Milk Duct Tissue Cancers Rose 55.3%

-For post-menopausal women, 1994 through 2002

by Paris Reidhead

Evidence of a strong link between certain human cancer risks and a high level of blood-borne, Insulin-like Growth Factor-1 (IGF-1) is now indisputable.

Is cancer genetically ordained? Or could diet, or other outside environmental factors, raise IGF-1 levels in some persons' blood?

Samuel S. Epstein, M.D., of the University of Illinois-Chicago, is a world-class environmental toxicologist who has strongly warned for nearly two decades that elevated IGF-1 levels in milk from dairy cows injected with recombinant bovine growth hormone (rbGH) posed cancer threats to the milk-drinking public. Epstein's 1996 article in the *International Journal of Health Sciences* clearly warned of dangers of high levels of IGF-1 contained in milk from rbGH-injected dairy cows.

Epstein postulated that IGF-1 in rbGH-milk could be a potential risk factor for breast and gastrointestinal cancers.(1)

To the readers of *The Milkweed* ...

For nearly two decades, critics have warned of potential human cancer concerns that could result from consuming milk from cows injected with recombinant bovine growth hormone (rbGH). That drug is trademarked and marketed to dairy farmers by Monsanto as "Posilac"—a synthetic, cow growth hormone that spurs the cow's mammary tissue cells to produce more milk.

Human health concerns about rbGH focus on a secondary hormone: Insulin-like Growth Factor-1 (IGF-1). IGF-1 is produced mainly by the liver in mammals, in response to blood-borne levels of growth hormones (natural and synthetic). Injecting rbGH into dairy cows dramatically boosts their IGF-1 output. IGF-1 levels of milk from rbGH-injected dairy cows are higher. In late 1993, when FDA approved "Posilac" for commercial sale, the agency contended that any extra IGF-1 in cows' milk would be destroyed by the digestive acids in the stomachs of persons drinking that milk. During the past decade, numerous scientific studies have shown that IGF-1 in milk survives digestion and passes into the human bloodstream.

IGF-1 is the key metabolic agent for spurring cellular growth and function. Structurally, IGF-1 in bovines and humans IS EXACTLY THE SAME.

In this article, writer Paris Reidhead has carefully researched two highly controversial subjects for the U.S. dairy industry:

1) The history of scientific findings linking IGF-1 to a variety of human cancers—breast, prostate, and colorectal.

2) The dramatic increase in post-menopausal women's milk duct tissue cancers from 1980 to 2002 in the U.S. Starting in 1994 (the first year rbGH was commercially used by dairy farmers), the rate of women's milk duct tissue cancers increased by 61.6%, through 2002.

Human milk duct tissue cancers in the U.S. are a key measure of concern, because the secondary hormones produced by rbGH injections in dairy cows target cows' mammary tissue metabolism. Logically, if additional quantities of IGF-1 are in the public milk supply, due to rbGH injections for cows, then if the IGF-1 in that milk survives pasteurization and human digestion to enter the human blood stream, where are the logical receptors for that IGF-1 to spur cellular metabolism? The human breast.

The following article does not claim to prove a direct link between additional IGF-1 in the U.S. milk supply due to dairy farmers injecting cows with rbGH and increased breast cancers. However, many serious questions arise, which are beyond the resources and information available to this publication.

Pete Hardin – Editor/Publisher

In 1990 researchers at Stanford University reported that IGF-1 promotes the growth of prostate cells.(2)

This finding was followed by the discovery in 1993 that IGF-1 accelerates the growth of breast cancer cells.(3)

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 pancreas and prostate.(4)

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.(5)

Other researchers provided evidence of IGF-1's link to breast and colon cancers.(6)

The January 1998 report by the Harvard researchers confirmed the link between IGF-1 levels in the blood and the risk of prostate cancer. The effects of IGF-1 concentrations on prostate cancer risk were found to be astoundingly large - much higher than for any other known risk factor. Men having an IGF-1 level between approximately 300 and 500 ng/mL were found to have more than four times the risk of developing prostate cancer than did men with a level between 100 and 185 ng/mL. The detrimental effect of high IGF-1 levels was particularly pronounced in men over 60 years of age. In this age group men with the highest levels of IGF-1 were eight times more likely to develop prostate cancer than men with low levels. Elevated IGF-1 levels were present several years before an actual diagnosis of prostate cancer was made.(7)

Chan, Stampfer, *et al.* in Vol. 23 of *Science* (January 23, 1998) wrote a paper called "Plasma Insulin-Like Growth Factor-1 and Prostate Cancer Risk: A Prospective Study".(7)

The bulk of this data was tallied at the Harvard School of Public Health. In this study, the authors stated that IGF-1 has mitogenic effect (i.e., IGF-1 impacts cellular division) on normal and transformed prostate epithelial cells. Most circulating IGF-1 originates in the liver, but IGF bioactivity in tissues is related not only to circulating IGF and IGF binding protein (IGFBP) levels, but also to local production of IGFs, IGFBPs, and IGFBP proteases (enzymes digesting such proteins).

Chan, Stampfer, *et al.* also determined that IGFBP shows growth inhibiting properties, and thus tends to reduce the bioactivity of IGF-1. They then theorized that high levels of IGFBP were inversely related to risk of prostate cancer. IGF-1 was shown to be significantly associated with prostate cancer risk in studies where only this single variable was being analyzed. Blood IGF-1 was measured in 152 men in the study; its values were expressed as nanograms/milliliter (ng/mL). In this study these values ranged from 99 to 500. An increase of 100 ng/mL doubled the risk of prostate cancer, as shown with a two-fold increase of PSA (prostate specific antigen).

Chan and co-workers were convinced that higher levels of blood IGF-1 are associated with increased prostate cancer risk, but they did not delve into possible external sources of this hormone—particularly IGF-1 ingested in dairy products originating with cows treated with rbGH. Later in 1998, the British journal *The Lancet* published a study entitled, "Circulating concentrations of insulin-like growth factor-1 and risk of breast cancer". (8) (It was written by Harkinson, Willett, Pollak, *et al.*)

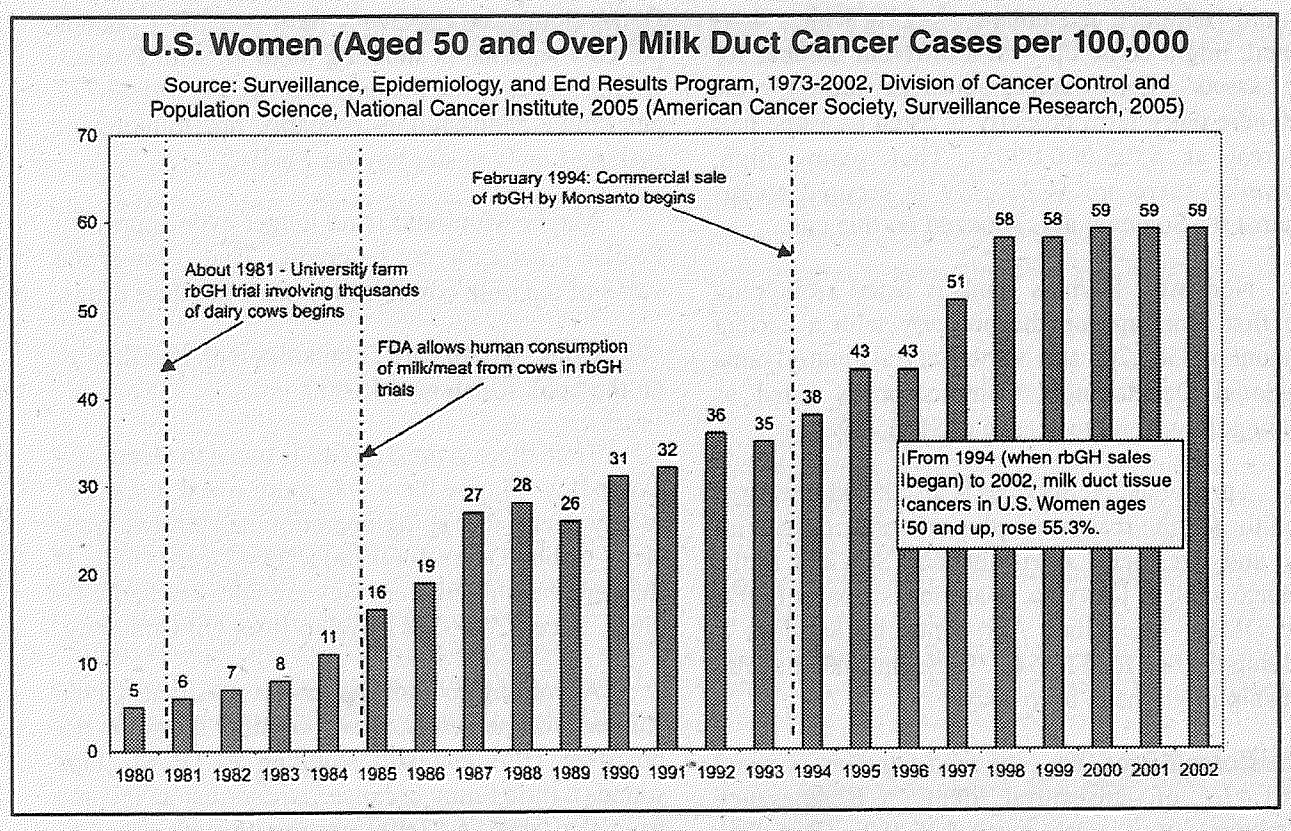
Much of this work was performed through the Harvard School of Public Health, as well as the Jewish General Hospital and McGill University in Montreal, Canada. These authors postulated that IGF-1, with its cancer-causing properties, could affect the growth of breast epithelial cells, and thus have a role in breast cancer. The authors believed that high circulating IGF-1 levels in the blood concentrations would be associated with increased risk of such cancers. This article will review some of the key points of these research findings.

A positive relation between circulating IGF-1 concentration and risk of breast cancer was found among pre-menopausal, but not post-menopausal, women. These workers found substantial evidence that the "IGF-1 axis not only affected the proliferative behavior of breast cancer, but also stimulates proliferation of normal breast epithelial cell." Moreover, that increased turnover in certain epithelial-cell populations was "associated with greater risk of neo-plastic transformation". Then they investigated the relation of circulating IGF-1 concentrations and the risk of breast cancer in women.

Harkinson, Willett, Pollak, *et al.* evaluated medical records of a group called the Nurses Health Study cohort. The Nurses Health Study started in 1976 when 121,700 female registered nurses ages 30-55 years completed and returned a mailed questionnaire. Then in 1989-90, blood samples were collected from 32,826 women, aged 43-69, in a study which was approved by the Committee on the Use of Human Subjects in Research at the Brigham and Women's Hospital. As was the case with the Chan *et al.* prostate cancer study, it appeared that IGFBP decreased the bioactivity (directly or indirectly) of IGF-1 as a factor in causing breast cancer. Once the mitigating impact of IGFBF was factored out statistically, there was clearly a positive association between IGF-1 concentration and breast cancer in pre-menopausal women.

Thus IGF-1 concentrations are a marker of breast-cancer risk among pre-menopausal women. Quoting Harkinson and associates in *The Lancet*, "The up to seven fold increase in breast-cancer risk among pre-menopausal women 50 years and younger suggest that the relation between IGF-1 and risk of breast cancer may be greater than that of other established breast-cancer risk

3% in U.S. Following rbGH Approval



factors". (As was the case with the prostate-centered IGF-1 study, the possibility of this secondary hormone concentration being enhanced by ingesting milk from rbGH-treated cows was not investigated.)

The link between rbGH and elevated IGF-1 in humans

But the year following the above two cancer studies' publication, IGF-1 from milk of rbGH-injected cows came further under the gun as a carcinogen… that gun being the pen of Dr. Michael Hansen, research associate with the Consumer Policy Institute, a division of the Consumers Union (publisher of *Consumer Reports*). He gave a lecture on June 17, 2000, at an anti-rbGH conference in Washington, D.C., the purpose of which to ban rbGH. The text of his speech appeared in its entirety in the July 2000 issue of *The Milkweed*.(10) Since Hansen's insights so well support this subject, a review of some of the high spots of his lecture is in order.

Dr. Hansen explained that natural bovine growth hormone is a protein hormone which is 190 amino acids long. The synthetic (recombinant) form of this hormone is called rbGH and is 191 amino acids long, with the addition of one amino acid (methionine). (A single methionine makes it possible for rbGH to be produced by *E. coli, bacterium* in economical quantities.)

Concern about negative impacts of rbGH on humans drinking milk from rbGH-treated cows was cleverly discounted by Monsanto. ("Posilac" ultimately was the brand name Monsanto gave this synthetic hormone.) Monsanto officials said that any bovine growth hormone is different from human growth hormone; therefore that any rbGH making it into the milk drunk by people would have no impact on them. Monsanto told the FDA, in comparing the human and bovine growth hormones, "they are about 35% different in terms of their amino acid sequence", and that rbGH wouldn't affect humans, even if it were injected into them.

Although there *are* significant differences between the growth hormones of bovines and humans, another hormone actually serves as the intermediary for the growth hormones. That's IGF-1, which is **exactly the same** between these two species. So the growth hormones work through this subsidiary molecule, which in turn greatly dictate the functions of mammary, bone formation, and other systems. (Note: IGF-1, in both bovines and humans, is a 70 amino acid polypeptide which plays an important role in regulating growth and fuel metabolisms; its biological activity is in turn modulated by IGFBPs.)

In quoting Dr. Hansen again: "The data was showing that IGF-1 levels in milk from cows treated with rbGH are higher than in non-treated cows. Even the FDA's own study in 1990: there are statistically significant, from 25 to 80% higher… they knew that IGF-1 was a potent growth promoter, and there were suggestions that it was linked to a number of tumors."

Additional research in 1997 showed that the vast majority of IGF-1 in milk (be it natural or that spawned by rbGH) survives digestion in rats, thus making it through the gut wall into the circulatory system. Turns out the IGF-1 in milk is shielded by casein, a major protein component in milk. In the digestive tract, unprotected IGF-1 has a half-life of 5 seconds. Enshrouded with casein, that figure increases to 85 seconds.

Also in 1997, Japanese researchers fed radioactively labeled IGF-1 (protected with casein) to adult rats. This labeling made it easy to distinguish introduced IGF-1 from that produced by the rat's body. In 1997, according to Hansen, new epidemiological data was tallied, showing that "IGF-1 is linked to the major cancers that we find in the West—particularly cancers of the breast, lung, prostrate, and colorectal".

New wrinkle in the cancer picture

One critical research paper dealt with one specific type of breast cancer, a paper which casts a new dimension on this disease, written by Li *et al.* and titled, "Age-Specific Incidence Rates of In Situ Breast Carcinomas by Histologic Type, 1980-2002." (10)

The following graph shows the increase in detection of milk ductal carcinoma per 100,000 women aged 50 and over. These values are rounded to the nearest unit and are *in situ* data. *In situ* is defined "in the natural or living place", as opposed to *in vitro* which means "outside the living body or in an artificial environment".

The rapid increase of human milk duct tissue cancers in the U.S. between 1980 and 1987 may be due largely to greater use of mammographic screening and increased early detection of breast cancers too small for self-detection. With the introduction of mammography during that period, the incidence of smaller tumors ($\leq$ 2.0 cm) more than doubled, while the rates of larger tumors ($\geq$ 3.0 cm) decreased by 27%. Most of the increase during the charted period (1980-2002) represents increased detection of ductal carcinoma in situ (DCIS) which from 1998 to 2002 accounted for about 85% of the in situ breast cancers diagnosed. Incidence rates of DCIS increased more than sevenfold during the period 1980-2002. The increase was observed in all age groups, but was most pronounced in women aged 50 and over.

The most dramatic increases in DCIS occurred between 1990 and 1998. a period following that of mammography's introduction and widespread adoption. Is it more than coincidence that this particular carcinoma's rapid increase coincides with the rapid commercial introduction of recombinant bovine growth hormone (rbGH) in U.S. dairy herds in early 1994?

Commercial sales of rbGH started the first week of February 1994. However, rbGH was widely used in many land grant university herds, as well as an unknown number of commercial herds, prior to that time.

Once we can accurately determine the actual quantities of Posilac marketed during each of the years analyzed by Li and associates, it may be possible, to scientifically determine a clear-cut relation between the increase in milk duct cancers and the use of Monsanto's rbGH. It is critical that good science be honored as such data is tallied. Goodness knows there was enough bad science employed in the research, development, and FDA approval of Posilac.

We now know there is a documented strong correlation existing between increased human twinning rates and consumption of milk from rbGH-treated cows. It may be a simple leap to examine the Li data, pawing through the epidemiology in a fashion similar to these twinning studies.

It would also be the hope of family dairy farm supporters, advocates of humane animal treatment, and proponents of food safety that some new, future scientific data materializes. Namely, as the use of Posilac vanishes entirely, the incidences of milk duct cancers, as well as many other cancers in the U.S., are significantly reduced.

Paris Reidhead is a sustainable farming activist in Hartwick, New York.

Bibliography

(1) Epstein, Samuel S. Unlabeled milk from cows treated with biosynthetic growth hormones: a case for regulatory abdication. *International Journal of Health Services*, Vol. 26, No. 1, 1996, pp. 173-185.

(2) Cohen, Pinchas, et al. Insulin-like growth factors (IGFs), IGF receptors, and IGF-binding proteins in primary cultures of prostate epithelial cells. *Journal of Clinical Endocrinology and Metabolism*, Vol. 73, No. 2, 1991, pp. 401-407.

(3) Stoll, B.A. Breast cancer: further metabolic-endocrine risk markers? *British Journal of Cancer*, Vol. 76, No. 12, 1997, pp. 1652-1654.

(4) LeRoith, Derek, et al. The role of the insulin-like growth factor-I receptor in cancer. *Annals New York Academy of Sciences*, Vol. 766, September 7, 1995, pp. 402-408.

(5) Mantzoros, C.S., et al. Insulin-like growth factor 1 in relation to prostate cancer and benign prostatic hyperplasia. *British Journal of Cancer*, Vol. 76, No. 9, 1997, pp. 1115-1118.

(6) Cascinu, S., et al. Inhibition of tumor cell kinetics and serum insulin growth factor I levels by octreotide in colorectal cancer patients. *Gastroenterology*, Vol. 113, September 1997, pp. 767-772.

(7) June M. Chan, Meir J. Stampfer, Edward Giovannucci, Michael Pollak, et al. Plasma insulin-like growth factor I and prostate cancer risk: a prospective study. *Science*, Vol. 279, January 23, 1998, pp. 563-566.

(8) Susan E Harkinson, Walter C. Willett, Graham A. Colditz, Michael Pollak, et al. Circulatin concentrations of insulin-like growth factor-1 and risk of breast cancer. *The Lancet*. Vol.351, May 29, 1998. pp.1393-1396.

(9) Hansen, Michael. rbGH: Appropriate Studies Haven't Been Done. *The Milkweed*. Issue No. 252. July 2000. pp. 5-8.

(10) Li. C.I., Daling, J.R., K.E. Malone. Age Specific Incidence Rates of *in situ* Breast Carcinoma by Histologic Type. *Cancer Epidemiology, Biomarkers, and Prevention*. Vol. 14, April 2005. pp. 1008-1011.