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Cancer

Cancer, a leading cause of mortality, results from the interaction of multiple genetic and environmental factors over time. Among the environmental factors, diet and nutrition, including milk and milk products, have received considerable attention as modifiers of cancer risk. This report reviews scientific evidence for the potential role of consumption of milk and milk products and their nutrients, particularly calcium and vitamin D, in reducing the risk of colorectal cancer, breast cancer, and prostate cancer. Also reviewed are other potential protective and some alleged harmful dairy food components on cancer risk. More research is needed to determine the role of milk and milk products in reducing the risk of cancer and the mechanisms involved.

Scientific Status Report

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Introduction

Cancer is the second most common cause of death in the U.S., exceeded only by heart disease, and accounts for nearly one in every four deaths.[1] A complex interplay of genetic, environmental, behavioral, and socio-cultural factors influence the development of cancer.[1,2] Some factors are modifiable (e.g., use of tobacco, diet, physical activity), whereas others (e.g., genetic predisposition) are not. Because only a small proportion of cancers are inherited, opportunities exist to modify lifestyle factors to help reduce risk of this disease.[2] Among lifestyle factors, diet and nutrition are recognized as important modifiers of cancer risk. [2,3,4] In 2007, the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) released its second expert report summarizing scientific evidence linking diet and nutrition, including milk and milk products and their nutrients, to the prevention of and risk for specific cancers.[2] Numerous studies (laboratory, experimental animal, and human epidemiological and clinical studies) have examined the role of milk and milk products and their nutrients, particularly calcium and vitamin D, especially in colorectal cancer, breast cancer, and prostate cancer.[2,3,5,6,7,8] A recent review of the science states that "milk and milk products may have both beneficial and adverse effects with regard to the risk of different cancers. The evidence indicating healthful effects of milk and milk product consumption on prevention of cancers is considerably greater than those representing harmful impacts."[3]

Colorectal Cancer

Recent scientific evidence accumulated since the 2007 WCR/AICR report supports its conclusion that milk and calcium probably protect against colorectal cancer. Although new findings suggesting a potential beneficial role of vitamin D in colorectal cancer are promising, further investigation is needed.

Colorectal cancer is the third most commonly diagnosed cancer in adults and the third leading cause of cancer death in the U.S.[1] The 2007 WCRF/AICR report, based on reasonably consistent evidence from cohort studies supported by strong evidence from dietary calcium studies and evidence for plausible mechanisms, concluded that milk and calcium probably protect against colorectal cancer.[2] The report graded the strength of evidence in four categories: convincing (strongest evidence), probable, limited, and "substantial effect on risk unlikely." With respect to dairy products other than milk, the report indicated that findings related to cheese are inconsistent and that "there is limited evidence suggesting that cheese is a cause of colorectal cancer".[2]

Subsequent findings related to milk and milk products and colorectal cancer build on the 2007 WCRF/AICR conclusions.[3,8,9,10] In an effort to keep the scientific evidence related to diet and cancer current, the WCRF/AICR, in collaboration with Imperial College London, is undertaking the Continuous Update Project (CUP). In its 2011 report on colorectal cancer, the CUP panel concluded that, based on recent evidence, milk probably protects against colorectal cancer, which is consistent with the conclusion of the 2007 WCRF/AICR Second Expert Report.[2,9] The 2011 CUP panel found that increased milk intake was associated with decreased risk in eight of 10 new cohort studies on colorectal cancer.[9] The panel added that any effect of milk consumption on reducing colorectal cancer risk may be explained at least in part by increased calcium. According to the CUP meta-analyses, increasing dietary calcium by 200 mg/day decreased risk of colorectal cancer by 6 percent. The 2011 CUP panel agreed with the 2007 WCRF/AICR report that there is limited evidence suggesting that cheese is a cause of colorectal cancer. Likewise, the 2011 CUP panel agreed with the 2007 WCRF/AICR report that findings related to vitamin D and colorectal cancer are inconsistent, and there is limited evidence suggesting that vitamin D or foods containing vitamin D protect against colorectal cancer.[9]

A recent systematic review and meta-analysis of 19 cohort studies found that the milk and total milk products categories were significantly associated with reduced risk of colorectal cancer. However, when studies examined specific types of dairy products (e.g., cheese, cottage cheese, yogurt, butter, etc), there was no significant association with colorectal cancer, although the number of studies was small.[11] This meta-analysis showed that the greatest reduction in colorectal cancer risk was observed at higher levels of intake

of dairy products (i.e., equivalent to two to three glasses of milk per day). These findings are consistent with those of previous studies.[12,13,14,15] A meta-analysis of 14 cohort studies showed a 10 percent decreased risk for colorectal/colon cancer with highest versus lowest consumption of milk.[14] A large prospective cohort study (the NIH-AARP study) of nearly half a million adults aged 50 to 71 who were followed for seven years found that those who consumed more calcium and dairy foods a day had a decreased risk of cancers of the digestive system, especially colorectal cancer.[15] In both men and women, those who either consumed nearly three servings of dairy foods a day or about 1,000 to 1,300 mg of dietary calcium a day had an approximate 15 to 30 percent lower risk of colorectal cancer for men and women, respectively, compared to those who consumed less than 500 mg of dietary calcium a day.[15] A 15 percent reduced risk of developing colorectal cancer was found in individuals who consumed more than a glass of milk (≥ 250 g/day) compared to those who consumed < 70 g/day, according to a pooled analysis of data from 10 cohort studies.[12] This study also found a 14 percent decreased risk of colorectal cancer for groups with the highest dietary calcium intakes.[12]

Although the WCRF/AICR report stated "there is limited evidence suggesting that foods containing vitamin D or vitamin D status protect against colorectal cancer,"2 newer studies suggest a potentially protective effect of vitamin D against colorectal cancer.[16,17] An updated meta-analysis of prospective cohort studies reported a modest, although significant, inverse association between vitamin D and risk for colorectal cancer.[16] The researchers suggest that improving vitamin D status could potentially reduce the risk of colorectal cancer, but call for further investigation. When Japanese researchers analyzed data from 737 people with colorectal cancer and 703 healthy, cancer-free individuals, the results showed that colorectal cancer was 36% lower in people with the highest vitamin D status than those with the lowest average vitamin D levels.[17] Further, specific sections of the vitamin D receptor gene were associated with greater risk reductions in colorectal cancer risk.

The majority of studies examining the relationship between dairy/dairy nutrients and colorectal cancer are observational, not randomized controlled trials which provide more compelling evidence. A randomized clinical trial in 832 adults with a history of colorectal adenomas (i.e., precursors of colon cancer) found that increasing calcium intake by 1,200 mg/day significantly reduced the risk of recurrent adenomas by 19% during 4 years of follow-up, and reduced the risk for having at least one adenoma by 24%[18] According to a meta-analysis of three randomized clinical trials, researchers found that intake of 1,200 to 2,000 mg calcium per day was associated with a significant 20% reduction in the development of colorectal adenoma in patients with a history of colorectal adenomatous polyps, but not in those without elevated risk.[19]

Several mechanisms may explain a protective effect of calcium on colorectal cancer. In experimental studies, calcium binds pro-cancer secondary bile acids and/or free fatty acids, reducing their proliferative effects in the colonic epithelium, and induces colonic epithelial differentiation and apoptosis (programmed cell death).[3,9,10,20]

Some studies have examined overall recommended dietary patterns, which include combinations of foods and nutrients consumed together, and risk of colorectal cancer.[21,22] Findings show that adhering to the Dietary Approaches to Stop Hypertension (DASH) eating plan, which is a low-fat diet rich in fruit, vegetables, and low-fat dairy products, is associated with reduced risk of colorectal cancer.[21,22]

Breast Cancer

Inconsistencies in studies examining associations between consumption of milk and milk products and breast cancer risk do not permit conclusions. More study is needed to determine whether milk and milk products, calcium, and vitamin D have a neutral or potential beneficial role in reducing risk of breast cancer.

Breast cancer is the second most common newly diagnosed cancer and the second leading cause of cancer death among women in the U.S.[1] Although numerous studies, primarily epidemiological, have examined the association between milk and milk products and breast cancer, no clear link has been established. The 2007

WCRF/AICR report, based on 24 cohort and 56 case-control studies, concluded that the available evidence was insufficient to establish associations between intake of milk and milk products and calcium and risk of breast cancer in premenopausal or postmenopausal women.[2] This conclusion was supported in the CUP's Breast Cancer 2010 report.[23]

A recent large prospective cohort study of African-American women followed for 12 years found no statistically significant associations between consumption of milk (total, whole, and 2%), other types of dairy products (e.g., skim milk, hard cheese, yogurt, ice cream), dietary calcium, and dietary vitamin D and risk of breast cancer in premenopausal and postmenopausal women.[24] Likewise, in a population-based prospective cohort study among Norwegian women, total dairy consumption and various dairy products (milk, yogurt), as well as adult and childhood milk consumption, were not significantly associated with breast cancer in either premenopausal or postmenopausal women.[25] Although total calcium intake tended to be inversely associated with breast cancer risk, particularly among premenopausal women, the association was not statistically significant.[25]

A case-control study in China showed that dietary calcium intake was significantly associated with reduced risk of breast cancer, whereas no association was observed between dairy product consumption (total dairy, low-fat dairy and high-fat dairy) and breast cancer risk after controlling for confounding factors.[26] A meta-analysis of 18 prospective cohort studies involving over a million participants found a modest inverse association of total dairy intake and breast cancer risk, but there was considerable variability in study designs that make comparisons difficult.[27] When the limited number of studies looking at dairy subgroups was analyzed, the inverse association of total dairy with breast cancer risk was stronger for low-fat dairy than high-fat dairy intake and for premenopausal than postmenopausal women.27 A recent study in 1893 women with invasive breast cancer found that overall intake of milk and milk products was not significantly associated with breast cancer recurrence or survival, whereas intake of high-fat dairy, but not low-fat dairy, was linked to higher risk of mortality.[28] Calcium and vitamin D were not associated with breast cancer outcomes.[28] In the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study, a large prospective study in which diet information was collected from 319,826 women, no significant association was observed between consumption of milk and milk products and breast cancer risk.[29]

Other studies suggest that calcium and vitamin D have protective effects against breast cancer.[30] A meta-analysis found that calcium intake and vitamin D intake and status were inversely associated with breast cancer risk, which the researchers concluded provides evidence that calcium and vitamin D protect against breast cancer. Based on a pooled analysis of data from 11 case-control studies, higher blood levels of 25-hydroxyvitamin D, an indicator of vitamin D status, were associated with reduced risk of breast cancer.[31] According to a recent case-control study in Saudi Arabian women, a group at high risk of vitamin D deficiency, vitamin D status was inversely associated with risk of breast cancer.[32]

Epidemiological findings of associations between intake of milk and milk products and dietary calcium and breast cancer risk are inconclusive. Researchers call for more well-designed prospective studies to confirm any potential protective effects of milk and milk products and/or calcium on breast cancer risk.[25,26]

Prostate Cancer

While overall findings fail to establish a consensus of an adverse effect of increased intake of calcium or milk and milk products on prostate cancer risk, the need for further research is acknowledged.

Prostate cancer is the second most common cancer and the second leading cause of cancer death among American men.[1] The WCRF/AICR Second Expert Report, based largely on epidemiological studies published prior to 2007, concluded that there is only a "limited-suggestive" association between dairy food consumption and an increased risk for prostate cancer and that diets high in calcium (1,500 mg or higher a day) are a "probable" cause of prostate cancer.[2]

Since the 2007 WCRF/AICR report, a number of epidemiological studies and meta-analyses of milk and dairy products, calcium, and vitamin D and prostate cancer have been published.[6,8,33,34] In general, these studies provide little support for an association between consumption of milk and milk products and prostate cancer.[6,8,33] Inconsistencies in study findings may be explained in part by such factors as the different types of dairy products or total dairy products examined, the stage/grade of prostate cancer or whether all prostate cancers are grouped together as a single outcome, subjects' lifestyle habits (e.g., smokers vs. non-smokers), and study endpoints (e.g., cancer incidence, death). A Japanese study found that while the highest intakes of milk, yogurt, and total dairy products were significantly associated with total prostate cancer, total dairy consumption was positively associated with localized, but not advanced, cancer.[34] Based on data from a meta-analysis of 26,769 prostate cancer cases from 45 observational studies, there was no clear evidence of an association between dairy products, calcium, and vitamin D and prostate cancer.[35] Increased intake of milk and milk products may reduce the risk of current, but not former, smokers from aggressive prostate cancer, according to an 11-year follow-up study.[36]

Some studies suggest that the specific type of milk/milk product consumed is associated with prostate cancer, although the findings are inconsistent. A large prospective investigation found that among prostate cancer patients, overall milk and milk product intake consumed after diagnosis was not associated with increased risk of lethal (metastasis and death from prostate cancer) prostate cancer.[37] However, when low-fat dairy and whole milk were examined separately, highest intakes of low-fat dairy reduced risk of progression, whereas highest intakes of whole milk increased risk of lethal prostate cancer compared to the lowest intakes. The researchers speculate that people who consume low-fat milk/dairy may be more health conscious and pursue more healthy lifestyle habits than those who drink whole milk.[37] In contrast to the above, several studies reviewed by Parodi[33] found that high intake of skim milk, but not whole milk, was associated with increased risk of prostate cancer. A recent prospective study among U.S. male physicians found that increased consumption of skim/low-fat milk was associated with a higher risk of non-aggressive prostate cancer, whereas intake of whole milk was associated with higher risk of developing advanced or fatal prostate cancer.[38] However, the risk estimates from this study were not robust and the suggested biological explanations cannot be substantiated.

Similar to findings related to milk and milk products, reviews of epidemiological studies of calcium intake and prostate cancer risk reveal inconsistent findings.[8,33] These studies generally show no association or a marginally positive association between calcium intake and prostate cancer risk. In the large population-based NIH-AARP study, calcium, even at very high intakes (≥ 2,000 mg/day), was not associated with prostate cancer.[15] A recent case-control study that examined the association between calcium intake from food and prostate cancer risk in U.S. veterans concluded that "calcium from food is associated with lower risk for prostate cancer, particularly among [African American] men, and lower risk for high-grade prostate cancer among all men".[39] A neutral or potentially beneficial effect of calcium on prostate cancer risk was demonstrated in a secondary analysis of data from a randomized, placebo-controlled clinical trial in which 672 men received either 1,200 mg of calcium or a placebo daily for four years and were followed for up to 12 years for development of prostate cancer.[40]

In vitro studies demonstrate that high levels of circulating vitamin D inhibit prostate cancer by promoting cell differentiation and apoptosis and inhibiting cell proliferation, and cell adhesion.[8] It has been suggested that high intakes of calcium could indirectly increase prostate cancer risk by suppressing circulating levels of vitamin D, a potentially anti-carcinogenic agent. However, epidemiological evidence of a protective effect of vitamin D status against prostate cancer is limited and controversial.[33,41,42,43] Some recent case-control studies suggest that there is no evidence of an association between plasma levels of 25(OH)D (a marker of vitamin D status) and overall prostate cancer risk, but that higher levels of 25(OH)D may reduce the risk of aggressive (advanced) or lethal prostate cancer.[41,43]

Further studies are needed to determine the effect of consumption of milk and milk products on prostate cancer risk.[8,33]

Dairy Food Components and Cancer Risk

Although milk and milk products contain alleged harmful and potential beneficial components for cancer risk, the healthful effects of dairy foods (milk, cheese, yogurt) greatly outweigh any harmful impact on cancer risk.

Several milk components have been examined for their potential harmful or beneficial association with risk of certain cancers.[3,33] Based on a recent comprehensive review of milk components and cancer risk, the authors concluded that "the evidence indicating healthful effects of milk and milk product consumption on prevention of cancers is considerably greater than those representing harmful impacts".[3] The review also suggests that any harmful cancer-related effect of dairy food consumption is dose-dependent.

Suspected cancer-promoting milk components. Dairy food components proposed to increase the risk of specific cancers include dietary fat/animal fat (saturated fat), insulin-like growth factor 1 (IGF-1), and estrogens. [3,33]

- Dietary fat/saturated fat. High dietary fat, particularly animal fat, and saturated fat, has been thought to increase the risk of some cancers including colorectal, breast, and prostate cancers.[3,33] Findings reviewed in the 2007 WCRF/AICR and more recent 2011 CUP reports indicate that there is limited evidence suggesting that consumption of foods containing animal fats cause cancer.[2,9,23] A review of dietary fat and risk of prostate cancer cited several studies demonstrating no association between intake of total fat or saturated fat and prostate cancer risk.[33] The positive association of dietary fat and cancer risk in many early studies could be explained by the failure to adjust for energy intake.
- IGF-1. Although considerable attention has focused on the association between high levels of IGF-1 and risk of some cancers (e.g., colorectal, breast, prostate), cow's milk contains a minuscule amount of IGF-1 and milk-derived IGF-1 has no biological activity in humans since it is broken down in the intestine and not absorbed.[3,8,33] It is suggested that blood levels of IGF-1 may be considered a marker of cancer, not a causative factor for prostate cancer.[33]
- Estrogens. While estrogens have been implicated in cancer at hormone-responsive sites (e.g., mammary and prostate glands), it is unlikely that the very small amount of milk-derived estrogen, which is extensively inactivated in the gastrointestinal tract, influences cancers at estrogen-responsive sites.[44]

Potential cancer-preventative components in milk and milk products. In addition to calcium and vitamin D, minor milkfat components including conjugated linoleic acid (CLA), sphingolipids, and butyric acid, protein and bioactive peptides, and probiotics added to some dairy foods have been investigated for their potential role in reducing cancer risk.[3,33]

- Milkfat components. The fat in cow's milk is the major source of CLA in the diet and CLA is found in greater amounts in higher fat dairy products such as whole milk, cheese, and butter than in fat-free or reduced-fat milk and milk products.[3,45,46] A potential anti-carcinogenic effect of CLA, particularly the predominant CLA isomer in milkfat (i.e., rumenic acid), has been demonstrated in animal and cell culture studies.[45,47] Although the mechanism(s) by which CLA may protect against cancer is unknown, several possibilities have been proposed, including its ability to reduce cell proliferation, induce apoptosis, regulate gene expression, and exert antioxidant effects.[48,49] Moreover, relatively few human studies have examined CLA's potential anti-carcinogenic effects and these studies are limited to epidemiological investigations, which do not prove a cause and effect relationship.[48,49] Findings from recent reviews of epidemiological studies of CLA and cancer are inconsistent.[46,48,49,50] Although a protective effect of CLA on specific cancers has yet to be established, researchers suggest that, based on the doses used in animal and cell culture studies, humans would need to substantially increase their CLA intake to an amount difficult to achieve with diet alone.[47,49,51]

Considering the limited number of human studies and inconsistent findings, researchers are calling for further study, especially controlled trials, to determine CLA's potential anticancer effects and the mechanism(s) involved.[46,49,50]

Dairy foods, particularly milk, are a rich source of dietary sphingolipids.[52] Because sphingolipids are a structural component of the milk fat globule membrane, but are not present in the fat droplet, low-fat and fat-free as well as full-fat milk and milk products are dietary sources of sphingolipids. Bioactive sphingolipids (e.g., ceramide, sphingosine, sphingomyelin) regulate cell growth, differentiation, and apoptosis.[52] Because of these functions, bioactive sphingolipids may have an anti-carcinogenic role. *In vivo* and *in vitro* studies have shown that specific sphingolipids may inhibit early and late stages of colon cancer.[52,53,54] A study in mice treated with a chemical carcinogen found that intake of dairy sphingomyelin reduced the proliferation of colonic cells and the appearance of aberrant crypt foci.[53] And in mice fed a mixture of sphingolipids similar to the amount and type in milk and milk products, the number of tumors in all regions of the intestine was reduced.[54] Another study in mice treated with a chemical carcinogen found that sphingolipids fed in amounts that can be achieved in the human diet were effective in preventing tumors and for early treatment.[55] Levels of ceramide in human colon cancer cells have been shown to be decreased compared to levels in normal colon cells from healthy patients.[56] It is plausible, but as yet unproven, that dietary sphingolipids, including dairy sphingolipids, could have a role in reducing cancer risk. Further study is needed to determine the role of sphingolipids from dairy foods in reducing cancer risk and the mechanism (s) involved.

Butyric acid is another potential anti-carcinogenic component in milkfat.[45,57] In a variety of cancer cell lines (colon, leukemia, prostate, breast), butyric acid inhibits the proliferation and induces differentiation and apoptosis.[45,57] At the molecular level, butyric acid is associated with down-regulation or inactivation of the expression of cancer genes.[45] It also may inhibit tumor invasiveness and metastasis.[45] Although butyric acid is an anti-carcinogenic agent, whether butyric acid in milkfat has anti-carcinogenic effects in humans as a result of dairy product consumption remains to be established.

- Milk proteins and their peptides. In recent years, animal and *in vitro* research has focused on the ability of milk proteins, casein and whey and their bioactive peptides, to reduce the development of cancer.[58,59] Caseins (80% of total milk protein) and whey proteins (20% of total milk protein) are the two major proteins in cow's milk.[59] These proteins, especially whey proteins, have been demonstrated in animal models and *in vitro* studies to suppress tumor development at various sites such as the breast, colon, and prostate gland.[58,59] Although several whey proteins such as β-lactoglobulin, α-lactalbumin, serum albumin, and lactoferrin have been shown to have anticancer potential, most attention has focused on lactoferrin, a minor whey protein.[59] Lactoferrin, an iron-binding protein, is known for its inhibitory action on cell proliferation, as well as its anti-inflammatory and antioxidant abilities.[58,60] When the effects of bovine milk lactoferrin were examined in two types of human breast cancer cell lines, lactoferrin decreased cell viability (an indication of cell growth potential), reduced cell proliferation, and increased apoptosis.[60] The findings led the researchers to suggest that intake of milk and milk products or foods enriched with lactoferrin may help prevent or treat breast cancer.[60]

- Probiotics in dairy foods. Findings from some experimental animal, *in vitro*, and epidemiological studies suggest that probiotic cultures, such as specific lactic acid bacteria, or dairy products with probiotic cultures may reduce the risk of some cancers or possibly help mitigate the side effects of cancer treatments.[3,61,62,63] Probiotics are defined as "live microorganisms, which, when administered in adequate amounts, confer a health benefit to the host."[63] Several potential mechanisms have been suggested to explain the anti-carcinogenic effects of fermented dairy products with live lactic acid bacteria.[3,62,63] These include enhanced immune responses, inhibition of procarcinogenic enzymes,

alterations in microbiotic species and metabolism, binding or inactivation of carcinogens, and increased apopotosis.[3,62,63] A 12-year prospective study of more than 45,000 Italian volunteers found a significant inverse association between yogurt consumption and colorectal cancer.[64] Although few human studies have directly examined the effect of consumption of dairy foods with probiotics on cancer (i.e., the endpoint), the findings are considered to be promising.[62,63] However, further research is needed before recommendations can be made regarding intake of fermented dairy foods or dairy foods with specific probiotics to help reduce the risk of certain cancers.

Dietary Guidance for Cancer Prevention

To prevent cancer, the American Cancer Society recommends that Americans maintain a healthy weight throughout life; adopt a physically active lifestyle; consume a healthy diet with emphasis on plant foods; and limit consumption of alcoholic beverages.[65] To reduce the risk of colon cancer, recommended intake levels of calcium (i.e.,1,000 mg/day for adults 19 to 50 years and 1,200 mg/day for people older than 50), primarily from food sources such as low-fat or fat-free dairy products and some green leafy vegetables, and ensuring sufficient vitamin D status is advised.[65] The WCRF/AICR Expert Report, based on its comprehensive review of the literature on diet, physical activity, and cancer, issued the following recommendations for cancer prevention:

- Be as lean as possible within the normal range of body weight.
- Be physically active as part of everyday life.
- Limit consumption of energy-dense foods. Avoid sugary drinks.
- Eat mostly foods of plant origin.
- Limit intake of red meat and avoid processed meat.
- Limit alcoholic drinks.
- Limit consumption of salt. Avoid moldy cereals (grains) or pulses (legumes).
- Aim to meet nutritional needs through diet alone.[2]

Milk and milk products are not included in these WCRF/AICR recommendations because these recommendations only focus on foods to limit to reduce cancer risk.

Conclusion

An extensive body of research has examined the potential of milk and milk products and their nutrients (e.g., calcium and vitamin D) to reduce the risk of specific cancers, such as colorectal cancer, breast cancer, and prostate cancer. In general, scientific findings indicate that milk and calcium probably protect against colorectal/colon cancer. While emerging findings suggest a potentially protective role of vitamin D in this cancer, more research is needed. In contrast to colorectal cancer, there is limited evidence that milk and milk products, calcium, or vitamin D reduce breast cancer risk. While some evidence has suggested that consumption of milk and milk products and diets high in calcium are a "probable" cause of prostate cancer, overall findings from most recent epidemiological findings do not support an association between increased calcium or dairy food intake and risk of prostate cancer.

Milk and milk products contain components (e.g., dietary fat/saturated fat, IGF-1, and estrogens) alleged to increase the risk of specific cancers, and those suggested to potentially reduce cancer risk (e.g., calcium, vitamin D, milkfat components, protein and bioactive peptides, and probiotics). According to a recent review of the scientific evidence on the effects of consumption of milk and milk products on cancer risk, the authors state that "the proven health benefits of dairy foods greatly outweigh the unproven harm".[3] They add that "dairy foods should be encouraged as part of a varied and nutritious diet" to help maintain health and prevent diseases, including some cancers.[3] According to another review, evidence suggests that the "recommended intake of milk and dairy products (3 servings/day) is safe and, importantly, does not seem to increase the risk of prostate cancer and seems to be protective against bladder, breast and colon cancer".[8]

Cancer is a complex disease resulting from the interaction of multiple genetic and environmental factors over time. For this reason, determining the effects of a specific food group such as dairy, individual dairy foods, or dairy nutrients on human cancer is challenging. Further, the study of milk and milk products and cancer risk has relied primarily on epidemiological associations, which cannot establish causality. More research is needed to determine the role of milk and milk products in reducing cancer risk and the mechanisms involved.

References

[1] American Cancer Society. *Cancer Facts & Figures 2013.* Atlanta, GA: American Cancer Society, 2013. http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2013/index Accessed November 21, 2013.

[2] World Cancer Research Fund/American Institute for Cancer Research. Second Expert Report. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective.* Washington, DC; AICR, 2007 www.dietandcancerreport.org. Accessed August 30, 2013.

[3] Davoodi, H., S. Esmaeili, and A.M. Mortazavian. Effects of milk and milk products consumption on cancer: A review. Compr. Rev. Food Sci & Food Safety 12: 249-264, 2013.

[4] Gonzalez, C.A., and E. Riboli. Diet and cancer prevention: contributions from the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Eur. J. Cancer 46: 2555-2562, 2010.

[5] Miller, G.D., J.K. Jarvis, and L.D. McBean. *Handbook of Dairy Foods and Nutrition*. 3rd ed. Boca Raton, FL: CRC Press, 2007, pp. 141-179.

[6] Lampe, J. Dairy products and cancer. J. Am. Coll. Nutr. 30(suppl): 464s-470s, 2011.

[7] Rock, C.L. Milk and the risk and progression of cancer. Nestle Nutr. Workshop Ser. Pediatr. Program 67: 173-185, 2011.

[8] Chagas, C.E.A., M.M. Rogero and L.A. Martini. Evaluating the links between intake of milk / dairy products and cancer. Nutr. Rev. 70(s): 294-300, 2012.

[9] World Cancer Research Fund / American Institute for Cancer Research. Continuous Update Project Report. Food, Nutrition, Physical Activity and the Prevention of Colorectal Cancer, 2011. www.dietandcancerreport.org/cancer_resource_center/downloads/cu/Colorectal-Cancer-2011-Report.pdf. Accessed September 22, 2013.

[10] Vargas, A.J., and P.A. Thompson. Diet and nutrient factors in colorectal cancer risk. Nutr. Clin. Pract. 27: 613-623, 2012.

[11] Aune, D., R. Lau, D. Chan, et al. Dairy products and colorectal cancer risk: a systematic review and meta-analysis of cohort studies. Ann. Oncol. 23: 37-45, 2012.

[12] Cho, E., S.A. Smith-Warren, D. Spiegelman, et al. Dairy foods, calcium, and colorectal cancer: a pooled analysis of 10 cohort studies. J. Natl. Cancer Inst. 96: 1015-1022, 2004.

[13] Larsson, S.C., L. Bergkvist, J. Rutegard, et al. Calcium and dairy food intakes are inversely associated with colorectal cancer risk in the Cohort of Swedish Men. Am. J. Clin. Nutr. 83: 667-673, 2006.

[14] Huncharek, M., J. Muscat, and B. Kupelnick. Colorectal cancer risk and dietary intake of calcium, vitamin D, and dairy products: a meta-analysis of 26,335 cases from 60 observational studies. Nutr. Cancer 61: 47-69, 2009.

[15] Park, Y., M.F. Leitzmann, A.F. Subar et al. Dairy food, calcium, and risk of cancer in the NIH-AARP diet and health study. Arch. Intern. Med. 169: 391-401, 2009.

[16] Touvier, M., D.S.M. Chan, R. Lau, et al. Meta-analyses of vitamin D intake, 25-hydroxyvitamin D status, vitamin D receptor polymorphisms, and colorectal cancer risk. Cancer Epidemiol. Biomarkers Prev. 20: 1003-1016, 2011.

[17] Yamaji, T., M. Iwasaki, S. Sasazuki, et al. Association between plasma 25-hydroxyvitamin D and colorectal adenoma according to dietary calcium intake and vitamin D receptor polymorphism. Am. J. Epidemiol. 175: 236-244, 2012.

[18] Baron, J.A., M. Beach, J.S. Mandel, et al. for the Calcium Polyp Prevention Study Group. Calcium supplements for the prevention of colorectal adenomas. N. Engl. J. Med. 340: 101-107, 1999.

[19] Carroll, C., K. Cooper, D. Papaioannou, et al. Supplemental calcium in the chemoprevention of colorectal cancer: a systematic review and meta-analysis. Clin. Ther. 32(s): 789-803, 2010.

[20] Norat, T., and E. Riboli. Dairy products and colorectal cancer. A review of possible mechanisms and epidemiological evidence. Eur. J. Clin. Nutr. 57: 1-17, 2003.

[21] Fung T.T., F.B. Hu, K. Wu, et al. The Mediterranean and Dietary Approach to Stop Hypertension (DASH) diets and colorectal cancer. Am. J. Clin. Nutr. 92: 1429-1435, 2010.

[22] Miller, P.E., A.J. Cross, A.F. Subar, et al. Comparison of 4 established DASH diet indexes: examining associations of index scores and colorectal cancer. Am J. Clin. Nutr. 98: 794-803, 2013.

[23] World Cancer Research Fund / American Institute for Cancer Research. Continuous Update Project Report. Food, Nutrition, Physical Activity, and the Prevention of Breast Cancer, 2010. www.dietandcancerreport.org/cancer_resource_center/downloads/cu/Breast-Cancer-2010-Report.pdf Accessed September 22, 2013.

[24] Genkinger, J.M., K.H. Makambi, J.R. Palmer, et al. Consumption of dairy and meat in relation to breast cancer risk in the Black Women's Health Study. Cancer Causes Control 24: 675-684, 2013.

[25] Hjartaker, A., M. Thoresen, D. Engeset, et al. Dairy consumption and calcium intake and risk of breast cancer in a prospective cohort: The Norwegian Women and Cancer study. Cancer Causes Control 21: 1875-1885, 2010.

[26] Zhang, C.-X., S.C. Hu, J.-H. Fu, et al. Dairy products, calcium intake, and breast cancer risk: a case-control study in China. Nutr. Cancer 63: 12-20, 2011.

[27] Dong, J.Y., L. Zhang, K. He, et al. Dairy consumption and risk of breast cancer: a meta-analysis of prospective cohort studies. Breast Cancer Res. Treat. 127: 23-31, 2011.

[28] Kroenke, C.H., M.L. Kwan, C. Sweeney, et al. High- and low-fat dairy intake, recurrence, and mortality after breast cancer diagnosis. J. Natl. Cancer Inst. 105: 616-623, 2013.

[29] Pala, V., V. Krogh, F. Berrino, et al. Meat, eggs, dairy products, and risk of breast cancer in the European Investigation into Cancer and Nutrition (EPIC) cohort. Am. J. Clin. Nutr. 90: 602-612, 2009.

[30] Chen, P., P. Hu, D. Xie, et al. Meta-analysis of vitamin D, calcium, and the prevention of breast cancer. Breast Cancer Res. Treat. 121: 469-477, 2010.

[31] Mohr, S.B., E.D. Gorham, J.E. Alcaraz, et al. Serum 25-hydroxyvitamin D and prevention of breast cancer: pooled analysis. Anticancer Res. 31: 2939-2948, 2011.

[32] Yousef, F.M., E.T. Jacobs, P.T. Kang, et al. Vitamin D status and breast cancer in Saudi Arabian women: case-control study. Am. J. Clin. Nutr. 98: 105-110, 2013.

[33] Parodi, P.W. Dairy product consumption and the risk of prostate cancer. Int. Dairy J. 19: 551-565, 2009.

[34] Kurahashi, N., M. Inoue, M. Iwasaki, et al. Dairy product, saturated fatty acid, and calcium intake and prostate cancer in a prospective cohort of Japanese men. Cancer Epidemiol. Biomarkers Prev. 17: 930-937, 2008.

[35] Huncharek, M., J. Muscat, and B. Kupelnick. Dairy products, dietary calcium, and vitamin D intake as risk factors for prostate cancer: a meta-analysis of 26,769 cases from 45 observational studies. Nutr. Cancer 60: 421-441, 2008.

[36] Neuhouser, M.L., M.J. Barnett, A.R. Kristal, et al. (n-6) PUFA increase and dairy foods decrease prostate cancer risk in heavy smokers. J. Nutr. 137: 1821-1827, 2007.

[37] Pettersson, A., J.L. Kasperzyk, S.A. Kenfield, et al. Milk and dairy consumption among men with prostate cancer and risk of metastases and prostate cancer death. Cancer Epidemiol. Biomarkers Prev. 21: 428-436, 2012.

[38] Song, Y., J.E. Chavarro, Y. Cao, et al. Whole milk intake is associated with prostate cancer-specific mortality among U.S. male physicians. J. Nutr. 143: 189-196, 2013.

[39] Williams, C.D., B.M. Whitley, C. Hoyo, et al. Dietary calcium and risk for prostate cancer: a case-control study among U.S. veterans. Prev. Chronic Dis. 9: E9, Epub 2012 Jan. 12.

[40] Baron, J.A., M. Beach, K. Wallace, et al. Risk of prostate cancer in a randomized clinical trial of calcium supplementation. Cancer Epidemiol. Biomarkers Prev. 14(3): 586-589, 2005.

[41] Gilbert R., R.M. Martin, R. Beynon, et al. Association of circulating and dietary vitamin D with prostate cancer risk: a systematic review and dose-response meta-analysis. Cancer Causes Control 22: 319-340, 2011.

[42] Yin, L., E. Raum, U. Haug, et al. Meta-analysis of longitudinal studies: serum vitamin D and prostate cancer risk. Cancer Epidemiology 33: 435-445, 2009.

[43] Shui, I.M., L.A. Mucci, P. Kraft, et al. Vitamin D-related genetic variation, plasma vitamin D, and risk of lethal prostate cancer: a prospective nested case-control study. J. Natl. Cancer Inst. 104: 690-699, 2012.

[44] Parodi, P.W. Impact of cows' milk estrogen on cancer risk. Int. Dairy J. 22: 3-14, 2012.

[45] Parodi, P.W. Anti-cancer agents in milkfat. Austr. J. Dairy Technol. 58: 114-118, 2003.

[46] McCrorie, T.A., E.M. Keaveney, J.M.W. Wallace, et al. Human health effects of conjugated linoleic acid from milk and supplements. Nutr. Res. Rev. 24: 206-227, 2011.

[47] Kelley, N.S., N.E. Hubbard, and K.L. Erickson. Conjugated linoleic acid isomers and cancer. J. Nutr. 137: 2599-2607, 2007.

[48] Bhattacharya, A., J. Banu, M. Rahman, et al. Biological effects of conjugated linoleic acid in health and disease. J. Nutr. Biochem. 17: 789-810, 2006.

[49] Gebauer, S.K., J.-M. Chardigny, M.U. Jakobsen, et al. Effects of ruminant trans fatty acids on cardiovascular disease and cancer: a comprehensive review of epidemiological, clinical, and mechanistic studies. Adv. Nutr. 2: 332-354, 2011.

[50] Dilzer, A., and Y. Park. Implication of conjugated linoleic acid (CLA) in human health. Crit. Rev. Food Sci. Nutr. 52: 488-513, 2012.

[51] Larsson, S.C., L. Bergkvist, and A. Wolk. Conjugated linoleic acid intake and breast cancer risk in a prospective cohort of Swedish women. Am. J. Clin. Nutr. 90: 556-560, 2009.

[52] Kurek, K., B. Lukaszuk, D.M. Piotrowska, et al. Metabolism, physiological role, and clinical implications of sphingolipids in gastrointestinal tract. Biomed. Res. Int. 2013: 908907, 2013 [Epub 2013 Sept. 5].

[53] Schmelz, E.M., M.C. Sullards, D.L. Dillehay, et al. Colonic cell proliferation and aberrant crypt foci formation are inhibited by dairy glycosphingolipids in 1,2-dimethylhydrazine-treated CF1 mice. J. Nutr. 130: 522-527, 2000.

[54] Schmelz, E.M., P.C. Roberts, E.M. Kustin, et al. Modulation of intracellular B-catenin localization and intestinal tumorigensis *in vivo* and *in vitro* by sphingolipids. Cancer Res. 61: 6723-6729, 2001.

[55] Lemonnier, L.A., D.L. Dillehay, M.J. Vespremi, et al. Sphingomyelin in the suppression of colon tumors: prevention versus intervention. Arch. Biochem. Biophys. 419: 129-138, 2003.

[56] Selzner, M., A. Bielawska, M.A. Morse, et al. Induction of apoptotic cell death and prevention of tumor growth by ceramide analogues in metastatic human colon cancer. Cancer Res. 61: 1233-1240, 2001.

[57]Parodi, P.W. Milk fat in human nutrition. Austr. J. Dairy Technol. 59: 3-59, 2004.

[58] Parodi, P.W. A role for milk proteins and their peptides in cancer prevention. Curr. Pharmaceut. Design 13: 813-828, 2007.

[59] Pepe, G., G.C. Tenore, R. Mastrocinque, et al. Potential anticarcinogenic peptides from bovine milk. J. Amino Acids 2013; 2013: 939804.

[60] Duarte, D.C., A. Nicolau, J.A. Teixeira, et al. The effect of bovine milk lactoferrin on human breast cancer cell lines. J. Dairy Sci. 94: 66-76, 2011.

[61] Saikali, J., C. Picard, M. Freitas, and P. Holt. Fermented milk, probiotic cultures, and colon cancer. Nutr. Cancer 49: 14, 2004.

[62] Kumar, M., A. Kumar, R. Nagpal, et al. Cancer-preventing attributes of probiotics: an update. Int. J. Food Sci. Nutr. 61: 473-496, 2010.

[63] Sanders, M.E., F. Guarner, R. Guerrant, et al. An update on the use and investigation of probiotics in health and disease. Gut 62: 787-796, 2013.

[64] Pala, V., S. Sieri, F. Berrino, et al. Yogurt consumption and risk of colorectal cancer in the Italian European prospective investigation into cancer and nutrition cohort. Int. J. Cancer 129: 2712-2719, 2011.

[65] Kushi, L.H., C. Doyle, M. McCullough, et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention. CA Cancer J. Clin. 62: 30-67, 2012.

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