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MATHEMATICAL MODEL IN PREVENTION OF CANCER

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Abstract:

Cancer is one of the diseases which are flourishing very rapidly throughout the world due to which mortality rate is also going to increase world widely. Cancer is a leading cause of death globally. The World Health Organization estimates that 7.6 million people died of cancer in 2005 and 84 million people will die in the next 10 years if action is not taken. More than 70% of all cancer deaths occur in low- and middle-income countries, where resources available for prevention, diagnosis and treatment of cancer are limited or nonexistent. But because of the wealth of available knowledge, all countries can, at some useful level, implement the four basic components of cancer control – *prevention, early detection, diagnosis and treatment, and palliative care* – and thus avoid and cure many cancers, as well as palliating the suffering. Mostly cancer treatments are based on selective killing of the cancer cells but not normal cells. Chemotherapy is the most widely used treatment for a large number of cancer types. Drugs that are used to help prevent cancer are highly regulated to insure quality and safety. Most drugs that are suggested by doctors to help prevent cancer are for a specific population that is at a high risk of developing certain cancer types. These drugs are not suggested for all people because they can cause other problems that may not be worth the cost of protection. In this paper, the prevention of cancer by using renewal process is discussed.

Key Words: Palliative, Oral Cancer, Anti Oxidants & Free Radicals

Prevention of Cancer:

One of the key problems in the treatment of cancer is the early detection of the disease. Often, cancer is detected in its later stages, when it has compromised the function of one or more vital organ systems and is widespread throughout the body. Methods for the early detection of cancer are of utmost importance and are an active area of current research. After the initial detection of a cancerous growth, accurate diagnosis and staging of the disease are essential for the design of a treatment plan. This process is dependent on clinical testing and the observations of physicians. It is important for cancer patients and their families to understand the results given to them so that they can take an active role in the planning of the treatment protocol to be used. Even the healthiest substances can cause harm if taken in large amounts [3]. In fact, there has been some recent evidence linking antioxidants to the spread of cancer. The benefits of antioxidants aren't limited to healthy cells; it seems they can support the survival and spread of cancer cells too.

Each cancer type is different in origin, composition, and responsiveness to treatment, reliable prevention techniques are very difficult to identify. Evidence that an activity or dietary item prevents cancer is difficult to confirm because the goal of cancer prevention is to produce an outcome where nothing changes (i.e. cancer does not develop). There is increasing emphasis on improving cancer survivors' overall well-being and quality of life through the application of principles of disease self-management and the promotion of healthy lifestyles, such as avoiding tobacco, maintaining a healthy body weight, avoiding intense ultraviolet radiation exposure, and being physically active throughout life [1]. Despite the conflicting evidence, the National Cancer Institute contends that the best way to help prevent cancer is to exercise, as well as eat a low calorie diet containing fiber, fruits, and vegetables. They also suggest that people should avoid a sedentary lifestyle, animal fats, and grilled meats to lessen the risk of developing cancer. Research suggests that a combination of different essential nutrients is better than consuming a large amount of a single item.

Another way to help prevent cancer is to avoid behaviors that are generally accepted to increase your risk of cancer. Some of the behaviors linked to cancer development are tobacco use, alcohol consumption, obesity, and sun exposure. The American Cancer Society suggests that a third of all American cancer deaths are linked to poor diet and lack of exercise. Additionally, another third of all cancer deaths are preventable by avoiding tobacco products. The World Health Organization believes that 40% of cancer deaths world-wide could be prevented with proper diet, exercise, and tobacco avoidance [4].

Even the healthiest substances can cause harm if taken in large amounts. In fact, there has been some recent evidence linking antioxidants to the spread of cancer. The benefits of antioxidants aren't limited to healthy cells; it seems they can support the survival and spread of cancer cells too. In one study, mice were given an anti-diabetic drug that activated a protein, called NRF2, in their cells. This protein increases the levels of antioxidants in cells. Drugs that are used to help prevent cancer are highly regulated by the federal government to insure quality and safety. Most drugs that are suggested by doctors to help prevent cancer are for a specific population that is at a high risk of developing certain cancer types [3]. These drugs are not suggested for all people because they can cause other problems that may not be worth the cost of protection. Nevertheless, some drugs have been shown to decrease the risk for cancer and have been approved by the US Food and Drug Administration for cancer prevention. The prevention of cancer is the ultimate goal of cancer researchers and clinicians. One good way to accomplish this is to prevent infection with agents (viruses, bacteria, and parasites) known to cause cancer. Vaccines have been developed and approved to prevent infection with hepatitis B virus, a cause of liver cancer, and the human papilloma virus, the major cause of cervical cancer and a cause of cancers of the head/neck and urogenital tract of men and women [2].

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Cancer in India:

Non-communicable diseases including cancer are emerging as major public health problems in India. These diseases are lifestyle related, have a long latent period and needs specialized infrastructure and human resource for treatment. The risk factors of the major non-communicable diseases (Diabetes Mellitus, Cardiovascular Diseases, Diabetes, and many types of Cancer) are tobacco, dietary habits, inadequate physical activity and alcohol consumption. Tobacco consumption either as chewing tobacco or smoking tobacco will account for 50% of all cancers in men. Dietary practices, reproductive and sexual practices etc will account for 20-30% of cancers. Tobacco is the most important identified cause of cancer and is responsible for about 40 to 50% of cancers in men and about 20% of cancers in women. India has the added burden of tobacco chewing which is more prevalent than smoking in many areas. Tobacco chewing has resulted in a huge burden of Oral cancers and oral precancerous conditions. The main risk factors for these cancers are tobacco and alcohol. A diet rich in green and yellow vegetables has been shown to offer protection against oral cancer. Avoidance of tobacco and alcohol is the most important preventive action against mouth, throat and lung cancers [4].

Usual activities are those that are performed on a regular basis as part of one's daily routine. These activities include those performed at work (such as walking from the parking garage to the office) and at home (such as climbing a flight of stairs), as well as dressing and bathing). Usual activities are typically of low intensity and short duration. Intentional activities are those that are done in addition to these usual activities. These activities are often planned and done at leisure, as regularly scheduled physical activity or fitness sessions, such as a bike ride or a run. Other intentional activities may involve incorporating more purposeful physical activity into the day and making lifestyle choices to supplement or substitute other routine activities, such as walking to use public transportation or commuting by bicycle instead of driving. Usual and intentional activities are also classified by intensity. Light intensity activities include activities such as housework, shopping, or gardening. Moderate intensity activities are those that require effort equivalent to that of a brisk walk. Vigorous intensity activities generally engage large muscle groups and cause a noticeable increase in heart rate, breathing depth and frequency, and sweating. Evidence suggests that higher amounts of physical activity may provide even greater reductions in cancer risk. Although the optimal intensity, duration, and frequency of physical activity needed to reduce cancer risk are unknown, approaching and exceeding 300 minutes of moderate intensity activity per week or 150 minutes of vigorous activity per week is likely to provide additional protection against cancer [1].

Studies suggest that 300 minutes of moderate to vigorous intensity physical activity per week also helps to prevent weight gain and obesity. By helping to maintain weight and avoid weight gain, this amount of physical activity may thus have an indirect effect on reducing the risk of developing obesity-related cancers. Apart from the effects on body weight, physical activity appears to have a direct effect on reducing the risk of cancers of the colon, breast, and endometrium, as well as advanced prostate cancer, even when activity is initiated later in life [1].

Examples of Moderate and Vigorous Intensity Physical Activities [1]:

	Moderate Intensity Activities	Vigorous Intensity Activities
Exercise and leisure	Walking, dancing, leisurely bicycling, ice and roller skating, horseback riding, canoeing, yoga	ogging or running, fast bicycling, circuit weight training, swimming, jumping rope, aerobic dance, martial arts
Sports	Downhill skiing, golfing, volleyball, softball, baseball, badminton, doubles tennis	Cross-country skiing, soccer, field or ice hockey, lacrosse, singles tennis, racquetball, basketball
Home activities	Mowing the lawn, general yard and garden maintenance	Digging, carrying and hauling, masonry, carpentry
Occupational activity	Walking and lifting as part of the job (custodial work, farming, auto or machine repair)	Heavy manual labor (forestry, construction, fire fighting)

Suggested Ways to Reduce Sedentary Behavior [1]:

- ✓ Limit time spent watching TV and using other forms of screen-based entertainment.
- ✓ Use a stationary bicycle or treadmill when you do watch TV.
- ✓ Use stairs rather than an elevator.
- ✓ If you can, walk or bike to your destination.
- ✓ Exercise at lunch with your coworkers, family, or friends.
- ✓ Take an exercise break at work to stretch or take a quick walk.
- ✓ Walk to visit coworkers instead of sending an e-mail.
- ✓ Go dancing with your spouse or friends.
- ✓ Plan active vacations rather than only driving trips.
- ✓ Wear a pedometer every day and increase your number of daily steps.

Atoms are composed of a nucleus, containing particles called protons and neutrons, and a group of particles (electrons) that constantly circle the nucleus like satellites around the earth. In most molecules electrons travel in pairs around the nucleus. Free radicals are an exception. At least one atom in a free radical has a single (unpaired) electron circling the nucleus. This single electron gives the atom a charge, making it very attracted to other molecules. A molecule with an unpaired electron is said to be 'radicalized'. These radicalized compounds, or free radicals, can quickly react with other molecules. For this reason these compounds are also called *reactive* species. Oxygen is the most common reactive species found in the human body and when it acquires an extra electron it is called a reactive oxygen species (ROS). Free radicals 'steal' an electron from a nearby molecule so that all of their electrons are in pairs. The affected target molecule would then become a radical [2]. A chain reaction of electron 'theft' can occur within a cell. Free radicals can affect just about any structure in a cell, including DNA. If free radicals steal an

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electron from DNA, the genetic code can be damaged and cell function damaged. DNA damage caused by free radicals has been associated with aging, rheumatoid arthritis, inflammatory bowel disease, **a**cute **r**espiratory **d**istress **s**yndrome (ARDS), emphysema, and some types of cancer.

Mathematical Modeling:

In the classical Poisson process, the intervals between successive occurrences are independently and identically distributed with a negative exponential distribution. Suppose that there is a sequence of events E such that the intervals between successive occurrences of E are distributed independently and identically but have a distribution not necessarily negative exponential , we have then a certain generalization of the classical Poisson Process which is called renewal process[5].

Consider a sequence of repeated trials with possible outcomes $E_j, j = 1,2,3.....$ The trials need not be independent, we assume that trials can be repeated infinitely. Suppose that we are interested in a certain outcome in a trial or a pattern of outcomes in a number of trials. We denote this event by E^*. Whenever E^* occurs we say that renewal has occurred; if it occurs at nth trial, we say that a renewal occurs at trial number n. The interval between occurrences of two successive renewals is called renewal period of the process [5].

Denote $f_n = P_r\{E^* occurs \quad for \ the \quad first \quad time \quad at \quad the \ n^{th} trial\}$ ----------(1)

$p_n = P_r\{E^* occurs \quad at \ the \ n^{th} trial (not \quad necessarily \quad for \ the \quad first \ time\}$ ----------(2)

Define $f_0 = 0, \quad p_0 = 1$ ----------(3)

$$F(s) = \sum_{n=0}^{\infty} f_n s^n \ , P(s) = \sum_{n=0}^{\infty} p_n s^n$$ ----------(4)

Now $f^* = \sum f_n$ ----------(5)

is the probability that the renewal E^* occurs at some trial in a long sequence of trials. We have $f^* \le 1$ when $f^* = 1$ then $\{f_n\}$ is a proper probability distribution representing the distribution of the length of a renewal period T. i.e., $P\{T = n\} = f_n$. However $\{p_n\}$ is not a probability distribution. The renewal event is termed as persistant (recurrent) when $f^* < 1$.

The event E^* occurs at the nth trial may be a compound event such that E^* occurs for the first time at the rth (r < n) trial and again at the later trial number n(i.e., in subsequence n-r trials) and thus

$$P_n = \sum_{r=1}^{n} f_r p_{n-r}, \ n \ge 1$$ ----------(4)

The right hand side in a convolution relation $\{f_n\} * \{p_n\}$ between two sequences. Multiplying by $s^n, n = 1,2,3....$

$$p_n s^n = (f_1 s)(p_{n-1} s^{n-1}) + ...+ (f_n s^n) p_0$$

and adding $\sum p_n s^n = (f_1 s)\sum_{n=1}^{\infty} p_{n-1} s^{n-1} + (f_2 s^2)\sum_{n=2} p_{n-2} s^{n-2} + ...$

or $P(s) - 1 = p(s)\left[\sum_{n=1}^{\infty} f_n s^n\right] = P(s)F(s)$

Thus $P(s) = \dfrac{1}{1 - F(s)}$ and $F(s) = \dfrac{P(s) - 1}{P(s)}$ ----------(5)

Now from (5) it follows that $\sum p_n = P(1) = \dfrac{1}{1 - F(1)}$ is convergent if and only if F(1)<1

i.e., E^* is transient. In other words for E^* is transient if and only if $\sum p_n = P(1)$ is finite.

The probability that E^* ever occurs is given by $f^* = F(1) = \dfrac{\sum p_n - 1}{\sum p_n}$; E^* is persistent if and only if $\sum p_n$ is divergent.

For example we consider the damage of DNA in a cell is the event $E_j, j = 1,2,3.....$ as a sequence of repeated trials in cancer cells. The trials need not be independent; we assume that trials can be repeated infinitely. The possibility of repair or the cell goes to apoptosis is the outcome in a trial or a pattern of outcome in a number of trials which is E^*. Whenever E^* occurs we say

that renewal has occurred; if it occurs at nth trial, we say that a renewal occurs at trial number n. The interval between occurrences of two successive renewals is called renewal period of the process. i.e. the time taken to the two successive trials of repair the damaged DNA is the renewal period of the process. This renewal has been occurred either by drug-induced apoptosis or replace the damaged DNA by a new gene through gene therapy. If the event E^* occurs continuously, the cancer cells in human body can be easily eliminated. If the immune system is regulated by this renewal process, the formation of tumours is reduced.

Conclusion:

Mathematical modeling has been instrumental in the past 50 years in helping decipher different aspects of complex systems in biology. In particular, mathematical modeling has had an impact on our understanding of cancer biology and treatment. Normal cells have multiple independent mechanisms that regulate cell growth and differentiation. For cancer to begin and spread, several separate events need to occur to override these regulating mechanisms. Along with a greater understanding of the origin of cancer has also come a greater awareness of the heterogeneity of cancer. The tumor suppressor p53 plays a central role in cell fate decisions after DNA damage. Programmed Cell Death 5 (PDCD5) is known to interact with the p53 pathway to promote cell apoptosis.

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