Dairy Products and Cancer

October 15, 2009; By Dr. Anthony Kleinsmith

Dear consumer,

There has been considerable adverse publicity and confusion recently regarding the relationship between the intake of dairy products, particularly milk, and the development of certain types of human cancer. One of the most outspoken antagonists supporting programs that attack the intake of dairy products is Robert Cohen, who identifies himself as the Executive Director of the Dairy Education Board. In reality, Mr. Cohen is an investigative reporter who has found a cause to champion and uses the Dairy Education Board, an "organization" he founded, as a soapbox. Mr. Cohen has published a book on the subject, MILK--The Deadly Poison, and authors a website (www.notmilk.com) as a means to disseminate his views and those of his supporters.

When one looks at the website of Mr. Cohen, it is evident that although he professes to state only the facts, he has grossly distorted them to suit his own needs. For example, in a supposed factual newsletter written in June 1998, but still used on the website, Mr. Cohen reports that Virgil Hulse, MD, wrote a book entitled Mad Cows and Milk Gate in which he reported that most of the dairy cows in America have bovine leukemia, bovine immunodeficiency virus or bovine tuberculosis. Mr. Cohen then states "We drink body fluids from diseased animals in the name of good health".

Anyone familiar with the dairy industry in America, or who will take the time to properly investigate it, knows that all dairy cows are vaccinated against these diseases and that such vaccinations are mandatory if the dairy farmer intends to sell milk for human consumption. Further, virtually all milk sold in commercial outlets for human consumption is pasteurized at temperatures that would destroy these microorganisms even if they were present.

Mr. Cohen's attack on milk has focused primarily on insulin-like growth factor-1 (IGF-1) wherein he claims that this hormone makes human cancers grow. Throughout the website, he cites scientific articles by reputable authors from prestigious institutions that he claims state that IGF-1 is a key factor that promotes the growth of prostate, breast and colon cancers. The website contains an article written by Hans R. Larsen, a chemical engineer,

which makes similar misrepresentations of scientific findings. Mr. Larson cites numerous articles and then makes statements about them, such as the following.

"On January 23, 1998, researchers at the Harvard Medical School released a major study providing conclusive evidence that IGF-1 is a potent risk factor for prostate cancer." "In 1995, researchers at the National Institutes of Health reported that IGF-1 plays a central role in the progression of many childhood cancers and in the growth of tumors in breast cancer, small cell lung cancer, melanoma, and cancers of the pancreas and prostate."

"In September 1997, an international team of researchers reported the first epidemiological evidence that high IGF-1 concentrations are closely linked to an increased risk of prostate cancer. Other researchers provided evidence of IGF-1's link to breast and colon cancers."

These statements are inaccurate misrepresentations of the actual conclusions drawn by the scientific investigators in their publications. The investigators' findings have been distorted to try and lead the reader to the erroneous conclusion that the intake of IGF-1 will lead to enhanced tumor development in human cancers. The truth is that no one has ever demonstrated a cause-and-effect relationship between IGF-1 and cancer. In fact, when the quoted articles are reviewed, one finds that none of the investigators ever even suggested that IGF-1 was a causative agent in tumor development associated with human cancers, but, instead, found that people with certain types of tumors had high levels of IGF-1 in their circulation as a manifestation of their disease. The elevated levels of IGF-1 seem to occur very early in tumor development and several authors cited by Mr. Larson have actually suggested that measurement of IGF-1 in the blood of people may be an early warning indicator that a tumor could be developing in the body. They believe that making such measurements of IGF-1 could mean possible earlier diagnosis and treatment. This situation is analogous to the elevated white blood cell count seen in association with appendicitis. The elevated white blood cell count is a manifestation of the condition and an indicator of infection. No reasonable person would say that it caused the appendicitis.

What are the Real Facts about IGF-1?

Insulin-like growth factor-1 (IGF-1), and its closely related counterpart insulin-like growth factor-2 (IGF-2), are potent hormones that are found in association with almost all cells in the body. IGF-1 is the best described and

most potent of this pair. These molecules are produced by all mammals and, in every case, have a very similar chemical structure regardless of the species. IGF-1 is essential for normal cell growth and for the development of the fetus in the uterus (4). Both IGF-1 and growth hormone are required for normal post-natal development (7) and that is why they are both present in colostrum. The IGFs are structurally very similar to insulin and, in fact, in certain diseases the specific receptors for insulin on cells in the body are sometimes incapable of distinguishing between IGF-1 and insulin.

Scientific knowledge about the IGFs, what they do and how they act on cells in the body has evolved very rapidly during the past few years. It is now known that there are specific receptors on almost all cells in the body capable of interacting with IGF-1 and triggering a series of chemical events within the cell (8). There are also 6 different proteins present inside the cell and on cell surfaces that control the actions of IGF-1 on the cell after it binds to a receptor. These are called insulin-like growth factor binding proteins (IGFBPs). In addition, there are at least 87 other related proteins either capable of binding to IGF-1, altering its actions, or influencing the effects of the IGFBPs.

These are called insulin-like growth factor binding protein-related proteins (IGFBP-rPs). The entire collection of these proteins is referred to as the insulin-like growth factor binding protein (IGFBP) superfamily (9). The key event that triggers the effects of any of these proteins appears to be the interaction of IGF-1 with its specific cell-surface receptor, an event that some of these proteins regulate.

The multitude of available IGF-1binding proteins and related proteins available in the cell is indicative of the many potential effects that the binding of IGF-1 to its specific cell-surface receptor can have on cells. To keep these many effects under control, some of the binding proteins act as checks and balances, allowing the secondary chemical switches in a cell to be turned on and then turning them off when it is appropriate. Therefore, IGF-1 is like the captain of a ship. When it binds to its specific receptor, the ship can move forward, but there are all kinds of systems in place to keep it moving at the right speed and in the right direction. The main triggered events include activation of the process by which the cell grows and reproduces itself and maintenance of the metabolic pathways by which the cell converts glucose into glycogen and uses amino acids to create proteins.

The actual pathway by which the cell uses glucose and converts it to glycogen is first switched on by the binding of insulin to its specific cell

surface receptors. Glycogen is stored in the liver and muscles and is the main source of readily available energy when the muscles are exercised. The IGFBP superfamily also has a direct role in how the cell uses amino acids to build proteins. As we age, the ability of our body to create an adequate supply of IGF-1 is diminished. Thus, by eating a well-balanced diet and maintaining a constant supply of IGF-1 in our body, we can keep the ship moving at the right speed and in the right direction. And when we exercise this becomes even more critical since there is an increased demand for glycogen to provide energy to our muscles and the preference is to build more muscle protein. Even more importantly, as we age the cells in our body do not reproduce themselves as well and, since IGF-1 is a primary factor in the ability of cells to grow and reproduce, it is highly desirable to have an appropriate level of IGF-1 in the circulation through dietary supplementation to limit the ever increasing rate of cell senescence.

Why is there excess IGF-1 in the circulation in certain types of cancer?

You will recall that Mr. Hans Larsen, writing on behalf of Mr. Robert Cohen, drew the following conclusion in his article on Mr. Cohen's website. "In 1995, researchers at the National Institutes of Health reported that IGF-1 plays a central role in the progression of many childhood cancers and in the growth of tumors in breast cancer, small cell lung cancer, melanoma, and cancers of the pancreas and prostate."

In actual fact, in the 1995 article cited (1), these researchers reported that the cell surface receptors for IGF-1 mediate most of the effects of IGF-1 and, despite its structural similarity to the insulin receptor, the IGF-1 receptor is mainly involved in the support of growth and sends different types of signals than the insulin receptor. They concluded that the gene encoded for the IGF-1 receptor is expressed by most cells in an organism, which is consistent with the role of IGFs as survival factors, and that the receptor gene is modulated by many physiological and pathological factors, including developmental stage, nutritional status, hormones, growth disorders and malignancy. In 1996 (2), the same researchers reported that the IGF-1 receptors are integral cell membrane proteins that demonstrate important effects on the regulation of cellular processes. The same investigators and others (3) also found that the IGF binding proteins (IGFBPs) were made by cells and could be secreted such that they could accumulate on external cell surfaces. As such, the IGFBPs were found to be involved in regulating cell processes by modulating the interaction of the IGFs with their cell surface receptors. Later it was recognized that certain of the IGFBPs were growth inhibitory molecules and, as such, were

primary regulators of the effects of IGF-1 interaction with its cell surface receptor on cell growth (5, 6), Multiple studies have shown that there is an elevated level of IGF-1 in the circulation of patients with certain types of malignancies including, prostate cancer (11, 12, 13, 14, 15), breast cancer (17, 18, 19, 20, 21, 22, 23, 24, 25), colorectal cancer (26), acute lymphoblastic leukemia (27, 28), and non-small cell lung cancer (29). Many of these studies also reported other associated factors. A group from the Harvard School of Public Health investigated the relationship of intake of dairy products to the risk of prostate cancer and found such patients also had reduced circulating levels of vitamin D, a factor believed to be protective for prostate cancer (13). In several cases, increased circulating levels of IGF-1 were paralleled by extremely low levels of a particular IGFBP (IGFBP-3) known to be a very potent inhibitor of the cell growth-promoting effects of IGF-1 and IGF-1 receptor interaction (24, 25, 26). More recent studies have shown that levels of some of the IGFBPrelated proteins that control the inhibitory effects of IGFBP-3 are also altered in certain malignant diseases (15, 22). One study has shown that another IGF-binding protein (IGFBP-6) that is involved in programmed cell death is increased in non-small cell lung cancer (29). In some studies, associations have been drawn between the levels of certain hormones, increased circulating IGF-1 and cancer risk. In prostate cancer there have been proposed relationships to high levels of testosterone (10) and in breast cancer with the progestins, which seem to interfere with the interaction of IGF-1 and its cell surface receptors (18, 22).

It is difficult to understand how a comprehensive review of the scientific literature would lead one to the conclusion that IGF-1 is responsible for enhanced tumor development in certain types of human cancer. This is particularly true when it is seen that the same increased circulating levels of IGF-1 and modifications of certain controlling protein substances have been found in various nonmalignant diseases. For example, similar alterations in IGF-1 and IGFBP-3 are found in patients with benign prostatic hyperplasia (16). In both type I and insulin-resistant type II diabetes, patients demonstrate increased circulating levels if IGF-1 (30, 31, 32) and in type II diabetes patients an inverse correlation between levels of insulin and a particular IGFBP (IGFBP-1) has been shown (30). In another study from the Harvard School of Public Health, it has been shown that men with higher levels of testosterone are more likely to have vertex baldness and in those that additionally have higher than normal blood levels of IGF-1 the odds of vertex baldness is doubled (33).

Published studies have also shown that in growth-retarded individuals the

gene encoding for the IGF-1 receptor is defective and, as a result, these individuals have substantially elevated levels of circulating IGF-1 (34). There is no question that there is an increased circulating level of IGF-1 in patients with prostate, breast, colorectal, lung cancer and some leukemias. The effects of IGF-1 on the cells, which include cell growth, survival and transformation, are mediated through its interaction with IGF-1 receptors on cell surfaces. The interaction of IGF-1 with its receptors is further controlled by the IGFBPs, some of which can independently act on cell processes. The controlling aspects of the IGFBPs is further modulated by many additional regulating substances in both normal and disease processes (36, 37). Studies from the National Institutes of Health have shown that in malignant disease there are more than enough IGF-1 receptors on cell surfaces, but the ability of these receptors to interact with IGF-1 is significantly reduced. They were also able to demonstrate that the most frequently mutated gene in human cancer, p53, lowers the ability of the IGF-1 receptors to bind IGF-1 and function (35). Studies from Germany reported in September 2000 have added to the understanding of this process (38). These investigators found that a protein encoded by the human papilloma virus binds to IGFBP-3, which restricts cell growth following the interaction of IGF-1 with the IGF-1 receptor, and enzymatically degrades it. This protein is a product of the p53 gene and it has long been known that it can immortalize primary human cells and overcome cellular senescence.

Therefore, the underlying cause for elevated levels of IGF-1 seen in cancer is related to a cascade of events that began with an alteration of basic genetic information and culminated in an impaired functioning of the IGF-1 receptors on the surface of the cells. In this case, other IGFBP and related proteins that can act independent of IGF-1 interaction with its receptors have apparently redirected cell growth without the involvement of IGF-1. Since IGF-1 does not have operating, functional receptors to interact with, it naturally backs up in the circulation as a manifestation of the disease process.

To your good health - always.

Sincerely,
Alfred E. Fox, Ph.D.

Dr. Alfred E. Fox holds a Ph.D. from Rutgers University in Microbiology (Immunochemistry) and has more than 25 years of senior management experience at Carter-Wallace, Baxter Dade Division and Warner-Lambert, where he was responsible for research and development and regulatory

affairs. He was also the founder and president of two biotechnology companies focused on agribusiness and environmental monitoring, respectively. For the past 15 years, Dr. Fox has been the President of Fox Associates, a business and technology consulting firm serving small- to midsize companies in the human and animal healthcare fields. He focuses primarily on marketing and regulatory issues and for the past 10 years has continuously consulted to bovine colostrum manufacturers, where he has gained regulatory approval for their products, been a technical advisor, helped design and develop marketing strategies and served as an expert witness in legal matters.

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