CANCER

Few words strike as much fear and loathing in a doctor's office as 'cancer'. More than one hundred types are known, of varying levels of aggression. Many are treatable or even curable. Still, cancer is the second greatest cause of death in North America, after cardiovascular disease. One third of Americans will eventually die of some form of cancer. It must be emphasized that many cancers can be prevented through the threefold regimen of diet, avoidance of carcinogens and reinforced bodily defenses.

CARCINOGENESIS

Healthy cells have a built-in mechanism that only allows cellular replication for three purposes: normal growth, healing of injured tissue and replacement of cells lost in normal metabolism. But cells can lose their ability to regulate growth, replicating uncontrollably and eventually forming a clump of cancerous tissue. This tumor can grow sufficiently to crowd out normal tissue, sometimes releasing diseased cells that spread the cancer into other parts of the body by the process of metastasis. Symptoms develop when the growth begins to interfere with bodily functions or deplete energy resources.

It is not clear precisely how and why these cells lose their self-regulation, although many possible causes have been singled out. Certain environmental carcinogens will predictably initiate cancerous growth, including a variety of chemicals and high radiation levels. Other factors are less predictable. Differences in our genetic makeup or immune systems apparently protect some people better than others. We also know that susceptibility to certain cancers is sometimes inherited from the family or racial gene pool, but the triggering factors are still unknown.

Apart from genetic factors, we can identify the following casual factors: the pollution of cigarette smoke, fossil fuel exhaust, heavy metals, pesticides and others; the ionizing radiation of x-rays, nuclear waste, ultraviolet (UV) radiation from the sun intensified by a depleted ozone layer; poor diet is an important factor; finally, certain viruses can contribute to the development of cancer: AIDS, hepatitis C, Epstein-Bar disease and papilloma.

The American Cancer Society makes the following suggestions to minimize the risk of cancer: maintain appropriate body weight, eat a varied diet including daily fruits and vegetables, eat more high-fiber foods (whole grains, cereals, legumes, etc.), cut down on total fat intake and limit consumption of alcoholic beverages and salt-cured, smoked and nitrate-preserved foods.

Cancer starts with a mutation in the genetic code of the cell – a reprogramming of developmental patterns that results in uncontrolled growth. A combination of genetic and environmental factors including diet may contribute to this aberrant replication. One theory suggests that when free radicals form in the cell nucleus, its DNA code may be damaged. Another theory suggests that factors such as poor diet and cigarette smoke compromise the immune system and weaken bodily defenses which might otherwise destroy a newly cancerous cell at the outset, when it is still vulnerable. Regardless of

theory, we owe it to ourselves to pay attention to all possible factors and take advantage of any way to minimize the danger of cancer. One of these is by maintaining GSH levels.

GSH AND CANCER

Hundreds of medical articles have been written describing the role of GSH in cancer prevention and cancer treatment. They fall into three main groups: 1) prevention, including detoxification of carcinogens, antioxidation and heightened immune response; 2) therapeutic possibilities, such as anti-tumor methodologies and the treatment and prevention of malnutrition and wasting, and 3) a special role for GSH in chemotherapy and radiotherapy whereby it enhances the effectiveness of these arduous treatments while minimizing their side effects.

CANCER PREVENTION

A 1996 article in the European Journal of Cancer actually suggested that free radicals be listed as an important class of carcinogens. Because of its great capacity as the cell's major antioxidant GSH can soak up oxyradicals and other free radicals as they form in the cell. This prevents subsequent damage to various parts of the cell, particularly to the DNA in its nucleus. GSH has the additional benefit of enhancing the effect of other antioxidants such as vitamin C, vitamin E and selenium. This further strengthens the body's ability to destroy free radicals. To top it off, GSH also plays an important role in the synthesis and repair of DNA.

There is no doubt that a well-functioning glutathione enzyme system wards of cancer. This is clearly illustrated by a study published in the Journal of the National Cancer Institute. It focused on people deficient in the enzyme glutathione-S transferase-mu-I (GSTM1). GSTM1 is an important antioxidant that also detoxified common bladder cancer carcinogens such as tobacco smoke. Approximately one person in two inherits two defective copies of the GSTM1 gene, impairing the function of this enzyme. It was found that 25% of all bladder cancers occurred in people missing this enzyme. Heavy smokers missing this gene were six times more likely to develop bladder cancer.

There is a link between the loss of glutathione activity and the development of prostate cancer. Another glutathione enzyme, glutathione-S-transferase-pi-1 (GSTP1) almost always disappears in both cancerous and precancerous prostate lesions. It seems that prostate cancer begins with the inactivation of this glutathione enzyme. Many studies have made the connection between GSTP1 loss and malignant transformation of prostatic tissues. Similar studies have linked GSH-defective genes to breast and lung cancer as well, especially in smokers. Several scientists have suggested that people should be screened for these genetic or enzymatic defects as a way to determine their risk level.

GSH also plays a specific role in the detoxification of numerous well-known carcinogens and mutagens in our environment. Some of the most important are:

Aflatoxin B1	Dimethylnitrosamine
N-acetyl-2-aminofluorine	Ethyl methane sulfonate
Benzanthracene	N-methyl-4-aminoazobenzine
Benzapyrene	7-methyl-benzanthracene
Benzidine	3-methyl-cholanthracene
Dimethylhydrazine	1-nitropyrene

These cancer-causing substances are conjugated or neutralized by GSH and rendered into a form the body can eliminate. The role of GSH in detoxification simply can't be overstated. Since the liver is the body's principal detoxifying organ it is not surprising that it carries the highest concentrations of GSH in the body.

The Chemoprevention Branch of the National Cancer Institute (USA) has for the last decade been developing drugs to diminish the incidence of this dreaded disease. Substances that raise GSH levels, such as NAC and the selenium derivative selenomethionine, are on their short list of useful therapies. One of the major successes of their research efforts is their statistical demonstration that selenium protects against prostate cancer. Other studies have identified selenium as protecting against colon, rectal and lung cancers as well as colonic polyps. R.B. Balansky, C.C. Conaway, H. Witschi, and other American and European researchers have successfully shown that NAC can slow the growth of cancers induced by toxins including urethane, nitrosamines, doxorubicin, ethylnitrosourea and other cancer-causing agents.

NAC apparently protects against the carcinogenic properties of cigarette smoke. N. VanZandwijk from the Cancer Institute of the Netherlands writes, "NAC has emerged as a most promising cancer chemopreventive agent." S. De Flora summarized a very large chemoprevention trial sponsored by Project Euroscan and described the many positive effects of NAC as a cancer prevention agent. It reviewed potential uses against lung, breast, bowel and skin cancers, and the actual mechanisms by which NAC and GSH exert these protective effects.

One of the glutathione's effects upon the immune system is to control and balance the growth of T-cell lymphocytes (a type of white blood cell), thereby strengthening the immune response. Immuno-depressed individuals are often more prone to cancer, a good example being Karposi's sarcoma, a cancer found mostly in AIDS patients. Cancer specialists have recently developed a strategy called immunotherapy – an attempt to optimize the body's natural defenses against the cancer. Immunotheraphy consists of tools to stimulate the immune system. A Japanese team from Kyoto University showed that adding NAC to cytokines – a class of immunotherapeutic agents – stimulated immune cells and their biochemical products. They suggest that this may be an effective compliment for the treatment of primary liver cancer.

Other anti-cancer substances produced naturally by the immune system include TNF (tumor necrosis factor) and IL-2 (inter-leukin 2). Glaxo Wellcome Research and Development scientists showed that NAC acts against tumors by elevating TNF. In the laboratory NAC halt4ed tumor growth in more than one third of mice injected with

cancer cells. C.Y. Yim and J.B. Hibbs at the University of Utah had similar success in suppressing tumor growth by using NAC to stimulate IL-2 (a promoter of white blood cell activity) in lymphokine killer cells, a type of T-cell lymphocyte.

THERAPEUTIC POSSIBILITIES

Surgical removal of cancer is only feasible if the tumor is not widespread and its accessible. Radiation and/or chemical therapy can help, but both inflict great damage on normal as well as cancerous cells. A cornerstone of recent research has been the search for ways to limit the damage to normal cells by such anti-cancer treatments.

Chemotherapy is a controlled poisoning of the patient based on the idea that rapidly growing cancer cells are more sensitive to the poison than are normal cells. Many but not all chemotherapeutic agents produce particularly unpleasant side effects. Radiation therapy works in a similar way. The cancerous area is targeted and bombarded with radiation. The tumor is theoretically more sensitive to the radiation than the surrounding healthy tissue, but this treatment can also produce severe side-effects.

Recent experiments show that the GSH content of both normal and cancerous cells makes them more or less susceptible to damage. High GSH levels clearly help protect cells from chemotherapy, low levels make them vulnerable. It would be ideal if GSH levels were high in normal cells and low in tumorous cells, but many human cancer cells have particularly high GSH levels. Cancer is the only known condition under which the otherwise tightly regulated GSH levels are exceeded. It is characteristic of cancer cells to bypass normal regulatory controls.

Tumor cells high in GSH often show resistance to chemotherapy, so there has been some effort to reduce GSH levels in cancerous cells with GSH-depleting drugs like BSO. The trouble is, BSO reduces GSH levels in healthy cells too, magnifying the already intolerable side-effects of chemotherapy. So this approach is impractical.

Nevertheless, there may be a way to diminish GSH in cancer cells alone. Paradoxically, the precursors that raise glutathione levels in normal cells trigger the opposite reaction in cancerous cells. When GSH production is overstimulated in cancer cells, they shut down glutathione production in a process called negative feedback inhibition, making them more susceptible to destruction. Meanwhile, normal tissue uses the precursors to make glutathione, leaving it with better defenses.

This paradox was described as early as 1986 by A. Russo's team in the journal Cancer Research. When the GSH-promoting drug OTZ was added to human lung cancer cells, their glutathione level did not increase even though GSH levels in surrounding normal cells did. McGill University researchers Sylvain Baruchel, Gerry Batist and their team in Montreal showed that OTZ could deplete GSH in breast cancer cells while enhancing it in normal cells. This team later worked with Dr. Gustavo Bounous and published similar results in the journal Cancer Research, using the whey protein isolate Immunocal to provide dietary GSH precursors.

Studies with the same product were also carried out on patients with metastatic carcinoma – cancer that is spreading through the body. They were fed Immunocal for six months. Although it did not cure the cancer, a significant proportion showed either tumor regression or stabilization. Most also experienced the advantage of normalized hemoglobin and white blood cell counts. The same researchers showed that elevated GSH levels may enhance the anti-cancer action of certain chemotherapeutic agents.

Another Canadian team – this one from the University of Saskatchewan – conducted trials on patients with advanced progressive cancer. They were given toxic doses of acetaminophen as chemotherapy, plus NAC to raise glutathione levels. They hoped that NAC would raise GSH in normal cells only, and their results bear them out. More than half the patients showed either improvement or stabilization.

Nevertheless, cancer specialists are still concerned that elevating GSH non-selectively might in certain cases diminish the advantages of chemotherapy. Any GSH therapy should be an integral part of the whole cancer treatment. Cancer patients should never initiate it on their own and must first talk to their treating physician.

Additional studies have investigated the effects of nutritional proteins on cancer-causing chemicals in animals. Researchers doing similar experiments in Canada and Australia subjected rodents to the powerful carcinogen Dimethylhydrazine – which causes colonic cancer similar to humans – and fed them a variety of proteins. Animals fed on undenatured whey protein concentrate showed fewer tumors and a reduced tumor load. The scientists found that this protein offered "considerable protection to the host," more so than any other protein.

It is accepted as a fact of life that the incidence and mortality rates of cancer increase with age. Certain cancers may in fact be considered diseases of aging, especially cancer of the prostate gland. Specific changes of aging render patients more susceptible to cancer. They also have less protection against oxidative damage, and diminished immune response. The protective effect of GSH diminishes with age. We generally lose from 20 to 40% of GSH after age 65.

A recent study convincingly showed that normal levels of androgens (male sex hormones) in older men lead to decreased GSH levels in the prostate gland. Anti-androgen therapy – also known as chemical castration – is a common treatment for prostate cancer. Androgens are known to act as oxidative stressors and can upset the prooxidant-antioxidant balance. Lowered GSH levels lead to loss of antioxidant function and may trigger the mechanism of prostatic carcinogenesis.

The prostate specific antigen (PSA) blood test is used to screen for prostate cancer and to track the progress of men suffering from this cancer. Higher PSA levels usually indicate progression of the disease, while falling levels show the success of treatment. Studies following PSA levels in patients taking GSH-promoting substances are in progress. GSH therapy has minimal toxic potential and one hopes it will become a standard treatment.

PREVENTION / TREATMENT OF SIDE-EFFECTS

Chemotherapy and radiotherapy lead to huge increases in free radical formation and a build-up of toxic metabolites. If the problem is not addressed, the side effects grow worse. Numerous studies have shown that when patients eat well – especially when their diets include vitamins and supplements – their tolerance of these unpleasant therapies improves. Patients with higher intracellular GSH levels experience far fewer chemotherapeutic side effects and cells with higher levels of GSH carry more protection against radiation damage, thereby lessening the side effects of radiotherapy.

Radiotherapists studying the protective role of GSH have correlated higher pretreatment glutathione levels with fewer subsequent radiation burns. Pre-treatment or simultaneous treatment with products that raise and maintain GSH levels gives patients greater tolerance to therapy.

Women with cancer were treated at the University of California (San Diego) with the standard chemotherapy cisplatin and supplemented with intravenous glutathione. This enabled them to take higher doses of chemotherapy while experiencing fewer side-effects. A similar but much larger study was carried out at the Western General Hospital in Edinburgh, Scotland. Over one hundred and fifty patients being treated for ovarian cancer with cisplatin and glutathione were monitored for side effects, quality of life, and outcome. They were compared to another group receiving no glutathione. The first group showed statistically less depression, vomiting, hair loss, shortness of breath and neurotoxicity. Their mental concentration and kidney function improved measurably and there was a distinct trend toward better outcome.

The hair loss that often results from chemotherapy may not be life-threatening but it can be extremely distressing to patients, especially at a time when they don't need additional stress. Hair loss may also suggest damage inflicted on other cells that regenerate quickly, like those lining the intestine. Researcher J.J. Jimenez at the University of Miami and others have demonstrated that NAC can protect from the baldness caused by common chemotherapy agents like cyclophosphamide.

Evidence suggests that glutathione-enhancing strategies may make certain chemotherapy agents more efficient. These include Adriamycin, cyclophosphamide, cisplatin and others. However, patients absolutely must talk to their treating physician before beginning any GSH-enhancing therapy. There are theoretical instances when non-specific glutathione elevation may interfere with the anti-cancer treatment, although this is less of a risk after the course of chemotherapy or radiotherapy is complete.

MALNUTRITION / WASTING

Anti-cancer treatment is often accompanied by loss of weight, appetite, energy and strength. Good nutrition is critical and should include appropriate dietary supplements. The cancer itself, the anti-cancer treatment and the resulting state of nutritional compromise all decrease intracellular GSH levels. This greatly weakens antioxidant and immune defenses rendering patients more susceptible to other diseases and opportunistic

infections. Well-known German immunologist and researcher Wulf Droge has studied weight and muscle loss in cancer, AIDS, sepsis and other diseases. He has noted the similarities among them and points to a common cause - GSH depletion. He and others have gone on to test the possibility that glutathione enhancing therapy may slow or halt this process of degeneration.

Increased GSH synthesis depends on the intake of cysteine-containing foods. Rich sources of this GSH-precursor are very hard to come by and often are not well tolerated by the patient. Cysteine is available as a free amino acid and may be taken, but it has toxic qualities and is not recommended. The drugs NAC and OTC can raise GSH levels but their effects are short-lived. These pharmaceutical drugs also have little nutritional value. Whey proteins have excellent nutritional value but usually lack GSH-precursors. The ideal source of dietary cysteine should be natural, nutritional, bioactive and undenatured. The patented whey protein Immunocal fits these criteria. It is biologically active, sustains elevated GSH levels and has great nutritional value.

CASE HISTORIES

Quebeccer Ivy-Marie is a very active thirty-seven year-old breast cancer survivor. After undergoing her initial surgery, the pathologist's report suggested she undergo a dozen sessions of chemotherapy and radiotherapy. She experienced many side-effects, including profound weakness and fatigue – a new experience for her. After ten sessions of therapy and many visits to her doctor to treat side-effects, she was put on 30 gm/day of the whey protein concentrate Immunocal. Her strength and sense of well-being improved within a week and she tolerated her last two sessions of chemotherapy with few side-effects. She is back to her usual routine, and remains disease-free.

Complaining of abdominal pain, Louisa from Alberta was 54 when she found out she had ovarian cancer. While awaiting surgery, she fell ill with a persistent cough and malaise which turned out to be a metastasis (spreading cancer) which had traveled to her lung. She ultimately needed pelvic surgery to relieve her discomfort, but decided not to undergo treatment for her lung metastasis. She started taking Immunocal and multivitamins daily and noticed a great improvement after several weeks. Four months later, repeat chest x-rays showed no increase in tumor size. Nine months later the radiographs revealed a decrease in tumor size. Louise continues to enjoy tending to her family and household.

CONCLUSION

There are many types of cancer, and perhaps hundreds of potential causes, but most cases are accompanied by poor antioxidant defenses. To make matters worse, most anti-cancer therapies place an enormous burden on the body and may deplete whatever natural defenses remain. Cancer sufferers must place themselves in best possible medical hands, but must also take special care of their nutrition. Patients are heavily dosed with pharmaceutical drugs and suffer from poor appetite and low energy, especially while undergoing chemical or radiation therapy. A natural source of energy that can also reinforce antioxidant defenses may make all the difference for people undergoing this distressing disease and its noxious treatment. Undenatured, bioactive whey proteins are

an ideal way to increase GSH levels and simultaneously address protein requirements. Elevated glutathione replenishes antioxidant defenses, contributr4es to synthesis and repair of DNA and helps detoxify numerous carcinogens and mutagens.

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