dr. Rodrigo Rodriguez. She returned to Mexico several times over the next few years to continue treatment. The talk at the university was arranged by my friend when she had been three years in remission.

I was present at the talk, where Dr Rodriguez discussed the use of intravenous vitamins, injectable amygdalin and various other complementary treatments used at his hospital. At the end of the talk, one of the professors from the medical school launched into a very derogatory critique of these supposedly unscientific methods. With many of the students laughing in response to the witticisms of their professor,
my friend became upset and stood to announce that Dr Rodriguez had saved her life when he successfully treated her for secondary melanoma. The professor asked her how long ago this was. On being informed that the metastases had been found three years earlier, he pointed at P.S. and exclaimed “You have two years to live”. This professor had been one of the oncologists who had given P.S. a prognosis of around six months.

I found this display extremely disturbing on two levels. Firstly, there was no attempt at any rational discussion of the benefits or otherwise of Dr Rodriguez’s treatments. Secondly, a person charged with instilling the qualities needed in medical students to make them caring, ethical practitioners seemed to be gleefully wishing death on another to support his clearly biased position.

Fortunately, the professor’s prediction of two years was as inaccurate as his earlier prediction of six months. My friend, more than twenty years after the original melanoma, is still alive and well today.

**Direct Conflict with the Medical Establishment**

In 1994 I convened in Sydney an international congress (The First World Congress on Cancer), bringing together scientists and clinicians from 13 countries to discuss and present cutting-edge research on new cancer treatments. The resulting interaction and conflict between myself and what appeared to be the organised cancer business in Australia strengthened my concerns about the cancer establishment.

The presenters were well-credentialed and reputable, many holding tenure in universities and others acknowledged as authorities in their own countries. The speakers included:

- Professor Bjorn Nordenstrom, the inventor of both the fine needle biopsy and ECT, an electro-galvanic treatment for solid tumours,
- Professor Wassilij Gudov, a most honoured and decorated scientist from what was previously the USSR,
- Professor Wolfgang Köstler, President of the Austrian Society of Oncology,
Dr. Hans Neiper, Past President of the German Society of Oncology, and

Professor Kedar Prasad, President of the International Cancer and Nutrition Society and Head of the Centre for Vitamins and Cancer Research at Colorado University.

A telephone conversation with an executive director of a leading cancer research organisation was one of the first indicators of problems to come. I had approached the organisation for assistance in notifying appropriate associations and groups of the congress. When I informed them of the range of treatments to be discussed, he refused assistance and stated that “all that these people have is anecdotal evidence from survivors”.

I had assumed that there would be widespread interest in these new and promising approaches to cancer research among Australia’s oncologists. I was surprised, perhaps naively, by their conspicuous absence from the congress and by the virulence of the attacks that followed.

A media battle ensued that paradoxically helped the congress to become a great success. It also demonstrated to me the absolute refusal of the medical establishment to have open discourse with any scientist, clinician or medical researcher who works outside the narrow world of chemotherapy, radiotherapy and surgery.

Dirty tricks were used in an attempt to sabotage the conference. Although 25 000 brochures were sent by road transport to the offices of the Doctors’ Weekly for inclusion in their magazine, mysteriously they disappeared and were never recovered.

Leading Sydney oncologists and members of the NSW Cancer Council suggested that treatments such as intravenous vitamin C, coffee enemas and vaccines should be avoided as they could kill patients, and published articles in Sydney newspapers decrying the congress.
This had a major impact on my life and my beliefs. It initiated a growing interest in the ‘politics of cancer research’ and it certainly played a role in my resolve to carry out this research.

Since 1985 many cancer patients have been tested in our laboratory. Many are using a combination of conventional therapy with adjunctive complementary therapies. I have been fortunate to have developed relationships with many of these people. Some are short-term relationships: we may only meet a few times. I have come to know other patients well, after conversations that have spanned a dozen or so visits.

Many have asked questions that are not easy to answer. My resultant search for answers has also prompted this investigation.

**Scope of the Study**

It is not in the ambit of this research to provide a complete listing of cancer treatments and the changes in science that have led us to where we are today. I have attempted to provide only an overview.

My examination of research paths not followed is intended as an indicative rather than a definitive guide to promising research that has been ignored.

My intention is not to belittle in any way the dedicated work of doctors. I have the highest respect for medical practitioners who devote their lives to healing and to their patients. I do, however have serious concerns as to the state of the medical profession in its entirety.

My overview of cancer statistics should be regarded as just that—an overview. Any criticisms of universities, government institutions or regulatory bodies relate to events that have been often extensively reported prior to this research.

Oncology has increasingly become a reductionist based dogma perpetuated by what is, in practice, a closed system, imprisoned by its boundary conditions. Medical science has developed extremely stringent boundaries—maintained by biased peer review, doctrinal teachings in medical schools and by selective funding—that must
conform to the current medical model. Closed systems may tend towards equilibrium but by their very nature also tend towards entropy.\textsuperscript{8}

**Organisation of the Research**

**Part I: Background**

*Chapter 1, Methodology*, gives background to the researcher and to the methodology used in investigating changes in cancer research. It also discusses the background literature that has formed a framework for the investigation and prompted many of the questions raised.

*Chapter 2, A Century of Cancer Statistics*, sets out statistics relating to cancer occurrence and cancer deaths, and analyses the changes and increases in these statistics over the last 100 years.

**Part II: Research Findings**

*Chapter 3, History of Cancer Research: Cause and Treatment*, gives a brief history of the developments in cancer research over this last century, in particular, the exploration by science into cell change, DNA, genome mapping, and epidemiology. It then examines the development and efficacy of the most popular treatments for cancer: chemotherapy, radiotherapy and surgery.

*Chapter 4, Bacterial Involvement in Cancer*, examines the cancer research and treatments that initially showed promise yet have never been fully explored or developed. The research into a bacterial involvement in cancer has been largely ignored or even actively discouraged, through the withholding of research funding and the negating of research results.

*Chapter 5, Paths Not Followed*, explores the research on chemicals that are known to cause cancer but to which we are still routinely exposed in our environment. In this chapter, I also analyse treatments for cancer that have not been integrated into conventional oncology. The ongoing control of which treatments to support and which to ignore has created a rift between clinicians: some became ostracised, some were labelled quacks, but subsequent research has often confirmed earlier discredited
claims as valid. There appear to have been many lost years of research and many worthwhile research projects ignored.

Part III: Economics

Chapter 6, Following the Money, examines the corporations involved in producing the drugs and equipment used in cancer treatments. The wealth and power of the multinational corporations is known to the general public. The use of money by these corporations to influence, buy and pervert has not been common knowledge. The use of money to influence doctors’ prescribing habits, to encourage practitioners to lend their names for use in fraudulent research papers, to influence governments and government departments—established to regulate these same companies—has not been common knowledge.

This chapter pursues the argument that the companies are not ethical or moral establishments: It should not be expected that they be altruistic in their corporate life. They should also not be allowed to walk away unscathed from the illegalities and breaches of regulations that so many corporations have indulged in over so many years.

Chapter 7, Academic Freedom—Academic Funding, examines the role of the universities, medical schools, and government scientific establishments in cancer education, research, prevention etc. It is the universities who most influence the thinking of new doctors; it is the universities who are responsible for the training of doctors and for the inculcation of a truly ethical and moral relationship between doctors and their patients. Changes to the funding of universities have had a profound effect on both the research and the end results of this research. Because governments are contributing less and less to universities, this is forcing them to look for finances in other quarters.

Part IV: Philosophy

Chapter 8, The Philosophy, provides an overview of medical philosophy; focusing particularly on how philosophy has been narrowed to the lesser subsection—ethics. Medical philosophy is compared with that in another profession, and an overview of cultural changes affecting the way medicine is practiced in other cultures is provided.
The lack of a suitable framework of self-introspection as to the ‘why’ of medicine has contributed to the ‘what we can do’ attitude.

*Chapter 9, Autopoietic Systems—A Biological Analogy*, offers another viewpoint of medicine as a social structure and of the requirements of a social structure to be determined as ‘autopoietic’. I discuss the tentative hypotheses that medicine, as an autopoietic structure, has formed an intensive version of structural coupling with the pharmaceutical industry, and how in the process it has given up the goals and autonomy that are usually implicit in autopoiesis.

Throughout this study I have used numerical referencing to increase and simplify readability. In *Chapter 1, Methodology*, I have also introduced the Harvard system of referencing when alluding to particular books in general rather than to specific points or text within that book.

**The Hypothesis**

My hypothesis is that, throughout the 20th century, oncology became an autopoietic system: it has established strictly defined parameters and is autonomous and self-maintaining. Although the processes being discussed apply to the whole medical system, the focus of this research is only on oncology.

As a self-maintaining entity with very defined boundaries, oncology as a social structure may have a long and useful life. Knowingly or unknowingly, oncology has, however, incorporated another discrete and more powerful structure into its system: the corporate structure of the pharmaceutical companies. This incorporation, and resultant symbiotic relationship, has formed a very unhealthy alliance.

The anticipated benefits of this research are to not only ascertain why we have our current system of research and treatment, but also to make some sense of the key players in what has undoubtedly become one of the largest and most influential industries world-wide.
Key starting questions included the following:

- Which sectors involved in cancer research have exerted the most influence on the directions taken?
- How was such influence achieved, and what enabled it to occur?
- Who are, or should be, the guardians of science or, according to Juvenal, Sed quis custodiet ipsos? (Who guards the guardians?)

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PART I

BACKGROUND
Chapter 1

Methodology

My investigation is primarily a retrospective evaluation focussed on both general publications and the scientific literature on cancer research, in which issues within oncology have been raised over many decades. The purpose of my enquiry is to take a global view of how we have arrived at the conventional treatment modalities that are currently dominant and to what extent the main influences (research findings, economics or philosophy) have determined this situation.

Cancer research and, by extension, the treatments resulting from it, affects directly and/or indirectly a significant proportion of humanity. Discovering the intent, or at times the motivation, of such a large scale conglomerate as the ‘cancer industry’ is only possible through an examination of the literature of all parties involved.

From the documentary evidence, I seek to evaluate and question the actions and structures of the following interrelated groups:

- Medical science (as a discreet organism),
- The corporations that supply products (such as pharmaceuticals),
- The government agencies that direct and regulate this complex industry,
- The profession (primarily the medical practitioner), and
- The final user: the cancer patient.

The documentary evidence has been gained through both mediate access (examining evidence in the form of written texts) and proximate access (through interviews and questioning)\(^1\) of a variety of stakeholders, including cancer patients, medical practitioners and scientists. Because no single method of enquiry appeared sufficient for the investigation, I have combined the following three styles of qualitative methodology:

- Hermeneutics,
- Case studies, and
Literature Review Using a Hermeneutical Approach

The large quantity of data that I’ve accessed over time, and the need to extract and interpret meaning from this data, led me to adopt a hermeneutic approach. Hermeneutics was originally used in relation to legal and theological issues, but it has subsequently been developed, based largely on the work of Heidegger and Gadamer, into a broader methodology for understanding other human issues.

I have aimed to be objective in assessing the texts I have gathered. It is not possible to be completely objective, however, because our own understanding and history always unavoidably impinges to some degree on the interpretation of historical texts.

Hermeneutics allows for the historical retrieval of texts, framing them into a reconstruction of meaning in our society. It enables us to deepen our understanding of the historical past by including our own interpretation of it, and by framing it within the context of our specific enquiry. Instead of letting the text be limited by the author’s intent, hermeneutics can be used to place the text into our own history or life experience, to contribute to our understanding, interpretation and application. Betti, in *Teoria dell’Interpretazione*, has argued that text may be regarded as an objectified representation of human intention.

Early on I decided that hermeneutics would provide me with the best methodological framework for interpreting and understanding the events (through examination of the retrieved literature) that have brought us (Western society) to our current state of cancer research and treatment. As stated by Wiercinski et al in 2005:

Ideas are nested in historical, linguistic, and cultural horizons of meaning. A philosophical, theological, or literary problem can only be genuinely understood through a grasp of its origin. Hermeneutics is in part the practice of historical retrieval...

Documents are produced by people and are by-products of the thoughts and feelings associated with human experience, both from the present and the past. Sidney and Beatrice Webb were quoted by John Scott (1990) as having argued that each such document is:
...an instrument in language which has, as its origin, and for its deliberate and express purpose, to become the basis of, or to assist, the activities of an individual, an organisation, or a community.\(^7\)

I have not only provided the historical basis for our current position in terms of research and treatment (see Chapters 2 and 3), but have also provided a secondary historical record of scientific research that fell outside of mainstream enquiry (see Chapters 4 and 5).

**Case Studies**

I chose case studies as a second methodology to enable me to address the broad and complex nature of the topic. Yin (1994) defined the case study approach as:

...an empirical inquiry that investigates a contemporary phenomenon within its real-life context, especially when the boundaries between phenomenon and context are not clearly evident.\(^8\)

Although a single case study can be used to form a hypothesis, it can also contribute to the systematic testing of hypotheses and to the building of a theory (see Ruddin citing Caporaso et al\(^9\)). When multiple case studies are carried out (as in this research) judgements of their ‘typicality’ can be justifiably made.\(^10\)

My interest in the issues involved in cancer research and treatment preceded the formal initiation of my research topic. Because of this I had already begun to collect case studies as a by-product of this interest. To provide enough data to prove my hypothesis, however, entailed the use of additional collective case studies.\(^11\)

My investigation into the role of the companies, in relation to my research questions, involved not only hermeneutic examination of key texts, but also the use of selected texts as case studies. Information about the companies’ finances and their promotion of drugs has been obtained by examining these companies’ own documents as well as texts written about them.

*Chapter 6, Following the Money*, focuses on many of these companies and on events that involve them. These events were influenced by a complex of interrelated
contextual factors, including both the political and social conditions at the times they occurred.

Using case study methodology, I selected cases that focused attention on my research topic and discarded events that were not relevant to my theme. To show the global nature of events engendered by these companies it was necessary to document multiple case studies in which the aims and outcomes were shown to be largely similar across companies, showing that these events were not singular occurrences.

The actions of the pharmaceutical industry have impacted not only on the patients who are the end-users of the drugs produced, but also on the people working on health issues in government, universities and the medical profession, particularly oncologists. Case study methodology was required to assess the impact on all parties involved. As the phenomenon being researched is broad and complex, multiple case studies have helped to show the generality of actions, as opposed to a single case study showing a singular aberrant event.

This methodology was also employed in Chapter 7, Academic Freedom—Academic Funding, in which I used multiple events to demonstrate the changes that have occurred in universities throughout the 20th century and leading into our current decade.

Case studies have been used to examine how the privatisation and commercialisation of research, and of the universities themselves, have contributed to the control and direction of streams of research.

In Chapter 6, Following the Money, and Chapter 7, Academic Freedom—Academic Funding, my case studies are multi-perspectival: I have examined the interactions of multiple groups—of those touched or affected by the events—rather than just the isolated events.

**Qualitative Interviews**

A small but significant part of my investigation involved conducting a series of interviews. Qualitative interview methodology has enabled me to pose questions to a
variety of people in my effort to understand the significance of research changes historically, and to gauge the human impact these changes have induced. Qualitative research interviews may be defined as:

... attempts to understand the world from the subjects’ point of view, to unfold the meaning of peoples’ experiences, to uncover their lived world prior to scientific explanations. 12

Over the period of time of my candidature, I have been invited to present papers at two annual meetings of the German Society of Oncology (Deutsche Gessellschaft für Onkologie) and at two breast cancer conferences in Canada (see http://www.wcbcf.ca/).

As a member of the German Society of Oncology for the last 10 years, I have attended most of the annual meetings and have forged excellent relationships with many of the attending oncologists from Germany and Austria. This contact has allowed me to become involved in a series of discussions with European oncologists relating to the focus of this research.

Presenting at two World Breast Cancer Congresses in Canada enabled me to not only listen to presentations by a diverse range of researchers, but also to meet and discuss my interests with them and with others from around the world.

It becomes clear, when participating in such international conferences, that carefully constructed questions can reveal much about the cultural differences in medicine and science. Such discussions have contributed to my research, particularly in the areas of social structure and cultural variations between countries. Chapter 8, The Philosophy, focuses on the effects on society (and on cancer patients in particular) of the dominant directions taken in cancer research and the resultant treatments.

Having a work history that has centred on pathology testing has provided me with a social circle that is also medical-centric. Many of my friends are medical practitioners and have willingly allowed me to interview them and use them as sounding boards for musings on my research topic. I have attempted to maintain a certain distance from my findings to allow objectivity, but the experiences of my
friends in dealing with medical establishments, patients and pharmaceutical companies has given me access to their diverse views of this world.

Because of the nature of my work, I frequently see cancer patients while they are undergoing conventional treatment. Some patients are regular visitors to our laboratory, and over many visits a sense of rapport often develops. Many of these patients have shared with me their stories of their experiences in the medical system.

I have posed essentially the same questions to both patients and doctors through my qualitative interviewing, and have found considerable similarity in their answers. However, because most of the medical practitioners I interviewed are holistic in their outlook, their views would not be expected to be representative of conventional oncology practitioners. Many of these holistic doctors are involved in cancer treatment through the provision of adjunctive treatment and lifestyle care.

Interviews and dialogue have provided the foundation of my proximate access to the data that has shaped this research. Although I have not included many transcribed interviews, these interviews have nevertheless contributed significantly to my understanding gained through this research. The voice of the patient first set me on this enquiry and the other 'voices' I have listened to along the way have helped to form the direction and framework of this work.

**Literature Survey: Sources**

Many books have been written on topics relating to the central themes of my research. I have continually evaluated and had to severely cull to arrive at those that I selected as supporting references. Key criteria were that the books are well referenced, and that the findings are verifiable.

**Criticism in the Popular Press**

Established conventional medicine has often been criticised for its failure to adequately investigate and promote the prevention of cancer, concentrating its attention instead on treatment and diagnosis. Neglected areas include the environmental, workplace and dietary causes (and co-factors) of cancer.
Epstein (1998), in *The Politics of Cancer Revisited*, has questioned whether any significant improvement in treatment and survival rates has occurred over the last few decades, and he critiques the politics of the cancer establishment in exhibiting an indifference to prevention strategies.

The issue of pursuing only a relatively narrow path of research—where ‘other’ causes and treatments have not been considered or adequately researched and, in fact, have often been actively suppressed—has also been raised in Cantwell’s (2005) *Four Women Against Cancer*, in Carter’s (1992) *Racketeering in Medicine*, in Culbert’s (1997) *Medical Armageddon*, and in the many journal articles quoted in Chapter 5, *Paths Not Followed*.

The usual reason given by the ‘medical establishment’ for this situation, and in particular for the narrow research agenda, is lack of funding.

**Literature that Focuses on Quality of Life**

The question of the quality-of-life effects of cancer treatment has been raised by many authors, especially in the popular press: Schou and Hewison (1999) “Experiencing Cancer: Quality of Life in Treatment”. Many authors have promoted a variety of less damaging and less toxic treatments in place of the conventional more invasive therapies.

It is not my intent to review or discuss the possibilities of such treatments. However, Moss (1995), in *Questioning Chemotherapy*, has ably critiqued the results that current treatments utilising chemotherapy achieve. Also, Ulrich Abels (1992), in *Chemotherapy of Advanced Epithelial Cancer – a Critical Review*, has also critiqued the use of chemotoxics in epithelial cancers, the most common form of cancer and one that has a very low response rate to chemotherapy.

**Questioning the Medical Power Base**

Many authors have wondered aloud about a medical establishment that has prevented or eliminated alternative forms of treatment to maintain its power base, where business and money are placed before the wellbeing of the patient. Barlett and Steele (2004), in *Critical Condition: How Health Care in America Became Big Business &
Bad Medicine, provided an exposé of how devotion to the profit margin has damaged the medical system in the USA and lessened life expectancy among the population.

This has been further documented in works such as Brown’s (1986) Aids, Cancer & the Medical Establishment, Walker’s (1993) Dirty Medicine, and Moynihan’s (2001) Too Much Medicine.

Questioning the Influence of Industry

The role of the pharmaceutical companies in maintaining what appears to be a status quo (or merely an extrapolation of it) in cancer treatment has been repeatedly criticised. The relatively recent rapid growth in the power of corporations has changed the way science is now carried out.

Control is now exerted through monetary power, which is a main deciding factor as to which research paths to follow, how drugs and treatments are promoted, and what the public are told in publicity campaigns. Both Bakan (2004), in The Corporation, and Beder (2000), in Global Spin: The Corporate Assault on Environmentalism, clearly outline the dangers to public interest that corporate priorities and greed pose.

From Le Carre’s (2001) Constant Gardener, in which a pharmaceutical company that puts profit before life is cast as the villain, to Marcia Angell’s (2004) critique of Big Pharma in The Truth About the Drug Companies: How They Deceive Us and What To Do About It, popular literature shows a growing concern about the morality of the corporations.

As a former Editor-in-Chief of The New England Journal of Medicine, Dr Angell was placed in a position that allowed her to see clearly the power that Big Pharma exerted over both government agencies and the clinical trials of drugs. This influence has rippled throughout the scientific world with revelations of peer reviewers with no financial interests in industry being almost impossible to find, and of scientists signing their name to articles ghost-written by industry employees.¹³ ¹⁴

Cancer Industry and Wohl’s (1984) The Medical Industrial Complex have addressed the problems inherent in a system where the primacy of economic power enables corporations to control our health systems.

**Challenging the Halls of Academe**

Academia’s position has been shown by Krimsky (2003), in Science in the Private Interest, to reflect a somewhat tarnished Ivory Tower. As government funding to universities in most countries has declined, the need for universities to turn to industry for support has resulted in the establishment of an unhealthily close partnership between medicine and industry. This connection extends from whole medical schools and research institutes that receive extensive funding, to individual scientists and clinicians who are funded with monies from industry without openly appearing as employees of the companies involved.

Payer (1992), in Disease-Mongers: How Doctors, Drug Companies, and Insurers Are Making You Feel Sick, shows how marketing techniques can create new illnesses and new uses for drugs to increase profits. Epstein’s (2005) Cancer-Gate: How to Win the Losing Cancer War critiques the National Cancer Institute in the USA and documents the American Cancer Society’s conflicts of interest with industry.

**Promise or Statistics**

The statistics, used both politically and scientifically, that relate to the success of cancer treatments have been found wanting by such epidemiologists as John Bailar III in the USA and Ulrich Abel of Germany. According to Bailar, the much publicised War on Cancer, initiated by President Nixon when signing the National Cancer Act in 1971, has been a qualified failure and a war that has been lost.

With a World Health Organisation health report estimating that by 2020 global rates of cancer could increase by 50%, it is imperative that more attention be paid to prevention. Although much of this increase in cancer rate may be linked to life-style factors and poverty, there is also an alarming world-wide increase in hormonal cancers. Environmental campaigners have often linked this to the chemicals used in industry and agriculture.
Sources for Statistics

Statistics on cancer occurrence and treatment success have been sourced from the scientific literature, the World Health Organisation (http://www.who.int/en/), the Australian Government Bureau of Statistics website, (http://www.abs.gov.au/) and the SEER (Surveillance Epidemiology and End Results) programme database (http://seer.cancer.gov/).

Conspiracy Theories

Much has been written in the popular press about ‘conspiracy theories’ relating to drug companies and their financial hold on governments, for example, Griffin’s (2001) *World Without Cancer* and Proctor’s (1995) *Cancer Wars*.

Although much of the popular literature in this field tended towards conspiracy theories, such as control of medicine by the Rockefeller organisation and other powerful groups, this did not constitute part of my research. Whether these claims have any basis in truth is not what I was investigating. Rather, I was impressed by more reliable sources, such as Richard Horton’s (2001) editorial—*Lotronex and the FDA a Fatal Erosion of Integrity*—in *The Lancet*, and Coombes’ (2005) article *Drug industry’s new code criticised for lacking teeth* in the *British Medical Journal*.

Investigative Journalism

Several Australian Broadcasting Commission investigative journalism productions (Four Corners *Paying the Price*) and newspaper articles on revelations by whistleblowers in government or industry positions have raised issues relevant to my research. Also, a British House of Commons report (*The Influence of the Pharmaceutical Industry 2004-2005*) found that influence by pharmaceutical companies was excessive and contrary to the public good, and that the interests of patients, the National Health Service (NHS) and industry were at odds and did not serve the public well.

Popular press publications such as Rampton and Stauber’s (2001) *Trust Us, We’re Experts, How Industry Manipulates Science and Gambles with Your Future* have also highlighted the control and power of pharmaceutical corporations.
Historical Sources

The short history of oncology has been sourced from textbooks such as the *Encyclopaedia of Medical History* by McGrew (1985), from International Cancer Conference Proceedings (starting from the 1920s), journal articles on the history of Occupational Health, and from the American Cancer Society’s web site on cancer treatments.

Philosophical Sources

For papers relating to questions of philosophy and social enquiry, Project MUSE, (http://muse.jhu.edu.ezproxy.uws.edu.au/) and the Journals of Medical Philosophy were searched.

Most of the literature I relied on to review the philosophy of medicine was from bioethics and philosophy journals. The seminal work of Ivan Illich (1976) questioned the mechanistic approach of modern medicine in *Limits to Medicine. Medical Nemesis: The Expropriation of Health*.

The work of Thomas Kuhn (1962) in *The Structure of Scientific Revolutions*, on paradigm shifts in science, explains the difficulties that all fields of science have with the introduction of new thoughts and insights.

The writings of Erich Loewy 18 19 20, Professor and Chair of Bioethics at the Department of Philosophy, University of California, and his generous personal communications, were valuable in directing my searching of ethical and philosophical papers relevant to my research.

Sources for Social Systems

If oncology in practice, in university and in industry has formed a triumvirate that has morphed into an autopoietic system, then this needs to be clearly recognised. Paradigm shifts are difficult and often unpleasant for those holding on to a system that has become redundant, but often such a shift is required to bring about ‘progressive’ change.

All of these areas of literature are relevant to my enquiry, and much has been written on each specific issue. The need now is to examine the totality of these parts and to identify how and why the present dominant system of cancer treatment developed.

Only by examining the interrelationships between the diverse issues and the organisations involved can we be in a position to judge whether our current cancer treatments are the product of the best that scientific research could offer us over the past century. If this is not the case, the knowledge of how we came to be in this position is needed before any beneficial change can occur.

**Scientific Sources**

The dominant language of oncology (the mode of communication about cancer) is evident in the scientific papers and textbooks relating to oncology. To preserve authenticity and language of the documents used in this research, the scientific papers quoted have been sourced through the Ovid and Science Direct search engines or PubMed, the National Library of Medicine. The papers quoted are from high-ranking, peer reviewed journals that are routinely used world-wide by the scientific community.

Relevant key words were used in searches and often links to related articles broadened the fields of the searches. Full articles were obtained rather than any reliance on abstracts as these often failed to reveal essential information.

Although many of the earlier papers would no longer meet today’s criteria for publication, it was essential that I examined them, taking into account that they reflected the science of their time.
Newspapers, the Popular Press and Websites

Documentary evidence was also sourced through newspaper articles, some Australian, but many from international newspapers such as The New York Times, The Guardian, Wall Street Journal and Forbes. I have also examined relevant websites, such as Public Citizen (http://www.citizen.org/) and the Centre for Media and Democracy (http://www.prwatch.org/). These provided many useful articles and helped to guide my ongoing searching.

Much of the information concerning monetary factors, particularly relating to the pharmaceutical industry, had to be accessed, at least initially, from the popular press. I was well aware that documentation obtained via the printed media required an assessment as to the possibility of the press being used as part of spin-doctoring campaigns.

Governmental and Legal Sources

In relation to the pharmaceutical industry, I also examined various court and government documents, especially from the USA. The 2005 UK House of Commons Health Committee report\(^\text{21}\) on The Influence of the Pharmaceutical Industry was particularly useful.

Interpretation and Bias

Scientists’ choice of guiding theory can depend not only on the evidence gathered, but also on the particular social and political context. This had to be considered when examining the nature of the scientific evidence.

Similarly, to gain a deep understanding of the interconnectedness of the groups involved in this investigation required an interpretative approach in relation to understanding the various events that have occurred. These ‘events’ are evidenced in the documents that were produced during the time when they occurred. My various discussions, both in Australia and overseas, were invaluable in helping me to more fully understand the scientific literature of the time.
I was only able to answer my initial question—what forces had prompted and enabled change in the direction of cancer research?—by discussing this, where possible, with the people involved.

**Literature in the Context of People**

Cancer research, by its very nature, cannot be divorced from humans. Whether terms such as cancer victim, sufferer or patient are used, our concern should always be primarily with the people who develop this disease. For most cancer patients, the type of treatment they receive is decided, usually with no discussion of the full spectrum of choices available to them, by conventional medical oncologists. Only a minority of cancer patients decide to seek other forms of treatment. Opinions on the value of alternative treatments, among both conventional oncologists and patients, are often diverse and emotionally charged.

I was also driven to better understand the thinking and positions of the scientists involved, whether they were working in government, industry or university. Their stories were undoubtedly influenced by their social background and a range of constraints, whether from peer pressure or social changes in general, and by the effects of increasing commercialisation of science and medicine.

The third group of interest to me in this research was the companies themselves. Society places relatively clear moral obligations on its members, but corporations are not necessarily subject to these same obligations. The employees of corporations may not be held accountable in the same way as individuals within society. Directors and executives are often legally protected from the end results of their decisions.

Bakan (2004) notes, for example, that:

> The corporation’s legally defined mandate is to pursue, relentlessly and without exception, its own self-interest, regardless of the often harmful consequences it might cause to others.\(^\text{22}\)

By the end of the 19\textsuperscript{th} century, particularly as a result of a US Supreme court decision in 1886, the corporation had gained the status of an ‘entity’, imbued with
rights to a ‘due process of law’, as would any individual. Because of this, case studies relating to the moral obligations and practices of corporations should be viewed in the same way as one might view individuals.

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23 ibid., p16.
Chapter 2

A Century of Cancer Statistics

After all, facts are facts; and although we may quote one to another with a chuckle the words of the Wise Statesman, “Lies—damned lies—and statistics,” still there are some easy figures the simplest must understand, and the astutest cannot wriggle out of.

Leonard Henry Courtney, To My Fellow Disciples at Saratoga Springs

Over the last century, a steadily increasing flow of funds has been spent on cancer research, both on the process of cancer and on treatments. This expenditure should have produced an increasingly beneficial outcome for cancer patients. As scientific knowledge has increased, as more and more drugs or other treatments are produced as an outcome of this new knowledge, as more is learnt of cancer induction, one might rationally expect that the diagnosis and treatment of cancer would have become more effective and accessible, and that the rates of cancer incidence would have declined.

In this chapter I will examine the statistics on both the incidence of cancer and treatment outcomes for cancer patients. In particular I will examine:

- Whether research results over the last 100 years have given us lower rates of cancer and better cure rates than at the end of the 19th century?
- What factors may influence any increase in cancer incidence?
- The introduction and use of the ‘5 year’ survival rate.
- Whether the death rate from cancer has decreased?
- Differences in cancer rates between industrialised and third world countries.
- Whether cause of death (autopsy) results correlate with what is written on death certificates?
19th Century Death Toll from Tuberculosis

At the beginning of the 19th century, one-fifth of human mortality was caused by tuberculosis. In cities such as London, with crowded living conditions, the rate was even higher, often reaching 30%.

The death rate from tuberculosis steadily declined over the next 100 years. From 1812 until 1840, Boston, Philadelphia and New York recorded deaths of approximately 400 per 100,000, although Budapest, in 1884, lost double this number. By 1947, the death rate from tuberculosis in England was 69 (per 100,000), Canada 45.8 and the USA 41.3.²

Not only did the death rate decline, but there was also a change in the average age of those affected by this disease. Where earlier the average mortality of males had been in their 30s, by the early 1900s the disease was suffered more by the 50 to 60 age group. The only major increase in tuberculosis death occurred during both World Wars I and II, particularly in those countries that were directly involved.³

We now, however, now experiencing a steady increase in the incidence of this disease, mainly because of malnutrition and lack of hygiene. The increasing resistance of bacteria to our armoury of antibiotics also heralds the return of infective disease as a real danger for human health.

By the early years of the 20th century, as the incidence and death rate of tuberculosis decreased, there came an awareness of the steadily increasing death toll from cancer around the world.

20th Century Death Toll from Cancer

Escalation of Cancer to the Leading Cause of Death

According to H.W Keens (London, 1934):

...it appears that the earliest statistical record was made in 1838, and between that date and 1850 the death-rate from cancer was so small per million people living (roughly 200 per mill.), that no great importance was attached to this, any more than to any other disease having a similar death-rate.⁴
Increase of 245% in Cancer Deaths over 60 Years

The figures given in the Annual Returns of the Registrar-General for England and Wales show that the ‘Mortality per Million Living’ for cancer for the years 1856–1860 was 327. This figure steadily increased year by year and, by 1936, the mortality rate per million was 1,625. This was an increase of 245% in the death rate from cancer, over a 60 year period.

Australian Cancer Rates

In Australia, in 1921, the proportion of total deaths from cancer in males was 9.1% and in females, 11.4%. These figures steadily increased, and by 1988, deaths from cancer were 25.3% in males and 25.2% in females.

By 1991, cancer became the principal cause of death for females in Australia. It had already become the main cause of death for men a year earlier. Cancer has replaced ischaemic heart disease as the primary cause for death in this country.

From 1960, following the introduction of the pap smear test, there was a steady decline in the death rate from cervical cancer, but the age-standardised death rate from breast cancer has shown minimal change from 1940 death rates—almost no change in rates over the last 50 years.

Future Predictions

This steadily increasing cancer rate is a global trend. According to a World Cancer Report of 2003, published by the IARC (part of the World Health Organisation), the global rates of cancer could increase by a further 50% to 15 million by 2020. The report stresses the need to control this increase through the actions of governments and health practitioners by the promotion of healthy lifestyles.

This WHO report estimates that one-third of cancers could be prevented by an improvement in lifestyle—including the reduction of tobacco use, increased consumption of fruit and vegetables, and increased physical activity—and by providing screening programmes for such cancers where early treatment is known to increase survival rates.
Demographics of Cancer Increase

Increase in Smoking-Related Cancers
Smoking has been shown to increase the risk of lung cancer by 20- to 30-fold. In countries with elevated smoking levels, approximately 90% of lung cancers are attributed to smoking. It is estimated that 50% of bladder and renal pelvis cancers are from smoking, and cancers of the oral cavity, pharynx, larynx and squamous cell carcinomas are also increased by tobacco use (as reported in the 2003 IARC World Cancer Report).

Increase in Cancers Caused by Infection
The IARC report also documents a large variation in the incidence of cancers caused by infection between developed and undeveloped countries. In developed countries, approximately 8% of malignancies have infection as a cause; in undeveloped countries, up to 23% of malignancies are from infectious agents. These infections included Hepatitis B and C, Human Papilloma Virus and Helicobacter pylori.

Effect of Affluence on Survival Rates
Survival rates for cancer also differ between rich and poor countries. In affluent countries, approximately 50% of cancer patients die of the disease, whereas in poorer countries approximately 80% of patients die. Much—but not all—of this difference reflects later diagnosis in the poorer countries.

Whether or not we presently have the best system of cancer treatment available to us, our system is obviously more effective at prolonging life than treatments currently available to the poor. The malnutrition suffered by the poor also contributes to a lesser chance of surviving the disease.

There is however, an increase in the number of cancer cases in the developed world as compared to the undeveloped. The developed nations show an earlier use of tobacco, an earlier exposure to occupational carcinogens, and the Western lifestyle and nutrition. Whereas the poor may receive little or no treatment and have minimal nutrition with which to maintain health, our leisurely and well-fed society may be killing many of us.
Increase in Hormonal Cancers

The incidence of hormonal cancers is increasing rapidly. World Health Organisation estimates for 1997 rank breast cancer as the leading cancer, with a total incidence of 895,000, with 505,000 in the developed world and 390,000 in the developing world.⁸

Measures of Success: The Death Rate

What are the crucial questions for a cancer patient? Death rate remains one of the most important yardsticks by which to judge the success of cancer treatment. However, quality of life of the cancer patient, which will be addressed in a later section (see ‘Balancing Quality of Life Against Length of Life’ on page 247) is equally important.

Death Rate Statistics

Australian Figures

In Australia, according to Australian Government Statistics, by 1995 there had been a 4% increase in cancer death rate over the previous 20 years. 45% of all cancer deaths were caused by cancers of the lung, colon, breast and prostate. The most common causes of death were lung cancer (for men) and breast cancer (for women).¹⁰

By 2002, the leading cause of death in Australia was cancer, with lung cancer and prostate cancer having the highest incidence for men, and breast cancer followed by lung cancer the highest for women.¹¹

The figures, according to our Australian Bureau of Statistics, reflect an increase in longevity causing an increase in cancer death, particularly in older men. However, breast cancer, the leading cancer for women, tends more and more to be found in younger women, and is therefore not attributable to increased longevity.

USA Figures

The 1950 US cancer death rate (for all types of cancer) was 194 out of 100,000 people. In 2001, 50 years (and billions of dollars of research funding) later, the death
rate per 100,000 people was 196. Any advance in treatment appears miniscule or nonexistent.  

**Cancer Deaths in the Third World**

The difference in death rate from cancer between Western countries and the less developed nations is startling. In Europe, 19% of deaths are attributed to cancer, whereas in Africa, death from cancer is only 4%. There is no doubt that the rate of cancer is much higher in developed versus third world countries. People in developed countries live longer and are more likely to get cancer later in life, but the higher rate has also been attributed to an increased use of tobacco in Western countries. There is an expectation that, as tobacco use increases in developing nations, so will the lung cancer rate increase.

**Misclassification of Cancer Deaths**

There appears to be an issue with the reporting of cancer mortality, which may impact on the overall statistics of cancer death. Dr Gilbert Welch and Dr William Black of Dartmouth Medical School have argued that cancer mortality may have been underestimated by 0.9% in the USA, through the listing of the deaths of cancer patients within a month of diagnosis and surgical treatment as attributable to ‘other causes’.  

Welch and Black used data from the National Cancer Institute *Surveillance, Epidemiology and End Result* (SEER) programme for 1994 to 1998. They examined deaths not attributed to cancer in patients with 19 common tumour types who had died within one month of diagnosis and had received cancer-directed surgery.

Their study showed that, of 4135 patients, 41% were not shown on their death certificates as having died from cancer. These figures were broken down as follows:

- 42% of 1695 colorectal cancer patients,
- 34% of 525 lung cancer patients,
- 54% of 256 bladder cancer patients,
- 24% of 242 ovarian cancer patients, and
- 75% of 106 prostate cancer patients.
When the time period examined was extended to four months following diagnosis, the undercounting of cancer deaths was elevated by a further 2%.

The inclusion of deaths such as these on the cancer registers would severely impact on the apparent decrease in cancer mortality shown over the last decade.

**Cancer Deaths Classified as ‘Other Causes’**

How does this ‘undercounting’ or ‘misclassification’ of cause of death occur?

Studies of mortality rates taken from the NCI *Surveillance, Epidemiology and End Result* (SEER) programme, over the period 1973 to 1987, showed that out of 913,161 cancer patients, 40% were recorded as having died from cancer and 21.4% as having died of ‘other causes’.

The most common cause of death for the 21.4% of patients who had died of ‘other causes’ was: circulatory malfunction (i.e. acute myocardial infarction, chronic ischemic heart disease, cerebrovascular disease, cardiovascular disease, cardiac arrest and congestive heart failure) and respiratory disease (i.e. chronic airway obstruction, pneumonia and emphysema). It is unlikely that without the cancer and its subsequent treatment, these patients would have died of these conditions.

**Deaths from Cancer Treatments**

Many of the above conditions, resulting in ‘other causes’ of death, may be associated with certain cancers, but they are also definitely associated with cancer treatments such as chemotherapy or radiotherapy.

When cancer patients who died from ‘other’ causes were compared with known age- and sex-specific mortality figures (Population Hazard Rates), it was found that the overall non-cancer death rate was 1.37 times higher than expected for US age- and sex-specific mortality figures. These figures were garnered from a study of cancer patients diagnosed between 1973 and 1987. If these deaths were attributed to cancer, then the cancer death count would increase by 7.4%. This strongly suggests an increase in death from the effects of treatment; this potential increase is discussed further on page 41.
Disagreement Between Diagnosis and Autopsy Results

Another factor that gives a false (decreased) figure for cancer death rate is the misdiagnosis of cancer and false reporting on the death certificate. The regular use of autopsy as a check of cause of death has become a thing of the past. Most death certificates are now filled in by the attending physician without further verification of cause. Figures from the USA in 1998 put the number of autopsies at below 9% of deaths,16 with autopsies of nursing home deaths being only 0.1 to 1.0%.17

The track record of agreement between diagnosis and autopsy results has been rather poor, judging by published papers. In 1974, the concordance between the ‘gold standard’—the autopsy—and medical judgement was only 43%.18 This was an improvement on the 35% correlation achieved in 193819. However, with the vast changes in laboratory assay ability, equipment for scanning, and DNA technology, one would expect that diagnostic ability would have dramatically increased. Unfortunately, the statistics do not support this.

By 1983, the correlation between diagnosis and autopsy had improved to 47%20. As the following two studies show, one could generously say that by 2003 there had been no change.

In 1998 in the USA, when 1105 cases were reviewed by autopsy, the discordance between diagnosis and autopsy findings was 44%. The study showed that 111 malignant neoplasms had been either undiagnosed or misdiagnosed, and that 57 deaths were directly attributable to cancer without this appearing on the death certificates.21

Another similar study over a 10-year period found that the clinical diagnosis had been correct in only 40% of cases.22 Figures from Japan indicate that more than 10% of malignant neoplasms are either misdiagnosed or undiagnosed despite medical investigations.23 When death certificates and autopsy results at an academic institute, Vermont USA, were compared it was found that, of 50 death certificates reviewed, 17 (34%) had a wrong cause or manner of death listed and 82% showed multiple errors.24
If all deaths were to be autopsied, these papers suggest that the recorded cancer death rate would be increased to frightening levels.

**Are Published Figures Correct?**

Are the published figures on both the incidence and mortality of cancer generally agreed and accepted? Obviously the research scientists who carried out the studies on death rates mentioned above would dispute the published statistics.

There may never be total truth in the production of statistics. The belief and attitudes of those compiling the data must have an influence on the way that data is viewed and presented both to patients and clinicians. Compiling data to reflect a ‘best case scenario’ occurs in many fields of science. The use of the 5-year survival time is an example of this.

**Measures of Success: ‘5-Year’ Survival Rate**

The 5-year survival rate is commonly used as a measure of success of treatment and this has enormous effects on patient longevity statistics. It was originally intended *not* to be an end point but rather a point sufficiently removed from original treatment to allow conclusions as to efficacy of treatment regimes (Sutherland quoting Hawkins).  

When patients are followed for longer time frames, the statistics generally quoted begin to seem rather irrelevant. According to Sutherland in *Cancer: Significance of Delay*, a 1926 study by Moshcowitz et al showed that a survival rate of 34% at 5 years became 31% at 6 years, 26% at 7 years, and by 10 years from treatment only 4% of patients were still living.

In 1947, Finney, Merkel and Millar followed 298 breast cancer patients. This group of women at the 5-year point had 49% survival, but 15 years from initial treatments again only 4% were still living. Neither of these two early studies on longevity stated the age groups of patients followed, so it is difficult to know if the results given were age-standardised. Later papers are more inclined to use age-standardised figures.
An assessment of age-adjusted mortality rates for the period 1970 to 1994 in the USA showed that cancer mortality for 1994 (200.9 per 100,000) was 6.0% higher than the rate for 1970 (189.6 per 100,000).\(^{27}\)

Haydn Bush, in a 1984 article in Science, stated:

> If you take a close look at the statistics on cancer cures, it soon becomes apparent that we’re not curing much more cancer than we were a generation ago. The death rates on the whole just haven’t changed significantly...

> ... There has been very little progress on the biggest cancer killers of the last 25 years—cancer of the lung, the breast, the colon, and the prostate. The death rate has not declined appreciably for any of these, and for lung cancer it has actually risen. Of all the more common forms of cancer, death rates for only two have declined substantially in recent decades—stomach cancer and uterine cancer.\(^{28}\)

In fact, a 1978 examination of cancer statistics by Hardin Jones, Professor of Medical Physics at the University of California, led him to state:

> My studies have proven conclusively that untreated cancer victims live up to four times longer than treated individuals.\(^{29}\)

When cancer patients discuss their treatment with their practitioners, statistics are invariably quoted relating to 5-year survival rather than longevity outcome studies. Certainly, figures for 5-year survival are more encouraging to patients faced with the possibility of debilitating treatment regimes than studies such as those mentioned above, but it creates an illusion of success of treatment that is not supported by current statistics.

An article, published on 12 December 2001 in the *Medical Observer Weekly* titled *Australia has highest cancer survival rates*\(^{30}\), states that the cancer death rates are continuing to fall. It cites survival improvements in breast cancer, Hodgkin’s disease, kidney and colorectal cancer, cervical and prostate cancer. All improvements stated are based on 5-year survival rate rather than death rates or longevity rates for each cancer.
Are Treatments Increasing Cancer Statistics?

Chemotherapy Drugs As Carcinogens

An examination of the Hazardous Substance Fact Sheets[^1] for chemicals lists the following chemotherapy drugs as carcinogens:

- **Dactinomycin** (Actinomycin D): Used in the treatment of testicular, ovarian, germ cell cancers and osteosarcoma.
- **Cisplatin**: Used in the treatment of testicular, ovarian, lung, bone, cervical and mesothelioma.
- **Cyclophosphamide**: Used in the treatment of lymphoma, leukaemias, multiple myeloma, mycosis fungoides, neuroblastoma, retinoblastoma, breast, ovary, rhabdomyosarcoma, bone cancer and childhood non-Hodgkin’s lymphoma.
- **Daunorubicin** (Daunomycin): Used in the treatment of acute lymphocytic and myelocytic leukaemias.

This is a very small selection of the chemotoxic drugs available in oncology. Furthermore their cancer-inducing properties are not the only side effects caused by these drugs. Information on the use of these chemotoxic drugs is taken from the American Cancer Society web site at [http://www.cancer.org/docroot/home/index.asp](http://www.cancer.org/docroot/home/index.asp).

I do not wish to imply that all chemotherapy drugs are carcinogens, but I have not, to date, found any chemotherapy drug that has been listed as having *no* side-effects. Induction of a future cancer is certainly a most serious side-effect and one about which most cancer patients appear to be unaware.

Radiotherapy As a Carcinogen

The other main stay of cancer therapy—radiotherapy—is also known to potentially induce cancer.

[^1]: Accessed February 2007
Radiation treatment for prostate cancer has been linked to a 70% increase in rectal cancer. As there was no noticeable increase in other cancers in the colon, the effect appeared to be limited to tissue that received direct irradiation.\textsuperscript{32} As more than half of cancer patients treated, receive radiotherapy as part of their treatment, and as current treatment now uses intensity-modulated radiation therapy, (IMRT), which involves a larger volume of normal tissue being exposed to lower doses of radiation, this increases the risk of second cancers at a later date.\textsuperscript{33}

\textbf{Conclusions}

Over this last century the figures do not appear to support any major improvement for cancer patients as far as \textbf{real cure} is concerned. Not only are we seeing enormous increases in the incidence of cancer world-wide, but there is only a very minimal improvement in the long-term survival rates for patients diagnosed with cancer.

Any industry that has spent enormous amounts of money on cancer research that has given such poor results would have problems maintaining the illusion that the money has been well spent. Yet rather than seeing a shift in focus away from the relatively ineffective treatments (many of which have not changed over the last three quarters of the century) we have seen only a continuous repetition of the same. Despite the many calls for more funding to go to prevention, support for this remains minimal when compared to funding for research into new drugs for treatment (see \textit{Chapter 6, Following the Money}).

\begin{flushleft}
\textsuperscript{1} Courtney LH (1895), 'To My Fellow Disciples at Saratoga Springs', \textit{The National Review}, 26: 21-26.
\textsuperscript{3} ibid.
\textsuperscript{4} Keens HW (1934), 'Annual Returns', \textit{Medical World}.
\textsuperscript{5} Bayly MB (1938), 'Cancer - The Failure of Modern Research, A Survey', The Health Education and Research Council, London, UK.
\end{flushleft}


8 Kleihues P (2003), 'Global Cancer Rates could increase by 50% to 15 million by 2020', *World Health Organisation*, 3 April.


23 Inoue K, Yoshioka K & Kawahito Y (1999), 'Is the Discordance Rate of Malignancy Still High?' *Archives of Internal Medicine* 159(9): 1013.


26 ibid., p15.
PART II

RESEARCH FINDINGS
Chapter 3

History of Cancer Research: Cause and Treatment

Cancer is not a new disease for humanity but it does appear to have more impact today. This is because of our increased life expectancy, an emphasis on anti-aging medicine and greater exposure in the media. As shown in Chapter 2, A Century of Cancer Statistics, the overall rate of cancer in the populations of Western countries has steadily increased in recent decades.

Accumulated knowledge about the causes of cancer and the cellular changes that occur in cancerous growth has also steadily increased. Changes in the treatment of cancer have sometimes, but not always, followed these newer concepts and understanding of cancer. Are research findings and patient outcomes of treatment the only—or even the major—factors in the direction that cancer research and treatment has taken?

Cancer research during the 20\textsuperscript{th} century appears to have followed two streams: prioritised ‘conventional’ research, and the neglected, unconventional cancer research. The latter is available to those who search for it, but it has not been given its due place in the literature. This less known research is discussed in Chapter 5, Paths Not Followed.

In this chapter, I present findings from the ‘conventional’ cancer research over the last century. The mainstays of cancer treatment over the 20\textsuperscript{th} century have been the use of surgery, chemotherapy and radiotherapy. Only a brief history of these treatment modalities and the results achieved by them is presented.

Of particular importance is the research that has not been done—omissions in follow-up research on causes or oncogenesis, and in the research of other potential treatments—and on the many reasons for these omissions.


**Early Cancer Research**

Cancer has probably always existed. The word comes from the Ancient Greek: Karcinos, meaning the crab. Tumours have been found in dinosaurs from the Cretaceous Age, and mummies from 3000 to 2500 BC in of Egypt have shown signs of cancers. A 1600 BC papyrus discussed surgery as a treatment for cancer.¹

The following is a basic outline of the history of changes and additions to the knowledge of cancer causation within conventional medicine.

**Earliest Mentions of Tumours: Humors or Black Bile**

European literature from the 6th century began to regularly refer to the classification and treatment of cancer. Hippocratic medicine had introduced the concept of ‘humors’ and, within this framework, cancer was considered to be caused by the accumulation of the melancholic humor, black bile.

The Roman physician Galen of Perganum (129–199AD) was the author of the only text from antiquity specifically devoted to tumours: *De tumoribus praeter naturam*. It followed the Hippocratic teaching of humors, but specified that cancer is caused not just by an excess of black bile but by a cool, black bile. Galen’s teachings were followed² until the discovery of the lymphatic system in humans by Thomas Bartholin in 1652.³

Galen’s beliefs were held for almost 2000 years. One of the earliest known antagonists to Galen’s teachings was Dr Andreas Vesalius, who in 1543 published findings from his studies and dissections in *De Humani Corporis Fabrica*. Vesalius challenged the political, social, academic and church forces of the day, causing such a controversy that he was eventually forced to resign from the University of Padua in Italy.⁴

**18th Century: Tissue Capable of Destructive Growth**

The next major deviation from Galen’s teaching was by Deshaies Gendron of Italy in 1700. Through observation of cancerous cases, Gendron noted that the growths were not inflammations caused by ‘humors’ but rather were composed of “nervous, glandular and lymphatic vascular parts … capable of destructive growth.”⁵
Gendon’s views, however, did not change the dominant thinking within the profession—the chirgeons and physicians of the day.

**19th Century: Tumours Derived from Normal Cells**

Research during the 19th century into causes of cell proliferation leapt ahead with the work of Dr Rudolph Virchow, now referred to as the father of cellular pathology for his use of the microscope. Virchow was a student of the German pathologist Johannes Muller, who had found that tumours were composed of cellular tissue and not the ‘lymph’ as was previously thought. It was Virchow who proposed that chronic irritation was the likely cause of cancer. This belief carried through into the 20th century.\(^6\)

**Cancer from Normal Tissue, Metastasis via Blood or Lymph**

Two papers by Wilhelm Waldeyer, published in 1867, laid the foundations for an approach to cancer theory that is still in use today. These papers stated that:\(^7\)

- Cancers develop from normal tissue that grew and multiplied through cell division.
- Cancers can spread throughout a local region by the movement of cancer cells into adjacent tissue.
- Metastatic spread of cancer is caused by cancerous cells moving through the lymphatic system and/or the blood to distant sites.

These were the prevailing theories in oncology until the environmental and genetic causes of cancer were discovered in the mid 20th century.

**1920s: Respiration in Cancer Cells**

In the 1920s, Dr Otto Warburg studied glycolysis in tumours. He found that cancer cells show variations to their respiratory mechanisms, with an increase in lactic acid production, which he felt was involved in the neoplastic transformation of cells. Warburg’s theories became a central part of later treatments that used ozone and hydrogen peroxide to affect cell respiration.
The American Cancer Society web site states that these therapies, based on Warburg’s theories, have now been discredited.\(^8\)

**1928: Dismissal of Theory of Causal Parasite in Cancer**

In a lecture given at the International Conference on Cancer in 1928, Dr James Ewing, an influential American pathologist, stated:

> The theory of a universal cancer parasite stimulating the cell to incessant growth is the most popular explanation of the cancer process, and seems to satisfy many minds. It must be ruled out of court on the ground of no evidence. It raises more questions than it solves, and is inconsistent with the known facts about many tumours.\(^9\)

Ewing had written a widely used textbook, *Neoplastic Disease*, in which he noted: “few competent observers consider the parasitic theory as a possible explanation in cancer”. This signalled a halt to most research into this area of cancer cause.\(^10\)

**Epidemiology of Cancer**

The pioneer of observational epidemiology was Percival Pott (1714–1788), who proposed that the high rate of scrotal cancers in London chimney sweeps was caused by soot accumulating in the folds of the scrotum.\(^11\) With this observation, Pott gave birth to the field of occupational health.

In 1915, researchers in Japan found that cancer could be induced in laboratory animals by the application of coal tar to the skin, and this led to further studies of the environmental causes of cancer.\(^12\)

**Early Recognition of Tobacco As a Causal Agent**

Tobacco was first queried as a cause of cancer in the mid 19\(^{th}\) century by clinician John Hill, a query that was scientifically justified 150 years later.\(^13\)

Lung cancer was not a common cancer prior to the 20\(^{th}\) century. In a publication on malignant growths of the lung and bronchi, Adler questioned, “Is it worthwhile to write a monograph on primary malignant tumours of the lung?”.\(^14\) Differentiating between lung carcinomas and other diseases such as tuberculosis and pulmonary
disease was difficult, and the consensus of opinion was that primary malignant neoplasms of the lungs were rare.

The first statistical evidence of the link between lung cancer and smoking was published in 1929 by Fritz Lickint of Dresden\textsuperscript{15}.

In 1939, the German researcher Dr F. Muller published the paper \textit{Tabakmissbrauch und Lungencarcinom} in the \textit{Zeitschrift f"ur Krebsforschung}, in which he provided clear evidence of the link between smoking and lung cancer.\textsuperscript{16}

**1950s: Epidemiological Studies of Smokers**

By the 1950s, many epidemiological studies were investigating this link. The American Cancer Society funded one of the largest studies (beginning in 1959), in which around one million men and women answered questions about age, diseases and smoking histories. Questionnaires were updated every four years or so, and a death certificate was supplied when a participant died.

After about 12 years, the results showed that “the Standard Mortality Ratio from lung cancer increased dramatically with the number of cigarettes smoked and with the inhalation of smoke.” It was also found that the Standard Mortality Ratio for ex-smokers decreased as the time since quitting increased.\textsuperscript{17}

**Enzymatic Studies of Cancers**

The 1950s also saw the beginning of work on the enzymatic activity of neoplasms. This eventually led to the ‘convergence hypothesis’ of Dr J.P. Greenstein, whose experimentation suggested that cancer cells showed increases in their metabolic pathways.\textsuperscript{18} It was subsequently found that such increased pathways were common to many forms of cancers, but not to all.
**Genetic Studies of Cancer**

**Gene Repression from Oncogenic Agents**

Dr V.R. Potter, in the 1960s, proposed that the proteins lost during carcinogenesis were vital for controlling the enzyme systems involved in cell division. He proposed that:

Repressors, crucial to the regulation of genes involved in cell proliferation are lost or inactivated by the action of oncogenic agents on the cell, either by interacting with DNA to block repressor gene transcription or by reacting directly with repressor proteins and inactivating them.

Once repressor gene transcription is blocked, cell regulation is lost, and proliferation may begin.¹⁹

**DNA and Genome Mapping**

The discoveries of Watson and Crick have driven the direction of cancer research through the middle to late 20th century. The discovery of DNA, and the later mapping of the human genome, opened up numerous possibilities for cancer researchers. Some earlier theories of cancer cause were validated by this work. For example in 1914, Boveri had published *Zur frage der erstehung maligner tumoren*, describing how a “wrongly combined chromosome complex” might cause abnormal cell proliferation in somatic cells.²⁰

**Discovery of the Breast Cancer Gene BRCA 1**

The new science of molecular genetics gained an enormous boost with the search and discovery of a gene associated with breast cancer. In 1986, Mary-Claire King found a mutation on a particular gene (called BRCA 1) in her study group of women with breast cancer. The evidence for this had taken Dr King 15 years to accumulate.

In 1984, a special edition of the Journal of the American Association for the Advancement of Science (AAAS) was published, titled *The Making of a Cell: Cause—Cure—Prevention*. On the opening page, editor Allen L. Hammond acknowledged the great discoveries in cancer in the previous two years, but also admitted that:
People with the leading kinds of cancer are no more likely to survive than they were a generation ago. The best way to treat cancer, in this emerging view, is not to get it in the first place.

The first article, *Cancer: the New Synthesis*, was written by senior editor Boyce Rensberger with the aid of researchers from the National Cancer Institute, Drs Harry Gelboin and Stuart Yuspa. Here they argued that the common mechanisms of cancer causation are chemical carcinogenesis, radiation, viruses and chromosomal rearrangements.21

**Recognition of Viruses as a Causal Agent**

That various chemicals and radiation could induce cancer has been known for many years, and the new era of DNA work has shown that mutations of chromosomes is also a potential cause. There has been persistent opposition, however, to the idea of cancer being caused by an infective agent.

The AAAS journal special edition (discussed above) included an interview with Dr Stuart A. Aaronson of the National Cancer Institute, a geneticist who had isolated a virus that was capable of causing cancer in monkeys. He speculated that this virus transferred growth-factor-like genes to the host cells, causing the cells to begin an endless proliferation.

In this article, the author(s) noted that “Most researchers believe that viruses are not a major cause of human cancer”22, hence the paucity of research into infective agents as potential carcinogens.

**A Century of Chemotherapy Treatment**

Chemical poisons to treat cancer have been investigated and used since the sinking of the John Harvey, a Liberty ship, in the harbour at Bari, Italy on 2 December 1943. The John Harvey, which contained 2000 mustard gas bombs in its holds when it was bombed, had released this poison into the water. The survivors of other bombed ships were plunged into the water and broke out with skin irritations and ulcers. After several days, an expert in chemical warfare, Lt. Col. Stewart Alexander,
noticed that their white cell counts were decreasing rapidly and they were becoming anaemic.\(^{23}\)

This observation, in combination with earlier investigations into bone marrow aplasia due to mustard gas exposure during the First World War, led to its initial use in the treatment of lymphoma.\(^ {24}\)

**The First Chemotherapy Drugs**

In 1946, Cornelius Rhoads derived the first alkylating compound from nitrogen mustard. Over the next 20 years a series of similar drugs were produced.

In 1948, Seymour Farber found that folic acid could disrupt cancer cell metabolism. This is still used in treatments of leukaemia and certain other cancers.\(^ {25}\)

In 1954, the forerunner of the National Cancer Institute was established in Bethesda. Here Charles Huggins experimented with hormones in cancer treatment; George Hitchings developed purines and pyrimidines that interfere with cell metabolism; Charles Heidelberger developed fluorinated compounds; and Alexander Haddow experimented with urethane and other compounds.

Chemotherapy—the use of cytotoxic agents—became a standard treatment in advanced Hodgkin’s disease\(^ {26}\), disseminated testicular cancer\(^ {27}\), and as an adjunct treatment of breast cancer\(^ {28}\).

**Chemotherapy Usage**

Chemotherapy usage is intended to supply enough of the drug to eradicate the cancer without causing irreversible toxicity in the patient. The border between unacceptable toxicity and benefit varies from one patient to another, and is subject to a diverse range of co-factor relationships.

Commonly, a combination of chemotoxic drugs is administered. Each drug differs in its toxic side effects and in the type of damage it causes to the tumour, with the aim of making the tumour more susceptible and less likely to develop resistance to the
drug regime. However, some patients sadly still succumb to the toxicity of their treatment regime.\textsuperscript{29}

**Newer Treatments**

Newer treatments such as monoclonal antibodies are now used to direct chemotherapy drugs directly to the tumour. Biological agents such as interferons, interleukins and other cytokines are used to influence the natural immune response, altering the growth of cancer cells and aiding healthy cells in controlling tumour growth.\textsuperscript{30}

**The ‘Magic Bullet’**

The idea of the ‘magic bullet’—miracle medicine—began during World War II, with the use of antibiotics in managing battle wounds. The use of penicillin, morphine and sulphur drugs became widespread, and the concept of high-technology cures was introduced into the public mindset.\textsuperscript{31}

**A Century of Radiotherapy**

In 1895, X-rays were discovered by Wilhelm Conrad Röntgen in Würzburg, Germany. The same year saw the initial therapeutic attempt to use X-rays to treat a relapse of a breast carcinoma. In 1896, X-Rays were used by Victor Despeignes in Lyons to treat stomach cancer, and by Léopold Freund in Vienna to treat a skin tumour.

In 1898, Pierre and Marie Curie discovered radium. This was first used therapeutically for skin ‘brachytherapy’ at the Hôpital Saint-Louis by Dr Danlos in Paris. By 1934 Marie Curie had tragically died from pernicious anaemia, induced by exposure to the radium she had worked on.\textsuperscript{32}

**First Clinical Uses**

Charged-particle beams were first proposed for clinical use in 1946 by Wilson, and first used to treat human cancer patients in Uppsala, Sweden, by Leksell and Larsson. John Lawrence, in 1954, used the Berkeley cyclotron to irradiate the pituitary glands of patients with metastatic breast cancer, in an attempt to achieve hormonal
suppression (Tatter quoting Tobias\textsuperscript{33}. ) Lawrence used protons in this way to treat the first 30 patients, but later patients were treated using helium ions.

**Research into Heavy Particles**

Research has continued into the use of heavy particles other than protons, such as neutrons, carbon and neon light ions and pi mesons. Research has not been successful with pi mesons, but the other particles continue to be examined as they all exhibit different biological effects on cells. Unlike X-Rays, protons deliver a radiation dose up to—but not beyond—an energy-dependent depth.

**Utilising Radiation Damage to Cells**

Radiation causes immense damage to cells, and secondary electrons create an increase in free radicals in the intracellular material. These radicals can chemically induce breaks in DNA, causing both malignant and normal cells to die.

There is a small difference between the radiation response of normal and malignant cells. Although this differential response is not fully understood, it allows for normal tissue to be preserved while the tumour, and tissue in close proximity, is targeted.\textsuperscript{34}

**New Radiation Regimes**

New regimes such as ‘external beam radiotherapy’ are used for pain control, and they have replaced the older prolonged courses of radiotherapy\textsuperscript{35}. Strontium–89 and Samarium–153 are radioisotopes and radiopharmaceutical products, now widely used to reduce pain in cases of sclerotic bone metastases, breast cancer and prostate cancer.\textsuperscript{36} \textsuperscript{37}

**A Century of Surgery**

Prior to the discovery of anaesthesia, surgical procedures were grotesquely painful events that often caused death from shock and blood loss. With the advent of the use of nitrous oxide as anaesthesia by Horace Wells in 1848, surgery became—and has remained—a mainstay of medical treatment for many cancers.\textsuperscript{38}
Radical Mastectomy

Radical mastectomy was developed at Johns Hopkins University by Professor William Halsted in the 1890s. Halsted believed that removal of the tumour was curative and that the appearance of any future tumours were the result of a new cancer. The radical mastectomy remained the standard medical treatment for breast cancer for almost a century.  

Modern Surgery

Modern surgery is often combined with radiation therapy or chemotherapy, and is undoubtedly less disabling than earlier radical procedures. Newer techniques, such as cryosurgery or cryoablation, are being studied as potential treatments for some forms of localised cancers.

Success Dependent on Surgeon’s Skill

The ability of the surgeon has been shown to influence the nature of the outcome for the patient, as measured in increased survival times. Variations in survival rates in ovarian cancer patients have been found to be dependent on whether surgery was performed by general surgeons or by gynaecologists.

In one study, median survival time for patients operated on by general surgeons was 9.87 months, as compared to a median survival time of 29.1 months for patients of gynaecologists, i.e. three times as long. The ability of the surgeon is undoubtedly of gravest importance to the life span of the patient.

Forms of Surgery

There are eight primary forms of surgery:

- Radical,
- Limited,
- Tumour reduction,
- Evaluation,
- Relapse and metastasis,
- Palliative,
- Reconstruction, and
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➢ Pain reduction.  

Results of Research

Losing the War on Cancer

In 1986, John Bailar III, Professor of epidemiology and biostatistics at McGill University, published a lack-of-progress report on President Nixon’s ‘War on Cancer’. Later in 1994, he concluded—from data provided by the National Cancer Institute—that the US cancer death rate had increased by 7% between 1975 and 1990, i.e. the war appeared to have been lost. This increase did not reflect aging of the population; it reflected increasing death rates from cancers such as non-Hodgkin’s lymphoma, multiple myeloma and cancers of the prostate, brain, kidney, oesophagus and breast.  

Epithelial Cancers Increasing and Difficult to Treat

The most common cancers are the epithelial cancers: breast, ovarian, lung, prostate and colorectal. These cancers are increasing in occurrence and are often the most difficult to treat, advanced cases responding relatively poorly to chemotoxic treatments. Ovarian cancer shows some response to chemotherapy, but therapeutic benefit for the other epithelial cancers is very limited. Response to therapy (i.e. tumour shrinkage) in these patients does not indicate prolonged survival. Less aggressive treatment is often as effective as the standard, more aggressive regimes.

Chemotoxic Agents Have Little Impact on Most Common Cancers

Chemotherapy has become one of the major treatments for cancer over recent decades. The debate on whether this increase in usage is justified has continued in the medical literature for almost as long.

A large amount of chemotherapy is being prescribed with a palliative intent, not just in the hope of cure. Few studies on the effectiveness of chemotherapy have produced data that supports palliative use. Kearsley (1986) examined the impact of cytotoxic chemotherapy on the most common adult malignancies and produced the following chart showing the estimated number of people who benefit from chemotherapy in the USA.  

57
In 1992, a critical review of the benefit of chemotherapy for epithelial cancer was published by Ulrich Abel, from the Institute of Epidemiology and Biometry in Germany. In the following tables, he summarises the direct and indirect evidence for increased survival through cytotoxic therapy in some of the common epithelial tumours.\textsuperscript{47}

**Table 3-1: Direct evidence from randomised studies on the question of whether palliative chemotherapy prolongs survival**

<table>
<thead>
<tr>
<th>Site</th>
<th>Chemotherapy + X vs X alone (X = any treatment)</th>
<th>Immediate vs deferred therapy</th>
<th>Dose-effect studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung, small-cell</td>
<td>+</td>
<td>Ø</td>
<td>-</td>
</tr>
<tr>
<td>Lung, non-small cell</td>
<td>(+)</td>
<td>-</td>
<td>Ø</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>Ø</td>
<td>unclear</td>
<td>Ø</td>
</tr>
<tr>
<td>Stomach</td>
<td>-</td>
<td>Ø</td>
<td>-</td>
</tr>
<tr>
<td>Pancreas</td>
<td>-</td>
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</tr>
<tr>
<td>Bladder</td>
<td>Ø</td>
<td>Ø</td>
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</tr>
<tr>
<td>Breast</td>
<td>-</td>
<td>(-)</td>
<td>-</td>
</tr>
<tr>
<td>Ovary</td>
<td>Ø</td>
<td>Ø</td>
<td>unclear</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>Ø</td>
<td>Ø</td>
<td>-</td>
</tr>
<tr>
<td>Endometrium</td>
<td>Ø</td>
<td>Ø</td>
<td>Ø</td>
</tr>
</tbody>
</table>
Ø: There is no evidence of this type
+ or -: The evidence is definitely positive (negative, response)
(+) or (-): Unclear evidence, on the whole rather positive/negative. In case of (+) the effect is, if any, small.

**Table 3-2: Indirect evidence on the question of whether palliative chemotherapy prolongs survival.**

<table>
<thead>
<tr>
<th>Site</th>
<th>Randomised comparisons of different regimens</th>
<th>Non-randomised comparisons of patient cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung, small-cell</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Lung, non-small cell</td>
<td>unclear</td>
<td>-</td>
</tr>
<tr>
<td>Colon/Rectum</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Stomach</td>
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<td>Pancreas</td>
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<td>Bladder</td>
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<tr>
<td>Breast</td>
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<tr>
<td>Ovary</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Cervix Uteri</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Endometrium</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Explanatory notes: see Table 3-1.

Abel states that there is (as of 1992) no clear evidence that chemotherapy improves the quality of life of cancer patients, a rationale often used for offering chemotherapy. He concludes the article, writing that:

It should arouse concern, however, that according to opinion polls, many oncologists would decline to accept cytotoxic therapy in their own case. Also, the observation made by Holli et al on 252 patients with advanced breast cancer that the “risk” of receiving cytotoxic therapy was three times as high in the terminal stage as in the remainder of the patients, does not point to a use of therapy which is particularly geared to patients’ well-being.

A review of randomised clinical trials on 5-year survival—with the benefit attributable only to chemotoxic therapy—was published recently by Morgan et al (2004). The authors conducted a systematic review or meta-analysis of trials in adult malignancies that reported statistically significant increases in 5-year survivals. The trials included in the study were from 1990 to 2004.

The conclusion reached was that the contribution of curative or adjuvant cytotoxic chemotherapy to 5-year survival was 2.3% in Australia and 2.1% in the USA.
When individual malignancies were studied it was found that colorectal, breast, prostate, melanoma and lung cancer—the most common cancers that account for 56% of the total cancer incidence in Australia—showed a benefit of only 1.6% in 1998.

The less common cancers, such as Hodgkin’s disease, non-Hodgkin’s lymphoma, and cancers of the cervix, ovary and testis—that account for only 8.4% of cases in Australia—remain the most sensitive to chemotoxic agents and gave a benefit of 14%. The conclusion reached by Morgan et al was that the newer drugs and combination regimes have had little impact on survival times.

The three studies—Kearsley (1986), Abels (1992) and Morgan (2004)—show minimal change in the efficacy of chemotherapy over 21 years.

**A New Paradigm—Understanding Therapeutic Resistance**

A new theory has been proposed, which may explain the above lack of long-term benefit with chemotherapy. In 2003, Al-Hajj et al isolated and identified cancer stem cells from a primary human breast cancer.

Cancer stem cells, although comprising only 1% to 2% of the total tumour mass, have a greater proliferative potential than more differentiated cancer cells. Cancer stem cells possess many of the same characteristics as normal stem cells, i.e. the ability to self-renew, to produce differentiated progeny and to exhibit resistance to DNA damaging agents. However, because stem cells are the longest-lived cells in any organ, they may accumulate more mutagens than more mature cells with shorter longevity.

Huang et al (2007) have reviewed data showing cancer stem cells identification in leukaemia, breast cancer, brain cancer, multiple myeloma, prostate cancer, ovarian cancer, colon and pancreatic cancer.

Cancer stem cells however, appear more resistant to chemotherapy than normal cancer cells. Leukaemic stem cells have shown significantly less sensitivity to daunorubicin than leukaemic blast cells, and myeloma cancer stem cells have
shown greater resistance to standard therapies used in myeloma treatment (Al-Hajj quoting Matsui 2004). Most chemotherapy regimes have been developed to kill as many tumour cells as possible, yet if cancer stem cells survive therapy, the possibility of future tumour development increases.

Should we expect that this new understanding will be translated into a lessening of the use of chemotoxic agents for the treatment of solid tumours—the most common tumours? Will future research concentrate on treatments that target cancer stem cells? Will patients with cancers that are now known to contain these stem cells still be encouraged into chemotherapy regimes?

**Tamoxifen Has Negative Effects on Survival from Breast Cancer**

Tamoxifen is a drug commonly used as a cancer preventive agent. Not only has the drug made little difference to 5-year survival for breast cancer patients, but Tamoxifen also increases mortality for women with a uterus, particularly women at the lower end of the ‘high risk’ range for breast cancer. Tamoxifen gives a heightened risk of the development of endometrial cancer.

**Response Rate to Oncology Drugs Only 25%**

For several years, Dr Allen Roses held the position of vice president of genetics at one of the world’s largest pharmaceutical companies. His announcement in 2003 that the response rate of drug efficacy in oncology is only 25% is an astonishing admission of the failure of chemotoxic therapies, and casts doubt on the ability of chemotoxics to effectively treat cancer.

If 75% of patients treated with oncology drugs do not gain benefit and, indeed, often undergo immense pain and suffering from the treatment itself, it is difficult to understand the continuation of such therapies.

**Postoperative Radiotherapy Increases Mortality**

Radiotherapy is often given as an adjuvant treatment for breast cancer following mastectomy. The Imperial Cancer Research Fund in London conducted a study of the long-term survival of 7,941 patients. The study found no difference in 10-year
survival between radical mastectomy patients and simple mastectomy patients, but there was a significant excess of deaths in patients given radiotherapy.\textsuperscript{55}

In randomised, controlled clinical trials of patients with intermediate-risk endometrial cancer, postoperative radiotherapy decreased the incidence of cancer recurrence, but had no appreciable effect on overall survival.\textsuperscript{56}

Radiotherapy of the chest region is known to cause multiple cardiovascular complications, such as pericarditis, myocardial fibrosis, muscular dysfunction and valvular abnormalities. Patients at highest risk were breast cancer (post mastectomy) and Hodgkin’s disease survivors who had received radiotherapy. The risk of fatal cardiovascular disease increased with higher dose volumes of exposure to the heart, and with the youth of the patient.\textsuperscript{57}

**Future Harm from Radiotherapy**

There is no doubt that radiotherapy can shrink tumours. However, eradication of a tumour as the sole treatment necessary to ‘cure’ a patient is debatable; in most cases long-term survival is not significantly increased. The possibility of future harm after radiation must also be considered carefully. Patients need to not only be given informed consent, but also an informed choice of treatments and an explanation of all future repercussions.

**Conclusions**

Whether cancer patients are receiving the best treatments possible is a real issue—especially for the cancer patient. From a patient’s perspective, treatment types and styles have not changed significantly since the advent of chemotherapy in the middle of the last century. Fear of treatment itself is a significant factor for patients.

Surgery has improved in many ways, helped especially by new guided imaging techniques. Radiotherapy has also advanced, yet still has inherent after-effects and dangers for the patient. Chemotherapy has shown its worth in some of the rarer cancers, but overall improvement in cure rate and long-term survival for the most common cancers remains low.
As discussed in *Chapter 2, A Century of Cancer Statistics*, the results of current treatments are not indicative of major changes in treatment modes or of increasing efficacy in long-term control of the disease. The journals, books and articles reviewed in this research show a vast body of research into cancer cause, but the thrust of research has not expanded in as many directions as might be expected.

The infective causes of cancer have largely been overlooked and ignored by mainstream cancer researchers. Research into perhaps the most important area of neglect, bacterial induction of cancer, is discussed in the following chapter, *Chapter 4, Bacterial Involvement in Cancer*.

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13. (ibid.).
14 Adler IA (1912), *Primary Malignant Growths of the Lung and Bronchi*, Longmans, Green and Company, New York, NY, 3-12.
22 ibid.
40 (ibid.).


Chapter 4

Bacterial Involvement in Cancer

In this chapter I present another history of cancer research, an investigation of the research that has not received the same standing as the methods discussed in the previous chapter, in acceptance and practical usage, and in the acquisition of research funding and clinical trials. In particular, the discussion focuses on research that indicates a bacterial cause of—or involvement in—cancer.

Not only are these lesser-known areas of cancer research not mentioned in most medical textbooks, but information spread appears to have been actively discouraged. This suppression of information has occurred in three main ways and continues to occur:

- Failure to fund such research,
- Proclamations from people of importance in cancer medicine, trivialising and negating such research results, and
- Omissions from medical teachings of a complete history of research in fields differing from the dominant approaches.

The following discussion is supported by reference to selected papers, chosen on the basis of the standing of the researcher or the scale of the study. A comprehensive survey of this work is beyond the scope of this research.

Early Research on Bacteria

Pasteur: Bacteria as Cause of Disease

Louis Pasteur (1822–1895) dominated the scientific community of the day with his work on bacteria as a cause of disease. When Pasteur postulated that disease arose from germs attacking the body, his findings were debated hotly amongst the medical establishment. The notion that large organisms could be endangered by these tiny bodies appeared ludicrous at the time to many medical practitioners.
He continued with this work and later showed that anthrax was caused by a particular bacillus. Subsequently, he developed a vaccine, produced from the same organism in a weakened state. His work on the cause and treatment of rabies, through vaccination, led to the acknowledgement of his work and his eventual honour and fame.¹

**Koch: The Rise of Bacteriology**

The discoveries of Pasteur laid the foundation for the work of other scientists such as Robert Koch (1843–1910), eventually giving rise to the discipline of bacteriology. Koch isolated *Bacillus anthracis* and inoculated it into mice to cause anthrax, thus convincing the medical community that these tiny bodies—bacteria—actually could cause disease. Koch later also isolated and identified bacteria as causative agents for tuberculosis and cholera.

**Koch’s Postulates**

Koch is still remembered for his criteria—known as Koch’s Postulates—for judging whether a bacteria could cause a particular disease:

- The bacteria must be present in every case of the disease.
- The bacteria must be isolated from the host with the disease and grown in pure culture.
- The specific disease must be reproduced when a pure culture of the bacteria is inoculated into a healthy susceptible host.
- The bacteria must be recoverable from the experimentally infected host.²

Current bacteriology has subsequently discovered some exceptions to this definition. For example, the bacteria *Mycobacterium leprae* that causes leprosy cannot be grown in ‘pure culture’; and generally-accepted ‘harmless’ bacteria may cause immense damage if an immuno-compromised patient becomes infected.

**Monomorphism**

However, there is still an adherence to these principles. The work of Koch, Pasteur and a botanist named Ferdinand Julius Cohn established the concept of monomorphism—meaning that a bacterium has a constant form and does not change.
Cohn had been editor of the journal *Beitraege*, in which Koch’s work on anthrax had been published, and he was generally well respected in bacteriology.

The monomorphist approach to some extent survives today and becomes relevant to the discussion later in this chapter.

### 1884: Tumours Contain Parasites, But Are Not Caused by Parasites

In 1884, the President of the Royal College of Surgeons, Dr Henry Butlin, made the following statement:

> The theory of parasitism, applied to tumours, has during centuries been more or less popular with surgeons; for in no other way can some of the most complicated processes of malignant tumours be so well explained, as by assuming that the tumours or their elements are parasitic. But of late years the parasitic theory has been discredited by the discovery that the elements of even the most malignant tumours are derived more or less directly from the natural tissues of the body, and that they differ only in degree, and, perhaps, in certain properties which they have acquired from the natural elements.

> It is quite clear, therefore, that the view, formerly maintained, that malignant tumours are actually parasites is incorrect. But the recent discoveries of micro-organisms, and of the part they play in relation to certain diseases, have led me to consider whether the theory of parasitism may not again be applied to malignant tumours, with this difference, that the tumours are no longer now conceived to be parasites, but to contain them.°

This is the first reference I have found to the concept of a bacterial cause of cancer. The term ‘parasite’ was common when referring to ‘bacteria’ in earlier years. Certainly the search for the elusive ‘parasite’ did not cease then.

### 1889: Parasites Found in Cancers

This statement was followed in quick succession by several other scientists. Dr Thoma published a paper *Ueber-eigenartige parasitare Organismen in den Epithelzellen der Carcinome* (translated as Over-peculiar parasitic organisms in the Epithelial Carcinoma) in 1889 in the journal *Fortschritte der Medicin* (Progress of Medicine).
In 1890 in the same journal, a paper entitled *Ein parasitarer protozoaartiger Organismus in Carcinomen* (A Parasitic Protozoan Organism in Carcinoma) was published by the scientist Nils Sjobring.

1885: Cancer Vaccine from Bacteria

In 1885, a French scientist Thomson Doyen not only isolated a bacterium (that he named *Micrococcus neoformans*) from tumours, but he also produced a vaccine from the bacteria. He claimed that his vaccine produced cures in cancer patients.⁵

1899: Histology Shows Parasites in Active Parts of Tumour

The monograph *On the Aetiology and Histology of Cancer*, published in April 1899 by Dr H.G. Plimmer, outlined various staining and fixing methods to demonstrate cellular inclusions. Plimmer also stated that, over a six year period, he had examined tissue from 1278 cancers (excluding sarcomas) and had found parasitic bodies in 85% of these.

Interestingly, he did not find these organisms spread homogeneously throughout the tumours. The organisms only appeared at the growing edges of the tumours where the cells were active, and not where there appeared to be degeneration or reversal of the tumours.⁶

1911: Virally-Induced Cancer

In 1911, Peyton Rous published one of the earliest proofs of virally-induced cancer in *A Sarcoma of the Fowl Transmissible by an Agent Separable from the Tumour Cells*.⁷ Significantly, it took until 1966 for him to be awarded a Nobel Prize for this discovery.

1925: Micrococcus Cultured from Breast Cancer

Dr J. Nuzum, in 1925, cultured a minute gram-positive micrococcus (unidentified but possibly a member of the streptococcus group) from a breast tumour. Inoculation with this bacteria into mice and dogs caused the growth of some pre-cancerous lesions and, in some cases, mammary carcinomas. Control mice inoculated with cultures of other strains of streptococcus and staphylococcus did not develop such lesions.⁸
1925: Cancer Induced by Virus with an Irritant

Also in 1925, The Lancet published a section entitled New Research into the Origin of Cancer including papers from Gye and Barnard. Dr Gye had come to the conclusion that cancer was a disease caused by a virus or group of viruses. Although he found that the virus alone was insufficient to induce cancer, in the presence of an ‘irritation’ such as coal-tar or paraffin oils the virus would multiply in the cell, provoking the host cell to multiply.\(^9\)

Dr. Barnard’s paper was on microscopy techniques for the examination of small filterable spheroids. Consistency in microscopy techniques was needed to allow other researchers to view these small organisms.\(^10\)

1930: Pleomorphic Forms from Cancerous Tissue

In 1930, Dr T.J. Glover, working at the Hygienic Laboratory in Washington, found an organism that was shown in subculture to be highly pleomorphic: thus its life cycle included coccoids, rods, mycelial stages and filter-passing forms. These organisms were able to be stained in cancerous tissue, appearing as intra-cellular forms.

He obtained such an organism from an adenocarcinoma of the human breast. He inoculated the organism into the breast tissue of full-grown female guinea pigs and female albino rats. Tissue from the resulting lesions was cultured and the organisms obtained were sub-cultured several times, before being passed through four successive groups of rats. After the fourth passage, the rats developed peritoneal carcinomas with metastases to the upper abdomen, peritoneal endotheliomas with focal infiltration.\(^11\)

Glover found this organism in 85% of 3000 cases.

Further Studies on Pleomorphic Forms

Glover’s work was reproduced by Dr J.L. Engle in Philadelphia, and, subsequently in a larger study by Dr George A. Clark. Clark found that he could consistently isolate a highly pleomorphic organism from blood or tissue biopsies from his cancer patients.
In this study, the organisms were cultured from patient tissue and the filtrate injected into two guinea pigs. One was given 1 cc of the filtrate and the other 5 cc. The guinea pig receiving the larger dose died 45 hours later. A drop of blood was aspirated from the heart and the liver of this guinea pig. The blood was cultured and, by the next morning, the same motile bacillus could again be shown to be present.\(^\text{12}\)

In Canada, O.C. Gruner was also studying pleomorphic organisms and cancer. He isolated such an organism, which he named *Cryptomyces pleomorpha*, from a breast tumour. He found that:

- The organism could be detected in circulating blood by direct examination.
- It was detected amongst tumour cells in the original neoplasm.
- An organism of the same type was found in seven previous cases.
- It resembled a fungoid organism, but with additional distinctive features.
- The organism in living cultures mimicked the cell-elements of human blood.\(^\text{13}\)

**1941: Pleomorphic Forms from Hodgkin’s Lymphoma**

Dr Mazet, a French physician, in *Extrait de Montpellier Medecalle* (1941), wrote of finding a bacteria in a patient with Hodgkin’s disease. He then cultured an acid-fast organism from 12 Hodgkin’s patients. He regarded the organism as highly pleomorphic, with phases varying from small granules to fungal type elements, including coccoid forms, mycelia and rod forms. He inoculated blood from a Hodgkin’s patient into a mouse that, when sacrificed 15 days later, yielded the same organism from its brain tissue.

**1948: Siphonospora from Cancer Tissue**

In Germany in 1948, Von Brehmer published his work on an organism, which he named ‘*Siphonospora polymorphs*’, that he claimed caused cancer. He had published earlier (1934) on this organism, which he had cultured from human blood.\(^\text{14}\) He found that this organism parasitised epithelial cells, as well as erythrocytes and leucocytes. Von Brehmer developed a therapy that involved the use of pooled cultures of ‘*Siphonospora*’ isolated from several different types of neoplasm.
1952: Pleomorphic Studies of Micromyces

From more than 1000 samples of tumour tissue, blood and ascites fluids of cancerous patients, Franz Gerlach isolated a pleomorphic, filter-passing organism that he called *Micromyces blastogenes*. He later renamed this organism *Micromyces universalis innatus* and regarded it as a micro-fungus. Again, this organism was filterable (able to pass through a fine filter). One of the stages in its life-cycle resembled a Mycoplasma-like organism.\(^\text{15}\)

Gerlach produced a ‘polyvalent’ vaccine by passing the organism through numerous passages of culture media. He claimed his vaccine stopped the growth of cancers enabling many patients to go into remission, without side effects.\(^\text{16}\)

1955: Cancer ‘Virus’ Extracted from 1000 Cancers

Dr John E. Gregory published the last edition of his book “Pathogenesis of Cancer” in 1955.\(^\text{17}\) In it he described finding cell wall deficient forms, which he referred to as a cancer virus, extracted from tissue samples of 1000 human cancers.

In total, he examined 31 types of cancers and found the virus to be present in all but eight of the 1000 samples. The negative results were found in five Hodgkin’s blood cultures, although he obtained positive cultures from 10 lymph nodes of Hodgkin’s patients. He could not culture the virus from two lymphosarcoma patients’ blood cultures, but had positive results from five other patients with the same disease.\(^\text{18}\)

Gregory produced a culture from malignant melanoma, which he injected into mice and baby chickens: 25% of the injected animals developed cancers. These included cancers of the ovary, adrenal gland, breast and stomach, spindle cell sarcoma, myosarcoma and leukaemia. His control group, which was larger than the research group by a factor of ten, developed no malignancies.

Gregory found that the virus isolated from the induced cancers was the same as the injectable form, and could be re-cultured to again produce the same cancer. Because the types of cancer varied from the original melanoma, he concluded that the inoculations were not cancer cells from the host, but viral forms that induced a cancer.
Early Drugs Utilising Bacterial Effect on Virus

Gregory experimented with various bacteria to find if they would affect this virus he had found, and had some success in his treatment of cancer patients, using the bacteria *Bacillus subtilis* Tracy 1. He produced a filtrate of this bacteria, mixed it with a saturated magnesium sulphate solution, and gave this to patients as a daily injection.

He showed many remissions using this treatment, particularly in late-stage patients for whom no other treatments were used. Unfortunately, many of the patients developed albuminuria, indicating a renal problem with this drug. It is possible that this may have been caused by the magnesium sulphate.

Gregory produced four antibiotics in his search for a cancer treatment. Tracin and Magnesium Tracinate were produced from the *Bacillus subtilis* Tracy 1 bacteria. Gregomycin was produced from a *Streptomycetes* and the fourth—called Gregocin—was produced from an unnamed mould. Among these, Gregocin was the most effective in cancer treatment.

1955: Dark Field Microscopy Reveals Pleomorphic Forms in Blood of Cancer Patients

In Paris, Dr E. Villequez used dark field microscopy, noting what appeared to be bacteria in the blood of cancer patients. When cultured, the organisms were noted to be highly pleomorphic. He wrote that they had some characteristics that linked them to *Mycobacteria*, but that at other times they resembled spore-forming bacteria.19

1959: Scientist Self-Inoculates with Carcinoma Isolate

Clara Fonti wrote on the parasitic theory of cancer and the transmissibility of cancer, citing 30 cases from her own practice.20 To demonstrate transmissibility, she inoculated herself in the chest wall with fluid from a metastasising mammary carcinoma. After a few days, an erythematous papillary eruption developed between her breasts, growing into a nut-sized lesion with numerous small ancillary papules. These papules were diagnosed as baso-cellular epithelioma.
Fonti’s own blood was then transfused to a patient with multiple abdominal metastases, giving an amelioration of the patient’s condition.


Dr Virginia Livingston-Wheeler worked with many distinguished scientists throughout her long career, including Dr Roy Allen, an expert microscopist and histologist. In August 1948, Allen published *The Microscopy of micro-organisms associated with neoplasms*, in which he stressed the pleomorphic appearance of the microbe isolated from the blood of cancer patients. Cantwell quotes Allen:

> He described it as ranging in appearance from a rod-shaped or coccus shaped form. That the non-acid-fast coccal forms could appear as single, double, or as densely-packed round forms. That these coccal forms could vary in size from 1 micron to the smallest microscopic size the eye could detect with a microscope approx. 0.2 microns, and that the microbe could live both inside and outside the cells, and that the tiniest forms of the cancer microbe were filterable and virus sized.\(^{21}\)

Livingston-Wheeler collaborated for many years with three well-known women scientists who undoubtedly influenced her research and career:

- Eleanor Alexander-Jackson PhD, a Cornell University microbiologist. Her work with the tuberculosis mycobacterium gave her familiarity with the concept of pleomorphism, and she described some of these variants in her PhD thesis (published in the American Review of Tuberculosis).
- Irene Diller PhD, a cell cytologist at the Institute for Cancer Research in Philadelphia and editor of *Growth*, a biological journal.
- Florence Seibert, a well-known refereed tuberculosis researcher, famous for her development of the TB skin test.\(^{22}\)

The paper *Cultural Properties and Pathogenicity of Certain Microorganisms obtained from various Proliferative and Neoplastic Disease*\(^{23}\) was first published in 1950, a team effort by Virginia Wuerthele-Caspé (Livingston-Wheeler’s name from a previous marriage), Eleanor Alexander-Jackson, John Anderson, James Hillier and Roy Allen.
In this they described how they cultured pleomorphic organisms from human and animal neoplasms, and that these could not be cultured from normal controls. When inoculated into experimental animals, the cultured organisms induced characteristic pseudocaseous lesions.

**1966: Studies on the Rous Virus As a Pleomorphic Form of Mycoplasma**

An important paper was published in 1966 by Eleanor Alexander-Jackson, who had been working for some time with the Rous virus. She had isolated, many times and over many years, a highly pleomorphic, gram-variable mycoplasma from the blood and tumours of Rous virus-infected chickens and from other sources of the virus.

Dr Alexander-Jackson\(^24\) postulated that the Rous virus was:

\[
\text{... the virus-size stage and virus-like form of a single type of pleomorphic intermittently acid-fast organism with a mycoplasma transitional L phase, belonging under the Order}\ 
\text{Actinomycetales.}
\]

**1969: Livingston-Wheeler Cancer Clinic and Autologous Vaccine**

Livingston-Wheeler, in conjunction with Alexander-Jackson in 1970 and later with her husband Afton Livingston in 1972, published papers on their culturing of organisms with filterable cycles and acid-fast cycles.\(^25\)\(^26\)

Livingston-Wheeler established her first cancer clinic in San Diego in 1969 and produced an autologous vaccine (utilising her *Progenitor cryptoceides* organism) for the treatment of cancer patients. Her later husband, Owen Webster Wheeler, developed a malignant lymphoma of the neck in 1972, and he chose to treat it only with the vaccine. The lymphoma was reportedly gone in six months.\(^27\)

**Late 1990s: Positive Responses from Clinic Patients**

In the late 1990s (after her death in 1990) I visited the Livingston-Wheeler clinic and spoke with several patients being treated there. Most of these patients had been considered terminally ill by their conventional oncologists. They had gone through standard treatments and were now seeking ‘other’ treatments in their search for a cure or prolongation of life. They were unreserved in their praise of the treatments
received, which involved primarily injections of the cancer vaccine; several were in remission and were undergoing maintenance treatment.

1973: Link Between Bacterial Endocarditis and Colorectal Carcinoma

The possible association between bacterial endocarditis and colorectal carcinoma was raised in 1973 by Dr Daniel Roses and Dr Arthur Localio, following their investigation into three patients presenting with bacterial endocarditis and carcinoma of the colon or rectum. Each patient was treated with antibiotics for endocarditis followed by surgical removal of the carcinoma.

A causal link between the two conditions must be considered as speculative, but the authors suggested that in patients with no history of heart disease, the concurrent development of these diseases certainly warrants further research.

1970s–1980s: Histology of Pleomorphic Forms in Cancers

Between the late 1970s and early 1980s, Dr Alan Cantwell, a dermatologist who considered Dr Livingston-Wheeler somewhat his mentor, began to publish on the presence of pleomorphic organisms he had found in breast cancer, lymphoma, Hodgkin’s disease and pre-AIDS Kaposi’s sarcoma. When Dr Cantwell retired several years ago, he kindly sent me a collection of his histology slides, clearly showing the acid-fast bacteria that he had isolated from many of his patients.

Cell Wall Deficient Forms and Mycoplasmas

I have had a particular interest in pleomorphic forms from my 22 years of work with darkfield microscopy, examining and comparing the blood of patients with cancer to the blood of non-cancer patients.

I have been both intrigued and disturbed by the variable forms of organisms I have seen in the cancer patient’s blood but not in the blood of healthy subjects. I have travelled to many research centres over the last 20 years, discussing my findings and asking advice and explanations from many eminent scientists. Highlights from my discussions are presented below.
1993: Mattman on Cell Wall Deficient Forms

In 1993, prior to convening the 1st World Congress on Cancer in Sydney, I spent a week in the USA at the microbiology laboratory of Professor (now Emeritus Professor) Lida Mattman. I had been intrigued by the ideas in her book on Cell Wall Deficient Forms.\(^\text{33}\)

Her knowledge of cell wall deficient bacteria and of the strange group of divergent organisms called Mycoplasmas has been invaluable to most researchers interested in this field. Although not the first to work with cell wall deficient bacteria, Professor Mattman’s work has added greatly to the body of information on this phenomenon.

Bacteria that become cell wall deficient have the ability to make enormous changes in their appearance. They have the following characteristics:

- They may disintegrate totally if fixed on a slide by heating (the standard method of fixing).
- They usually grow on soft agar.
- They may grow within red blood cells.
- They are often serophilic.
- They often grow best in a hypertonic environment.\(^\text{34}\)

Working with cell wall deficient organisms is exceedingly difficult: They are more difficult and take longer to grow than the classical forms of the organisms. The appearance of a cell wall deficient form is totally unlike the classical form, making them difficult to identify by appearance. Identification may require promoting a shift back to classical form, for example, the addition of penicillin induces a reversion in cell wall deficient Candida to its classical form.

Late 20th Century: Mycoplasmas in Gulf War Syndrome Patients

The end of the 20th century saw an increase in the investigation of Mycoplasmas. Mycoplasmas are from the class Mollicutes, and are the smallest of the bacterial forms. Unlike other species of bacteria, Mycoplasmas are unable to make cell wall components. They do not enter a cell wall deficient stage, but they do share many of the characteristics of the cell wall deficient.\(^\text{35}\)
The work of Professor Garth Nicolson on the diagnosis and treatment of Gulf War Syndrome patients showed the pathogenicity of Mycoplasma infection. Infections of *Mycoplasma pneumoniae* were identified through antibody testing. Today, the Polymerase Chain Reaction (PCR) test is considered the ‘gold standard’ for identification of such organisms. Infections are treated with antibiotic therapy.

Many papers are now emerging that indicate that Mycoplasmas may play a major role in regard to human disease.

**Mycoplasmas Inducing Chromosomal Instability and Malignancy**

Researchers at the American Registry of Pathology at the Armed Forces Institute of Pathology, Washington, have shown that chronic infection, or colonisation by some Mycoplasmas in cell lines induced chromosomal instability and malignant transformation.

Their hypothesis was that chronic infection could promote tumour growth of mammalian cells. They also showed that infection by several—but not all—species of Mycoplasma would prevent murine myeloid cells from undergoing apoptosis, and that these Mycoplasma-infected cells gradually underwent malignant transformation over a period of four to five weeks. The two Mycoplasma strains used in this study were *M. fermentans* or *M. penetrans*.

**Affinity of Mycoplasmas for Cancer Cells**

One the most fascinating characteristics of the Mycoplasmas is their affinity for cancer cells. All scientists working with cancer cell lines must continually check them for Mycoplasma infection, and many papers are devoted to studies of how to eliminate Mycoplasmas from these cells.

Why these particular species are the most likely contaminants of cancer cells does not yet appear to be have been answered. Testing for contamination is now recommended, by DNA fingerprinting or cytogenetic analysis, as the effect of Mycoplasmas in the cell lines may render research data highly unpredictable and questionable. Much research—performed prior to DNA technology, utilising cell
lines—should be repeated with attention to possible infiltration of the cell lines by Mycoplasmas, in order to verify the published outcomes of the studies.

**Stats on Infection of Cancer Patients with Mycoplasmas**

The numbers of cancer patients who are infected with these bacteria is unknown, but where reasonable studies have been carried out the results are frightening. A study from China by Su Huang, published in *World Journal Gastroenterology*, gave the results shown below.  

![Table 4-1: Mycoplasma Infections in Cancer Patients](image)

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Number Positive for Mycoplasma</th>
<th>Total Patient Number</th>
<th>Percentage Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>25</td>
<td>63</td>
<td>39.7%</td>
</tr>
<tr>
<td>Colon Cancer</td>
<td>32</td>
<td>58</td>
<td>55.1%</td>
</tr>
<tr>
<td>Adenomorous polyp</td>
<td>10</td>
<td>49</td>
<td>20.9%</td>
</tr>
<tr>
<td>Gastric Carcinoma</td>
<td>50</td>
<td>90</td>
<td>56.0%</td>
</tr>
<tr>
<td>Oesophageal Cancer</td>
<td>27</td>
<td>53</td>
<td>50.9%</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>31</td>
<td>59</td>
<td>52.6%</td>
</tr>
<tr>
<td>Glioma</td>
<td>38</td>
<td>91</td>
<td>41.0%</td>
</tr>
</tbody>
</table>

**Connection Between *Helicobacter pylori* and Gastric Cancer**

Another bacteria, *Helicobacter pylori*, has been much in the news lately. A Nobel Prize was won by researchers showing its role in the induction of stomach ulcers. This bacteria was classified as a human pathogen in 1994, by the International Agency for Research on Cancer.  

*H. pylori* has a positive association with gastric cancer. According to Correa (2003), more than half the world’s population is infected with *H. pylori*.

**Early Misclassification of Mycoplasmas and Cell Wall Deficient Forms**

Viruses were distinguished from bacteria, particularly prior to 1940, based on their ability to pass through specific filters. Bacteria were larger so they were trapped by the filter, whereas viruses passed through. The size of the filters used at that time, however, allowed bacteria such as mycoplasmas to easily pass through, so they would have been mistakenly classified as viruses.

Recent work by Wainwright showed that the presence of the culture medium affected the ability of bacteria to pass through a 0.2 micron filter. When bacteria were given overnight incubation in a culture medium on the membrane, they formed...
small (cell wall deficient) forms that were able to pass through the filter. The bacteria that Wainwright used were all common human pathogens.

This finding has significant repercussions for the field of microbiology, and may indicate that studies carried out over the earlier part of the 20th century should be re-examined.

Renewed Interest in Bacterial/Viral Induction of Cancer
Following the large body of research from the late 19th century through the first three quarters of the 20th century, there has been a renewed interest in bacterial and viral induction, promotion of, and affinity with neoplasm.

High Incidence of Infection in Cancer
A 1997 paper by Pisani et al estimated that, in 1990:

- 15.6% of the worldwide incidence of cancer could be attributed to infection with either the Hepatitis B or C viruses, Helicobacter pylori, schistosomes or liver flukes.
- In developing countries, the prevention of these infections would lower the cancer rate by 21%.
- The papillomaviruses are attributed with causing 89% of cervix cancers.43

Salmonella Infections Linked to Gall Bladder Cancer
Strong epidemiological evidence supports a link between infections with Salmonella typhi and gallbladder cancer. Carriers of S. typhi have 8.47 times the risk of gallbladder carcinoma, compared with those who have had typhoid and have successfully cleared the infection.44 45 46

Chlamyphila pneumoniae in Lung Cancer
Chronic infections of Chlamyphila pneumoniae are now being found to correlate with an increased risk of lung cancer.47 48 49 An elevated IgA antibody titre to C. pneumoniae has been reported to be associated with a 50% to 100% increased cancer risk.50
**Escherichia coli and Streptococcus bovis in Colon Cancer**

Several bacteria have now been linked to chronic infections of the colon and an increased risk of colon cancer. These include *Escherichia coli* (McCoy and Mason suggested this in 1951\(^{51}\)) and, in more recent studies, *Streptococcus bovis*. Colon cancer incidence that may be associated with *S. bovis* has been estimated at 18% to 62%\(^{52}\).

**Infection in Oral Squamous Cell Carcinomas**

Over 90% of oral cancers are oral squamous cell carcinomas (OSCC). These have one of the lowest survival rates (based on 5-year survival statistics), with no noticeable improvements in the last few decades.\(^{53}\)

In a recent study, Mager et al used DNA identification of oral flora to test for 40 microbial species. *Capnocytophaga gingivalis*, *Prevotella melaninogenica* and *Streptococcus mitis* were elevated in the saliva of patients with OSCC. When testing the presence of these three species as diagnostic markers, the authors found that their presence could predict 80% of cancer cases and absence could predict 83% of controls.\(^{54}\)

**Conclusions**

Patients presenting with a cancer diagnosis are neither routinely tested for pathogenic infections, nor routinely treated for infections at any time during their cancer treatments. There do not yet appear to have been any studies showing the outcome for patients if such infections are identified and eliminated when cancer is first diagnosed.

Ignoring the possibility of bacterial induction of cancer in screening—or as a requirement in treatment—means that no understanding is gained of the possible benefits of such treatment for cancer patients. Future expansion of treatment modalities hopefully will answer this question and lead to improvements in survival.

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Chapter 5
Paths Not Followed

This chapter highlights some of the key aspects of the research—into the cause and treatment of cancer—that has not been absorbed into conventional medicine. In particular, I present:

- A summary of the chemical and environmental causes of cancer, an area that has not been given the significance it deserves in attempts to prevent cancer.
- A brief selection of research data, published from the 20th century to the present, on treatments that have not been integrated into conventional oncology. Some of these treatments have been relegated, by the medical establishment, to the negative category of ‘alternative medicine’.
- An investigation of why such treatments were proscribed and whether time has justified their initial rejection.
- The development of two contrasting treatment paths in oncology and what this has meant for patients.

Environmental Carcinogens

Numerous chemicals in our environment have been linked to cancer induction. Many of these are used in industrial processes, and convincing evidence has been found to link workplace exposure with various cancers.

There are three major criteria required in evaluating the potential of an environmental chemical to induce carcinogenesis in humans.

1. Does the agent have in vitro mutagenic potential.
2. Do experimental animals show increased incidence of specific types of cancer when exposed to the agent.
3. Do humans show increased incidence of the same types of cancer when exposed to the agent.
Role of Industrial Chemicals in Cancers

Based on studies from the Institute of Cancer Epidemiology, the Danish Cancer Society, the Cancer Registry of Norway and the Finnish Cancer Registry, it has been estimated if industrial carcinogens were eliminated in the world, then the following cancers could be avoided:

- 70% of mesotheliomas,
- 20% of cancers of the nasal cavity and sinuses,
- 12% of lung cancers,
- 5% of laryngeal cancers,
- 2% of urinary bladder cancers;
- 1% of leukaemias, and
- 1% of renal cancers.²

The National Cancer Institute (NCI), and the national Institute for Environmental Health Sciences (NIEHS), currently suggests that two-thirds of cancers are caused by environmental factors.³

Cancer Clusters

Cancer clusters are at times reported by the public. Investigation of such clusters is difficult for public health authorities as such investigation is difficult and often inadequately performed. Environmental cause was determined in the following two clusters.

- Angiosarcoma of the liver in workers exposed to vinyl chloride at a manufacturing plant.⁴
- Childhood leukaemias in residents exposed to contaminated drinking water.⁵ ⁶

The Danger of Close Proximity to Industry

Death certificates were examined for 28 children who lived in a residential area of Taiwan between 1981 and 1990, in close proximity to three petrochemical plants. An unusually high number of bone, bladder and brain cancers were found. The children were aged from birth to 19 years, and all but one of them had lived within two to three kilometres of the plants.
Pollution reports, compiled by the Environmental Protection Agency of the Republic of China, showed nine serious air pollution events that had released vinyl chloride and acrylonitrile. Polycyclic aromatic hydrocarbons were also released from the plants, and phenol had been found as a contaminant in well-water at levels far exceeding government safety guidelines.\(^7\)

**The Danger of Close Proximity to Pesticide Use**

Living in areas of high pesticide use has also been shown to increase rates of brain tumours. A 1996 study compared the home locations of 1,000 cancer patients to that of 1,000 patients dying of other illnesses. The study found that people living within 2,600 feet of a cranberry growing area had twice the risk for all brain cancers and nearly a seven-fold increased risk for astrocytomas.\(^8\)

Statistical data has shown that there is a higher incidence amongst farmers in industrialised nations of multiple myeloma, melanoma, prostate cancer, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, brain cancer, leukaemia and cancers of the lip and stomach.\(^9\)

Working with pesticides appears to increase brain cancer rates. A 1993 study followed the health of 2,310 Italian men, working with the application of pesticides, between 1972-1979. By the time the study ceased in 1988, there had been 207 deaths in the group. Of these deaths, seven were due to brain cancer. This is close to 2.5 times higher than the expected rate of 2.7.\(^10\)

A summary of scientific evidence of environmental and occupational links to nearly 30 types of cancer was compiled by the Lowell Center for Sustainable Production. The review, compiled by the Boston University School of Public Health and the Environmental Health Initiative, University of Massachusetts, Lowell, found strong causal links for: \(^11\)

- Metals such as arsenic and cancers of the bladder, lung, and skin.
- Chlorination byproducts such as trihalomethanes and bladder cancer.
- Natural fibres such as asbestos and cancers of the larynx, lung, mesothelioma, and stomach.
- Petrochemicals and combustion products, including motor vehicle exhaust and polycyclic aromatic hydrocarbons, and cancers of the bladder, lung, and skin.
- Pesticide exposures and cancers of the brain, Wilms tumour, leukaemia, and non-Hodgkin’s lymphoma.
- Reactive chemicals such as vinyl chloride and liver cancer and soft tissue sarcoma.
- Metalworking fluids and mineral oils with cancers of the bladder, larynx, nasal passages, rectum, skin, and stomach.
- Ionizing radiation and cancers of the bladder, bone, brain, breast, liver, lung, ovary, skin, thyroid, leukaemia, multiple myeloma, and sarcomas.
- Solvents such as: benzene and leukaemia and non-Hodgkin’s lymphoma; tetrachloroethylene and bladder cancer; and trichloroethylene and Hodgkin’s disease, leukaemia, and kidney and liver cancers.
- Environmental tobacco smoke and cancers of the breast and lung.

**Endocrine Disrupters in Cancer Formation**

Endocrine disrupters—such as diethylstilbestrol (DES), dieldrin, chlordane, hexachlorobenzene and triazine herbicides, which all have weak oestrogenic activity—are being investigated in a range of environments for their possible role in the increasing incidence of particular types of cancer.¹²

The European Commission Union Research on Endocrine Disrupters¹³ has identified PCBs (polychlorinated biphenyls), dioxin, benzo(a) pyrenes, phthalates (plasticisers), Bisphenol A, pesticides and heavy metals as having estrogenic effects. A more complete list of these chemicals is found at www.ourstolenfuture.com/Basics/chemlist.htm.

**Known Carcinogens in Foods and Personal Products**

Our chemicalised society is using more and more chemicals, many of which are known carcinogens, in the environments in which we live and for personal use:
Foods may contain antibiotics, pesticides, contaminants and additives.

Cosmetics and toiletries may contain talc, saccharins, fluorides, formaldehyde, dyes and preservatives.

Disinfectant sprays may contain orthophenylphenol (OPP).

Weed killers may contain sodium 2,4-dichlorophenoxyactic acid (2,4-D).\(^{14}\)

**Talc As Carcinogen**

The situation for talc is another example of the confusion and ambiguity that exists with respect to the regulation of potential carcinogens within our environment. If it does not contain asbestos, talc is not considered a carcinogen by the FDA. However, talc on its own is being investigated as a potential cause of ovarian cancer if used near the genital area.\(^{15}\) As well as being used in powder form, talc is also used in several drugs as a colouring agent.\(^{16}\)

A 1993 Toxicology and Carcinogenesis Study of Talc by the US National Toxicology Program found the following:

- Some evidence of carcinogenic activity of talc in male F344/N rats, based on an increased incidence of benign or malignant pheochromocytomas of the adrenal gland.

- Clear evidence of carcinogenic activity of talc in female F344/N rats, based on increased incidences of alveolar/bronchiolar adenomas and carcinomas of the lung and malignant pheochromocytomas of the adrenal gland.

- No evidence of carcinogenic activity from talc in B6C3F mice.\(^{17}\)

Should one err on the side of caution and not use talc? If talc was only available in talcum powder, it would be an issue for individual choice. However, talc is found in many products, from cosmetics to pharmaceutical drugs, making avoidance extremely difficult.

**A Sweet Danger**

Aspartame (Nutra-Sweet\(^\circledast\)), used world wide in diet drinks and foods, has been posed has having a potential role in the increase in brain cancer rates. Aspartame is composed of aspartic acid, phenylalanine and methanol. On digestion, the methanol
breaks down to formic acid and formaldehyde. Aspartame also decomposes to produce diketopiperizine (DKP).\textsuperscript{18,19}

The listing of aspartame as a safe product for human use is of extreme concern and has raised questions as to the probity of the FDA in this issue. The original manufacturer of aspartame was G.D. Searle in the USA.

In 1970, 11 years prior to the FDA approval for use of aspartame, Olney et al queried the potential of the chemical to cause neurotoxicity.\textsuperscript{20,21} Safety studies were carried out by the manufacturing company and submitted to the FDA as a basis for the chemical’s approval. These studies were questionable in both their scientific validity and their results in relation to safety.

One of these supporting studies was carried out in 1972. In this study, infant monkeys were given three levels of doses of aspartame over 52 weeks. All animals in the medium and high dosage groups exhibited seizure activity. One animal in the high dose group died after 300 days of treatment. The cause of death was listed as unknown. Seizures were observed for the first time following 218 days of treatment. Sporadic convulsions occurred inconsistently at various times and were of the grand mal type.\textsuperscript{22}

In 1976, G.D. Searle representatives received FDA permission to hire a private agency, the University Association for Education in Pathology, to validate 12 aspartame studies, at a cost of US $500 000.

Independent pathologists were informed that they were not to make a judgement about aspartame safety or to comment on the design of the studies.\textsuperscript{23} This documentation is of concern, not only in the sparsity of good science shown in the initial safety studies, but also in the legitimacy of the FDA ruling of aspartame as a ‘safe’ food additive.

In 1980, the FDA convened a Public Board of Inquiry with prominent neuroscientists W. Nauta, V. Young and P. Lampert, who were asked to evaluate two animal studies linking aspartame to astrocytic brain tumours. They concluded that one study was
bizarre and unreliable and that the other appeared to indicate that aspartame contributed to brain tumours. They recommended further research. Additional FDA experts concurred with the recommendations but studies suggested by the committee were never carried out.

In 1981, the newly appointed Commission of the FDA, Arthur Hayes, approved aspartame on the basis that the brain tumour risk was minimal.

When aspartame studies were surveyed in the medical literature for funding source and study outcome, it was found that:  
  1. 166 studies were relevant to questions of human safety.  
  2. 74 studies had received manufacturer-related (Nutrasweet®) funding.  
  3. 92 studies were independently funded.  
  4. 74/74 (100%) of industry funding studies found the chemical to be safe.  
  5. 84/92 (92%) of independent studies identified a problem.

A list of referred papers on Aspartame is found at http://www.dorway.com/peerrefs.html.

It has been shown that the aspartame molecule exhibits mutagenic potential. When brain tumour data (gathered by the National Cancer Institute) were analysed for the years 1975 to 1992, increases in incidence occurred in two distinct phases. The initial modest increase may have reflected improved diagnostic technology, but a secondary increase and shift towards great malignancy required explanation by other factors. The timing of the increases paralleled the increased social use of aspartame.

More recently, the European Ramazzini Foundation of Oncology and Environmental Sciences in Italy administered Aspartame in varying concentrations to male and female rats. The experiment followed the animals through to their spontaneous deaths. It was found that there was a statistically significant, dose-related increase in lymphomas and leukaemias in the female rats compared to controls. This dose level was very near those to which humans are exposed.
The European Food Safety Authority (EFSA) said it had evaluated the trial and concluded that “there is no need to further review the safety of aspartame…” EFSA found that the rats in the study had a high rate of chronic respiratory disease that may have predisposed them to cancer.27

The strength of the science is difficult to ascertain when industry pays the bill. There appears to be a plethora of studies on both the toxicity and safety of aspartame. With this chemical, the precautionary principle does not appear to have been followed.

Aspartame is currently found in around 6,000 products worldwide.

**NIH List of Environmental Carcinogens**

The US National Institutes of Health and National Cancer Institute have compiled lists of environmental chemicals and metals known to be carcinogenic. This list includes: 28

- **Pesticides**, such as ethylene oxide, DDT, lindane and lead acetate,
- **Ionizing radiation**, whether from medical procedures such as X-rays and cancer treatments or from the presence of radon in the soil in or around homes,
- **Estrogens**, Tamoxifen, and Diethylstilbestrol (DES),
- **Solvents**, such as benzene (known to cause leukaemia), chloroform and methylene chloride,
- **Fibres**, fine particles and dust, including asbestos, ceramic fibres and wood dust,
- **Dioxins** formed as by-products in paper bleaching, incineration of toxic waste and smelters,
- **Polycyclic aromatic hydrocarbons** produced by burning wood and fuels, in exhausts, and in smoked, barbecued or charcoal-broiled foods,
- **Metals**, such as arsenic, beryllium compounds, cadmium and cadmium compounds, chromium, lead and nickel.
The above list is indicative of a much large compilation of chemicals known to be carcinogenic. For example, the State of California’s Environmental Protection Agency provides a more complete listing on the website:

The environmental soup we live in contains many potential carcinogens, and this may explain at least part of the steady rise in cancer incidence world-wide. Humanity has always known danger from the environment. However, the increase in exposure to most of these carcinogenic chemicals is a new, largely invisible phenomenon.

Because we are exposed to synthetic and industrial chemicals in most areas of our lives, we must rely on governments and scientific organisations for protection from environmental carcinogens with potential to increase the incidence of cancer.

**Unconventional Medicine**

‘Alternative medicine’ in oncology is regarded, by the medical establishment, as an “unproven treatment, promoted for use instead of conventional therapy, claiming to treat the cancer itself”. ‘Complementary medicine’, more condescendingly, is considered to be a “therapy used for symptom management and to enhance quality of life, but is not meant to treat the cancer”.\(^{29}\)

In this chapter, these treatments are often referred to collectively as Complementary and Alternative Medicine (CAM). The treatments discussed may have benefit as stand-alone treatments or as adjunct therapies, to be used in conjunction with current conventional therapies. Integrative medicine is a title given to the combination of orthodox treatments with other forms of treatment.

The delineation between treatments that are conventional and those that are alternative or complementary is fluid. Therapies that are proven safe and effective may eventually, over time and as prejudices weaken, become absorbed into conventional health care. Chiropractic and acupuncture were resisted with vigour by conventional physicians, but they have now—with legal redress in the case of
chiropractic—largely become accepted as a standard health service by the public, if not by conventional medicine.

**Complementary and Alternative Medicine (CAM)**

Complementary therapies are regarded as ‘soft’ treatments, and include:

- Acupuncture,
- Traditional Chinese Medicine (TCM),
- Ayurveda,
- Homeopathy,
- Chiropractic,
- Herbs and nutritional medicine (to some extent),
- Hypnosis,
- Psychotherapy,
- Meditation,
- Massage.

Treatments that may actually kill cancer cells or affect the tumour are classed as alternative, and include:

- Cancer vaccines,
- Injectable glandular extracts,
- High dose injectable Vitamin C,
- Injectable laetrile,
- Mistletoe lectin (Iscador),
- Hyperthermia,
- Electrochemotherapy (Galvannotherapy).

**'Fringe' Science?**

The labelling of treatments as ‘alternative’ has not only deprived most cancer sufferers of access to them, but has also restricted future research possibilities. Being known as an alternative practitioner or scientist is not beneficial to anyone’s career future within the current medical community.
When or why a treatment modality is described as alternative is unlikely to be the decision of the research scientist or clinician involved. Many of the treatments listed above are regarded—by conventional oncologists—as fringe science or alternative medicine. The scientists involved do not necessarily share this view, particularly when their results are published in mainstream peer-reviewed journals. Once a modality is used routinely, it becomes conventional regardless of its origins.

**Criteria for ‘Alternative’ Classification?**

Why does a new and interesting treatment become labelled as ‘alternative’? Is it primarily because the new treatment requires such a paradigm shift that the current accepted dogma of medicine cannot face such a change (although this may not be the reason given by those doing the labelling).

Could money be the major reason? If no patent is available, there is no financial gain for a company to produce and promote a treatment. The R & D must then be funded by government or by a group motivated by altruism rather than profit. This is not to say that the profit motive is excluded from alternative medicine. Many companies and individuals have gleaned large incomes from the sales of alternative and complementary products.

**Herbal Medicine**

All civilisations have a history of the use of herbal medicine. Herbs have been used by all peoples to treat the diseases that ailed them. Today, the use of western herbal medicine, Traditional Chinese Medicine (TCM) and Ayurvedic Medicine (Indian herbal medicine) is increasingly common.

**Traditional Healing Methods**

Herbal use in European countries was often the domain of wise women, who (in the more male-dominated scientific medicine) were subsequently referred to and persecuted as witches. Today, herbal medicine is increasingly recognised in the health policies of Australian federal and state governments, and courses are available at several of our universities.\(^\text{30} \) \(^\text{31} \) \(^\text{32} \)

In 18\(^{th}\) century Europe a form of medicine called homeopathy was developed, based
on the “principle of similars”. Homeopathy was founded by Samuel Hahnemann, a German physician who developed his treatments by matching the symptoms produced by a drug to symptoms exhibited by sick patients. He emphasised all facets of a person’s health status, including emotional, mental as well as physical.\(^{33}\)

In China, a complex system of medicine was developed over 3000 years, involving not only the use of herbs but also of acupuncture, massage, diagnosis by pulse and a view of the workings of the human body that is quite distinct from the Western view.

Ayurvedic medicine was developed in India, based on ideas from Hinduism. Ayurvedic means “the science of life”. Their medical practice is based on the beliefs that all things in the universe are interconnected, that disease is disharmony of the person with the universe, and that disruptions may be physical, emotional, spiritual or a combination of the three. Treatments may be herbal, dietary, massage or yoga/exercise based.\(^{34}\)

**Effect of Scientific Medicine on Traditional Healing**

When scientific medicine came to the fore in Europe, it increasingly diminished the use of traditional healing. Women were banned from the study of medicine at universities. Many women who had worked as healers were burned as witches—primarily because of their religious beliefs, but their use of medicinal herbs attracted attention and persecution. ‘Wise woman’ was equated with ‘witch woman’.

Women were excluded from educational institutions, particularly medical schools, prevented from learning Latin (the prevailing language of medicine), and were told they were not allowed to practice because they were not qualified to do so. The women lay healers (particularly the midwives) were competition for the guilds so the medical profession appealed to the church for help, and the church re-sponded by persecuting women in one of the most vicious rampages in her-story.\(^{35}\)

As a consequence, cottage industry competitors in this area were eliminated, leaving the field open to control by universities and similar organisations.
Integration of Scientific Medicine into Traditional Systems

Countries such as China and India did not discard their traditional medicine in favour of the newer ‘scientific’ Western modalities. Over the last century, they have integrated such approaches into a system of medicine that combines TCM and/or Ayurveda with modern scientific medicine.

In contrast, in countries that had been colonised by Europeans, a social stigma has been attached to traditional medicine. In Singapore, for example, for many years it was not encouraged or tolerated. ‘Proper’ treatment—drug therapy—became something to aspire to if sufficient funds were available to pay for it.

Non-Delivery of ‘Cure’ by Conventional Medicine

If conventional medicine had successfully delivered the expected ‘cures’, then alternative and traditional medicine would have gradually disappeared, but this has not been the case. Over the last century there has been an increasing swing towards self-treatment and the use of treatments outside the control of the medical establishment. This swing may reflect:

- An increase in dissatisfaction with the treatments of science.
- A greater tendency for people to take control of their own health.
- A steady increase in scientific studies showing efficacy with the use of traditional methods.

Obstacles to Proving New Medical Treatments for Cancer

There have been two main obstacles to overcome in proving new medical treatments for cancer: cost and a social structure in medicine that is resistant to change of the current scientific paradigm.
Cost of Clinical Trials

Clinical trials must be large and well designed to satisfy current medical standards. Double blind, cross-over trials that meet the requirements of Phase I, II and III levels of testing are costly ventures. These trials are only affordable by large institutions that are funded by governments, donations and companies and, especially in the case of drugs, by pharmaceutical companies that have a vested interest in the outcome of the trials—a patented drug that will repay the investment over time.

Herbs that have been used for millennia cannot be patented. Consequently, unless an active component of the herb can be produced as a new (and patentable) entity, the funds to run large studies are difficult to source. Only governments or academic institutions can run large trials without the financial return of a patented medicine. As noted in Chapter 7, Academic Freedom—Academic Funding, this has become increasingly less likely to occur over time.

Resistance to Change

The second obstacle to proving new treatments is the attitude held by many scientists and doctors in the upper echelons of medicine. When those who have influence and power at the highest levels are resistant to change, change is only likely to occur through a paradigm shift. At what stage is a treatment ‘proven’? While a treatment or modality is resisted by the power brokers, it may never be accepted.

Rejection of Herbal Medicine by Orthodox Practitioners

A 2005 study, presented in the New England Journal of Medicine (NEJM), found that Echinacea did not prevent colds or ease their symptoms. An adjacent opinion piece on the Echinacea research, by a former Stanford physician, Wallace Sampson, dismissed herbal and other alternative remedies as implausible and unworthy of scientific support. Sampson had earlier called for the abolition of NCCAM, the body set up by Congress to investigate alternative medicine in the USA.

A response to the NEJM study—from the American Botanical Council—was that the dose used was too low, only one species of Echinacea was tested, and the group tested fell in the category of the healthy young. Dr. Sampson’s response is a common reaction by orthodox practitioners to studies of alternative medicine. It
reflects the objectivity difficulties one might expect to experience when a group with a dominant paradigm studies the theories and practices of another group, with a different paradigm.

The World Health Organisation promotes the use of herbs such as Echinacea, based on over 350 experimental studies showing the herb’s ability to boost important components of the immune system and for its anti-inflammatory effect.

**Unchanged Attitudes: Dr Rush (18th Century) to Dr Dwyer (21st Century)**

The prejudicial attitudes of some professors of medicine does not appear to have changed much over the last two centuries.

In lectures given by Dr Benjamin Rush, Professor of Medicine at Pennsylvania University from 1769 to 1813, his response to the idea of a healing power that might be found in nature was to treat it “in the sick chamber as I would a squalling cat – open the door and drive it out.” (Caldecott quoting Griggs, page 38). 39

More recently, in a 2001 lecture entitled *Dangers, Interactions and Adverse Events: Facts and Fallacies of Natural Therapies*, Dr John Dwyer, Professor of Medicine at NSW University, discussed the use of herbal medicine. 40 He stated that:

> Anecdotes flourish, and are strong enough to give a scientific encouragement that something should be tested, so we identify the agent that is responsible, test it, purify it, standardise it, subject it to level one placebo controlled trials and we have a winner.

The slide accompanying this stated, however, that “nature is intrinsically inferior”. Dr Dwyer went on to state:

> To suggest to people that something natural is inherently superior in a pharmacological sense, or to suggest that because it’s natural, it’s likely to be harmless, that’s nonsense.

Dr Dwyer may be correct in stating that natural does not equate to harmless. Many plants are highly toxic; the knowledge of toxic plants has been documented in the herbal pharmacopoeias for centuries. I disagree strongly, however, with Dr Dwyer’s assumption that extracting the active agent in the plant, then purifying and standardising it for testing, is the only way that these plants should be used.
There are many active chemicals in herbs, ranging from phenols, alkaloids and steroids to terpenes.\textsuperscript{41} \textsuperscript{42} \textsuperscript{43} Synergism—where the effect of the combination of the chemicals in the plant is greater as a whole, or where herbs used in combination give a heightened effect—is a time-tested mainstay of herbal medicine. Such synergistic effects are also employed in conventional oncology when combinations of chemotoxic drugs are given to improve efficacy.

The belief that only a treatment produced by a pharmaceutical company (scientifically produced) should be used in medicine seems naïve and simplistic. Dr Dwyer would seem to promote the use of only extracted active fractions and never the whole herb. Only the extracted fraction can be patented (if it is a new identity) and produced by the pharmaceutical industry as a commercially viable product.

Dr Rush\textsuperscript{44} had a profound effect on North American medicine in the 18\textsuperscript{th} century, with Pennsylvania University producing 75% of all medical practitioners trained during his tenure. Similarly, Dr Dwyer has had a large impact on the attitudes of medical practitioners in recent years in Australia. This impact occurred as Dr Dwyer headed a committee for the New South Wales Government into practices of complementary medicine in this state. His role was to give guidance and advice on the growing field of holistic medicine.

**Synergism in Naturally Sourced Drugs**

It was reported in 1999 that 62% of new anti-tumour and anti-infective agents, either in late stages of development or that were already available, were naturally-sourced drugs.\textsuperscript{45}

Researchers examining herbal products are learning of the difficulty of extracting all the active fractions from plants, and are becoming increasingly aware of the synergistic and additive effect that many of the chemicals in these plants may exert.\textsuperscript{46}

A combination of oregano and cranberry extracts was tested for antimicrobial activity against *Vibrio parahaemolyticus*. If ingested, this bacteria, (found in contaminated seafood) may cause diarrhoea, cramping, and nausea, or if entering
broken skin, may cause a serious skin infection. Both extracts showed antimicrobial activity, but the effect was enhanced by the mixture of the two. The researchers at the University of Massachusetts then further enhanced the antimicrobial effect by adding lactic acid to the mixture. They suggested that such synergistic ingredients would be useful for the food industry in food preservation.47

**Herbs that Are Cytotoxic to Cancer Cells**

As more and more herbs are being tested for efficacy in the treatment of cancer, an increasing number of their constituent compounds, alone and in combination, are found to be cytotoxic to cancer cells48, or to stimulate the immune system.

**Andrographis paniculata and Uncaria tomentose**

*Andrographis paniculata* (Indian echinacea) has been shown to contain immunostimulants49, and *Uncaria tomentose* (cat’s claw) extract has an anti-proliferative effect on breast cancer cells.50 Further studies have shown that *Uncaria tomentose* also causes a stimulation of interleukin-1 and interleukin-6, giving an immune enhancement effect.51

**Scutellaria barbatae**

A 2003 study on the Chinese herb *Scutellaria barbatae* (Scute Barbata) found that it was cytotoxic to 100% of the actively-proliferating ovarian cell lines tested, and to 50% of actively-proliferating breast cancer cell lines.52 As ovarian cancer and breast cancer are two of the most lethal gynaecological cancers, and many women diagnosed with cancer reportedly use herbal medicine53, it is timely that all potential treatments are explored.

**Curcumin**

Curcumin is an extract from the common spices of curry and turmeric. Studies on curcumin have shown it to be a powerful antioxidant, to have anti-inflammatory properties, and to be a potential anti-carcinogen.

Researchers at the University of Texas M.D. Anderson Cancer Center have shown that curcumin blocks a biological pathway required in the development of melanoma and some other types of cancer. Curcumin allowed an induction of apoptosis in
melanoma cell lines by shutting down a protein (NK-kB) known to induce an abnormal inflammatory response.\textsuperscript{54}

Rinaldi et al have suggested that curcumin is an oral cavity chemo-preventive agent because of its ability to inhibit carcinogen bioactivation.\textsuperscript{55} They also suggest that it has anti-tumour, anti-oxidant and anti-inflammatory effects, can induce apoptosis in varying cell systems\textsuperscript{56} and, in combination with cisplatin, gives synergistic anti-tumour activity.\textsuperscript{57}

\textbf{Artemesia annua}

\textit{Artemesia annua}, (Chinese Wormwood), has been the subject of extensive research, primarily for use as an anti-malaria treatment. Many forms of malaria have now become resistant to the dominant drug treatments, and the search for clinically effective treatments has centred on Artemisinin, an extract of Artemesia. The World Health Organisation now suggests Artemisinin as a last resort treatment for malaria.

Artemisinin appears to be effective for more than malarial treatment. Work by Professor Neranda Singh at Washington University has shown that, when compared with other types of chemotoxic drugs, Artemisinin use has resulted in a higher cancer cell death rate.\textsuperscript{58} When Professor Singh measured apoptosis in MOLT-4 Leukaemia cells, the Artemisinin killed 100\% of the cells in 8 hours, as shown in Table 5-1.

\begin{table}[h]
\centering
\small
\begin{tabular}{|l|c|c|}
\hline
Treatment & \% MOLT-4 Leukaemia Cells Killed & Time Taken (hours) \\
\hline
(dihydro) Artemisinin (200 \textmu M) & 100 & 8 \\
Sodium Ascorbate (2000 \textmu M) & 63 & 24 \\
Mitoxantrone (0.5 \textmu M) & 55 & 24 \\
Hydrogen Peroxide (176 \textmu M) & 40 & 8 \\
Novobiocin (800 \textmu M) & 23 & 24 \\
X-ray (100 rads) & 9.5 & 24 \\
Hyperthermia (44\textdegree C for 1 hour) & 5 & 24 \\
Control & 3.4 & 24 \\
\hline
\end{tabular}
\caption{Apoptosis in MOLT-4 Leukaemia Cells}
\end{table}

\textbf{Mistletoe Lectin 1 (Iscador)}

In 1653, Nicholas Culpeper, an English Physician, wrote and published \textit{The English Physician}, a herbal compendium:
In this early herbal study, Culpeper states that:

... both the leaves and berries of Misselto do heat and dry and are of subtle parts; the birdlime doth mollify hard knots, tumours, and imposthumes.

This appears to be the first published reference to mistletoe as a treatment for human tumours.

**Modern Use of Mistletoe**

The re-introduction of mistletoe as a modern cancer treatment came through Anthroposophical Medicine, based on the writings of Rudolph Steiner, and has since then been used extensively in European medicine. Proteins extracted from the oak mistletoe have been shown to be cytotoxic for leukaemia Molt-4 cells in culture, in six human malignant melanoma cell lines and in human colon cancer cell lines.

A study by Gabius et al (2001) suggested that there was a ‘stimulation’ of tumour proliferation in melanoma and sarcoma cell lines by clinically-relevant low doses of mistletoe lectin. However, Büssing et al (2003) analysed the same melanoma cell lines as used by Gabius, but was unable to replicate Gabius’s results. In fact they were not able to show any stimulation of cell growth by the mistletoe extract.

Most research papers on the use of mistletoe have been written in Europe, but increasingly research is coming from other areas of the world. In 2003, a study of mistletoe lectin-II (Park et al, 2003, Korea), showed that a particular lectin from the Viscum (mistletoe) plant induced apoptotic death in cancer cells. They showed that the lectin induced the production of pro-oxidants causing cellular death, and that anti-oxidants inhibited this process. They concluded that hydrogen peroxide, an oxidising compound, was generated during this process at a cellular level.
Many other studies have been carried out, especially in European countries, on the use of mistletoe, but it has seldom been used in conventional oncology in Western countries. The common rebuttal from conventional oncologists is that not enough studies have been carried out or that the study designs do not fit the new ‘evidence-based medicine’ guidelines.

Only one study appears to fit this criteria, where the use of mistletoe (Iscador) was compared to the standard treatment of interleukins—low-dose recombinant interferon-alpha 2 b (rIFN-α2b, 1 MU) or recombinant interferon gamma—and compared to a control group of malignant melanoma patients. A study group of 830 stage II and III patients at high risk was randomised and followed from 1988 to 1996. This was a well-planned study showing a good success rate, but did not show any statistical benefit in overall survival for either arm of the trial: patients assigned Iscador treatment or the interleukins had similar response rates.

**Nutritional Medicine**

**Gerson Diet**

An early proponent of nutritional medicine in the treatment of cancer was Dr Max Gerson of Germany, in the early 20th century. Gerson had developed a specific diet from personal experience, experimenting with changes in his diet to see if he could cure his migraines. He was successful in his own treatment and went on to trial the diet with his patients.

He achieved a recovery in a lupus patient with the diet, leading to its use for tuberculosis patients in the Charité Hospital and later in the Urban Hospital in Berlin. When Gerson saw advanced tuberculosis patients with poor prognoses recover and survive he became even more convinced of the benefits of this regime. The most difficult part was patient compliance with extreme dietary change.

Gerson’s treatments included juices, fresh liver juice, vegetable broths and foods high in potassium. He also had his patients use coffee enemas daily as a detoxification process.
Dr Gerson emigrated to the USA, and by the 1940s was treating cancer patients with his largely nutritional approach. In 1946, he was called to testify before a US Senate committee investigating cancer treatments. He supplied records of successful treatments, pathology reports, X-Rays, five articulate patients, and testimonials from many more patients.

**Gerson Therapy: Negative Reviews**

At the time of Gerson’s testimony, he was in private practice on Park Avenue in New York, with affiliation to Gotham Hospital, NY. The Senate Committee was headed by Senator Pepper. Although it was not unfriendly towards Gerson, it did not subsequently recommend a dietary-prevention approach to cancer treatment (Moss 1999). Following this testimony, the Gerson therapy was reviewed twice in the *Journal of the American Medical Association* (JAMA): both reviews, perhaps predictably, concluded that the treatment had no value.

Gerson published an article describing his treatment regime and the rationale for the diet and the use of caffeine enemas “*to cause dilation of bile ducts to facilitate excretion of toxic cancer breakdown products by the liver and dialysis of toxic products from the blood across the colonic wall*”. The use of coffee enemas seemed to cause derision from the medical profession (Moss 1999). Even at the end of the 20th century, coffee enema treatments were viewed with both concern and derision.

**Explanation of Gerson Therapy**

A partial explanation of why the Gerson diet may have shown efficacy was provided by Cope (1978). Cope suggested that such a high potassium and low sodium diet may have caused damaged cell proteins to return to their normal undamaged configuration, partly repairing the damage induced in the tissues by the cancer.

The Gerson diet was very strenuous and posed life and death issues for the seriously malnourished patient. Many alternative medicine clinics worldwide have incorporated selected aspects of the Gerson methods into their treatment regimes. However, the results achieved today by these dietary changes do not appear to achieve the high level of success reported by Gerson. The lower quality of our
currently available foods and increased exposure to environmental chemicals since Gerson’s time may provide some explanation for this decreased efficacy.

**Controlled Food Intake**

Other forms of dietary manipulation have been studied in relation to cancer. Professor Ray Kearney of Sydney University studied PAF (platelet-activating factor), a pro-inflammatory mediator of lipid metabolism. He found that test animals that had access to food for only six hours a day—without any reduction in their normal caloric intake—became resistant to a lethal challenge of PAF. Conversely, animals allowed to graze throughout the day, with continual access to food, were uniformly susceptible to fatal PAF-induced anaphylaxis.

Dr Gavin Greenoak, a colleague of Professor Kearney’s, took the controlled feeding study further. He exposed immune-competent hairless mice to simulated solar radiation. Mice allowed access to food for only six hours a day developed 93% fewer skin tumours than those allowed to graze throughout the day. All mice were allowed the same quantity of food.70

**Lack of Studies on Overeating**

The amount of food and frequency of consumption in developed countries is undoubtedly higher than in previous human history. The size of servings has increased dramatically, as shown rather graphically in the movie *Supersize Me* by Morgan Spurlock (producer and director, 2004). The effect of overeating ‘fast’ food for one month proved to be extremely damaging to Mr Spurlock’s health.

Most Western governments now encourage ‘good’ eating habits in their citizens to minimise obesity and its associated health issues. Slowly, there is growing concern regarding a link between overeating and the increased cancer rates in our society.

**Therapeutic Foods**

Studies have been carried out on specific foods historically associated with a therapeutic effect. For example, a trial studying the effect of miso (fermented soybean) with and without Tamoxifen on chemically-produced mammary cancer in rats produced the results shown in Table 5-2:
Table 5-2: Effect of Miso and Tamoxifen on Induced Mammary Tumours in Rats

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Incidence of Mammary Tumours</th>
<th>Multiplicity of Tumours (Mean Tumours/Rat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular (control) diet</td>
<td>91%</td>
<td>4.5</td>
</tr>
<tr>
<td>10% Miso diet</td>
<td>77%</td>
<td>2.4</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>68%</td>
<td>1.4</td>
</tr>
<tr>
<td>Tamoxifen + 10% Miso diet</td>
<td>10%</td>
<td>0.2</td>
</tr>
</tbody>
</table>

A second experiment studied the effect of the combination of miso and tamoxifen in established rat mammary tumours that had reached a 10–25 mm stage at 6 weeks, comparing the size of tumours before and after treatment. See Table 5-3.

Table 5-3: Effect of Miso and Tamoxifen on Established Mammary Tumours in Rats

<table>
<thead>
<tr>
<th>Test Group</th>
<th>Tumour Size at 6 Weeks vs Pre-treatment Tumour Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>160%</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>141%</td>
</tr>
<tr>
<td>Tamoxifen + 10% Miso diet</td>
<td>85%</td>
</tr>
</tbody>
</table>

These studies indicate a protective use for miso with mammary cancer and a possible potent antitumour effect, particularly when combined with tamoxifen.71

Attitudes to Nutritional Supplements by Oncologists

The use of high-dose nutritional supplements has become widespread amongst many cancer sufferers. Most oncologists in Australia do not encourage the use of these supplements during treatment with radiotherapy or chemotherapy. Some oncologists believe that high-dose antioxidants protect the cancer cells against radiation or chemotoxic damage, negating the benefits of treatments.72 73 74

However, a large body of evidence indicates that the use of antioxidants adjunctively with chemotherapy has a demonstrated benefit in reduction of tumour size and, possibly, increased longevity.75 76 77

Studies on Micronutrients in Cancer Treatment

Studies by several groups—particularly those led by Professor Kedar Prasad at the Centre for Vitamin and Cancer Research at the University of Colorado, Denver—have shown a sound scientific rationale for a micronutrient protocol. This protocol included high doses of Vitamin C, Vitamin E succinate and a natural form of β-carotene, as an adjunctive treatment in combination with radiation therapy.78
Professor Prasad established the International Society of Nutrition and Cancer as a group of clinicians and scientists committed to researching and publishing in this area.

A recent study from the NIH in the USA showed that high-dose intravenous vitamin C has a cytotoxic effect and can kill cancer cells\(^79\). This group showed that vitamin C leads to the production of hydrogen peroxide in cancerous tissue, inducing the death of cancer cells.

Intravenous vitamin C treatment has been an area of contention for many years between conventional and alternative/CAM practitioners. Many patients have been warned by conventional oncologists of the ‘dangers’ of intravenous vitamin C. A Sydney newspaper article published in 1994 listed vitamin C under the heading ‘You can Die of the Cure’, though the text stated only that it might cause ‘dietary irritation’. It seems unlikely at this time that hospital oncology departments in Australia will include this treatment in their modalities.

The research carried out by Professor Prasad on the benefits of a particular regime of micronutrients has been in published form for many years\(^80\)\(^81\). Work carried out by Dr Ewan Cameron and Professor Linus Pauling indicated a beneficial role for vitamin C in prolonging life expectancy of terminal cancer patients\(^82\). This work was published almost 30 years ago and has been overwhelmingly ignored or castigated by most in the medical establishment.

Despite this, many patients have availed themselves of these treatments, with or without the encouragement—or even the knowledge—of their oncologists. To have a potentially beneficial and inexpensive treatment ignored for so long is contradictory to the professed image of open-minded scientific oncology.

**Immunotherapy**

The use of bacterial toxins to treat cancer originated with the work of Dr William B Coley, who was the attending bone surgeon at Memorial Hospital in New York City from 1893 until 1936.
Early Work: Dr Coley

Dr Coley has been called by some the father of immunotherapy. He developed an interest in immunotherapy after a young sarcoma patient died of metastatic cancer despite radical surgery. He reviewed 100 cases of sarcoma treated at Memorial Hospital, and found that patients who had developed bacterial infections following surgery did much better than those who did not. For example, he found a patient who had four regressions of his cancer following an infection of *Streptococcus erysipelas*, a bacterium that normally produces a superficial infection of the skin.

Coley initially injected live culture of *S. erysipelas* into 10 patients with sarcoma. With repeated injections he found improvement, in some cases without producing the erysipelas infection, and postulated that toxins from the bacteria might be producing the tumour reduction activity. He began working with heat-killed bacteria, but the reactions were initially not as beneficial. Through trial and error, Coley eventually settled on a more potent mix of gram positive *Streptococcus pyogenes* and gram negative *Serratia marcescens*.

In 1896, Dr Coley presented a report outlining the benefits of his toxins to cancer patients. For over 40 years, this combination of bacterial toxins was used to treat patients with a significant degree of success.

Revival of Interest in Immunotherapy

There has been a recent revival of interest in this form of immunotherapy. It has been proposed that the mechanism of action of the toxins includes:

- Induction of interferon,
- Augmentation of natural killer cell activity,
- Stimulation of lymphoid tissues,
- Activation of macrophages,
- Induction of serum factor causing necrosis of tumours and stimulation of interleukin II (IL-2).

A retrospective study was conducted in 1999, comparing 10-year survival rates of patients treated with Coley’s toxins to patients treated with modern conventional...
therapies: 128 of Coley’s cases were matched with 1675 controls from the SEER (Surveillance Epidemiology End Result) cancer registry. The groups were matched by age, gender, ethnicity, stage and radiation treatment status.

The study showed no statistical advantage for the modern day cancer patients. Thus, in over 50 years of science, current treatments have not increased the benefit to patients when compared to the ‘bacterial toxin’ treatment that William Coley developed in the 1890s. 99

**Anticancer Effect of Newcastle Virus**

In Hungary, a chicken farmer, suffering from a metastasised stomach cancer, suddenly underwent a complete and lasting disappearance of his tumour. The treating physician, Dr. Laszlo Csatary, became very interested in this case. He discovered that there had been an outbreak of Newcastle virus amongst the farmer’s chickens. Newcastle virus is a well-known bird virus that usually causes no more than conjunctivitis in humans.

Dr Csatary began investigating whether this ‘spontaneous’ remission could have resulted from an infection of Newcastle virus. He first published his findings in 1971 90 and has devoted his life work to developing a treatment using this virus for chronic disease patients.

**Newcastle Virus Vaccine**

The anticancer effect of Newcastle virus was first reported in 1965 by Cassell. 91 It has since shown efficacy in the treatment of Glioblastoma multiforme, a highly malignant brain tumour with a median survival time of one year.

A study on the use of a Newcastle virus vaccine in a 14-year-old boy, first diagnosed with Glioblastoma multiforme, was carried out in September 1994. After standard treatment, consisting of surgical debulking of the tumour followed by radiation therapy and adjuvant tamoxifen, the tumour had recurred. Chemotherapy was then given, using cyclophosphamide and vincristine sulphate. When the MRI demonstrated progression of the tumour, the chemotherapy regime was changed to a
different cocktail. By March 1996, an MRI again showed enlargement of the tumour.

Treatment with Newcastle virus began in April 1996. By January 1997, all medication apart from the Newcastle virus treatment was discontinued. An MRI taken in September 1998 showed tumour shrinkage of approximately 95%. By March 1999 the boy had returned to school.

Two other children with the same form of brain tumour were also given this treatment. Prior to treatment with NDV vaccine, (Newcastle Disease Virus), both children had rapidly progressive cancers despite receiving conventional therapy. At 22 and 24 months, both were shown to have stable tumours, as measured by MRI. They were to continue the NDV vaccine treatment.\(^{92}\)

**Phase II Study on Newcastle Virus**

A Phase II study, using Newcastle virus as an oncolysate, studied the progression of Stage II malignant melanoma patients. The progression of the disease was considerably less in patients receiving the oncolysate than in the control group.\(^{93}\) The Newcastle virus was found to induce internucleosomal DNA fragmentation, a feature of programmed cell death. Only a brief exposure of 30 minutes was required to induce a full-blown apoptotic response.\(^{94}\)

This treatment appears to have no significant toxic effects, nor were neurotoxic effects noted in the glioma patients. For many years Dr Csatary worked in the USA trying to gain acceptance for this treatment. After almost 20 years of unsuccessful effort, he returned to his native Hungary to produce and trial his vaccine. He has since returned to the USA, as the use of Newcastle virus vaccine did not gain formal acceptance in Hungary.\(^{95}\)

Research continues into the use of this vaccine by Csatary and others at the United Cancer Research Institute in Virginia,\(^{96}\) in Hungary,\(^{97}\) and by researchers at the German Cancer Research Center in Heidelberg, Germany.\(^{98}\)
Other Research on Vaccines from Bacterial Isolates

As discussed in *Chapter 4, Bacterial Involvement in Cancer*, a large body of research exists on the possible bacterial cause of cancer. Several of the scientists already mentioned had developed and used forms of vaccination, produced from bacteria isolated from various tumours.

Glover and Livingston-Wheeler, for example, showed encouraging results with this form of treatment. Gregory developed several antibiotics as a response to the organism cultured from tumours, claiming particularly good results in the treatment of cancer with one antibiotic that he named Gregorcin.

**Hyperthermia**

Hyperthermia is a method of treatment based on the premise that cancer cells—even though they can reproduce indefinitely—are more fragile than normal cells. Cancer cells die at a temperature of around 43°C, whereas normal cells survive this temperature.

Hyperthermia is often used in conjunction with low-level chemotherapy, and is believed to increase the efficacy of chemotherapy without an increase in toxic reactions.\(^9^9\) It has also been shown to improve survival times of malignant melanoma patients when combined with radiotherapy.\(^1^0^0\)

Many forms of hyperthermia have been used historically. This treatment was first used by Julius Wagner von Jauregg (1857–1940), an Austrian neuropsychiatrist, when treating a patient suffering from dementia paralytica, the final stage of syphilis. He inoculated the patient with malaria. The patient developed the high fevers of malaria, and the fever stopped the progression of the syphilis. Dr von Jauregg received the 1927 Nobel Prize in Physiology and Medicine for this discovery of the therapeutic value of fever induction.\(^1^0^1\)

**Early Use of Hyperthermia in Immunotherapy**

The next and most well known use of hyperthermia, early in the 20\(^{th}\) century, was the induction of fever by bacterial toxins—the immunotherapy method of Dr Coley,

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already discussed on page 109. This technique was also used with apparent success by German physician Dr Josef Issels.

An adaptation of the immunotherapy fever was the use by mechanical means of raising the temperature of the tumour. Early methods used microwaves; later methods used infra-red and then radio-wave induction of heat.

Dr Issels gave patients a ‘fever shot’ once a month to raise the body temperature as high as 105°F (40.5°C). He induced active fever with the drug Pyrifer, made from specially-treated coliform bacteria. He then induced passive fever by hyperthermia. The patient was placed inside a cylinder containing electrodes that bombarded the body with ultra short waves.

Studies carried out by Professor Joan Bull at Anderson University in Texas have examined the use of infra-red hyperthermia using the Heckel Bed from Germany. She showed that 60% of patients with advanced pancreatic cancer had a significant response to the hyperthermia treatment, given in combination with chemotherapy and immune-modulating drugs.¹⁰²

**Electro-hyperthermia**

The use of ‘oncothermia’ (electro-hyperthermia) appears to be increasing in Europe. The most popular equipment design is from Professor Andras Szasz of St. Istvan University, Biotechnics Department, Budapest, Hungary.

A recently-published article examined the use of electro-hyperthermia in the treatment of advanced brain gliomas, alone and in combination with standard treatments such as chemotherapy or radiotherapy. Gliomas are a common brain tumour, usually with a fatal outcome.¹⁰³ ¹⁰⁴

Hyperthermia by itself has been shown to inhibit angiogenesis¹⁰⁵, and may induce translocation of apoptosis-inducting factor (AIF) and apoptosis in human glioma cell lines.¹⁰⁶
As an adjunctive treatment in combination with standard therapies, hyperthermia may well increase their efficacy, enhancing sensitivity to chemotherapy and radiotherapy, and it may help overcome chemo-resistance in human malignant glioma cells.

A phase II study, published in 2006, was carried out on relapsed malignant glioma patients in Florence, Italy. Eight patients were pre-treated with temozolamide-based chemotherapy and radiotherapy before hyperthermia was applied. One complete and two partial remissions were achieved with a response rate of 25%, indicating that electro-hyperthermia may have some effectiveness in relapsed glioma cases.

**ECT (Galvanno Therapy)**

While head of the Radiology Department of Karolinska University in Stockholm, Professor Bjorn Nordenstrom began working with the concept of treating tumours by the insertion of fine needle probes into tumours. A low electrical current was then pulsed through the tumour.

In the mid-1980s I travelled to Sweden and met with Professor Nordenstrom. At that time, he had used this method to treat 80 lung cancer patients, all of whom had been treated by conventional means and were considered to be in their terminal stages. Out of these 80 patients, Professor Nordenstrom had reversed the condition of approximately 28 of them.

Professor Nordenstrom was quick to correct me when I referred to the treatment as alternative. He was the head of his department and had previously served as the head of the Nobel Assembly, and felt that the label of ‘alternative’ was an insult to an established and well-respected scientist.

This method of treatment became known as galvanno therapy or Electrochemical Therapy (ECT).

scientific explanation of the traditional Chinese medical system of acupuncture, and it became widely used by those practicing oncology in China.

Professor Xin Yuling, Head of Thoracic Surgery at the China-Japan Friendship Hospital in Beijing, adopted this method of treatment. Professor Xin published many large studies showing the efficacy of this treatment, and by the early 2000s over 1200 hospitals in China were using the ECT method.

The use of ECT has continued in China and has since spread to several other countries. A small number of Australian patients have travelled to China for treatment but as yet, this treatment is not available to patients in Australia.

**Patient Choices and Information**

Most cancer patients who decide to use complementary or alternative treatments do not do so on the advice of their conventional practitioners, but rather through information from a variety of other sources.

**Sources of Information on CAM**

A 2005 study by Dr Molassiotis, on haematological cancer patients from 12 European countries, found that their main sources of information were friends, family and the media. This study confirmed earlier research (2002) on the sourcing of information relating to non-conventional forms of treatment.

Professor Ernst in England presented particularly different results. He stated in his 2003 paper that most cancer patients received information on non-conventional therapies from newspapers, books and, increasingly, the Internet. Interestingly, Professor Ernst sourced his information from European (British) cancer patients, as did Dr Molassiotis.

Walji et al (quoting Fox and Rainie, in *Vital Decisions: How Internet Users Decide What Information to Trust When They or Their Loved Ones are Sick*, from Pew Internet and American Life Project, Washington, DC (2002) suggests that 48% of health-related Internet searches are for information about CAM or experimental treatments.
The above papers show a significant difference in patients’ methods of sourcing information. However, there is general agreement that medical practitioners, be they oncologists, radiotherapists or surgeons, should not only be aware of possible interactions between the different therapies, especially herbal medicines, but should also increase their knowledge and understanding of CAM therapies so that they can offer informed and unbiased information to their patients.

**Common Choices of Therapy**

A study on the use of CAM treatments in 126 colorectal cancer patients found that the most commonly used therapies were:

- Herbal medicine (48.7%),
- Homeopathy (20.5%),
- Vitamins and minerals (17.9%),
- Spiritual therapies (15.4%),
- Medicinal teas (15.4%),
- Relaxation techniques (12.8%).

This study was conducted across seven European countries and showed that 87% of the patients received conventional treatment, and that of this group, 89% underwent chemotherapy. Most patients reported satisfaction with the use of CAM and felt that its use was effective. Only two of the 126 patients reported no benefit from their use of CAM therapies.

There have been many conflicting studies published concerning the possible benefits of alternative/CAM treatment in cancer patients.

**Demographics of CAM Users**

A study by Richardson et al (2000) cited several reasons for patients to use other forms of treatment:

- To attempt to control, or at least be involved in, their own treatments,
- To increase their sense of well being and decision making,
- To increase their own level of hope as to a positive outcome.
Molassiotis et al (2005) found that patients with colorectal cancer who chose to incorporate CAM techniques into their treatment regime tended to be younger, with non-manual jobs, and were most likely to have received previous conventional treatment for their cancer.  

The 2005 study by Molassiotis on patients with haematological cancers found that CAM users were from a variety of backgrounds:  

- 30% were in professional jobs,  
- 22% were university educated,  
- 28% were manual workers,  
- 25% were retired,  
- 76% were married,  
- They generally earned less than 10,000 GBP annually,  
- The most commonly used type of treatment was homeopathy (39%) followed by psychic therapies (use of mediums/healers) and herbal medicines, both at 22%,  
- A quarter of the herbal usage was with mistletoe.

The choice of homeopathy may reflect the long history of its use in Europe and its ease of access. The most common reasons for CAM use given by patients were:  

- To increase the body’s ability to fight the cancer,  
- To improve physical well-being,  
- To improve emotional well-being, hope and optimism.

There was a 44% perception of benefit for points 2 and 3 amongst the patients in this study, but it was not within the scope of the study to judge whether benefit was real or merely perceived. Molassiotis states “It is interesting to see that spiritual therapies (such as faith healing, Reiki or prayer) have been frequently reported in the literature as being used by cancer patients.”
Interest in Prayer and Spirituality

Having worked with many cancer patients over the past 20 years, I think most patients who face death tend towards some form of spirituality and prayer. I would suggest that for most people—when faced with their own mortality—prayer would be a natural choice rather than being, as this author suggests, somewhat surprising.

Patients with More Aggressive Cancers More Likely to Choose CAM

Another study that examined patients with a broad range of cancers (127 patients from three centres in Scotland and England) found similar results. An improvement of physical well-being was reported by 44% of patients, whereas 67% reported an improvement in emotional well-being and an increase in levels of hope. It is interesting that the range of CAM practitioners discussed in the study did not include ‘holistically-trained’ medical practitioners and that, in most cases, no practitioners were involved in the choice of treatments, treatments were patient driven rather than practitioner recommended.

A 5-year follow-up of the long-term benefits of CAM treatments did not show increased survival rates among CAM users in this particular study. However, the authors of the study stated that this could be because disease was extensive in this group of CAM users.

A Norwegian study of the survival rates of patients using CAM techniques showed an increase in death rate of patients using these treatments. However, the study pointed out that the use of CAM treatments was more common among patients with symptoms relating to their cancer, those receiving only palliative treatment, patients with metastatic disease and those diagnosed with cancer more than three months previously.

The authors of the study did not feel that the use of CAM treatments directly influenced survival times, but that patients who turn to these treatments may have suffered worse symptoms during cancer treatment. The more severe symptoms might suggest a more aggressive disease, hence their turning to other treatments in an attempt to alleviate suffering.
Patients have reported that their use of CAM therapies brought psychological benefits—being more optimistic about the future, feeling calmer and emotionally stronger—and an improvement in their physical well-being, with more energy and a reduction in the nausea associated with conventional treatments.\textsuperscript{120, 121}

**Paediatric Patients Choosing CAM Therapies**

A study on the use of CAM treatments amongst paediatric patients in the United Kingdom\textsuperscript{122} showed that 33\% (of 49 respondents) used some form of CAM treatment, with the most common therapies being multivitamins, aromatherapy, massage, diet and music therapy. These therapies played a substantial role in helping the children through conventional treatments.

There has been a marked increase in CAM usage by children with cancer. In a study published in 1977\textsuperscript{123}, only 9\% of parents indicated that they had used some other kind of therapy. By 1994\textsuperscript{124}, a publication from Australia showed an increase in this level of use to 46\%.

This trend in increased use appears in other countries also, with a Canadian study of 366 patients showing that 42\% had used some form of CAM therapy.\textsuperscript{125}

A study from the USA in 2000 showed that 84\% of children with cancer were receiving at least one type of CAM therapy while undergoing conventional treatment.\textsuperscript{126}

From the Netherlands, Grootenhuis et al (1998)\textsuperscript{127} showed an increased usage of CAM therapies if the child with cancer had a lower survival chance; 46\% of children using these therapies had suffered a relapse, whereas only 16\% of children in remission used such therapies.

The highest reported use of CAM therapies (sourced to date) in childhood cancer treatment is of 73\% of patients using some form of adjunctive treatment in Taiwan.\textsuperscript{128}
Adult Cancer Patients Choosing CAM Therapies

For adult cancer patients, studies from the UK estimate that the use of CAM therapies ranges from 32% in patients undergoing radiotherapy\textsuperscript{129} to 16% in unselected oncology patients.\textsuperscript{130}

Five studies undertaken in Turkey since 1998 showed that CAM treatment usage ranged from 39% to 60%, with the most commonly used therapy being herbal medicine.\textsuperscript{131}

An Israeli study showed that approximately one-third of adult cancer patients surveyed used CAM treatments. Most patients were satisfied with the results and the effect achieved by these therapies, and the authors noted that no adverse effects were reported from these treatments.\textsuperscript{132}

In Australia, it has been reported that 22% to 52% of medical oncology patients use non-conventional medicine\textsuperscript{133,134}, and that 40% of those were being treated palliatively.\textsuperscript{135} As this last figure was published in 1993, the true percentage in 2005 will be much higher if Australia follows world-wide trends.

Attitudes and Understanding of Oncology Practitioners

On the whole, conventional cancer specialists appear to have a very negative approach to CAM therapies. Even though studies have shown that most CAM therapies are used to assist with the often debilitating and horrific side-effects of conventional treatments, and that reports of interactions of CAM therapies with conventional treatments have been reported only rarely\textsuperscript{136}, many practitioners still have a strong distrust of their use.

Oncologists Surveyed on CAM Therapies

A study published in 2000 surveyed Australian oncologists’ knowledge and attitudes about the CAM therapies used by cancer patients. Of the 265 surveys posted out, 161 oncologists responded as follows:\textsuperscript{137}

- Oncologists reported knowing most about acupuncture, antioxidant therapy and meditation.
The therapies considered most likely to be harmful were coffee enemas, psychic surgery, Iscador therapy and diet therapies. (There was no explanation of the reason for concern for the use of Iscador therapy, but it may be because of the injectable nature of the treatment or the perceived possibility of it having anti-cancer effect.)

There was a distinction between therapies being used for palliative as compared to curative treatment, with acupuncture and the psychosocial therapies considered helpful for palliative patients.

A higher level of harm was feared from the use of therapies that might actively affect the cancer itself. (Note the distinction between ‘soft’ and ‘alternative’ treatments. The soft treatments do not actually target the tumour, as opposed to alternative treatments that may have anti-cancer effects.)

Many of the oncologists overestimated the use of CAM therapies amongst palliative patients, particularly the use of aromatherapy, coffee enemas, herbal therapies, naturopathy, homeopathy, magneto-therapy and shark cartilage therapy.

The therapies that oncologists reported knowing most about—meditation, relaxation, visual imagery and antioxidants—were the therapies most used by their patients.

The patients likely to use non-traditional therapies were those with the most advanced cancers.

Even though a large number of the oncologists considered that they had a good knowledge of the use of antioxidants, there still appears to be no standard use in Australia of antioxidant/micronutrient therapy in combination with conventional treatments.

Note that this study used self-reporting rather than any objective assessment of the oncologists’ actual knowledge about these therapies.

**Lack of Understanding of CAM Therapies**

This survey of oncologists appears to indicate an acceptance of the use of non-conventional treatments once no hope is left for the patient, when the patient is in
palliative care. The hostility shown, even with no understanding of the treatments used, is not a particularly scientific stance.

Many of the treatments described by this particular group of oncologists as ‘harmful’ have been validated by research published in refereed journals, available through PubMed.

Is it a question of scarcity of time in busy practices, so research papers are not read? Could the attitude be that if these treatments were acceptable we would all be using them, so it would be best to wait until all oncologists embrace these treatments? Could the belief patterns of Australian oncologists have more to do with an emotive response than with hard science?

**Bias in Medical Journals**

The evidence indicates a strong bias in conventional medical journals against alternative forms of treatment.

Two articles on complementary and alternative medicine were published in 1998 in leading medical journals. One was an editorial on the risks of alternative medicine, published in the *New England Journal of Medicine* (NEJM), and the other a study on ‘therapeutic touch’, published in the *Journal of the American Medical Association* (JAMA).

An evaluation was undertaken as to whether the information and opinions presented in these articles were objective. It was found that, at best, these articles showed a lack of understanding of the concepts of alternative medicine. At worst, misinformation was regarded as a possibility.\(^{138}\)

Professor Ernst of Exeter University in the UK showed that two identical papers—one listing the treatment discussed as an orthodox treatment, the other as an unconventional treatment—received quite different responses from journal reviewers. The manuscripts referred to a study on treatment for obesity.
Ernst recruited 398 reviewers via Medline searches to receive one or the other version of the paper. The reviewer graded the paper as (a) 1 – 5 in level of importance and (b) whether the paper should be accepted or rejected. The response rate was 41.7% (141) of reviewers. When responses were compared, Ernst found a significant difference in favour of the ‘orthodox’ version.  

Such a response from reviewers raises questions about the ethics of the reviewing process, with its apparent prejudice against alternative interventions. It also highlights the difficulties in producing and publishing good science for any method outside the standard usage accepted by orthodox medicine. What has been viewed as paranoia by alternative practitioners may be the truth regarding current scientific attitude.

Studies must be funded to fully investigate:

- The efficacy of CAM therapies as stand-alone therapies,
- The use of CAM therapies as adjunctive therapies,
- Possible detrimental interactions with conventional treatments. In particular, the potential for interaction between herbal therapies and chemotoxic drugs should be examined. For example, St John’s Wort, a herb often used for mild depression, lowers levels of the chemotoxic drug irinotecan, reducing effectiveness of the chemotherapy regime.

**Bias Against Acupuncture**

A paper entitled “Acupuncture may be associated with serious adverse events” was published in the *British Medical Journal*, stating:

We conclude that acupuncture continues to be associated with occasional, serious adverse events and fatalities. These events have no geographical limits. Most of these events are due to negligence. Everyone concerned with setting standards, delivering training, and maintaining competence in acupuncture should familiarise themselves with the lessons to be learnt from these untoward events.

A letter of response from John Heptonstall, Director of the Morley Acupuncture Clinic and Complementary Therapy Centre at West Yorkshire, pointed out that:
In 55,000 treatments using acupuncture there had been 44 adverse events. When compared to the level of adverse events in conventional medicine, this result is miniscule.

Dr Kim Jobst, Honorary Research Fellow at Glasgow Western Infirmary, had examined the literature regarding acupuncture in 1994–5 and had stated that: “of the comparatively few ADRs to acupuncture most of these were associated with doctors practicing acupuncture.”

In the same discussion it was pointed out by Sean Walsh, a post-graduate student and acupuncturist, that in Australia:

- A general practitioner practicing acupuncture was able to treat after 250 hours of practice.
- An alternative practitioner of acupuncture and TCM had to achieve a minimum of 2500 hours, 1500 of which was TCM/acupuncture.

This would indicate that a medical doctor trained in conventional medicine receives less education to practise outside their field than do alternative practitioners, sometimes with regrettable results.

**Quackwatch**

CAM is viewed by some members of the conventional medical community as an attempt to replace good scientific medicine by charlatan’s methods. These methods may pose as medical treatments but lack medical usefulness or scientific validity, and exist only to take money from the innocent public. CAM is often considered to be lacking in critical thought and scientific rigour, and is often referred to as ‘quackery’.

A web site of the Lake Macquarie City Council (in NSW) states that one should “Be aware that alternative health and healing covers everything from pure hogwash to promising and proven therapies.” This web site then gives links to web sites of various modalities of holistic medicine, research sites and associated government sites.
The first link shown is to a US site called ‘Quackwatch’, describing it as a “consumer guide to health fraud, quackery, and intelligent decision making on traditional and alternative health topics.” This description is taken from the Quackwatch site itself, a site run by Dr Stephen Barrett.

Dr Barrett is the vice-president of the National Council Against Health Fraud, and is a Fellow of the Committee for the Scientific Investigation of Claims of the Paranormal. Quackwatch and other related sites show Dr Barrett’s involvement in several court cases, as an expert witness giving evidence against practitioners of alternative medicine (see also www.bolenreport.net).

Dr. Barrett’s Quackwatch web site, has articles deriding most forms of alternative and complementary medicine, including the article titled High Doses of Vitamin C are Not Effective as a Cancer Treatment.

The recent publication of a study from the US National Institutes of Health (NIH)\textsuperscript{145}, showing that intravenous vitamin C does kill cancer cells, has not prompted the withdrawal of Dr Barrett’s article. The kindest explanation is that the web site is not updated frequently enough to remove articles once scientific studies have validated the claims of CAM therapies. (The use of high dose vitamin C against cancer is discussed on page 108.)

**Australian Skeptics**

In Australia, a group called the Skeptics\textsuperscript{146} has the stated aim of investigating subjects such as paranormal and pseudo-science (which includes vitamin supplements). Their web site provides links to similar sites, including the Australian Council Against Health Fraud and the RatbagsDotCom site. These sites are extremely critical of alternative and complementary therapies, but do not list any articles querying dangerous drug regimes or ADRs (Adverse Drug Reactions).

**Conclusions**

With approximately one-third of cancer patients world-wide now using some form of complementary or alternative treatment, it is imperative that researchers investigate fully both the benefits and disadvantages to patients of these treatments.\textsuperscript{147}
In the papers referred to above, most authors agree that the main use of CAM therapies amongst cancer patients is by:

- Patients in palliative care, when their conventional treatments have been unsuccessful.
- Patients who are seeking higher levels of pain control than others, perhaps indicating more advanced or serious conditions.

When treatment by CAM therapies is sought by this cohort of cancer patients, it should be expected that any form of non-conventional treatment has less likelihood of success. These are not patients who have just been diagnosed with cancer, but rather patients who have already undergone chemotherapy, radiotherapy, surgery and/or hormone therapy.

Such a patient may have elevated levels of toxicity (post chemotherapy), a seriously depleted immune system (from chemotherapy, radiotherapy and surgical intervention) and a tumour that has been changed by chemotherapy and radiotherapy from the original cancer that was diagnosed. The response from such a patient will always be different to the response of a patient at first diagnosis who, apart from the cancer, is more likely to be in a reasonable state of health.

To compare the results of treatments on such differing cohorts of patients is likely to be biased, unrealistic and unscientific. For patients who have already undergone standard conventional treatment and who then turn to alternative treatments as a last resort, any benefit from that treatment should be viewed as a significant and beneficial result.

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Jennie Burke – April 2007
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PART III

ECONOMICS
Chapter 6
Following the Money

As a believer in the pursuit of self-interest in a competitive capitalist system, I am not going to bash business for not being socially responsible. I can't blame a businessman who goes to Washington and tries to get special privileges for his company. That’s his business. He has been hired by his stockholders, as it were, to make as much money for them as he can within the rules of the game. And if the rules of the game are that you go to Washington to get a special privilege, I can't blame them for doing that. I'm going to blame the rest of us for being so stupid and foolish as to let them get away with it.

Milton Friedman

Few trends could so thoroughly undermine the very foundations of our free society as the acceptance by corporate officials of a social responsibility other than to make as much money for their stockholders as possible.

Milton Friedman

The incidence of cancer has increased world-wide throughout the 20th century, with a corresponding increase in the monies invested in related research. In this chapter, I examine:

- The monies associated with treatment and research,
- Recipients of the monies generated in cancer research,
- Contributors to the funding and the science.

Growth of Pharmaceutical Companies

The amount of money involved in cancer research and treatment is beyond the understanding of ‘the man in the street’. To gain some concept of how this has happened, this discussion follows the growth of those corporations that have come to be known as ‘Pharma’.

The beginning of the 20th century saw the burgeoning of the new chemical companies, such as I.G. Farben in Germany and the Standard Oil Company in the USA (owned by the Rockefellers). By 1927, Farben and Standard Oil had formed a
cartel agreement, whereby the two companies did not compete with each other, but agreed to mutually develop and exploit new scientific breakthroughs.

By the 1940s, I.G. Farben was the largest chemical company in the world. They then held interests in American I.G. Chemical, Lederle Laboratories, Sterling Drug, Winthrop Chemical, Hoffman-La-Roche, Bristol Myers, and Squibb and Sons Pharmaceuticals.³

By the end of World War II, General Eisenhower reported that I.G. Farben had stock interests in 613 corporations, 173 of them in foreign countries. When I.G. Farben was dismantled in 1946, some sections—such as Bayer, Hoechst and BASF—survived in Germany, whereas others were absorbed internationally into the Rockefeller empire.

**Wealth and Power of Pharma**

Pharmaceutical companies have become among the richest, most influential businesses in the world, wielding enormous political power through their effects on national economies and their use of lobbyists and political donations. Their ability to fund medical research has strongly influenced the direction and the dominant paradigms in medical research and educational institutions.

Pharmaceutical companies are among the most profitable businesses in the world. Their worth puts them into the number one or two ranking according to the Fortune 500 analysis of businesses in the USA in 2000, a rank that has been consistent for the past few decades. According to David Earnshaw, a former director of SmithKline Beecham and now leader of Oxfam’s campaign on access to medicines:

> Put together, the market capitalization of the four largest (pharmaceutical) companies is more than the economy of India.⁴

**Excessive Profits on Prescription Drugs**

In 2001, the 11 top US pharmaceutical companies showed rates of profit that were three to four times more than the median of all other industries listed in Fortune 500.
Pfizer has shown an increase in stock prices over the last decade of 1,454%. In 2000, Merck, the largest of the US drug companies, made profits of US $6.8 billion, giving it higher returns than the combined profits of the airline, entertainment, food production, metals and hotel/casino/resorts industries.\textsuperscript{5}

In the early 1990s, it was becoming obvious that the pharmaceutical manufacturers were making astounding sums of money. A US Congress report from the Office of Technology Assessment (OTA) stated that the pharmaceutical companies were making excessive profits on prescription drugs, and that they were spending too high a proportion of this on promotion. The OTA estimated that the 1981–1983 New Chemical Entities (NCE’s) delivered cash flows of US $341 million per compound. The net after-tax value of the cash flows for these NCE’s was $230 million.\textsuperscript{6} The report stated that the figures for revenue and cost assumptions were very uncertain as they knew little about cash flows from global sales.

The Pharmaceutical Manufacturers Association estimated that worldwide drug sales by US pharmaceutical companies in 1992 was $75.2 billion, an increase of 11.7% over 1991 sales. Global sales of ‘ethical’ pharmaceuticals—prescriptions and over-the-counter medications—were said to have been $63 billion in 1991, with a market share in the USA of $43 billion.\textsuperscript{7}

The sales and profits of some of the larger pharmaceutical companies for 1999, 2000 and 2001 (depending on availability of data) are shown in Table 6-1.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
\textbf{COMPANY} & \textbf{YEAR} & \textbf{SALES (in US$ billion)} & \textbf{PROFIT (in US$ billion)} \\
\hline
Abbott & 2000 & 13.7 & 2.8 \\
Amgen & 2000 & 3.6 & N/A \\
AstraZeneca & 2001 & 16.5 & 4.2 \\
Aventis Group & 2001 & 5.8 & N/A \\
Baxter & 2000 & 6.8 & N/A \\
Bayer & 1999 & 8.9 & N/A \\
& 2001 & 10.1 & N/A \\
Bristol-Myers Squibb & 2000 & 20.0 & 4.7 \\
GlaxoSmithKline & 2001 & 24.8 & N/A \\
Immunex & 1999 & 0.542 & N/A \\
Novartis & 2001 & 19.1 & 4.2 \\
Pharmacia Group & 2000 & 18.1 & N/A \\
\hline
\end{tabular}
\caption{Profits by US Pharmaceutical Companies}
\end{table}
Note: The figures above are in US dollars, and are sourced from District Court documents of Massachusetts in the Class Action against Multiple Pharmaceutical Companies (Civil Action: 01-CV-12257-PBS).

In July 2003, *Fortune* magazine listed the world's largest corporations showing their steady increase in revenue over the 2001 to 2002 period. The figures in Table 6-2 are taken from www.crikey.com:

**Table 6-2: Profits by World’s Largest Pharmaceutical Companies**

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<tr>
<td>Pfizer (USA)</td>
<td>3.9</td>
<td>45.9</td>
</tr>
<tr>
<td>GlaxoSmithKline (Britain)</td>
<td>7.45</td>
<td>35.0</td>
</tr>
<tr>
<td>Bayer (Germany)</td>
<td>1.5</td>
<td>32.3</td>
</tr>
<tr>
<td>Novartis (Switzerland)</td>
<td>5.0</td>
<td>24.9</td>
</tr>
<tr>
<td>Roche Group (Switzerland)</td>
<td>2.3</td>
<td>23.2</td>
</tr>
<tr>
<td>Merck (USA)</td>
<td>6.8</td>
<td>22.5</td>
</tr>
<tr>
<td>Bristol-Myers Squib (USA)</td>
<td>3.1</td>
<td>20.9</td>
</tr>
<tr>
<td>Aventis (France)</td>
<td>2.2</td>
<td>20.2</td>
</tr>
<tr>
<td>AstraZeneca (Britain)</td>
<td>3.0</td>
<td>18.9</td>
</tr>
</tbody>
</table>

According to Harvard Business School Professor Debora Spar, corporations:

...are not institutions that are set up to be moral entities… They are institutions which have really only one mission, and that is to increase shareholder value.

**Importance of Patents**

The research and development costs associated with bringing a new drug to the marketing stage are high. The ownership of a patent gives a pharmaceutical company the length of time needed to recoup its investment. Purchasing patents gives a company the ability to supply a drug with no competition—if it is a novel entity—for years. Patents are therefore protected as sources of major value.

Between 2002 and 2007, it is estimated that 35 patents will expire for drugs that currently have an aggregate global sales worth of more than US $73 billion per year. However, only 14 new blockbuster drugs were expected to acquire patents in 2006.

After 1899, the flood of new drugs continued to rise for half a century. Few of these turned out to be safer, more effective, and cheaper than well-known and long-tested therapeutic standbys, whose numbers grew at a much slower rate ... Many of the new
drugs (after WWII) were dangerous, and ... few were demonstrably better than those they were meant to replace. Fewer than 98 percent of these chemical substances constitute valuable contributions to the pharmacopeia used in primary care ... Opinions vary about the actual number of useful drugs; some experienced clinicians believe that less than two dozen basic drugs are all that will ever be desirable for 99 percent of the total population. Ivan Illich

Cost of New Drugs

With the development of new drugs that appear to extend lives and are less toxic than those routinely used in standard chemotherapy, the cost to consumers is a growing issue, at least in the USA.

Some current examples of costly drugs (prices given in US dollars) are as follows:

- Iressa, used in the treatment of lung cancer, costs approximately $1,800 per month. Patients may need to take the treatment for many months, if not years.
- Gleevec, taken for long periods of time in the treatment of chronic myeloid leukaemia, costs more than $500 per month.
- Erbitux, used in the treatment of advanced colorectal cancer, costs from $18,000 to $30,000 for a seven-week course, perhaps longer if patient response is favourable.
- For patients in the USA who have health insurance, a standard regime for advanced colon cancer would cost close to $250,000 for 19–20 months of treatment. The patient would be expected to pay 20% of this cost—around $50,000. Patients without health coverage may apply for a patient assistance scheme—to which drug companies donate free cancer drugs each year—and hope they will be accepted.
- The older chemotoxics are not necessarily much less expensive. An eight-week course of Irinotecan (an older class of chemotoxic) would cost close to $9,500.

When these high prices are queried, the response from the industry is that the prices help pay for future drug development and clinical trials. A spokesperson for Bristol-Myers Squibb stated, for example, that the price of Erbitux would fund 60 trials.
involving Erbitux. According to a spokesperson for AstraZeneca, manufacturer of Iressa, these prices are “in line with other cancer treatments”.

**Fair Price?**

Whether these prices are realistic and fair becomes questionable when it can be shown that prices have been raised for other reasons. A leprosy drug, Thalomid, was found to be effective in the treatment of multiple myeloma and other cancers. The manufacturer, Celgene Corp, raised its price from US $4,000 to more than $35,000 per year, with an average five-month treatment plan. The company spokesman, Brian Gill, stated that Celgene had “increased the drug’s price to reflect its therapeutic value.”

Until recently, the standard treatment for colorectal cancer was Fluorouracil (5-FU) combined with a vitamin, Leucovorin, costing around $500 for a course of treatment. With the newer drugs, the standard treatment for colorectal cancer—including Eloxatin, Erbitux and Avastin—costs almost $250,000.

Despite the high costs, these treatments do not guarantee a cure. Patients on the 5-FU treatment had on average a life expectancy of around 11 months; the new treatments give patients a life expectancy of around 19 to 22 months.

A price cannot be put on months of life. However, a gain of another 8 to 11 months—with no assurance that quality of life is improved—for a 500% increase in cost is not impressive. Devastated families may be left to cover these costs following the death of a loved one.

**Loss of Patent: Generic Drugs**

The loss of a patent—with the resultant rapid decrease in income—is a huge issue for a company. Loss of patents over the next few years could cost Pfizer up to US $14 billion in annual sales. The only way forward for Pfizer is to create new drugs with long patent times in which to recoup their investment.

It was noted in 2001 that the patents of several large brand-name drugs would terminate by 2006. Over this five-year period, these drugs would have combined
USA sales approaching $20 billion. The loss of the patent meant that other companies could manufacture generic forms of the drugs at a fraction of the price.\textsuperscript{14}

**Extending the Life of a Patent**

USA federal authorities have led numerous investigations into whether anti-competitive practices have been carried out to stifle the launch of generic drugs.

In 2000, seven drug companies were accused of arranging deals, by which they paid their generic competitors to keep their cheaper drugs off the market.\textsuperscript{15} \textsuperscript{16} One such investigation was related to a deal between Bristol-Myers Squibb Co. and American Bioscience Inc. regarding Taxol (Paclitaxel), a cancer drug.

**Drug Patents and Generic Drugs**

Many battles between companies holding patents on drugs and companies producing generic (and cheaper) copies of such drugs are being waged currently in courtrooms worldwide.

In 2000, Ivax Corporation sought to market a cheaper, generic version of the cancer drug Taxol—called Paxlitaxel—that would have saved cancer patients in the USA more than US $500 million annually. Bristol-Myers Squibb, who held the original patent, challenged Ivax’s right to produce the generic drug.

Bristol-Myers Squibb eventually lost the court case, but the legal process meant that Ivax took 30 months to obtain the legal right to manufacture Paxilitaxel. Bristol-Myers Squibb earned around US $3 million a day from Taxol sales, so it gained 30 months more sales time—and several billion dollars in sales—before the generic version was able to be produced and marketed.

With the generic version available, the cost of the drug fell by approximately one-third in the first six months and by half after that.

Bristol-Myers Squibb claimed that around US $1 billion had been spent in R & D on Taxol, including funding for 600 clinical trials. However, the truth was that Taxol had been discovered by the National Cancer Institute (NCI), which is funded by
taxpayers. Kurt Blum, an NCI scientist, discovered the anti-cancer properties of the Pacific Yew tree bark in 1963. Bristol-Myers Squibb took over the development of Taxol in 1989, receiving FDA approval for its use in December 1992. In this case, as in most others, no profit was returned to the taxpayers.\textsuperscript{17}

**Extending a Patent for Testing on Children**

Another way in which companies can extend the life of a patent is to investigate the potential use of their drugs in the paediatric market. As very few drugs are tested on children, their use in childhood remains scientifically largely unknown.

The USA ‘Best Pharmaceuticals for Children Act’ gives brand-name pharmaceutical manufacturers an extra six months of exclusivity if they test their products on children. This act, originally passed in 1997, was renewed in 2001 to the discomfort of many legislators: the longer the patent times, the higher the cost of the drugs to the community. When the Act was renewed, Rep. Henry Waxman (Democrat, California) stated:

> If we look at just 25 more drugs that are coming up for exclusivity soon, this law will add at least $11 billion to $12 billion to the nation’s healthcare bill.\textsuperscript{18}

**Patent Buyouts**

The worth of a patent depends on the value (and marketability) of the drug involved. The US $1.3 million paid by Eisai to Elan, for the patent on a pain-killing drug for cancer patients, is on the lower end of the scale of payments. A patent buyout between Immunex and Schering AG was settled at US $380 million in 2002. Patent licensing agreements in 2003 were settled at US $330 million (Novartis and Idenix Pharmaceuticals) and $295 million (Eli Lilly and Galen Holdings).\textsuperscript{19}

**Patent Lawsuits**

Lawsuits abound in the field of patents, with many speciality law firms devoted purely to the practice of patent law. Suing for breach of patent is relatively common, albeit expensive. These lawsuits are not restricted to company versus company but have, on several occasions, involved universities as sources of research.
In 1999, the University of Minnesota sued Glaxo Wellcome PLC over the issue of royalties from the drug Ziagen, an AIDS drug containing antiviral compounds discovered by researchers at the university. The University received a patent settlement payment of US $300 million, and established a Graduate Fellowship Endowment with the royalties generated by sales of Ziagen.

The lawsuit involving the Michigan State University and their technology-licensing company, Research Corporation Technology (RCT), is discussed in detail on page 207 in Chapter 7, Academic Freedom—Academic Funding. Following the lawsuit, four generic drug companies are contesting the patent held by Michigan State University. The responsibility of protecting this patent will fall upon RCT. A statement on the web site for the university outlining these cases ends with 20:

In short, Cisplatin has produced not only physical, but also monetary, side effects. In the past few years, there have been two lawsuits contesting how the profits of Cisplatin should be distributed.

When large sums of money are involved, human nature seems to dictate arguments over the distribution of funds. The amounts involved in such legal action appear enormous, but in the context of potential earnings from a ‘blockbuster’ drug, the investment may be a justifiable and reasonable outlay for the companies.

**Abbreviated New Drug Application (ANDA)**

The Hatch-Waxman Act, passed by the US Congress (Drug Price Competition and Patent Term Restoration Act) in 1984, was meant to streamline the approval of generic drugs, while protecting the patent-holding company’s legal interests.

The Hatch-Waxman Act introduced the Abbreviated New Drug Application (ANDA), whereby a generic manufacturer could bypass the long and involved process of safety and efficacy testing if they could show that their generic drug was the same as, and bioequivalent to, an already patented drug.

To apply for ANDA, the applicant must show that either:

- No patent information has been submitted to the FDA on the drug product that is the subject of the ANDA;
Changes in Cancer Research: Research Findings, Economics, Philosophy

Chapter 6 – Following the Money

An existing patent has expired;

An existing patent will expire on a particular date; or

An existing patent is invalid or will not be infringed by the manufacture, use or sale of the drug product for which the ANDA is submitted.21

Companies filing for ANDA would then give notice to the patent holder of their application. If the holder of the patent wished to challenge the ANDA, they would need to initiate a patent infringement notice against the applicant within 45 days. If no infringement notice was filed, the FDA approval would proceed according to the FDA’s expedited schedule. If a patent infringement suit was filed, FDA approval would be held until the date of the patent expiration.

The Act was intended to benefit all parties, particularly consumers. This initiative followed a 1998 Congressional Budget Office study that found generic drugs saved US consumers $8 to $10 billion in retail pharmacy sales in 1994.

The Cost of Protecting Patents

Protecting a patent against generic alternatives has in some cases proved to be a costly business. In mid–1999, the US Federal Trade Commission settled an anticompetitive agreement between Abbott Laboratories and Geneva Pharmaceuticals, Inc., an indirect wholly-owned subsidiary of Novartis Corp. Geneva had filed an ANDA for the production of a generic version of Terazosin HCl (trademarked Hytrin for BPH), used in treatment of Benign Prostatic Hyperplasia.

Geneva filed an ANDA for both capsulated and tablet versions of Hytrin. Abbott sued Geneva for patent infringement for the tablet version of Terazosin HCL but, through error, did not file against the capsule version. When Geneva was granted FDA approval to market the generic capsule version, they informed Abbott of their intention to market the drug unless Abbott paid them not to.

Abbott and Geneva then entered an agreement whereby Geneva would not market Terazosin HCL until the patent infringement litigation for the tablet Terazosin HCL was resolved, or until the entry of another generic Terazosin HCL product. Abbott agreed to pay Geneva $4.5 million per month until the final resolution of litigation.
Abbott had estimated that sales of a generic version would cost Abbott over $186 million in sales in just six months.\textsuperscript{22}

When profit margins for one drug are so high, the lengths to which companies may go to protect patent rights becomes easier to understand.

\textbf{Research & Development}

Research and Development (R & D) has to be the life-blood of any company involved in the competitive business of selling drugs. It might be expected that a large percentage of revenue would be directed to R & D, and that innovation would either increase or be maintained at the current level. Over the last few years, this does not appear to be the case.

\textbf{Decrease in New Drug Development by Pharma}

In 2000, according to pharmaceutical analysts at the investment bank Dresdner Kleinwort Wasserstein, costs for launching a new molecular entity (drug) were about US $800 million.

By 2003 this cost had risen to US $1.4 billion and the numbers of new drugs had fallen ten-fold. This shortfall in output was attributed to a loss of efficiency of research in the pharmaceutical company laboratories. The fastest growth area in pharmaceuticals became the manufacture of generic drugs.\textsuperscript{23}

Why has research into new molecular entities diminished?

With the new mergers between drug companies, the numbers of competing discovery groups has decreased. It has become easier to use combinatorial chemistry to find minor variations or modifications for existing drugs, rather than look for chemical diversity in natural products. More than half the drugs currently approved have been either natural products or related to them. Eliminating natural products as a source of new drugs lessens true novelty in the search for new products.\textsuperscript{24}
R & D in Government Laboratories

Not all the cost of research and development is borne by the pharmaceutical industry. The Division of Cancer Treatment at the National Cancer Institute (NCI) contains a section—the Developmental Therapeutics Program (DTP)—that is funded by both government and industry. The DTP includes the Laboratory of Drug Discovery Research and Development and the Drug Synthesis and Chemistry Branch.

The Laboratory of Drug Discovery Research and Development assists in the development of agents with high priority for the treatment of cancer or HIV.

The Drug Synthesis and Chemistry Branch acquires, screens and evaluates the therapeutic potential of new compounds.25 This NCI department has assisted in the successful development of many cancer therapeutic drugs, such as the following small sample:26

- Hydroxyurea: the NCI discovered this drug and provided major input in its clinical trials—marketed by Bristol-Myers Squibb.
- Carboplatin: the NCI played a significant role in the pre-clinical studies and a major role in clinical trials—marketed by Bristol-Myers Squibb
- L-Asparaginase: discovered at Cornell University, with significant pre-clinical and clinical trial assistance by the NCI—marketed by Merck.
- Streptozotocin: discovered at the NCI with major clinical trial assistance—marketed by Upjohn.
- Taxol: considered one of the block-buster drugs, Taxol had its development funded by the National Institutes of Health (NIH)—marketed by Bristol-Myers Squibb without return to tax payers.27

Public Funding, Corporate Gain

In 1997, the Cambridge Healthtech Institute (CHI) followed more than 45 000 references from US patents to the scientific research papers quoted. It was found that 70% of the citations used in US industry patents came from public science, that is, science carried out in universities, government laboratories or other public agencies.28
It appears that most of the drugs passing through the FDA have received money either from the National Institutes of Health or the FDA to assist in discovery, development or testing.²⁹

Quoting DeAngelis, in the *Journal of the American Medical Association* (JAMA):
In 1999, the National Institutes of Health (NIH) provided $17.8 billion for research, and the major proportion was expended for basic research; the top 10 pharmaceutical companies spent $22.7 billion, primarily on clinical research. ³⁰

It appears that the commercialisation of drugs—the clinical trials needed to show improvement over previous drugs—is handled by the pharmaceutical companies. However, the basic research into new molecular entities is funded mainly by government.

**How Much Does Pharma Spend on R & D?**

How much pharmaceutical profit is spent on research and development of new drugs? Are the figures given by Dresdner Kleinwort Wasserstein (see page 149) agreed generally as being the cost of R & D in pharmaceuticals?

A study carried out at the Tufts Center for the Study of Drug Development in 2001 stated that the average cost of discovering and developing a new drug had risen to US $802 million, from the $231 million the same Tufts group had estimated in 1987. The leading author of the study, Joseph DiMasi, stated that the largest increase in cost was for clinical trials, which had risen by 12% because of larger numbers enrolled in trials.³¹

The consumer watch-dog group *Public Citizen* has queried this study on several counts:

- The drugs listed by DiMasi did not receive any government support at any stage of their discovery and development. This is contrary to the norm, where many, if not most, new drugs do have government input;
- The estimate of $802 million cost included figures for ‘opportunity cost of capital’ of $399 million, which is a theoretical calculation of the value of the R & D investment if invested elsewhere;
Federal Tax laws provide a deduction of 34% of R & D expenses, making the after-tax outlay around $240 million per drug at that time.\textsuperscript{32}

According to \textit{Public Citizen}, the Tufts Center for the Study of Drug Development is funded to a large degree by the pharmaceutical industry, and these figures are used to justify increased pricing of drugs.

The production of new drugs is a hugely expensive affair, yet the amount of revenue allocated to R & D may not be as high as the pharmaceutical industry projects. According to \textit{Public Citizen}, only 12% of revenue went into R & D, whereas 30% was spent on marketing and administration\textsuperscript{33}.

The US Office of Technology Assessment (OTA) produced a paper in June 1994, assessing multiple studies on the costing of pharmaceutical R & D. Between 1970 and 1982, the after-tax cost per drug—that successfully achieved FDA approval for the market—lay somewhere between US $140 and $194 million (in 1990 dollars).\textsuperscript{34} This is markedly less than quoted by DiMasi ($231 million) in his 1987 study.

\textbf{Profits from New Drug Exploration}

How financially rewarding is new drug exploration? The after-tax R & D outlay for new drugs in the 1980s in the USA was approximately $65 million (in 1990 dollars), with each drug taking around 12 years to bring to fruition. This brought the total after-tax cost to approximately $194 million, but the return was at least $36 million more than the R & D investment.\textsuperscript{35}

With the enormous amounts of money—government and industry sourced—spent on R & D for new drugs, what has been the effect for the end-user, the patient?

The OTA study found that most new drugs being marketed offered little therapeutic advantage over the older drugs already in supply.\textsuperscript{36} A 1990 European study was quoted as finding that, between 1975 and 1989, only 30% of new drugs “added something to therapy”, meaning that over half of all drugs introduced into the USA were judged as offering no new therapeutic benefit.
**Pharma and Governments**

There has always been a distinction between government, representing the people, and industry, representing its own select group of people in a money-making enterprise. Government has a responsibility to its people to protect them from harm, whereas industry has responsibility only to its shareholders.

The separation between government and the pharmaceutical industry has become blurred, even in sections of the government charged with the responsibility of regulating the industry and of protecting the public.

**Growth of the US Food and Drug Administration (FDA)**

In the USA, the Food and Drug Administration (FDA) oversees the production and public use of products manufactured by the pharmaceutical industry. The Food and Drug Act was passed in 1906 to force manufacturers to list ingredients on the packaging of medicines and to maintain purity of foods. For many years, the agency involved in the enforcement of this Act was small.

In 1938, a liquid form of sulphanilamide was found to contain a lethal solvent, diethylene glycol, which had been added to sweeten the formula. The manufacturers of the drug, the Massengill Company of Bristol, Tennessee, shipped out the first lots on 4 September, 1937.

In October, Dr James Stephenson asked the American Medical Association (AMA) for details of the composition of the drug, as six of his patients had died immediately after taking it. Massengill provided the AMA with the list of ingredients, on the proviso that they were kept ‘secret’. The AMA had laboratory tests carried out and determined that the problem was diethylene glycol.

At the time, the FDA could not legally investigate or prosecute unless it could be shown that the labelling on the bottles was incorrect. By the time the FDA managed to recall all bottles of the drug, 107 people had died. Another death occurred with the suicide of the Massengill chemist who had added the diethylene glycol to the
formulation of the drug. The company was eventually fined $26,000, the largest fine levied by the FDA to that date.

This event resulted in passing the Food, Drug and Cosmetic Act, whereby manufacturers had to list all ingredients on their labels and submit a New Drug Application (NDA) to the FDA, demonstrating that the new product was safe for its intended use. 37

This new law resulted in major increases in the size and duties of the FDA.

FDA Funding for New Drug Approvals

The approval of new drugs has become the largest and most highly funded section of the FDA. The budget for new drug review in 1992 was 53% of the total budget, but by 2003 it had increased to 79%. The corresponding increase in the numbers of staff involved with new drug approval meant that funding was diverted from FDA laboratories and drug safety experts.

Reduced Funding for Monitoring Drug Safety

The concentration of resources into the drug approval section has meant that the FDA is less able to efficiently monitor the ill-effects of drugs that are already on the market. This has meant a reliance on voluntary reporting of problems by the companies manufacturing the drugs.

Monetary input by the pharmaceutical industry has also extended to FDA new drug reviewers. Their budgets gave them the perks of travelling to conferences and attending courses that were denied to those officers in the drug safety section, which is not funded by industry. 38

Stripping whole sections of the FDA to enable the most funding to be channelled into new drug classification—eliminating half of the FDA in-house scientists and lessening their access to laboratory equipment—does not bode well for patient safety.
This search for more money and staff did not only occur internally. As was pointed out in a 2001 editorial in *The Lancet*, during a six-year period in the 1990s the FDA hired close to 700 medical officers for new product review.

This hiring was made possible through a stipulation in the 1992 Prescription Drug User Fee Act that allowed US $300 million (required for the hiring) to be sourced from industry funding. These new officers—funded by industry—would review new drugs from their original source of wages. A survey of the FDA medical officers blamed this ‘arrangement’ as a reason for the decline in standards in drug approval.39

**FDA Suppression of Commercially-Sensitive Data: the Vioxx Scandal**

The FDA has also caused concern with incidents where they appear to have actively suppressed access to data on prescription drugs, apparently because of its commercial sensitivity.

This problem was revealed on a large scale with the Vioxx scandal. Investigators from *The Independent* newspaper in England found that 28 pages of data relating to Vioxx—a non-steroidal anti-inflammatory drug (NSAID)—had been removed from FDA files because of confidentiality. The newspaper also stated that Dr Peter Juni, who had raised issues concerning the safety of Cox-2 inhibitors, claimed that his efforts were being obstructed by the FDA, and he was told that data on trials of Celcoxib (NSAID) and Valdecoxib (NSAID) had been deleted because they contained trade secrets.

A report by Dr David Graham, Associate Director of the FDA Office of Drug Safety, stated that patients on Vioxx suffered five times as many heart attacks as those on Naproxen (NSAID). Dr Graham’s supervisors refused permission for him to present his findings at a meeting in France. They later attempted to interfere with the publication of his study in *The Lancet*.40

The story of the eventual Vioxx recall made headlines worldwide. It became known that Merck had used a consistent pattern of intimidation to silence scientists who were questioning the increase in heart risk with the use of Vioxx. Merck had developed a training manual to help company staff fend off questions about safety
issues. The scandal destroyed Merck’s credibility and led to class actions against Merck.41

**FDA: Servant of Industry?**

The cosy arrangement between Pharma and government is viewed with scepticism by many people, with justifiable concern as to the transparency of decisions by FDA officials.

The editor of The Lancet, when writing on “Lotronex and the FDA: a fatal erosion of integrity” discussed the ethical issues raised by the Center for Drug Evaluation and Research (CDER), a section of the FDA.42 The financial ties between overseer and industry brings “an impossible conflict for safety issues to be overseen by a centre that receives funding from industry to review and approve new drugs.” Dr. Horton then goes on to refer to the FDA, and the CDER in particular, as becoming the servant of industry.

**Lack of Constraints on Pharma**

Perhaps surprisingly, the value of reputation for the pharmaceutical companies does not appear to be hugely diminished by adverse publicity and fines. There may be a drop in share prices, as there was for Merck following the Vioxx scandal, but without any lasting effect. Patients who wish to buy drugs from ethical companies are not given a choice. The prescription is written by a third party, the prescribing doctor, who is unlikely to choose a drug based on company ethics.

**British Pharmaceutical Industry—‘Voluntary’ Code of Conduct**

The UK situation is broadly similar to that in the USA. In April 2005, the Association of the British Pharmaceutical Industry published a tougher code of conduct, following criticism that self-regulation had failed to stop misleading claims being issued about products. The criticism came in the form of a report from a health select committee, which cited “examples of breaches of advertising regulations; cover-ups of negative medical information; and giving misleading information to prescribers.” MPs also criticised the long delays by the industry in investigating complaints.43
This new code of conduct however is a voluntary code: there are no legal penalties for breach of the code. The major changes to the previous code relate to tighter rules governing hospitality, in that delegates sponsored by companies may only be given economy airline tickets and should not be lodged in ‘lavish’ accommodation.

The medical advertising for a drug may now be no longer than two pages; all promotional material should include information regarding adverse drug reactions; and companies should make no more than three mail-outs to physicians in the first six months of a drug launch.

According to Andrew Hotchkiss, the managing director of Lilly UK:

The key thing for us is the reputation of the industry. ‘Naming and shaming’ is the biggest sanction. At the end of the day any company can pay a fine – whether it be £100 or £10 000 but more valuable is the company’s reputation.

The harshest penalty available to the Association of the British Pharmaceutical Industry for breaking the codes of conduct of the Association would be expulsion. This has never happened. In fact the board has never required a company to publish a corrective statement.

**Ineffectiveness of ‘Naming and Shaming’**

‘Naming and shaming’ seems to have provided little incentive for companies to restrain from hard-sell techniques. The reputations of the pharmaceutical companies do not seem to be held in much esteem world-wide.

John Le Carre’s 2001 novel *The Constant Gardener*, and the film released in 2005, set a pharmaceutical company as the evil protagonist of the story. The concept of the great Pharma giants ruthlessly using and eliminating people reached the public stage without there seemingly being any disbelief from the public. Perhaps the public mind already has a distrust of the morals of these monolithic companies. The Vioxx scandal confirmed, for many, the lengths to which companies would go to make a profit, but ‘naming and shaming’ of Merck has not resulted in any permanent economic repercussions for the company.
The section titled *Litigation* (see page 179) shows increasing and unashamed corporate malfeasance, indicating that ‘naming and shaming’ is of no consequence in any endeavour to induce social responsibility in corporate decisions.

As staff members of the regulating agencies are often drawn from the industry they police, they view their role as one of partners rather than overseers.44

**Australian Pharmaceutical Benefits Scheme (PBS)**

In Australia, we have benefited from a unique system of government payment for the drugs we require. When Howard Florey’s role in discovering penicillin became known, in a flush of national pride the Labor government of the time (1948) decided that all Australians should benefit from this drug, regardless of their financial situation. The government introduced our Pharmaceutical Benefits Scheme (PBS), which ensured that government paid the cost of needed drugs.

**Reference Pricing to Keep Prices Low**

We are one of the few countries to have such a scheme, one that is dramatically different to the medical system of the USA. The PBS scheme was revamped in the early 1990s, when Professor David Henry became the driving force in the Scheme to contain the rising prices of drugs. He introduced a system whereby each drug would undergo a rigorous cost-effective analysis, prior to being listed on Medical Benefits.

This system of ‘reference pricing’ means that the price of a new drug must be compared with the price of drugs of the same class. If a new drug cannot be shown to offer more in performance than the cheapest available product, then the new drug receives the same price as the cheapest product.45

Because of reference pricing, a drug with the potential to be a block-buster (in profit terms) may achieve minimal sales on the Australian market unless listed by the PBS.

This has caused many conflicts between the Pharmaceutical Benefits Advisory Committee (PBAC) of the PBS, and the pharmaceutical companies attempting to have new drugs listed. The pharmaceutical companies intent is to gain the highest price possible, whereas the PBAC tries to obtain the best price for the public.
An ABC *Four Corners* story, *Paying the Price*, examined the politics and dealings that occurred prior to major changes to the PBAC.\(^{46}\)

**Politics and Industry Put Pressure on the PBS**

Professor Henry was visited in 1997 by the new Australian Medical Director of Pfizer US, who made it clear that Pfizer were very unhappy about the way their products were being dealt with by the PBS of Australia.

The new Managing Director of Pfizer in Australia, Dudley Schleier, developed strong connections with the current Liberal government and became one of the founding members of a Commonwealth Government industry work group, established in June 1998. This group was made up of the CEOs of six drug companies and two Cabinet ministers—the Minister for Health, Dr Michael Wooldridge, and the Minister for Industry, Senator Nick Minchin.

Details of the meetings of this group were not available to the Pharmaceutical Benefits Advisory Committee (PBAC) of the PBS. However, *Four Corners* accessed ministerial briefing notes showing that most of the discussion had centred on the PBS and the pharmaceutical companies’ dissatisfaction with their Australian income.

**Government Staff Become Industry Lobbyists**

A year later, Professor Birkett (Chairman of the PBAC) and Professor Henry met with the two ministers, and were informed that the ministers were experiencing significant pressure from the pharmaceutical industry. They later learned that the ministers’ principal adviser had resigned and joined a pharmaceutical company that subsequently became involved in legal proceedings against the PBAC.

By early 2000, the first assistant secretary at the Department of Industry, Alan Evans, had been recruited as a lobbyist for the pharmaceutical companies. Mr Evans began a series of columns in the Australian Pharmaceutical Manufacturers Association (APMA) newsletter, titled ‘Alan’s Antidotes’.
A selection from Alan’s Antidotes states:

The pressure to suppress prices is overriding all other factors. It can be and will be redressed.

…having been at the centre of policy making in Canberra for quite some time, I can recognise policy paralysis when I see it …

... But in some ways this might not be a bad thing as it will allow us to set the agenda and develop policy options which best suit us …

... We might have to break a few eggs to make the omelette, but it will be worth it in the end.47

The Tambling Review

The industry continued to press for change and the Government set up the Tambling Review, with an industry wish list on the agenda. Even though this review was never made public, Four Corners obtained a copy, revealing that the industry had directly lobbied government to have one of their representatives positioned on the Pharmaceutical Benefits Advisory Committee. The Tambling Review concluded, however, that this “could result in an untenable conflict of interest.”

The Tambling Review recommended that a time limit be placed on the length of time that members of the committee could serve, eight years for committee members and twelve years for the chairman. Professor Henry had already spent ten years as a committee member, with two years left of his contract. At their regular meeting in December 2000, the committee was notified that legislation would be pushed through the Senate, and that all members who had been on the committee for more than eight years would have to leave the committee.

Four weeks prior to this, the Prime Minister, John Howard, had met with the CEOs of the pharmaceutical companies located in his electorate. A copy of the confidential background paper (sourced by Four Corners) listed the membership of the PBAC as an issue and stated that “Industry is greatly concerned about membership of the PBAC, particularly the public hostile attitude of some members and staff to industry.”
When the new committee convened, its twelfth member was Mr Pat Clear, who had been a senior executive with Bayer and Glaxo Wellcome for 20 years, with five years as the CEO of the industry’s lobby group. Mr Clear was, at the time, a director of a biotech company working in product development.

One of the very unsettling outcomes of this story was that the pharmaceutical industry succeeded in gaining higher prices than had been previously allowed for Celebrex and Vioxx, two drugs that the expert committee had previously judged to be not cost-effective. This resulted in a $150 million blow-out in the PBS budget, which boosted the profits of Pfizer, Merck and Pharmacia. (The scandal over Vioxx involving Merck and the FDA is discussed on page 155.)

**Repercussions of the Free Trade Agreement on Australia’s PBS**

On 18 May 2004, Mr Mark Vaile, Minister for Trade (Australia), signed the Australian–USA bilateral Free Trade Agreement. Australians have been repeatedly assured by our government that this Free Trade Agreement would not change the PBS. However, there has been an insertion into the Free Trade Agreement that may lead to unwanted repercussions for the Australian people.48

Annex 2-C of the Free Trade Agreement relates to pharmaceuticals. Clause 2 is titled ‘Transparency’ and subclause (f) commits Australia to “make available an independent review process” of decisions by the PBAC.

According to Professor Peter Drahos of the Australian National University Law faculty:

If the Australian Government resisted, then there would be the threat of litigation, and if the threat of litigation was not enough, the US would ultimately bring an action because it would be pressured to do so by US industry, which would be presumably disappointed by the outcome of the independent review.

How this agreement might change pharmaceutical pricing is as yet unknown. Australia has only a 1% share of the world-wide drug market. Professor David Henry has stated that the concern for US drug manufacturers is that the Australian system is being copied by other countries, often with referral from the World Health
Organisation. The outcome for Australian pricing of drugs may have serious repercussions for Australians, but equally importantly it may also have world-wide significance for the pharmaceutical industry.

**What Price Political Influence?**

Lobbying of political parties occurs in most democratic countries. Most industry groups participate in some form of lobbying. The more money involved in the industry, the more there is to give to political parties to curry favour.

**Donations to Australian Political Parties**

The following table shows donations given to the two leading Australian political parties for the years 1998 to 2005, at both federal and state levels (for NSW). These donations are listed under the Pharma/Health Industry category.

**Table 6-3: Donations to Australian Political Parties by the Pharma/Health Industry**

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<thead>
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<th>PARTY</th>
<th>AMOUNT</th>
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Notes:
- The figures above are taken from www.democracy4sale.org; accessed on 8 September 2004.
- Federal elections were held in October 1998, November 2001 and October 2004. NSW State elections were held in April 1999 and March 2003.

Contributions to the Liberal Party have been approximately double that of contributions to the Labor Party, at both federal and state levels. Given that the Liberal Party held power in federal politics, whereas the Labor Party was in power in NSW, the disparity in donations clearly had more to do with party policies than with who held the seat of power at the time.

**Donations to USA Political Parties**

The situation in the USA is similar, where the two major parties have broadly similar philosophical beliefs to the two main Australian parties. The Australian Liberal Party is similar to the USA Republican Party and the Australian Labor Party is similar to the USA Democrats. The following are figures taken from www.opensecrets.org/industries, with thanks to the Center for Responsive Politics.

<table>
<thead>
<tr>
<th>Election Cycle</th>
<th>Total Contributions</th>
<th>Contributions from Individuals</th>
<th>Contributions from PACs</th>
<th>Soft Money Contributions</th>
<th>Donations to Democrats</th>
<th>Donations to Republicans</th>
<th>% to Dems</th>
<th>% to Repubs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006*</td>
<td>$10,432,530</td>
<td>$3,889,743</td>
<td>$6,542,787</td>
<td>N/A</td>
<td>$3,235,336</td>
<td>$7,199,024</td>
<td>31%</td>
<td>69%</td>
</tr>
<tr>
<td>2004*</td>
<td>$17,897,820</td>
<td>$8,510,111</td>
<td>$9,387,709</td>
<td>N/A</td>
<td>$6,021,651</td>
<td>$11,851,794</td>
<td>34%</td>
<td>66%</td>
</tr>
<tr>
<td>2002</td>
<td>$29,445,451</td>
<td>$3,335,540</td>
<td>$6,957,382</td>
<td>$19,152,529</td>
<td>$7,686,772</td>
<td>$21,733,672</td>
<td>26%</td>
<td>74%</td>
</tr>
<tr>
<td>2000</td>
<td>$26,688,292</td>
<td>$5,660,457</td>
<td>$5,649,913</td>
<td>$15,377,922</td>
<td>$8,225,197</td>
<td>$18,402,165</td>
<td>31%</td>
<td>69%</td>
</tr>
<tr>
<td>1998</td>
<td>$13,169,694</td>
<td>$2,673,845</td>
<td>$4,107,068</td>
<td>$6,388,781</td>
<td>$4,722,879</td>
<td>$8,408,570</td>
<td>36%</td>
<td>64%</td>
</tr>
<tr>
<td>1996</td>
<td>$13,771,496</td>
<td>$3,430,216</td>
<td>$3,584,217</td>
<td>$6,757,063</td>
<td>$4,693,810</td>
<td>$9,054,632</td>
<td>34%</td>
<td>66%</td>
</tr>
<tr>
<td>1994</td>
<td>$7,712,082</td>
<td>$1,940,929</td>
<td>$3,477,146</td>
<td>$2,294,007</td>
<td>$3,388,028</td>
<td>$4,339,984</td>
<td>44%</td>
<td>56%</td>
</tr>
<tr>
<td>1992</td>
<td>$7,924,762</td>
<td>$2,389,870</td>
<td>$3,205,014</td>
<td>$2,329,878</td>
<td>$3,442,821</td>
<td>$4,509,323</td>
<td>43%</td>
<td>57%</td>
</tr>
<tr>
<td>1990</td>
<td>$3,235,192</td>
<td>$771,621</td>
<td>$2,463,571</td>
<td>N/A</td>
<td>$1,497,179</td>
<td>$1,750,973</td>
<td>46%</td>
<td>54%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$130,277,319</strong></td>
<td><strong>$32,602,332</strong></td>
<td><strong>$45,374,807</strong></td>
<td><strong>$52,300,180</strong></td>
<td><strong>42,913,673</strong></td>
<td><strong>$87,250,137</strong></td>
<td>33%</td>
<td>67%</td>
</tr>
</tbody>
</table>
Table 6-5: Pharmaceutical Manufacturing — Long-Term Contribution Trends

<table>
<thead>
<tr>
<th>Election Cycle</th>
<th>Total Contributions</th>
<th>Contributions from Individuals</th>
<th>Contributions from PACs</th>
<th>Soft Money Contributions</th>
<th>Donations to Democrats</th>
<th>Donations to Republicans</th>
<th>% to Dems</th>
<th>% to Repubs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006*</td>
<td>$5,711,219</td>
<td>$1,577,220</td>
<td>$4,133,999</td>
<td>N/A</td>
<td>$1,573,720</td>
<td>$1,439,329</td>
<td>28%</td>
<td>72%</td>
</tr>
<tr>
<td>2004*</td>
<td>$9,887,445</td>
<td>$3,612,266</td>
<td>$6,275,179</td>
<td>N/A</td>
<td>$2,913,675</td>
<td>$6,954,645</td>
<td>29%</td>
<td>70%</td>
</tr>
<tr>
<td>2002</td>
<td>$21,763,755</td>
<td>$1,533,183</td>
<td>$5,436,068</td>
<td>$14,794,504</td>
<td>$4,328,753</td>
<td>$17,412,495</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>2000</td>
<td>$19,344,597</td>
<td>$3,231,334</td>
<td>$4,588,705</td>
<td>$11,524,558</td>
<td>$4,364,311</td>
<td>$14,941,356</td>
<td>23%</td>
<td>77%</td>
</tr>
<tr>
<td>1998</td>
<td>$9,028,646</td>
<td>$1,214,935</td>
<td>$3,181,744</td>
<td>$4,631,967</td>
<td>$2,807,263</td>
<td>$6,216,658</td>
<td>31%</td>
<td>69%</td>
</tr>
<tr>
<td>1996</td>
<td>$9,264,843</td>
<td>$1,393,124</td>
<td>$2,823,154</td>
<td>$5,048,565</td>
<td>$2,708,062</td>
<td>$6,544,977</td>
<td>29%</td>
<td>71%</td>
</tr>
<tr>
<td>1994</td>
<td>$5,379,522</td>
<td>$908,086</td>
<td>$2,768,621</td>
<td>$1,702,815</td>
<td>$2,133,172</td>
<td>$3,261,940</td>
<td>40%</td>
<td>61%</td>
</tr>
<tr>
<td>1992</td>
<td>$4,903,427</td>
<td>$1,185,783</td>
<td>$2,385,144</td>
<td>$1,332,500</td>
<td>$2,378,054</td>
<td>$2,547,705</td>
<td>48%</td>
<td>52%</td>
</tr>
<tr>
<td>1990</td>
<td>$2,341,170</td>
<td>$442,354</td>
<td>$1,898,816</td>
<td>N/A</td>
<td>$1,027,861</td>
<td>$1,322,419</td>
<td>44%</td>
<td>56%</td>
</tr>
<tr>
<td>Total</td>
<td>$87,624,624</td>
<td>$15,098,285</td>
<td>$33,491,430</td>
<td>$39,034,909</td>
<td>$24,234,871</td>
<td>$63,341,524</td>
<td>28%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Notes:
- The numbers in Table 6-4 and Table 6-5 are based on contributions of $200 or more from Political Action Committees (PACs) and individuals to federal candidates, and from PAC, soft money and individual donors to political parties, as reported to the Federal Election Commission.
- Although election cycles are shown as 1996, 1998, 2000, and so on, they actually represent two-year periods. For example, the 2002 election cycle ran from 1 January 2001 to 31 December 2002.
- Data for the current election cycle were released by the Federal Election Commission on Monday, May 29, 2006.

Again, a vast disparity exists between donations to the two parties, with almost double the amount of funding being given to the Republican Party. Both the Australian Liberal Party and the US Republican Party support business as a major priority in their electoral campaigns. It was the Labor Party, not the Liberal Party in Australia, who introduced our PBS system.

Prior to the Bush versus Kerry election, there was great unease as to possible repercussions for pharmaceutical companies and their investors in the event of a Democrat win. Richard Evans, the pharmaceuticals analyst at Bernstein & Co., stated in 2004:

> If Kerry were to win, and do what the drug companies are afraid he’ll do—authorize the secretary of Health and Human Services to negotiate prices—I think that would be a fairly constant pressure on the industry, and would change the nature of that investment forever.49

Lobbying money is often well hidden, and so does not always appear in tables such as those shown above. The American Association for Retired Persons (AARP)—a non-profit organisation for people 50 years and over—reported in their AARP...
Bulletin (2003) that they had examined tax records for three non-profit organisations that represented older Americans.

They found that the United Seniors Association received more than one third of its funding in 2001 from drug industry sources, including the Pharmaceutical Research and Manufacturers of America (PhRMA)—the trade association for the industry—as well as Citizens for Better Medicare (a PhRMA-funded non-profit group) and Pfizer Inc. The industry contribution was at least $3 million. These groups were known to advocate for industry-friendly policies.

PhRMA has not restricted its lobbying to only the US government. CanWest News Service reported, on 9 June 2003, that US $1 million had been contributed to fighting the Canadian drug regulatory system. PhRMA spent $450 000 to target the Canadian Internet pharmacy industry, which provides Americans with cheaper prescriptions drugs than are available in the USA.

PhRMA applied pressure through lobbying both the USA and Canadian governments to prohibit Canadian doctors co-signing prescriptions for U.S. patients and to introduce new requirements that patients must appear in person to have prescriptions filled.

**Pharma and the Medical Profession**

It would seem natural that there be some form of connection between medical practitioners and the suppliers of the medications they use in their practices. Doctors make choices as to which drugs to prescribe in their treatments and, often, which particular make of drug.

**Importance of Doctors to Pharma**

Doctors, and the way they are trained, determine the types of treatment that are given for varying conditions. It is doctors who enrol patients in clinical trials and who find new applications for drugs that result in the use of off-label marketing.

Medical doctors, therefore, are critically important to the pharmaceutical companies. With influence from the industry exerted throughout the educational process and
(later) in the clinics, there must be strong ethical checks and balances in place to protect the concerns of the patient.

The primary goal of any advertising or marketing tactic is to convince the recipients (the doctors) to use the manufacturer’s products. How much influence can a company exert on doctors before ethics and morals are breached? Doctors who are influenced financially by industry could be cynically likened to non-salaried salesmen: providing a true bonus to any supplier.

**Industry Support of Universities**

Industry money flowing into universities is not a new phenomenon. It certainly occurred in the earlier part of the 20th century, but it increased greatly over the second half of the century. Often funding comes from foundations, usually with strong ties to industry, thus providing companies with tax relief.

By mid-1970 (Griffen quoted in Culbert (2000)), it was estimated that ‘the great tax-free foundations’ had invested over a billion dollars in the nation’s medical schools. Half the schools received a part of their income from foundation ‘research’ grants, whereas 16% of medical schools were funded entirely in this manner. The main donors were the Ford Foundation, Kellogg Foundation, Sloan Foundation, Macy Foundation, and the Commonwealth Fund, which has been described as a Rockefeller ‘interlock’.52 This money was and is regarded as an investment, rather than a no-strings-attached gift.

At the end of university life and the beginning of their medical careers, doctors have already had considerable exposure to the pharmaceutical industry through lectures and symposia funded by industry. This exposure does not cease once practice begins. If anything, ties may become stronger.

**AMA Code of Ethics**

The comfortable relationship that exists today between medical practitioners, research scientists and the pharmaceutical industry has not always been in place. The initial code of ethics of the American Medical Association (1847) regarded the patenting and advertising of medicines to the public as unethical.
Early in the 20th century, the peak body representing scientists in pharmacology was the American Society of Pharmacology and Experimental Therapeutics, founded in 1908. According to their bylaws:

No one shall be admitted to membership who is in the permanent employ of any drug firm… Entrance into the permanent employ of a drug firm shall constitute forfeiture of membership.

This prohibition was not changed until 1941.53

Medical School Funding by Industry

In Chapter 7, Academic Freedom—Academic Funding, the connections between industry and academic research are explored, as well as academia’s growing reliance on industry for income, not only for trials but also for the running of departments. As governments decrease funding for universities and other centres of science, the shortfall is being made up by industry.

Doctors graduate from teaching schools that meld medical teaching and industry. From industry comes money to support schools and their expensive research trials. From industry come the very tools of the modern medical practitioner: access to pharmaceutical drugs. Doctors are taught to treat by prescription; to rely on the offerings of the manufacturers for medicaments to treat their patients.

How well can an ethical boundary be established between treating a patient by the best and most inexpensive means and prescribing a treatment for self-benefit?

‘Financial’ Barriers to Oral Chemotherapy

Some of the most disturbing articles I have found relate to choices made by oncologists in prescribing chemotherapy for their patients.

Bowers, Silberman and Mortenson (2002) conducted a study on the use of oral oncology products by interviewing oncologists in 12 private-practice oncology clinics.54 Oral forms of chemotherapy are being developed that are easier to use and may be used alone or in combination with other chemotherapy products. This study
examined issues that could arise such as: patient compliance with taking medication on schedule; informing their oncologist as to side effects; payment by insurance companies for oral chemotoxics; and ease of administration.

In a section of the paper headed “Barriers to Expanded Use”, the primary barrier was listed under the heading “Financial”: they found that interviewees considered loss of income to be one of the major drawbacks for oral chemotherapy use.

Many oncology practices derive revenue from the treatment of patients with injectable chemotherapy drugs, both from the administering of the drugs and from the sale of the drugs themselves. If the practice does not dispense the drugs, then the income from providing this service is lost.

**Discount Drugs**

Another recent study, conducted by the Universities of Michigan and Harvard and reported in the *New York Times*, found that although payment variations for treatment did not cause oncologists to favour chemotherapy over other treatments, if chemotherapy was chosen as the intended treatment, then the reimbursement figures did influence the type of chemotherapy given. Oncologists can profit from the sale of these drugs through a chemotherapy concession, and can purchase the drugs at a lower price than the insurance reimbursement.

The article quoted a government study as saying that discounts were as high as 86% on some chemotoxics and that the doctors commonly pocketed the difference. This profit margin was the major influence on the choice of drugs prescribed, rather than drugs being chosen for their appropriateness to the patient’s particular need.

**Visits From Drug Representatives**

Many studies have examined the ethics of doctors accepting gifts from pharmaceutical representatives in exchange for prescribing a specific drug: the drug that the representative is selling. The money invested by industry can bring strong returns, but when the gift process is uncovered it can become a large and expensive scandal, as elaborated below.
Exposure to pharmaceutical promotion begins in medical school and appears to continue throughout the working life of most medical practitioners. A USA national survey of third-year medical students (from eight medical schools) in 2005 found that 97% of students had eaten lunches provided by the drug companies, 94% had accepted small gifts (cups and pens) and 87% had attended drug company sponsored Grand Rounds.  

**Managing Drug Company Gifts**

Several papers highlight the need to educate doctors in the critical skills needed to manage visits from drug representatives (if they are considered necessary), encouraging them to forego the acceptance of gifts and samples and to refer to scientific sources for the most reliable information on particular drugs.

An international cross-sectional survey was conducted by the World Health Organisation (with responses from 700 deans of medicine and pharmacy worldwide) into the education given to medical and pharmacy students about drug promotion. It was found that, throughout their university training, students usually had less than one day devoted to learning about drug promotion. In almost one-third of cases, the medical faculties devoted only one to two hours to this. The survey also showed that medical schools generally gave less time to this topic than did pharmacy schools.

Many studies have shown an agreement amongst doctors that there are ethical issues with the acceptance of gifts from industry, but most feel that although ‘other’ doctors may be swayed by this, they are not personally affected.

**Payments to Doctors to Prescribe Drugs**

When the former manager of Abbott Laboratories in Spain turned whistle blower and instigated legal action against Abbott, it was revealed that Abbott annually budgeted US $2.7 million for payments to doctors for prescribing specific drugs manufactured by Abbott.

Four years later in Italy, there occurred one of the largest inquiries into the marketing practices of the drug industry. Police listed almost 5000 people to be charged,
of whom were medical doctors, including 1700 specialists. It was found that GlaxoSmithKline had spent €228 million on such ‘sweeteners’ to doctors.

Of even more concern was evidence of a programme involving oncologists, pharmacists and sales representatives designed to promote Hycamtin, which is used to treat lung and ovarian cancers. In some cases, doctors were receiving a substantial pro rata payment based on the numbers of patients treated with Hycamtin.\textsuperscript{83}

**Drug Samples as a Marketing Technique**

The giving of drug samples has long been a marketing technique by drug manufacturers. In 2005, resident physicians at a primary care clinic, associated with a teaching hospital in Minneapolis, were studied in relation to their exposure to free samples of drugs. Compared to residents with no free samples, those with access to samples were more likely to write prescriptions for the heavily advertised drugs and less likely than their peers to recommend over-the-counter drugs.\textsuperscript{64}

Other studies have similarly found associations between prescribing habits and the receipt of free samples. In 1998, it was estimated that 2.4 billion free samples were distributed to USA medical centres. When a family medical centre was examined in 1992, it was found that over a four-week period there were 5 546 free samples in the practice, worth US $19 273, based on their average wholesale price.\textsuperscript{66}

Large sums of money are spent on marketing in this way to doctors. As figures on this form of promotion have increased over the years, it seems safe to assume that such marketing is profitable for the companies.

**Effects of Drug Marketing on Level of Medical Care**

What effect has this drug marketing had on the level of medical help given? Do doctors easily identify the difference between scientific fact and sales hype?

In 1995, Ziegler et al conducted a study on the accuracy of drug information provided by pharmaceutical representatives. Out of the 106 statements examined:

- 12 were inaccurate but were favourable towards the drug in question.
A large difference was noted between statements relating to competitor drugs: none were favourable statements but all were accurate.

Only seven of the 27 physicians (the recipients of the presentation) recognised false statements by the representatives.

Ten of the physicians said that they were influenced in their prescribing of drugs by the sales representatives.66

In a much earlier study (1982), Avorn et al found that, although physicians claimed that scientific sources were more important in influencing their prescribing habits than pharmaceutical sources, when questioned about two classes of drugs where the scientific viewpoint was directly opposed to the commercial literature, the understanding of most doctors reflected the commercial information.67

For most doctors, provision of information on drugs by drug representatives has become an important source of education and influence, and this is often accorded greater weight than the scientific evidence.68 69 70 71

The most influential driving force affecting the prescribing habits of general practitioners has been shown to be the pharmaceutical representative, with hospital consultants and observations of hospital prescribing taking second place.

It was found to be rare for doctors to initiate their own active information search. It was, however, likely that they would be influenced by a patient request for a specific drug.72 This fairly new concept of patients requesting brand-name drugs is discussed in the issue of direct-to-patient advertising of drugs. See page 176.

**Continuing Medical Education (CME) for Doctors**

The use of industry-funded continuing medical education for doctors has increased over the years and is an expanding field. An Australian study from Newcastle on the value of industry-funded ‘educational’ meetings found that 62% of general practitioners, 71% of psychiatrists and 24% of physicians attended at least three such industry-organised meetings every year.
This study showed that the topic and speaker were the most important reason for attendance, rather than attaining Continuing Medical Education (CME) points, and that industry CMEs play an increasingly important role in clinician education.

However, this study was conducted by the Hunter Postgraduate Medical Institute (HPMI), an independent Newcastle and Hunter Valley CME provider.\(^73\) The HPMI, according to its web page, receives no money from government and is funded solely by members and sponsors. The list of sponsors includes Roche Products P/L., Altana Pharma, AstraZeneca, Bayer Australia Ltd., Boehringer Ingelheim P/L., Bristol-Myers Squibb Aust. P/L., Eli Lilly Australia P/L., Glaxo SmithKline, Janssen-Cilaq P/L., Merck Sharp & Dohme (Aust.) P/L., Novartis Pharmaceuticals Aust P/L., Pfizer P/L., Sanofi Aventis, Schering-Plough P/L (Essex Pharma Division), Servier Laboratories (Aust.) P/L., and Solvay Pharmaceuticals.\(^74\)

How credible is such a study that shows the benefits of industry-funded meetings likely to be when it is funded by industry?

**Pharmaceutical Company Funding of CME**

The use of independent providers for CME points has been described as a ‘win–win’ situation in the USA. If the medical education and/or communications company (MECC) is accredited by the Accreditation Council for CMEs, it offers the education programme on its own. It then recruits academic physicians to deliver the lectures.

Payment to the MECC comes in the form of ‘educational grants’ from pharmaceutical companies, and the recruited academics are given a small share of the ‘grant’. If the MECC does not have the appropriate accreditation in its own right, then it goes through a medical school that supplies the necessary accreditation (also for a share of the grant), and certifies it free of commercial bias.\(^75\) Such a situation is clearly open to bias.

The listing of such monies spent in promotion as ‘educational grants’ makes the deciphering of monies spent on marketing and promotion by pharmaceutical companies very difficult to ascertain.
Bowman’s paper “The impact of drug company funding on the content of continuing medical education”, quoted in Lexchin, found that.⁷⁶

- Funded meetings were biased in favour of the sponsoring drug companies’ products.
- The sponsoring company’s drugs were mentioned more often and were more likely to be attributed with positive clinical effects.
- When reference was made to competing drugs, these references were more likely to be negative.

Katz et al (2002), noted that the range of topics offered by industry-funded CME providers is narrower than when funded independently of such support.⁷⁷

**Prescribing Habits Affected by Industry-Funded Meetings**

When prescribing habits have been examined following attendance of industry-funded CME meetings, a marked increase is evident in the prescribing of drugs that were the subject of the symposium. One study showed a threefold increase from 81 units +/- 44 prescriptions to 272 +/- 117. Prescription patterns were tracked for 22 months prior to the symposium and for 17 months post symposium.⁷⁸

This increase in prescriptions is also likely to be influenced by the acceptance of ‘all-expenses-paid’ tickets to such symposia.⁷⁹

Most doctors interviewed in the above studies have voiced concern in relation to industry funding. Whereas the majority of doctors do not expect their own clinical judgement to be influenced in such a manner, the end result unfortunately is, that when industry has a role in providing education to doctors, it does so as a marketing exercise and profits from this exercise.

**Pharma and the Medical Journals**

When an industry-funded symposium is published in a peer-reviewed journal, the benefit of the investment increases exponentially with the numbers of subscribers to those journals.
These symposia have been found in many cases to focus on unapproved therapies of a particular drug, without having undergone the peer reviewed process that submitted papers to a refereed journal would.\textsuperscript{80} The appearance in a well-known journal gives a veneer of scientific validity that is worth much to a company.

**Drug Advertising in Journals**

Pharmaceutical companies also pay for advertising in those journals that permit this. When the information given in the advertisements has been critically appraised by external medical reviewers, doubts have been raised as to their accuracy.

A 1992 examination by three reviewers of 109 full-page advertisements in ten leading medical journals found that:

- In 30\% of the advertisements, two out of the three reviewers disagreed with the advertising claim of the ‘drug of choice’.
- Reviewers agreed with a balance on efficacy versus side effects and contraindications in 49\% of the advertisements, but regarded 40\% of advertisements as unbalanced.
- In 44\% of the advertisements, the information given would lead to incorrect prescribing if physicians relied only on information in the advertisement.
- 57\% of advertisements had little or no educational value.
- The reviewers would not recommend for publication 28\% of the advertisements and would require major changes in another 34\% before publication.\textsuperscript{81}

A 2001 study of four major refereed journals (containing 187 advertisements) found that the advertisements generally did not provide adequate study design and statistical information to allow an accurate assessment.\textsuperscript{82}

An examination of advertisements for anti-hypertensive and lipid-lowering drugs published in six Spanish medical journals found that, in almost 50\% of the advertisements, the promotional statement was not supported by the reference provided, usually because the drug was being recommended for different patient groups than the approved group.\textsuperscript{83}
The following two issues for medical journals have emerged in the last decade:

- The problem of finding peer reviewers who are independent of industry.
- The problem of industry ghost writers being the ‘hidden’ authors of articles submitted.

**Papers by Industry Ghost Writers**

Ghost writing in science has become more prevalent over the years. Medical writers, often with a science background, either writing freelance or working for drug companies or universities, provide papers for publication supposedly written by scientists.

An informal poll by the American Medical Writers Association found that 80% of 71 freelance writers had written at least one paper that was accredited to another person.84 A 1998 study of 809 articles found that 11% showed evidence of ghost authors, 19% had evidence of honorary authors and 2% had evidence of both.

They found that the ghost-authored papers were more likely to be found in smaller circulation journals, and they were more likely to be reviews.85 This study found that one in four articles “demonstrated misapplication of authorship criteria and inappropriate assignment of authorship.” These findings were similar to previous studies of this issue.86 87 88

The situation has not improved greatly, even with a growing awareness of the problem. A later study (Mowatt et al, 2002) looked at Honorary and Ghost Authorship in 577 reviews published in the Cochrane Library, and found that 39% of the reviews showed evidence of ghost authors and 2% had evidence of both ghost and honorary authors.89

**Lack of Independent Peer Reviewers**

The independence of peer reviewers of papers submitted to medical journals is of importance with respect to validity. Many journals do not have policies in place on reviewers’ conflicts of interest. Fewer than 50% of biomedical journals have any policy at all, and only 3% publish the reviewers’ conflict disclosures.90
**Pharma and the Patient: Direct to Consumer Advertising**

The direct-to-consumer advertising phenomenon is most prevalent in the USA and, to a lesser extent, in New Zealand. The pharmaceutical industry garners patient support for particular drugs in two ways:

- The advertising of specific drugs in varying media outlets, particularly print and television, and
- The ‘third party technique’ (explained below).

In 1996, a submission was made to the Food and Drug Administration by the Health Research Group of *Public Citizen*, following an FDA request for comment on direct-to-consumer (DTC) drug promotion. This submission showed that, in 1988, US $25 million had been spent on DTC advertising, but that this had increased to between $225 to $250 million by 1994.⁹¹

**Effect of DTC Advertising on Doctors’ Prescribing Habits**

Successful companies are only likely to spend money on advertising if the campaigns increase revenue. The drugs involved are often prescription-only drugs. Not only does the patient become more likely to ask for a particular drug following such advertising campaigns, but the prescribing habits of the physicians involved are also changed by such campaigns.

According to *Public Citizen* figures, in 1989 only 84% of physicians said they would prescribe a particular drug if requested by the patient. By 1995, 99% of physicians agreed to such a patient request and would prescribe on demand.⁹²

According to Charatan:

Last year [2002] pharmaceutical companies spent $1.8 bn on ‘direct to consumer’ advertising mostly on television. Advertising expenditure in 1999 rose by 38.5% from the 1.3 bn spent in 1998, and was 33 times the amount spent on media advertisements in 1991.⁹³

Does it work? According to Charatan, it works exceptionally well:
Doctors wrote 34.2% more prescriptions in 1999 than in 1998 for the 25 drugs promoted direct to consumers that contributed most to overall drug spending. Doctors wrote only 5.1% more prescriptions for all other prescription drugs.

Later figures (2003) now show a DTC expenditure of around US $3 billion per year. 94

**FDA Allowing Prescription Advertising**

The overwhelming success of Vioxx was attributed to its massive PR campaign. Following the failure and recall of Vioxx, the FDA in the USA has not restricted companies’ ability to advertise.

In fact, the FDA is studying a proposal to relax the rules on advertising, allowing the companies to simplify print advertisements to make them more user-friendly and summarising risks with typographical symbols. Prescription advertising has been allowed by the FDA since 1997, and has grown to a business worth US $3.8 billion per year in the USA. 95

The most important issue, however, for patients is whether they have benefited in terms of improved treatments?

**Third Party Technique by PR Companies**

The third party technique used by PR firms develops a ‘grass roots’ organisation that operates with no acknowledgement of the company it serves or that funds it.

One example of this ploy in Europe aimed at selling a HPV (Human Papilloma Virus) test kit produced by a USA biotech company, Digene. In 2003, celebrities and high profile women were enlisted to lobby the House of Commons in London to encourage the NHS to support the use of this test.

*The Observer* newspaper in London tracked the origins of this campaign to one of the world’s largest PR companies, Burson-Marsteller, based in Brussels. The celebrities contacted by the newspaper had no knowledge that they were in effect
providing free PR for Digene by pressuring the UK government to introduce the new screening test. 96

**Benefit for Patients?**

The main concern for patients is that they receive the best possible treatment for their cancers and have the best possible quality of life available to them. This does not always occur—indeed, many prescribed treatments tragically have little chance of success.

Many patients with cancer receive chemotherapy at the end of life, even if their kind of cancer is known to be unresponsive to the drugs, according to a study reported at the (2001) annual meeting of the American Society of Clinical Oncologists held in San Francisco. 97

Dr Ezekiel Emanuel, at the American Society of Clinical Oncologists, noted that treatment for a patient at the end of his or her life could cost $38,308 in the final year, compared to $27,567 for a patient not in the final year of life. What kind of financial burden may be left to families who have spent their life savings on treatments for a family member dying of cancer?

**Pharma and Marketing**

If one company epitomizes the modern drugs industry it is Pfizer. Just a decade ago, it was regarded as an industry also-ran. But the US company has powered its way up the global ranking list to its unassailable position thanks mainly to its marketing prowess… ...While some of Pfizer’s research has been excellent, its success stems largely from its ability to turn drugs, often ones licensed in from its competitors – into multi-billion dollar products.

David Pilling (in a 2001 issue of the *Financial Times*) 98

**Pharmaceutical Marketing Budgets**

The Office of the Attorney General in the State of Vermont has, for three consecutive years, 2002-2005, released figures on pharmaceutical marketing in his state. These reports document the monies spent on fees, travel expenses, and payments to doctors, hospitals and universities in Vermont from the companies.
Disclosures of these figures have come from the companies and do not include free samples, compensation for clinical trials, payments under $25, some educational scholarships and grants for continuing medical education.

- **July 1st 2002 to June 30th 2003:**
  44 companies spent $2.47 million with the largest spenders being GlaxoSmithKline, Bristol-Myers Squibb, Merck, Forest Pharmaceuticals and AstraZeneca. These five accounted for 72% of the total expenditure.

- **July 1st 2003 to June 30th 2004:**
  48 companies spent $3.11 million with the largest spenders being Merck, Amgen, GlaxoSmithKline, Forest Pharmaceuticals and Eli Lilly. These five accounted for 72% of the total expenditure. The largest recipients were physicians and other prescribers receiving 54% of the total.

- **July 1st 2004 to June 30th 2005:**
  68 companies spent $2.17 million with the largest spenders being Forest Pharmaceuticals, Eli Lilly, GlaxoSmithKline, Sanofi Aventis and Merck. These five accounted for 50% of the total expenditure. Physicians and other prescribers received 81% of expenditure, with hospitals, clinics and universities receiving 12% of the total.

Vermont has a population of 623,050. The population of the USA is 296,410,404. Thus this enormous marketing expense has been directed at only 0.2% of the US population.

Recently, the state of Maine approved new laws requiring manufacturers to file annual reports with their Department of Human Services, beginning on 1 January 2004. The State of Oregon passed legislation requiring the disclosure of economic benefits provided by the pharmaceutical companies in 2005 with disclosures to be made annually by the 15th February.

If all countries followed this procedure the amount of marketing money spent by the companies would be more easily accessible, rather than being hidden under varying headings of expenditure.
Marketing Through ‘Scientific Experts’

A slightly more sinister (I believe) form of advertising has been used very successfully: through supposedly independent ‘scientific’ expert groups or think tanks.

One such scientific group is the American Council on Science and Health (ACSH), whose website is http://www.acsh.org/. The ASCH describes itself as “a consumer education consortium concerned with issues related to food, nutrition, chemicals, pharmaceuticals, lifestyle, the environment and health.” Founded in 1978 by a group of scientists concerned with public policies being based on poor science, it was originally proposed as a means for bringing common sense views to the public.

ASCH began with a commission from Pfizer to write a paper on the ‘Delaney Clause’. This is the part of the Food Additive Amendment of 1958 that restricts the addition of cancer-inducing chemicals into the food supply.

Initially they accepted no industry funding but in 1980 Dr Fredrick Stare, one of the founders, contacted Philip Morris (tobacco company) requesting financial support. Since that time ASCH has produced papers and given interviews downplaying risks from chemical pollutants, dioxin, DDT and asbestos, to name just a few.

The ASCH has become an influential journalistic source of commentary on public health. Although they no longer publish lists of funding companies, past lists include: The Bristol-Myers Fund, Inc., Ciba-Geigy Corp., Dow Corning Corp., E.I. Du Pont de Nemours & Co., Johnson & Johnson, and Merck Co. Foundation.

The pharmaceutical companies, naturally enough, have been extremely reluctant to provide details of the monies spent on public relations (PR) in any form, whether on advertising or promotion of drugs, gifts to physicians or direct-to-patient advertising.

A move to legally force this disclosure in West Virginia was unanimously agreed upon by the state Pharmaceutical Cost Management Council in November 2005. However, the move was challenged by the lobby group PhRMA on the grounds that
all company financial information is confidential and not subject to the Freedom of Information Act.\textsuperscript{106}

Recent legislation in the states of Minnesota, Vermont, California, Maine and West Virginia mandates disclosure laws between the pharmaceutical industry and health professionals. In Vermont and Minnesota, payment disclosures are publicly available. A Mount Sinai School of Medicine study found in Vermont, that 61\% of payments were not released to the public as the pharmaceutical companies had designated them as trade secrets and 75\% of the disclosed payments did not identify the recipient. In Minnesota, only 25\% of companies reported data.\textsuperscript{107, 108}

\section*{Litigation}

The commercial morality and ethics of pharmaceutical manufacturers has been increasingly challenged by legal actions over the last few decades. It seems an overly simplistic and naïve viewpoint that corporate ethics and social responsibility would be achieved and maintained through market forces rather than by regulation.

Corporations can be dissolved under charter revocation laws. As stated by New York Attorney General Eliot Spitzer during a 1999 election campaign, when commenting on these laws, if:

\begin{quote}
... a corporation is convicted of repeated felonies that harm or endanger the lives of human beings or destroy our environment, the corporation should be put to death, its corporate existence ended, and its assets taken and sold at public auction.\textsuperscript{109}
\end{quote}

What follows is an account of some of the litigation involving pharmaceutical companies over the last several years. Whether this is a relatively new phenomenon or whether these companies have dealt in such a cavalier attitude with courts and settlements through the life-time of their corporations is unclear.

When the monies paid out in fines and settlements are very large and yet do not appear to cause any financial distress to the companies—or induce better corporate morality—it is difficult to imagine what would cause a change in their activities.
Fraudulent Drug Pricing and Marketing Conduct: Boston

In 2001, following an investigation by the USA Attorney’s Office in Boston, TAP—a joint venture between Abbott Laboratories and Takeda Chemical Industries of Japan—agreed to pay US $875 million relating to fraudulent drug pricing and marketing conduct.

The charges related to TAP’s sales and marketing of the prostate cancer drug Lupron during the 1990s, when Lupron was competing for the market place with Zolodex, another prostate cancer drug. Lupron was severely discounted or given as free samples to doctors, with the intent that doctors should fraudulently bill Medicare for the drugs.110

Following the settlement of the government action against TAP, separate actions have been launched by Empire Health-choice Inc., Blue Cross and Blue Shield of Massachusetts to recover overpayments made through the Medicare and Medicaid HMO programmes111.

In 2001, the Citizens for Consumer Justice (a coalition of consumer groups) filed a lawsuit in the Federal District Court in Boston against Abbott Laboratories Inc, alleging overcharging of drugs estimated at more than US $800 million in 2000 alone.

The allegations include discounts being given to physicians, ranging from 13% to 34% lower than the AWP costing and, in some cases, reaching between 65% to 85% for particular drugs. These discounts were given to doctors to encourage the use of Abbott’s drugs rather than those of their competitors.112 Doctors could buy Abbott’s drugs at reduced cost, sell them to their patients for the Medicare or Medicaid listed price and pocket the difference.

Overcharging US Medicaid Through Relabelling: USA

In 2003, Bayer agreed to pay US $257 million to the US government for supplying the drug Cipro to Kaiser Permanente (a health care organisation) at a lower price than Bayer was selling to Medicaid. This violates a federal law requiring the
pharmaceutical industry to supply Medicaid with drugs at the lowest price charged to any customer.

Bayer hid the cost of the drug sales to Kaiser by relabelling the drugs and giving a false drug identification number. Bayer also pleaded guilty to a criminal charge associated with the case.

**GlaxoSmithKline**, in a similar case involving relabelling of medicines for Kaiser, agreed to pay $87.6 million, settling civil charges of overcharging the Medicaid programme for their drugs Paxil and Flonase.\(^\text{113}\)

**Rigging of Vitamin Prices: USA, Europe and Australia**

**Hoffman La Roche** was found guilty of rigging vitamin product prices during the 1990s and in 2005 was ordered to pay fines of US $500 million in the USA and €462 million in the European Union.\(^\text{114}\)

Roche Holdings colluded with **BASF AG** (Germany) and **Rhone-Poulence** (France), over at least a nine-year period, to set prices of vitamins and ‘premixes’ used to enrich cereals and processed food.

Rhone-Poulenc cooperated with authorities and therefore was not held criminally liable for its participation in the cartel, however, the former director of worldwide marketing for Roche (Kuno Sommer) was ordered to serve four months in a USA prison and fined US $100,000 for fraud. BASF was fined US $225 million for its role in the price fixing.\(^\text{115}\)

In Australia, a 2006 court action resulted in **Roche BASF** and **Aventis** agreeing to pay more than $30 million in compensation relating to the above mentioned 1990s vitamin price-fixing cartel.\(^\text{116}\)

**Blocking Access to Generic Drugs: Europe**

The European Union antitrust regulators, again in 2005, fined **Astra Zeneca PLC** US $73 million for keeping the price of their ulcer drug ‘Losec’ artificially elevated by blocking market access to generic versions between 1993 and 2000. According to
the EU officials, Astra Zeneca’s actions “constitute serious abuses of its dominant market position” and that they gave “misleading information” therefore gaining extended patent protection.¹¹⁷

**Stockpiling Inventory to Overstate Revenue: USA**

Again in 2005, **Bristol-Myers Squibb** reached an agreement with the USA attorney in Newark whereby Bristol-Myers paid to their own investors an amount of US $300 million and, in a separate settlement to four investors who sued outside the class action, a further payout of $89 million.

The company had been accused of ‘channel stuffing’. Channel stuffing is where wholesalers are paid to stockpile inventories, making it appear as if sales were higher than the reality. This overstated their revenue by about $2.5 billion from 1999 to 2002. Bristol-Myers negotiated a ‘deferred prosecution’ where charges would be dropped if the company complied with the prosecutor’s demands.¹¹⁸

**Off-Label Marketing and Conspiracy: USA**

More recently, in August 2006, the **Schering-Plough Corporation** was ordered to pay US $435 million for the off-label marketing of Temodar, a drug approved for the treatment of anaplastic astrocytoma (a brain tumour). Schering-Plough had promoted the drug for the treatment of other brain tumours and for cancers that had spread to the brain as secondaries from other tumours.

Schering-Plough pleaded guilty to conspiracy in this case and agreed to pay a further $255 million in resolution of civil aspects of the investigation. With court approval yet to ratify this agreement, a subsidiary, Schering Sales Corporation, has also agreed to pay a criminal fine of $180 million following a plea of guilty to one count of conspiracy in making false statements to the government.

This is not the first court settlement for Schering. Two years earlier a settlement of $346 million was paid on charges of a kickback to a health insurer, protecting the market of their allergy drug Claritin.¹¹⁹
Multiple Ill-Effects of Drugs: USA

In 2005, Eli Lilly settled against 10,500 lawsuits relating to its anti-psychotic drug Zprexa and its causing of diabetes or high blood glucose. Seroquel (AstraZeneca’s anti-psychotic drug) also faced similar claims in court. The income from Seroquel in the USA for 2005 was $2.8 billion.\textsuperscript{120}

Conspiracy to Inflate Drug Prices: Class Action, USA

Legal actions against pharmaceutical companies are not only taken by the government enforcement agencies, but increasingly are being filed by health plans and consumer coalitions.

The most recent and largest legal action to date has been taken against multiple (16) pharmaceutical manufacturers in the United States District court in Massachusetts. This is a Class Action with five subclasses as plaintiffs. It was initiated by multiple HMOs and Health Funds.\textsuperscript{121}

Part of the allegation in this case is that:

For the last decade, the Defendant Drug Manufacturers have conspired with others in the pharmaceutical distribution chain, including but not limited to physicians and hospitals … to collect inflated prescription drug payments from Plaintiffs and the Class. More specifically, the Defendant Drug Manufacturers report to trade publications a drug price – the Average wholesale Price (or “AWP”) – that for many drugs is deliberately set far above the prices that these drugs are available in the marketplace. The AWPs for these drugs are deliberately false and fictitious and created solely to cause Plaintiffs and the Class members to overpay for drugs.\textsuperscript{122}

Charges of breach of the US RICO law (US Racketeer Influenced and Corrupt Organizations Act) have also been brought against the defending companies.

The District Court filed notice of action against the following companies: AstraZeneca, the Bristol-Myers Squibb group, GlaxoSmithKline, the Johnson & Johnson Group, and the Schering-Plough Group.
One of the defendants, **GlaxoSmithKline**, agreed (with no admission of liability) to a settlement payout of US $70 million in August 2006. A Bristol Myers Squibb, Johnson & Johnson, AstraZeneca and Schering-Plough, however, were set to go to trial to answer the above charges.

**Misleading the Patent and Trademark Office: USA**

*GlaxoSmithKline* settled in the USA District Court on 13 October 2005, over charges of misleading the Patent and Trademark Office to obtain a patent for Relafen, an anti-inflammatory medication. The amount of settlement in this case was US $75 million.

**‘Transfer Pricing’ to Offshore Low-Tax Countries: USA**

To continue the GlaxoSmithKline saga, the latest payout for this company is a $3.4 billion settlement to the US Internal Revenue Service over ‘transfer pricing’, whereby companies claim most of their earnings in countries where taxes are low. A company spokesperson, Patty Seiff, stated “Our estimates would have shown that the potential exposure here—total exposure—could have been $14 billion to $15 billion.”

**Inadequate Testing of HRT Drugs: Class Action, USA**

Monday 11 September 2006 saw the opening day of a USA federal trial in a class action brought by between 5,000 and 8,300 women against *Wyeth*, for failing to adequately test for and warn of potential risks (including breast cancer) with the use of their hormone replacement drugs Prempro and Premarin. The annual sales for 2005 of the two drugs were $909 million in the USA alone.

**Pharmaceutical Industry has Highest Lawsuit Count in USA**

The highest numbers of product liability lawsuits in 2005 were taken against the pharmaceutical industry, with 17,027 cases. The USA is seen by many other countries as being especially litigious. However, when compared to cases against the chemical industry (2,875), the manufacturing industry (3,236), financial services (2636) and the insurance industry (1,926) more harm appears to be done by big Pharma than most others.
The term ‘regulatory capture’ was introduced by George Stigler, an economist in the 1960s, to describe corporations’ control and domination of regulatory agencies through lobbying and selective information transfer.

How much stronger must such ‘regulatory capture’ be when corporations are funding the agencies?

According to Bakan in 2004:

Many corporations regularly breach regulatory laws, confident that they won’t be caught or that, if they are, the financial benefits derived from the breach will exceed the costs of the fines assessed against them; regulatory agencies tend to be understaffed, unaccountable, and peopled by bureaucrats – many of whom are drawn from the industries being regulated – who see themselves as partners with industry, rather than its overseers. 128

**Conclusions**

In this chapter I have examined the growth in wealth and power of the pharmaceutical companies. In spite of the decrease in new drug development over recent years and the ongoing expiry of patents for existing drugs, Big Pharma has thrived and continued to grow.

Close relationships with governments have allowed Pharma to operate with few constraints. The courting of the medical profession has proven to be a formidable marketing tool. Direct-to-consumer advertising has ensured public help in driving pharmaceutical sales.

Overshadowing all this is the high level of litigation involving the pharmaceutical industry, with most of the major companies being under scrutiny for fraud, price rigging, conspiracy, inadequate testing, and so on. It seems that the needs of the patient for safe, affordable treatments are being sacrificed for the needs of the stock holder.

In Chapter 7, Academic Freedom—Academic Funding, the relationships between universities, governments and industry are examined, to determine if
scientific/medical research has retained its independence in both public and private sectors.

22 Ibid.
36 Ibid.: p311.


Ibid.


92 Ibid.


(2002). Scrutiny of Pharmaceutical Industry Continues As Private Lawsuits Follow Record-Setting TAP Settlement. Law Watch. 02.

Ibid.


127 Ibid.
Chapter 7

Academic Freedom—Academic Funding

The purpose of universities is to develop society’s human resources, and to generate, transmit, and disseminate knowledge. Historically universities have had considerable autonomy from regulation because they are supposed to foster academic freedom and protect it from outside interference.

Marsha Woodbury

In this chapter, I explore the university and government scientific institutes as the training grounds for future medical practitioners of oncology and as centres of research into cancer cause and treatments. In particular, I discuss the following:

- Funding for these institutions has changed greatly over the last century. What effect has this had on academic output?
- Have funding changes caused any conflict of interest in the institutions, and how has this affected the quality and type of science in academia?
- What effect has the growing power of the pharmaceutical industry had on the universities and institutes?
- To what extent is the patient—the end user of cancer treatments—benefiting or being disadvantaged by these changes?

The concept of academic freedom—the ability to ethically investigate fields of knowledge without repercussion—has been part of the foundation of universities for hundreds of years. Universities were established to foster this freedom and protect it from outside interference, to explore the world around us without undue influence or manipulation from external bodies.

History of the University

The classical model of the university was a feudal institution, beginning in the 13th century and changing little until the 19th century. Access to university was mostly
confined to the wealthy and was strongly allied to the church. The appearance of the research university² was accompanied by the state actively promoting research at universities as a supporting mechanism for the national economic interests of the country.

Over the last 2000 years, three models of intellectual process have prevailed in the Western world:

- First came the monopoly of the Catholic Church over knowledge production and its distribution. Under the feudal system of the Catholic Church, all belonged to the church. Patronage was defined by Burke as “the tribute opulence owes to genius” and by Rousseau as “the consideration riches owe to talent”.

- The Renaissance and Enlightenment followed, when knowledge was produced under royal and aristocratic patronage. Thinkers of the Enlightenment often had many patrons and did not feel obliged to produce to demand for any single patron.

- Now knowledge comes from the professional staff of universities, government institutes and capitalist corporations. Businesses have generally not been expected to fund research that would be critical of their activities or products, thus bringing a change to the freedom of thought and expression.⁴

**Autonomy of Universities Under Threat**

Infringements of the ‘right of autonomy’ of the university have occurred in the past. For example, in World War II, the governments in totalitarian societies such Germany, Italy and the Soviet Union,⁵ sought to impose their state/party lines onto the activities of the universities, in both research and teaching.

In the face of these infringements, checks and counterbalances have been built into university charters to protect the autonomy of the university from government interference and restriction.

But what of the choice of universities to sell their autonomy to industry? Academic science was once considered an altruistic search for the truth, for the greater good of
humanity. Today, much of this ‘free thinking’ science is being displaced by ‘controlled’ industry science.

**Following the Corporate Model**

Peters and Roberts note the move from the traditional university to one closer to a corporation, with its corporate language, mission statements, performance indicators and focus on strategic planning:

Contemporary universities function as performance-oriented, heavily bureaucratic, entrepreneurial organisations committed to a narrow conception of excellence generated by the imperative of international competitiveness.⁶

Universities of the Western world have traditionally gathered funding from student fees, government grants and donations and endowments. Now these institutions draw larger and larger amounts of funding from industry through collaborations, contracts, and partnerships with the private sector.

Can autonomy be maintained by institutions that accept large amounts of money to carry out research for the commercial gain of the donor corporations?

**Bias in Research Reports**

Studies have repeatedly shown that research funded by ‘companies’ shows a much higher positive outcome for the products of those companies than studies carried out by independent scientists or institutes.⁷ ⁸

Trials with positive results for the funding company are reported quickly by the researcher. However, if the trial has a negative outcome—for example, if the test product was found to be either harmful or non-beneficial when compared to a placebo, or was shown to be inferior to another product (e.g. a drug)—it can take twice as long for the results to be published as for a positive result.⁹

Of even more grave concern is when negative results are not released.¹⁰ ¹¹ A report on clinical trials for cancer therapeutics found that approximately one-quarter of trials did not reach the public domain for many years after completion or not at all.
Dr. Richard Sullivan, head of clinical programmes for Cancer Research UK, a charitable organisation, commented at the group’s Festival of Science that:

If only positive results are published this can distort medical literature and leave doctors thinking a treatment is more effective than it actually is.

Although there may well be benefits from industry funding of clinical researchers, the deleterious effect could far outweigh the benefits. The risks are:

- Universities could become totally dependent on commercial funding if governments worldwide continue to decrease their contributions to university coffers.
- The full and truthful reporting and publishing of results could be undermined.
- The agenda of research studies could become driven only by profit and share prices.

**Governments, Grants, Endowments and Industry**

Universities have traditionally taken money from the community in some form or another. Fellowships and grants have been part of university income for the last hundred years, contributing to the running of the university and to student support.

**Fellowships in Science**

Following World War 1, in 1925, ‘fellowships’ in science were established with the creation of institutions such as the Guggenheim Foundation. These fellowships were given to graduate students wishing to gain research experience in their chosen fields and who met the criteria.

One of the first graduates to receive these monies was Linus C. Pauling, who had just graduated from the California Institute of Technology (Carter quoting Donas in *The Circuit Rider*). Pauling has delivered an exceptional return in science for this modest outlay of fellowship money.

These somewhat small amounts of money continued to flow into universities, but only covered costs incurred by individual students. They did not provide the increasingly large amounts needed to fund institutions that were growing to monolithic sizes; some campuses with their own police departments (in the USA),
and most with multiple research centres, restaurants and car parks. Grants, however, were often large enough to assist at least in maintaining the existence of the universities.

Prior to World War II, the total available funding for scientific research in universities in the USA came mostly from these endowments and grants, as well as from the fees charged to students.

**Growth of Government Funding**

The use of science (both good and bad) in World War II—the development of nuclear energy, chemical warfare and leaps in physics research—and the growing reliance of governments on the universities in wartime research projects changed the nature of funding. Following the war, government became the major benefactor of universities. In 1940, the total USA Government support to universities was worth US $31 million. Within 40 years, this support had grown to exceed US $3 billion. ¹³

**The Advent of Corporate Sponsorship**

During the late 1970s, money from corporations to fund research universities began a steady increase in the USA, rising from US $264 million in 1980 to over US $2.3 billion by 2000. The USA Government funded approximately US $17.5 billion for university research in 2000, with corporate sponsors contributing an estimated 12% of research funding. ¹⁴

Research grants come from diverse sources. From the initial funding of the Association of American Medical Colleges in 1876 to the mid 1970s, according to Culbert (quoting Griffin in *Medical Armageddon*¹⁵), foundations such as the Ford Foundation, the Kellogg Foundation, Macy Foundation and the Commonwealth Fund had invested over a billion dollars in USA medical schools. By the 1970s, these ‘research grants’ covered 16% of the costs of many USA medical schools. This funding also directly contributed to the income of the research faculty.

**Corporate Funding in Australia**

Most universities today accept funding from private sources, some for paid research work and some as donations or endowments. Australia certainly has progressed
along the path, first established by the USA, whereby virtually all research institutes, universities and medical schools now compete with one another for funding from the private sector.

The ABC television investigative programme *Four Corners* aired *The Degree Factories* (on 27 June 2005), exploring the monetary crises in Australian Universities, with a discussion of the causes of and solutions to these problems by academics and students.

Professor Ian Chubb, Vice Chancellor of the Australian National University (ANU), described the decrease in government funding as causing Australian universities to become very heavily privatised. He stated that the Australian Government had decreased funding by billions of dollars in recent years.

Professor Peter Doherty (a Nobel prize winner, and a member of the Department of Microbiology, Melbourne University) was also interviewed on the *Four Corners* programme. He stated that Australian universities had not yet caught up to universities in the USA in acquiring funding from private organisations, but that as we become more entrepreneurially-oriented we will inevitably head further along this path.

A slightly different view—of both necessity and outcome of this path—was expressed in an interview for the programme by Professor Allan Luke, Foundation Dean of the Centre for Research in Pedagogy and Practice at the National Institute of Education, Nanyang Technological University, Singapore. Professor Luke stated:

In this whole process of corporatisation and marketisation, we’ve got to make sure that we actually protect the very core functions of the university, which are research and teaching. We can’t get entrepreneurial just to be entrepreneurial for some sake … Universities will lose their soul. They’ll lose some of their very powerful historical functions as social critics, as forms of alternative knowledge, as sources of aesthetic and intellectual activity and wealth—the kind of thing that, as corporations come and go, they’ll never be able to recover.
It is not premature to reflect whether our universities are already prioritising financial concerns over educational issues. *The Chronicle of Higher Education* stated that university presidents are more preoccupied with financial issues than with education. How does this impact on the quality of education being offered?

A survey of 764 presidents of universities in the USA showed that more than half of them spent a significant amount of each day on fund-raising. The next most frequently-mentioned daily activity was dealing with their budget and financial matters. Only 29% of those surveyed attended to student matters on a daily basis.¹⁷

To what extent have our universities been transformed into financial institutions that are selling education?

**Industry Funding of CSIRO**

By 1996, the Commonwealth Scientific and Industrial Research Organisation (CSIRO) was gaining roughly one-third of its total external income from direct industry funding. This figure has been slowly increasing over the past 10 years. It is highly unlikely, however, that the general public is aware that this has resulted in Australia’s premier research institute being in business to an increasing extent for itself, rather than being a taxpayer-funded scientific research centre that searches for solutions and scientific advancement for the benefit of all Australians.

The annual Reports for CSIRO give the following figures.¹⁸

<table>
<thead>
<tr>
<th>Year</th>
<th>% Income</th>
<th>External Sources (in $ million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993-1994</td>
<td>29.6</td>
<td>206.7</td>
</tr>
<tr>
<td>1995-1996</td>
<td>32.6</td>
<td>201.8</td>
</tr>
<tr>
<td>1996-1997</td>
<td>33.2</td>
<td>221.4</td>
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<tr>
<td>1999-2000</td>
<td>33.3</td>
<td>240.8</td>
</tr>
<tr>
<td>2000-2001</td>
<td>32.3</td>
<td>242.3</td>
</tr>
<tr>
<td>2001-2002</td>
<td>34.7</td>
<td>267.0</td>
</tr>
</tbody>
</table>
CSIRO is also in the business of establishing ‘start-up’ companies, formed on the basis of research completed in CSIRO laboratories and then sold to private enterprise companies. Australian universities and medical research institutes also establish ‘start-up’ companies to provide revenue. Following is data from the Australian Government’s Department of Education, Science and Training for the years 2001 and 2002 (taken from http://www.dest.gov.au/sectors/research_sector/policies_issues_reviews/key_issues/commercialisation/nsrc.htm#table2).

Table 7-2: Commercialisation in Universities, Medical Research Institutes and CSIRO in 2001

<table>
<thead>
<tr>
<th></th>
<th>Universities n = 35</th>
<th>Medical Research Institutes n = 33</th>
<th>CSIRO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start-up companies formed</td>
<td>46</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>% of companies in which equity was held at the end of the year.</td>
<td>71%</td>
<td>89%</td>
<td>86%</td>
</tr>
<tr>
<td>Value of equity holdings ($m)</td>
<td>91.16</td>
<td>6.25</td>
<td>29.83</td>
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</table>

Table 7-3: Commercialisation in Universities, Medical Research Institutes and CSIRO in 2002

<table>
<thead>
<tr>
<th></th>
<th>Universities n = 38</th>
<th>Medical Research Institutes n = 35</th>
<th>CSIRO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start-up companies formed</td>
<td>45</td>
<td>13</td>
<td>3</td>
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<tr>
<td>% of companies in which equity was held at the end of the year.</td>
<td>82%</td>
<td>92%</td>
<td>33%</td>
</tr>
<tr>
<td>Value of equity holdings ($m)</td>
<td>85.95</td>
<td>10.69</td>
<td>18.99</td>
</tr>
</tbody>
</table>

This has the ring of a commercial business venture, rather than taxpayer-funded institutions. In 2002 to 2003, the private sector invested $108.8 million in CSIRO research. This was 40% of all external revenue, with $67.1 million (or 64%) being spent by large companies.

On the CSIRO website, “Our Strategy” states “We are on a journey from being an Australian research institution to a research enterprise with global reach.”19
Today’s emphasis in the CSIRO, and in our other academic institutions, is on ways to increase commercialisation (see http://www.csiro.au/org/ps1gx.html).

Does the taxpayer lose anything by this? If research projects now need commercial validation and to be able to show future profits, who will carry out the non-profitable research. For example:

- Who will research non-patentable cancer treatments?
- Who will follow up on so-called spontaneous remissions?
- Who will work on the investigation of non-drug treatments for cancer?

**Industry Funding of Teaching Hospitals**

The financial position of institutions associated with our major teaching hospitals is similar. The Garvan Institute of Medical Research is the research institute attached to St Vincent’s Hospital. Based in Sydney, their financial reports show that for the years 2000 to 2004:

- 5–13% of their income came from commercial collaboration,
- 15–18% came from the NSW Government,
- 21–25% came from ‘other’ grants, and
- 27–37% of their income was from NHMRC grants.

The category ‘other grants’ was not explained in the financial report.

Melbourne is the home of the Walter and Eliza Hall Institute, another prestigious centre of medical research. Whereas the annual report for 1997/98 shows government support of the institute at 51%, by 2001 the Government funding had dropped to 31%. To survive, the institute must make up this missing 20% support from external sources (primarily the industry sector of the community).²⁰

The report for 2003-2004 showed strong increases in the numbers of IP (intellectual property) transactions. This was attributed to the “growing identification of potential commercial opportunities by our scientists.”²¹
Should our science degrees now also include subjects from business and marketing? What might be the end result of this commercialisation of our scientists in the health arena?

**Money and Ethics—Conflict of Interest**

An anonymous editorial in *The Lancet* of March 2000, entitled *Medicine’s Rude Awakening to the Commercial World,* raised the issue of changes in attitudes in biomedical science:

Today’s universities are increasingly encouraging their scientists and doctors to be entrepreneurs and to commercialise their intellectual property. However, the collaboration between industry and academia or the combining of private and public interest can easily end in tears.

Could an example be the restriction of research into only those areas of science that will produce profits? This trend towards our universities and research institutes becoming commercial places of science appears to be occurring in most countries.

**Private Funding at the Karolinska Institute in Sweden**

In Sweden, even though the universities are state-owned, one-third of professorships at the Karolinska Institute, the country’s leading university, are financed by private companies.

The Swedish newspaper *Torsdag* reported that Astra-Zeneca funds the salary of a professor of neurology and, in return, has exclusive rights to his research. This would give Astra-Zeneca the right to refuse publication to any research not complimentary to their products or, if they so choose, to delay publication of results. Of more concern, however, is that Astra-Zeneca has been given these rights, even though some of this research is partially funded by the Swedish National Medical Research Council.

**Private Funding at the University of California Berkeley**

In 1994, the University of California Berkeley (UCB) found that the state government would meet only 34% of their budget because of funding cuts. Their newly appointed Dean, Dr Gordon Rausser, approached 16 companies with a
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Proposal: The university would choose one company with which to form a research partnership.

The partnership went ahead with Novartis, bringing UCB an income of US $25 million over the next 5 years. Two-thirds of this funding was allocated for so-called unrestricted research, with the rest going to infrastructure, costs and so on. The agreement was as follows:

- UCB had rights to any patent coming from any research done by a UCB scientist and the right to a joint patent if the discovery was made by a scientist employed by Novartis.
- Novartis gained the ‘first right to negotiate a licence’ from any discovery gained by their paid research.
- Novartis researchers would sit on the internal university research committees.
- Once confidentiality agreements had been signed by researchers, no publications would be possible without agreement from Novartis.

By December 1998, most faculty members (30 out of 32) in the Department of Plant Microbial Biology at UCB had signed an agreement to participate in the Novartis/UCB collaboration.

**Concerns from Senate Hearing Into UCB/Novartis Collaboration**

By 2000, the Californian Senate was holding hearings on whether such an agreement between industry and academia would engender conflicts of interest. The hearing, led by Senator Tom Hayden, asked Dean Rausser if the University would support a faculty member who had signed confidentiality agreements with Novartis, but who wished to speak out on results as a matter of conscience.

The response was that the University had no duty or obligation to defend a scientist who broke their contracts with the company. ³⁴

The hearing raised concerns as to the compromised role of universities in being able to deliver independent research. Although the hearing did not change the agreement

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between UCB and Novartis, it underlined the dangers that flow from universities and industry becoming bedfellows.

**The Biotechnology Boom and Tax Benefits**

The growth of biotechnology has been a major driving force for the expansion of entrepreneurial university science. In 1980, the Stevenson-Wyndler Technology Innovation Act was introduced to encourage technological innovation. This Act was followed the next year by the Economic Recovery Tax Act, which gave tax breaks to companies that contributed research equipment to universities. It also promised tax benefits for the development of collaborations between universities and business.

Even by 1984, biotechnology research in universities was estimated to be worth US $120 million per year, approximately 42% of all monies being put into US universities by big business.\(^{25}\)

**Congressional Hearings: Concern About Autonomy**

At the time of these developments, politicians in the USA were aware of the potential dangers inherent in this type of partnership. Between 1981 and 1990, several congressional hearings were held to discuss the issues.

At one of the earliest hearings (in 1982), Congressman Al Gore, co-chair of the proceedings, stated:

> We return with a continuing concern that our universities, the source and foundation of these technologies, may be permanently altered by the increasing number of commercial agreements they are developing.

By 1990, a study by the US Congress House Committee on Government Operations, Subcommittee on Human Resources and Intergovernmental Relations—*Are Scientific Misconduct and Conflicts of Interest Hazardous to Our Health?*—was examining cases reflecting the problems of industry–university collaborations. The chair of these hearings, Ted Weiss, urged the Department of Health and Human Services to restrict financial ties for researchers who conduct evaluations of products and treatments in which they held vested interests.\(^{26}\)
So, more than 20 years ago, the US government acknowledged the dangers inherent in universities giving up their autonomy. At this time, although the US government committees called for stops and checks to be applied to such practices, the response was minimal.

There has certainly been more and more public recognition of these issues, but the problems and scandals continue to multiply.

**Case Study: Michigan State University**

In 1950, Michigan State University (MSU) signed an agreement with Research Corporation, stating that royalties gained from any discoveries patented by MSU would be shared between the two: 15% of royalties would go to the inventors, with 85% split between the two partners.

Research Corporation was a charitable non-profit organisation, established in 1912 with the stated mission of promoting “the advancement and extension of technical and scientific investigation, research, experimentation, and education.” The revenue brought in to Research Corporation by such deals was subsequently given out in grants.

In the early 1970s, Barnett Rosenberg and co-workers at MSU discovered Cisplatin, which was approved in 1978 for the treatment of genitourinary tumours. In 1989, a related compound of Cisplatin—called Carboplatin—was approved by the FDA for ovarian cancer treatment. Between 1978 and 1999, these two drugs had provided MSU with over US $160 million in royalties.

In 1985, Research Corporation established a daughter company, Research Corporation Technology (RCT), to manage dealings related to ‘technology transfer’. 27

This offshoot of Research Corporation, rather than using its income for providing research, used it to invest in the creation of new companies, in the commercialising and licensing of new discoveries. RCT became an independent, non-profit company,
paying tax but with no shareholders. RCT now maintains royalty-sharing agreements with over 100 universities in the USA.

RCT and MSU both did very well from this arrangement until 1995, when MSU sued RCT and moved to terminate the contract. According to MSU, RCT were not using the profits made from royalties to invest in new scientific projects, but were giving large wage increases to high-ranking administrators within RCT.

If this legal action had been successful, the termination clause in the original contract meant that MSU would have received the full 70% of royalties from the two drugs mentioned above.

A settlement was achieved between the two parties prior to court, with RCT still managing patent and licensing details, but with changes to the allocation of royalties. MSU received an increase in the royalties on Carboplatin (by 1999, worth more than six times the royalties of Cisplatin). RCT also agreed to pay MSU $4.5 million over the next two years.

This was a somewhat toxic end to a blend of academia and the corporate world.

‘True’ Science?

An early naïve hope was that the monies allocated to universities in these ‘sweetheart deals’ would contribute greatly towards the costs of running the universities, and would enable research to be carried out that would otherwise be financially non-viable.

It was also hoped that such alliances would not result in any unethical compromises for the universities. However, documented examples do not indicate such clean partnerships, examples are provided below. Money buys compliance and may affect such fundamental principles of academia as objectivity.

Conflict of Interest at Harvard University

The prestigious Harvard University also has been besmirched with the taint of compliance for cost.
Public Citizen, in March 2001, released a 130-page report entitled Safeguards at Risk: John Graham and Corporate America’s Back Door to the Bush White House. This report was released at the time that John Graham was nominated by Bush to head the Office of Information and Regulatory Affairs, a part of the Office of Management and Budget.

Public Citizen was, however, concerned with the record of Graham’s role as founding director of Harvard’s Center for Risk Analysis (HCRA). The report showed the following:

- John Graham, on behalf of the HCRA, had solicited financial contributions from a cigarette company while the centre agreed to downplay the risks of passive smoking.
- HCRA had produced a report opposing a ban on the use of mobile phones while driving. This report was funded by AT&T Wireless Communications.
- The newsletter published by the HCRA also downplayed the risk to children exposed to pesticides and bio-active synthetic chemicals such as bisphenol-A and phthalates. The newsletter did not, however, advise readers of the funding received by the centre by the chemical companies producing these chemicals.
- In 2001, the HCRA received funding from over 100 corporations and trade associations, including DOW, Monsanto and Du Pont, and trade groups such as the American Chemistry Council.\(^\text{30}\)

Whether companies can give monies to a university and expect no consideration in return from the university is questionable. Most shareholders would understandably consider that giving donations without any expectation of a return would be naive.

According to Marcia Angell,\(^\text{31}\) the Harvard Medical School once had the following strict guidelines for its researchers: They were prohibited from owning more than $20 000 worth of stock in companies whose products they were studying. However, this guideline has subsequently been softened, according to the executive Dean for academic programmes, to curtail the loss of key faculty members to other schools.
Academic Staff as Shareholders

The Harvard story is not an isolated instance of ‘closeness’ between universities and private corporations.

Stanford University School of Medicine has no fixed limits of stock ownership for their academics. It is only when faculty members own more than US $100,000 in stock, or own 0.5% of a company, that they must notify the university.

Massachusetts Institute of Technology’s ruling on this question is that notification is only necessary when the academic’s equity in a company may be large enough to influence prices of the company’s stock.32

Boston University apparently had no qualms about questions of conflict of interest when, in 1994, it established a spin-off pharmaceutical company called Seragen. David Blumenthal reported in Growing Pains for New Academic/Industry Relationships that:33

The university itself, individual members of its board of trustees, the president of the university, and members of its faculty own substantial equity in this company, which is also funding research at the university.

Positive results of research from the university would provide direct benefit to these members of faculty. Surely this should raise questions of any research carried out for the benefit of Seragen.

Further Conflicts of Interest

Krimsy, in Science in the Private Interest34, lists the results of a 2000 national survey on conflict of interest, showing 127 medical schools and 170 research institutions receiving monies from the National Institutes of Health (NIH) and the National Science Foundation (NSF).

In November 2000, the New England Journal of Medicine35 published a national survey in relation to conflict of interest. The survey achieved an 85% response rate, giving a sample size of 250 medical schools and institutes. These institutions received over US $5 million in grants from the NIH and the NSF.
Fourteen respondents had no policy on conflict of interest. Of those respondents with such policies, 92% had instituted them after 28 June 1994, the date the federal draft guidelines on conflict of interest was released.

A further report, released by the General Accounting Office in November 2001, found that at that time most universities left the decisions on conflict of interest up to the faculty in question and that monitoring of compliance was non-existent. The attitude and general response from the centres was “that the management of conflicts and the penalties for nondisclosure were totally discretionary.”

Dirty Money

Funding from the Tobacco Industry

A 2004 study, published in the Canadian Journal of Public Policy, stated that 11 of Canada’s 16 medical schools had accepted funding from the tobacco industry in the late 1990s. This figure may have been higher if the other five faculties of medicine in Canada had agreed to disclose whether they also had received research grants or donations from the tobacco corporations.

The study was conducted by the Ontario Tobacco Research Unit. The authors, not surprisingly, warned that the acceptance of this money:

...may present major conflicts of interest that undermine public health and have implications for the scientific integrity of the medical research enterprise.

Head of the research group, Dr Pamela Kaufman (PhD), stressed that the findings may underestimate the links between tobacco companies and academia, because the issues of specific faculty members accepting money for acting as expert witnesses or reviewers for the industry was not included in the study.

Studies Show Industry-Positive Bias

Most now agree that universities accepting such funding from tobacco companies is unethical. Professor Simon Chapman of the School of Public Health analysed 484
papers published in *Indoor and Built Environment* since the journal’s inception in 1992.

The analysis showed that 60% of studies on environmental tobacco smoke had findings judged ‘industry positive’. In 90% of these cases, at least one author was shown to have links with the tobacco industry. Professor Chapman stated that the tobacco industry had a long history of using money and sponsorship to infiltrate and influence both the scientific community and hospitality industry.  

**Australia Phases Out Tobacco Company Support**

The Public Health Association of Australia (PHAA), in their 1998 Annual General Meeting, adopted the stance that the Council of the PHAA would, within three years of the meeting (i.e. by 2001):

> ...take all reasonable steps to ensure that support from tobacco companies and related entities is removed forthwith from the formula for calculating ‘Mechanism A’ funds to Australian universities.

This step was taken following a review of 106 scientific reviews of evidence on passive smoking and health from 1980 to 1995. It is hard to believe that 37% of these reviews concluded that passive smoking is not harmful to health; this may be partly explained, however, by the fact that 74% of these reports were written by authors with tobacco industry affiliations. The conclusion of this PHAA review was that the only factor associated with this non-harmful finding was whether an author was affiliated with the tobacco industry!  

The University of Sydney web site states that, from 1 September 2003, the university will no longer accept funding from any tobacco manufacturer or agent. No reason was given for the two-year gap between the suggested cut-off point of 2001 for ceasing tobacco company funding—as per PHAA policy—and the date of the University of Sydney Senate’s policy statement on this.

The figures given in relation to positive results of trials associated with funding from the tobacco industry are uncomfortably close to the statistics on the pharmaceutical industry funding of drug studies, both involving scientists with links to industry. I
am not suggesting that the use or sale of tobacco is the same as the use and sale of pharmaceuticals, but rather that business is business and most companies will do what they can to increase profits.

**Conclusions**

In this chapter, I have examined the relationships between universities, research institutions, governments and industry. The changes in funding have created academic institutions that are less and less independent and therefore less free to provide unbiased comment and critiques of social developments. The science itself, in many cases, may be tainted as the money buys the results required. As governments decrease their funding of academia, the corporations are stepping in to buy the science, with the benefits going to the stock holder rather than to the patient.

There is also a strong secondary effect of this partnering of universities and industry—the education and training of our future medical doctors. The belief patterns instilled in them by what must only be seen as the benevolence and natural working relationship between doctors and the ‘industry’ is examined in Chapter 8, *The Philosophy*, with particular emphasis on the current trend towards the use of medical specialists in both private practice and salaried practices in research projects funded by industry.

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1 Flawn PT (1990), *A Primer for University Presidents: Managing the Modern University*, University of Texas Press, Austin, TX.


14 ibid., p10.


16 Fullerton T (2005), 'The Degree Factories', *Four Corners*, Australian Broadcasting Corporation.


24 ibid., pp35-37.

25 ibid., p32.

26 ibid.


36 ibid.


PART IV

PHILOSOPHY
Chapter 8

The Philosophy

I apprehend, this dignity is not to be supported by a narrow, selfish corporate spirit, by a peculiar formality in dress and manners, or by affected airs of mystery and self-importance.

John Gregory 1770

In this chapter, I examine the philosophy of medicine as it applies to cancer research and treatment, by asking:

- What effect could this philosophy have on cancer patients and on doctors’ attitudes to their work and patients?
- In what ways have changes over the last century been beneficial or detrimental to both doctors and their patients?
- What cultural differences exist in philosophical attitudes and what are the indications of such differences?
- In what ways has the philosophy of medicine induced changes in cancer research?

Philosophy, when used in a particular field of knowledge, denotes the general laws and principles under which all the phenomena and facts relating to that subject are comprehended.

A search of the medical literature using the search term ‘medical philosophy’ yielded surprisingly few results. Papers have been written on medical ethics—bioethics—but ethics is a subset of philosophy, a functional area rather than a self-reflective stance.

Ethics and Philosophy: Are They the Same?

The field of ethics is based on principles that are regarded as true, and that therefore cannot be challenged. Any concepts that challenge these basic principles are dismissed as not worthy of consideration. This attitude leads to a dogmatic
approach that stifles critical reflection and innovation. Any suggestions that basic
tenets may not be true and correct are vigorously opposed.

The indoctrination of conformity to these unquestionable ‘truths’ begins in medical
schools; and the ‘brotherhood’ of medicine maintains this conformity throughout the
professional life of a doctor.³

Medical schools tend to focus primarily on the development of their students’
clinical competence. However, physicians must also understand and take into
account their patients’ psychology, attitudes, values and social standing; areas that
receive much less attention in medical schools today. How can doctors perform
ethically for their patients’ benefit without this understanding?⁴

**Resistance to Change**

Most people tend to become quite set in their ways and do not easily deal with
change or challenges to their belief patterns. Dogmatism, which regards opinions as
truths, is only likely to change as a result of a radical paradigm shift.

Thomas Kuhn⁵ stated that a scientific community must have a set of received beliefs
to perform its role in science and society. The preparation required to become a
member of that community—by being “rigorous and rigid”—enforces these beliefs
strongly in the student’s mind. Challenges and changes to these beliefs must be
resisted by the establishment, for a change may introduce a new establishment. Such
is the nature and challenge of a paradigm shift.

The 19ᵗʰ century witnessed the introduction of ‘positivism’, which sought to separate
science from any corrupting influence of subjective values.⁶ Medical science of the
20ᵗʰ century maintains a perception that it is based solely on fact. As we move into
an age of ‘evidence-based medicine’ this may increasingly become its reality.
Despite this, we still use many procedures and hold many beliefs that have not been
subjected to rigorous testing.
Conservatism in Medicine: the Cartesian Approach

For the last five decades, physics has shown that it is not only ‘matter’ that is important, but also dynamics. Little has changed, however, in medical thinking. The conservatism of medicine has prevailed.\footnote{7}

Our modern medical science has become a science of reductionism. George Engel, has described scientific medicine as being based on:

...the notion of the body as a machine, of disease as a consequence of breakdown of the machine, and of the doctor’s task as repair of the machine.\footnote{8}

This adherence to the Cartesian separation of mind and body—a concept developed over 300 years ago—has meant that medical science regards disease primarily as a mechanistic breakdown; and cancer, as a cellular malfunction. Such a view is likely to neglect the interaction of body and mind, both in the understanding of the disease, and in its treatments.

Moral Judgements in Medicine

Evidence-based medicine relies primarily on laboratory and physical data. In this way, a positive feed-back loop is established that reinforces the belief that medicine is abstract, numerical and sterile.

The art of medicine, however—dealing with sick unhappy patients, with illness and death—cannot be solely reliant on fact. It also requires a moral epistemology. Doctors must make choices in therapy and in disclosure, choices that are based on individual patients, and on their beliefs, various needs and wants.

Treatment decisions are necessarily complex and must be made wisely: whether to use a particular drug, to advise no treatment and offer palliation, or to listen to a patient’s enquiries about adjunctive treatments. These decisions are essentially moral judgements and need to be based on a clear philosophical stance of ‘service’ to the patient.

Clinical encounters and choices arising from just laboratory reports form a rather sterile text. However, when the doctor and patient are able to form a caring and
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vis enough for them to see the patient as a whole
being, rather than just the disease?

University Ethics Committees

The philosophers are not readily visible or eminent in the current medical system. However, universities have Ethics Committees; and some even have medical ethicists. The number of doctors who read papers on medical philosophy is unclear but, in my experience, philosophy is rarely discussed at medical conferences.

Today, medical ethicists are regarded as essential members of the medical establishment. Their role, however, is limited to helping physicians to make decisions about rights and wrongs in treatments or research projects, possibly to minimise the possibility of litigation. They provide a service, rather than being viewed as major components of medicine and medical practices.

Ethics Committees decide whether the proposed study is ethical. Ethicists are not involved in discussions about why treatments are done:

- What is the goal of a treatment: To what extent is it the goal of the practitioner or of the patient?
- What are the rights of the patient in the proposed treatment plan?
- How much of a patient’s informed choice is based on the type of information presented by their oncologist and on the way it is presented?

Does Medical Philosophy Exist?

In 1992 Caplan, from the Center for Biomedical Ethics, postulated that for the field of Medical Philosophy to exist it must fulfil the following criteria:

- It must be well-integrated with other cognate inquiries and disciplines.
- It must have an established canon of key books, textbooks, anthologies and articles.
- It must have a set of distinctive and defining problems.

With reference to those criteria, Caplan concludes that:
The philosophy of medicine as it currently exists fails to satisfy these criteria and, thus, fails to exist as a field of inquiry...

...Bioethics is fundamentally a normative enterprise. The aim of its inquiries is to understand ethical problems in health care in order to make recommendations as to whether there is a need for normative change or not…. The philosophy of medicine tries to examine how it is that doctors, nurses, public health experts and other medical professionals believe or know things about health, disease, dysfunction, disability, illness and suffering.

Until there is a clearly defined field and teaching of the philosophy of medicine, all that remains is a sub-section of philosophy, that is, ethics.

**The Ethics**

Ethics should be taught as an intrinsic part of medicine. The primary reason for the teaching of ethics is to arm medical students with the concepts required to address future patients’ problems. Enabling doctors to become introspective or to develop their own moral and ethical lives is seen as beneficial but not necessary.¹²

**Helsinki Declaration**

Doctors have sets of guidelines laid out in charters such as the Helsinki Declaration. The section of the declaration that sets out any form of philosophical stance states that:

1. It is the duty of the physician to promote and safeguard the health of the people. The physician’s knowledge and conscience are dedicated to the fulfilment of this duty.

2. The Declaration of Geneva of the World Medical Association binds the physician with the words, “the health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that, “A physician shall act only in the patient’s interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.
The Helsinki Declaration, however, was never meant to provide a philosophical or moral stance for doctors, but rather a list of what may ethically be done to human subjects in the name of research. See Appendix 1, World Medical Association: Declaration.

**Australian Medical Association (AMA) Code of Ethics**

On the web site of the Australian Medical Association (AMA) can be found its (2006) Code of Ethics for Australian doctors. This code has been developed from two sources: the Canadian Medical Association Code of Ethics and the World Medical Association International Code of Medical Ethics.  

This code covers conduct relating to:

- the doctor and the patient,
- clinical research,
- clinical teaching,
- the dying patient,
- transplantation,
- the doctor and the profession,
- advertising,
- referral to colleagues,
- professional independence,
- the doctor and society.

In the preamble to the code of ethics, the AMA states that this body of ethical principles is to guide doctors in the conduct of their relationships with patients, colleagues and society.

The naïve public perception in Australia, however, is that all doctors swear the Hippocratic oath on graduation.

**Swearing of Oaths in Australian Medical Schools**

Although medical practitioners may be read the Hippocratic Oath, they are not required to formally swear to uphold the principles on graduation. (See Appendix 2,
Hippocratic Oath—Classical Version.) Depending on which university Australian doctors attend, they may or may not swear an oath:

- The University of Western Australia\(^\text{14}\) does require swearing of the oath.
- James Cook University\(^\text{15}\) students recite an oath written by the Medical Student Association.
- The University of Adelaide\(^\text{16}\) has a Declaration Ceremony at which an oath may be taken. However, it is not compulsory to attend or to read the oath, and the ceremony is an internal faculty event, not a university function.
- At the University of NSW\(^\text{17}\) students write their own ‘oath’ to recite at graduation.
- Monash University\(^\text{18}\) and Sydney University\(^\text{19}\) graduates have not taken a formal oath in many years.

**World Medical Association (AMA) Code of Medical Ethics**

The World Medical Association International Code of Medical Ethics (see Appendix 3, Pledge—World Medical Association) has an almost identical list of guidelines to the Australian code, with one interesting difference: the requirement for the swearing of an oath on admission as a medical practitioner, consecrating one’s life to the service of humanity.

Both the British Medical Association and the American Medical Association no longer require the swearing of an oath. However, oath taking on induction as a medical practitioner is still carried out in many European countries.\(^\text{20}\) In the French *Code de Déontologie*, it states:

> The new doctors take the Hippocratic Oath, this oath has been established, nearly twenty-five centuries ago, with rules that are always valid; probity and devotion of the doctor who must preserve life, do no harm, respect the sick people, their interests, their private life and medical secrecy, and be just.\(^\text{21}\)

There appear to be philosophical differences between English and non-English speaking countries in their attitude to oath taking.
According to the Enquiries Officer at the General Medical Council of England\textsuperscript{22}, popular belief in England is that an oath is sworn. In reality, this is not done, rather doctors are expected to adhere to a set of ‘Good Medical Practice’ principles.

Although the major associations in the UK and USA do not require any oath be sworn on admission, some universities, for example the Johns Hopkins School of Medicine in the USA\textsuperscript{23}, still continue the tradition (see Appendix 4, Hippocratic Oath—Johns Hopkins University.)

**Shift in Responsibility from the Doctor–Patient Contract**

The Hippocratic Oath was developed in a market-place era of medicine, when the contract was between the doctor and the patient: Either the patient paid for the treatment or was treated as a charity case.

Australian doctors are now paid by government (from Medicare rebates), usually with additional funds being contributed by the patient. However, this means that doctors are answerable not only to their patient but also to the government that acts as their employer. This creates a shift in responsibility and in the nature of the contract between patient and doctor.

Doctors in Australia are now expected to follow guidelines for ethical behaviour, rather than swearing an oath dedicating their lives to the service of medicine and humanity. Although these guidelines are posted on the AMA web site, there is no requirement for Australian doctors to be members of the AMA.

**Ethics in the Legal Profession**

Medical practitionerers are not the only profession with a Code of Ethics. The Statement of Ethics of the Council of the Law Society of New South Wales declares that: “The true profession of law is based on an ideal of honourable service.” It also states that the legal profession serves the interests of justice.

On becoming a legal practitioner, an oath is taken whereby the applicant sincerely promises and affirms that they will truly and honestly conduct themselves, in the practice of a Legal Practitioner of the Court, according to law and to the best of their
knowledge and ability. The same oath is sworn in all the states and courts of Australia.

When evidence is given in a Court of Law, an oath or affirmation is taken that the truth will be told. A witness is not asked if they hold a Code of Ethics that binds them to the truth. The swearing of an oath is to enforce the seriousness of the giving of evidence, just as the swearing of the oath of service to the law enforces, for lawyers, the seriousness of the profession they are entering.

The practice of medicine often entails life and death decisions, and is surely a profession that should be taken seriously enough to warrant the taking of such an oath.

**Protectionism Among Medical Practitioners**

The fraternity of medical practitioners—the brotherhood of doctors—plays a major role in the professional life of doctors. The Code of Ethics for Australian doctors states:

“*Report suspected unethical or unprofessional conduct by a colleague to the appropriate peer review body.*” However, in the recent cases of the Campbelltown, Camden and Bundaberg hospitals, it was the nurses who were the whistleblowers rather than the doctors. Nurses have invariably been the ones who have raised the alarm when patients’ lives have been put at risk.

This attitude of the protection of the status quo begins in medical training. It has been shown that medical students are less likely to report aberrant behaviour at the end of their medical training than at the beginning.

External reviews of the inadequacy of health care delivery have been conducted at the Canberra Hospital (Australia), Mt Druitt Hospital (Australia), Royal Bristol Infirmary (Britain) and Winnipeg Hospital in Canada. All reviews have shown that the medical staff—the doctors—turn a blind eye to unethical and unprofessional conduct by their colleagues.
In 1976, Professor Holman of Stanford University’s School of Medicine blamed the ‘professionalization of medicine’ for providing an insulation from criticism and alternate views, and for creating an establishment protective of its own social power rather than the selfless pursuit of knowledge.27

The AMA’s Code of Ethics28, however, does state that the physician should: “Consider first the well-being of your patient.” This attitude needs to be instilled in medical school and maintained throughout the professional life of a doctor. Swearing an oath at the beginning of professional life does not guarantee that the oath will always be upheld, but it does raise awareness and make possible the enforcement of what that professional life should represent.

**Self-Regulation within the Medical System**

The medical system is self-regulating. Unless there is a breach of the law of the land, any breach of the code of ethics is dealt with internally by the system itself. The de-registration of a doctor, for example, is carried out only in extreme situations.

An analysis of medical disciplinary actions, such as license suspension or de-registration, for physicians whose negligence caused multiple malpractice payments in the USA was carried out recently by *Public Citizen*. The study was based on NPDB figures (National Practitioner Data Bank).29 *Public Citizen* found that:

- 89.61% of doctors who made two or more malpractice payments were disciplined by their state board.
- 11.71% of doctors who made three or more malpractice payments were disciplined.
- 14.75% of doctors who made four or more malpractice payments were disciplined.
- Only 33.26% of doctors who made 10 or more malpractice payments were disciplined. This means that two-thirds of doctors in this group were not disciplined at all.
Conflict of Interest in Bioethics

Bioethicists are those who provide the framework for the ethics and therefore this part of the philosophy of medicine. It is the Bioethicists who have written on conflict of interest in medical practice and in research.

Yet monetary factors appear to have even invaded this sector of the medical system, the very core of medical ethics:

- Centres of Biomedical Ethics, such as the Stanford Center for Biomedical Ethics, have had programmes funded by SmithKline & Beecham.
- Merck has provided funding for ethics centres in many countries.
- The Midwest Bioethics Centre received half a million dollars in funding from Aventis Pharmaceuticals in 2000 to establish the Research Integrity Project.
- The US AMA Council on Ethical and Judicial Affairs in 2001 planned to educate doctors about the ethical problems associated with the acceptance of drug industry gifts. This educational programme was funded by monies from Eli Lilly and Co., GlaxoSmithKline Inc., Pfizer, Astra Zeneca Pharmaceuticals, Bayer Corporation, Procter and Gamble Company and Wyeth-Ayerst Pharmaceuticals.30

It appears that ethics may be being taught in a ‘do as I say not as I do’ manner?

Doctors’ Relationships with Industry

It has become well publicised that it is unethical for doctors to accept gifts from pharmaceutical companies, yet this publicity does not appear to have ended the practice.

Drug industry rules suggest that hospitality provided to doctors at education events should be ‘simple and modest’, yet Roche has recently been fined $75 000 for spending $65 000 on wining and dining doctors at exclusive restaurants. The fines followed a complaint to Medicines Australia—the drug industry’s overseer of conduct—from the Therapeutic Goods Administration. This complaint followed the publication of an article regarding this conduct a recent issue of the The Australian.31
In 1994, the Royal Australasian College of Physicians drew up and released their guidelines on ethical relationships with the pharmaceutical industry.\textsuperscript{32} It warned doctors that, although they are not the consumers of the products, they act as agents for the consumers. It warned against the acceptance of product samples, as this was usually:

\begin{itemize}
  \item a marketing exercise designed to accustom the physician to prescribing a certain product or to establish a cohort of patients on long term treatments with a particular drug
  \item particular care should be taken in the light of a trend to the provision of lavish dinners disproportionate to the content of the accompanying scientific presentation.
\end{itemize}

The guidelines were, however, fairly vague as to which gifts were acceptable and which were not, saying merely that there is a “gradient of acceptability.”

**Industry Funding Throws Doubt on Research Results**

The medical structure appears to be so intrinsically tied to the pharmaceutical industry that delineation between the two has become blurred, and doctors find it very difficult to be clear about and maintain a healthy separation. When it is found that a doctor or medical researcher has accepted industry funding and concealed it, because the potential bias cannot be accurately evaluated, the research results cannot be regarded as trustworthy.

It has recently been revealed that one of the ‘greats’ in medical research, Sir Richard Doll, had in fact been on the payroll of Monsanto for many years. Doll was one of the first epidemiologists to point to a clear link between cigarette smoking and lung cancer. He became a figure of enormous standing in epidemiology and public health.

A recent paper, however, in the American Journal of Industrial Medicine\textsuperscript{33} showed that Doll had been secretly retained as a paid consultant by several international chemical companies. At the same time, he was acting as an impartial scientific expert investigating and reporting on suspected links between these companies’ products and the development of cancer.
During the 1980s, Doll received $1,500 per day from Monsanto. This was during a decade when Monsanto was at the centre of the debate as to whether Agent Orange (a Monsanto product) is carcinogenic.

During this period, Doll gave testimony to an Australian Royal Commission investigating claims by Vietnam servicemen who had been exposed to Agent Orange. His statement that there was no evidence to suggest that the product was carcinogenic must now be regarded as highly suspect. He did not disclose at that time or since that he was a paid consultant to Monsanto.

**Paradigm Shifts**

**Signs of Self-Delusion?**

When *The Lancet* published an editorial in 1993 entitled “*Breast cancer: have we lost our way?*” we may have expected some intense soul searching into current treatments and attitudes relating to breast cancer and, just possibly, a subsequent small paradigm shift.

The editorial pointed out that the overall mortality from breast cancer has remained static and that there is no reliable data to suggest that screening reduces mortality in the youngest or oldest groups of patients. It also suggested that researchers were too impatient to wait for the ultimate end-point of the disease—a long survival time but usually with cancer recurrence causing death—instead relying on markers such as disease-free survival and early diagnosis.

The editorial discussed primary prevention—not taking steps to prevent the occurrence of a tumour, but rather using Tamoxifen with high risk women. (Note that uterine cancers can be a side-effect of the use of Tamoxifen.)

The author(s) also discussed secondary prevention—again, not true prevention but rather early diagnosis through mammography—in the hope of finding cancers prior to the expression of their metastasising potential. However (as mentioned above), screening in this way does not reduce mortality in the younger or older groups of women.
The editorial was written to announce the *Lancet’s* April, 1994 conference, *The Challenge of Breast Cancer*. Was the result of this conference a shift in treatment possibilities or in true prevention of the disease? My answer would have to be ‘no’, as little change eventuated following the meeting, and certainly it did not herald any form of paradigm shift.

Papers presented included the following:

- Jim Devitt from Ottawa reminded attendees that breast cancer is only a manifestation of a widespread disorder.
- Joyce Taylor-Papadimitriou and Ian Hart, both of London, spoke of investigating adhesion molecules such as E-cadherin and the integrins.
- Vincent Guinee of Houston noted that young women diagnosed with breast cancer during or within a few years of pregnancy have a higher risk of death from the cancer than those who have not been pregnant.
- Harry Burke from Reno spoke of outcome prediction as a new form of prognosis.
- Valerie Beral reported that there was no evidence to indicate that oral contraceptives increased the risk of breast cancer.
- Leslie Bernstein of Los Angeles encouraged women to exercise, as 5 hours minimum per week had a protective effect against cancer.
- N. Krieger of Oakland reported a nested case-control study dismissing the risk of breast cancer from exposure to organochlorines.
- Breastfeeding gave a protective effect against premenopausal cancer, Clair Chilvers of Nottingham reported.
- Michael Sporn of Bethesda spoke of primary prevention using several chemopreventive manipulations.
- Richard Margolese from Montreal pointed out that, even though there may be dissatisfaction with the current treatments, we should not dismiss the benefits of ‘conventional’ chemotherapy and hormonal therapy.
- Harvey Schipper from Winnipeg urged that thinking should be moving towards cellular regulation rather than cell killing. 35

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The final word came in the post-conference editorial from *The Lancet* April 30, 1994:

So, have we lost our way, as we asked in the Lancet editorial that announced the conference in February of last year? With confidence we can say no, to judge by the reactions of the conference participants … there were few signs of self-delusion and none of self-congratulation.36

This conference took place over 12 years ago. Since then, the treatments and success rates have shown minimal change. According to the American Cancer Society web page, the current standard treatments remain surgery followed by radiotherapy and/or chemotherapy, with the addition of Herceptin or hormone-blocking drugs.37

Little has changed in the last decade. The participants of the conference may have felt no self delusion, but for an outsider it is difficult to see how the conclusion that the ‘way was not lost’ stands up to scrutiny.

**Prevention or Early Diagnosis?**

A disturbing trend is the use of the word ‘prevention’ to refer to early diagnosis. This concept of prevention has been used in the past in relation to mammography for women, and was again referred to at *The Lancet* conference, noted above.

The public perception of prevention may be more about staying healthy and therefore not developing a tumour, rather than having a tumour already, but finding it early enough to permit a more favourable prognosis.

**Calls for a Paradigm Shift**

A 1993 paper by Schipper and colleagues from the University of Manitoba, Winnipeg, not only called for a paradigm shift in cancer treatment but also offered a new model and view of the cancer process.38

They emphasised the need for a change from the current strategy of hoping for a cure by killing every last cancer cell. This strategy regards the cancer as an entity, an
‘enemy’ that needs to be eradicated, rather than as a process of aberrant cell regulation.

Their view of malignancy describes cancer as a process rather than a morphologic entity, thus questioning the long-standing concept of current cancer therapies.\textsuperscript{39}

There are some new chemical agents that may re-regulate cells, such as inhibitors that block ras-oncogene activation and metalloproteinase inhibitors to block the enzymes involved in tissue invasion.\textsuperscript{40} Sadly, the suggestion of “rethinking cancer” has not produced any noticeable shifts in standard oncology treatments.

**Opposition to Paradigm Shifts**

When attempting to introduce a new viewpoint in science one invariably must face many hurdles. Pressure from peers to conform to standard perspectives is known to influence not only funding possibilities, but also advancement in academic circles.

Opposition to new thought has been known throughout medical history. Semmelweis, a Hungarian doctor working in Vienna, observed in 1847 the death of a colleague who had cut his finger during an autopsy. The symptoms were similar to puerperal fever. Semmelweis instituted a procedure whereby doctors washed their hands in a chlorine solution after autopsies and before delivering babies. The death from puerperal fever at his Viennese hospital dropped from 13\% to 2\%.

Despite this success, however his actions were seen as a criticism of the hospital director and Semmelweis’ promotion was blocked. He returned to Hungary, continued experimenting (washing instruments as well), and wrote of his findings to overwhelmingly poor reviews. He subsequently suffered a nervous breakdown and died at the age of 47.\textsuperscript{41}

In our modern society, being known as a leading scientist does not make it easier to challenge standard thinking. Linus Pauling, the two-times Nobel Laureate, was repeatedly denied grants to study the use of Vitamin C in cancer treatments.\textsuperscript{42}
Protecting the current status and monopoly of the medical profession has, at times, taken regrettable turns. When chiropractors were seen to be encroaching on areas belonging to the medical profession, a systematic campaign of libel and slander was undertaken by the AMA in the USA. This campaign ended in a court case *Wilk vs. AMA* in 1987, in which the judge found against the AMA for “*systematic, long-term wrong-doing with the long-term intent to destroy a licensed profession.*”\(^{43}\)

**A Doctor’s Philosophical Stance**

A man’s ethical behaviour should be based effectually on sympathy, education, and social ties; no religious basis is necessary. Man would indeed be in a poor way if he had to be restrained by fear of punishment and hope of reward after death.  


Doctors are taught to maintain an air of confidence with their patients. When there are clear outcomes in relation to a patient’s prognosis and treatment options, a happy relationship is maintained between doctor and patient. However, if the outcome of suggested treatments is not clear—because of poor prognosis or risk of severe adverse effects from the treatment—it becomes increasingly difficult for doctors to maintain an atmosphere of certainty in this doctor–patient relationship.

**Honesty in Discussing Treatment Options**

Doctors are ethically required to give patients full disclosure, thus encouraging the patients’ fully-informed consent to treatments. This is often problematic for doctors, and can result in nondisclosure, poor discussion techniques and oversimplification. Patients may misinterpret the doctor’s explanation of prognosis and treatment, or the doctor may exhibit over-confidence in the treatment being recommended, and discourage the patient from considering alternative treatments.

Many patients wish to rely solely on the advice of their oncologist, but they are often unaware of the level of certainty associated with the various treatment options.

It has been claimed that doctors who are honest with patients about their uncertainty in the outcome of treatments are more likely to reduce the confidence, trust and satisfaction of their patients, and that:
Patients may not understand the statistics relating to uncertainty of outcome.
Patients may be harmed by the revelation of uncertainty.
The doctors’ authority and effectiveness may be undermined.
If trust and satisfaction is undermined, patients may sue.44

A 2004 survey on a group of patients with advanced cancer evaluated the content and amount of information given to them by oncologists, as follows:

- 53% of the oncologists explained the course of the disease,
- 35% spoke of symptoms,
- 39% gave a prognosis,
- 84% informed patients of the absence of cure,
- Watchful-waiting was discussed with only half of the patients,
- Most discussed ‘active’ treatment plans.45

**Misinformation to Patients**

Over the last 20 years, I have spent long periods of time in conversation with cancer patients. I have often been surprised by statements they have attributed to their oncologists, ranging from non-existent statistics to prognoses of x number of months to live. Patients may be given informed consent, but do not usually have informed choice.

One breast cancer patient informed her oncologist that she wished to treat her cancer with natural therapies rather than conventional treatments. She was told: “If I had 100 women with your type of cancer in this room and they used proper treatment, at the end of five years 70 would still be alive, but if they used natural therapies at the end of five years only five would be alive.”

As there has never been a study on breast cancer patients using only natural therapies, this was patently untrue. There was no discussion about the type of natural therapies the patient wished to use. It appeared that for that oncologist only conventional treatment could be effective. This was a doctor trying to persuade a
patient to follow standard protocols, possibly with the best interest of the patient in mind, but with a blatant lack of ethics.

**Oncologists Lack Interest in ‘Other’ Treatments**

As discussed on page 121, surveys of Australian oncologists show that most lack any detailed knowledge or understanding of ‘other’ therapies, such as complementary and alternative therapies. Most patients find it difficult to discuss these therapies with their oncologists, whose response they generally suspect will be dismissive. The issue is not that oncologists should be required to have this knowledge, but that they should admit their lack of knowledge to the patient and if requested by their patient, collaborate with those who do have this knowledge.

Many patients who have used adjunctive therapies in conjunction with their orthodox treatments and who have responded surprisingly well, have reported that their oncologists have said: “keep doing whatever you are doing”. Nevertheless, to date, I have not been told of any oncologist who has asked for information on any of these adjunctive therapies, with the view to assist other patients not doing well.

I interviewed a group of medical practitioners, many of whom give such adjunctive therapies to cancer patients. I asked their opinion on why oncologists do not feel obliged to offer all possible help to patients. Doctors MM and RB both felt that there is enormous peer pressure to conform to conventional treatments and to offer all standard protocols, partly to be seen to have ‘treated well’ and partly to avoid possible litigation.

**What Treatments Would Doctors Choose?**

Whether oncologists would choose to undergo the same treatments they routinely offer their patients is a question that has been raised in the past. In a 1986 study, by the McGill Cancer Center, questionnaires were sent to 118 doctors involved in the treatment of non-small-cell-lung cancer. The doctors were asked which of six randomised chemotherapy trials they would enter, if they were themselves diagnosed with non-small-cell-lung cancer.
Many of the doctors queried were involved in recruiting patients for trials and in the trials themselves; 79 doctors responded to the questionnaire:

- 64 of the 79 doctors stated that they would not consent to a trial containing Cisplatin.
- 58 of this 64 stated that they would not enter any of the trials offered because of the ineffectiveness of chemotherapy in this cancer and the unacceptable level of toxicity.46

It is known that cytotoxic treatments that do not (and are not expected to) achieve therapeutic benefit may be offered by oncologists. This is usually justified on the basis of providing a degree of ‘hope’ for the patient.47

**Informed Consent or Informed Choice?**

The difference between informed consent and informed choice lies at the heart of one of the dilemmas of medical philosophy (as opposed to medical ethics). Doctors in this scientific age increasingly rely on the technical aspects of medicine, rather than the human or moral aspects. Thus they tend to rely on the scientific data—the laboratory results of tumour markers, scans and so on—rather than considering each patient’s situation in ethical terms.48

The Law Reform Commission of Victoria in 1989 published *Informed Decisions About Medical Procedures: Doctor and Patient Studies*49, in which they found that information was given to patients to ensure compliance to treatment, rather than to enable clear decision making by the patient. They found the common attitude amongst doctors was that the patient’s best interests were served by the doctor deciding what information should be provided and what treatment the patient should undertake.

In terms of treatment, there is a vast difference between what is possible and what is desirable. Medical science in this past century does not have a history of offering clear treatment choices to their patients.50 51

If patients truly understood the repercussions of the treatment plans offered, would their decisions remain the same? If oncologists—who do understand the expected
side-effects and level of efficacy of the drugs—would decline to personally take these treatments, it is difficult to find a sound ethical basis for their suggestions that patients should do so.

**GEMZAR: “Overall Survival Difference ... Not Significant”**

I have previously mentioned the Lilly Oncology drug GEMZAR (in *Chapter 2, A Century of Cancer Statistics*). It is difficult to understand a fully-informed patient agreeing to use this drug for ovarian cancer. The advertisement produced by Lilly Oncology is unlikely to sway a patient’s decision—unless it is read quickly. It is even more difficult to understand a doctor recommending this treatment to a patient.

The advertisement (see Appendix 5, GEMZAR Phase III Trial) provides data of a randomised trial comparing carboplatin to carboplatin plus GEMZAR in patients with advanced ovarian cancer. Bold letters announce that GEMZAR/carboplatin offers a superior progression-free survival, in fact, a 49% improvement over carboplatin alone. Bold letters again claim a 53% improvement in overall response rate.

However, with continued close reading, one eventually reaches the statement:

“Overall survival difference between GEMZAR/carboplatin (18.0 months) vs carboplatin (17.3 months) was not significant (p=0.8977).”

The advertisement also shows a comparison of the adverse effects of each treatment. The GEMZAR/carboplatin group showed significant increases in most adverse effects, including anaemia, the need for blood transfusions, and an increase in neutropoenia and leucopoenia (an abnormally low number of neutrophils and leucocytes in the blood), which would require the patient to avoid contact with any relative or friend with an infection. An increase in most of the unpleasant side effects of chemotherapy was also reported.

GEMZAR may have given some of the patients an extra couple of month’s survival, but at what cost? When faced with death, not being able to be close to friends and relatives would be particularly arduous for most people. It is difficult to understand
how such a drug was ever approved for release or how difficult this drug must be to sell.

**The Ethics of Accepting Money from Pharma**

In *Chapter 7, Academic Freedom—Academic Funding*, I discussed the effect of pharmaceutical money on universities, research and the medical profession. The acceptance of money for favours is often disguised in diverse ways.

**ASIC Recommendations**

When financial advisors are consulted to give advice on the best ways to invest, it is expected that impartial and proper advice should be given. When financial advisors take money from investment managers, this has been shown to influence the advice, often to the detriment of the investors. Investigation into these kickback practices has been of concern to ASIC (Australian Securities and Investment Commission) for many years.

In April 2006, ASIC released a report on financial planners, after surveying 306 instances of advice given to investors. They found that:

- When financial planners received some form of commission 35% of advice given was not reasonable, compared to 6% of poor advice given when commission was not involved.
- At the corporate level, when commission is involved 32% of advice given was poor, compared to 11% with no commission involved.\(^52\)

The recommendation from ASIC is that all forms of commission—whether in the form of free office equipment, overseas trips, share options and cash bonuses—could influence the recommendations of the advisor, and need to be clearly declared\(^53\).

**Influence on Prescribing Habits**

Studies have shown that prescribing habits by doctors are influenced by gifts from the pharmaceutical industry (see *Chapter 6, Following the Money*). However, there still appears to be reluctance within the medical profession to resist this acceptance of gifts.
In a 2006 poll conducted by Medscape, the following question was asked: 54

“Recent reports have described the practice of pharmaceutical companies providing lunch to medical practices while reps pitch their drugs to the physicians. The companies say the lunches are modest and fall within industry guidelines. Opponents say that modest or not, they still influence prescribing practices. Do you favor or oppose the free lunch?”

Responses to the poll were from physicians, pharmacists and nurses:

➢ The total response in favour of accepting a free lunch was 56%, that is, 2748 were in favour from a total of 4823 responses.
➢ The response from physicians only was 65%.

In the words of Shirley Chisholm (2006, in http://www.econsultant.com/quotes):

When morality comes up against profit, it is seldom that profit loses.

**Cancer Care As a Corporate Entity**

Professor Fritjof Capra of the University of California Berkeley wrote, in 1982, that healthcare needed to be liberated from the pharmaceutical industry, and that drugs would eventually be used sparingly and as specifically as possible, and only in emergency cases. 55

Unfortunately, healthcare has certainly not yet become liberated from the pharmaceutical industry. Indeed, the connections over the last 25 years have become even more tangled, and there has been no major move away from our current drug-based medical system. In fact, at least in the USA, cancer care has become a large corporate entity in its own right.

US Oncology is a large cancer care service company. Founded in 1999, it now manages 1,000 oncologists and treats one in seven cancer patients. US Oncology manages the business affairs of the doctors on its books and injects practices with “financial savvy and a competitiveness seldom seen in medicine.” 56

US Oncology is now the largest purchaser of chemotherapy drugs and can negotiate a 24% discount on the wholesale price of the drugs. This contributes to the profit margin of the company, which in 2005 showed revenue of US $2.5 billion.
The company also sells data on patients, and consults with the pharmaceutical industry. There is now a move for the company to purchase equipment such as PET scanners and linear accelerator machines, which would be turned over to oncologists for a cut in the profit from the machines.

This is certainly corporate medicine with a view to the profit margin, rather than medicine as an art, with a view of the patient as the sole recipient.

**The Patients**

Socially, we have changed in our view of cancer. The mass media’s continual reference to ‘cancer cures’, ‘cancer risk’ and ‘cancer prevention’ have brought to the forefront of our thinking a sense of living with risk and the inevitability of risk management.

**‘Experts’ Promoting Fear**

We are continually bombarded with appeals for money to fight cancer: Daffodil Day, Pink Ribbon Day, CanSurvive Day, and the list goes on. Experts are seen on television and heard on radio, talking of the latest breakthroughs in treatment, of the need to fight the war: the War on Cancer. That these reports are from ‘experts’ makes their message seem both more credible and more frightening.

This promotion of fear generates millions of dollars for research centres and hospitals, and provides income for members of cancer societies worldwide.

Historically, the role of the doctor was to encourage healing and ease pain. In the current system, a doctor’s role is to diagnose ‘illness’—whether the patient is aware of it or not—and then treat the illness with purchased products. This is disease-based medicine.

For women, the constant promotion of fear—specifically in relation to breast cancer—has changed the way we relate to our bodies. The historian Barbara Duden has examined the diaries and letters of 18th century women. She found that women of that era considered health and sickness as being to do with the flow of blood.
Women went to doctors not because they were ill but because they felt ‘blocked up inside’. They were motivated by fear of blockages. This was also the fear from the time of Hippocrates: congestion, non-movement, an internal non-flowing.

Present-day society has made our breasts a matter of concern, of fear, of risk of possibilities that may never occur, of malignancy—a fear of possible disease that may never eventuate.57

**Patients As End-Users**

Cancer patients are the end-users of oncology. In commercial terms, it is usually the end-user who chooses the products they will use, but this does not occur in oncology or in medicine generally. Patients rely on third parties—the oncologists—to decide for them which treatment protocol they should undertake. In other fields this is not the situation. The Ford Pinto story is an example of consumer power.

**Consumer Power: Ford Pinto**

In the 1960s, Ford faced strong competition in the American small-car market from Volkswagen and Japanese competitors. Ford rushed through production of the Pinto in 25 months, when the usual time was 43 months.

Before production began, engineers at Ford discovered a flaw in the design that caused the Pinto fuel system to explode easily on rear impact. At the time of manufacture, Lee Iacocca was head of development. He had specified that the car was not to weigh over 2000 pounds and should not cost more than $2000. Modification to the design to ensure safety would take the car over these specifications.

It was estimated that there would be potentially 2100 burned vehicles, causing 180 serious burn injuries and 180 burn deaths. Estimates were that each death would cost the company $200 000, each major burn injury would cost $67 000 in compensation, and the average repair cost for each car involved would be $700.
To correct the fault would cost the company $137 million—$11 per car—which was much greater than the cost of compensation and other payouts, calculated at $49 million.

Ford’s cost-benefit analysis found that it was not profitable to make the $11-per-car changes to the car. (Experts later found that their calculations were inaccurate and the cost of settlements would have been closer to the cost of correcting the problem.) The safety issue was dismissed, as it was decided that trunk space was a larger issue in the competition to sell cars.

A report by Eugene Trisko, prepared for the national Highway Traffic Safety Administration (NHTSA), found that the Ford Company made 24% of the cars on American roads, yet 42% of collision-ruptured fuel tanks were occurring with Ford cars. The NHTSA also commissioned a report by Robert Nathan and Associates, who found that 400,000 cars were burning each year, causing 3000 deaths through burns.

By 1972, the NHTSA had been researching and analysing car fires for four years. Over that period there had been 9000 deaths and tens of thousands of injuries involving burns and scarring. This four-year delay allowed over 10 million unsafe vehicles to be sold.

In May 1978, the Department of Transport, a division of the NHTSA, announced a ‘safety related defect’ in the Pinto. One month later, Ford recalled 1.5 million Pintos.58 59

This scandal came close to destroying the Ford motor company, as consumers realised that there had been a conscious decision to put profit before human lives. Ford sales were low for many years after this.

**Consumer Lack Of Power In Medicine: Merck/Vioxx**

The Ford Pinto scandal is somewhat similar to the Merck/Vioxx situation, in which Merck failed to alert consumers to the potential for cardiac adverse events associated with the use of Vioxx.
During a clinical trial, the Advantage trial, eight patients suffered heart attack or sudden cardiac death, compared with one taking the rival drug Naproxen. This difference in adverse events was statistically significant, but Merck did not disclose the data. An earlier study, the Vigor study, had also showed that patients taking Vioxx were more likely to suffer heart attacks than those taking Naproxen.

Email messages from Dr Edward Scolnick, Merck’s leading scientist, and from Dr Alise Reicin, vice president for clinical research, indicated that Merck had concerns about data that contradicted the safety of Vioxx. In one of Dr Scolnick’s emails, he expressed concern to other Merck scientists that this study could result in the FDA demanding that the Vioxx label indicate its cardiac risks.

The Advantage trial was published in 2003 with Dr Jeffrey Lisse as first author. Dr Lisse later declared that, although he was listed as first author, the report had been written by Merck, and that Merck had designed, paid for and run the trial. He had been approached after the trial and asked to edit the paper.60

It has also come to light that Merck attempted to reformulate Vioxx by the inclusion of a thromboxane inhibitor to provide cardiac protection, filing a patent application in 2001. According to Rep. Henry Waxman, a review of Merck documents showed that:

- 3000 sales people were given misleading information about the safety of Vioxx.
- They were instructed to show physicians a pamphlet indicating that Vioxx might be 8 to 11 times safer than other anti-inflammatory drugs.
- They were told not to discuss heart risks associated with the drug with doctors.61

There is a large difference here between consumers of cars—deciding not to purchase a particular manufacturer’s product—and patients, who are consumers of drugs, but who have no say in which manufacturer’s product they use. Patients must rely on their oncologist/doctor to make this choice on their behalf. They have some
consumer power in medicine: They can change doctors, but this is their only voice, their only source of any choice.

**Lack of Impartial Government Regulation**

Uncovering the malfeasance of Merck has also exposed corruption and weaknesses in the government agencies responsible for regulating the companies and their products.

The FDA advisory committee that voted to continue to allow sales for Cox-2 inhibitors, including Vioxx, comprised 32 members, of whom 10 had previously been paid consultants to the drugs’ manufacturers.

Much of the information on the FDA’s inaction relating to Merck and Vioxx have come from a whistleblower, Dr David Graham, a scientist with 18 years experience working at the FDA. Dr Graham performed a 3-year study with Kaiser Permanente and concluded that high-dose Vioxx significantly increased the risk of heart attack and sudden death.

Senior management at the Office of Drug Safety attempted to pressure Graham into changing his conclusions and recommendations. When he resisted this pressure, the FDA refused clearance for the publication of his findings. Shortly after this, the FDA approved Vioxx for use in children with rheumatoid arthritis.\(^{62}\)

**Patients’ New Role in Their Own Health Management**

Patients put their faith and trust not only in their doctors, but also in the government agencies that regulate the pharmaceutical industry. If neither manufacturers nor government agencies show complete trustworthiness, then patients are at the mercy of both.

There is, however, a growing change in the patient’s role in their own health management, as we enter a third age of information transfer.\(^{63}\)

The first age of information transfer was the age of the book, when widespread use was limited to the elite. We have seen this limitation continue in medical science,
where information has remained the prerogative of the elite. Patients rarely have access to full print papers or journals, and the information in these is extremely specialised, with its own elitist language. To be published in these journals, the information must conform to the positions and standards of the ‘gatekeepers’, the editors and reviewers.

The second age of information transfer came with the introduction of television. Access to television is potentially available to all (dependent on one’s wealth status) but information placement is costly. Those with the largest budgets have their information viewed most often.

The third age is the age of Internet. This new information source has caused the largest change for patients, where they can now not only access enormous amounts of information but can also share their stories with other patients. This scale of patient story-sharing has never been experienced before, and it is starting to have large effects on the treatment choices patients may make.

The quality of information from the Internet is often problematic, but patients can now access abstracts of papers through PubMed and many spend vast amounts of time learning about their own particular types of cancer. Patients once relied on information from their oncologists, who may only have told them what they felt they needed to know. They edited information and often felt that the best interest of the patient was served by the doctor making the decision as to which treatment was best suited.

**Changing View of the Doctor**

Our society has taught us to respect physicians. We grew up with television programmes that idealised doctors. We watched Dr. Kildaire and others walk the corridors of hospitals, saving lives and bestowing their blessings on the common folk. The medical profession were seen to be endowed with paternalistic qualities, and their decisions were acknowledged as being authoritarian and unquestionable.

To some extent this no longer holds sway, but doctors are still not treated the same as veterinarians, engineers or others with a good education. Most people have no
problem with gathering multiple opinions on fixing their cars and electrical appliances, and with sacking and changing their legal representatives. However, the choice of doctors does not seem so easy.

Many of the patients I have spoken to over the years have not been happy with the oncologist treating them. But they have often baulked at seeking another oncologist, in case the first was offended or the second may have been friends with the first. The end result is that the patient is unhappy with their treatment.

**Fear of Death in Modern Western Culture**

Our modern culture views death in ways different both to our ancestors and to non-western cultures. In many less industrialised cultures, death is still viewed as an essential part of life—part of the human experience—that cannot be avoided.

**Planning for a Good Death**

Our Western culture focuses primarily on living. For most, dying well is a concept that is neither spoken of nor thought about until we have no other choice. We run from death and are taught to fear it, rather than plan a good death. Our social structure is built on the denial of death, our anti-aging medical movement and the celebration of youth. We are not taught how to deal with dying people, whether they be relatives or friends.

The last three decades have witnessed various attempts to improve the quality of life of dying patients, with the availability of hospices and the legal right of patients to refuse life-sustaining care.

Medically, the attempt to ease dying and improve care for the dying patient has been mostly to do with technology for symptom relief. However, surveys of patients indicate that their concern is mostly about loss of dignity, loss of control and of being a burden on their loved ones.

The experience of dying is not purely physical but is psychological as well, taking in social relationships, hopes, expectations and spiritual beliefs. Quality of life is relative to individual patients rather than being an absolute assessment, but often
when palliative chemotherapy is offered it is regarded by patients as still striving for length of life. There is often a tendency in palliative cancer treatment for oncologists to focus most attention on discussion of an ‘active’ treatment programme.\textsuperscript{67 68}

\textbf{Balancing Quality of Life Against Length of Life}

We now live in a society where death is no longer considered a natural event but rather an enemy. Once a ‘good death’ was where the dying person was surrounded by their loved ones and died in their own bed peacefully. Death is now regarded as the enemy and the extension of life is seen as worthwhile, even at the loss of quality and function. We now undergo aggressive care, rather than accepting death and taking palliative care.

Do ethics committees examine the effect of treatment rather than the nature of the action that brought that effect?\textsuperscript{69} Should skilled support in other ways, such as emotional support, help patients face the reality of a cancer beyond cure?

\textbf{European Attitudes to Cancer Patients}

When attending oncology conferences in Germany and Austria, and when visiting cancer clinics in those and other European countries, I have found that there is quite a different attitude to cancer patients. Many of the clinics I have visited use art and drama therapy to help a patient express the emotions, fears and concerns that are part of the diagnosis of cancer. In Denmark, a cancer clinic headed by Dr Fin Andersen holds a weekly dance for, as Dr. Andersen remarked, “How can patients get well if they are not happy?”

In 1991, I attended a conference in Moscow and was invited to meet for lunch with Dr. Eugene Stranadko, a leading oncologist in Moscow. This was during the time of the overthrow of communism when hospitals were very poorly funded. I remember there being holes in the walls of the oncology unit.

Dr. Stranadko spoke of having healers working the wards with the patients, particularly prior to surgery. He said he did not believe that this really did anything, but he allowed it as it made the patients feel better.
Whether the healers caused any effect is not the point. Rather, allowing the use of harmless treatments—solely to enhance the patient’s sense of well-being—is very much to the point. I cannot imagine a hospital oncology ward in Australia inviting healers into the wards with the blessing of the oncologists, simply because this makes the patients feel better.

**Cultural Differences in Science and Medicine**

There are strong cultural differences worldwide in our views of science and medicine and, to a large extent, our cultural backgrounds help to define our philosophy.

Lynn Payer, in her book *Medicine and Culture*, examined differences between English, German, French and North American (USA) medicine. She described the French system of medicine as being Cartesian in its love of logic and theory, and as more inclined to emphasise the importance of aesthetic, sexual and psychological concerns. The French have always valued the thinkers of their society. French medicine has long been concerned with the *terrain* of the body, and treatments meant to boost the body’s own resistance to disease have long been practised. Immunotherapy for cancer treatment fits well into the French psyche.

The German medical thinking, however, has romanticism at its core and values feelings rather than thinking. German doctors have always been more holistic in their approach to medicine, and are more inclined to look at the whole rather than just part of the body. A large percentage of German doctors practice homeopathic medicine and the work of Rudolf Steiner is still held in high regard in Germany. Steiner taught that disease was caused by an imbalance between the polarities of the body and that the spiritual world of the body must be healed as well as the physical.

Payer found that British medicine was dominated by a sense of economy. Where French surgeons were disinclined to radical mastectomy because of their sense of aesthetics, the British surgeons leaned towards lumpectomy as it was an easier operation. The British tendency is to equate the cause of disease as being external. Disease was often regarded as a malevolent entity outside the body, owing nothing to the *terrain*. 
Medicine in the USA, however, was found to be aggressive and often invasive, with an overwhelming need to be doing something, often as much as possible. The presence of many self-described ‘type A’ personalities in American medicine appeared to be a result of a difference in the types of students attracted to a medical career. The attraction of being a doctor in the USA was often because of the social and academic prestige. Fear of litigation has influenced much of American medicine, with a need to act being preferable to a watch-and-wait attitude. The ‘more is better’ philosophy of American society is reflected in their medicine.

**Conclusions**

Whether cancer patients are now offered the very best treatments possible remains an issue, not only for the patients but also for the families and the medical teams involved.

Very few significant changes in treatment types and styles have occurred since the advent of chemotherapy. There is no doubt that surgery has improved in many ways, with new guided imaging techniques, and radiotherapy has also improved, yet both still have inherent after-effects and dangers for the patient. Chemotherapy has shown its worth strongly in some of the rarer cancers, yet overall—for the most common cancers—improvement in cure rate or long term survival is depressingly low.

The philosophy of medicine is taught to students in the form of ethics, but it appears to be a dogmatic approach that does not encourage innovation and introspection. New approaches are vigorously opposed and adherence to a standard format is enforced. The medical view remains essentially reductionist and mechanistic.

Consultations do not allow time for a patient’s wants and needs to be truly understood. Visits to the oncologist are timed (Medicare payments are on a time scale) and explanations in relation to treatments rarely involve giving full disclosure, therefore not allowing true informed consent or informed choice by the patient.

The cessation of swearing an oath on admission as a medical doctor may, in the long term, make no difference to the morality of the delivery of medical treatment, or to
the morality of individual doctors. It is, however, an indication of a change in the viewpoint of medicine. Oath taking highlights the serious nature of what is being undertaken, whereas guidelines remain just that—a guide to doing what is allowed and expected, and often, in practice, what one can get away with.

Monetary influences are evident not only in the funding of ethics centres by pharmaceutical companies, but also in the belief of doctors that their acceptance of gifts from companies is not ethically wrong. Doctors are now partially in the employment of government, with Medicare repayments being a central part of their income. They are therefore government employees, rather than being solely advocates for their patients.

The cancer patient, the end-user of oncology practice, is left reliant on the advice of their doctor and on the regulation by government as to best clinical practices. Unfortunately the end-user has little say as to treatments offered, and informed choice for a patient does not fit with our current medical system.

Our Western culture’s view of death and dying encourages dramatic struggles to prolong life, often with little consideration of the quality of life. Quality of life issues should be an integral part of oncology.

The choice of whether to administer treatments with inherent risk to the patient, compared to palliative pain control at the end stages of life, requires a deep understanding of a patient’s beliefs, values, needs and wants, to ensure the best possible treatment for a particular patient. Improving quality of life should be the endpoint aim of palliative cancer therapy. Often quality of life is improved by giving less aggressive treatment.

There is, I feel, a great need for a paradigm shift in oncology. This would—as is the nature of paradigm shifts—be exceedingly difficult in its implementation, but would be extremely beneficial to the cancer patient. The profession of medicine has shown itself to be highly protective of its status and of its monopoly on cancer treatments.
Sadly, the philosophy of medicine, as taught and practiced in most countries, does not appear to have had any great input into changes that have taken place in oncology.

If the physician possesses gentleness of manners, and a compassionate heart, and what Shakespeare called ‘the milk of human kindness’ the patient feels his approach like that of a guardian angel administering to his relief: while every visit of a physician who is unfeeling and rough in his manners, makes his heart sink within him, as at the presence of one who comes to pronounce his doom. Men of the most compassionate tempers, by being daily conversant with the scenes of distress, acquire in process of time that composure and firmness of mind so necessary in the practice of physick.

John Gregory. 73

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26 Faunce TA and Bolsin SN (2003). If doctors don't understand ethics, it's time to start teaching them. Sydney Morning Herald, Sydney.
34 Editor (1993). "Breast cancer: have we lost our way?" The Lancet 341: 343-344.


Chapter 9
Autopoietic Systems—A Biological Analogy

To attempt a deeper understanding of ‘how’ and ‘why’ our system of medicine has brought us to our current situation, I have sought to use the concepts of Maturana and Varela’ in their work on autopoietic theory.

Using the biological theory of Maturana and Varela on living systems—that is, on systems that are self-producing and self-constructing—one may draw comparisons with the social structure of both medicine and the corporate world. The interaction of these two differing types of structure may better elucidate the triggers and events that have led to our current system of oncology.

**Autopoietic Systems**

Living systems are open systems, whereby input from external sources is allowed and expected and causes a response. In closed systems, external influences are not possible. Autopoietic systems, however, have both open and closed qualities.

**The Concept of Autopoiesis**

Luhrmann defined autopoietic systems as systems that use their own output as input and are (in this sense) their own product. Although an autopoietic system does not allow external events to enter and disturb the entirety of the system, it will allow external events to ‘deform’ its autopoiesis. A ‘deformity’ may then induce some form of adaptation within the system. All operations of the system are self-referenced and exist within the confines and boundaries of the system.

The word autopoiesis has been formed through the conjunction of the Greek words auto, meaning self, and poiesis, meaning creation or production.

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* For this section, I will use the term “medicine” to encompass the entirety of the social structure, i.e. medicine, of which oncology is a sub-branch.
The concept of autopoiesis—systems that are self-producing or self-constructing—was developed in the late 1970s by Maturana and Varela, both Chilean biologists, who used the term to describe the nature of living, as opposed to non-living, entities.

In the 1990s, the sociologist Niklas Luhmann applied the concept to society, together with action theory and social systems theory. Luhmann also stressed the difference between psychical and social systems, with social systems operating on a foundation of communication. Social systems evolve, maintain their specific identity and reproduce themselves through their internal communication. They relate to other social sub-systems in the environment through this communication.

**Maintaining Autopoiesis**

Maturana and Varela consider that autopoietic systems are defined by their organisation. Once such a system has been attained, it recursively interacts within itself to maintain its structure.

Maintaining the structure may be equated to maintaining power and control. Whereas an open system must readily adapt to survive, an autopoietic system maintains stability as an ongoing process, providing members of the system with their identity. Even though the members of the system change over time, the system is maintained in its totality rather than as a sum of the individual components.

The structure of such a system must identify anything outside of itself as being non-self, as established by the demarcation of boundaries of the structure.

Gunther Teubner has been a proponent for the interpretation of the legal system as an autopoietic entity. Whittaker (1995) states that this is seen as: ... the application of cybernetic principles to the ongoing debate among legal theorists concerning the status of law as either (a) ‘autonomous’ and ‘self-referring’ or (b) ‘derivative’ of the sociocultural setting in which it is realized.
Language As Communication

Law and government are intrinsically connected, however it is the social and cultural settings that produce the ‘events’ that change the communication boundaries of the legal structure.

Plain English in Legal Texts

The legal system in Australia changed its language because of adverse publicity over many years and public distrust. No longer is modern law written in the Dickensian language of the past. The use of Latin has ceased.

The principle of the Rule of Law is based on the understanding that those affected by a law must be able to ascertain its meaning and effect. This use of plain English has not meant that lawyers are no longer required. Lawyers are needed to interpret law, to understand and search for specific applications and meanings in the law, and to apply law to fact scenarios that have endless computations.

Our society expects to understand documentation and laws that affect our lives. This public need was recognised in 1983 when the Australian Government introduced Plain English and Simpler Forms Programmes. The US, Canadian and British governments all now have plain language policies.10

To produce a text in language that is not contemporary restricts public access; it produces and maintains a hierarchy with the public at the lowest level. This is similar to the ancient guilds, where access to knowledge was restricted to only the few.

The legal profession has adapted and changed the boundaries of its system to ideally allow access to all, at least in the area of terminology. Where law may have been a self-contained, self-reproducing closed system, it has been forced to broaden its language and therefore its boundaries.
In contrast, medicine has yet to do this. The medical language still tends to be mysterious and unintelligible to those who have not studied medicine or a related field.

The legal system has gained operational closure by controlling the concepts of legal/illegal and thus has retained exclusive control of the legal social structure. Laws, incorporating the concept of ‘legal/illegal’, are the basis of the construction and reproduction of their social system.

**Structure of the Medical System**

With medicine the concepts are not quite so clear cut. Medicine is not a system of disease/health: There are many stages in between the two. Cancer patients may be healthy while still having a tumour, and may then become extremely unwell during treatments to kill cancer cells.

Mingers (2004) has outlined two definitive requirements for a system to be autopoietic:

- Autopoiesis is concerned with the processes of production: the production of the components that themselves constitute the system.
- An autopoietic organisation has clear demarcations or boundaries that are constructed and maintained by the system.

The medical system is a total and complete structure, in which medical schools at universities begin the process by training young doctors in very well-established and agreed-upon curricula. There is generally little variation in the teachings in medical schools within a country.

Differences in cultural background cause variations in the forms and data used, but generally medical doctors are easily recognisable as members of a global fraternity. The new doctors may become researchers or clinicians or may, in turn, teach new influxes of students.
The role of medical research is to improve treatments, develop new testing procedures and improve medical techniques, all of which continue in the system as tools of the system.

**Maintaining Autopoiesis by Self-Production**

Medicine has maintained itself as an autopoietic system by its self-referencing and self-production. Medicine as a social system produces and provides treatment, research and more members: more medical practitioners. This means that medicine as a structure imports energy from the environment—bringing in people, government support, diverse resources and so on—then uses this energy to create a product.

The product is the training of new people, the scientific research, the treatments provided, and the energy required to continually maintain the structure and to reproduce these events over and over again. The structure maintains and directs the activities and behaviour of its members.

Such a hierarchical structure allows the discourse of the powerful medical and health system to overrule the voice of the less powerful, the public.\(^{14}\) According to Mingers:

> Organizational closure does not imply interactive closure or isolation from the environment. Clearly organisms do, necessarily, interact with their environment. The point is that such interactions also continue the ongoing process of autopoiesis; otherwise, they would not occur. They form part of a circular, self-sustaining process. The result of organizational closure is autonomy – the organization demarcates itself from its environment and, through its own self-referential processes, maintains its self.\(^ {15}\)

**Boundaries of the Medical System**

Borders and boundaries of the medical structure have been clearly delineated for many years. The members are trained and work within the medical social structure and the structure acts as a totality rather than as a collection of individual members. This gives the structure stability and provides the individual members with their identity.
The boundaries are established through the legal and government acts that define the permitted practitioners of medicine and through the psychological boundaries that are imposed on the members themselves.

The following is taken from my discussions in 2007 with a medical practitioner on the inculcation of such boundaries.

I started medicine after an Arts degree, working and extensive travel. Consequently, medical school was quite a shock. I had expectations that this was a deeply intellectual and spiritual profession, as it needs to be. But, what I experienced was a rigid dogma and closely controlled set of stereotypic practices. In fact, the medicine I was taught is substantially pattern recognition where the patient’s symptoms are fitted into stock responses of investigations and treatments. And, despite the good intentions of many doctors, patients aren’t usually cured of their illness. Rather, their symptoms are managed and a doctor documents their decline into worse health.

The 50 billion dollar question is why do these highly educated professionals adhere to the dogma and continue often unsuccessful patterns of behaviour when there are many successful alternative treatments described in the scientific literature? One reason is Medicare and its support for brief consultations. Five to fifteen minutes isn’t enough time to do a thorough history, examination or treatment. It’s only time to have a stock response.

Another reason is pervasive fear. I began to experience in my first years of med school a free-floating anxiety. In part, this was a fear around competence and my ability to memorise the long lists of information so I wouldn’t kill patients. However, there was a second fear and this almost stopped me from practising altogether on a number of occasions. This is the well-based fear that if I don’t follow the prescribed pattern of investigations and treatments then if anything went wrong I’d be abandoned by my profession and medical insurance. And conversely, if I did follow them it’s unlikely there’d be any adverse consequences for me.

The fear of medico-legal problems or investigation by the medical profession and government regulatory bodies effectively stops doctors from critiquing the profession or stepping outside its dogma and narrow practices. Little wonder doctors are so conservative and protective of their own.16
The induction of such anxiety to remain within the safety of the system is a very powerful boundary—it controls and enforces the need to conform and maintain dogma. Unfortunately it also stifles innovation.

**Self-Regulation Within the Medical Structure**

The medical structure self-regulates, with the legal demarcation of its powers fixed by Acts of Parliament, each State enacting its own Medical Practice Act.\(^\text{17}\)

Complaints about medical practitioners, such as unsatisfactory professional conduct, which can cover many situations, are dealt with in Australia by the Medical Board or the Health Care Complaints Commission. Serious complaints are dealt with by the Medical Tribunal. The Commission and Tribunal have the power to caution, reprimand, counsel, fine, suspend or deregister the practitioner. An appeal of a Committee’s decision is heard by the Tribunal, but an appeal of the Tribunal’s decision must be taken to the Supreme Court.

The regulatory capacity of this system replaces many of the normal legal situations for other members of our society, and shows the strength and power of the medical system to control its own fate and that of its members.

The British Columbia College of Teachers has published a monograph, *Understanding Professional Self-Regulation in British Columbia*, that provides two examples of definitions for self-regulating professions.\(^\text{18}\)

The first example, from Ryan and Cooper’s book *Those Who Can, Teach*, 1988, states that a self-regulating profession:

1. Renders a unique, definite and essential service to society. Only people in the particular profession can render the service, and the service rendered is considered so important that it is available to all people in a society.
2. Relies on intellectual skills in the performance of its service.
3. Has a long period of specialised training.
4. Provides both individual members of the profession and the professional group with a considerable degree of autonomy and decision-making authority.
Professional groups regulate their activities rather than having outsiders set policies and enforce adherence to standards.

5. Requires its members to accept personal responsibility for their actions and decisions.

6. Emphasises the services rendered by its partners more than their financial rewards.


8. Has a code of ethics that sets out the acceptable standards of conduct for its members.

The second example, from Michael Doherty of the BC Public Interest Advocacy Centre, states that:

(Professionals are) those who are willing to accept the honour, status and other benefits of the designation (of professional) in exchange for which they agree to place the welfare of those whom they serve foremost and to avoid any conflicting biases of confounding relationships. (Emphasis added by the BC College of Teachers.)

**Is Self-Regulation in Medicine Working?**

There have been failures in medicine relating to both the above definitions. According to Ryan and Cooper’s first point, medicine should provide an essential service that is available to all members of society. In sections of our society, certain groups—because of poverty—are denied the same access to treatment that is available to wealthier groups.

With respect to the fifth point, although the profession may ‘expect’ that its members will accept responsibility for their personal actions, in many cases, where monetary gain has been involved, this has not been the case.

In this regard, the quote from Doherty is particularly applicable to members of the medical profession, as a reminder of how to behave when confronted by monetary offers and ‘gifts’ from industry.
History of Medicine as a Profession

The establishment of medicine as a profession began with the institution of university medicine in the 1400s. A parliamentary act in 1815 in the UK recognised surgeon-apothecaries as general practitioners. The Medical Reform Act of 1858 then created a council that oversaw all medical practice in the UK, stipulating that only universities and the established corporations of surgeons, apothecaries and physicians could grant medical licences.19

Such decision making has been strongly held by the profession, which has control over most of the legal, economic and institutional areas of medical care. This control has also extended to influencing the decisions made by associated entities, such as hospitals, medical schools, private health insurers, other health care practitioners and government agencies (as discussed in previous chapters).

Suppressing the Competition

The issue of the medical profession’s control of its own structure and its self-replication—as in the certification of medical specialists—has potentially suppressed the emergence of competing sources of information by restraining the production and dissemination of ‘other’ information.

This suppression has been possible through the assumption that the medical profession knows best what society’s needs are and how they should be managed.20 This then leads into potential areas of legal wrong-doing, such as anti-trust laws in the USA and anti-competition laws in Australia.

Abuse of Privilege

The latter part of the 20th century has witnessed abuse by the medical profession in its privileged status and public trust, and in the flaws exposed in its regulatory processes, as described by Cruess in 2005:

Medicine was further criticized by the lack of openness and transparency in regulatory procedures and for the absence of public involvement in them. In short, the system appeared to lack accountability.21
A 2005 editorial in the British Medical Journal (BMJ) stated that the General Medical Council (GMC) of Britain has:

... broken its contract with the public—to protect patients in exchange for the privilege of self regulation... 22.

The editorial referred to an analysis of the situation by the last president of the GMC, Sir Donald Irvine, who critically stated that:

The culture is wrong. It is reactive rather than proactive, prefers that doctors should be trusted rather than held accountable, places consensus before leadership, is driven by expediency and compromise, and in the last analysis will put fairness to doctors ahead of patient protection.

**Dealing with Offenders**

The self-regulating capacity of the medical profession is evident in the handling of offences committed by a member of the medical profession. Most offences are dealt with internally, rather than in other venues such as legal courts, as set out by the Medical Practitioner Acts (State Acts). The Medical Tribunal is the body that deals with serious complaints; only when an appeal is made on a decision of the Medical Tribunal is the matter taken to the Supreme Court.

**Negative Response to Whistleblowers**

The effectiveness of the profession to self-regulate has been criticised, particularly when external reviews of the adequacy of health care in hospitals have been initiated. Reviews initiated by whistleblowers—all of whom were treated poorly because they sounded the alarm—were held at the following hospitals:

- The Bristol Royal Infirmary Paediatric Cardiac Surgery Inquiry, 23
- The Winnipeg paediatric cardiac surgery scandal. 24
- The Camden and Campbelltown hospitals (NSW), the Canberra Hospital (ACT) and the King Edward Memorial Hospital (WA). 25

The protective position of many in the medical profession toward whistleblowers stems from beliefs instilled in medical school.
Medical School Encouraging a Guild Mentality

A 2003 study of medical students’ attitudes found that—when students were challenged with identical ethical problems in their first and final weeks of a four-year medical course—there was no increase in ethically correct decisions being made. There was a 40% correct response at both beginning and end of four years of ethics training.

More disturbing, however, is that although only 13% of students at the beginning of the course confirmed that they would report unethical behaviour, by the end of four years of training this figure had dropped to less than 5%.26

What we can recognise here is a profession, and structure, that consciously and habitually seeks to maintain a guild-style mentality, where devotion to and protection of other guild members, and their shared organisation, takes precedent over the needs of the patient. This establishes and maintains boundaries of the structure and attempts to internalise any regulation.

There appears to have developed in medicine a culture of ‘us’ and ‘them’ that is very similar to the police culture exposed in Queensland by the Fitzgerald Inquiry of 1989. Fitzgerald found that there was an unwritten police code that allowed misconduct to flourish. This code exaggerated the need for and benefits of mutual loyalty and support. The code meant that police could not be criticised by anyone outside the police force and that “police [could] not enforce the law against other police, nor co-operate in any attempt to do so, and perhaps even obstruct any such attempt.”27

Structural Coupling

‘Structural coupling’—in which social sub-systems are linked through the sharing of selective communications—occurs when ‘deformities’ or ‘irritations’ from their environment or from another social sub-system impinge upon the system.28
Structural Coupling with the Pharmaceutical Companies

Medicine has formed a permanent structural coupling with the pharmaceutical companies. There is a common language that is shared, yet the aspirations and central thrust of each of these structures is intrinsically different.

The social system of medicine has developed in response to the greater environment’s need for health management. The ‘need’ is for people to be cured, for help with pain management, for diagnosis and prevention of disease. The science of medicine is engaged in research into these areas for a greater understanding of cause and effect, for the understanding of cellular processes, all ultimately aimed towards the benefit of the people within the greater social structure.

The ‘need’ or aim of a corporation, however, is not only the self-maintenance of the corporation, but also for the production of the wealth of that corporation. This production of wealth is of benefit to the ‘members’ of this social structure, that is, to the owners (share-holders) and staff employed by the structure. The requirement that profit is the end goal of the corporation places economic rationality in an inflated position. The need for profit downgrades other concerns that are important for the healthy functioning of a corporation, such as workers’ health and well-being, critical participation by all members of the corporation, and care for the environment.29

Effects of Divergent Goals of Medicine and Pharma

When two autopoietic systems are structurally coupled over a period of time, they affect one another’s structures and consequently also the behaviour they both manifest.30

If medicine had developed into a discrete autopoietic system it could self-replicate, self-maintain and self-regulate, because the goals for this system would be shared by the entire system. However, when medicine became structurally coupled with systems that have a variance in goal, this variance created a ‘deformity’ or ‘irritation’ deep within the medical social system. The system then adapted to the deformity without changing its structure irrevocably. Thus the divergent goals caused extensive changes in the system’s structure.
The coupling of medicine and commerce has progressed to a level where ‘medicine’ is dependent upon commerce for a large percentage of its funding. This funding produces research and new products—products that should be solely in the domain of the manufacturers. The funding is also needed to run and maintain the medical system.

Without funding from industry, many medical schools could not survive. Industry funding pays for many research projects; it pays for a large part of medical continuing education; and it rewards doctors for prescribing products that increase profits for the companies.

When an autopoietic system reaches the stage where the benefit of internalising change does not outweigh the detriment, it must either change or collapse. With the declining government responsibility for the funding of medical schools and research centres, the medical system has chosen to change by seeking alternative funding rather than collapse. The benefits to industry of this opportunity to increase its influence and control are obvious—they can be seen within their ledgers in increased profit margins. As a result of this changed situation, it seems likely that the benefits to society might be compromised. Whether this change will be beneficial for the greater society and whether this change will continue to maintain the medical structure is yet to be thoroughly examined and evaluated.

**A Biological Analogy**

This comparison of the medical system as a living system enables us to view it as an autonomous entity. Thus, as an autopoietic structure, the medical system has established itself in our society with its own carefully set boundaries, as a self-regulating and self-maintaining structure. Because of this, it will require major deformations to its structures and processes to bring about the sort of transformative change that would make an innovative structural shift.

**Parasitisation by Industry**

The incorporation of industry, the pharmaceutical companies, into this self-maintaining system is eroding its autopoietic nature. In biological systems, this can be seen when cells and organisms become parasitised.
The parasite derives benefits from its association with the host cell. Facultative parasites can survive both in the host and as a free form. If they induce harm in the host they are termed *pathogenic*. Parasites are referred to as *commensals* when the relationship is symbiotic, when there is some mutual benefit to those involved.\(^{37}\)

A host and parasite may co-evolve to maintain a relationship that does not kill the host, as this would also be detrimental to the parasite. Generally, however, the parasite causes harm to the host, even if the harm is subtle. The host and the parasite may be forced over time to modify their behaviour to survive.

**Conclusions**

How long a parasitised structure (or cell) can survive is dependent on many factors. In a social setting, the change induced in a structure by relinquishing much of its autonomy to an external body may cause perturbations to the structure, and may even change the structure’s intrinsic quality and nature. This would certainly appear to be the case with the expanding intrusion of the pharmaceutical industry into the medical system.

The basic nature of an industry or corporate structure is one of a commercial, money-producing system. The ideal nature of the medical structure, however, is one where the output—the research and practice of medicine—has as its goal the prevention and treatment of disease for the benefit of the greater environment, the people.

As presented here, it is clear that the current medical system is increasingly a money-making venture. The amount of money to be made in oncology is enormous. Billions of dollars can be made from one ‘block-buster’ drug, for example, and cancer patients may be prescribed many such drugs.

Money as a central theme may be the unfortunate end result for a system that has changed its ‘intrinsic quality and nature’. This ongoing transformation of the medical system has resulted from having its core co-opted by an external system that has money-making as its goal.
When two systems with divergent goals and different levels of power merge, it is predicted that the more powerful will increasingly determine the nature of the less powerful partner. Thus, in this case, the financial goal is overpowering the altruistic goal of equitably serving the health needs of the population.

26 Goldie J, Schwartz L & McConnachie A (2003), 'Students' attitudes and potential behaviour with regard to whistleblowing as they pass through a modern medical curriculum', *Medical Education* 37: 368-75.
CONCLUSIONS

What factors have shaped the theory and practice of oncology today? What factors have led to today’s dominant forms of treatment? To what extent has it been the result of research by well-intentioned investigators; to what extent has economics influenced both the outcomes and the areas where money has been spent; and how has the resultant medical philosophy affected the field of oncology?

In an ideal situation, research findings should guide fields of enquiry that are systematically explored, followed or rejected, and these findings should enable the adoption of the best possible treatments. Ideally these treatments should extend the life expectancy of cancer patients, be humane and generally support good health. However, because the ultimate form of cancer treatment is prevention, this is logically where most research needs to be occurring.

My study has, I believe, clearly shown that cancer research—in the past and present—is far from the ideal scenario. The following research findings support this conclusion. Supporting references are provided throughout the thesis.

Indicative Research Findings

- Long-term survival rates for the most common cancers have not substantially improved over the last century. In fact, mortality rates in the USA increased between 1970 and 1994 by 6.0%.
- The incidence of cancers in the world is increasing. Cancer statistics do not reflect the common misclassification of cancer deaths and the declining use of autopsy. Correct classification and routine autopsy would increase published cancer death rates.
- Prevention has not received, and is not receiving, the emphasis needed to address this increase. Furthermore, prevention is commonly confused with early detection.
- Potential ‘alternative’ cancer treatments—such as herbal remedies, Traditional Chinese Medicine (TCM), Ayurvedic, nutritional medicine, mistletoe therapy and ECT (electrochemical therapy)—have received little...
serious study by the conventional medical establishment. Their ‘alternative’ label has generally been used to relegate them to the fringes of science and, largely because of this, they have been ignored.

- Modern day conventional treatments have shown no statistical advantage over the use of Coley’s toxins. Other similar treatments—employing bacterial isolates by scientists such as Glover, Livingston-Wheeler and others—have shown encouraging results, but they have not been examined in clinical trials for efficacy.

- Micronutrient use in combination with radiation therapy, and hyperthermia in conjunction with chemotherapy, may both have potential in future treatment protocols, yet these approaches are still largely being ignored in current treatment procedures.

- Research into the diverse causes of cancer—such as bacterial induction—has been largely neglected and has not been adequately used by conventional oncology.

- Surgical techniques and radiation therapy, on the other hand, have improved over the last century. However, over the last 60 years the focus has centred on chemotoxic drugs and, more recently, on monoclonal antibodies and other biological agents—even though 5-year survival studies with the most common cancers, being treated only with chemotherapy, resulted in just 2.3% of patients benefiting in Australia and 2.1% in the USA.

- Recent research has indicated that, in the common cancers, the presence of cancer stem cells may provide one explanation for the poor response to chemotherapy regimes. Will these new findings provide enough stimuli to induce a paradigm shift in the way most cancers are treated?

**Indicative Economics Observations**

- It must be understood and acknowledged that industry (Pharma) has as its primary goal the production of profit for shareholders. It is naïve to expect that this industry’s main aims are to service the community and act altruistically with respect to patient wellbeing.
When trials are funded by Pharma, research findings may be suppressed or delayed if results are counter to these economic priorities of industry. Pharma-funded trials with their products have been found to be more likely to show a positive outcome than independent trials on the same products.

The common practice of Pharma hiring professional science writers to ghost write research papers has created problems for journals and raised issues as to the validity of published studies.

Pharma funds many universities and corporate ties are held by significant numbers of academics—many of whom become shareholders—raising issues of conflict of interest. This extends to the funding of continuing medical education and bioethics centres. This affects the medical system at its core.

Pharma funds advertising in medical journals. Indeed, it is becoming increasingly difficult to find journal reviewers who do not have a conflict of interest because of industry connections.

Pharma regularly gives ‘gifts’ to doctors to encourage the use of their products. This does not support ‘best medical practice’.

Strong links have developed between Pharma and government bodies at state, national and international levels. The movement of personnel between Pharma and regulatory bodies, in particular, links industry and government in ways that may encourage bias and minimise constraint.

**Indicative Philosophy Observations**

Ethics is a sub-set of philosophy, not a philosophy in itself. The medical structure has tended to substitute ethics for a ‘philosophy of medicine’. There has been a de-emphasis on the use of oaths as an enforcement of the bond and contract between doctor and patient. This failure to take an oath shows that the medical mindset is, at least to some extent, on other things. The oath is a ‘spiritual’ binding or a binding by sanctions. Lack of enforcement of the seriousness or, indeed, any ‘spiritual’ side of medicine becomes a reflection of Pharma being just a business. This does not support and encourage the concept of medical doctors being ‘in the service of humanity’.
Our medical system is limited by ‘received beliefs’—dogmas—making most innovation difficult to accomplish within our current system. Significant beneficial change would require a major paradigm shift.

- Although current ethics guidelines may stop some unwarranted treatment, they do not necessarily promote a genuine informed ‘choice’ among therapies for patients.

- Inadequate time allotment for consultations (merely sufficient to prescribe a curative drug rather than investigate and address the causes) do not allow for deep understanding of a patient’s long-term and holistic needs. All Medicare payments are ‘time-scaled’.

- Many of the treatments that are commonly given lower the quality of life of cancer sufferers and some may induce further tumours and result in other negative consequences.

- Interestingly, a study by Abel (see Chapter 3, History of Cancer Research: Cause and Treatment, page 59) indicated that some oncologists stated that they would refuse chemotoxic treatments if they themselves were diagnosed with cancer.

**In Conclusion**

There is no disputing the wealth, political influence and power of today’s pharmaceutical companies over the theory and practice of oncology. Indeed, they are amongst the most influential and wealthiest of all industries.

We should have no expectation that the pharmaceutical companies will not do their utmost to make large profits. However, we should expect them, if only because of regulations, to pursue profits legally and ethically. The many cases of corporate malfeasance in Pharma would indicate that the drive for profit commonly compromises ethics. It is naïve for those in the medical system not to realise that industry has any greater motive other than the making of money.

There is now no area of medicine that Pharma has not infiltrated. The medical structure may have been able to resist this push from industry if there had been a strong enough philosophical base when our ‘health services’ and systems were first
established. However, once the core of the medical structure had been infiltrated, the entire structure became increasingly compromised.

The concepts of autopoiesis and structural coupling provide a framework for further research into the increasing integration of medicine and industry. Both oncology and the medical system have boundaries that are maintained to exclude and constrain any threats to the status quo or progressions from it. Medicine has put in place these boundaries—legal boundaries via legislation as well as psychological boundaries—to constrain and maintain unquestioning compliance.

The structural and procedural coupling of oncology and the pharmaceutical industry has produced a parasitised structure that has two very divergent goals.

Patients naively rely on a system in which their welfare, health and survival is the ultimate goal. Monetary, profit-making goals have been shown to be detrimental to this patient goal. When industry-funded trials give a higher percentage of positive outcome than independent trials, because of manipulation of the results, then the patient receiving therapy based on industry-funded research may be at risk. At the very least, the suppression of research that questions the dogma of the day has cost us many decades in which potential treatments and identification of causes could have been thoroughly explored.

My research has focused on systems and structures, with individual cases being provided as examples of pathology within the larger system of science and oncology/medicine. For those medical practitioners who read this, I would like to stress that the problems appearing in the basic functions of oncology are largely systems problems and not ‘failures of physicians’. I am not inferring that oncologists lack compassion and care but rather that they are operating within a system in which their choice of treatments are limited and, as a result, are not generally successful. I believe that most young doctors commencing their oncology specialisation do so with a genuine desire to palliate suffering and to cure cancer. Unfortunately the system does not adequately support this desire and does not enable doctors to put their patients’ needs above all else.
The purpose of this research was not to provide a detailed or definitive analysis of cancer research, treatment and philosophy. Rather it was designed to offer an overview of these areas using individual cases to illuminate problems within the dominant system.

The biological analogy of autopoietic systems and structural coupling provides a basis for further analysis and understanding of these connections. A deeper understanding of these issues will, I believe, allow for progressive change to occur and for research findings to become the true arbiter of directional change in cancer theory and practice.
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APPENDIXES
Appendix 1

World Medical Association: Declaration of Helsinki

Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000
Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002
Note of Clarification on Paragraph 30 added by the WMA General Assembly, Tokyo 2004

A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

1. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

2. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

3. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

4. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

5. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

6. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.
7. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

8. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

9. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

10. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

11. The subjects must be volunteers and informed participants in the research project.

12. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

13. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

14. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

15. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
16. When a subject deemed legally incompetent, such as a minor child, is able
to give assent to decisions about participation in research, the investigator
must obtain that assent in addition to the consent of the legally authorized
representative.

17. Research on individuals from whom it is not possible to obtain consent,
including proxy or advance consent, should be done only if the
physical/mental condition that prevents obtaining informed consent is a
necessary characteristic of the research population. The specific reasons for
involving research subjects with a condition that renders them unable to
give informed consent should be stated in the experimental protocol for
consideration and approval of the review committee. The protocol should
state that consent to remain in the research should be obtained as soon as
possible from the individual or a legally authorized surrogate.

18. Both authors and publishers have ethical obligations. In publication of the
results of research, the investigators are obliged to preserve the accuracy of
the results. Negative as well as positive results should be published or
otherwise publicly available. Sources of funding, institutional affiliations
and any possible conflicts of interest should be declared in the publication.
Reports of experimentation not in accordance with the principles laid down
in this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED
WITH MEDICAL CARE

1. The physician may combine medical research with medical care, only to the
extent that the research is justified by its potential prophylactic, diagnostic
or therapeutic value. When medical research is combined with medical care,
additional standards apply to protect the patients who are research subjects.

2. The benefits, risks, burdens and effectiveness of a new method should be
tested against those of the best current prophylactic, diagnostic, and
therapeutic methods. This does not exclude the use of placebo, or no
treatment, in studies where no proven prophylactic, diagnostic or therapeutic
method exists.

3. At the conclusion of the study, every patient entered into the study should
be assured of access to the best proven prophylactic, diagnostic and
therapeutic methods identified by the study.

4. The physician should fully inform the patient which aspects of the care are
related to the research. The refusal of a patient to participate in a study must
never interfere with the patient-physician relationship.

5. In the treatment of a patient, where proven prophylactic, diagnostic and
therapeutic methods do not exist or have been ineffective, the physician,
with informed consent from the patient, must be free to use unproven or
new prophylactic, diagnostic and therapeutic measures, if in the physician's
judgement it offers hope of saving life, re-establishing health or alleviating
suffering. Where possible, these measures should be made the object of
research, designed to evaluate their safety and efficacy. In all cases, new
information should be recorded and, where appropriate, published. The
other relevant guidelines of this Declaration should be followed.
Note: Note of clarification on paragraph 29 of the WMA Declaration of Helsinki

The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or
- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

Note: Note of clarification on paragraph 30 of the WMA Declaration of Helsinki

The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.

The Declaration of Helsinki (Document 17.C) is an official policy document of the World Medical Association, the global representative body for physicians. It was first adopted in 1964 (Helsinki, Finland) and revised in 1975 (Tokyo, Japan), 1983 (Venice, Italy), 1989 (Hong Kong), 1996 (Somerset-West, South Africa) and 2000 (Edinburgh, Scotland). Note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002.

9.10.2004
Appendix 2

Hippocratic Oath—Classical Version

I swear by Apollo Physician and Asclepius and Hygieia and Panaceia and all the gods and goddesses, making them my witnesses, that I will fulfil according to my ability and judgment this oath and this covenant:

- To hold him who has taught me this art as equal to my parents and to live my life in partnership with him, and if he is in need of money to give him a share of mine, and to regard his offspring as equal to my brothers in male lineage and to teach them this art - if they desire to learn it - without fee and covenant; to give a share of precepts and oral instruction and all the other learning to my sons and to the sons of him who has instructed me and to pupils who have signed the covenant and have taken an oath according to the medical law, but no one else.
- I will apply dietetic measures for the benefit of the sick according to my ability and judgment; I will keep them from harm and injustice.
- I will neither give a deadly drug to anybody who asked for it, nor will I make a suggestion to this effect. Similarly I will not give to a woman an abortive remedy. In purity and holiness I will guard my life and my art.
- I will not use the knife, not even on sufferers from stone, but will withdraw in favor of such men as are engaged in this work.
- Whatever houses I may visit, I will come for the benefit of the sick, remaining free of all intentional injustice, of all mischief and in particular of sexual relations with both female and male persons, be they free or slaves.
- What I may see or hear in the course of the treatment or even outside of the treatment in regard to the life of men, which on no account one must spread abroad, I will keep to myself, holding such things shameful to be spoken about.
- If I fulfil this oath and do not violate it, may it be granted to me to enjoy life and art, being honored with fame among all men for all time to come; if I transgress it and swear falsely, may the opposite of all this be my lot.

(Translation from the Greek by Ludwig Edelstein. From The Hippocratic Oath: Text, Translation, and Interpretation, by Ludwig Edelstein. Baltimore: Johns Hopkins Press, 1943.)
Appendix 3

Pledge—World Medical Association

AT THE TIME OF BEING ADMITTED AS A MEMBER OF THE MEDICAL PROFESSION:

- I SOLEMNLY PLEDGE TO CONSECRATE MY LIFE TO THE SERVICE OF HUMANITY
- I WILL GIVE to my teachers the respect and gratitude that is their due;
- I WILL PRACTISE my profession with conscience and dignity;
- THE HEALTH OF MY PATIENT will be my first consideration;
- I WILL RESPECT the secrets that are confided in me, even after the patient has died;
- I WILL MAINTAIN by all the means in my power, the honour and the noble traditions of the medical profession;
- MY COLLEAGUES will be my sisters and brothers;
- I WILL NOT PERMIT considerations of age, disease or disability, creed, ethnic origin, gender, nationality, political affiliation, race, sexual orientation, social standing or any other factor to intervene between my duty and my patient,
- I WILL MAINTAIN the utmost respect for human life;
- I WILL NOT USE my medical knowledge to violate human rights and civil liberties, even under threat;

I MAKE THESE PROMISES solemnly, freely and upon my honour.

Appendix 4

Hippocratic Oath—Johns Hopkins University

I do solemnly swear ... by that which I hold most sacred ...

That I will be fully committed to those I serve ... and just and loyal to the profession of medicine and its members ...

That I will lead my life ... and practice my art ... in uprightness and honor ...

That into whatsoever house I shall enter ... it shall be for the good of the sick ... to the utmost of my power ... holding myself aloof from wrong ... from corruption ... and from the tempting of others to vice ...

That I will exercise my art ... solely for the care of my patients ... and will give no drug ... and perform no operation ... without justifiable purpose ... far less suggest it ...

That whatsoever I shall see or hear ... of the lives of men and women ... which is not fitting to be spoken ... I will keep inviolably secret ...

These things I do promise ... and in proportion as I am faithful to this my oath ... may happiness and good repute be ever mine ... the opposite if I shall be forsworn.
For Oncology Professionals
Clinical Data: GEMZAR for Ovarian Cancer

Pivotal Phase III Trial
GEMZAR was studied in a randomized phase III study of 356 patients with platinum-sensitive¹ advanced ovarian cancer. Patients were randomized to receive either GEMZAR plus carboplatin or single-agent carboplatin as the control arm.

Randomization Schema and Dosing
Pivotal trial design: Randomized phase III study (N=356)

Primary Endpoint
Progression-free Survival

Secondary Endpoints
Overall response rate
Duration of response
Overall survival
Toxicity

GEMZAR Plus Carboplatin Versus Carboplatin in Ovarian Cancer
Baseline demographics and clinical characteristics

<table>
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<th></th>
<th>GEMZAR/carboplatin</th>
<th>Carboplatin</th>
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<td>Median age, years</td>
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</tr>
<tr>
<td>6-12 months</td>
<td>39.9%</td>
<td>39.9%</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>59.0%</td>
<td>59.6%</td>
</tr>
<tr>
<td>First-line therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platinum-taxane combination</td>
<td>70.2%</td>
<td>71.3%</td>
</tr>
</tbody>
</table>

¹ Platinum-sensitive patients are defined as those who develop disease progression at least 6 months after completion of a platinum-based chemotherapy regimen.
² Nine patients, (5 on the GEMZAR plus carboplatin arm and 4 on the carboplatin arm) did not have baseline Eastern Cooperative Oncology Group (ECOG) performance status recorded.
³ Three patients (2 on the GEMZAR plus carboplatin arm and one on the carboplatin arm) had a platinum-free interval of less than 6 months.
<table>
<thead>
<tr>
<th>Platinum-nontaxane combination</th>
<th>28.7%</th>
<th>27.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum monotherapy</td>
<td>1.1%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

In the GEMZAR plus carboplatin arm, dose reductions occurred with 10.4% of GEMZAR injections and 1.8% of carboplatin injections vs 3.8% on the carboplatin arm. 13.7% of GEMZAR doses were omitted and 0.2% of carboplatin doses were omitted compared to 0% of the carboplatin doses on the carboplatin arm. There were no differences in discontinuations due to adverse events between arms (10.9% vs 9.8%, respectively).

**Superior Progression-Free Survival**

GEMZAR/carboplatin offers superior progression-free survival (PFS) and superior response rates over carboplatin alone, providing better disease control\(^4\) with a generally manageable toxicity profile. The addition of GEMZAR to carboplatin resulted in a statistically significant improvement in PFS (nearly 3 months), overall response rate, and complete response rate when compared to carboplatin alone.

**Kaplan-Meier Curve of Progression-Free Survival**

Hazard ratio = 0.72 (95% CI [0.57, 0.90])

**Progression-Free Survival**

GEMZAR in combination with carboplatin offered 49% improvement in PFS vs. carboplatin alone.

**Overall Response Rate**\(^5\)

There was a 53% improvement in overall response rate.

**Complete Response Rate**\(^6\)

The combination of GEMZAR/carboplatin doubled the complete response rate when compared to carboplatin alone.

Overall survival difference between GEMZAR/carboplatin (18.0 months) vs carboplatin (17.3 months) was not significant (\(p=0.8977\)).

**Generally Manageable Toxicities**

The combination of GEMZAR and carboplatin is an effective regimen for the 2nd-line treatment\(^7\) of platinum-sensitive advanced ovarian cancer with generally manageable toxicities.

**Adverse Events from Comparative Trial of GEMZAR Plus Carboplatin Versus Single-Agent Carboplatin in Ovarian Cancer**\(^8\)

CTC Grades (% incidence)

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\(^4\) Disease control is defined as the combination of response rate and progression-free survival outcome.

\(^5\) Investigator-reviewed.

\(^6\) Data on File, Eli Lilly and Company. ONC20060627.

\(^7\) Second-line treatment is defined as treatment given to a patient who has not yet been treated for her first recurrence.

\(^8\) Grade based on Common Toxicity Criteria (CTC) Version 2.0 (all grades ≥10%).
Changes in Cancer Research: Research Findings, Economics, Philosophy  
Jennie Burke – April 2007  
Appendix 5 – GEMZAR Phase III Trial

<table>
<thead>
<tr>
<th></th>
<th>GEMZAR plus carboplatin N=175</th>
<th>Carboplatin N=174</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades</td>
<td>Grade 3</td>
</tr>
<tr>
<td>Laboratory³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematologic Anemia</td>
<td>86</td>
<td>22</td>
</tr>
<tr>
<td>RBC transfusion¹⁰</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>90</td>
<td>42</td>
</tr>
<tr>
<td>Febrile neutropenia¹¹</td>
<td></td>
<td>1.1</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>86</td>
<td>48</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>78</td>
<td>30</td>
</tr>
<tr>
<td>Platelet transfusion¹²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-laboratory¹³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>49</td>
<td>0</td>
</tr>
<tr>
<td>Neuropathy-sensory</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>69</td>
<td>6</td>
</tr>
<tr>
<td>Fatigue</td>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>46</td>
<td>6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26</td>
<td>3</td>
</tr>
<tr>
<td>Anorexia</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Stomatitis/pharyngitis</td>
<td>22</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Constipation</td>
<td>42</td>
<td>6</td>
</tr>
</tbody>
</table>

There were no differences in discontinuations due to adverse events between arms (10.9% versus 9.8%, respectively).

G-CSF was not used prophylactically in this trial. Actual use: 23.6% and 10.1%, respectively.

Myelosuppression is usually the dose-limiting toxicity with GEMZAR therapy.

See the complete Warnings, Precautions, Adverse Reactions, and Dosage and Administration sections in the full Prescribing Information for safety and dosing guidelines.

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For more information about cancer, contact your doctor or other healthcare professional.

MG28487

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9 Percent of patients receiving transfusions. Transfusions are CTC-graded events. Blood transfusion included both packed red blood cells and whole blood.

10 Regardless of causality.

11 Grade based on Common Toxicity Criteria (CTC) Version 2.0 (all grades >1% and ≤10%).

12 Regardless of causality.

13 Percent of patients receiving transfusions. Transfusions are CTC-graded events. Blood transfusion included both packed red blood cells and whole blood.