

## Alternative Approaches in Cancer Chemotherapy

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### Abstract and Keywords are not provided

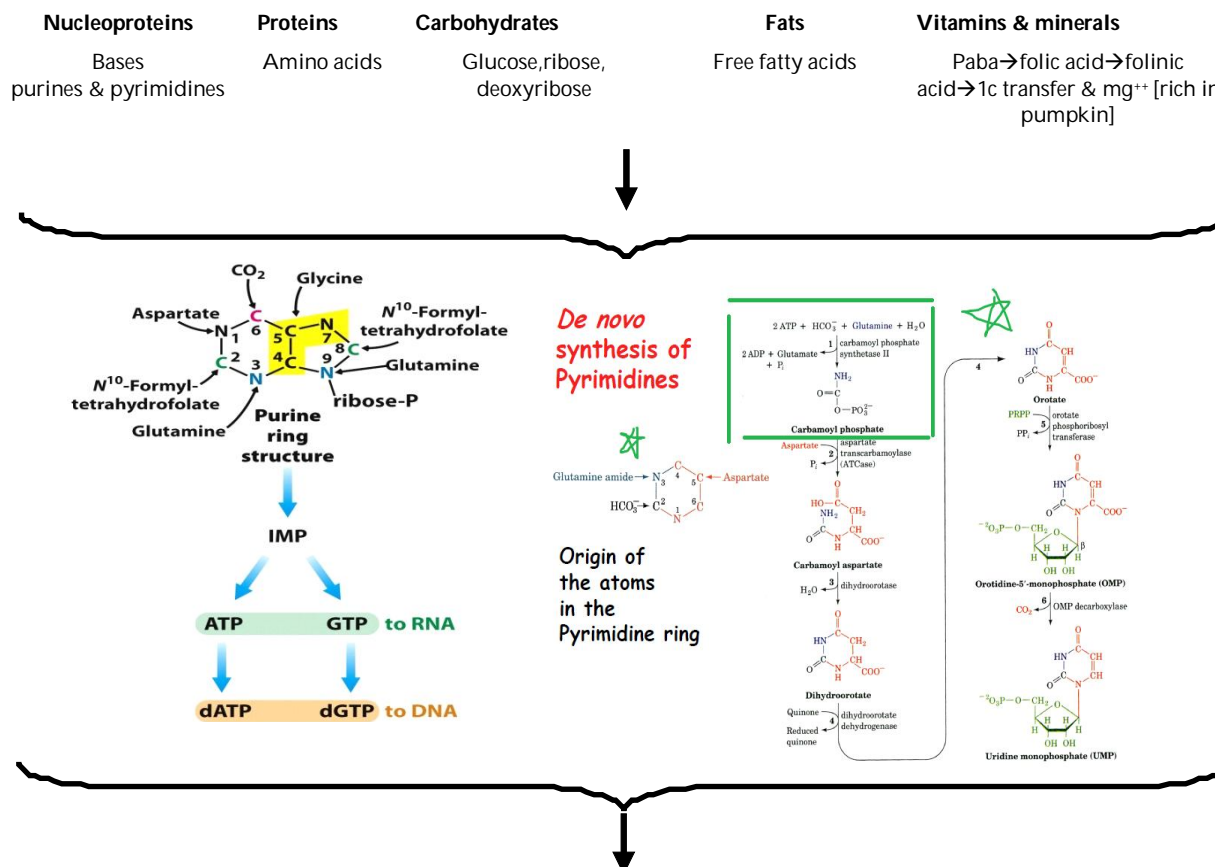
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DNA (deoxyribonucleic acid) expresses a large number of proteins through the process of transcription which are mainly responsible for the cell division (replication). Nucleoproteins of DNA are derived from the food we eat which give rise to nucleoproteins by salvage pathway or through de novo synthesis of purines and pyrimidine from the nutrients we consume as food. Various amino acids in the food like fumarate, glutamate, glycine,

methionine, S-adenosyl methionine etc give rise to various atoms in the synthesis of purines and pyrimidines. One carbon atom is transferred from folic acid, in addition gaseous materials like oxygen and carbon dioxide also contribute in the synthesis of DNA. Magnesium plays a key role in the synthesis of DNA [1]. Further, ribose and deoxyribose are attached to synthesize DNA are also obtained from carbohydrate we eat (Fig 1).



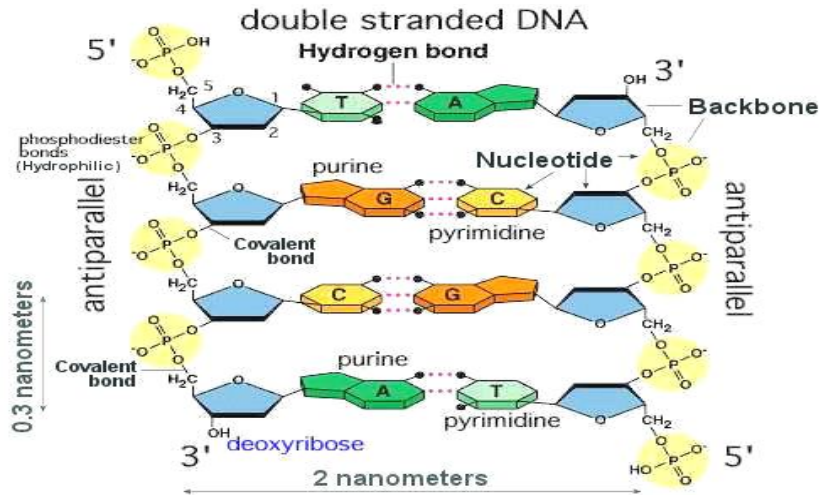


Fig. 1: Dna synthesis with food materials [de novo/ salvage pathways]

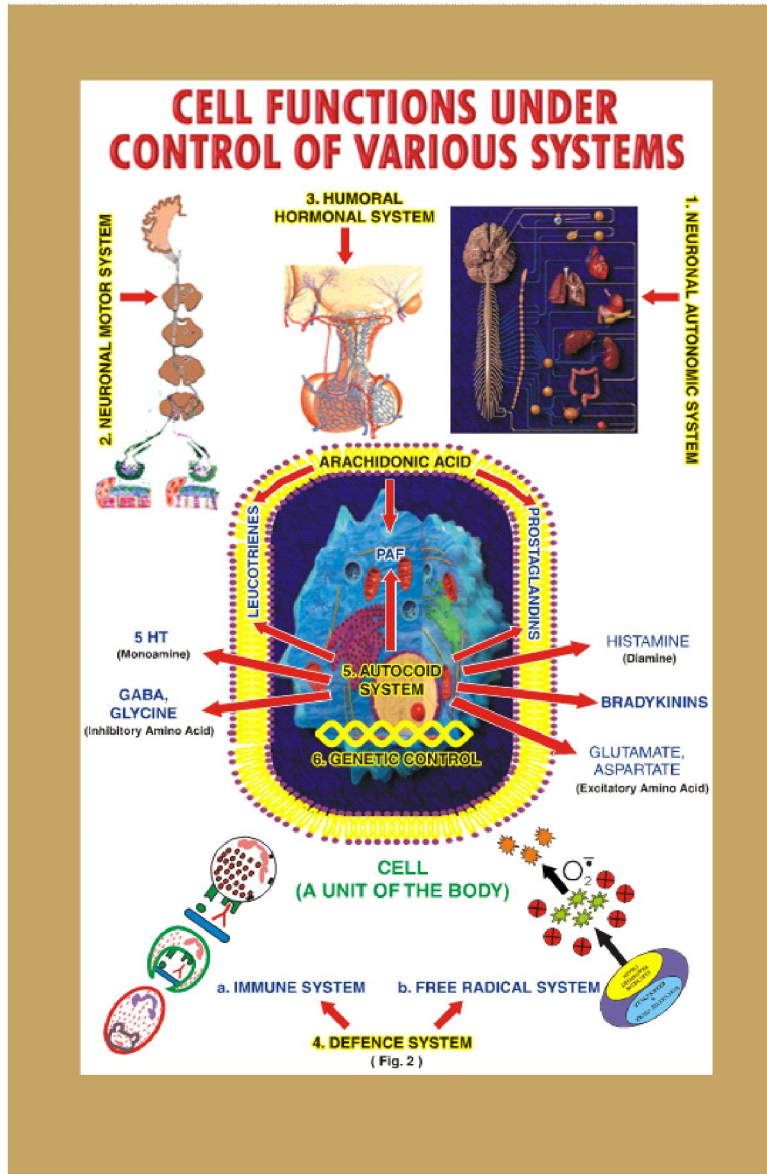


Fig. 2: Cell functions under different chemicals

		Second Position									
		U		C		A		G			
		code	Amino Acid	code	Amino Acid	code	Amino Acid	code	Amino Acid		
First Position	U	UUU	phe	UCU	ser	UAU	tyr	UGU	cys	U	
		UUC		UCC		UAC		UGC		C	
		UUA	leu	UCA		UAA	STOP	UGA	STOP	A	
		UUG		UCG		UAG	STOP	UGG	trp	G	
	C	CUU	leu	CCU	pro	CAU	his	CGU	arg	U	
		CUC		CCC		CAC		CGC		C	
		CUA		CCA		CAA	CGA	A			
		CUG		CCG		CAG	CGG	G			
	A	AUU	ile	ACU	thr	AAU	asn	AGU	ser	U	
		AUC		ACC		AAC		AGC		C	
		AUA		ACA		AAA	lys	AGA	arg	A	
		AUG		ACG		AAG		AGG		G	
	G	GUU	val	GCU	ala	GAU	asp	GGU	gly	U	
		GUC		GCC		GAC		GGC		C	
		GUA		GCA		GAA	glu	GGA		A	
		GUG		GCG		GAG		GGG		G	

Fig. 3: Merely from 64 codons code for required amino acids which inturn forms thousands of proteins

Thus DNA is basically involved either in the synthesis of large number of proteinous materials like enzymes, receptors, channels, carriers or pumps which are embedded in various bio-membranes of variety of cells but otherwise enzymes are also available in serum which are responsible for the synthesis of variety of neurotransmitters and autacoids as well as hormones which are very much important for normal physiological functions of the body in association with charged particles like the cations and anions. In addition even for our defense mechanism of the body, various antioxidants play a major role in addition to transcribed different kinds of immunoglobulins [2] and the feedback mechanisms. It is only due to our defense mechanisms, we often say "our body itself is a doctor" (Fig 2)

Thus proteins are very crucial for our body functions. These proteins in turn are synthesized from 20 essential amino acids and semi essential amino acids which are picked up by transfer RNA and are arranged in a specific sequence to transcription perform a specific proteinous material under the directive of codon [3] which gives rise to thousands of specific and nonspecific proteins to perform a specific function. (Fig 3)

#### Part: B

Replication i.e., producing like ones as per the law of nature (niyati) which again involves the contribution of a large number of proteins like aurora

kinases, tubulin proteins etc.

Thus the process of replication and transcription are independent to each other and are closely related to each other. Further activity of many catalytic enzymes are in turn dependent on many minerals eg metalloenzymes involved in various biological reactions. These are also involved in oxidative defense mechanism as well as in nucleoprotein synthesis eg divalent cations like Mg, Mn containing enzymes and in electron transport chain for the delivery of ATP, currency of our body.

#### Cancer and Cell Division

There are 3 types of the cells in our body

1. Nondividing cells like neurons or cardiac cells (now are also known to be induced and also inhibited although at a very slow rate).
2. Slowly dividing cells like that of liver cells which regenerates after partial hepatectomy and
3. Very rapidly dividing cells eg hair cells, bone marrow cells, gametes, mucosal cells, foetal cells which are also inhibited by anti cancer chemotherapeutic agents as these are well known to be inhibitory in nature whether these are pathological cancerous cells or naturally multiplying physiological cells. This is the major drawback with the anticancer drugs causing adverse drug reactions, quite often fatal in nature.

Thus, the need oriented cell division as well as its differentiation is of utmost importance in relation to

the existing cell population in the body. In relation to cancer, there are 3 types of genes

1. Oncogenes: which are replicating and cell dividing oncogenes (OG).
2. Proto-oncogenes: which accelerate the process of cell division resulting in cancer or malignancy ie these are proliferating genes (POG).

3. Anti-oncogenes or tumor suppressor genes (TSG) which retard the rate of cell division.

Thus these two opposite wings (POG & TSG) maintain the balance of the cell population by controlling the activity of OG. When POG are excited and TSG activity is attenuated, ie balance becomes a disbalance's excessive proliferation occurs resulting in cancer or malignancy [3].

### Herbs are Soft Drugs and ACT Slowly Through DNA Modulating Many Molecular Targets without Undesirable Effects

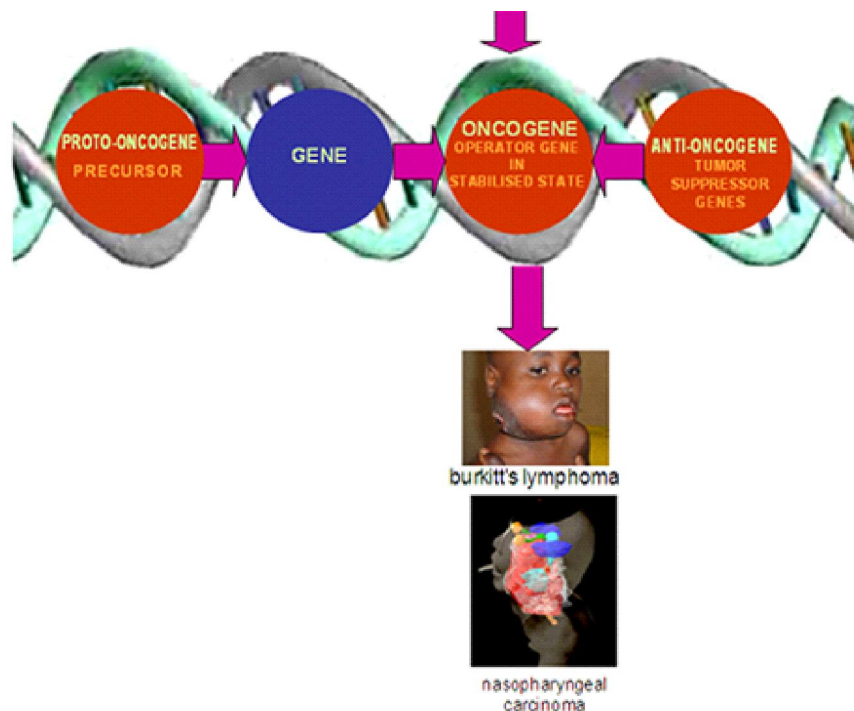


Fig. 4:

#### Storage of DNA Bases

Telomeres are the two caps at the terminal ends of DNA, obviously consisting of base pairs which act like bio molecules storage sites of base pairs. The rate of multiplication of cells is indirectly proportional to the telomere bio molecules and the life of an individual ie

Rate of transcription or Replication (Cell Division)  $\propto \frac{1}{\text{Number of base pair in telomeres or life of DNA or of a man}}$

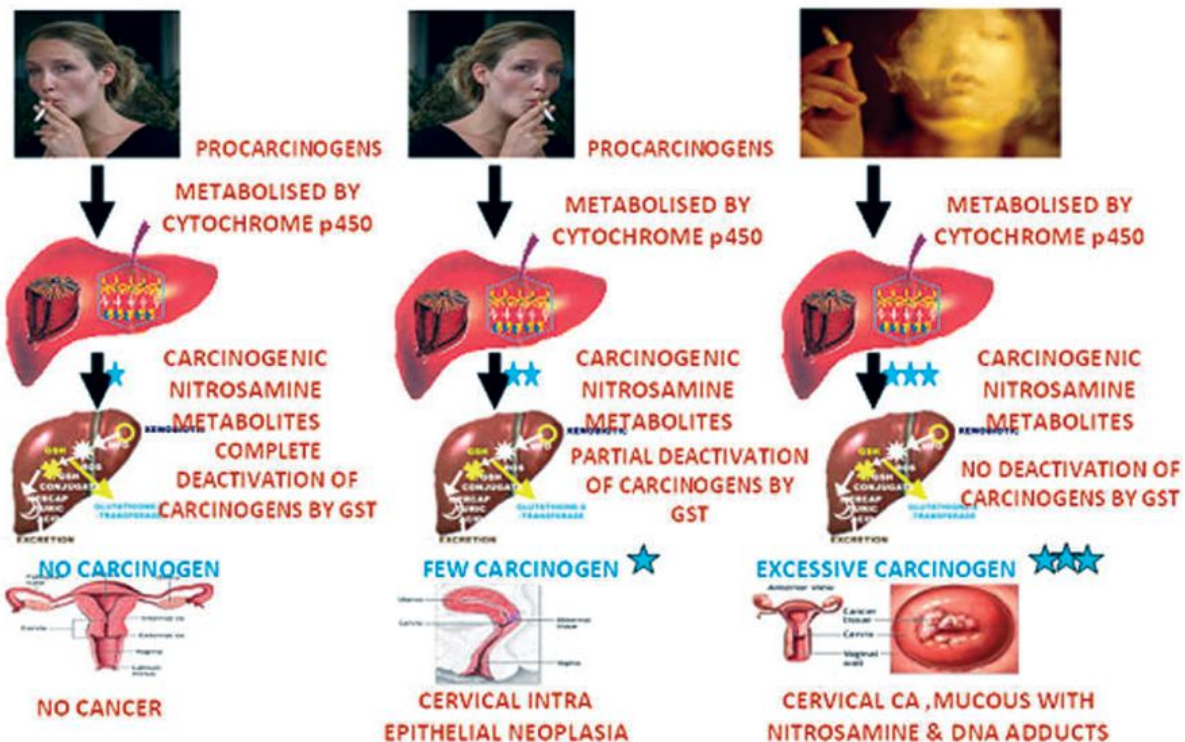
There are large number of adaptogens which are likely to enhance the number of telomeres such as Haldi, Giloy, Shilajit, Oscimunsanctum (Tulsi), Gurch etc., Causative Factors Involved in Pathogenesis of Cancer

There is not one but many risk factors which leads

to cancer formation. These can be categorized as follows:-

1. Genetic factors which include age, sex, race, hereditary;
2. Dietic factors;
3. Chemical factors such as endocrinal or hormonal factors, pollutants and contaminants and food additives;
4. Iatrogenic for example chloramphenicol induces leukemia or secondary cancer by anticancer drugs;
5. Many physicochemical factors;
6. Biological factors like bacteria, nematodes and oncogenic viruses. These are summarized in the following figure.

## CIGARETTE SMOKING : A CO-CARCINOGENIC FACTOR



**Fig. 5:**

Among these the most common cause of oral and cervical cancer in females is smoking habit where in there is an interplay between its procancerogenic metabolites like nitrosamine and protective glutathione-S-transferase (antioxidative enzyme). If earlier dominates over the later cancer sets in.

### *Disbalance Leads to Cancer*

In the whole universe there is fixed amount of energy as well as fixed amount of particulate matter and in case of disbalance between the two, these are inter-convertible as per our Puran and Einstein ( $E=mc^2$ ) theory of energy. Exactly in a similar way in our body, there are defence forces like immune system, oxidative system, feedback mechanisms and normal bacterial intestinal flora which protect our body from invaders i.e., the causative factors. Thus there is interplay between our defence mechanisms and the invaders. If invader dominates, cancer sets in.

Defence System  $\longleftrightarrow$  Invading system

That is why if our defence forces are strong as compared to invading forces, cancer or any other disease does not occur. Thus, only some of the

individuals are susceptible to cancer and others are not.

As far as cancer is concerned interplay occurs at different levels as is given below.

It has been mentioned above that disbalances in our exogenous system of the environment or the endogenous system are the root cause of diseases like cancer, which means excess of anything is not desirable or too much shortage is not desirable (*Ati ke bhala na bolna, ati ki bhali na chup*). Excess may produce more of toxins and damaging substances where as shortages may decrease one's defensive forces.

Activity of oncogene is of utmost importance in this regard. Hypogenism can cause decrease in our defence mechanism for eg there may be lesser production of defensive biomolecules for eg immunoglobulins, white blood cells (granulocytes as well as agranulocytes) as well as the antioxidative enzymic biomolecules like the superoxide dismutase, catalase, glutathione peroxidase and other such molecules like hydrogen peroxide and glutathione etc. (Fig 2)[2]. As a result of that more of toxins or free radicals dominate which are likely to cause damage or aberration of oncogenes [2] producing large number

of cells that is there is excessive proliferation of the cells. Obviously due to enhanced rate of production of cells, many of the immature cells can be seen as these immature cells do not get sufficient time for maturation. Malthus law says, if there is over population, nature tries to balance the population by reducing the excessively produced population either by floods, earthquakes, draught or epidemics and likewise. Law of nature are same everywhere. Thus when cell population of a particular type of the tissue increases in a specific type of cancer, body tries to overcome the situation to bring back the normal number of matured cells by way of apoptosis of overpopulated immature cells. Apoptosis is a naturally occurring programmed cell death phenomenon. This is the end stage of oxidative apoptosis for maintenance of cell population. Thus the process of proliferation of cells and killing of excessive cells by apoptosis merely occurs to maintain the normal functioning cell balance.

Proliferation (cellproduction)  $\rightleftarrows$  Apoptosis (killing of cells)

Thus, proliferation of cells control apoptosis and vice versa but when this feed back mechanism fails, proliferation dominates resulting in cancer. Thus the aim of the cancer therapy must be directed to enhance our body defence mechanism and to cut down our

overpopulated cells in the body.

If causative factors of chromosomal aberration are eliminated or are engulfed, cancer will ameliorate. To illustrate this fact I give a simple example of smoking or tobacco chewing. If in an individual, nitrosamine metabolite produced by metabolism of constituents of cigarette is in excess than glutathione, a part of our defensive system, disbalance occurs. Those who have excessive or sufficient amounts of glutathione like defensive molecules to take care of nitrosamine like invaders, person does not get oral cancer or cervical cancer but if our defensive molecule glutathione is short one gets cancer (Fig 5)[3].

Lacunae in Present Approaches of Cancer Therapy

There has to be three approaches for cancer therapy as follows:-

1. *Preventive*: Stop the entry of the precancerous agents is the best approach but once cancer sets in, it becomes very difficult to revert back the irreversible damage done to the chromosomes.
2. Once provocative factor enters in the body, body tries to inactivate such xenobiotics but can also produce toxic metabolites like nitrosamines. Hence, either destroy the xenobiotic or destroy its toxic products.
3. The chromosomal aberration is a gradual process which occurs in stages as can be seen in the following Fig 6.

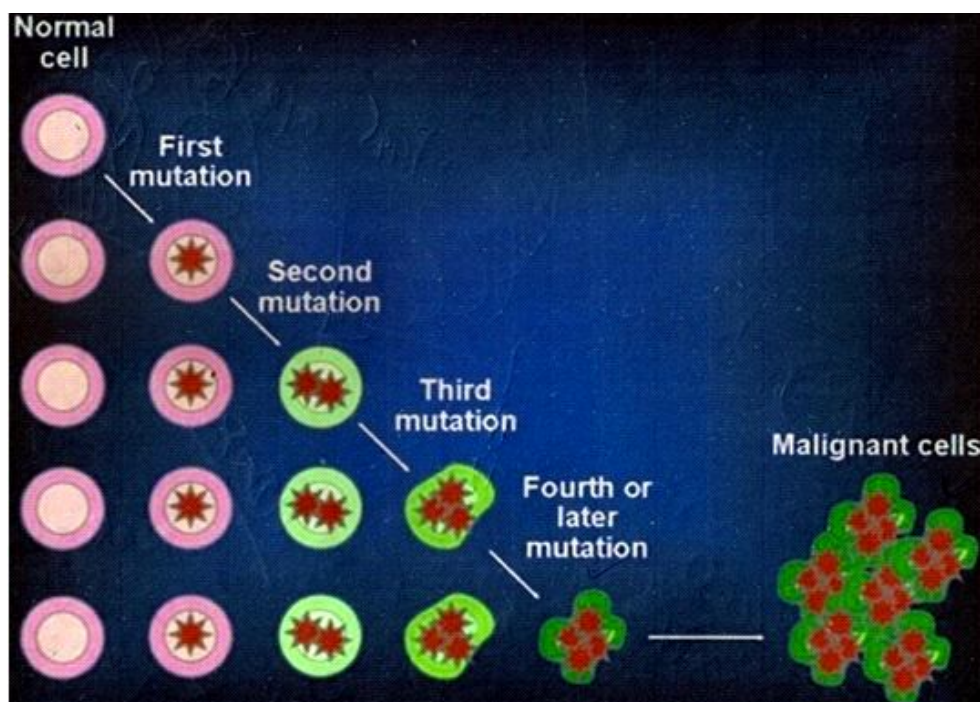


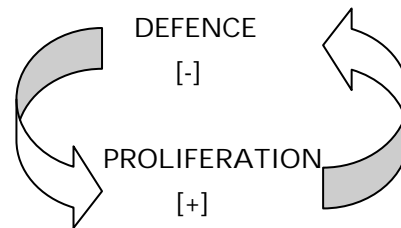
Fig. 6: Stepwise process of mutation in cancer which is clonal

Therefore, prevent this gradually occurring chromosomal aberration by boosting up of the defence mechanism of the individual. However, the gradual change in chromosomes/oncogenes is so silent and subclinical that it cannot be assessed clinically. Here regular health checkups, studies with general biomarkers may be useful to screen the population at risk for eg:-

- Estimation of survivin;
- Glycosylated oligosaccharide;
- Human chorionic gonadotropin hormone [HCG]

These biomolecules are concerned either with the physiological proliferation of the cells eg in the foetal stage or in the pathological stage of cancer. On the other hand p53 protein, a policeman like molecule which guards the cells during reparative process of the chromosomal damage is also equally of importance. Onco-viruses like other viruses enter into the cell silently without creating any signs or symptoms [subclinical stage]. But once they increase in the population, symptoms appear. Since, these oncoviruses share the biomolecules of the host for their existence, eliminating viruses by eliminating the biomolecules of the host is likely to produce

adverse drug reactions. Such is the situation which exists in almost all types of cancer. Hence we say cancer is a silent killer. But once the irreversible chromosomal abnormalities occur over a period of time, prevention becomes very difficult as excessive proliferation further weakens our defence mechanism and the vicious circle continues.



But still if our defence system is enhanced in cases of cancer, it can prolong the life of the patient along the quality of the life, if it cannot be saved.

Once irreversible chromosomal abnormality sets in and preventive defensive system fails we use cancer chemotherapy to prevent proliferation of cells by using variety of anticancer agents affecting different stages of cancer. Hence, these drugs are merely symptomatic support with many adverse drug reactions.

## Therapeutic Approaches in Cancer Prophylaxis

### PRECANCEROUS SILENT STAGE

#### Prophylaxis Stage-1

[if defence system is strong cancer will not occur]

#### Prophylaxis Stage-2

Enhancement of defence system of our body to cope with xenobiotic or its metabolites by using:

- Food supplements to repair DNA damaging state eg proteins, vit furtheramins like folic acid etc
- Prophylactic vaccine working through T cells and B cells of lymphocyte of our immune system eg HPV vaccine for cervical and oral cancer
- Enhancement of oxidative and antioxidative balance system by the use of Vitamin A, D, E, C etc
- Intake of rasayanas [adaptogens] which increases nonspecific immune resistance [NSIR] and being adaptogens, they bring back the pathological state to physiological state within limits
- Immunoenhancers like yoga, exercise, herbs like tulsi, haldi, giloy etc.
- Even autourine or cows urine therapy as immunity enhancer [no clinical trials reported with authenticity]

#### Post Cancerous Clinical Stage Prophylaxis Stage-3 to stop further proliferation

Once irreversible chromosomal abnormalities occur and defence system goes to its low ebb, such prophylaxis as mentioned in stage 2 can help and support cancer patients to live long who can perhaps be cured if irreversible changes are made reversible which is a challenging but a possible task for the oncologist

Prevention of exposure of procarcinogen

Prevention of actions of Xenobiotic or its toxic metabolites like nitrosamine

Irreversible damage leading to cancer

Modern chemotherapeutic approaches mainly rather only look after the inhibition of proliferation of cells at different stages of cell cycle and do not bother for the defence enhancers hence patient is killed earlier due to decreased defence as well as due to adverse drug reactions occurring with such drugs.

Drugs which enhance defensive system to defend against the continuous ongoing exposure of carcinogens along with apoptosis enhancers will be of more value than only antiproliferative drugs.

#### *Therapies Available*

1. **Modern Chemotherapeutic Agents:** Modern chemotherapeutic approach basically is dependent on all processes concerned with inhibition of replication which includes changing of base pairs or inhibition of various stages of cell division leading to cell division by inhibiting the excitatory proteins.

These modern chemotherapeutic drugs do reduce the rate of proliferation of rapidly multiplying cancer cells relatively quickly to give a better clinical response apparently but these drugs also reduce the rate of proliferation of normally and much needed physiologically rapidly multiplying cells of the body creating many drug reactions which may be even fatal. For example bone marrow cells if depressed will cause erythrocytopenia, anaemia, pancytopenia, bleeding disorders, neutropenia, immunodeficiency, secondary infections against the needs of the body which are required to keep normal counts of RBC, platelets, WBC to defend our defensive mechanisms. Obviously invaders like carcinogens will be encouraged to do more harm to our body. Similarly gametocytes inhibition causing infertility will also disturb our endocrinal system and such may happen with retardation of the growth of the hairs causing alopecia. The mucosal surfaces of our gut will get ulcerations and denudations which are again of great importance for the maintenance of our immunity. What I wish to clarify that these drugs weaken the protective defensive mechanisms of our body which obviously will give invaders a better chance to invade and enhance the process of carcinogenesis.

2. **Herbal:** Here also cells of the plants divide and cell division is very tightly controlled one but to keep up a balance, these contain both proto-oncogenic as well as anti-oncogenic substances. Thus if one isolates an active principal, it will be effective but it is bound to be associated with

adverse drug reactions such as seen quite frequently with vincristine, vinblastin or topoisomerase II inhibitors. Therefore, plant or its part must be used as a whole and not as its active principle only which will be of greater value than its active principle although the onset of action may be slow as these are the soft drugs of the nature. Plant as a whole is more useful as it is itself a complete one by nature. If one takes out an active heart or brain of a person, do you think, it will ever function for a long in vitro conditions. Such has been very well documented with other drugs obtained from nature eg reserpine isolated from rauwolfia serpentina causes CNS depression and suicidal tendency and deaths. Isolated principle will immediately stop the proliferation but will not take care of defensive system, hence, it is bound to be harmful although apparently it will appear to be useful as we are observing the same in our day today practice. This aspect has to be considered seriously.

3. **Homoeopathy:** These drugs have been discarded many a times because one can not estimate their drug levels as one does pharmacokinetics with modern drugs. But it is not so important to estimate the drug in the blood or other body tissues so far these drugs produce pharmacodynamic activities. One is concerned with the effects. These are working at subatomic levels and perhaps at energy levels at the site of transport of positively charged cations and negatively charged anions. But in cancer if the chromosomal aberration has become irreversible especially in late stages, it may not act as anticancer agent but certainly can enhance the defense mechanism and that is what is required to be searched in homoeopathy by estimating different immunological parameters.
4. **Unani and Tibatti:** same holds true for these systems also as holds true for herbal therapy.
5. **Urine Therapy (Shivambu Therapy):** Isolated reports of urine therapy have been reported in the literature from different parts of the world especially from India and herein either the cows urine (especially Sahali, cows urine) or human urine or the urine of the patient himself has been employed both internally as well as externally. However, no authentic clinical trials have been reported. It would be interesting to use this therapy either in the terminal stages of cancer or if the patient is so poor that he/she can not afford the costly modern drug therapy or in the absence of the availability of anticancer drugs. However, it requires all ethical consideration as one does in doing a clinical trial in human beings.



Lyophilised Urine concentrates are available in the market.

A large number of bioactive substances and hormones have been reported to be secreted in the urine and urokinase is very well documented to be used as thrombolytic agent. Urine basically contains many hormones and growth factors which are important for cell division eg human chorionic growth hormone (HCG) in addition to other growth hormone, colony stimulating factors, epithelium growth factor, gonadotropins and perhaps anticancer substances like antineoplaston, directin, 3 methyl gloxal, H-11 beta indole acetic acid as well as some minerals and vitamins like magnesium and folic acid important for nucleic acid synthesis, If human being is himself a doctor and can cure himself within limits by its own defensive systems of immunity, oxidative systems and feed back mechanisms, can urine and other secretions of the body like saliva be useful in such conditions may be seen in scientific way using modern methodologies to prove or disprove such claims.

6. Yoga and Transdental Meditation: each of our thought or emotion produced some or the other chemical in the body which alters rather expresses our behavior. These chemicals are basically DNA expressed proteins and enzymes which help in the synthesis of neurotransmitter, hormones, oxidative and antioxidative enzymes and immunoglobulins concerned with our physiological functions of our body including cell divisions. It is worthwhile to explore this field in the management of cancer as an adjuvant therapy in future. Yoga and TM helps in the energy management and cancer like diseases are basically energy disorders as when a cancer patient dies, cancer cells do not proliferate.
7. Obviously this is in addition to surgery and radiotherapy having their own advantages and disadvantages.

### Conclusion

Thus it would be desirable to enhance the defensive mechanisms of the body of a cancer patient by any means to strengthen immunity, oxidative and anti oxidative mechanisms, feed back mechanisms by using methodologies of any of the alternative systems of medicine concomitantly which have no undesirable side effects if used in the natural forms which will help in ameliorating the cause of cancer along with or without modern therapy. However,

these alternative agents have to be given in combination as early as possible to give a chance to them to work and not really in the end irreversible stages. This field needs to be explored as it is the need of the day as well as a challenging task for the oncologist.

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