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Beyond the Calorie

The concept of the calorie as a unit of heat measurement (and the potential source of metabolic fuel) came from physics. As vitamins came to be better understood, it was recognized that other factors could activate specific steps within metabolism.

As background for the interview with Dr. Bruce Ames that is featured in this issue, Dr. Bland discusses the evolution of the understanding of nutrients. Dr. Ames, who is now considered one of the most-cited scientists, was preceded by pioneers Dr. Roger Williams and Dr. Linus Pauling. Concepts such as biochemical individuality, genetotrophic disease, and orthomolecular medicine are central to understanding how nutrients play roles in the functional health of an individual. Dr. Bland synthesizes the historical information together with more recent examples, including a 2010 article on vitamin D, and a 2009 article by Dr. Ames and his colleague, Dr. Joyce McCann, on vitamin K. REF #1-4

Triage Theory and Vitamin K

Published in the *American Journal of Clinical Nutrition* in 2009, the article by Dr. Ames and Dr. McCann is titled "Vitamin K, An Example of Triage Theory: Is Micronutrient Inadequacy Linked to Diseases of Aging?" Triage theory is a concept Dr. Ames has developed. It is described in the paper as: "The triage theory posits that some functions of micronutrients (the approximately 40 essential vitamins, minerals, fatty acids, and amino acids) are restricted during shortage and that functions required for short-term survival take precedence over those that are less essential. Insidious changes accumulate as a consequence of restriction, which increases the risk of diseases of aging."

For 16 known vitamin K-dependent (VKD) proteins, Dr. Ames and Dr. McCann evaluated the relative lethality of 11 known mouse knockout mutants to categorize essentiality. From this evaluation, they concluded that genetic loss of less critical VKD proteins, dietary vitamin K inadequacy, human polymorphisms or mutations, and vitamin K deficiency induced by chronic anticoagulant (warfarin/coumadin) therapy are all linked to age-associated conditions. A triage perspective reinforces recommendations of some experts that much of the population and warfarin/coumadin patients may not receive sufficient vitamin K for optimal function of VKD proteins that are important to maintain long-term health. REF #5

Clinician/Researcher of the Month

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Dr. Bruce Ames is a Professor of Biochemistry and Molecular Biology at the University of California, Berkeley, and a Senior Scientist at Children's Hospital Oakland Research Institute (CHORI). He is a member of the National Academy of Sciences and was on their Commission on Life Sciences. He was a member of the board of directors of the National Cancer Institute, the National Cancer Advisory Board, from 1976 to 1982. Dr. Ames has been the recipient of many prestigious awards during his career. His over 450 publications have resulted in his being among the few hundred most-cited scientists (in all fields).

Dr. Ames' research involves various aspects of tuning-up metabolism to optimize health. A major contributor to aging is mitochondrial decay due to oxidation of RNA/DNA, proteins, and lipids. In his lab, experiments with animals have led to considerable progress in understanding the mechanism of action of two mitochondrial metabolites, acetyl carnitine (ALC) and lipoic acid (LA). Inadequate intakes of vitamins and minerals from food can lead to DNA damage, mitochondrial decay, and other pathologies. Dr. Ames suggests that evolutionary allocation of scare micronutrients by enzyme triage is an explanation of why DNA damage is commonly found on micronutrient deficiency. He and his colleagues are developing sensitive assays for measuring DNA damage in human blood so as to determine what level of each micronutrient is optimum for keeping DNA damage to a minimum. Dr. Ames feels that an optimum intake of micronutrients and metabolites, which varies with age and genetics, should tune up metabolism and markedly increase health at little cost, particularly for the poor, obese, and elderly.

Dr. Ames was last interviewed for *Functional Medicine Update* in 1999. Dr. Bland asks him to tell listeners about the work he and his colleagues have been doing over the last 10 years. Dr. Ames discusses his ongoing research on aging, micronutrients, and his focus on mechanism, covering a range of topics from vitamin D deficiency to iron excess. He talks at length about vitamin K, triage theory, and collaboration with his colleague, Dr. Joyce McCann, who has published a series of reviews on the developing brain. Dr. Bland calls this interview "iconic." He describes this opportunity to hear from Dr. Ames about his zeal for investigation and discovery a privilege for all. REF #6-16

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