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A Review of Cancer Immunotherapy and Nutritional Therapies

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Abstract

The recognition that oxidative stress induces neoplasia and the formation of cancer cells has expanded the prevention and management of cancer to include eliminating factors that induce inflammation and strengthening the immune system through the use of nutrients and natural remedies as complements to surgery, radiation and chemotherapy.

Keywords: Immunotherapy; Cancer; Nutritional Therapies; Neoplasia

Introduction

More than 160 years ago, the German biologist Rudolf Virchow proposed that cancer occurred at sites of chronic inflammation. Today, scientists have affirmed that he was correct [1].

Oxidative stress resulting from prolonged exposure to toxins, especially in combination with cells that have not been properly nourished, oxygenated, hydrated and cleansed, is the primary cause of cancer. Over time the resulting inflammation leads to dysfunction in cellular mitochondria. This leads to a cellular defense mechanism in which cells revert to a more primitive form of respiration (glucose fermentation), refuse to die, multiply and form a protective barrier around them as a tumor.

Chronic inflammation also can lead to the production of DNA-damaging molecules that cause mutations. This combined with signals to produce new cells and grow new blood vessels—hallmarks of wound healing—can create fertile ground for the emergence and growth of cancer cells. Root causes of inflammation include: 1) diet, 2) environmental toxins in air, water and soil (pesticide, heavy metal and fossil fuel pollution), 3) alcohol, 4) excess body weight, 5) excessive ultraviolet radiation, 6) electromagnetic pollution, 7) infections (viruses, bacteria, fungi); 8) pharmaceutical medications, 9) nutritional deficiencies, 10) lack of exercise, 11) genetic predisposition, and 12) emotional stress.

Oral contraceptives also may influence cancer risk both as taken in medication form and in tap water [2]. Naturally

occurring estrogen and progesterone have been found to influence the development and growth of some cancers. Birth control pills contain female hormones. Population studies to examine associations between oral contraceptive use and cancer risk have not always been consistent. Overall, however, the risks of endometrial and ovarian cancer appear to be reduced with the use of oral contraceptives, whereas the risks of breast, cervical, and liver cancer appear to be increased.

The medical community has an obligation to inform the public about the hazards environmental factors poses by inducing oxidative stress that contributes to neoplasia [3].

Literature Review

Immunotherapies

Immunotherapies are assuming prominence in the treatment of cancer. Because each immunotherapy draws upon an aspect of the immune system, a combination of immunotherapies most closely resembles the ways in which the immune system works.

Immunoediting is the process in which aberrant cells develop mechanisms to permit their multiplication with three possible outcomes: 1) through immunosurveillance the immune system distinguishes between aberrant and normal cells and can eradicate aberrant cells; 2) some aberrant cells withstand the pressure exerted by immunosurveillance and may be either killed at the same rate as a tumor grows or permitted to remain as dysplastic benign tumors by immune system avoidance mechanisms; and 3) some aberrant cells grow unrestrained by immunosurveillance and become cancer cells in the neoplastic process. In this way, normal cells subject to carcinogenic stimuli undergo transformation through neoplasia to become cancer cells [4,5] (**Figure 1**).

Immunotherapies can be classified in the following categories:

Active immunotherapy: Active immunotherapy aims to stimulate a patient's innate immune response to neoplasia, either nonspecifically or specifically. Vaccines attempt to get the body's immune system cells to respond more effectively by exposing them to specific cancer antigens.

Adoptive immunotherapy: In contrast, adoptive immunotherapy involves removing immune system cells from

a patient, boosting their anti-cancer activity by genetically recoding them to identify and seek out proteins present on cancer cells, growing them in large numbers and then returning them to the patient.

Restorative immunotherapy: Restorative immunotherapy is the direct and indirect restoration of deficient functions of immune system cells through any means other than removing them from a patient. Examples are reactivating NKTC, unblocking NKTC proliferation and NKTC Receptor Bispecific Therapy.

Passive immunotherapy: Passive immunotherapy is infusing a patient with antibodies to antigens on the patient's cancer cells and thereby destroying the cells. Examples are monoclonal antibodies, Epithelial Mesenchymal Transition Therapy, Transient Photoactivation and Laser Assisted Immunotherapy that block the "don't-eat-me" signal on cancer cells and train the immune system to attack the tumor.

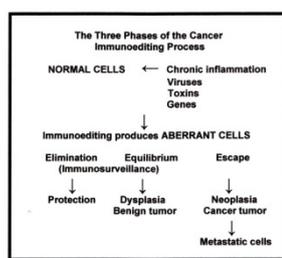


Figure 1: Three phases of the cancer immunoediting process.

By 2015, twenty-five immunotherapy antibodies had been approved by the FDA and many more are currently being evaluated in clinical trials [6,7].

Complementary nutritional elements in cancer therapy

A comprehensive nutritional assessment to identify daily goals for carbohydrates, fats and proteins should be carried out with cancer patients. A dietitian can monitor the patient's nutritional status throughout cancer treatment and make modifications as needed to address side effects and prevent treatment interruptions before they arise.

Mitochondrial dysfunction is at the core of virtually all diseases—cancer especially. Hence strategies that support and optimize mitochondrial function, such as nutritional ketosis (achieved by a high-fat, low-carbohydrate diet), intermittent fasting and high-intensity exercise are all helpful. One of the basic reasons why a high-fat, low-carbohydrate diet works so well is because it decreases inflammation, especially when it results from obesity.

Otto Warburg's discovery that neoplastic cells consume excessive glucose, later named the Warburg effect, is estimated to occur in up to 80 percent of cancers [8-10]. It is so fundamental to most cancers that a positron emission tomography (PET) scan—an important tool in the diagnosis of

cancer—works simply by revealing the places in the body where cells are consuming extra glucose. In many instances, the more glucose a tumor consumes the worse a patient's prognosis. Cancer cells have low oxygen levels because they stop taking in oxygen for respiration as part of the neoplastic process itself. Consequently, the neoplastic process causes the body to become increasingly acidic. The body labors mightily to maintain a blood pH within a narrow range (7.35 – 7.45) and, as the cancer progresses, it becomes increasingly acidic.

Since two-time Nobel Laureate Linus Pauling announced his finding in 1979 that high-dose intravenous Vitamin C had anti-neoplasia and cancer cell killing effects, numerous studies have replicated his results [11].

The kinase eEF2K cell signaling factor can be exploited by tumors to support adaptation to metabolic stress. The development of therapeutic strategies to neutralize the eEF2K in tumors, especially aggressive human brain tumors, warrants further investigation [12].

Nutritional therapies include a low carbohydrate diet, ubiquinol, curcumin, impower (AHCC), milk thistle and Vitamin D3. The most effective approach is to use all of them as a "cocktail" because of the possible synergetic effects they might have, as suggested by Dr. Raymond Chang in his book *Beyond the Magic Bullet: The Anti-cancer Cocktail* [13].

In general, a low carbohydrate diet is appropriate for the prevention of cancer. Cruciferous vegetables, such as broccoli, Brussels sprouts and cauliflower, are rich in powerful glucosinolates, which break down to form isothiocyanates that can cause cancer cells to commit suicide [14].

Most, if not all, cancer cells have a high demand for glucose compared to benign cells of the same tissue and conduct glycolysis even in the presence of oxygen (the Warburg effect). In addition, many cancer cells express insulin receptors (IRs) and show hyperactivation of the IGF1R-IR pathway. Evidence exist that chronically elevated blood glucose, insulin and IGF1 levels facilitate carcinogenesis.

It may be beneficial for cancer patients to adopt a ketogenic diet. Those who adhere to it may have positive results. Thus, the use of a ketogenic diet as a complement to cancer therapy merits further study in rigorously controlled trials [15]. Epidemiological and anthropological studies indicate that restricting dietary carbohydrates could be beneficial in decreasing cancer risk. High fat, low carbohydrate diets are safe and likely beneficial, in particular for advanced stage cancer patients. The beneficial effects of calorie restriction and fasting on cancer risk and progression are well established. Carbohydrate restriction thus opens the possibility to target the same underlying mechanisms without the side-effects of hunger and weight loss. A multitude of mouse studies proved anti-tumor effects of ketone bodies for various tumor types, and a few case reports and pre-clinical studies showed promising results in cancer patients as well [16]. At the same time, aspartame in diet sodas is associated with a higher risk of leukemia, multiple myeloma and non-Hodgkin's lymphoma [17]. In contrast, stevia is a safe natural sweetener.

Discussion

One of the most promising areas of research focuses on identifying substances that will inhibit nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), a protein complex that activates the genes and pathways that increase inflammation. Research has shown that the ongoing activation of NF- κ B is linked with most cancers and major diseases. Curcumin is a natural substance in curry that inhibits NF- κ B. Curcumin does not adversely affect healthy cells, suggesting that it selectively targets cancer cells. Research also has shown that it works synergistically with certain chemotherapy drugs by enhancing the elimination of cancer cells [18].

More specifically, curcumin's anti-cancer properties include:

- Suppresses NF- κ B and other inflammatory compounds in the body
- Stimulates apoptosis
- Inhibits blood supply to tumors
- Inhibits the invasion of cancer cells into tissues
- Inhibits metastasis of cancer cells
- Reduces the side-effects of chemotherapy
- Reduces the cancerous compounds found in smokers

Meriva, Curcumin C3 Complex[®], Theracumin[®] and Curamed are much more absorbable than regular curcumin.

Ubiquinol the naturally occurring product in the body of Coenzyme Q10 helps prevent healthy cells from undergoing malignant changes. It also reduces chemotherapy side effects and inflammatory damage inflicted on the body by cancer cells [19-22].

Ubiquinol's role as the body's natural, powerful antioxidant that removes free radicals probably is responsible for its benefits in aging, cancer and other diseases. Antioxidants (a misleading term because they do not remove oxygen) are molecules that can safely remove free radicals before they damage cells. Free radicals are atoms or groups of atoms with an odd (unpaired) number of electrons and can be formed when oxygen interacts with certain molecules. Oxygen itself can become a free radical when it loses electrons and becomes a "superoxide anion". Free radicals are formed naturally in the body. In addition, some environmental toxins may contain high levels of free radicals or stimulate the body's cells to produce more free radicals. Free radicals are highly reactive and have the potential to cause damage to cells that may lead to cancer.

AHCC (Active Hexose Correlated Compound) is an extract of fermented mycelia of a Japanese medicinal mushroom which has been shown to strengthen the body's immune system and inhibit the growth of cancer cells in mice [23].

Links between emotional stress and cancer can arise in several ways. For example, people under stress develop behaviors, such as smoking, overeating or excessive alcohol use, that increase their risks for cancer. Stress also can indirectly promote cancer by weakening the immune system through releasing high levels of cortisol and epinephrine. Many studies have shown that these hormones make breast,

ovarian and prostate cancer cells resistant to destruction [24-26].

Taking charge of one's life with cancer by becoming knowledgeable about one's own cancer can play a key role in reducing anxiety and stress that inevitably accompany having life-threatening cancer [27,28].

Following is the Complementary Cancer Treatment Protocol:

- Ketogenic diet
- Ubiquinol
- Curcumin
- Immpower (AHCC)
- Milk thistle (silymarin)
- Vitamin D3
- Stress relieving meditation
- Exercise
- Support system—media and/or interpersonal

Conclusion

Scientific knowledge of the prevention and treatment of cancer is based upon preventing, redirecting and stopping the process of neoplasia. For this reason, both strengthening the immune system and destroying cancer cells by surgery, radiation and chemotherapy are necessary and complementary factors in managing cancer.

The fact that both pharmaceutical and natural medications and nutrients have important roles in the prevention and treatment of cancer is changing the medical approach to cancer so that its management can become more effective.

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