

Nutrition, Cancer, and The Degenerative Diseases of Aging

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Aging appears to be in good part due to the oxidants produced as by-products of normal metabolism by mitochondria. The degenerative diseases of aging such as cancer, cardiovascular disease, cataracts, and brain dysfunction, are increasingly found to have, in good part, an oxidative origin. The main source of dietary antioxidants is fruits and vegetables. The quarter of the American population that eats the fewest fruits and vegetables (5 portions a day is advised) has about double the cancer rate for most types of cancer of the quarter that eats the most. Deficiency of antioxidants causes the same damage to DNA as radiation.

Many micronutrients protect against DNA damage. For example, folate deficiency is one of the most common vitamin deficiencies, occurring in nearly half of low income (mainly African-American) elderly, and adolescents. Folate deficiency is associated with increased chromosome breaks cancer, heart disease, neural tube defects in the fetus, and cognitive defects in adults. Folate deficiency causes extensive incorporation of uracil into human DNA (4 million/cell), leading to chromosomal breaks. Elevated DNA uracil levels and chromosome breakage are reversed by folate administration. This mechanism is the likely cause of the increased cancer risk and cognitive defects in humans and emphasizes the importance of fruit and vegetable intake for a healthy life.

Men with low Vitamin C intake have low Vitamin C in their seminal fluid and much more oxidative damage to the DNA in their sperm. Male smokers are particularly at risk as they have depleted antioxidant pools (cigarette smoke is extremely high in oxidants). A smoker must eat 2 to 3 times as much Vitamin C as a non-smoker to maintain an equal plasma level, yet smokers tend to eat worse diets than non-smokers. Indeed, male smokers may have a considerably higher risk of having children with birth defects and childhood cancer.

Two major causes of cancer are smoking (1/3 of cancer & 1/4 of heart disease) and dietary imbalances (excess fat and calories; inadequate intake of fruits, vegetables, fiber, and micronutrients). Another major contributor to cancer is chronic infections leading to chronic inflammation (hepatitis B and C viruses, *Helicobacter pylori* infection, schistosomiasis, etc.). Chronic inflammation is a major cause of cancer in the world because it releases powerful oxidants which both stimulate cell division and are mutagens. Gamma-tocopherol, the main source of Vitamin E in the diet, is a mutagen trap and defends against NOx and other mutagens released during inflammation or smoking, and thus complements alpha-tocopherol, the antioxidant sold as a supplement. Past occupational exposures might cause about 2% of current human cancer, a major part being asbestos exposure in smokers, and industrial or synthetic chemical pollution causes less than 1%, in my view. The age-adjusted cancer death rate in the U.S. for all cancers combined (excluding those attributable to smoking) has declined 15% in the U.S. since 1950, while life expectancy increases every year.

Two factors are critical in the formation of mutations: lesions in DNA, formed when DNA is damaged, and cell division, which converts DNA lesions to mutations. Agents increasing either lesions or cell division increase mutations and as a consequence increase cancer incidence. Hormones stimulating cell division increase cancer incidence (e.g. levels of estrogen in breast cancer and testosterone in prostate cancer); hormones may be a risk factor in about 20% of human cancer.

Animal cancer tests, which are done at the maximum tolerated dose (MTD), are being misinterpreted to mean that low doses of the chemicals tested and found positive are thereby relevant to human cancer. Animal cancer tests are mainly done on synthetic chemicals and industrial pollutants, yet half of all natural chemicals that

have been tested at the MTD are rodent carcinogens. It is argued that the explanation for the high frequency of positive results in animal cancer tests is that high dose animal cancer tests are mainly measuring increases in cell division due to cell killing and compensatory cell division; this is a high dose effect that does not occur at low doses. In any case, 99.9% or more of the chemicals we eat are natural. For example 99.99% of the pesticides we eat are natural chemicals that are present in plants to ward off insects and other predators. More than half of those natural pesticides tested in high dose animal tests are rodent carcinogens. There are about 10,000 of so different natural pesticides in our diet, and they are usually present at enormously higher levels than synthetic pesticides. Cooking food also generates thousands of chemicals. There are over 1000 chemicals reported in a cup of coffee. Only 26 have been tested in animal cancer tests and more than half are rodent carcinogens; there are still a thousand chemicals left to test. The amount of potentially carcinogenic pesticide residues consumed in a year is less than the known amount of rodent carcinogens in a cup of coffee.

The reason we can eat the tremendous variety of natural chemical rodent carcinogens in our food is that animals are extremely well defended against all chemicals by many general defense systems. These enzymes, e.g. DNA repair and glutathione transferases which defend against reactive compounds such as mutagens, are all inducible (more of them are made when they are in use). They are equally effective against natural and synthetic reactive chemicals. Thus, animals are extremely well defended against low doses of chemicals. One does not expect, nor does one find, a general difference between synthetic and natural chemicals in their carcinogenicity, and though less well studied, the same would be expected for mutagenicity, teratogenicity, and acute toxicity.