# Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage

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Contributed by Bruce N. Ames, October 6, 2006 (sent for review September 20, 2006)

**Inadequate dietary intakes of vitamins and minerals are widespread, most likely due to excessive consumption of energy-rich, micronutrient-poor, refined food. Inadequate intakes may result in chronic metabolic disruption, including mitochondrial decay. Deficiencies in many micronutrients cause DNA damage, such as chromosome breaks, in cultured human cells or *in vivo*. Some of these deficiencies also cause mitochondrial decay with oxidant leakage and cellular aging and are associated with late onset diseases such as cancer. I propose DNA damage and late onset disease are consequences of a triage allocation response to micronutrient scarcity. Episodic shortages of micronutrients were common during evolution. Natural selection favors short-term survival at the expense of long-term health. I hypothesize that short-term survival was achieved by allocating scarce micronutrients by triage, in part through an adjustment of the binding affinity of proteins for required micronutrients. If this hypothesis is correct, micronutrient deficiencies that trigger the triage response would accelerate cancer, aging, and neural decay but would leave critical metabolic functions, such as ATP production, intact. Evidence that micronutrient malnutrition increases late onset diseases, such as cancer, is discussed. A multivitamin-mineral supplement is one low-cost way to ensure intake of the Recommended Dietary Allowance of micronutrients throughout life.**

Poor nutrition has been linked to an increased risk of many diseases, including cancer, heart disease, and diabetes. The human diet requires both macronutrients, which are the main source of calories, and micronutrients (≈40 essential minerals, vitamins, and other biochemicals), which are required for virtually all metabolic and developmental processes. The leading dietary sources of energy in the United States are abundant in carbohydrates and fats (1) but deficient in micronutrients (i.e., they are energy-dense and nutrient-poor) (2). Such foods are inexpensive and tasty and as a consequence are consumed excessively, particularly by the poor (3). Thus, even in the United States (4), inadequate intake of some vitamins and minerals is common (Table 1). Suboptimal consumption of micronutrients (4) often accompanies caloric excess (6, 88) and may be the norm among the obese and contribute to the pathologies associated with obesity.

Significant chronic metabolic disruption may occur when consumption of a micronutrient is below the current Recommended Dietary Allowance (RDA) (7–10) but above the level that causes acute symptoms. When one component of the metabolic network is inadequate, there may be a variety of repercussions in metabolism, including acceleration of degenerative diseases. The optimum intake of each micronutrient necessary to maximize a healthy lifespan remains to be determined and could even be higher than the current RDA, particularly for some populations (7, 10). For example, folic acid intakes above the RDA appear to be necessary to minimize chromosome breaks (10, 11).

**Table 1. Selected micronutrient inadequacy in the U.S.**

| Nutrient | Population group | % ingesting less than the EAR from food |
|---|---|---|
| Minerals | | |
| Iron | Women 14–50 years old | 16 |
| Magnesium | All | 56 |
| Zinc | All | 12 |
| Vitamins | | |
| B6 | Women >71 years old | 49 |
| Folate | Adult women | 16 |
| E | All | 93 |
| C | All | 31 |

Less than the EAR is used as a measure of inadequacy in populations (4, 5). The RDA is defined as 2 standard deviations above the EAR. Data are from Moshfegh *et al.* (4).

## Micronutrient Deficiencies May Accelerate Mitochondrial Decay and Degenerative Diseases of Aging, Such as Cancer

Mitochondrial decay appears to be a major contributor to aging and its associated degenerative diseases, including cancer and neural decay (12). Mitochondria from old rats compared with those from young rats generate increased amounts of oxidant by-products (13) and have decreased membrane potential, respiratory control ratio, cellular oxygen consumption, and cardiolipin (a key lipid found only in mitochondria). Oxidative damage to DNA, RNA, proteins, and lipids in mitochondrial membranes contributes to this decay (9, 13–16) and leads to functional decline of mitochondria, cells, tissues, and eventually organs such as the brain with an accompanying loss of ambulatory activity (9, 13–16).

The importance of optimizing metabolic function to prevent mitochondrial decay is illustrated by feeding the mitochondrial metabolites acetyl carnitine (ALC) and lipoic acid (LA) to old rats. Carnitine is used for transporting fatty acids into the mitochondria; the main form of carnitine in the plasma is ALC. LA is a mitochondrial coenzyme and is

Author contributions: B.N.A. wrote the paper.

Conflict of interest statement: B.N.A. is a founder of Juvenon, a company that has licensed the University of California patent (B.N.A. and T. Hagen, inventors) on acetyl carnitine plus lipoic acid for rejuvenating old mitochondria. Juvenon sells acetyl carnitine plus lipoic acid supplements and does clinical trials on them. B.N.A.'s founder's stock was put in a nonprofit foundation at the founding in 1999. He is director of Juvenon's Scientific Advisory Board, but he has no stock in the company and does not receive any remuneration from them.

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reduced in the mitochondria to a potent antioxidant. LA is also an effective inducer of ≈200 phase 2 antioxidant and thiol-protective enzymes, including those required for glutathione synthesis (17–19). ALC and LA when added as a supplement can act, in some cases synergistically, to restore much of the lost mitochondrial function in old rats (13–16), which appears to rejuvenate the mitochondria and improve cognition and other functions (9, 13–16).

One possible mechanism of mitochondrial decay is that, with age, increased oxidative damage to mitochondrial proteins causes structural deformation of key enzymes that lowers their affinity for the enzyme substrate (16). Feeding old rats the substrate ALC with LA for a few weeks decreases oxidative damage, allowing the synthesis of new carnitine acyl transferase with normal binding affinity ($K_m$). This partially restores mitochondrial function; decreases oxidants, neuronal RNA oxidation, and mutagenic aldehydes; and increases rat ambulatory activity and cognition (13–16). ALC and LA are not thought of as micronutrients, because they can be synthesized in the body, but they are illustrative of many normal metabolites that may be beneficial in the elderly.

The association of several micronutrient deficiencies with degenerative disease, DNA damage, cancer, and mitochondrial decay is discussed below.

**Magnesium Deficiency.** Magnesium intakes for ≈56% of adults in the United States are below the Estimated Average Requirement (EAR) (Table 1). Intakes below the EAR are especially prevalent among the poor, teenagers (78% of 14- to 18-year-old males and 91% of 14- to 18-year-old females), the obese, African Americans, and the elderly (81%) (4, 20–24). In humans, magnesium deficiency has been associated with colorectal and other cancers (25–28), hypertension, osteoporosis, diabetes, and the metabolic syndrome (5, 29, 89). In a study of 4,035 men followed for 18 years, the highest quartile with serum magnesium at baseline compared with the lowest had a 40% decrease in all-cause mortality and cardiovascular disease and a 50% decrease in cancer deaths (30). In primary human cells in culture, magnesium deficiency leads to mitochondrial DNA damage, accelerated telomere shortening, activation of cell-cycle arrest proteins, and premature senescence (D. W. Killilea, B.N.A., unpublished observations). Magnesium deficiency in rats leads to chromosome breaks (31) and cancer (25). In rats, a diet moderately deficient in magnesium increased mortality, blood pressure, inflammation, and oxidants and decreased resistance to oxidants compared with a standard or magnesium-supplemented diet (32). This evidence suggests that supplementation programs should be considered, because there is little risk of magnesium toxicity (5). A standard multivitamin–mineral (MVM) supplement does not contain sufficient magnesium (or calcium) because it would make the supplement too bulky.

**Vitamin D Deficiency.** The dark skin of people indigenous to southern India, Africa, and other tropical regions protects against excessive UV light exposure from the sun. On the other hand, dark skin interferes with the formation of vitamin D in the skin, which requires UV light. Thus, dark-skinned people in northern latitudes are often vitamin D-deficient. For example, African Americans as a group are particularly deficient in vitamin D (33, 34). In The Netherlands there is a very high level of vitamin D deficiency during pregnancy in dark-skinned women (35, 36). Inadequacy is prevalent in Caucasians as well (37). Vitamin D deficiency has been estimated to account for 29% of cancer mortality in males (38) and has been strongly associated with colon, breast, pancreatic, and prostate cancer (38–44). It also has been associated with a variety of diseases with long latency periods, including cardiovascular disease (45–51). A study of independent, community-dwelling elderly people reported that nursing home admissions, and possibly mortality, were strongly associated with vitamin D inadequacy (52). A large prospective study (50) in women reported that intakes of ≥400 I.U. of vitamin D per day from supplements was associated with a 41% lower risk of multiple sclerosis compared with women that did not consume vitamin D from supplements. It was not possible to definitively attribute the effect to vitamin D, because it was mostly consumed in MVM supplements, which were also associated with lower risk; the authors concluded that vitamin D was the most likely explanation. Some evidence in humans and rodents suggests that vitamin D deficiency is associated with cognitive dysfunction (90, 91). Numerous authors have suggested that efforts to improve vitamin D status by supplementation could reduce disease incidence and mortality at low cost with few or no adverse effects (39, 41, 49, 53). Many experts suggest the current RDA for vitamin D should be raised (54, 55).

**Other Micronutrient Deficiencies Associated with Chronic Degenerative Diseases.** Calcium deficiency is common; it has been associated with chromosome breaks (56) and diabetes (48) in humans and colon cancer in mice (57). Selenium deficiency in mice induces genes linked to DNA damage and oxidative stress (58), and it has been suggested that selenium protects against cancer (59, 60). Potassium in table salt in elderly men was associated with a 40% decrease in cardiovascular disease compared with normal table salt in a randomized controlled trial (RCT) (61). Omega-3 fatty acid deficiency is associated with melanoma and other cancers (62) as well as cognitive dysfunction (63). The effect of B vitamin deficiency on mitochondria was reviewed recently (64). Vitamin B12 deficiency is common in the population (4); it is associated with cognitive dysfunction (65) and multiple sclerosis (66) and induces chromosome breaks (11). The cognitive dysfunction associated with B12 deficiency improved with supplementation within the first year of onset (67). Folate deficiency also causes chromosome breaks (11, 56, 68) and is associated with several human cancers (69, 70). Marginal thiamine deficiency in rats induces the formation of colonic aberrant crypt foci, a preneoplastic lesion in a model for detecting colon carcinogens (64). Thiamine deficiency is also associated with brain dysfunction and diabetes (64). Niacin deficiency in cellular and animal studies appears to be genotoxic (64, 71). Choline deficiency in humans increases DNA damage in lymphocytes (72). In rats, choline deficiency has been associated with brain dysfunction (73), oxidant release, and mitochondrial damage (72).

We and others discussed the need to set micronutrient requirements high enough to minimize DNA and mitochondrial damage (7, 8, 10, 11, 56, 64, 74). For each micronutrient we are investigating the level of deficiency that causes DNA and mitochondrial damage in humans because neither studies using human cells in culture nor studies using rodents can provide this information. End points such as DNA damage in humans might be useful indicators for refining EARs and upper limits (ULs) to more closely approximate the levels required for optimal health.

**Some Micronutrient Deficiencies Impair Heme Synthesis, Which Can Result in Mitochondrial Decay, DNA Damage, and Cell Senescence.** Seven micronutrients (pyridoxine, pantothenate, zinc, riboflavin, iron, copper, and biotin) are required for heme synthesis in mitochondria (Table 2). It is likely that a deficiency in any of these seven will cause a deficit of heme and therefore of complex IV, of which heme-*a* is an essential component (7, 8, 75, 83, 85, 86). The results to date

**Table 2. Micronutrient deficiency and heme: effects on human cells in culture and animals**

| Micronutrient deficiency | Heme deficit | Complex IV deficit | Oxidative stress | DNA damage | Early senescence |
|---|---|---|---|---|---|
| Pyridoxine | 75 | | | **A** | **A** |
| Zinc | | **A** | 76–78 | 76–78 | |
| Riboflavin | 75 | | | | |
| Iron | | | 79 | 79 | |
| Copper | 80 | 81 | 82 | | |
| Biotin | 83 | 83 | 83 | 83 | 83 |
| Pantothenate | 75 | 84 | | | |

Numbers represent references. **A**, H. Atamna, S. Askree, and B.N.A., unpublished data.

are in Table 2. The normal complement of complex IV keeps oxidants to a minimum; deficits of complex IV result in oxidant leakage, DNA damage, accelerated mitochondrial decay, and cellular aging (8, 83, 85). Table 2 is incomplete because the effects of some deficiencies on human cells in culture have not yet been determined. Deficiencies of iron, zinc, and biotin are discussed below.

***Iron.*** Iron deficiency is the most common micronutrient deficiency in the world, and anemia is widespread in underdeveloped countries (87). Iron intake in U.S. menstruating women is low; ≈16% are below the EAR (4). Hispanic women and the obese are at greater risk of being iron-deficient (6). In humans, iron deficiency anemia is associated with poor cognitive development in toddlers (92), suggesting that iron deficiency in humans during critical periods of development harms the developing brain (92). Severe iron deficiency causes loss of mitochondrial complex IV in selected regions in the brain of neonatal rats (93) and other changes in function, morphology, and physiology of the brain (88, 94). Iron deficiency in rats damages mitochondria and causes oxidant release, oxidative DNA damage, and decreased mitochondrial efficiency (79).

Iron deficiency also is associated with diminished immune function and neuromuscular abnormalities (95, 96). The primary measure used to identify iron deficiency in most human populations is a reduction in hemoglobin to the point of anemia (malaria, HIV, and other nutrient deficiencies may also lead to anemia). The effects of iron deficiency occur along a continuum (88, 97), and subclinical iron deficiency may have deleterious effects on heme biosynthesis. Iron deficiency without anemia can also occur in newborns exposed to intrauterine hypoxia, such as infants of preeclamptic or diabetic mothers (98). In such cases, iron is prioritized to erythroid and hemoglobin synthesis, putting the nonerythroid tissues at risk of iron deficiency and hence heme deficiency (99, 100). Dietary iron deficiency in the absence of anemia decreases aerobic capacity and physical work performance, which are improved by iron supplementation (101). Iron deficiency has not been adequately studied as a possible risk factor for cancer, and the results are discordant (102). However, many studies are looking for a monotonic relationship and do not take into account that one might expect cancer at levels of iron that are both too low and too high (79), as in hereditary hemochromatosis, a known risk factor for cancer (103).

***Zinc.*** Zinc inadequacy is common in adults, ≈12% of whom are below the EAR (4). In human cells in culture, zinc deficiency causes complex IV deficiency and the release of oxidants, resulting in significant oxidative damage to DNA (76–78). Zinc deficiency also causes chromosome breaks in rats (31) and is associated with cancer in both rodents and humans (104). As discussed above, these observations reinforce the need to determine what degree of deficiency in humans results in DNA damage. We think it is likely that the trigger for decreased heme synthesis is the inactivation of the second enzyme of the pathway, δ-aminolevulinate dehydratase, which contains eight atoms of zinc (85, 105). Zinc deficiency in human cells also inactivates other zinc-containing proteins such as the tumor suppressor protein p53 and the DNA base excision repair enzyme, apyrimidinic/apurinic endonuclease, with a resulting synergistic effect on genetic damage (76, 77).

***Biotin.*** Biotin deficiency is more common than previously thought; ≈40% of pregnant women who do not take a multivitamin show metabolic signs of deficiency (106). Marginal biotin deficiency is teratogenic in mice (106). Biotin is a prosthetic group in four biotin-dependent carboxylases (three of which are solely present in mitochondria) that replenish intermediates in the tricarboxylic acid cycle (107). Biotin deficiency decreases the activity of these enzymes, leading to a decrease of two heme precursors, mitochondrial succinyl-CoA and glycine, thus resulting in heme deficiency (83). Biotin deficiency in normal human lung fibroblasts in culture caused a 40–50% decrease in heme content, oxidant release, premature senescence, and DNA damage (83). The relationship of these effects to human intake needs to be determined (108).

## A New Hypothesis: Allocating a Scarce Micronutrient by Triage

Is there an explanation for the observation that many micronutrient deficiencies are associated with chromosome breaks and cancer in humans, cause DNA damage in rodents or human cells in culture, and, where assayed, cause early senescence? I propose DNA damage and late onset disease are consequences of a triage allocation mechanism developed during evolution to cope with episodic micronutrient shortages. For example, living creatures always have required ≈15 metals/minerals for their metabolism, which are distributed very unevenly throughout the Earth. Thus, episodic shortages probably were common, as probably also was the case for vitamins and other essential micronutrients. Natural selection is known to favor short-term survival at the expense of long-term health when they are in conflict. I hypothesize that as the scarcity of a micronutrient increases, and after homeostatic adjustments, such as induction of transport proteins (109), a triage mechanism for allocating scarce micronutrients is activated that favors short-term survival at the expense of long-term health, in part through an adjustment of the binding affinity of each protein for its required micronutrient.

The consequences of such triage would be evident at all levels. For example, in metabolic reactions, enzymes involved in ATP synthesis would be favored over DNA-repair enzymes; in cells, erythrocytes would be favored over leukocytes; and in organs, the heart would be favored over the liver. Isozymes with different binding constants for the coenzyme or metal in the heart or liver could be one of several ways to accomplish this end. Physiological triage is well known: "when $O_2$ delivery to the tissues is inadequate . . . vital organ function is maintained by intrinsic neurohormonal compensatory mechanisms resulting in distribution of organ blood flow primarily to the heart, brain, and adrenal glands and away from other 'nonvital' organs" (110). Similarly, under conditions of deficiency, organs such as the liver lose certain micronutrients first, before other more vital organs (111–116, 150).

The triage hypothesis suggests additional mechanisms that may be used by the body to allocate scarce resources. This hypothesis is testable, and, if validated, suggests that it may be necessary to optimize intakes of micronutrients according to the needs of the most dispensable organ or cells in order to maximize longevity and retard cancer and other degenerative diseases of aging. There is increasing evidence that nutritional inadequacies during development can have consequences later in life (117). For example, fetal malnutrition during the Dutch famine in 1944–1945 was associated with coronary artery disease in adulthood (117, 118), although both micronutrient and macronutrient malnutrition may have contributed to this late-onset disease. Broadly, such protein triage would represent an instance of "antagonistic pleiotropy," as proposed almost 50 years ago by Williams (119) in which a single allele (e.g., an isozyme with a low affinity for a micronutrient) may encode both a beneficial (short-term survival of episodic deficiency) and a harmful (an increase in degenerative disease) phenotype. The concept of enzyme triage is also broadly consistent with recent evolutionary theory about aging, which stresses that selection for reproductive success early in life may involve trade-offs that shorten lifespan (120). Malnutrition has been discussed in relation to "investment priorities" in birds (151), fetal programming in humans (152, 153), and type of immunocompetence (154).

Moderate reduction in dietary intake of macronutrients (calorie restriction) with adequate micronutrients extends lifespan in various animals (121) but is not inconsistent with the triage hypothesis because the normal level of calories fed controls could be in excess of what is optimal for maximum lifespan.

## Should People Take an MVM Supplement for Insurance?

The National Health and Nutrition Examination Surveys (NHANES) (4) indicate that the diets of many in the United States do not provide adequate intakes of all of the vitamins and minerals recommended by official bodies (Table 1). From NHANES and Table 1, it seems likely that actual intakes of various micronutrients from food are not only inadequate for the poor, teenagers, menstruating women, the obese, and the elderly, but for much of the rest of the population as well. However, decades of public health efforts to improve the American diet have not been very successful, particularly among the poor. Why not recommend that a MVM supplement be added to a healthy lifestyle? This approach, focusing on micronutrient malnutrition, with additional attention to food fortification, in addition to continuing efforts to improve diet, might be more successful in improving health. It may be easier to convince people to take an inexpensive MVM supplement than to markedly change their eating habits. Evidence is accumulating that a MVM supplement, or smaller combinations of vitamins and minerals, also improve long-term health, reducing heart disease, cancer, and cataracts and improving immune function for those who consume inadequate diets (122–137, 155). The potential benefits of an MVM in infection have been critically reviewed (138).

Should it be necessary to first demonstrate efficacy for preventing or delaying long-term chronic diseases such as cancer in RCTs before recommending MVM use (45, 156)? RCTs for micronutrients and long-term effects are extremely difficult to do correctly for many reasons (45): decades are sometimes required in long latency diseases (139, 140); there are different, and often multiple, consequences of each micronutrient deficiency; large populations are required; this type of RCT is very expensive, and, unlike for drugs, there is no commercial incentive to do trials; and compliance is difficult to maintain for many years, particularly in controls, who can take readily available MVM supplements. For all of these reasons it is unlikely that it will be possible to obtain definitive results from this type of RCT, whether it be targeted at single micronutrients or MVMs. For example, two very large RCTs examined effects of supplementation with a limited number of vitamins and minerals on cancer risk (134, 135). Although both of these RCTs reported a reduction in cancer incidence or mortality with supplementation, methodological concerns have been raised to argue that the results are not definitive (156).

Instead of relying only on long-term RCTs (156), all scientific evidence should be taken into account in making supplementation recommendations (45, 141). RCTs on short-term end points such as DNA damage (10) or markers of inflammation (125) are feasible and are more likely to yield definitive results. Many other types of experiments in humans and animals, including biochemical, mechanistic, and epidemiological, are also relevant.

One does need to be concerned that cumulative effects of supplementation and fortification might exceed ULs. Increasing consumption of supplements and increasing fortification emphasize the need for vigilance to prevent overconsumption of certain micronutrients. For example, consuming too high a dose of many of the minerals is toxic (e.g., iron, zinc, copper, and selenium, and some of the vitamins, such as vitamin A). Vitamin A was of particular concern until most MVM manufacturers switched recently to using more provitamin A. Excess iron is also not difficult to achieve in men and postmenopausal women, who should take readily available MVMs without iron and should limit red meat consumption. In mice, both low (one-third of normal) intake of a mixture of vitamins and a 5-fold excess caused an increase in intestinal neoplasia (142). In rats, both too little and too much iron resulted in mitochondrial damage, release of oxidants, and DNA damage (79). However, the percentage of the population consuming more than the UL from food is very low compared with the percentage consuming less than the EAR (4). Thus, micronutrient deficiencies are likely to be a far more important public health problem than excess consumption (4). This conclusion is supported by the many epidemiological and other human studies cited in this article. Thus, taking a daily standard MVM supplement is unlikely to be of concern, because these amounts of micronutrients are not close to the UL (4).

Despite the lack of definitive proof of efficacy, I and others believe that public health officials and physicians should recommend that people take a MVM supplement in addition to leading a healthy lifestyle (133): there are widespread low intakes (4); an impressive array of evidence for MVM supplementation exists, and there is an absence of realistic safety concerns. If this simple change could be implemented, and particularly if MVMs could be made available to the poor, a marked decrease in the prevalence of micronutrient intakes below the RDA would result.

Fortification of food, such as folate fortification, is another approach that has been shown to improve health and is valuable. Fortification, however, might not be sufficient for population subgroups that have special needs. For example, most African Americans are very low in vitamin D despite milk fortification (33); 75% are lactose-intolerant (53); and it seems prudent for African Americans to take a vitamin D or MVM supplement (54). Fortification is also problematic when some groups in the population would be benefited and some harmed. This is relevant for iron, because menstruating women need more than men or older women, some of whom may be getting too much.

## Other Possibly Useful Supplements

Other useful supplements include fiber, and omega-3 fatty acids from fish oil, particularly eicosapentaenoic acid and docosahexaenoic acid, which appear to be important for brain function and have potent antiinflammatory activity (63, 141, 143). Inadequate fiber intakes, both soluble and insoluble, are widespread and have adverse health consequences (144); supplementation is inexpensive. Advice to take MVM supplements, fiber, and omega-3 fatty acid supplements should always be coupled with advice to eat a good diet, because we also need other nutrients and probably phytochemicals that may not be present in supplements (145).

## Variable Optimal Requirements

The elderly may need more or less of certain vitamins and metabolites compared with younger people, but this issue has not been thoroughly examined (146, 147). For example, ≈25% of Dutch adults >70 years of age showed mild-to-severe vitamin B12 deficiency (148), most likely because of malabsorption rather than low dietary intakes (4). Vitamin B12 intakes at levels many times the RDA reversed the deficiency (65, 148). Most smokers have an inadequate intake of vitamin C; 76% are below the EAR (4). The optimal intake of micronutrients and metabolites can also vary with genetic constitution (146, 147, 149) (e.g., iron requirements vary with age and gender as discussed above). A study of a common polymorphism in the gene for mitochondrial manganese superoxide dismutase demonstrated that selenium, $\alpha$-tocopherol, or lycopene protected against prostate cancer, and the combination of all three showed a 10-fold gradient of risk across quartiles in one form of the polymorphism (149). A variety of MVM supplements have been developed that reflect different needs depending on one's age and gender, and more are likely to be developed with new knowledge.

## Conclusion

Although many results are not definitive and much more research is needed, a large literature suggests that micronutrient inadequacy can lead to cancer and other long-term deleterious consequences. I present a triage theory that explains why these consequences might be expected. Short-term RCTs using end points associated with long-term disease, such as DNA damage and inflammatory markers, are likely to identify populations at risk and further refine levels of micronutrients required for optimum long-term health. Micronutrient inadequacies are widespread in the population, and a MVM supplement is inexpensive. A solution is to encourage MVM supplementation, particularly in those groups with widespread deficiencies such as the poor, teenagers, the obese, African Americans, and the elderly, in addition to urging people to eat a more balanced diet.

I am indebted to G. Ames, S. Askree, H. Atamna, K. Beckman, G. Block, B. German, L. Gold, H. Helbock, D. Killilea, J. King, T. Klask, A. Lal, G. Li, M. Mietus-Snyder, J. Nides, M. Stampfer, J. Suh, J. Vance, F. Viteri, P. Wakimoto, W. Willett, and especially to J. McCann for their suggestions and contributions. This work was supported by National Foundation for Cancer Research Grant M2661, National Center for Minority Health and Health Disparities Grant P60 MD00222, National Center for Complementary and Alternative Medicine Grant R21 AT001918, and Research Scientist Award K05 AT001323.

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