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# PREVENTION OF CANCER: EVOLUTION OF CONCEPTS AND STRATEGIES

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Medical scholarship of nineteenth and twentieth century modernization provided many new ideas and theories for disease – diagnosis, treatment and prevention. Cancer, a disease earlier considered synonymous with death, was declared to be treatable and even preventable in many cases. Ancient Indian medical texts had considered cancer to be a result of life style errors such as unhealthy food, poor hygiene, physical trauma and environmental exposure. Advances in understanding of cancer during the last two centuries support these ancient contentions. Moreover, with the identification of causal factors and revelation of the mechanism of cancer initiation and progression, it was suggested that about one third of all cancers, in principle, may be prevented and that up to one third of cancers may be curable. Therefore, the concept of public health efforts for control of cancer took root which is now strongly emphasizing on preventive measures which include early detection and vaccination. It is now firmly established that preventive medical practices can indeed play a major role in global cancer control. The present article is an attempt to trace the history of conceptual evolution of preventive strategies for cancer, which is still a leading cause of mortality and morbidity worldwide in the current time.

**Key words:** Cancer risk factors, *Caraka saṃhitā*, Carcinogenesis, Life cycle modification, Preventive oncology, *Suśruta saṃhitā*

The antiquity of man on this earth has not yet been determined with certainty, but it is unquestioned that disease is as old as life itself. Interestingly the studies on the history of medicine suggest that most of the diseases from which man suffer today also afflicted our remote ancestors of prehistoric times (Major, 1954). It is therefore imperative that there existed healing practices for alleviating human suffering from varied ailments.

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In early India, preservation of health was emphasized through recommendation on life style, behaviour and religious practices. The Vedic prayers reflect the keen desire for youthfulness and preservation of health[1,2]. The rich heritage of Indian medicine with its important medical texts attracted scholars to delve into the depth of existing knowledge base. These studies have provided detailed information on the understanding of health and disease as well on the existence of different diseases, their diagnosis and treatment practices over the ages. However the preventive aspect with focus exclusively on specific diseases remains largely unexplored. In recent times preventive medicine has emerged as a special branch of medical science and it would be of interest to look back and try to analyse the current concepts in disease prevention in the light of that prevailing in the early times. The objective of the present investigation is an endeavour towards this end.

The earliest available document of Indian medicine is the *Atharva veda*, but the first creative and exhaustive compilations of medical thought and practice of Ancient India are the *Caraka saṃhitā* (600 BC - 200 AD), *Suśruta saṃhitā* (completed by the 2nd century AD) and *Aṣṭāṅga saṃgraha* of Vagbhaṭa (6-7th century AD) (Kutumbiah, 1999). Caraka belonged to the Atreya school of medicine which was most intimately connected with *Atharva veda* and the *Caraka saṃhitā* deals with the philosophic background of medicine and its interrelation with religious thought and Hindu spirituality.[3] *Suśruta saṃhitā* is the main source dealing with surgery although it has included other important components of medicine as well. The *Aṣṭāṅga saṃgraha* is a compendium of General Medicine – a collection and collation of relevant materials from *Caraka* and *Suśruta* which has been arranged harmoniously into a treatise on the prevailing medical practices. Vāgbhaṭa II's *Aṣṭāṅga Hṛdaya* is more close to *Suśruta* in that it has emphasized on the surgical elements.

Cancer as a disease is known from time immemorial. In ancient Indian medical texts cancer is referred to as *Karkaṭa* and tumour at different sites of the body as *Arbuda*, *Gulma* or *Granthi* and described in detail with respect to their appearance, nature and treatment (Sharma, 1981, Bhisagratna, 2006, Murthy, 1999, 2000). Some of the tumours were considered to be treatable while others were mentioned as untreatable forms.[4] Medical or surgical treatments were recommended for the former types while the latter

ones were to be best left untreated with just palliative care for the patients. No specific mention or any suggestion for their prevention can be found. Similar view of therapeutic measure of different types of tumour is to be found in the subsequent texts also (Bhisagratna, 2006, Murthy, 1999, 2000). However general preventive measures suggested in the different medical texts of ancient India concerning with a complete mental and physical well being of individuals in accordance with the principles of Āyurveda, as we now understand, can also ward off cancer. The sole aim of Āyurveda, it appears, is preservation of good health free from diseases by prescription of proper diet, regimen of life, avoidance of disease causing substances and medication if necessary. This allows equilibrium (*sāmya*) of the elements (*dhātu*) which control body function. Thus preventive measures of that time consisted of *dhātu-sāmya* or maintenance of body equilibrium to prevent diseases which are results of *dhātu-vaisamya*. Interestingly, this principle is applicable for all human ailments, particularly the non-communicable diseases, even if it is interpreted in modern medical terms.

The general guidance for proper food is to be found mentioned in medical texts to assure healthful and happy life free from diseases.[5] It has also been suggested that food should be taken in proper quantity and have variety without continuing a particular item all the time along with avoidance of over consumption of meat, milk products and black gram.[6] Avoidance of aetiological factors (although not well defined) and unwholesome diet is a recommendation for remaining free from diseases (Devraj, 2003). Good conduct, pure mind and yoga are considered to be conducive to good health and one should follow the code of conduct and acquire virtues for healthy life.[7] Regular physical exercise[8] and avoidance of excessive exposure to sun are also recommended as a prophylactic measure for sound health.[9] These aspects have been considered in current times with respect to cancer prevention. The practice of responding to natural urges of the body when they appear (like shedding tear, passing urine and faeces, sleep etc) and not suppressing them are some other measures mentioned for prevention of diseases.[10] The removal of excrements of the body are essential, as we now know that many of them are toxic materials and their retention for prolonged periods in the system are likely to cause cellular damages associated with the causation of cancer. Sound body, mind, behaviour, knowledge of habitat and one's self, right living are mentioned as methods to prevent origin of

diseases.[11,12] The concern for environment in early India (Das, 2003) is another instance that can be interpreted in terms of the current call for a "clean environment" free from carcinogens (cancer causing agents) to reduce cancer risk.

The creative period of ancient Indian medicine culminated in *Caraka saṃhitā* and *Suśruta saṃhitā* having established the final synthesis of practices in medicine, surgery and health protection. These works remained as the basic frame of subsequent medical practices in this country. Many of the essence of these great works have found place in modern world medicine although in a highly modified form. The post *Caraka-Suśruta* documents may be considered as offshoots in specific areas of medical knowledge. For example the *Mādhava Nidān* of Mādhavakāra (12th century AD) deals with diagnosis of diseases in more details (Murthy, 1993), Sharangadhara's *Śāraṅgdhara saṃhitā* (14th century AD) is an extensive work on Pharmacology (Murthy, 1984) and meant to be a practitioner's handbook while the *Bhāvaprakāśa* of Bhāvamiśra (16th century AD) is a comprehensive treatise on basic doctrines, aetiology and symptomatology as well as treatment of diseases (Murthy, 1998). Although these works have emphasized on diagnosis and treatment, it may be presumed that perceptions and practices of disease prevention continued to remain similar to that of the earlier texts. Subsequent Indian medical literature (from medieval period onwards) records the growing importance of physicians and medical professionals, who were committed to diagnosis and management of diseases, and development of public health measures and hospitals (Rejari, 2001, Verma, 1970). More researches are necessary to decipher the status of disease prevention which was a responsibility of the practicing physicians. An interesting anecdote may be mentioned in this connection, where there is a mention of a physician Hakim Ali Gilani warning Akbar to refrain from tobacco smoking which is offered by a young Portuguese guest as a gift to the Emperor (Rejari, 2001, Verma, 1970). This incident perhaps suggests there was awareness of the ill effects of tobacco on health. It is now well established that tobacco use in any form causes severe damage and is identified as a causative risk factor for many non-communicable diseases viz. heart disease and cancer.

During the Mughal period both Āyurvedic (Indian) and Unāni (Graeco-Arab) systems of medicine were followed; gradually a new hybrid Muslim-

Hindu system developed known as Tibb (Kumar, 2001). Their emphasis was on diagnosis and therapeutics, probably because the major diseases encountered at that time were considered manageable. The concept of individual case studies developed during this period and hospitals and dispensaries were established (Rejari, 2001, Askari, 1957, Reddy, 1957). Perceptions in disease prevention of this period remain largely unknown as reports in translated literature available do not throw light on this aspect. A number of European physicians visited Mughal India in the 18th century who gradually tried to incorporate the Western system of medicine into the existing ones. None of these systems could however develop a comprehensive theory in disease causation and so treatment was based on observational diagnosis (Kumar, 2001). In the absence of sound knowledge on the etiological factors, it is most likely no new preventive concepts could be visualized and developed during this period.

Human societies had to face the realities of disease and death in all ages. It can be seen through the eyes of history how societies conceptualized and coped with diseases and developed methods to contain them. The approaches for control of disease form a part of world view associated with religious practices and belief as well as growing scientific understanding concerning diseases. Development of concepts in preventive strategies in the modern age progressed with the knowledge on the natural history and causal factors of each disease. Evolution of preventive medicine therefore revolved round an understanding of disease source, their occurrence and nature of spread and genetic predisposition which became known in phases. This in turn enabled planning and organization of public health measures as well as medical actions for protection of health and control of diseases in a population.

Communicable diseases were constant companions before the discovery of penicillin, antisepsis and germ theory. The establishment of the 'Germ theory' and identification of infective agents by Antony van Leeuwenhoek in 1676 and the revolutionary works by French and German bacteriologists Louis Pasteur and Robert Koch in the eighteen seventies and eighties provided a strong impetus for treatment and prevention of infectious diseases in the 19th century (Carter, 1991). The scientific revolution of the 17th-19th centuries, described and analyzed the spread of all diseases that emerged out of the effects of industrial revolution like hazardous work exposure, crowded living condition, polluted environment and life style

changes. From 1970s to the end of the 20th century a new focus was thrown on prevention of non-communicable diseases which surfaced following the control of infectious diseases worldwide. Cancer, cardiovascular diseases and diabetes were some of the notable among them.

The colonial period in India is abound in data on the infectious diseases, including preventive strategies (which is not under the perview of this study), but this was not so with respect to the non-communicable diseases. It seems that the non-communicable diseases were not as serious a threat as the communicable diseases and control of these life threatening epidemics was given a priority in health care. The shortened life expectancy also did not allow diseases like cancer, which usually manifests later in life, to surface. The very idea of cancer prevention was unthinkable and diagnosis and treatment for this disease was generally poor. Comprehensive and dedicated facilities for cancer detection, diagnosis and treatment were only available in the country after the establishment of the cancer hospitals in the mid nineties (Das, 2003, 2011).

Cancer as we now know is a highly complex disease which develops through a long drawn process, continuing for as many as 20-30 years, known as carcinogenesis. Modern science has made major strides in unraveling the mysteries surrounding this disease. The causation of this disease is multifactorial and the disease process differs at different sites. A host of causative factors have been identified like environmental exposures, certain infection and genetic predisposition which play important role in carcinogenesis. Advances in medical technology have largely improved the methodology for detection and treatment of cancer during the 20th century. Comparatively the progress in the field of cancer prevention had lagged behind for a fairly long period because emphasis of modern medicine remained on the diagnostic and curative aspects until the mid 20th century. In this connection it may be mentioned that gains in long term survival for patients with advanced cancer has so far been modest due to heterogeneity of tumors which allows evasion of therapeutics by tumor cells. So it would be much better to try to reduce the burden of cancer or improve survival through prevention and early detection.

Observational studies since late 19th century and through the 20th century revealed strong association between many environmental exposures

and modifiable life style factors and cancer (Kolonel, 2004). This provided the impetus for formulating suitable preventive measures. Researches on carcinogenesis in animal models supplemented these findings and role of life style and environmental factors as well as some infective agents in the causation of cancer was established. Perhaps the first observation on life style association was that from Ramzzini (1700) who had noted that breast cancer was to be found more often in nuns, which he thought to be due to derangement of the womb (Boylan, 1980). The other landmark observations were those of Hill in 1761 who found a link between frequent occurrence of cancer of the nasal passage in men with tobacco habit in the form of chewing, smoking or using snuff (Boylan, 1980) and that of Percivoll Pott in 1775 (Brown, 1957) describing scrotal cancer among chimney sweepers exposed to chimney soot, suggesting a occupational risk for malignancy. Pott's report is referred to as a milestone in chemical carcinogenesis, preventive oncology, environmental health and occupational medicine. Over half a century elapsed after the first publication of Rehn (1895) on the evidence that exposure to aromatic amines used in dye industry was responsible for bladder cancer before the International Agency for Research on Cancer (IARC) took up a programme on identification of chemicals which were carcinogenic to humans. About 420 chemicals have been evaluated since 1971 and some 20 volumes of monographs published identifying human carcinogens (Loeb & Harris, 2008).

Scientific evaluation of human cancer risk factors were also started in India since the 1940s, particularly for the more prevalent forms in this country. Khanolkar was among the first in India to clarify the causal relationship of habit and life style with cancer pattern in the country. For example oral cancers were associated with tobacco chewing habits (Khanolkar, 1944, 1945, Jussawala, 1962). Early age of marriage and repeated child birth was etiologically associated with cancer of the uterine cervix in India (Mitra, 1962). Chronic mechanical injury due to tying of garments (*dhoti* and *sāri*) tightly around the waist was found to be responsible for a type of skin cancer among Indian men and women (Khanolkar, 1945). A high incidence of oesophageal cancer among people of Kashmir was related to consumption of excessive red chillies, spices along with hot salted tea, reported for the first time by Matto in 1974 and Maqbool in 1976 (Mattoo & Kaul, 1974).[13] A similar association was also noted in Karnataka (Deka, Palit & Joshi,

1978). Further extensive studies were undertaken in this area (Goswami, 1987, Siddiqi, 1988, 89, 92).

Ancient Indian medical science had also considered cancer to be a result of life style errors such as unhealthy food, poor hygiene, poor behaviour, physical trauma and environmental exposure. These were believed to lead to imbalances of *vāta*, *pitta* and *kapha* resulting in injury to the inner layers of dermis (*rohini*,the sixth layer of the skin) and formation of abnormal branches of blood vessels (Das, 1987), now referred to as angiogenesis which is associated with development of tumor.

Although the genetic background of an individual is likely to influence cancer development in some cases, particularly breast cancer, the vast majority of human cancers were found to be linked to exposure to environmental carcinogens and other life style practices, as revealed by modern scientific assessment of cancer risk (Moore, 1999). Data generated through exhaustive researches in causal factors of cancer laid the foundation of the concept of Preventive Oncology, initially with a subtraction approach i.e. elimination of risk, which subsequently evolved to a multidimensional approach for cancer prevention which impacted on the cancer scenario at the turn of the 21$^{st}$ century. The contemporary concepts in cancer prevention is a product of late 19$^{th}$ century and from the 20$^{th}$ century it became increasingly clear that answer to cancer prevention is to be found in our lifestyle, as well as the environment.

It had started to become quite clear since 1970s that treatment procedures could at best prolong the survival in only a section of people with advance cancer. Soon the importance for early detection, through mass screening, was realized to be a feasible strategy for cancer control. Early detection was likely to yield better treatment outcome following an early intervention that was likely to be comparatively easy and more effective. Though theoretically accepted there were practical difficulties in implementation of this approach, more so in an over populated and under educated country like India. So screening drives were preceded or coupled with mass awareness programmes since the 1980s as a first step towards cancer prevention. Education of the public about the disease to remove cancer fear was also started around the same time, otherwise it was found difficult to draw people to come forward for screening and early detection.

The initiatives were taken by the first three cancer institutes in the country at Bombay, Calcutta and Madras who also gave the lead for the formation of a National Cancer Control Programme in 1975-76, which played an important role in prevention of cancer as per guidelines of WHO (WHO, 2002, Dinshaw, 2005). According to this programme cancer prevention involves action at three phases : (1) Primary prevention, to create awareness on the risk along with advocacy for risk reduction so as to prevent the very onset of the disease. For example, by minimization of exposure to carcinogenic chemicals, cessation of tobacco habit, limiting exposure to high intensity sunlight and radiation, inclusion of green leafy vegetable, fruits and grains in diet (high fibre diet), reduction of high fat intake (minimization of high caloric diet), avoidance of sedentary life style as far as possible, avoidance of early onset of sexual activity and multiple partners and oral hygiene (to reduce HPV infection), vaccination (HBV & HPV) etc. (2) Secondary prevention, to ensure early diagnosis by screening (clinical examination, cytology, X-ray, endoscopies, mammography etc) and (3) Tertiary prevention, to take care of checking recurrences as well as prevention of long term impairment or disabilities, restoration and maintenance of optimal function, rehabilitation and palliative support. The final choice of strategies for cancer prevention however has to be made according to prevalence and incidences of cancer type in a region. In India, major thrust is on early detection, and recommendation on life style modification (Agarwal, 2002). Visual inspection and cytological tests of oral cavity and cervix uteri and anti tobacco advocacy forms an important procedure for cancer screening because cancer of the head and neck continues to be highest among males and cancer of uterine cervix being highest in females closely followed by lung cancer in males and breast cancer in females.

The consensus among cancer researchers in carcinogenesis that the process can be inhibited, restricted or reversed at the molecular level has initiated a search for anti-carcinogenic agents since mid 20$^{th}$ century (Wattenberg, 1979). During the next decades researches on diet and nutrition in relation to cancer development, immune system and tumour growth gave rise to a new branch of medical science - Nutritional Oncology. There was an endeavour to find critical link between metabolic control, genetic and epigenetic homeostasis, cellular repair mechanism and cancer in the light of nutritional science (Herber, 2006). The synthesis of these two areas of research

on anti-carcinogenesis and nutritional oncology paved the path for development of a new concept in cancer prevention termed – Chemoprevention of cancer. The concept of cancer chemoprevention is based on the fact that carcinogenesis can be stalled by administration of natural or synthetic agents. Many of the natural agents comprise of micronutrients and vitamins as well as non-nutrient phytochemicals present in plant food. No wonder our ancient medical thought and traditional wisdom had asserted the importance of vegetables and fruits in our daily diet for preservation of health and protection from diseases.

Assessment of nutritional status and dietary habit of cancer patients in India as well as epidemiological observation on cancer pattern in the country offered guidelines for possible preventive interventions based on this concept, targeted towards those at high risk for cancer or where early pre-cancer signs and symptoms are detected. Extensive experimental studies from different laboratories in this country during 1990-2010 supported the contention that components of Indian food and spices indeed could influence and modulate carcinogenesis. The first department of cancer chemoprevention of India was started at the Chittaranjan National Cancer Institute in 1995 (Carter, 1991). Poor nutrition and low vitamin status was found to be associated with risk of cancer cervix in India. A pilot study on women at risk for this cancer, receiving chemopreventive intervention with supplemental vitamins, revealed regression of pre-cancerous lesions of the cervix (Ganguly, 1999, 2001). Similarly, consumption of black tea was reported to protect from tobacco related DNA damage in oral mucosa cells which in turn is likely to reduce risk of oral cancer among tobacco chewers (Pal, 2007). It is unfortunate that not many controlled human studies have been reported from India to assess the chemopreventive efficacy of food and dietary items. One of the limitations for implementation of supplemental strategy for cancer prevention in our country is non-compliance of the subjects treated and skepticism of the practicing oncologists. However, awareness drive has been taken up by scientists and NGOs to impart information on the anti-cancer components and the chemopreventive potential of plant food and beverages.

The hypothesis of zur Hausen published in 1976[14] that human papilloma virus (HPV) plays an important role in cancer cervix (Hausen, 1977) and the identification of HPV 16 and 18 in cancer cervix samples in 1983-84 made possible the development of a vaccine introduced in 2006

(Lowry, 2006). Prevalence of HPV infection among women varies from 7-14% and high risk type 16 and 18 were found in 80% of cancer cervix in India (Sankarnarayan, 2008). Currently a vaccination programme against human papilloma virus has been initiated. The vaccine was shown to provide almost 100% protection against pre-cancers and genital warts caused by HPV type 16/18 (Sharma, 2008). A multicentric HPV vaccination project, co-coordinated by the Screening Group of International Agency of Research on Cancer (WHO), Lyon, France, in collaboration between Programme for Appropriate Technology in Health (PATH), an International non-profit USA based organization, and Indian Council of Medical Research (ICMR), New Delhi was launched in 2009 to generate critical data on effective strategies for public-sector HPV immunization for prevention of cancer cervix. Vaccine and screening which are complimentary and synergistic now constitute the new paradigm for prevention of cancer cervix.

Advances in understanding of cancer during the last two centuries has given rise to the now prevailing concept in cancer prevention, which holds that only a multi-pronged strategy, integrating life style and medical approach, coupled with governmental regulation for addressing the significant public health problem of cancer, is the only answer to the fight against this human malady. Fortunately for India, the predominant cancer types are life style oriented and therefore preventable. Based on the internationally prevailing concepts, the strategies applied for cancer prevention since the past two decades or so, are likely to impact on the cancer scenario in the current century. The initiatives taken should succeed in stabilizing the cancer figures by checking the upward trend as more and more pre-cancer cases are detected and their progress halted by the use of various preventive methodologies that have evolved over the years. An analysis of the concept of health protection in ancient Indian medical treatises (*Caraka* and *Suśruta saṃhitās*), in the light of current understanding of prevention of non-communicable disease, reveals that the early medical philosophy remains as the basic foundation on which the cancer preventive concepts have evolved. The seed of origin of modern Preventive Oncology was already there. Advances in scientific knowledge and medical technology have only facilitated the revalidation and reaffirmation of the same and made possible an improved designing of strategies and their implementation.

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7. *CS. Sū* 8.30-33, 46-47.
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