



Vitamin D and Colorectal Cancer

Colorectal Cancer in Hong Kong

The incidence of colorectal cancer has increased markedly over the past 10 years in Hong Kong. Among the 24,342 new cancer cases registered in 2007, there were 4,084 cases (16.8%) of colorectal cancer which is ranked the second most common cancer after lung cancer. It is expected to surpass lung cancer in the coming 5 years to become the most common cancer affecting our community. Leading to a total of 1,690 deaths in 2007, colorectal cancer is the number two cancer killer in Hong Kong.¹ The rising incidence and mortality mean that the need for more public health input into colorectal cancer prevention is greater than ever.

New study links higher levels of vitamin D to lower colorectal cancer risk

A recent observational study² funded by the World Cancer Research Fund (WCRF) global network examined the association between circulating vitamin D concentration and the risk of colorectal cancer. The nested case-control study was conducted within the EPIC study, a cohort of more than 520,000 participants from 10 European Countries. The largest ever study on the subject revealed a strong inverse association between circulating vitamin D concentration and colorectal cancer risk ($p < 0.001$), which supports the findings of previous small observational studies.

Among 1,248 cases of incident colorectal cancer, participants with the highest levels of circulating vitamin D (≥ 100 nmol/L) had a 40% lower risk of colorectal cancer than those with the lowest levels (< 25 nmol/L, $p < 0.001$). Participants with lower levels of circulating vitamin D (< 50 nmol/L) had a higher risk of colorectal cancer than those with mid-range levels (≥ 50 to < 75.0 nmol/L), whereas participants with higher levels (≥ 75 nmol/L) did not have a significant further decrease in their cancer risks. In addition, dietary vitamin D intake was not associated with colorectal cancer risk. The results were adjusted for potential confounders, not altered by corrections for season or month of blood donation, and did not vary by sex.

Despite this large study showing strong inverse associations, the findings should be treated with caution. Before any public health recommendations can be made for vitamin D supplementation, further randomised controlled trials are required to assess whether increases in circulating vitamin D concentration via supplementation can effectively decrease colorectal cancer risk without inducing adverse events. The potential cancer risk benefits of higher vitamin D levels should be balanced with caution for the potential toxic effects of vitamin D overdose. Previous findings of randomised trials of vitamin D supplementation on colorectal cancer risk have been inconsistent. Besides, there have been few studies into the long-term health effects of very high circulating vitamin D levels from supplementation regime.

WCRF HK's recommendation regarding vitamin D supplements

WCRF HK recommends not using supplements to prevent cancer and instead choosing a balanced diet with a variety of food.³ Normal healthy individuals require 5 μ g of vitamin D daily, as recommended by Chinese Nutrient Reference Values.⁴ Natural sources of vitamin D are fatty fish such as salmon, herring and mackerel, and eggs. Endogenous vitamin D production from sensible sun exposure (5 to 30 minutes, twice a week), together with a balanced diet, can provide an adequate amount of vitamin D.⁵ Certain subgroups may benefit from taking the supplements, such as pregnant women, lactating mothers, or homebound elderly.

It is estimated that about 30% of colorectal cancer cases in Hong Kong could be prevented through appropriate food, nutrition, physical activity and body fatness.⁶ The recommendations for lowering colorectal cancer risk remains to be maintaining a healthy weight, being physically active every day, consuming more dietary fibre and less red and processed meats, limiting alcohol and stop smoking³, unless the WCRF/AICR cancer prevention recommendations have to be further updated. The evidence linking foods containing vitamin D to lowering colorectal cancer risk is limited suggestive.³

The WCRF/ AICR Continuous Update Panel has identified colorectal cancer as the next cancer site, after breast cancer and prostate cancer, to be added to the rolling programme of literature updates.⁷ The Continuous Update serves as a basis for reviewing and where necessary revising WCRF/AICR's cancer prevention recommendations based on the 2007 WCRF/AICR Second Expert Report. No changes to the recommendations have been made so far.

Reference:

1. Hospital Authority: Hong Kong Cancer Registry website. www3.ha.org.hk/cancereg/e_stat.asp (accessed February 2010)
2. Jenab M et al. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case-control study. *British Medical Journal* Jan 2010;340:b5500.
3. World Cancer Research Fund/ American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. 2007 (www.dietandcancerreport.org)
4. Food and Environmental Hygiene Department: Centre for Food Safety. *A closer look at Nutrition Label How to read Nutrition Label*. 2009.
5. Holick MF. Vitamin D Deficiency. *N Engl J Med* 2007;357:266-81.
6. World Cancer Research Fund/ American Institute for Cancer Research. *Policy and Action for Cancer Prevention: Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. 2009 (www.dietandcancerreport.org)
7. World Cancer Research Fund/ American Institute for Cancer Research. *Continuous Update Project – Cancer Site*. (www.dietandcancerreport.org/cu)

High Blood Glucose Level and Cancer Risk

A recent large prospective study¹ of 6 European cohorts investigated the association between blood glucose and cancer risk. The study, funded by the WCRF global network, was part of the Metabolic Syndrome and Cancer Project (Me-Can), which tracked 274,126 men and 275,818 women for an average of 10 years. The findings suggested that elevated blood glucose levels were associated with increased cancer incidence and mortality, independent of BMI and smoking status. The association is stronger in women than men. This raised the possibility that good blood glucose control may reduce cancer risk. It is worthy to note the limitation of this study – there were no data on other possible confounding factors such as genetics, physical activity or dietary factors, which are linked to both cancer risk and blood glucose levels.

Insulin and Insulin-like Growth Factor-I (IGF-1) are thought to be the possible links between glucose and cancer, as hyperglycaemia induces elevation of these hormones that stimulate tumour growth. Besides, glucose may have a direct tumour-promoting effect, as glucose is used as an energy substrate in tumour cells.

Results from this study and those from the largest study on the subject in Korea² were largely congruent. Together these studies provide some evidence that high blood glucose is a risk factor for cancer. However, more studies on the subject are needed to obtain enough evidence on the possible link between blood sugar levels and cancer risk.

Optimum blood glucose control can be achieved by eating a healthy diet, being physically active and staying lean, all of which are supported by WCRF HK's three Guidelines for Cancer Prevention³.

Reference:

1. Stocks T et al. Blood Glucose and Risk of Incident and Fatal Cancer in the Metabolic Syndrome and Cancer Project (Me-Can): Analysis of Six Prospective Cohorts. *PLoS Med* Dec 2009;6(12):e1000201.
2. Jee SH et al. Fasting serum glucose level and cancer risk in Korean men and women. *JAMA* 2005;293:194–202.
3. World Cancer Research Fund / American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. 2007 (www.dietandcancerreport.org)

WCRF HK's Health Professional Survey

To find out how you view cancer prevention and our *Informed* Newsletter as a health professional, we would like to hear from you. It will be very much appreciated if you can spend a few minutes to complete the online questionnaire. Please go to the following URL:

<http://www.surveymonkey.com/s/MK9KGTM>

Complete your survey today and receive a limited edition copy of Chapter 8 of the WCRF/ AICR Policy Report – this chapter specifies recommendations for actions from all sectors of society to prevent cancer. Please provide us with your contact details at the end of the questionnaire. Survey results will be shared in the next issue of *Informed*.

Links between Obesity and Cancer

There is convincing evidence that excess body fatness increases risk of several common cancers.¹ Some of the mechanisms by which body fatness increases cancer risk are well understood. Obesity increases the levels of cancer-promoting hormones and growth factors, such as insulin, insulin-like growth factor (IGF-1), leptin, and sex steroid hormones including oestrogens and progesterones. In addition, insulin resistance is increased, in particular, by abdominal fatness. Obese individuals also have elevated levels of circulating tumour necrosis factor (TNF)-alpha, interleukin (IL)-6 and C-reactive protein, which contribute to a status of chronic inflammation.

A study² published in a recent issue of the journal *Cell* offered another possible explanation for the obesity-cancer link. It is shown that the enzyme monoacylglycerol lipase (MAGL) is highly expressed in aggressive cancer cells. The over-expressed MAGL breaks down fat stores into large amounts of free fatty acids (FFAs), which serve to synthesise cell membranes and protumorigenic signalling molecules. The MAGL-FFA pathway promotes migration, survival and growth of tumour. It is also found that exogenous FFAs from a high fat diet could promote malignancy in cancers which lack MAGL-FFA pathway. It has provocative implications for the obesity-cancer link. The researchers postulated that excessive fat accumulation may exacerbate the development and progression of cancer. The findings further strengthen WCRF HK's Recommendations for Cancer Prevention¹: be as lean as possible without being underweight, and limit consumption of energy-dense high-fat foods.

Reference:

1. World Cancer Research Fund/American Institute for Cancer Research. *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. 2007 (www.dietandcancerreport.org)
2. Nomura DK et al. Monoacylglycerol Lipase Regulates a Fatty Acid Network that Promotes Cancer Pathogenesis. *Cell* Jan 2010;140(1):49–61.

Check List

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