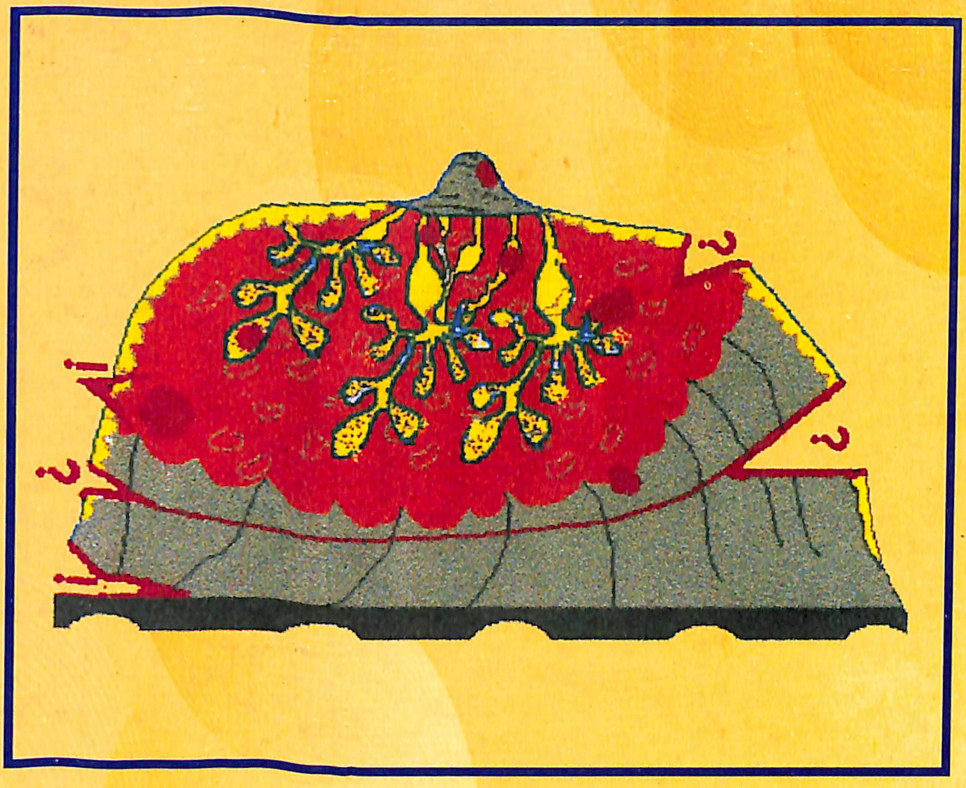
POLITICAL ECONOMY OF (BREAST) CANCER



STHABIR DASGUPTA

CADEMY OF SOCIAL SCIENCES

Breasts that are symbols of beauty, sexuality and nurturing, sometimes are troublesome organs that threaten women's lives. This occurs when cancerous diseases manifest themselves in the breasts. Breasts, of course, are not the exclusive preserves of the women only, but the beauty, sexuality and nurturing are. This is the reason why, despite male breast cancer being more dangerous, when we talk about breast cancer we have the women in our mindset. Moreover, women's health is one of the important parameters in the evaluation of the state of health of a society. This is also the reason why, so much myths have developed around breast cancer. Some examples from among the hordes of such myths are: Breast Cancer Is A Genetically Hereditary Disease; Oral Contraceptive Pills Cause Breast Cancer; If a Breast Lump is Painful, Then it is Not Cancerous; The Best Place To Practice Breast self-examination (BSE) Is In The Shower; Women Who Have Had Breast Cancer In The Past Should Not Become Pregnant, and so on and so forth. Myths are cooked by the media, media are fed by the industries, industries maintain sometimes holy and at other times unholy relationship with the scientists, scientists have got to publish or to perish, and the clinicians who are at the ground level seem to be perplexed. They do not find specific answers to the point blank questions from their patients. The patients, therefore, remain more perplexed. Meanwhile, cancer as a phenomenon, and particularly breast cancer as a perplexing phenomenon is playing havoc. In 1900, cancers caused 3 per cent of all deaths. Now it is more than 33% and, is still rising! As the death rate from cancer rises, so does the rate of diagnosis. Today, 10 million new cancer cases are diagnosed globally each year, and the figure is expected to rise to 20 million by the year 2020. A comprehensive estimation of the overall incidence and mortality in cancer, done in 2000 showed that there has been 22% increase as compared to 1990. What is more disturbing to note is that 70% of these patients will live in countries that between them will have less than 5% of the resources for cancer control. Since health related reliable statistics in our country are difficult to obtain, the precise state of cancer care can only be assumed; but in the other developed countries such as U.K. over one third of hospital beds are already occupied by cancer patients. The figures are: 30% in 1980, 40% at present, and the estimated figures for 2010 is 50%. If similar rates of increase remain the same then in 2080 the figure will be 100%!

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BY

STHABIR DASGUPTA

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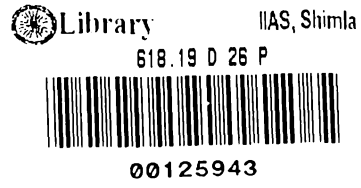

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IN MEMORY

OF

LATE PROFESSOR RAJAMMAL P. DEVADAS,

THE FORMER PRESIDENT

OF

THE INDIAN ACADEMY OF SOCIAL SCIENCES

WHO

ALL HER LIFE STRUGGLED FOR IMPROVING

THE QUALITY OF LIFE AND HEALTH

OF

THE OPPRESSED AND DOWNTRODDEN

PEOPLES OF INDIA

AND

REMAINED A STRONG PROTAGONIST OF

'HEALTH FOR ALL' TILL SHE BREATHED LAST

FOREWORD

Science is in crisis. The crisis in science is deepening day by day. What does it mean? Science means knowledge as well as method or methods by which knowledge is acquired. As a knowledge science means objective knowledge of a thing or an object or an individual or a society. To be precise science is a **mirror** of Nature-Man-Society. It has no colour, no weight, and no size of its own. However, science does reflect colour, weight and size of the thing/object/individual/society correctly and precisely. 'Crisis in science' or 'science is in crisis', therefore, means crisis in objective knowledge of a thing or things, object or objects, individual or individuals, society or societies. That is to say, the objective knowledge of Nature-Man-Society is in crisis. Science involves close association/interaction between theory and practice. The crisis in science, would, therefore, mean absence of such interaction/association between theory and practice, which in turn would reduce its objectivity. 'Crisis in science', therefore, would mean science is no longer 'mirror' of 'Nature-Man-Society'. As a result, scientists themselves may begin questioning the very notion of objectivity, repeatability and verifiability of science. This distinction between science and no science or science and metaphysics may get blurred. Thus, science may become metaphysical. Creeping of **divinity** in science heralds crisis in it.

Through science man is able to (a) comprehend Nature-Man-Society complexity, (b) to solve his/her needs of survival and growth, (c) ensure continuous improvement in his/her quality of material, cultural and spiritual life, (d) create better social conditions and social orders and (e) devise methods for establishing harmonious relations between and among Nature, Man and Society. A study of history and philosophy of science shows all this, although in varying degree. The 'crisis in science' or 'science is in crisis', will, therefore, mean man's inability to advance science of Nature-Man-Society which in turn will imply

his/her inability to achieve a better social order and a harmonious relations with Nature and Society. It will mean crisis in society and breakdown of harmony between Man and Nature, between Society and Nature. It will mean turmoil and chaos all over the world. It will mean increase in violence of all kinds all over the world. It may lead to ethnic strife and world war of a very high magnitude involving destruction of entire mankind. It may mean regression to barbarism and jungle **raj**. Such are the likely serious implications of 'crisis in science' or 'science is in crisis'. In other words 'crisis in science' would imply crisis in society or vice-versa. However, it would be wrong to assume straight or direct relationship between the crisis in society and crisis in science. Also, it is not easy to separate 'crisis in science' from crisis in society. The relationship between 'crisis in science' and 'crisis in society' is systemic/ organic.

When can this happen? This can happen only when a few individuals or groups use science as a tool for enhancing their interests at the cost of all other members of the society. In such situations instead of liberating science becomes effective and powerful instrument of **enslaving** and **oppressing** others. **Equalizing power of science**, in this process, is lost and scientists of all denominations get alienated from Society and Nature. Whether scientists of today are socially alienated or not is a moot question that needs separate treatment.

Thus, it is apparent that the nature of crisis in science is social. What does it mean?

In order to comprehend nature and dynamics of 'crisis in science' the Indian Academy of Social Sciences (ISSA) in association with Indian Association of Social Science Institutions (IASSI), therefore, organised a symposium on "Crisis In Social Science" during the Silver Jubilee of the Indian Social Science Congress in January 26 – February 01, 2002 at University of Kerala, Thiruvananthapuram. The term 'Social Science' was used

in a broadest sense in order to include all branches of science – Physical, Chemical, Biological, Agricultural, Ecological, Historical, Philosophical and Social. That science is primarily a social phenomenon was our underlying assumption in the conference? The scientists of all disciplines were invited to participate in the symposium. Although the response was not very positive, yet some presentations at the symposium were very encouraging and thought provoking. The paper on **"Political Economy of (Breast) Cancer"** by Dr. Sthabir Dasgupta, is indeed, a brilliant paper and explains the 'crisis in science' brilliantly and creatively.

Medical Science is concerned with the life-processes of man directly. A study of history and philosophy of Medical Science shows enormous progress in it. It has great social use-value for the well being of entire mankind. Today it is possible to ensure better, healthier, longer and happier life to all human beings through appropriate, effective and uniform use of Medical Science. But alas, it has not yet happened and it is not happening. Large number of peoples of the world live a very poor quality of life while suffering from all forms of diseases and large number of them die prematurely without receiving any kind of medical care. This is so notwithstanding average increase in life expectancy. The slogan "Health For All' remains a slogan on paper. It has not yet become a reality even in advanced countries of Europe and America. Afro-Asian and Latin American countries are far, far away from achieving '**Health for All**'. Question arises why?

In his paper on 'Political Economy of (Breast) Cancer' Dr. Sthabir Dasgupta addresses to this question 'Why' and makes an in-depth comprehensive scientific inquiry. His analysis shows a deep crisis in Medical Science. In a process of its development Medial Science became integral part of the social processes and structures of the given society at a given point of time. Perhaps, it was natural. In today's world politics controls every thing. There is nothing, which is free from politics. Economics is under control of

politics. So is science and so is Medical Science. Thus Medical Science like other sciences has been transformed into a commodity. It is very much under the control of market forces: Giant Multinational Corporations control Medical Science and use of Medical Science. It is their goal of maximization of profits and minimization of losses that guide the growth and use of medical science in contemporary world. The Medical Science has become an easy and effective tool of the process of *the 'enrichment of the few'* and *'impoverishment of the majority'*. In the process, it has lost its *elan vital*. All the wonderful discoveries that have taken or that are taking place in fields of Medical Science are primarily concerned with the maximization of profits of drug manufacturing companies. This is exemplified by intensive case study of advances in the field of cancer in general and breast cancer in particular by Dr. Dasgupta. His inferences that crisis in Medical Science is related to the crisis in contemporary political economy of capitalism and that there is no way of doing away with this crisis so long as the modern world capitalism continues to exist are very serious inferences. Whether one agrees with him or not, one will have to examine it scientifically. Herein lies the theoretical significance of the monograph "Political Economy of (Breast) Cancer".

Crisis also offers an opportunity for creativity, innovations and newer initiatives. It all depends upon the people affected by the given crisis. The people concerned may seize the opportunity to discover newer ways to tide it over and use their newfound discoveries for ending it. Although crisis keeps on recurring in cyclic order, the revolutionizing discoveries rarely occur. One, therefore, can hope at the cost of being seen as a wishful thinker that the scientists and peoples together will discover newer ways of overcoming the present social crisis and creating better social order in which science will touch newer heights. Readers, however, are advised not to expect much on this score from Dr. Dasgupta as it is not part of his concern here. But all of us need to remember that the 'Health for All' shall remain a dream or wishful thinking so

long as an alternate Political Economy of Peoples does not replace the present Political Economy of Capitalists. Thus warns Dr. Dasgupta.

Dr. Dasgupta is a well-known oncologist. But he is not known as an expert social scientist. His treatment of the subject in this monograph shows his command over Social Science as well as Medical Science. Most of the medical scientists, I am sure, would envy his expertise and depth. Quality of science in our country will improve tremendously if our scientists, particularly the younger scientists emulated (not imitated) Dr. Dasgupta. There is a lot to learn from him.

No doubt, the scientists, the social thinkers, the policy planners, the administrators, the social activists and the people in general would find the monograph very stimulating and thought provoking.

Allahabad
March 14, 2002

(N.P. Chaubey)
General Secretary

PREFACE

"Only two things are infinite, the universe and human stupidity, and I'm not sure about the former." – *Albert Einstein*

Over the years, while treating the cancer patients, discussing with them about the various aspects of the disease and its treatment and counselling them, the present author has observed certain unfortunate and disturbing phenomena that eat into the vitals of this branch of medical science. It is known that the scientists (and clinicians) are not immune to pride and prejudices. Whether this is due to the methods practised by them or despite those is open to discussion. However, the results seem to be disturbing because potentially scientific discussions often end into sterile arguments stemming out of ready-made ideas that are more dangerous than no ideas at all. This is true to the professionals as well as the laymen. Ready-made ideas lead to dogma and an illusion that we know what a group of facts means. This is, perhaps, a far greater obstacle to progress than simple ignorance. Of course, scientists (and clinicians) have got to work from the facts, but it is not difficult to understand that a static frame of mind is supposed to impose restrictions on free thinking.

Medical curriculum today has been overloaded with factual information leaving no room for philosophy. This seems to be the breeding ground of a static frame of mind. The resultant condition finds expression in the style of thought of this 'post modern' epoch. It also finds unique expressions in the daily interaction of the participating practitioners. Since consumerism has become the motive force in all our social activities, there is a consistent endeavour on the part of the relevant authorities to fit the health care system of our country into the unique styles of consumerism. As a result, our health care system has earned the notoriety in making a calculated caricature, ending into callousness. Medical

practitioners with a static frame of mind are prone to accept this state of affairs as a *fait accompli*.

Where do the cancer patients stand in this situation? While the oncologists heavily medicalise their illness, the patients simply require safe and at the same time effective treatment. Modern oncological practice, however, found it difficult to offer; and simply installing newer treatment regimens with newer technology seems to have become a comparatively easier task. This baffling paradox has compelled the present author to look into the issues from a sociobiological point of view.

Needless to say that the present author is aware of his limitations. He is neither an expert in the field of oncology, nor he is a trained social scientist. The present discourse is for the perusal of all who are similarly disturbed but refuse to yield ground.

Kolkata
March 14, 2002

Sthabir Dasgupta

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CHAPTER I

INTRODUCTION

"What we observe is not nature itself, but nature exposed to our method of questioning." [Werner Heisenberg]

Modern medical science has offered a very simple equation to the modern society. It demands that the society must make major investment towards medical research so that the valid human goal of achieving better health and longer life can be reached. While the society obliges, the medical science faces two problems: First, the commodification of the fruits of medical research results in grossly unequal access to them; and the Second, from time to time medicine realises that it fails to approach the reality, since the latter *changes incessantly, renews itself and moves away from us at the same pace as we are advancing*[1]. The first problem forces medicine to maintain a balance between its academic exercises and the economics of the society; while the second one compels medicine from time to time, to look back, reevaluate, and change its paradigm. The first problem signifies that if commerce becomes the motive force of a society, a perfect breeding ground for decadence is developed. As a result, the whole idea of medical research in a decadent society becomes perverted. The second problem stems out of the medical science itself since the changing and evolving beauties are its inherent properties.

The state and nature of a society depend primarily on its economics, the infrastructure so to say, while science plays its role at the level of superstructure only. Although one is aware that a complex interrelationship exists between the infrastructure and the superstructure, modern medicine has realised that the former plays the decisive role. For instance, any medical practitioner with an

objective outlook must have sensed in the recent period that an Age of Commerce has totally replaced the earlier Agrarian and Industrial Ages, and commodification has engulfed all the realms of social activities. The very objective of medical science, to use the fruits of research for the benefit of the society, therefore, remains untouched. On the other hand, we have witnessed the most rapid changes in medicine and medical practice during the last 50 years or so, thanks to the tremendous surge in technological development. The impressive achievements of technology in various fields have, of course, created a new style of living and thinking as well, in the society as a whole, and so in medical practice also. This again has influenced many practitioners drift into the assumptions that technologies, therefore, will decide the course of civilisation, and the future of modern medicine as well. Thus, medicine has been seduced by technology. Today, we can prescribe a procedure for practically every symptom. Many medical practitioners of our country are thus, easily swayed by the claims arising out of the technological brilliance occurring in the western countries. They take inordinately long time to realise that in modern medicine, technology glitters, but is, often, not gold. In essence, therefore, the elementary questions on health, disease, treatment and its outcome are being overshadowed by an idea of technological determinism. As a result, medicine finds that it is indeed difficult to maintain a balance between its objectives and the ground reality. Since it has failed on this issue healthcare has ceased to be a right now; it is a good, to be marketed like cars. And *'Health' is now a Humpty-dumpty word (it means what I say it means) and is thus indefinable*[2]. Medicine could have maintained the balance, only if it had a suitable political theory to guide. This seems to be far cry in an *increasingly atomised and demoralised society*[3]. The conspicuous absence of such a political will has left medical science with inevitable tensions within the existing frameworks. These tensions compel it to reevaluate itself from time to time.

'Have Heads for Figures!'

"Nothing in life is to be feared; it's only to be understood".

It is indeed intriguing to think that the breasts that are symbols of beauty, sexuality and nurturing, sometimes are troublesome organs that threaten women's lives. This occurs when cancerous diseases manifest themselves in the breasts. Breasts, of course, are not the exclusive preserves of the women only, but the beauty, sexuality and nurturing are. This is the reason why, despite male breast cancer being more dangerous, when we talk about breast cancer we have the women in our mindset. Moreover, women's health is one of the important parameters in the evaluation of the state of health of a society. This is also the reason why, so much myths have developed around breast cancer. Some examples from among the hordes of such myths are: Breast Cancer Is A Genetically Hereditary Disease; Oral Contraceptive Pills Cause Breast Cancer; If a Breast Lump is Painful, Then it is Not Cancerous; The Best Place To Practice Breast self-examination (BSE) Is In The Shower; Women Who Have Had Breast Cancer In The Past Should Not Become Pregnant, and so on and so forth. Myths are cooked by the media, media are fed by the industries, industries maintain sometimes holy and at other times unholy relationship with the scientists, scientists have got to publish or to perish, and the clinicians who are at the ground level seem to be perplexed. They do not find specific answers to the point blank questions from their patients. The patients, therefore, remain more perplexed. Meanwhile, cancer as a phenomenon, and particularly breast cancer as a perplexing phenomenon is playing havoc. In 1900, cancers caused 3 per cent of all deaths. Now it is more than 33% and, is still rising[4]! As the death rate from cancer rises, so does the rate of diagnosis. Today, 10 million new cancer cases are diagnosed globally each year, and the figure is expected to rise to 20 million by the year 2020[5]. A comprehensive estimation of the overall incidence and mortality in cancer, done in 2000 showed that there has been 22% increase as compared to 1990[6] What is

more disturbing to note is that 70% of these patients will live in countries that between them will have less than 5% of the resources for cancer control[7]. Since health related reliable statistics in our country are difficult to obtain, the precise state of cancer care can only be assumed; but in the other developed countries such as U.K. over one third of hospital beds are already occupied by cancer patients. The figures are: 30% in 1980, 40% at present, and the estimated figures for 2010 is 50%. If similar rates of increase remain the same then in 2080 the figure will be 100%[8]!

In India there are estimates by the National Cancer Control Programme (NCCP) that some 700,000 new cases are detected each year and 300,000 are suffering perish. NCCP has also suggested through the media that by 2026, every year more than 1.4 million people will be falling in the grip of cancer. At present 30 -40% of cancers occur in the oral cavity, food pipe and the stomach in the males. In females the dominant sites are uterine cervix and breast[9] If we just change our perspective, we shall see that internationally, the overall incidence of breast cancer has in fact increased by 60%, from 1950 to 1998[10]. There is a controversy around the veracity of such a staggering figure. But controversies notwithstanding, breast cancer by far has become the most common malignant disease in women [22% of all new cancer cases][11], and overall it is the second most frequent cancer in the world[12]. In India, breast cancer accounts for 11% of cancer-related diseases and is prevalent among urban women. Over 80,000 new cases of breast cancer are reported every year in India[13]. The incidence is steadily rising and posing a great threat. This alarming situation forces our women to question: Is breast cancer becoming an epidemic? But another question that makes our patients more anxious, is that how long they are going to survive after having breast cancer, or in other words are they going to be cured? There is no way to predict whether or how long any individual woman will survive after a diagnosis of breast cancer. There are a number of variables that influence the results of treatment. There is no way either, to predict how long a woman with breast cancer is going to survive, if she is

not treated with modern therapies. If we go simply by the size of the tumour only, the statistics show that 80% of those having a tiny cancer, less than 1 cm and strictly localised in a certain small corner of the breast are expected to survive for 10 years, with treatment. This, of course, will be an accident since we normally don't find those tumours in practice. Our normal practice is to find them when they are 3 - 4 cm; and 55% of these cases are expected to survive for 10 years. If the tumour is larger still, for instance 5 - 7 cm, the expectation would be 45% only. Of course, this is gross simplification, for the other and numerous variables must be taken into consideration. However, most of our cases are 'metastatic breast cancers' [MBC], meaning that the disease has already crossed the boundaries of the breasts. And only 15 - 40% of them are expected to survive for 10 years. Thus, at the end of the day we cannot save most of our breast cancer patients from the eventual death. The question that now disturbs not the patient anymore, but the people around is what kind of a disease is this? ... Can't we find an answer? ... What the hell our science is doing?

What is it, Actually?

'Omnis cellula a cellula': each cell descends from another cell.

The term 'cancer' refers to more than 100 forms of the disease. Still, the basic processes that produce these diverse diseases appear to be quite similar. There are 30 trillion cells in a normal, healthy human body, and unlike the human communities they live in a complex condominium, in the sense that they are uniquely interdependent, regulating one another's development and activities. This collaboration ensures that each tissue maintains a size and architecture appropriate to the body's needs. The cancer cells violate this unique scheme and tranquility of the body. When the normal cells become cancerous they become deaf to the friendly suggestions of the other cells and follow their own internal agenda. The agenda comprise of relentless reproduction, migration

from their original sites and invasion of the other sites. These insidious properties of the cancer cells make them more and more aggressive over the time, and ultimately they become lethal by disrupting the tissues and organs needed for the survival of the host. But how does a cell become such a savage, that we call it malignant?

The malignant transformation of a cell comes about through the accumulation of mutations in specific classes of the genes within it. These genes provide the key to understanding the processes at the root of cancer. However, mutations occur daily in our cells for a variety of reasons; and some of these are even cancer-related while the others are not. Repair mechanisms at the same time function within the cells; and repair enzymes are involved in this. Most of these damaged cells [due to mutation] die so long as the repair mechanism remains intact. If repair enzymes are not working, that damage won't get corrected, and we're off the races.

Two gene classes play major roles in triggering cancer: 'Proto-oncogenes' that encourage growth, whereas 'tumor suppressor genes' inhibit it. There is a unity of the opposites. These two classes of genes are normal genes, and they must remain intact in order to have a normal life. When the proto-oncogenes are mutated they yield too much of proteins or their active forms that stimulate cellular growth. Tumor suppressor genes, when mutated fail to counterbalance the proto-oncogenes, and thus growth remains uninhibited. So, cancer is supposed to occur when both these classes of genes are mutated. Of course, this is a simplified story, for there are other classes of genes that also play very important roles in the genesis of cancer. However, for the present moment, this is the standard or conventional view on cancer. A legitimate question now arises: Does cancer occur just by switching on a genetic mechanism?

When a cancer-related mutation occurs, some cells get damaged. The damaged cells are called 'initiated' cells. It is not that these 'initiated' cells now start growing uncontrollably. They will not do so until several more things happen to it. A continuous transmission of messages takes place back and forth between a cell and the body it inhabits. The damaged cell has to be 'promoted' by some agents that interfere with this message transmission. In some instances, x-rays or certain chemicals and in other instances some female sex hormone, such as estrogen can 'promote' the damaged cells. The result of such 'promotion' is an expanded cluster of abnormal cells, waiting to become true cancers. Still these promoted cells do not multiply uncontrollably unless something else happens to them. The *something else* is called 'progression' and it results from more physical injury to the cell's DNA. Again, x-rays and certain chemicals (in cigarette smoke, for example) might cause 'progression'. Thus cancer is a multi-step process, requiring perhaps 5 or 6 (or more) *insults* to a cell before cancer develops. When a cell is sufficiently damaged and become cancerous, it takes the insidious properties as mentioned above. It is now a cancer cell and, left alone, it will multiply (grow) until it kills its host. There are very few things on earth that have the ability to do the three jobs in a row: to initiate cancer, to promote it and to make it progress. Things that have such ability are called 'complete carcinogens'. Radiation is a complete carcinogen (including cosmic radiation from outer space, which we cannot avoid) for instance; but most carcinogens are not. Most carcinogens can do any of those three jobs as mentioned above. However, in sum, if we are to avoid cancer, we are to find out the means to avoid contact with carcinogens. This is the environmental explanation of cancer. Therefore, if we view cancer just as a switching mechanism, we might be wrong.

Moreover, while it is true that the accumulation of genetic changes over the years to perhaps decades, is the basic cause of cancer in all cases, it has to be remembered that no single genetic change is sufficient to give rise to cancer. Since a set of genetic

changes is needed, cancer is also a *polygenic disease*. Yet it is not unique in that sense, since polygenic inheritance as it is called, has been invoked to explain a wide variety of other diseases also, ranging from congenital malformations to porphyria to peptic ulcer. All these diseases are different, in the sense that they have their unique characteristics and unique life histories. Cancer as a polygenic disease always remains a matter of chance or probability in its occurrence at the individual level, although it might exhibit a *predictable certainty at the level of a community*[14]. In other words, if it is seen that world over, the overall cancer occurrence is one in five humans, that would be a matter of certainty; but which one, is that of probability. Why there is probability, in stead of certainty at the individual level? This is because, *it is not the genes of an individual that decide the presence or absence, static or progress of a disease, but the abstract relationship that the individual bears to the whole environment*[15].

We can view cancer as an interesting phenomenon also, in the following manner. We know that if the species were to survive, the primary prerequisite would be to have a stable Genome. In other words, if the genes are imperfect, the Genome becomes unstable, and thus the very survival of the species becomes *jeopardised*[16]. Since cancer stems out of genetic instability, in order to survive the species will try to eliminate those individuals harbouring actively triggered dormant cancer. In this way it will maintain the integrity of the common gene pool of the human society, thus serving a definite advantage. And again, since the nature of the link between cancer and death is debatable as may be realized from the computation, were cancer eliminated altogether from mankind, *it would just add a little more than a year to the human life span*[17]. Of course, this sounds like a fatalist view, but different views are to be taken into consideration any way.

If this is the phenomenon of cancer, can we do anything about it? We have, indeed, three options: We can try to prevent the

occurrence of cancer; we can try to identify people destined to develop cancer, or detect them as early as possible so that we can cure them; and we can devise such methods of treatment that could make the life of our patients comfortable, even if they are not cured. But before we discuss these options, let us look at the nature of our medical practice today.

CHAPTER II

THE NATURE OF CLINICAL PRACTICE AN APPRAISAL

[The Bad, The Good and The Ugly?]

Needless to say that we have learnt a lot during the last couple of thousand years. Susruta knew very well that some tumours were to be removed surgically, while others should be left out to be treated with 'potions' [whatever that meant at that period]. Susruta as well as Galen believed that cancer was due to imbalance of bodily humours. The Egyptians also documented tumours well. That cancer is a cellular disease has been proposed and explained, however, only after the invention of microscope. Things changed in this fashion. Concepts, therefore, also changed. The early 20th century was an era of radical surgery, because it was conventional to think that cancer arises in a specific organ, grows centrifugal and then spreads in a predictable manner. It was a glorious period in the history of cancer surgery, and at the same time, it was tragic. Oncology practice has come a long way since then. Of late, we are witnesses to the legalisation and legitimisation of the so-called alternative therapies in cancer. These alternative therapists stand at one extreme, believing that modern medicine has utterly failed to deliver substantial benefit to the cancer patients. At the other extreme are the mainstream oncologists who believe that we are gaining ground each day, exploring newer arena and achieving newer benefits. Between the two extremes we see the so called complimentary therapists who are of the opinion that the biomedical model of disease, though powerful, does not explain all known facts about cancer, and they argue that a broader theoretical framework, which includes other non-traditional approaches, has to be taken into serious consideration. They believe that they try to integrate the best of these two different

approaches to help patients achieve an optimal medical outcome and the best quality of life. However, our present concerns are the mainstream oncologists who still dominate the arena of techno-medical complex.

There are now three methods in mainstream oncology practice. There are the *Empiricists*, the *Methodists*, and the *Rationalists*. We shall discuss the essence, advantages and limitations of these methods with our social perspective in mind.

It is said that 'all clinicians need good judgement; good judgement comes from experience and experience comes from bad judgement'. There is a great deal of truth in that statement. The *Empiricists* are those who rely entirely, or mostly on experience. In any critical juncture they tend to cite their own experiences as well as the anecdotes. We, as healthcare professionals, operate in a culture that places great emphasis on anecdote and experience, the values of which cannot be undermined. However, the values of the newer evidences and theories cannot be undermined either. Our empiricists are not really blind to the changing theories and newer evidences; but these simply fail to attract much attention from them. An 'experience-based' practice is the most widely used by medical practitioners worldwide. This method depends too heavily on art and past experience and far too little on available newer scientific data. The final outcome after all, is what is important to them. They think that all arguments about the relative virtues and vices of various treatment modalities in the developed and not-so-developed countries do not have a great impact as far as the final outcome is concerned. For example, the life expectancy and pattern of recurrence of disease in the cancer patients across the countries is almost the same, even if we treat them in the most sophisticated manner. The patients suffer just as their counterparts do in the other countries, and eventually die, albeit rather later and more expensively. So there is nothing great in the newer theories or hypotheses. The greatest problem with this kind of thinking is

that the managing physician suffers from cynicism or frustration that results from the morbid outcome of treatment of oncological events. They are indeed *bad* in the eyes of the others!

Then there are the *Methodists* who refuse to pay undue attention to the past experience and the anecdotes. Neither they are very keen to depend on the changing causal theories. They rather put all oncological problems down to the *Evidence Based medicine* [EBM]. The main factor that eventually encourages the medical practitioners today into utilizing an 'evidence-based' methodology is to bring forth a kind of discipline among them. The 'evidence-based' practice stands on the pillar of 'Clinical Trials'. These clinical trials are wonderful documents to provide us with guidelines for clinical practice. Protocols and algorithms are all supported by the EBM. Another factor that has encouraged the use of EBM very recently is medico-legal. The changing pattern of the society at large and medical practice in particular now need the 'expert opinion' at many junctures; and these 'opinions' obviously call for evidence-based information in the medico-legal platform. The level of evidence determines the strength of the recommendation. These clinical trials are variously designed, and although they have some limitations they contribute to avoid arbitrary practice and to reduce practice variability among professionals. On the other hand, practically every week something comes across somebody's desk emphasizing results of some clinical trial showing loosely bound benefits of certain pharmacological molecules. Moreover, these clinical trials are important to provide information in patient populations, and not the individuals. The difficulties arise when we tend to mix our own experience with latest evidences found in the other countries. A cross-contamination occurs between the values of our own experience and evidence-based values that came out of a newer pattern of study. The most widely publicized studies that we very often tend to refer to have been implemented in tightly controlled *methodological environments*[18]. Our clinical environment on the other hand, is socially and historically not so tightly controlled. It

is doubtful, therefore, whether the outcomes of clinical trials performed elsewhere can be readily and beneficially transformed to the less structured milieu of this country. If we decide that we shall perform the 'trials' in the same manner as practised in the western societies, we shall come across an insurmountable problem of obtaining reliable evidence because '*risk assessment, confidentiality, recruitment, randomization, informed consent, and monitoring*'[19] that *are* so essential and critical issues, are supposed to pose unique barriers. Moreover, in traditional Indian philosophy, death is viewed in the context of passage to another life. Death is a relief from suffering, with a destination to eternal *atman* or rebirth. In contrast, the very essential stimulation towards the progress of modern medical science originates from a *death-denying* society. If we bluntly accept the value outlook of such a society, a problem of different nature and magnitude might evolve in course of time. If on the other hand, we stick to our own tradition nullifying the newer ones, there is danger of medicine being stuck to a *narrow domain*[20]. This means that the evidence obtained from other countries should be applied to our patients with due caution. Given *doses of drugs or administration schedules*[21] may not be entirely suitable to our people. Even if we overlook these problems, the largest single obstacle to evidence-based clinical management is the *bias*[22] against the reporting of studies with negative findings. This is to be remembered that most of these trials are *sponsored*, and the sponsors are not always above suspicion! For example, there is a great suspicion that the pharmaceutical-industry-sponsored trials could be biased, *'due to selective reporting of studies... wherein unfavourable results are incompletely described'*[23]. It has been observed that most of clinical practice in management of various cancers is *not supported by high quality evidence*[24]; they are rather based on opinions. True Methodists are those who tend to strictly adhere to these trial results, applying them on all patients, whatever the perspectives or circumstances are. Thus they are sometimes called *evidence-biased*! There are, therefore, clear advantages and disadvantages in both the methods

described above; but the Methodists are *good* at least in the present arena of stereotyped medicine!

What now, if the clinician uses the guidelines born out of clinical trials as adjuncts to clinical judgement, not recipes for making decisions in the individual patient? What if, a physician uses his judgement, not only based on evidence but also and more so, on experience, and thus rationally avoiding the risk of cross-contamination? The clinicians after all, are free to base their judgement on well-defined observational studies in contrast to the EBM. These observational studies could be more reliable and less costly. Moreover, they may possibly more accurately reflect the practical use in a broader range of patients, particularly in a country like ours. This is to be mentioned here that the doctors in our countries are equally able to exercise judgment as their colleagues in more-developed nations. This is not because they have improved access to diagnostic and therapeutic resources as well as contemporary information, [that they have, of course] but because they have historically acquired a clinical skill that seems to be deficient in many countries. Medical questions are commonly very complex and the application of best practice obtained from clinical trials is a rarity rather than the norm. Therefore, to follow EBM slavishly without interpretation in the context of our own practice environment is akin to driving a highly sophisticated automatic car without a driver. And this is also to be remembered that *evidence-based medicine imposes the questions that are important to rich countries and the relevant answers on less-developed countries*[25] A third group of practitioners, therefore, who base their clinical judgement mostly on reason are the *Rationalists*. Specific circumstances and perspectives are more important to them, rather than a hard and fast rule of practice. Of course, they look at the pre-specified theory of cause and effects, but these theories are not sacrosanct to them. These practitioners are indeed *ugly* in the eyes of the trial-driven medicine of today! However, these rationalists are not the 'true' ones. The essential approach of a true rationalist would be to look for the exact cause

and effect. We are now living in a fascinating time for medicine, in that the first draft of the human genome is on the brink of completion. If it is considered that the elementary cause of malignancy lies in the genes, then the most rational approach would be gene therapy, of course. Clinical trials in this respect in some types of cancer have just started. Although these novel treatment methods are still in the infancy, the true rationalists would hope that these are the only rational methods to treat cancer. There are other rationalists who would consider the malignant diseases from another perspective; e.g., the immune system. Their rationale says that all cures carried out since the days of William Harvey [1628] in the name of *Scientific Medicine* have not been effective, only because the *immune system* in its proper perspective has never been addressed. So they believe that the assertion of today's scientific cures will prove to be barbaric travesties tomorrow. But these kind of true rationalists are rare birds to see. Our rationalists may not be so in the truest sense of the term, for while they place keen attention to the theories of cause and effect, they also realise at the same time that the cause and effect phenomena do not always fit well into the domain of medicine. They base their clinical decision making on rational pathophysiologic principles, and yet they know that every patient is a unique individual who may or may not conform to a *population profile*[26]. Thus, they place more attention to the specific rationality of a specific treatment in the specific circumstances. In other words, they feel that whatever is rational may not be reasonable, and whatever is reasonable may not be rational at the theoretical level at least. Therefore, the approach they pursue most of the time seems to be down-to-earth. The present era of ascendancy in the 'clinical trials' is indeed an era of numerical/statistical reasoning. Numerical reasoning after all, is an empirical knowledge. An empirical knowledge cannot exist without a mechanistic reasoning, and mechanistic/deterministic reasoning leads to *theoretical dogma*[27]. *'Medicine may have moved from mystic certainty towards scientific uncertainty, yet many of its practitioners still behave as if Galileo had never lived'*[28]. Karl

Popper was primarily a philosopher, but he was also interested in science and the scientific method. He characterised science as *'the art of systematic over-simplification'*[29]. Today's EBM [evidence-based medicine] resulting out of 'clinical trials' may be just as fallible as other reasonable sources of information, and is again a systematic over-simplification. Many oncologists in our country feel that their patients' interests are better served by good traditional observational studies than by EBM. This outlook, however, does not fit well with the market economics of medicine. Our rationalists, therefore, look *ugly*.

THE MARKETPLACE

"Birds may not violate the letter of the law of gravity, but they violate its spirit".

Today, such practitioners who tend to refuse the spirit of the market are exceptional. Socially amoral forces are driving all the existing systems of the country, including the health care system. In oncology practice, *the slippery slope of drug-company money has already influenced us in many ways and boundaries between industry and academic medicine have become blurred*[30] The idea of the physician taking enormous time to make a bedside clinical judgement or the remote scientist in an ivory tower, where the jingling of coins is never heard is now a nonsense idea. Clinicians now allow themselves to be piled with expensive gifts, opulent feast and trips to luxurious settings. It is not difficult to understand that the costs of the industry-sponsored trips, meals, gifts, conferences, and symposia are simply added to the prices of anticancer drugs and devices. There is now considerable evidence that researchers and clinicians with ties to drug companies are indeed *more likely to report*[31] results that are favourable to the products of those companies than those without such ties. Indeed, the pharmaceutical industry has of late, dominated the field of clinical research in oncology. This is also evident that the incentives of the marketplace have led to an overusing the

oncological drugs that is of nobody's interest except of the companies only. This also has to be remembered that whereas all oncological drugs have a number of side effects, most important side effect of the newer generation of such drugs is their cost! It is true that cost containment is a difficult and debatable issue in oncology practice. But certain things are simple to understand; for example, a random prescription of advanced drug therapy protocols discussed in western journals has jacked up treatment cost to such levels that these programmes cannot be applied to *more than 80% of our patients*[32]. This is to be mentioned here that the average gross national product per person per year in our country is $350 as opposed to $23090 of developed countries[33]. On the other hand, within a span of 14 years, from 1980 to 1994 the global pharmaceutical sales have skyrocketed from *22 billion dollars in 1980 to 259 billion*[34]. The market forces have changed the face of medicine in the recent years, in the other ways also. For instance, this era has been particularly vitiated by the fact that we are now more concerned about subversion by litigious patients than offering rational suggestions. The public sees us as becoming *double agents*[35] who would purportedly serve the patient but in fact limit care for the financial benefit of the sister organizations, such as the investigation clinics. We are aware that the rewards of medicine are many, including service to humanity, intellectual stimulation, professional respect, and financial remuneration. However, because the first three rewards are fast diminishing, it seems inevitable that our concern for compensation will become most important. It is not that the ground reality in clinical decision making compels us to get more and more sophisticated in terms of back-up investigations; it is the very misleading concept of modernity in medical practice that has made us forget to knit our brows and get a clinical clue. In this context, some have stressed that the physicians must be *mindful* so that their *mental quality*[36] would direct them to take proper clinical decisions. However, it is difficult to understand as to how this can be achieved when we have already lost, or neglected our mentors of the yesteryears in the name of progress!

A society that is solely governed by trade and business is a demoralised society. Today the Cancer Business has grown so huge that it is *second in size*[37] to the petrochemical industry. In the U.S.A. alone the cancer business is estimated to be worth *$1 trillion* and in the U.K. it is estimated to be worth *£5 - £6 billion*[38] In cancer medicine, there are a number of profit centres: ranging from the realm of advocacy, through detection or early diagnosis, to treatment and terminal care. The most flourishing profit centre today in cancer care is the drug market. Generally, active cancer agents that have been used for the last 30 years are not very expensive. It is the second and third-line chemotherapeutic agents that have flooded the market during the '90's are so expensive – and, presumably, so profitable. Today, we have a tendency to prescribe these agents at random in the name of 'favourable' results published in the western literatures. Of course, there is some discounting on these drugs, particularly in sales to poorer countries. But, in general, drug companies are very reluctant to cut their prices in particular markets for fear that those same drugs will find their way back to more profitable Western markets as parallel imports. This is where mercantilism can be seen to cut both ways. It is true that combination of capitalism and medicine can make great breakthroughs, but meanwhile big business, absolved of guilt, can rake in the bucks. Moreover, in poorer countries like ours, there are problems with drug patent laws that prevent generic production, thereby putting the drugs beyond the reach of the common people. It has been proved that with generic production, drug prices of AIDS drugs, for instance, in third world countries may be reduced to 82% lower than the prices in US. This has also been documented elaborately[39] that because the 1970 Patent Act in India did not allow product patent in medicine, during a period of almost 30 years, from 1971 to 1998 the number of registered pharmaceutical producers had increased from 5,000 to 24,000, and the production of pharmaceutical products also grew 48- fold from Rs. 250 crore to over Rs. 12,068 crore. In a short period of less than 10 years, exports increased from Rs. 228 crore in 1987-88 to Rs. 4,090 crore in 1996-97. This in effect had created self-reliance

in medicines and kept the prices of medicine within reach of the common man. In contrast, if the US patent monopolies are globalised through TRIPS then millions of victims in the third world will be denied affordable treatment. The politics of Medicare in our country have changed over the decades, and the present politics which is again the brainchild of an unfair social order, have compelled our governments to look at the World Bank or the IMF as the saviour. We know, however, that neither the World Bank nor the IMF is going to stop the pharmaceutical companies arbitrarily pricing their drugs out of the reach of billions of common people who need them most. The industrialists talk about viability. When some essential drugs are discontinued, they say it is because they are not commercially viable. When we say that the price of some anticancer product is unusually high, they say that the costs of R & D are very high. Yes, we agree they are, but so are the profits and returns of the pharmaceutical industry. The industries now say, well Sir, let us share the profit! The essence of this debate is whether the availability of health care would be determined by the industry alone? If it is so, then this is in essence a kind of terrorism.

As a profession medicine put the interests of the patients first, whereas commerce serves the shareholders first. The medical community of our country never offered due attention to this age-old conflict. Medicine was a half-hearted business from the very beginning. The professionals used to maintain a half-hearted relationship with true commerce, and used to be paid for their service either in kind or in coins. This constipated relationship on its turn allowed the professionals to enjoy a certain kind of prestige in the society. This scenario existed for the last 2000 years. Commerce did not bother too much with medical profession because the market ethos was weak. This scenario has changed; and particularly during the last half of the last century, when the market theory gained in strength it tried to set a newer relationship with the medical profession for its own interest. The market forces, particularly the corporate bodies bound the profession to their

profit mission. Medical profession just like other professions yielded to this mission. Thus, medicine as a profit making business became legitimate. However, this legitimacy did not find an even support from the community as a whole. Society remained awestruck at first when the professionals started speaking in languages akin to commerce. This is because the value outlook of the community did not change at the same pace as the market mechanism. The values of the society are, of course, changing; but the hangovers of the yesteryears refuse to give adequate support to the newer value outlook of the profession. Market forces ultimately have changed the whole concept of doctor-patient relationship. Today patients are known as consumers; they are nothing less and nothing more. The increased public expectations and increasing fragmentation of care fractured the previously mutual relationship between the doctors and the patients. As medical care has been fragmented, *so more professions have come to play the decision-making and technologically sophisticated roles in patient care*[40], challenging thereby the dominant status of medicine. The medical professionals responded to this phenomenon in their own way: developing and maintaining close commercial relationship with the companies. Since the technology on which rests the present euphoria of modern medicine is at the hands of the companies, the professionals have become victims of their own success. As a corollary the cost of medical intervention has increased spirally. Since the cost does not match the benefits of medical intervention most of the time, the consumers find solace in litigation. Popular media played a very important role in this situation. The media's ideal role was to inform the community about the advances in medical research in fair and accurate way as far as possible. They fell far short of it, raising false hopes, undue anxiety or unnecessary alarm largely because they are more interested in 'stories' that sell. In other words, consumerism took its toll there also. Thus, *'they have already warned us that holidays make us less intelligent, as our brain misses out on its daily workout.... Why rabbits don't smoke.... Carrots and cigarettes' are a lethal combination, as vitamin A reacts with tobacco smoke to cause*

deadly carcinogens.... What's more, smoking also causes penis shrinkage.... And having sex twice a week can prevent colds and flu'[41] Modern media have been overwhelmingly successful because at long last they have been able to produce a narcissistic obsession with the body's personal cosmos and technology; but in essence they have reduced themselves into mere *'cheer squads'*[42], or sometimes castigators.

The underdeveloped countries have refused to learn from the failures of the developed countries so far as the high technology approaches to medicine (e.g., in imaging) are concerned. These approaches are really reaching the point of diminishing returns. This spills over into the Third World. So many developing country doctors look to the US for their training; they are, of course, being trained in newer studies in medicine. But the point is to put a social dimension to these studies. For example, the studies in genetics of health and cancer might have an impact in the realm of public health in the long run if the theme of 'individual susceptibility' is addressed properly. This is imperative because this theme is persistently being propagated in order to relegate the responsibility of the disease on the individuals, despite the fact that the *'environmental explanations were reinforced by numerous tests and by increasing knowledge of the impact of chemicals in causing mutations*'[43, 44]. In this way, if we apply our wisdom, we shall refuse to read cancer in a mechanistic model, and forsake the idea of viewing health as biological agents, chemical agents, physical factors, or our own genetic make-up only. The fact is that all these factors play their respective roles in turn, or in combination, in the genesis of cancer. This method of scientific practice also, in the long run becomes an economic question; but primarily it is a question of principle. The question of principle has its strings attached to the society. If society does not exist as such, the questions of morality, right or wrong become out of place. Medicine as such does not have a moral purpose, but the practice of medicine has. If left alone, medicine remains unpredictable, baffling, ambiguous, fallible, and absurd; it becomes lively and

purposeful only when it is practiced with a social perspective in mind.

PREVENTION?

"The chief cause of poverty in science is imaginary wealth. The chief aim of science is not to open a door to infinite wisdom, but to set a limit on infinite error." [Bertholt Brecht, Galileo]

We have been trained in the traditional western view of science and medicine. This view inspires the search for eternal laws, which could make the universe move in predictable, mechanical ways. The Newtonian mechanistic and reductionist world-view brought by Claude Bernard to the 19th century[45] as new scientific method has still dominated our ideas on health and diseases. Thus, although in our practice we see that the relationships between cause and effects are multifactorial, contextual and non-linear, we are almost instinctively forced to presume a linearity of events. It also seems today that the history of medicine runs in close unison with the socioeconomic history of the world. For instance, the period of Thomas Hobbes who had propagated that nothing existed except matter and motion was the unique period of mercantilism. Then we saw the birth of capitalism during which Hobbes' influence passed down to us via Charles Darwin. The slogan of the *survival of the fittest* fitted well with the conception of expansion of the 'free' market. Together they acted like a 'ball-and-socket' joint. Sociobiology has passed through many ups and downs since then. Lately, biology has been dominated by the double helix of DNA (deoxyribonucleic acid), the genetic material. And from its very inception the genetics have been viewed in a mechanistic manner, at least by a strong group of scientists. According to this view, since all the biochemical reactions in our body are catalysed by the proteins, it is implied that the genes ultimately control and determine all the characteristics of the organism. Environmental influence cannot

directly change the genes and genomes, and if this influence occurs at all, it can be neatly sorted from the genetic. Therefore, there is nothing in the world, no societies or communities except the *selfish genes*[46] (or, *selfish individuals* only). Even these individuals serve only as a vehicle for the genes. Since the vehicle is of less importance because it will not last long, but the gene will; all that is good in human beings, love and compassion etc is also less important. Competition is the one and the only one that has a lasting importance. Today we see that mechanistic science (biology, in this instance) has created an environment where globalised economy fits nicely. A linear outlook in the genetics of diseases has now become more of a faith than a science. This faith arises out of the idea that despite a hump, a camel's spine is straight! The camel's spine is indeed straight, but does it help us in riding it? This is bad science of reductionist biology. *Thus, genetic predisposition to everything: from cancer to diabetes, from behaviour patterns to homosexuality, and from animal instinct to sanity are being reported almost daily in the scientific literature*[47]. We must not forget that this very outlook gave rise to such discipline called 'eugenics' in the recent past, which propagated the concept of "race purification" and prevention of immigration from countries judged inferior. Today, we are being told that with the tremendous growth in the field of biotechnology that can tamper with the very blueprint of life, we may be served with special prescriptions of lifestyles based on our particular genetic makeup. At the same time, commerce has been interested with renewed vigour. Some companies in the USA and UK for instance, have started a sort of population-based genetic screening, advertising its own genetic tests for breast cancer and other diseases on the website, and claim that they will even give 'well-being advice'. This despite the fact that population-based genetic screening for cancer has been cautioned against by *many scientists*[48]. Thus, a philosophy of 'genetic determinism' in essence, is being propagated in a subtle manner.

In this context it will be worthwhile to mention that there are two types of genetic determinism, namely *'puppet determinism' and 'promethean determinism'*[49]. The first one assumes that we are victims of our genes, or in other words we are simply puppets at the hands of the DNA that determines everything. It has been propagated by some that it is the individual's developmental programme that is the sole issue. *'If it [cancer] is not a part of his programme, nothing can cause it; if it is, nothing can prevent it'*[50]. These assumptions of 'puppet determinism' have already been contradicted by the discovery of, for instance, the recombinant DNA (rDNA) technology. Many other discoveries subsequently showed that under certain conditions the genes could be silenced, or inactivated or even eliminated from the genome. We have of late, come across such terms like 'fluid genome' that tell us that genes can undergo changes due to environmental perturbations. All these scientific developments point towards *nullification*[51] of the ideas of 'puppet determinism'. However, at the same time all these developments equally lead us towards another concept that is called `Promethean determinism`. It means that we can tamper with our genes and genetic make up, and thus we can act as the guardians of our genes. This view propagates the idea that we are invincible and, therefore, some day we shall logically land into the fields of preventive vaccination, molecular screening, tailored chemotherapy, gene therapy, and the overcoming of drug resistance through genetic manipulation. *The future of oncology may lie here only*[52]. If we stretch this view to some extent, we can even question the necessity of death, and mortality becomes no more *a priori necessity*[53]. According to *many molecular biologists*[54], however, this determinism in any form is a myth, since all these might be possible only at the expense of being *dehumanised*[55]. We will no longer remain human at the present sense of the term! Not only it is a myth, it is dangerous too, for this notion in the long run, will direct a biomedicalised man to realise that what he had wished for was not exactly what he had wanted; but that will be a painful and late realisation indeed. Thus, fatalism [puppet determinism] and invincibility of the humankind

[Promethean determinism] are in effect the two sides of the same coin. They are mutually opposite, but they arise out of the same outlook. However, both these views ultimately lead to *social deterioration*[56]. Science may be neutral and disinterested but its applications never are, and neither should they be.

How do we propose to prevent cancer, then? Prevention works at the population level. Plain logic in genetics suggests that we shall be able to know beforehand, with the help of a data bank whether an individual has any genes for this disease, and, therefore, exposed to high risk. But let us pause for a minute; we are talking about *high risks*, not the *inevitability* of the disease. Researchers have identified two genes on chromosome 17, BRCA1 (breast cancer gene 1) and BRCA2 (breast cancer gene 2), that may increase breast cancer risk, although more genes that affect breast cancer risk may also exist. However, only *5%-10%*[57] of breast cancer cases are thought to be due to these abnormal genes. And because nine out of ten tests for the *BRCA1* mutation among women related to breast-cancer patients will be negative, the genetic test does not live up to its earlier promise[58]. Furthermore, a mutated BRCA gene is only one of the risk factors for developing breast cancer. Other high risk factors include: age, family history, high fat diets, obesity, previous breast biopsy showing benign or non-cancerous conditions, menstruation beginning at an early age, menstruation continuing past age 50, not having children, having a first child after age 30, etc. Also, *up to 80%*[59] of women who get breast cancer have no identifiable risk factors. Of course, the genes people inherit from their parents also influence cancer development, but they are responsible for the development of *less than 5 percent*[60] of fatal cancer cases. Serious *researchers*[61] have studied the role of changing environment and ways of life in the relatively recent and rapid increase in breast cancer, and have hypothesized that this role is greater than the role of solely genetic abnormalities. Using modern tools might identify genetic abnormalities, but they will remain academic exercises as long as

we fail to address the question of prevention from the sociobiological point of view.

Even before we propose to study breast cancer from the sociobiological point of view, we need a solid and reliable data bank. The history of maintenance of tumour registry in India is a sad story to tell. The importance of collecting information on the incidence of cancer was realised by the Government of India as early as 1965 when the setting up of a National Cancer Registry Programme (NCRP) was suggested. It took 17 years to establish NCRP. The NCRP has brought out just seven registry reports till date, and the last report was published in 1992 for the year 1988-89. It plans to publish the next set of data only in 2002 — after an entire decade. In a sadistic display of insensitivity, information of cancer registries is never shared, crippling future research. This only displays the callousness and insensitivity of our medical establishment to read cancer with a down-to-earth attitude.

The growing incidence of breast cancer has been blamed on a growing tendency for *late marriage, nulliparity, and stress*[62] All these factors have social, political and economic connotations. It is already well known that the amount of time between menarche and first pregnancy is a crucial risk factor. Possibly, many do not know that at the turn of the last century, breast cancer was a relatively unusual disease. Its incidence has steadily mounted since the 1930s. Many reasons have been cited for this rise, including rising diagnoses due to developed diagnostic tools; but the inexorable fact is that the emergence of breast cancer as a widespread health problem is tied to the extraordinary transformations in women's lives in the modern times. These changes seem to make the women more vulnerable to certain cancers, especially the breast cancer. If we see from the physiological point of view, we shall appreciate that most of the women in the past used to ovulate perhaps only twenty times in their entire lives due to late menarche, multiple pregnancies, long

nursing times, and early menopause. The picture was very grim indeed. Women today are exposed to reproductive hormones over a much longer span than in the past. In modern societies, in contrast to the traditional ones, menarche occurs earlier, at age 12 or 13 and the first pregnancy decades later or never, resulting in a huge number of menstrual cycles. They may have around 400 menstrual cycles, twenty times as many as their ancestors had, exposing their breasts to historically unprecedented numbers of hormonal cycles. As a result the breast cells multiply more. This simple increase in cellular multiplication is believed to increase the likelihood of genetic accidents. Most cancers are believed to arise from such accidents indeed. It seems now that the more "modern" a society becomes, the more crucial becomes the risk factor towards breast cancer. Of course, it is overtly simplistic to ask the women to get pregnant in their teens in order to prevent breast cancer later; but it is equally difficult to refute the rationale either. Late marriage, late motherhood and nulliparity are to be seen in this perspective only. Stress also, is a distinct feature of modern civilisation.

As industrialization has proliferated, so, too, have the suspected causes of cancer. Among these suspected causes all manner of modern conveniences have been questioned, ranging from pesticides to cellular telephones. If we accept that all these amenities have their carcinogenic effects if used indiscriminately, we must also remember that they do not act in the same way, and their harmful effects are hard to verify because they generally result from exposure to *several carcinogens at a time*[63], but broadly speaking, they comprise agents *that damage genes*[64] involved in controlling cell proliferation. In 1981, Richard Doll and Richard Peto, famous British *researchers*[65] looked at cancers in every country where statistics were available. They looked for the lowest rates for each type of cancer and on that basis they estimated that the "natural" level of cancer in humans is about 1/5 of the then cancer rate in the U.S. In other words, they estimated that 80% of U.S. cancer cases were *avoidable and preventable*[66] It

implies that if we really want to prevent, we are to prevent contamination of our air, water and food with cancer-causing, hormone-disrupting chemicals. Environmental pollution is a direct effect of rampant urbanisation. In fact, during the last 50 years and particularly during the last two decades, we have witnessed an unplanned migration of the rural population to the cities, resulting in the rise in the urban component of the population from *23% to 42%*[67]. This phenomenon is the direct result of rampant urbanisation, uneven development and a trade-based economy; and at the same time this is one of the most important causes of changes in life style with accompanying health hazards. That women's health can be used as an indicator, of the state of the environment, is a perspective not often taken. But increasingly well documented evidence supports the fact that *women (and consequently children)*[68] are the first to experience the effects of environmental degradation. We have been fooled earlier by a sophisticated misinformation campaign of the tobacco industry, and we wasted 50 years debating the importance of cigarettes. We cannot afford to make the same mistake again. Evidence has been provided by *many studies*[69] that breast cancer epidemic is related to exposure to a wide range of environmental contaminants, including DDT, other carcinogenic pesticides, and hormone stimulants. *There are over 70,000 chemicals in current commercial use today and 1,000 new ones are added each year*[70]. A chemical may not of itself instigate cancer but it may work, in combination with many other substances, both natural and synthetic, to contribute towards the risk of developing disease, including breast cancer. *"One teaspoonful of concentrated pesticide could pollute the water-supply of 200,000 people for a day"*[71], and at least 168 of them are linked to major *diseases of the immune system, cancer, allergies, infertility and problems of foetal development*[72]. There are many who defend their efficacy and safety, for they bring about agricultural benefits. However, while they may keep particular pests away from crops, the very pests they are designed to keep away can become resistant to one pesticide, thus the greater need to use other pesticides. This seems to be vicious circle. One can get

out of it only by changing the very outlook towards progress. We are so fond of using plastics, for another instance. Since the 1930s we have depended on an ever-growing range of products made from various sorts of plastic. It wasn't until studies were carried out on people working with Polyvinylchloride [PVC] that it was discovered it could contribute to the death rates from breast and testicular cancer[73a&b]. Let us take another example. From before birth and throughout the whole of our lives hormones control many of our vital body functions (e.g. growth, reproduction, metabolic rate, intelligence and behaviour). Oestrogen, the main hormone implicated in breast cancer, controls a variety of different processes in women's bodies.e.g. regulation of menstrual cycle and cholesterol levels, maintenance of bone mass. Its production varies over a lifetime, beginning at birth, reaching a peak at puberty and then leveling off. Excessive oestrogen can stimulate the growth of breast and uterine cancers and the more oestrogen we are exposed to in our lifetime, the greater our risk of developing breast cancer. *We have strong scientific evidence about toxic chemicals in the environment that mimic female sex hormones and overload a woman's hormonal system, a known cause of breast cancer*[74]. Now a days there is a tendency on the part of many practitioners to suggest 'Hormone Replacement Therapy' [HRT] to women after their natural or artificial menopause. Of course, this therapy has its advantages, but at the same time we must be honest with patients, and let them know that there is also an ongoing debate as to the risk of breast cancer involved with this[75]. In the 1980s studies in Long Island showed no link between the incidence rates for breast cancer and the environment. The local women, who had noticed that incidence rates were 10% to 20% higher in Long Island than in the rest of New York State, set about drawing their own maps of the area to demonstrate the need for further investigation. As a result, *"in 1994, the New York State Department of Health released the results of a case control study of Long Island women that showed a significant association between residence near chemical plants and risk of contracting breast cancer"*[76,77]. This event is being cited only to emphasise the role of public motivation. This

role is of greater magnitude today, if we take into account some of the examples of modern life styles. One may speculate, however, that if it is so, then why so little attention has been paid so far to these factors? It is because *prevention is less glamorous than treatment, and fewer profit financially if it succeeds*[78]

Today, the traditional third world cancers, such as those of the liver, cervix and stomach are slowly but steadily being outnumbered by those of the breasts, colon and prostate, presumably due to improvement in living standards; or in other words due to westernisation of the traditional societies. If westernisation per se means progress, then we are progressing no doubt, but only at the expense of more stress and by ignoring the relative safety of our traditional society. What has happened to our traditional society? At the community level we are witnessing a dramatic flux in the relationships between individuals and their social groups. At the macro level the relations among governments are changing fast, while at the micro level the international economy has left individuals not only economically vulnerable but *socially exhausted*[79] as well. We have already lost many traditional guideposts, and have loosened the social ties that bind. Thus, the late 20th century and the upcoming 21st century have been thought to be the *most individualist society in human history*[80]. Mutual concern and the protection of cherished values are thought to be the old notions, and so they have disappeared. They are being replaced by the *strategic special interests*[81] between man and man. They exist free of conventional time and space limitations, and via communication technologies. Since these communities are simply need and self oriented they are typically very heterogeneous. All societies, homogeneous and heterogeneous are in essence fearful about the future; but the contemporary societies are more fearful because of their heterogeneity that makes them numerically and psychologically weaker. Therefore, whatever be their apparent nature, they are destined to lose confidence in their own way of life. When faced with a fearful situation, the people will, therefore, seek emotional solace and security in the safe certainty either of

the past or of the future. The past is past, but what about the future? Is there anything in its treasure that can give solace and security? The way we are progressing, the way we are engaging ourselves in mutual destruction, the way we are vitiating our own atmosphere, and the way we are encouraging our future generation to accommodate a bizarre life style are all potent indicators that we are heading towards a disaster, and thus solace and security will remain the things of the past. The future indeed seems bleak.

Indeed, the world is not a safe place today! Those who imagine that environmental hazards are unique in the less developed countries should remember that they are at fault. In fact the same hazards are eating into the vitals of the USA in such a great length that a number of oncologists had to meet in a press conference[82] to call on the President to *phase-out the manufacture and use of industrial carcinogens and institute a crash program to develop safer alternatives. Expand the testing of chemicals and chemical compounds for carcinogenicity*. There are people to say that if prevention means banning of so many chemicals, then this signifies the end of experimentation, and, therefore, progress. One should remind these people that the molecular biologist and physician, John Gofman, argued in the following manner: If we don't know if there is a safe dose and we pollute, we are performing an improper experimentation on people without seeking their informed consent. On the other hand, if we know that there is no safe dose with respect to cause some more cases of cancers, then we are committing premeditated random murder. Either way, we are violating the human rights. But who are violating our human rights? Who are polluting the environment? Today, Corporations, in the name of globalisation have hijacked our sovereign power and are using it against us; and if we see cancer in that perspective, we realise that cancer, and particularly breast cancer is a political disease. To be more precise, it is no more a biogenic disease, it is a biopolitical one. Thus, in order to prevent the menace we will need to reassert the sovereign power of the people to promote the general welfare. We simply have no

other choice. However, this seems to be an overtly simplistic attitude; for you just cannot identify a number of corporate bodies, label them, and blame them in order to isolate them straightaway. The problem of environmental pollution is of a far greater magnitude and of far deeper significance. We have become victims of our own newly adapted life style. In effect, we feel that we are progressing, while the very progress is eating into our vitals. In effect, we are 'doing better, but feeling worse'. You might ask: What is the right answer here? The answer is: There is no right answer. Like so many things that happen in medical science, there are risks and there are returns. People differ in their attitude toward risk. They also differ in their willingness to pay to avoid risk. If the environmental hazards are to be removed, it invites participation both at the public and at the government levels. And they have a strong political connotation. There is also a danger of trying to move the wheels of history in a reverse direction. Medicine is political science, it is said. The major issues in medicine, when they come to the point of implementation, become political issues. If we envision health care as our right, and thus reducing cancer incidence as our right, then we need the concept of a welfare state. When it was first proposed one hundred or even fifty years ago, it was conceivable that governments could actually implement such a right. Today, we have come to understand that this is not possible.

At the same time, we also know that the social structures are mutable. A vast number of social structures throughout the human history have risen and fallen, only because they were mutable. The current structure that we live in should not, therefore, be an exception. This is more so because the social system that we are carrying on is environmentally not sustainable. Going by statistics alone it seems that it is imperative to control cancer in a global context. There were 10 million new cases, 6 million deaths, and 22 million people lived with cancer in 2000. It has been estimated that if the current rates remain unchanged, there will be 15 million new cases and 10 million new deaths in 2020[83]. This means that we don't enjoy anymore the luxury of playing the role

of silent spectators. However, we must be practical in our assessment, and must not act impulsively out of simplistic conclusions. It means that no change should be fuelled by brashness and egoistic dissatisfaction, but by an authentic understanding of what is truly necessary and feasible. For instance, we must be aware that many of the proven causes of cancer today are hard to control, including nuclear experimentation and radiation, viruses, sunlight, rampant medical procedures and abuse of drugs, industrial pollution, unplanned urbanisation, and the addictive habits of cigarette smoking, chewing, overeating, drinking alcohol and inherited genetic defects. It is, of course, politically expedient to attack one or the other known cause, and sometimes we find satisfaction out of it; but this kind of expedience never gives any lasting result. For instance, in the USA, reduction in smoking has, of course, resulted in the decline in death from cancers as a whole; but at the same time the incidence of cancer in the young men has increased by 4 times and in the young women by 50%. For another instance, it is well known that radiation causes genetic mutation. What is not well known is that there is no safe dose of radiation, according to the U.S. Environmental Protection Agency. Furthermore, radiation dosage is cumulative throughout life, and there is no programme in place to monitor patients' cumulative lifetime radiation exposure, even though the technology exists. So the moot point is that in this respect there is nothing much that we can do. Similarly, it is important to consider that most women who get breast cancer have none of the currently accepted risk factors for the disease. In fact, the currently agreed-upon risk factors explain less than half of all cases. This is not to imply that it is naive to think about prevention since it does not make much difference; but to emphasise that although, prevention is indisputable, it might not be feasible. We are aware that it is unclear today how to establish a viable, free, logical and humane system of health care. We are also aware that in the absence of such a system in concrete terms and forms, the very notion of an alternative system has a utopian air about it.

EARLY DETECTION ?

"First they told us the world was flat. Then they told us it was round. Now they are telling us it isn't even there!" [Irving Oyle]

If prevention of breast cancer is so difficult as such, let us examine if we can screen our population so as to detect *presymptomatic* breast cancers and *early* breast cancers, for in that case we may be able to reduce the morbidity and mortality at least.

The recent developments in the genetic-testing techniques indicate that the identification of 'presymptomatic' breast cancers might be possible, although in terms of economics, there is no evidence that this kind of screening care will be feasible. Most techniques of screening care, however, do not save money; they cost money. But they do save lives. Breast cancer screening, cervical cancer screening and colorectal cancer screening with molecular techniques will be really costly; and the *cost will escalate exponentially*[84] if we move to screen say, three-yearly, then two-yearly, and then yearly. But we would also possibly save lives. If we catch cancer in its early stages, we will prevent a lot of expensive treatment later on, thereby saving money in the other manner also. The problem is, in order to find the one person who has cancer, we have to screen several thousand people who do not. That is why the aggregate costs will be so high relative to the benefits. Apart from that, as we have already pointed out, the identification of gene-related marker is one thing, and inevitability of the disease is another. To *complicate matters further*,[85] some genotypes may increase the risk of one cancer but decrease risk of another. There are other adverse psychological consequences of presymptomatic genetic testing also. Someone with a positive result may respond fatalistically, while someone with a negative result may develop a *false sense of security*[86]. Even if we eulogise the importance to the genetic component, we still *do not understand*[87] the mechanism of changes occurring there inside the DNA. It is, of course, expected that one day we shall understand

the underlying mechanism, but till date it is not clear whether understanding a problem will really teach us how to control it. We understand sunspots, but there is no question of controlling them. Most diseases, like coronary heart disease, cancer, diabetes, arthritis and mental illness have genetic components, but multifactorial diseases have both genetic and environmental components which contribute in *different proportions*[88] in a given patient or family. Thus, in effect the whole purpose of molecular screening will remain largely either an academic, or a commercial exercise. Thus any assumption that gene studies in cancer will virtually eliminate the disease is a false assumption.

What can we do about *early* detection, clinically? Most of the time and almost by instinct, we advocate *Breast self-examination* [BSE]. Despite all our insistence for breast self-examination over the past 30 years, we see from our experience that most women do not do it and the vast majority doesn't do it properly. Even if they do it properly, is it true that they are helping themselves? A recent report from the Canadian Task Force on Preventive Health Care, however, says that BSE should not be taught routinely to women aged 40 to 69 years and there is *little evidence*[89] to suggest it is a useful screening tool at other ages. In other ways, it has simply increased the rate of biopsies in normal breasts. Unnecessary anxiety, followed by unnecessary investigations and eventually unnecessary surgery are all destined to produce a commercially viable project, but that is the reason why report says that it is *proven*[90] that BSE is rather harmful.

Can we depend on Mammography? Let us look at the science of oncology at the elementary level. One divides into two. That is the basic law of nature, as that of the cells. One cancer cell divides into two, then four, then eight and so on and so forth. We call it doubling, and the time taken for one doubling is called doubling time. A tumour is a sum of cancer cells plus the normal cells. The cancer cells are descendants of one cell that had

transformed and then doubled for several times. Therefore, the number of cancer cells can be described by the equation 2^n [n = number of doublings]. If we ignore the normal cells, then 1 cc tumour consists of 1 billion cells, e.g., 2^30, approximately. On an average, a breast cancer cell takes 100 days for one doubling [the range being from 25 days to 1000 days]. Therefore, 30 doublings take 8 years approximately [30 x 100 days]. We know that it is theoretically possible for a mammogram to find out a breast tumour at 1 cc which in effect, means we are already late by 8 years before we could detect a so-called early breast cancer! If now the tumour is left untreated and the doublings continue, then by another 10 doublings [total 40 doublings] the volume of the tumour will be 1000 cc [1000 cc = 10^12 cells = 2^40]. This volume of a breast tumour is lethal. Thus, when we are to treat breast cancer diagnosed at mammography at the earliest stage, we are to deal with only 25% of the total life history of the disease. However, this is only a linear measurement, and one must be aware that there are many realistic limitations also. In clinical practice, when we find a breast tumour on palpation, it is about 3 cm in diameter, containing about 45 billion cells. It has, therefore, completed 35 doublings. If this tumour is still localised in the breast only, we call it early disease. What difference does it make if we insist on diagnosing a tumour after its 30th doubling, instead of 35th doubling [e.g., mammography Vs palpation]? The available data suggest that there is *no evidence*[91] to prove that a breast cancer starts spreading only during the last 5 doublings [from 30 to 35]. Therefore, although, mammography has its utilities as any other investigation, it is illogical to assume that our newfound ability to observe breast tumours between the thirtieth and thirty-fifth doublings means that it is a great achievement in terms of prognosis. Why do we insist on mammography then? It is simply because it is there! It seems that the proponents of mammography *continue to ride roughshod over scientific evidence, driven by emotional, commercial, and political compulsions*[92]. And thus mammogram is *oversold*,[93] and screening for breast cancer with mammography according to a number of *studies*[94, 95] is unjustified because mortality from breast

cancer is not reduced in this way. Some *researchers*[96] even have gone to the extent to say that it is a risky procedure, in that the compressive force used in order to obtain useable mammograms may be enough to dislocate and spread any existing cancer cells. In fact in the UK the force used to squeeze the breast as flat as possible corresponds to placing twenty 1-kilogram bags of sugar on each breast. According to these researchers the number of cancer sites can increase by as much as 80% when tumours are manipulated mechanically in this way. Dr. I. Mittra of Tata Memorial Hospital in Bombay had *estimated*[97] that the cost of mammography was 5-10 times higher than the cost of physical examination. He has also pointed out that mammography may cause anxiety in women awaiting their test results and often leads to unnecessary biopsies and treatments. On the other hand, mammography misses 10-15 per cent of the so-called early breast cancers thus providing a *false sense of security*[98]. Women over 40 years of age have long been advised to have an annual mammogram, while it is seen that only *1 in every 20,000 women*[99] screened actually receive a benefit, it is clear that there is no wisdom in this advice; rather it a sheer wastage of resources.

There are other interesting questions also. For example, some *researcher*[100] refuse to see breast cancer either as a local or as a systemic disease. To them it is not a question of early versus late. Breast cancer does not necessarily go from 0 to 1 to 2 to 3 etc; it may start as 4 or 3 or 2 or 1! Thus, according to these researchers no matter how small the disease, if it is cancer it has to grow and spread, resulting in an eventually unchanged statistics of the mortality for breast cancer.

It appears thus, that there is in fact no reliable, dependable and acceptable way either for screening, or for early detection of breast cancer. The only possibility of prevention rests at the public level, therefore. However, there are scientists who refuse to believe it either. Dr Emil J Freireich, a pioneer of modern oncology says

that *Cancer treatment is always better than prevention... Public health strategies won't work, prevention strategies that affect individual strategies will never work. We will always have cancer; it is one of the greatest challenges to the human intellect*[101]. So, we have been told that we should intensify our search for more effective treatment. Let us now see our prospect at that level.

TREATMENT?

"The human brain is a remarkable organ. It begins working the moment you are born and never stops until you stand up to speak in public".

Our contemporary practice is to start treating a breast tumour as soon as we find it by whatever means. We treat it with surgery and chemotherapy almost always, in their various techniques and forms; and by radiotherapy and hormone therapy most of the time. Almost always we tend to impress upon the patient that this is urgent to start treatment. The medical community raises many hue and cries as soon as a case of breast cancer is diagnosed in an advanced state. Sometimes the patients are accused of their ignorance and callousness and at other times the attending clinicians are castigated. This is done despite the fact that whether delay in diagnosis at any level really influences the prognosis adversely is still an extremely *debatable issue*[102]. This is, of course, not to indicate that any such delay is desirable, for earlier diagnosis certainly reduces morbidity and saves money; but at the same time this has to be propagated that breast cancer is *not a medical emergency*[103]. Almost always our surgeons come out of the operating theatre to say that they have 'got it all', meaning, of course, that they have eliminated the primary tumour. And elimination of the primary tumour marks the beginning of a prolonged treatment most of the time. At the end of the day, the women having 'bad' type of breast cancer that we call 'invasive', always remains at 16 times higher risk of dying prematurely than women without breast cancer. Postoperative therapies are

important advances, in that they buy time; and we go on treating most of these patients with larger and larger doses of anticancer drugs with the hope that *the tumour will die (just) before the patient does*[104]. In 1935, 26.2 out of every 100,000 women died of breast cancer. In 1992, the latest year for which figures are available, the adjusted rate of mortality was 26.2 women per 100,000--*the same as in 1935*[105], despite our latest chemotherapy activism. It is true that the journey through conventional chemotherapy followed by aggressive chemotherapy, followed by high-dose chemotherapy and marrow transplantation, followed by even targeted therapy have all resulted in gradually improved response rate in breast cancer. It is also true that they have excellent role to boost the quality of life for some time may be even in terms of years; but the outcome in terms of mortality remains unchanged, and thus the resultant benefit remains *inconclusive*[106]. Response rate alone is a poor parameter in order to assess therapeutic benefit. For instance, according to conventional teaching [Cecil's TextBook of Medicine, Ed 18, 1988] the overall response rate in advanced breast cancer is 75%, whereas the disease-free survival is rare. The overall survival after having an advanced breast cancer has not improved during the last 30 years. Even if we take 'response to treatment' as a useful advancement, we shall have to quantify it; for instance, how long a particular response is going to sustain. In terms of weeks, or months, or years, or decades? The novel pharmacological approaches that have developed during the nineties are already immensely expensive; newer approaches are going to be more. But do the percentages of response after using these drugs make their use worthwhile? And moreover, does the period of response balance the *cost involved*[107 (a)&(b)]? The answer to both the questions is unfortunately: NO! For instance, if the total cost of first line chemotherapy programmes in breast cancer is a few thousand rupees only, that of the second lines will be around 5 times more, and that of the third line will be 10 times more than the last one. Surely, the improvement in treatment modality is incremental, but so is the cost! The question, however, is how much progress is

possible with this incremental approach? The latest treatment modalities in breast cancer have become the exclusive preserves of the filthy rich people only. Those who think that these financial constraints are unique for the poorer countries only are utterly wrong. In fact, since the health-care budgets in the developed countries are already tight, the increasing expenses of cancer treatment have already created *political problem*[108] and there are going to be more such. Again those who think that the insurance companies will bear the budget are equally wrong. There are indications already that they will *refuse to oblige*[109]. In that sense, we are indeed reaching an intellectual impasse.

This has led us reach a critical point where we are disappointed with the further progress in treatment. We have relied too much on chemotherapy. This has to be reaffirmed that cancer is not a polygenic disease only, it is heterogeneous also because of the unique interactions between the individual and the gene protocol. And not only that; gene mutation also results in a population of cells with significant heterogeneity. Cancer cells within individual neoplasms are also a heterogeneous collection of sub-populations. These sub-populations of cells differ even in their *sensitivity to treatment*[110]. This means that most treatments will not eradicate all the cells. Some cells will remain resistant. This again implies that we are unlikely to find general treatments that will work for all, or even most, patients. One of the problems in our mindset is that we tend to believe in generalisation and oneness in regard to disease and its treatment. This possibly arises out of our concept of the universe. We believe in the basic oneness of the universe at a deeper and fundamental level. Cancers are also the same at the deeper and fundamental level; but the cancer cells are indeed a heterogeneous population, and they consist of different traits. In chemotherapy, we use agents that interact individually and effectively with each cancer cell. Chemotherapy wipes out 95 to 99.9 percent of the residual cancer cells in a patient's body, after surgery or radiotherapy. This figure as such, seems to be impressive, but as far as the actual impact is concerned only those

cancer cells along with some normal cells are affected that express a *particular trait*[111]. As a result, therefore, the other cancer cells escape the attack. The remaining cells, May be say, 10000 which are resistant to chemotherapy, will keep on proliferating, at the same or even a greater rate. Thus the tumour burden will revert back to its original position after a few doublings. *Cruelly, chemotherapy helps least those who need it most*[112]. And let us not forget that the prolongation of death is not the same as the prolongation of life. It appears that while relying too much on chemotherapy, we have relied too much on pharmaceutical industry.

Despite enormous amounts of hype and optimistic puffery, pharmaceutical research is actually *failing*[113]. The annual number of new chemical entities submitted for approval is steadily falling in spite of the enthusiasm for techniques like combinatorial chemistry, high throughput screening and pharmacogenomics. Nowadays an urge to merge is being seen in the pharmaceutical industry; but even this drive to merge is also driven by failure, not by success. Even if we examine the claims of the pharmaceutical industry, we find that they are so shaky that the two biggest successes, the beta blockers (now widely used in treating hypertension) and the histamine-2 antagonists (effective against peptic ulcers), had to come from the mind of one man, Jim Black. This view may be contested, but that is a matter of outlook. Of course, we have made progress against several uncommon forms of cancer, in the improvements in palliation in several other forms of cancer, and in the extension of the productive years of life in some of them; but we cannot escape the summary conclusion that *Chemotherapy is known to have 90% of it's successes in 10% of all cancers, namely, Hodgkin's diseases, acute lymphocytic leukemia and testicular cancer, as well as certain rare cancers. No disseminated neoplasm incurable in 1975 is curable today*[114]. It seems that the cancer industry in conjunction with certain scientists has forgotten that the continuing euphoric projections of the successes in anticancer treatment, despite a *minimal overall*

improvement in the last 15 years[115] are more likely to be targeted at the stock market, rather than at the scientific community, much less the public. As a result, both the clinicians as well as the public, after having passed through decades of optimism, are now becoming more and more skeptic.

The technological triumphs in medicine in this century outweigh our aggregate achievements in the entire past. We now carry Rs. 10 lakhs worth of equipment in our car; but that does not essentially mean that we now are able to cure more diseases. Of course, technology does what it has been designed to do, and as such it is effective; but what it just cannot touch becomes crucial. It seems that we need to face the inevitability of cancer, since cancer is the price we pay for being sophisticated organisms. It has to be reaffirmed that rather than anything else it is the higher incidence of neoplasm's occurring subsequent to survival of other diseases, that is the basic reason of the rise in cancer mortality. It has been *suggested*[116] that in the present century a third to a fourth of all deaths will be cancer-related, at least in the developed world.

Scientists say that we are making progress since newer discoveries are on the line. In breast cancer, the 'BRCA' genes and 'Herceptin' were going to be discovered sooner or later, because they were there. Discoveries in science are not essentially beneficial; some might be harmful also. It remains to be seen what net benefit we will be offered out of the new discoveries in breast cancer; but meanwhile millions of our patients will be consumed by anxiety because they will think that the new discoveries have only robbed them of their purse. Are we really making progress? This question seems to be pertinent because the newer developments in cancer research sometimes have a real potentiality to lead us to unnecessary treatment, by means of *overdiagnoses as well as overtreatment*[117]. This happens equally in other diseases as well[118]. Medical researchers estimate that 80 per cent of all angiographic procedures are inappropriate and that half of all

bypass operations performed in the United States are unnecessary or of no benefit[119]. Similarly, more spine X-rays and MRI lead to more back surgery, and that more prostate tests lead to more prostate surgeries[120]. Clinical care, as it seems has been largely dominated by diagnostic batteries resulting in the down gradation of wisdom and experience in favour of *'spurious objectivity'*[121]. It seems, therefore, that rationality has become the greatest victim of circumstances. The absence of rationality leads us towards a state of *overoptimism*[122] wherefrom, we tend to believe that we are gaining ground each day. All these we believe because essentially we believe in linear progress in science. The concept of linear progress in science, however, was strongly propagated by an extraordinary school of economics, by courtesy of the governments of some developed countries, particularly USA and UK. They propagated the ideas of *"Endogenous Growth Theory"* which stated that economic growth depended on scientific and technological advances. The fallacy and emptiness of this theory were *exposed*[123] long back and it was convincingly explained that science demonstrates diminishing returns, as a result of which economic growth will decisively slow down. In cancer medicine, we have witnessed great efforts by great scientists, marked by great fanfare. The great fanfare did not match with the net outcome, however. One of the latest examples is the gene therapy in cancer.

What really is offered by the genetic studies is the structure of the evolutionary history of the humankind. The structure does not explain the whole building; nor does it describe the interior decoration. Nevertheless, gene therapy in cancer has already promised too much. We hope that one-day gene therapy will be used to treat cancer in more than one way. One of the approaches that is comparatively easy to understand is that the cancer cells will be isolated and taken out of the body. They will be altered genetically and will be returned to the body. These cells will now act as cancer vaccine. Some questions, however, will still disturb us. Will the new gene, randomly lodged in a cell's chromosome,

trigger a new cancer? After all, these are all 'engineered genes', and one does not know whether the cells will remain capable to keep them dormant. What if the engineered gene makes its way into the germ cells and get passed on to the children? Certainly, the results will be *catastrophic*[124]. The risks have been claimed to be minimal, but they are *real*[125]. At the present moment, however, although the description of an n-dimensional arrangement of hyper-cubes in gene studies is impressive to us, but not yet useful in practice. Promising too much is an understandable but unnecessary error, for we must not forget that Johannes Fibiger was awarded with a Nobel Prize as back as in 1926 for finding the cure for cancer. And it took the Nobel committee a long time to *live down the award*[126] since it became apparent after some period that his model was not the solution that everyone was looking for.

Biology indeed is not engineering, and neither there is any scope of arithmetic *understanding*[127,128] of the *evolving issues*[129] of genetics of cancer. Everything evolves, but man knows that he evolves, develops and then deteriorates until the eventual death. He must also know that the strands of DNA that direct the development of the trillions of cells in a human body ultimately lead it to death[130]. The human body fails because there are flaws in the intricate design the human body is made of. Nature does not overspend. It does only what is sufficient. It does not seem to be bothered with perfection[131]. Thus, we would like to remind those who think that the perfectionists will successfully chase cancer with a linear model in hand, and will one day find out the *philosopher's stone*[132], that the future explorers will prove someday that they were thousands of miles wrong in their conclusions. Should we now try to imagine the nature of our future explorers? Will they be mathematicians, or the clinicians, or the biologists, or a combination of all of them? What could be the nature of their exploration? But before we start reading these explorations, let us look at the so-called *alternative therapies*.

CHAPTER III

ALTERNATIVE THERAPY ?

The history of medicine has been explored and elaborated in various ways. We can also summarise the history in brief, in the following way[133]:

I have an earache.

2000 BC: Here, eat this root.
1000 AD: That root is heathen, say this prayer.
1850 AD: That prayer is superstition, drink this potion.
1940 AD: That potion is snake oil, swallow this pill.
1985 AD: That pill is ineffective, take this antibiotic.
2000 AD: That antibiotic is artificial. Here, eat this root.

It seems that at the last lap of the last century, *progress through science* had been replaced by *back to nature*, at the popular level. If we start eating the root in order to get relief from earache, it only signifies that we are trying to elevate the natural world above human attempts to modify it, which means that we have lost faith in science. Of course, this outlook has evolved out of glaring social crisis. The wars and man-made disasters have made general public lose confidence in science and technology. Science has moved at a pace that has outstripped the ability of law, morals, and ethics to keep up. Science, often viewed by the public as identical to technology, has scared many people. They feel that science is intimidating, and so they search for something simpler, more understandable and more caring. This results in an overly simplistic belief that anything that is natural is curative and can't hurt. In an objective analysis, it seems that science itself cannot be blamed for this loss of confidence in it; rather it is the manner of its use that is largely responsible. This is a crisis within the population level. Moreover, the linear progress in science, the way medicine has developed in the recent times has pretended to establish its

dominant nature in the society, thereby creating a gap between our expectation and the stark reality. The proponents of the so-called alternative therapies so as to rationalise their approach eventually magnify this gap. There is a myriad alternative cancer therapies available all over the world and all of them enjoy support from various quarters, ranging from religious leaders to political spokesmen. Laetrile, Shark cartilage, Antineoplastones, Antineoplastin (from Kolkata!), Gakacu (from Mumbai), homeopathy, Sarbapisti and other Ayurvedic products, and Di Bella Multitherapy are only a few to be named. There are host of others known and unknown. All claim to cure or at least contain cancer for a long period; and some of these are explained in curious languages, like altering the vibration of cancer cells, making cancer burst onto the skin and so on and so forth. They are most of the time claimed to be inexpensive and without toxicity. However, none of them so far, could stand scrutiny of the standard and accepted methods[134]. Meanwhile, these alternative therapies, in the name of holism, as opposed to fragmentary approach to the problems of health and disease, have been legitimised to a large extent and professionalised to some extent[135].

If this is a crisis at the popular level, there is a more important crisis at the scientific level also. It is the gap between evidence and reality. This crisis leads us to consider newer approach at the scientific level. It appears as some eminent oncologists are beginning to believe that we must undergo a radical shift in our thinking - an intuitive leap so dramatic that it will completely transform our approach to cancer treatment. Voltaire said, "God is on the side not of the heavy battalions, but of the best shots". We are no more interested in heavy battalions as we have seen enough of an enormous cancer industry. It is far better to have fewer, properly funded, highly motivated individuals getting on with producing new insights. It is better if we can *"shake off some of the more ludicrous mental strait-jackets we're currently wearing"*[136].

CHAPTER IV

NEWER APPROACH?

There is about 200 times more gold in the world's oceans, than has been mined in our entire history.

Today's oncology practice, particularly in the field of breast cancer has been largely dominated by chemotherapy. The logic used in chemotherapy of breast cancer patients is intimately tied to growth patterns of the cancer cells. Our conventional idea is that in an advanced breast cancer the cells there are relatively slow growing. Therefore, we remove most of the cells by means of surgery, sometimes followed by radiotherapy. The remaining cells are smaller in number, and so they grow faster. Since they grow faster they are more supposed to be killed by chemotherapy. This is Gompertzian model. Chemotherapy is advised according to this model; it is continued for sometime until limited by toxicity and then stopped. Then we hope for the best. However, this reasoning is valid in animal models, and we have had only modest improvements in survival rates over the decades. Apart from tumour heterogeneity that we have discussed before, the main reason why chemotherapy fails to cure breast cancer is the repopulating of surviving cells after some level of tumour-cell kill. Thus what we achieve after cytotoxic therapy is a temporary remission only. If we are to counter some of the effects of repopulating, cytotoxic treatment has to be done with a lethal dose. Since it is impractical it is difficult to agree with the Gompertzian growth model itself. Clearly, a *different model*[137] for tumour-cell kill is required. Although, mathematical modeling in oncology have *serious drawbacks*[138], such as the absence of a unifying concept, the presence of some assumptions which might be unrealistic in many practical situations and etc, of late a *'stochastic' model of tumour growth*[139] has been developed. Research using this model predicted that tumour growth was mostly erratic, with

alternating growth phases and periods of no growth or temporary dormancy[140, 141,142,143,144]. This work challenged the Gompertzian model, and has shown that the evidence to support the Gompertzian model in breast cancer at least, is very weak. On the other hand, there is much well documented evidence to support temporary dormancy in the *natural history*[144, 146] of breast as well as other cancers. In most of our breast cancer patients we see a distinct design in the recurrence of the disease. There is a first peak of recurrence around 18 months after breast cancer surgery – suggesting that tumour cell stimulation at the time of surgery may be implicated. The next peak for recurrence is 5-7 years after surgery, but this cannot be explained in the similar way. This has been described as a *spontaneous occurrence*[147]. This spontaneous occurrence has been described in the following way. Some tumours produce a substance called angiostatin. When we detect a malignant breast tumour, we detect a tip of the iceberg only; for there might be millions of cancer cells at the microscopic level at the sites quite distant from the breast tumour. We call them 'micrometastases'. These cells do not have adequate blood supply, and so they can not proliferate. This avascular state is maintained by the substance, *'angiostatin'*[148]. It is, indeed, interesting to note that the mother tumour itself maintains its children and grandchildren in this manner! When we remove the breast tumour surgically, we remove the source of angiostatin. As a result, the micrometastases start growing over time. They take several years to manifest themselves, and thereby to be detected clinically. Of course, we put our patients on chemotherapy after surgery, but most of these cells are not very sensitive to chemotherapy as they are basically slow growing. Thus, chemotherapy is expected to kill most of the rapidly growing cells that have been implicated after surgery, but not those micrometastases. In effect, therefore, we might be successful in fighting the first peak of recurrence, but not the 'spontaneous' ones. The possibilities of the presence of micrometastases as well as their volume do not correspond with the size of the primary breast tumour. A small tumour as such is not so innocent in so far as its ability to harbour micrometastases is

concerned. In these cases the possibility of 'spontaneous recurrence' seems to be more. Thus, it has been predicted[149] that only 15% of patients with small breast tumours would benefit from chemotherapy, whereas 51% of those with large tumours would do so. This means that the smaller the tumour, the less effective is the therapy. This is, of course, against our conventional outlook. In this way, it is becoming more and more apparent that the patients who relapse under the second peak may be treated not by conventional chemotherapy, but by some other method, such as *'anti-angiogenic therapy'*[150]. These observations compel us to look for a new paradigm.

Needless to say that the results of our present anatomo-histological approach to treat breast cancer are numerous, irrefutable and sometimes specific, and it generates a wealth of valid data; although no one seems to know how to translate this into progress. There are *scientists*[151], however, who consider that this approach based on assumption of linear biologic reality and simple cause and effect relationships might be erroneous, because it presupposes the predictable outcomes and summation of parts to equal the whole. According to them, this paradigm has *outlived its usefulness*[152]. On the contrary, if we step out of this one-dimensional approach into a multidimensional world, we see that the whole is more than the sum of the parts if the physiological and pathological processes of the disease are taken in their full complexity. We all see in our practice that in the life history of a particular cancer in a particular patient, predictability is possible only on a short-term basis, and unpredictability sets in over the long run[153]. We have come to know that the relationship between cause and effect is not linear, since multiple factors and variables that are contextual and non-linear[154] influence it. Even the dynamic interactions of the genes with the environment and the consequent development of heterogeneity cannot be explained by a linear model[155]. In a non-linear model the meaning and use of evidence itself will require further revision and new *refiguring*[156]. The application of nonlinear dynamics has shown that small,

appropriately selected changes may yield disproportionate social and cultural benefits that impact health, disease, and prevention. Slight changes in cholesterol levels or in coronary artery diameter for instance, yield disproportionate benefits in clinical outcome[157]. There is, indeed, documented evidence that much lesser treatment in breast cancer in terms of enormity has yielded comparable results. For example, it has been shown that 58% overall survival at 21 years could be achieved with limited surgery followed by radiotherapy followed by short course of 'non-aggressive' chemotherapy[158]. The experiences of our yesteryears might also endorse the values of such studies. The prevention, cure or more effective treatment of cancer thus, may reside in multiple *smaller input at critical points*[159]. Let us not forget that there is only a difference of less than two percent in the basic genetic make-up of human beings and chimpanzees a difference that can be quantified in terms of molecular chemistry. This small dissimilarity has made an enormous difference between one species and another. In a non-linear model, however, it might be difficult to define cancer since there is a gray area between latent and active disease. Many scientists have legitimately considered cancer as an inevitable consequence of life and of the aging process. Maybe cancer is a consequence of life, which we will all develop if we live long enough. Almost all of us can be considered to suffer from latent cancer if we consider the almost inevitable existence of 'in-situ' cancers within the breast, prostate or thyroid gland. It might also be difficult to define what we mean by 'cure'. There are many other potential areas for exploration. Even if we set aside the fact that some animals - some species don't get cancer, such as Newts, and some human societies are known to suffer more cancer than others do. Shamans in Amazonian Indian tribes smoke prodigious amounts of tobacco in healing rituals – and don't get cancer. There are other relevant questions: such as, the question of occasional spontaneous remission. We usually ignore it because we don't understand it. But there must be some process somewhere in the conceptual mists that may reverse the malignant process. There are determinants, as we know, of emergence and non-emergence of

cancer. These determinants are not linked to each other in a linear, predictable manner, and, therefore, also form a complex system. If we try to read this complex system with a non-linear model, there are strong possibilities that we can refine our *'diagnosis by revealing new disease categories, improve prognosis by linking clinical heterogeneity to biological diversity, and offer the prospect of new treatments'*[160]. If things go in the right direction, as it is being expected, the clinicians with the help of the scientists will eventually create a new period of marvelous medical discovery.

Throughout the history of science other disciplines astronomy, particle physics, etc. have been advanced when the fundamental ideas governing the discipline were redefined. These redefinitions are often termed *paradigm shifts*[161]. Earlier scientific theories are reinterpreted, sometimes discarded and replaced by newer ones. We have witnessed these changes in the realms of medical science over the centuries. The miasma theory of infection has been replaced by the germ theory, now part of the current biological theory of disease[162]. Disease models also, therefore, change. The era of 'randomised trial' possibly began in 1948 with the publication of Streptomycin trial[163]. Since then the era of diagnostic skill is slowly but steadily fading away. This era will be slowly but steadily replaced by another era that is destined to force a revision of the accepted certainties about life, disease, disease classification and treatment. Today, we claim that we have been able to increase the human life span. Of course, our maximum life span as compared to the earlier centuries has increased. But this may also be due to the fact that there may have been evolutionary selection for longer human lives. In spite of our much arm-waving and frequent hopeful statements on treatment and research, there is no evidence whatsoever that science or medicine has done, or ever will do, anything to influence the maximum human life span. The overall mortality of any human population in any period of 125 years is 100%. In other words, the overall mortality in any 100-year period is way over 99%. Thus it is 90% in any 80 -year period, and so on and so forth. It seems that people survive to near their

own *internally programmed limit*[164]. Medicine, therefore, has not increased the life span of an individual, and neither that has been its task. It has only tried to make life more comfortable and more adaptive. So far as the diseases are concerned medicine certainly sometimes cure and often relieve. However, its main task was to console always; and at that sphere it has failed miserably. Thus the crises of modern science if it can be said so, lies in its failure to introduce humour. Thus, we tend to forget that because of increasing longevity on the other hand, deaths from cancer will increase: in India this rate will rise by *285% as life expectancy increases by 9 years between 1995 and 2025*[165]. Today, medical research is being done so obsessively and with so little humour, that it is being governed by the false belief that human existence per se can be reduced to a formula. And when we find discrepancies we adjust them by *approximations and statistical manipulation*[166]. It seems therefore, that the linear concept is no longer able to explain the diverse and complex events of the present time. As a result, a novel idea of *nonlinear dynamics* that has been developed since 1975 has gained access in medicine. It has turned out that almost all laws of nature (especially in biology and medicine) are nonlinear[167]. Non-linear dynamics exhibit not only apparently random unpredictability, but also a degree of determinism in that randomness[168]. In the ancient times the patients used to get protected during disease by the *healing force of nature*[169]. This force has now been replaced by technology. With advances, technology now can detect even the minuscule aberrations in health and disease. In oncology, the newer advances direct us to detect the tiniest cancer cells in the making. Still, we do not know if these *abnormal* cells are destined to cause disease. Will the normal physiological process, called 'apoptosis' eliminate them? Will they remain dormant, and if so, for how long? Should we kill them; and if so at what advantage? In this way, it seems that we have reached a conceptual impasse. In contrast to the previous era, therefore, the question that haunts us now, is not how to treat, for we are convinced we shall come to know fairly enough about it; it is what are we supposed to treat, and more importantly, when?

CHAPTER V

THE FUTURE

"Not only will men of science have to grapple with the sciences that deal with man, but---and this is a far more difficult matter---they will have to persuade the world to listen to what they have discovered. If they cannot succeed in this difficult enterprise, man will destroy himself by his halfway cleverness."
[Bertrand Russel]

The present social system describes both the 'economic' and 'sexual' man as isolated, asocial, greedy and competitive by nature. These convenient fabrications of man's nature fit well with the present medical system. The nature of cancer research fits still better, and is held in high esteem. But in essence, this system is incapable of meeting human needs when expressed in collective terms. If we see health as a collective property, the role of a competitive system that seeks only to maximize wealth and power, and thrives only on market relationships, comes down to the level of anti-human and intolerable. Hence, what we need is a radical structural transformation, challenging our ideological fallacies, our thought and our action on the other. The Newtonian Universe taught us that small changes in a process will produce small effects, whereas larger changes will have larger effects, meaning that the effects are proportional to the changes made. In practice, however, we are seeing that a small change in a process creates larger and disproportionate effects, and that there are small time predictability with large time unpredictability of the effects of our actions when we are dealing with the individual patient. This non-linear dynamics is going to be our next conceptual paradigm in the future. With the help of the new paradigm, *'we shall realise the wisdom of the ancient Aristotelian approach to the study of nature, which means that we shall no longer regard disease as a 'mechanical fault in the human machine' but as a disturbed life*

process. We shall apply the theories of open systems and non-linear dynamics to medical problems, and we shall reach a fuller understanding of the development of disease. We shall use our new knowledge to invent new effective therapies, but we must not harbour the illusion that we shall ever be able to eradicate disease"[170]. It can be safely predicted that during the next century, our ways of life will undergo radical changes, and, therefore, we can also predict the emergence of new diseases. There will be no "health for all", even by the year 2100.

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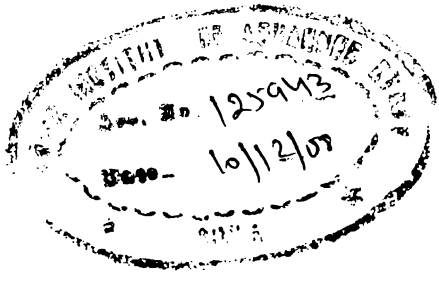

Dr. Sthabir Dasgupta (b.1950) joined the medical curriculum in the year 1965. He had studied in RG Kar Medical College & Hospital, Kolkata, West Bengal. After receiving training in the different branches of medical science, his interests were drawn into the field of cancer. He had received extensive training in the field of cancer treatment. At present he practices oncology in his private capacity. He is also attached to Duncan Gleneagles Clinic and Suraksha Hospital, Kolkata.

COMMENTS

The author from the start of his medical profession has been working as an oncologist for more than 20 years. His keen vision on various facets of management of breast cancer is nicely depicted in this monograph. He has elaborated the crux of the pr[illegible] mind the new and the old ideas [illegible] nerce oriented treatment with th[illegible] tried to impress the dilemma [illegible]. In conclusion he has mentio[illegible] the future ones to provoke more interest of the readers. The entire monograph is filled with information and rich with references.

— **Prof. Tarun Deb Moulik**