# The Functional Assessment of Nutritional Status: Principles, Practice and Potential

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*The relatively high prevalence of biochemically diagnosed marginal malnutrition has raised the issue of health significance of the so-called "deficient" and "low" values for certain biochemical parameters on which such diagnoses are usually made. In fact, it is well known that many cut-off points suggested as the borderline of adequate intake for a given nutrient are rather arbitrary. They have usually been obtained by studying the distribution of an individual biochemical parameter in the populations with different degrees of clinical appearance of malnutrition, and are meant to represent only the guidelines for expressing the levels of nutrients, not to quantify deficiency status. There seems to be little justification for accepting those cut-off points as diagnostic criteria for the impairment of health status due to the deficiency of a respective nutrient.*[1]

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Malnutrition in various forms—induced by disease or its treatment, by dietary practices or by environmental conditions—is a serious problem throughout the world. Keusch[2] notes that whereas selective deficiencies of specific nutrients can be produced in experimental animal models, deficiencies of several nutrients often occur together in human malnutrition. He states, "Human protein-energy malnutrition (PEM) is in fact a mosaic of alterations in, not only protein and energy nutriture, but in vitamin, mineral and trace element balance as well."[2] Diagnostic techniques for assessing human nutriture have not kept pace with developments in experimental nutrition, and, to some extent, diagnostic assessment has not sufficiently exploited newer knowledge of nutritional biology. In the present review, we examine the concept of nutritional status assessment based on functional indices and make suggestions for the improved application of this approach in clinical and public health nutrition.

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## Static Indices of Nutritional Status

Since it is well-recognized that some period of depletion of body stores precedes the manifestation of classical clinical signs and symptoms of nutrient deficiency syndromes, nutritionists have endeavored to develop sensitive diagnostic tests that reflect the depletion of stores. Most approaches to nutritional assessment of humans are based on the determination of levels of given nutrient (for example, serum iron, plasma vitamin A, hair zinc, urinary N-methyl nicotinamide) or on the measurement of some protein or protein-derivative that is dependent on a given nutrient (for example, whole blood hemoglobin concentration for iron, erythrocyte glutathione peroxidase for selenium, white cell cytochrome C oxidase for copper and urinary creatinine excretion for nitrogen).

Such laboratory determinations of biochemical "levels" of nutrients, metabolites, nutrient-dependent proteins, etc., represent static indices of total-body nutriture, which are, how-

**TABLE I**

**A Systems Classification of Functional Indices of Nutritional Status**

| *SYSTEM* | *NUTRIENTS* |
|---|---|
| *Structural Integrity* | |
| Erythrocyte fragility | Vitamin E, Se |
| Capillary fragility | Vitamin C |
| Tensile strength of skin | Cu |
| Experimental wound-healing | Zn |
| Collagen accumulation in implant sponge | Zn |
| Lipoprotein peroxidation (breath ethane/pentane) | Vitamin E, Se |
| *Host Defense* | |
| Leukocyte chemotaxis | P/E,* Zn |
| Leukocyte phagocytic activity | P/E, Fe |
| Leukocyte bactericidal capacity | P/E, Fe, Se |
| Leukocyte metabolism (glycolysis, iodination, etc.) | P/E |
| Serum opsonic activity | P/E |
| White cell interferon production | P/E |
| Lymphocyte (T-cell) blastogenesis | P/E, Zn |
| Delayed cutaneous hypersensitivity | P/E, Zn |
| Rebuck skin window | P/E |
| *Transport* | |
| i) Intestinal absorption: | |
| Iron absorption | Fe |
| Cobalt absorption | Fe |
| ii) Plasma/tissue transport: | |
| $^{65}Zn$ uptake by erythrocyte | Zn |
| $^{75}Se$ uptake by erythrocyte | Se |
| Retinol relative-dose-response | Vitamin A |
| Post-glucose plasma chromium response | Cr |
| Post-glucose urine chromium response | Cr |
| Thyroid radioiodine uptake | I |
| *Hemostasis* | |
| Prothrombin time | Vitamin K |
| Platelet aggregation | Vitamin E, Zn |
| *Reproduction* | |
| Sperm count | Energy, Zn |
| *Nerve Function* | |
| Dark adaptation | Vitamin A, Zn |
| Color discrimination | Vitamin A |
| Central scotoma | Vitamin A |
| Olfactory acuity | Vitamins A & $B_{12}$, Zn |
| Taste acuity | Vitamin A, Zn |
| Nerve conduction | P/E, Vitamins $B_1$ & $B_{12}$ |
| Skin conductivity | P/E |
| Abducens (VI cranial nerve) function | Vitamin $B_1$ |
| Electroencephalography | P/E |
| Sleep pattern | P/E |
| *Work Capacity/Hemodynamics* | |
| Task performance/endurance | P/E, Vitamins $B_1$, $B_2$ & $B_6$, Fe |
| $\dot{V}O_2$ max | P/E, Fe |
| $\dot{V}O_2$ submax | P/E, Fe |
| Heart rate (cumulative) | P/E, Fe |
| Vasopressor response | Vitamin C |
| *Unclassified* | |
| d-Uridine suppression test | Vitamin $B_{12}$, Folic Acid |

* P/E = protein-energy nutriture

Tests of pathways in intermediary metabolism and those of the whole individual have not been included in this classification system.

TABLE II

Functional Methods for Appraising Nutritional Status

*IN VITRO TESTS OF IN VIVO FUNCTIONS*

Leukocyte chemotaxis
Leukocyte phagocytic activity
Leukocyte bactericidal capacity
Leukocyte glycolysis
Leukocyte iodination
Leukocyte reduction of NBT
Serum opsonic activity
Lymphocyte (T-cell) blastogenesis
White cell interferon production
Erythrocyte fragility
$^{75}Se$ uptake by erythrocytes
$^{65}Zn$ uptake by erythrocytes
Prothrombin time
Platelet aggregation
d-Uridine suppression test
$^{14}C$-formate conversion in lymphocytes
Tensile strength of skin

*INDUCED RESPONSES AND LOAD TESTS IN VIVO*

Experimental wound-healing
Collagen accumulation in implant sponge
Rebuck skin window
Delayed cutaneous hypersensitivity
Antibody formation
Vasopressor response
Radioiron absorption
Radiocobalt absorption
Thyroid radioiodine uptake
Retinol relative-dose-response
Post-glucose plasma chromium response
Post-glucose urine chromium excretion
Mixed-function oxidase ($^{14}CO_2$) breath test
$^{14}C$-histidine ($^{14}CO_2$) breath test
$^{14}C$-serine ($^{14}CO_2$) breath test
Histidine load test for urinary FIGLU
Histidine load test for urinary hydantoin propionic acid
Purine load test for urinary xanthine
Sulfur amino acid load test for abnormal sulfur-containing metabolites
Sodium bisulfite load test for blockage of sulfur amino acid catabolism
Glucose Load: exercise test for lactate and pyruvate accumulation in blood
Tryptophan load test for urinary xanthurenic acid excretion
Leucine load test for urinary 3-hydroxy-isovaleric acid

*SPONTANEOUS IN VIVO RESPONSES*

Dark adaptation
Central scotoma size
Color discrimination
Taste acuity
Olfactory acuity
Abducens (VI cranial nerve) function
Nerve conduction
Skin conductivity
Electroencephalography
Sleep pattern
Muscle function/work capacity
Volatile hydrocarbon excretion breath test
Capillary fragility (Hess) test
Sperm count

*RESPONSES OF INDIVIDUALS OR POPULATIONS*

Work productivity
Lactation performance
Cognitive performance*
Growth velocity
Sexual maturation
Birthweight
Fertility/Fecundity
Social competence

* Cognitive performance as a functional index of nutritional status will be discussed in a companion review article.

true potential as an index of nutritional status will emerge only as an understanding of its components is acquired.[22] To date, however, it has been shown that in vitro blastogenic transformation in short-term culture with mitogenic agents is impaired in PEM[31,36-40] and in zinc deficiency.[41]

A correlation between the production of the endogenous antiviral agent, interferon, by white cells, and severe, but not mild, protein-energy deficiency has been observed.[42,43]

The maintenance of membrane integrity of red cells in vitro in the presence of oxidative stress was first suggested as an index of vitamin E nutriture in 1956.[44] It has subsequently been used to gauge vitamin E nutriture,[44-47] and extended to assess another antioxidant nutrient, selenium.[47,48]