

## **Central Obesity & Dementia; Diet, Vitamin D, Calcium, & Colon Cancer**

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### **CENTRAL OBESITY & DEMENTIA**

We are, quite plainly, the heaviest society in the recorded history of mankind. More than 60% of adult Americans are overweight, and one-fourth of the U.S. population is frankly obese.

There is ample clinical evidence showing that obesity is associated with an increased risk of high blood pressure (hypertension), diabetes, heart disease, stroke, arthritis and premature death. Some cancers also appear to be more common among obese patients, including cancers of the breast, pancreas, esophagus, stomach, colon, rectum, uterus and kidney.

Although generalized obesity is a risk factor for all of the life-threatening diseases that I have described, the accumulation of excess body fat within and around the abdomen (central obesity) appears to be linked with an especially high risk of obesity-associated illnesses. Now, a new research study, just published in the journal *Neurology*, suggests that dementia may also be more common among patients with central obesity. This study was conducted by the Kaiser Permanente Division of Research in Oakland, California, in collaboration with Göteborg University in Sweden, the University of California in San Diego, the University of Michigan, and the University of California in San Francisco.

In this study, more than 6,500 patients within the Kaiser Permanente Northern California system participated in this study. Between 1964 and 1973, these patients had their abdominal diameters measured (sagittal abdominal diameter), and were then followed, for an average of 36 years, through clinical records of

their subsequent visits for medical care at Kaiser Permanente healthcare facilities. In addition to the incidence of dementia in this large group of patients, the researchers also considered the following patient factors: gender, age, ethnic background, level of formal education, marital status, and the presence or absence of diabetes, hypertension, elevated cholesterol (hyperlipidemia), stroke and heart disease.

Out of the approximately 6,600 patients evaluated in this long-term study, 1,049 (16%) were ultimately diagnosed with dementia. When these patients with dementia were further analyzed, it was determined that the patients with the greatest abdominal diameter had nearly 3 times the risk of developing dementia when compared to patients with the smallest abdominal diameter. Because both diabetes and hypertension also increase the risk of dementia, the researchers in this study adjusted their analysis to account for these two other dementia risk factors. However, following this adjustment, the nearly three-fold incidence of dementia associated with central obesity persisted.

To summarize, this long-term analysis of a very large group of patients enrolled in a comprehensive healthcare maintenance organization (HMO) appeared to show that central obesity was, *by itself*, a significant risk factor for dementia. As this study was not designed to assess the mechanism, or mechanisms, whereby central obesity might be increasing the risk of dementia, it will be necessary to follow-up the findings of this study with a more focused clinical research trial in order to gain a better understanding of how central obesity affects the risk of dementia. However, the results of this study offer additional and compelling data that obesity, and central obesity in particular, appears to be associated with an increased risk of dementia, in addition to the increased risk of other life-threatening illnesses that have previously been identified.

## **DIET, VITAMIN D, CALCIUM & COLON CANCER**

Regular readers of this column already know that I have a very strong interest in disease prevention, particularly through lifestyle modifications. These modifiable lifestyle factors include, principally, diet, natural products and dietary supplements, and physical activity levels. It has been estimated by cancer epidemiology experts that somewhere between 60 and 80% of all cancers could be eliminated through relatively moderate lifestyle modifications, although this conclusion receives shockingly little emphasis within our current healthcare system. (A forthcoming book of mine, "A Cancer Prevention Guide for the Human Race," extensively covers the currently available scientific and clinical evidence supporting specific lifestyle modifications that appear to reduce the risk of the most common causes of cancer-related death.)

The scientific evidence related to dietary factors and colorectal cancer risk remains a bit unclear at the present time. Indeed, some recent research studies have called into question a few longstanding and conventional assumptions about diet and colorectal cancer risk. For example, for decades, we've been telling our patients that a high-fiber diet will reduce their risk of developing colorectal cancer. However, recently published clinical research has suggested that there may not be a significant relationship between the amount of fiber in your diet and the risk of developing pre-cancerous polyps (adenomas) of the colon and rectum. To complicate matters further, however, other recent clinical studies have suggested that at least certain types of dietary fiber *may* actually reduce the risk of adenoma formation in the colon and rectum. So, the jury would appear to still be out on the issue of dietary fiber as a possible colorectal cancer prevention strategy (although there are many other documented health benefits to eating a diet rich in natural high-fiber foods!).

The role of Vitamin D and calcium in preventing colorectal cancer has also been an area of intense study, lately. Once again, as is unfortunately often the case with clinical research, there is a considerable amount of contradictory research data with respect to the effectiveness, if any, of Vitamin D and calcium in the prevention of colorectal cancer. However, several high quality epidemiological studies in recent years have suggested at least a moderate protective effect against colorectal cancer associated with higher levels of Vitamin D and calcium in the blood (blood levels of calcium are primarily controlled by Vitamin D, in the diet, and parathyroid hormone, which is secreted by small glands located near the thyroid gland in the neck).

A newly published research study in the journal *Cancer Research* takes a further look at potentially adverse health effects associated with the typical highly-processed, high-fat, low-fiber "western diet." (Most nutrition experts consider the typical western diet to be deficient in fruits and vegetables, fiber, and other important nutrients, including Vitamin D and calcium.) This study was conducted by researchers at Cornell University, Rutgers University, Stony Brook University and the Albert Einstein College of Medicine.

In this study, laboratory mice were fed the "rodent-equivalent" of a western diet for most of their lifespan (an average of 2 years). The researchers noted that a long-term western diet was associated with an increased risk of colon tumors in these mice, when compared to mice that were fed standard "mouse chow." Seeking to learn more about the exact causes of the observed increase in colon tumors associated with a prolonged western diet, the scientists then supplemented the western diet of these laboratory mice with individual nutrients known to be deficient in the human western diet.

When the researchers added Vitamin D and calcium supplements, the increased incidence of colon cancer previously observed in the mice that received the western diet essentially disappeared. However, supplements of *fiber*, folate

(Vitamin B-9), choline and methionine, all of which are deficient in the human western diet, failed to reverse the increased incidence of colon cancer observed in these laboratory mice that were fed a western diet.

The scientists then studied the function of genes known to be associated with the development of colorectal cancer. Specifically, the effects of a prolonged western diet on these cancer-associated genes were evaluated, and with rather startling findings. Gene expression studies revealed that a prolonged western diet, in laboratory mice, was associated with changes in cancer-associated gene function that is more typically observed in patients who inherit a gene mutation (the APC gene) that is associated with a very high risk of developing a hereditary form of colorectal cancer. Among those mice that received supplements of Vitamin D and calcium, in addition to a western diet, these cancer-associated genetic changes were *not* observed in the cells lining the animals' colons.

To briefly summarize, an animal model of colon cancer was developed in this research study, using laboratory mice that were fed a "western-diet-equivalent" throughout most of their lifespan. The animals placed on a western diet experienced an increased incidence of colon tumors, although Vitamin D and calcium supplements appeared to reverse this increased risk. At the level of genetic changes known to be associated with colorectal cancer development, a western diet appeared to be associated with a high level of cancer-associated changes in gene expression. Once again, however, these cancer-associated genetic changes appeared to be prevented by adding Vitamin D and calcium supplements to the animals' diet.

A few caveats before you run out to the drugstore and load up on Vitamin D and calcium pills. First, as always, it is important to remember that what works in laboratory mice and rats doesn't always carry over to human physiology. There have been numerous research studies of treatments that have shown dramatic effects in laboratory animals, but have then gone on to fail in human clinical trials. So, this animal study, including the cancer-associated gene expression studies, will have to be replicated in human clinical studies before the findings of the animal study can be confirmed in humans as well. Secondly, there have already been several human studies that have looked at blood levels of Vitamin D and calcium, as well as clinical studies that incorporated supplements of these nutrients. Some of these studies have shown no apparent protective effects against colorectal cancer by these nutrients, while other studies have shown a modest-to-moderate protective effect, at best.

On the whole, a considerable number of well-designed and well-executed human clinical research studies suggest that vitamin D and calcium may have a modest-to-moderate protective effect against colorectal cancer. However, *none* of these human studies have shown as dramatic a protective effect with Vitamin D and calcium as was observed in this laboratory animal study. Once again, the methodology used in this animal study will need to be translated into a human

clinical trial before anyone can definitively say that Vitamin D and calcium supplements are highly effective in the prevention of colorectal cancer. For now, however, it is prudent to ensure that your diet is at least sufficient in these two very important nutrients.

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