Applications of Nutritional Biomarkers in Global Health Settings

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The global public health burden of micronutrient deficiencies is concentrated within the world’s poorest populations that are now largely confined to Sub-Saharan Africa and South Asia. In these regions, there are multiple overlapping applications for biomarkers of the nutritional status ranging from individual clinical diagnosis, through group screening for targeting interventions, to population surveillance.

Screening for gross nutritional sufficiency of protein-energy supply tends to still focus on simple anthropometric indicators assessing stunting (height-for-age z score), underweight (weight-for-age z score), and wasting (weight-for-height z score), and mid-upper arm circumference. Protein status assessment still relies on crude indicators based on plasma protein concentrations (e.g. albumin), which are insensitive to all except gross protein deficiency. In these aspects, there has been little notable movement towards next-generation indices of the nutritional status. One exception is the use of noninvasive tools to determine body composition, which is crucial for body fat, lean tissue, and muscle mass assessments, with bioimpedance assessment being the only practical method for low-income clinics or field applications.

Assessment of the micronutrient status also remains a major challenge with few significant breakthroughs that have been adequately validated in recent years. The challenges are manifold. First, micronutrients can be divided into type-1 and type-2 micronutrients [1]. For type-1 micronutrients, the category that includes all vitamins and most minerals, physical growth continues in the face of deficiency and hence tissue levels are depleted, and, at extremes of deficiency, characteristic clinical signs become visible. However, these only surface at extreme levels of deficiency. For type-2 micronutrients (e.g. zinc and protein), growth slows rapidly and hence tissue levels tend to be maintained making detection of deficiency very challenging. Second, for many nutrients, the blood levels (the customary biopsy tissue) are homeostatically maintained by reserves in the liver or other tissues. Thus measuring circulating levels of vitamin
A, for instance, provides only a crude measure of nutrient status and is more useful at the population level than the individual level. The modified relative dose response is an example of an innovative test which aims to overcome this problem. Third, the circulating levels of many micronutrients are profoundly altered by inflammation, which raises challenges as to how to correct for these effects especially in low-income settings where infections are common. Such problems over the validity of existing biomarkers for a status create problems regarding the development of new tests; namely, there is no gold standard against which to reference new techniques.

Ideally, next-generation biomarkers would be based on functional tests. Some of these tests already exist. For instance, the erythrocyte glutathione reductase activation coefficient test assesses the percent saturation of erythrocyte glutathione reductase with its riboflavin-derived cofactor flavin adenine dinucleotide. This has been shown to be robustly correlated with the activities of other flavo-enzymes in other tissues thus providing a comprehensive assessment of the status. There are a few other examples of such functional indicators, but others are required.

It appears that the discovery of the iron-regulatory hormone hepcidin provides a step forward in assessing the iron status; consequently, hepcidin is allocated a full chapter in this workshop [2]. A next step will be to develop a point-of-care diagnostic that could indicate ‘ready-and-safe-to-receive iron’.

The Gates Foundation/NIH-sponsored programs on BOND (Biomarkers of Nutrition for Development) [3] and INSPIRE (Inflammation and Nutritional Science for Programs/Policies and Interpretation of Research Evidence) [4] provide excellent resources describing the range of biomarkers currently available and those in development.

References