# Vitamins/minerals and genomic stability in humans Editorial

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FROM ABSTRACT

Recommended dietary allowances (RDAs) of micronutrients have been traditionally defined as those levels necessary to prevent symptoms of deficiency diseases.

There is increasing evidence that higher levels of many such micronutrients may be necessary for various DNA maintenance reactions, and that the current RDAs for some micronutrients may be inadequate to protect against genomic instability.

Supplementation of a normal diet, with either vitamins and/or minerals or with isolated plant polyphenols, is very common, but becoming increasingly common in most Western populations.

However, there is no clear agreement as to how much supplementation should occur, if at all, and genotypic differences are not accounted for.

The 14 mini-reviews in this special issue summarise the role of specific micronutrients in various aspects of DNA maintenance: DNA synthesis, DNA repair, DNA methylation, gene mutation, chromosome breakage, chromosome segregation, gene expression, oxidative stress, necrosis and apoptosis.

THESE AUTHORS ALSO NOTE:

Dietary imbalance may increase gene mutation and chromosome aberrations in human populations, similar to exposure to radiation, mutagens and carcinogens.

"Diet may well be a key factor in determining genomic stability since it impacts on all relevant pathways, i.e. exposure to dietary carcinogens, activation/detoxification of carcinogens, DNA repair, DNA synthesis and apoptosis."

"Many micronutrient minerals and vitamins act as substrates and/or co-factors in key DNA maintenance reactions, and the exact concentration of these in the cell may be critical."

Sub-optimal levels of key micronutrients required for DNA maintenance will reduce genomic stability, "producing similar effects to inherited genetic disorders or exposure to carcinogens."

“The current recommended dietary allowances (RDAs) for vitamins and minerals have been derived from levels known to prevent deficiency diseases, including scurvy (Vitamin C), anemia (folic acid) and pellagra (niacin).”

“Micronutrients may also be essential to prevent degenerative diseases including cancer, cardiovascular disease, Alzheimer's disease and premature aging, and their role in maintaining genomic stability is likely to be critical to those functions.”

“Uracil in DNA caused by low folate intake and oxidised DNA bases caused by low antioxidant diets may either independently or in synergy cause the production of DNA breaks.”

“Carotenoid intake from fruits and vegetables is linked with reduced cancer risk, dietary interventions with supplements of beta-carotene did not prove to be effective against cancer.”

“Foods that are naturally rich in Vitamin C are associated with reduced risk for cardiovascular, neurodegenerative disease and various cancers.”

“There is no case to recommend the consumption of ascorbate supplements to replace diets rich in fruits and vegetables which may deliver many other anti-oxidant and anti-cancer agents.”

Vitamin E is an antioxidant vitamin with an important role in the prevention of lipid peroxidation. **[IMPORTANT]**

Niacin has an intimate role in DNA synthesis, DNA repair and cell death.

Folate plays a direct and critical role in the prevention of uracil incorporation into DNA, which causes chromosome breakage.

“Both folate and Vitamin B12 deficiency independently or together have been shown to cause chromosome damage and micronucleus formation in vivo in humans.” **[Micronuclei are the best biological marker for the development of future cancer][There is evidence that the 4-inch radius around your cell phone antennae causes micronuclei damage]**

“Intakes in excess of 200 microg folic acid and 2 microg Vitamin B12 would be needed to minimize chromosome damage.”

“Micronucleus frequency in humans is minimized when plasma homocysteine is less than 7.5 micromol/l.”.

“It is clear from these studies that optimal dietary intakes for minimizing genomic stability depend on age and genotype.”

"The age factor is particularly important for folate and Vitamin B12 because the capacity to absorb these vitamins declines markedly with increasing age."

"Vitamin D exerts antioxidant activity by increasing glutathione levels in normal cells and induces apoptosis in cancer cells."

The current RDA of 5 microg per day of Vitamin D is not adequate for the biomarkers of cancer prevention.

Plant polyphenols are ubiquitous in our diet, and they "play a critical role in modifying gene expression, anti-oxidant status and cancer/cardiovascular disease risk in humans."

It is unknown "whether plant polyphenol supplements provide any advantage over a simple recommendation to eat five servings of fruits and vegetables each day."

"The daily intake of magnesium in most industrialised countries is currently significantly below the RDA levels and marginal magnesium deficiencies are very common."

"A deficiency of this element appears to decrease membrane integrity and function, and increase susceptibility to oxidative stress, cardiovascular diseases and accelerated aging."

"Magnesium is essential for all metabolic pathways, as an essential co-factor in almost all enzymatic systems involved in DNA processing."

Selenium inhibits the production of carcinogens and retards oxidative damage to DNA, lipids and proteins.

"The upper limit of desirable selenium intake may be around five times higher than suggested by deficiency methods of defining RDA."

"Excessive amounts of selenium may cause oxidative damage leading to, rather than preventing genomic instability."

Copper is a co-factor for a number of critical enzymes.

"An intake of 1-3 mg per day [copper] has been suggested as adequate for humans, and these levels may be adequate for maintaining genomic stability."

"A deficiency of iron leads to anaemia, especially during active growth periods such as early childhood, adolescence and pregnancy."

However, high levels of iron are likely to increase oxidative stress.

"Although a certain level of iron is essential, iron overload could create serious problems especially enhanced oxidative stress."

"Zinc deficiency is associated with developmental defects and increased DNA damage rates."

"The most early effect of zinc deficiency is growth retardation."

"Very little is known about the impact of dietary factors on the stability of mitochondrial DNA."

The authors note that mitochondrial DNA also requires micronutrients to avoid mutation, maintain cell function and prevent disease.

Mitochondrial DNA regulates the amount of ATP generated by the cell.

Mutations in the "mitochondrial genome can lead to an inefficient electron transport chain leading to electron leakage and generation of elevated oxidative stress."

This will require elevated levels of Vitamin E to prevent the damaging effects from increased oxidative stress.

KEY POINTS FROM DAN MURPHY

(1) The recommended dietary allowances (RDAs) of micronutrients are based on the levels necessary to prevent symptoms of deficiency diseases.

(2) Higher than RDA levels of micronutrients are necessary to protect DNA integrity and to protect against genomic instability.

(3) Micronutrients are also essential to prevent degenerative diseases including cancer, cardiovascular disease, Alzheimer's disease and premature aging.

(4) This article reviews the importance of Carotenoids, Vitamin C, Vitamin E, niacin, folate, Vitamin B12, plant polyphenol, magnesium, zinc, selenium, copper, and iron.

(5) These authors stress the benefits of ingesting micronutrients from foods rather than from supplementation.