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On The COVER



Safe and Effective

Cancer Prevention

Using natural therapies for the prevention of breast and other forms of cancer

Last month we told you about the approval of tamoxifen chemotherapy for healthy women. Despite a lack of evidence, tamoxifen has been approved by the FDA for "reducing the incidence of breast cancer in women at high risk for developing the disease." This wordy description has been translated into "prevention" by the media. While one study shows that tamoxifen reduces the relative risk of certain women to develop breast cancer in the short-term, two long-term studies do not. Tamoxifen doubles, triples or quadruples a woman's risk of endometrial cancer, and it has never been proven to prevent one case of breast cancer.

Cancer is a reality for everyone: men have a 50/50 chance of contracting the disease, women-one in three. This year over 500,000 people will die of cancer. The disease is the leading cause of death in people 45-64 years, surpassed at 65 only by heart disease; it is the second leading cause of death for all ages. The incidence of certain types of cancer has skyrocketed. According to *Eat to Beat Cancer*, prostate cancer increased 266% between 1950 and 1992. The number of cases has increased more than 25% since 1980.

It has been estimated that 70-90% of all cancers are caused by environmental chemicals. Even with the most careful attention, one cannot avoid the onslaught of chemicals that have invaded the environment. Chemicals are insidious in that their effects may not show up for decades. Just as skin damage from sunbathing shows up two decades later, so can the effects of chemical exposure.

America is experiencing a cancer epidemic that coincides with the introduction of billions of tons of chemicals-including chlorine-based chemicals that mimic estrogen-into the environment. Chlorine-based chemicals are ingredients in plastic wrap and baby toys, DDT and "Agent Orange." Most people believe that because DDT has been banned, it has disappeared. It has not. Millions of tons of it are served up on America's dinner plates every year in beef and produce from South America, Mexico and other countries where the pesticide is still legal.

Chlorine-based chemicals have been implicated in the dramatic rise of breast and prostate cancer in the U.S. African-Americans are particularly hard-hit by prostate cancer, with an astounding 3% increase between 1992 and 1995. Prostate cancer is striking at an earlier age. In 1992, the proportion of men under age 60 who contracted prostate cancer was 21.3%. Now it's 29.8%.

Some believe the answer to estrogen overload is estrogen blockers. The drug tamoxifen is one such drug. The American Cancer society and others have hailed it as a cancer preventative, yet the drug's ability to prevent cancer in healthy women has never been proven. Conversely, its ability to increase uterine cancer is proven. Tamoxifen's dark side is rarely mentioned. It, like other estrogen regulators, can both block and promote estrogen, depending on the tissue. This probably accounts for tamoxifen's ability to promote endometrial cell growth.

Zeneca Pharmaceuticals, manufacturer of tamoxifen, is part of one of the largest chemical manufacturers in the world. Along with tamoxifen, Zeneca makes insecticides, paints, dyes, adhesives, fungicides, plant growth regulators and herbicides, including a version of "Round-Up." Although the role that chemicals play in human cancer is controversial, their long-term safety in humans has never been proven. The safety of combinations of chemicals (including drugs) has never been proven. Enough data exists for the prudent person to assume that until a safe environment is restored, they are at risk. The most rational approach is to take steps now towards preventing cancer in the future.

The National Cancer Institute (NCI) is in the preliminary stages of investigating three natural substances that have decades of research behind them as cancer preventives in the test tube and animals. All three, curcumin, green tea and genistein, have been a part of non-Western diets for centuries.

Although they seem simple compared to compounds created by drug companies, the three are showing activity just as sophisticated, and in some cases even more so, than drugs.

Curcumin

Curcumin is the yellow part of turmeric, a spice used frequently in Indian cuisine and curries. Turmeric comes from the root of a plant related to ginger. Its antioxidant ability is greater than vitamin E, plus it enhances natural antioxidant enzymes in the liver. It has powerful anti-inflammatory action.

Several anti-cancer activities have been discovered for curcumin. In the test tube it induces cell death (apoptosis) of human cancer cells. Researchers in Poland have observed that curcumin can either inhibit apoptosis or promote it, depending on the type of cell. They also report that curcumin's apoptosis is different than that caused by chemotherapeutic chemicals.

Standard chemotherapy causes death to cancer cells by halting the cell cycle. All cells, including cancer cells, proliferate by dividing. The process of division-the cell cycle-is categorized into various steps (G1, G2, etc.). These are orchestrated by signals from both inside and outside the cell. Chemotherapy interferes with those signals, so as to stop division at one point in the cell cycle. The cell then dies. The reason chemotherapy is so toxic is because it's not cancer-specific. It targets any quickly dividing cell, which means it stops the division of normal cells such as the ones that line the mouth and gut.

Curcumin has the ability to stop cell division at more than one point in the cell cycle (G1 or G2), depending on the type of cell. Plus, it has the surprising ability to inhibit cell death, depending on the type of cell. This means that curcumin has the potential to selectively kill cancer cells, while sparing normal ones. Is curcumin "smart" chemotherapy? Test tube evidence says yes.

Another feature of curcumin is that it can act as an antioxidant or prooxidant, depending on the dose and whether metals are present. And, strangely enough, it can either deplete or enhance glutathione, depending on the cell and whether certain carcinogens are present. These features may eventually be exploited for cancer therapy. The secret to its dual personality may lie in its ability to regulate more than one molecular pathway. In other words, curcumin can send different signals to different cells.

Curcumin appears to be well-suited to go up against environmental chemicals, as it has shown to greatly reduce the number of tumors in rodents exposed to such toxins. It is particularly powerful against skin, stomach and colon cancer. In one study, a form of curcumin known as tetrahydrocurcumin reduced aberrant crypt foci, a precancerous condition, by 50%. Curcumin has been shown to stop the growth of two types of human colon cancer cells by 96% within 48 hours. In a rodent study on oral cancer, curcumin gave a stellar performance, significantly reducing both DNA damage and the number of tumors.

Curcumin and Green Tea

Researchers at Sloan-Kettering have been able to enhance the cancer preventive effect of curcumin by combining it with green tea. They tried the combination on three different types of oral cancer, plus normal cells. The researchers found that the combination blocks the cell cycle at more than one point, increasing the likelihood that more cancer cells will be killed. The reason that cancer patients undergo therapy with different types of chemotherapies is to stop as many cells as possible from dividing. Not every cell is going to be in the same point of the cell cycle, so multiple drugs are used to get at dividing cells in different stages of division.

Adding green tea to curcumin not only produced a synergistic effect, it also enabled the dose of each to be reduced. This theoretically could reduce toxicity (although no significant toxicity of these two has ever been shown). In fact, curcumin itself protects the heart from the toxicity of adriamycin (doxorubicin), a common chemotherapy used for breast cancer. (There is some evidence that SAME can also protect against cardiac toxicity caused by adriamycin.)

Regulating p53

Curcumin has potential to regulate p53 ("p" is for protein), a tumor suppressor gene. It is estimated that mutations in p53 are involved in half of all malignancies. P53 is important because it affects cancer growth-it helps regulate the cell cycle, controls cell death, and affects the way cells respond to growth factors. Restoring a functional p53 gene in cancer patients is a major focus of gene therapy.

Skin cancer of the non-melanoma type is an area in which mutated p53 regularly shows up. In 1998, re-searchers reported that curcumin's ability to induce cell death in skin cancer cells is mediated through p53. Other studies support curcumin's ability to stop cancer growth through p53, but the mechanisms are not yet known.

An exciting aspect of curcumin is that it may have the ability to counteract dioxin. Dioxin and other chlorine products have been implicated in the increase of prostate and breast cancer because they have the ability to mimic estrogen. Dioxin itself causes major oxidative stress. It has been characterized as the most toxic chemical known-so toxic, in fact, that the EPA allowable daily amount

is .006 trillionths of a gram per kilogram of body weight.

One of the reasons dioxin is so dangerous is because the body thinks dioxin is natural. It readily allows the chemical to interact with a protein known as the "aryl hydrocarbon receptor" (AhR) that transports it to human DNA. There, the AhR binds another protein. Together, the natural protein and its attached imposter can activate genes and do damage.

NIH researchers have discovered that curcumin can also interact with AhR. And this is good news because it means that curcumin can potentially block dioxin. Unfortunately, however, curcumin is not as good at latching onto the AhR as dioxin, so it can't block the chemical completely. But it has been shown to counteract some of the effects of the breast carcinogen, DMBA, which provokes the same kind of changes in the cell as dioxin. Researchers have proven that in human cells, curcumin reduces DNA damage caused by DMBA.

The only other beneficial substance known to interact with AhR is a phytochemical found in cruciferous vegetables such as cauliflower and brussels sprouts.

Green tea

More exciting research was published last year on green tea and its anti-cancer qualities. A new report from Japan demonstrates that green tea goes way beyond antioxidant protection. If the study is confirmed, it will propel the ancient beverage squarely into the middle of 21st century science.

One of the factors that sets cancer cells apart from normal ones is that they have telomerase, an enzyme that maintains telomeres on the ends of DNA. Most normal cells do not have telomerase to maintain their telomeres. Every time a normal cell divides, telomeres are lost. When all the telomeres are gone, the cell dies.

Cancer cells' ability to maintain their telomeres may be the secret to their immortality. Consequently, inhibiting telomerase and causing cancer cells' telomeres to shorten has become a focus of cancer therapy. Theoretically, if telomerase could be inhibited, telomeres would shorten to the point that the cancer cell would die.

The first natural telomerase inhibitor has been discovered-green tea. Japanese researchers have been able to show that green tea inhibits telomerase in two different types of cancer cells in the test tube. Green tea extract (EGCG) causes cells of both leukemia and the solid tumor type to die. Although the mechanism is not yet known, the researchers were able to see EGCG being transported into living cells. Within a month, some of the cancer cells began dying. Within two months more, most were dead. The experiment has been repeated several times with the same result.

While it is great to kill cancer cells by inhibiting their telomerase, those familiar with the telomere theory of aging might ask what effect green tea has on normal cells. The answer is that they don't have to worry. The few normal cells that possess telomerase (germ cells and hematopoietic cells which eventually become blood cells) have longer telomeres to begin with, and their telomerase is very weak. If green tea had an adverse effect on these cells, then it would be expected that the Japanese (who drink lots of green tea) should have decreased life expectancy. Instead, they have the greatest, with Japanese women who practice the tea ceremony having half the mortality of those who don't. As with curcumin, the effects of green tea may depend on the type of cell. It may even turn out that green tea has a beneficial effect on the telomeres of normal cells. The researchers who conducted the telomerase/tea study are now focusing on that issue.

While the finding about green tea and telomerase is exciting for test tubes, it is far from being proven for humans. Yet this experiment is another example of the hidden sophistication of natural substances. One of the reasons the scientists undertook this study was to find ways that green tea might work against cancer besides its antioxidant action. The surprising result is particularly exciting to breast cancer researchers because telomerase has been detected in 95% of advanced cases.

Another group of Japanese researchers have proven that green tea prevents several types of cancer. In a follow-up study, they decided to focus on breast cancer. Rather than looking at prevention, they looked at what effect green tea might have on women already diagnosed with breast cancer. Surprisingly they found that drinking green tea affected a woman's response to therapy and whether she had a recurrence of the cancer. After seven years of study, they concluded that women with stage I and II breast cancer who had drunk five cups or more of green tea a day before they got sick had a recurrence rate of 16.7% compared to 24.3% for women who drank less than four cups daily. Statistically, this is a significant difference. In addition, the number of metastasized lymph nodes in premenopausal women was slashed almost in half by five to seven cups of green tea per day, and further reduced with more cups. (Postmenopausal women had to drink more than eight cups of green tea a day to see a significant effect.) The tea drinkers also had more cancers that were estrogen and progesterone-receptor positive-the more treatable types of cancer. The study also suggests that green tea can help prevent new cancers from occurring. Five of six patients who contracted a new cancer drank less than four cups of green tea a day. While the number of patients in this study is too small (472) to be more than an indication, taken together with other published data, it shows green tea's potential.

Like curcumin, green tea has shown promise against chemical carcinogens. In this case nitrosamines, which are formed when chemicals called nitrates or nitrites come in contact with organic substances. Researchers frequently use nitrosamines to create cancer in animals. Nitrates and nitrites are used as food preservatives-particularly in such products as hot dogs, bologna and bacon-although human brain cancer has been connected to preserved meats containing nitrite. Cigarette smoke and car exhaust also generate nitrosamines. Antioxidant vitamins C and E counteract nitrosamines, but green tea is stronger.

Research shows that green tea may enhance chemotherapy. In a study from Germany, researchers took human colon cancer cells that were resistant to doxorubicin and treated them with EGCG and EGC from green tea. These tea extracts sensitized the cells to killing by the drug. On the other hand, EGCG seems able to protect against the toxicity of chemotherapy. Researchers in Turkey have discovered that EGCG protects against doxorubicin-induced heart damage in rats. Chemotherapy generates large amounts of free radicals, and it is likely that EGCG works through its free radical scavenging mechanism.

For those who rather swallow than sip, green tea is available in highly concentrated capsules that contain extracts of the specific polyphenols that have proven cancer-fighting properties. Be aware that other kinds of tea cannot be reliably substituted for green tea. The main difference between green tea and others is that green tea is not heated (heating causes oxidation). Although black tea and others contain EGCG, the amount is less than what occurs in green tea. For example, a cup of Sencha, the most common variety of green tea, contains high amounts of EGCG compared to very low levels for Oolong tea. Boiling water degrades EGCG, so use less-than-boiling water when making green tea-the traditional way to prepare the beverage.

Phytoestrogens-genistein

The amount of genistein in a plant-based diet is 30 times higher than a meat-based one. Genistein is found abundantly in soy beans, and has been pegged as a cancer fighter. It inhibits angiogenesis (the growth of new blood vessels) in vitro, and inhibits cell proliferation-both important features in stopping cancer growth. The much lower incidence of breast and prostate cancer in Asians who eat a traditional diet is thought to be partly due to the phytoestrogens they eat. (It should be pointed out, however, that the amount of fat from meat in the Asian diet is about a third less than in Western diets. Some studies link high dietary fat to cancer, other studies show that fat has little effect on cancer incidence.)

The tendency of researchers and the public alike is to downplay the potential of dietary components. It's hard to believe that something as simple and common as soy could act in a manner as scientifically sophisticated as a drug. Yet genistein has repeatedly been proven to have very advanced mechanisms against cancer cells. Several important new studies leave no doubt that phyto-estrogens from soy inhibit several types of breast cancer. It has been discovered that genistein regulates a tumor suppressor gene, p21, which works in tandem with p53 to regulate cancer cell growth.

In addition to regulating p53, genistein also induces cancer cell death, and regulates cyclin-a substance that sends "grow" signals to cancer cells. Furthermore, researchers at the University of Southern California report that genistein also neutralizes a factor that activates stress proteins. Tumors use stress proteins to protect themselves from destruction by the immune system.

Research also shows that genistein blocks the ability of a chemical (DMBA) to cause breast cancer. Scientists at the American Cancer Foundation report that pretreatment of rats with genistein stopped the chemical from damaging DNA and causing cancer. Researchers at the University of Alabama report that genistein inhibits the activation of factors that prostate cancer uses to get a foothold.

The best evidence so far that phyto-estrogens prevent cancer in humans is the millions of Asians who eat it everyday. Their incidence of cancer is much lower than in Americans. This isn't science, however, and definitive data is still lacking.

Although large-scale studies have not been conducted, three controlled studies do demonstrate a clear preventive effect of soy on breast cancer in premenopausal women. A fourth study on both pre- and post-menopausal women was conducted in Australia. The study was very elaborate: women were tested for phytoestrogens right after they were diagnosed with breast cancer, before chemotherapy was started. Five separate phytoestrogens were measured. (Unfortunately, problems with the assay prevented genistein from being measured.) The study showed that women with higher levels of phytoestrogens had up to a four-fold decreased risk of breast cancer.

Natural Cancer Prevention

For optimal prevention the best plan is to take a variety of cancer fighters. However, it must be cautioned that more is not necessarily better. Especially regarding curcumin, this is true. At high levels, antioxidants such as curcumin become pro-oxidant, i.e. they promote free radicals rather than inhibit them. For prevention purposes, 500-900 mg a day of curcumin with a heavy meal is suggested. The minimum amount of soy isoflavones to prevent disease has been estimated to be about 50 mg per day. Since soy is water-soluble and has a short half-life in the body, it is recommended that soy supplements be taken twice a day to maintain constant levels in the blood. An ideal dose would be 50 mg in the morning and 50 mg in the evening. A study in Japan showed that green tea worked better at 10 cups than five. Those who enjoy a constant jolt of caffeine throughout the day should consider

switching from coffee or colas to green tea. Many people do not tolerate high caffeine levels and instead choose green tea supplements. Since the amount of active disease-fighting polyphenols in green tea beverages varies, depending on how green tea is brewed and the type of green tea used, it is sometimes difficult to ascertain the optimal number of green tea extract capsules to use everyday. For prevention purposes, a minimum dose of green tea polyphenols might be 200 mg per day, while an optimal dose may be in the range of 1000 mg per day.

The bottom line is that natural cancer prevention works. A decade of science now stands behind green tea, curcumin, phytoestrogens and other plant extracts as safe and genuine cancer preventers. The National Cancer Institute has studies underway on all three. A Phase I study is underway to look at genistein and prostate cancer. Another NCI study is looking at curcumin for the prevention of colon cancer. Yet another is comparing a low-fat, high fiber, soy, fruit, vegetable, green tea and vitamin E diet to a regular NCI diet for prostate cancer. A green tea study is in the first stages only to look at how much can be tolerated, while a breast cancer study using soy, fish oil and low-fat is being organized. It will be years before the results of these studies are known, but people wanting prevention now can benefit from data already published on these natural cancer preventers. Don't wait until cancer strikes to begin thinking about preventing it.

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For more information on chlorine-based chemicals, see:

"Chlorine Crisis: Time for a Global Phase-Out" and "Dow Brand Dioxin" at www.greenpeaceusa.org

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