Nutritional Science: Evolving approaches to Molecular Homeostasis

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ABSTRACT

Consumption of whole organisms by one another forms natural characteristic of food chains and apparent determinant of consistency of basic molecular constitution of live beings through the evolutionary sojourn. Progress in nutrition science appears best in consistency to nature’s health code in whole dietetic patterns, programmed for molecular homeostasis. Food production, consumption and utilization have been changing, posing challenges to address disturbances in homeostasis. With simple beginning of defining standard daily intakes, the task in nutrition science progressively gets complex. Impact of disturbed homeostasis is neither transient nor isolated as revealed by metabolic and genomic studies. It may cover within its fold the vulnerabilities from host-pathogen interactions to genesis of variety of chronic diseases and disability. Multidisciplinary advances in science including recent surge in genomics redefine approaches to address perspectives of molecular homeostasis. The very science of human nutrition however may sail to aspired destinations through disciplined adherence to holistic pursuits with new and traditional means and simultaneous awareness to environmental and social facts besides biomedicine.

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1. Introduction to Dietetic Ecology

Living organisms from the most primitive to the most evolved, exhibit persisting unity in constitution by same amino acids, vitamins minerals etc. Live organisms also constitute food chains for diverse environmental communities in nature, where whole organism (not select pieces) becomes food of another, as order of the nature. Philosophic dicta that ‘we are’ what we eat’ may imply that ‘we eat what we are’. Mahatma Gandhi, the greatest seeker of truth, had intensely experimented on self-sufficient nutritional solution for masses. He promoted resort to barely cooked and unprocessed, self-grown natural whole food consumption. Constancy of basic ingredients in such
diets is now proposed as health secret. Consumption of wide variety of natural foods is means to obtain all that is needed (Williams, 1962). Food in its natural form is a non random mixture of variety of molecular constituents. The latter are assembled in unique community of ingredients as evolutionary processes best suited to maintain life of the organism, which becomes food. Concerted role of biologically determined combination of nutrients and bioactive substances in food has biological implications. Such food synergy concept is perhaps, a natural programming for health (Jacobs, 2011).

Hierarchial choice in dietary consumption is guided by accessibility profile of consumers (Satter, 2007). Food insecure people select foods to fill hunger. It comprises of energy dense items with disregard of nutrient values. Next level of economic strength fosters conscious resort to ordinary food items for consumption on regular basis. More assured consumers embark on food-stock for future. Scope emerges consequently of menu planning, catering to appetite perspective. Novelty of food is still avoided, fearing the risk of food wastage. Higher stratum with enough to enjoy food goes for variety. Choice may be guided by desired physical, cognitive or spiritual gratification. This is exemplified in eating or avoiding particular food items for resisting disease, prolonging life, or enhancement of mental and emotional functioning. Appreciation of individual’s position in the spectrum of food choice hierarchy invokes social and environmental dimensions of nutrition science that is key determinant of success for nutritional counselling. It was long realised that large majority of people would benefit by removal of negative ingredients in diet like, extra oil, sugar etc, even before advent of elaborate wisdom on health needs and provisions. Individuals were categorised as fast and slow oxidizers, who respectively are better with either high protein and fat diet or high carbohydrate diet (Watson, 1972). The subjective phenotyping were attempted through questionnaire, using additional glucose tolerance test. The propositions appear in conflict to current dietary management in diabetes. A category of balanced oxidizers indicate those, who could tolerate wide variations of food.

3. Nutritional Homeostasis and Health

Human disorders implied in premature birth, inherited metabolic disorders, infections, chronic disease, use of medications etc pose special dietary needs to address, over and above the recommended daily intakes. Studies of medical genetics reveal frequent individuals bearing some degree of inherited metabolic aberration, emphasizing nutritional cognizance. Availability in food is itself no guarantee of nutrient functionality, which depends on kinetics and dynamics of the nutrient interacting with biological system. Medical practitioner orthodoxy tends to assume perfect functionality of nutrient system until severe metabolic dysfunction causes overt clinical manifestations. Prospects of restoration are significantly compromised by the time. Nutrition science is study of the totality of relationships between functional (metabolic, behavioural) characteristics of the organism and its dietary environment, focussed on individual nutrients and the diet as a whole. This encompasses study of all processes of growth. Maintenance and repair of living body that depend on assimilation and activity of molecules derived from environment through food (Young, 2003). Nutrition research creates and practice applies scientific knowledge to promote an understanding of the effects of diet on health and well being. Realization of relation of food chemistry to metabolism advanced the biomedical knowledge of nutrition, now traversing through genomics.

Notwithstanding progress on physiological, biochemical, genomic and medical understanding reached the concepts of energy balance, dietary deficiency and inadequacy and quality composition of food are still scientifically fragile. Increasing
longevity and prevalence of chronic diseases calls for new nutritional understanding on how health advantage could be obtained in face of apparent diverse risks.

### 3.1 Assessment of Nutritional Status and Needs

Interaction of constituents of food and diet, as a whole with biological systems provide understanding on strategies to prevent disease and sustain health of individual and populations (Beauman et al, 2005). Patients responding feebly to nutritional measures deserve functionality evaluation of the system, irrespective of manifest specific signs of nutritional disorder. Biochemical individuality, multiplicity of inherited aberrations in nutritional system and hence, need for broader functionality evaluation, then merit consideration. Urinary amino acids reflect biochemistry of the body. By tracing back along described metabolic pathways, some insight to functionality of mineral activators in enzyme mechanism can be obtained. Problems of digestion and possibly metabolism, efficiency of Kreb’s cycle, state of urea cycle etc may be looked at. Food sensitivities are suggestive in patients having difficulty with metabolism of specific amino acid. Problems relating deficient precursor supply for neurotransmitter synthesis may be detected. Heightened patient expectations from the health care agency will progressively dictate depth of the endeavours, and advance of basic and applied knowledge and technology.

While scientific clarity is desirable, results of nutritional interventions are subtle and gradual not dramatic. Enlightened intervention only improves the number of beneficiaries and extents of benefit. Nutrients, especially vitamins act in concert with other factors. Thus, more the information on state of nutrient functionality, more accurate is diagnosis of situation and contemplated therapeutic interventions. Chrono-biologic patterns of some nutrients deserve cognition as kind of effects and their extent would be subject to time of administration during the day. Optimal benefit without adverse consequences depends on correct quantity administered. Kind and degree of environmental variation (i.e. pollution) as well as, level of physical/ emotional stress influence immediate nutrient needs. Dynamicity of demand/ supply balance of nutrients and choice from available food resources is quite challenging in nutritional management. Innovative, integrative, sustainable and cost effective nutritional management is aspired for human well being and health, for which developments in environmental and social, in addition to biomedical perspectives are simultaneously warranted (Beauman et al., 2005; Leitzmann et al., 2005; Wahlquist, 2005).

Homeostatic mechanism allows adaptation to a broad range of nutrient intakes employing regulation to increase absorption and decrease excretion of nutrient. Biochemical measurements are used to assay the balance and functionality of nutrients and recommend standard daily intakes (Food and Nutrition Board, 2001a-c). Surrogate markers of impact of external and internal environments on specific biochemical systems, are valuable means in this context, but only few are currently available for valid functionality analysis. The fact that exercise and diet constitute the most economical and effective measures for chronic disease prevention justifies worth of developing biomarkers for assessment. Advent of genomic analysis would facilitate accurate assessment of qualitative and quantitative nutrient requirements (Sunde, 2001).

### 3.2 Assessment of Nutrient System in Post genomic Era

Impact of nutrient deficit or excess on genome-wide map and the homeostatic genes controlling aberrations in specific nutrients can be identified by use of micro-array techniques (Petrik, 2001). Also the sensors for disturbance in nutritional homeostasis lye encoded in the genome. These may
be defined along with related signalling proteins, enzymes and mRNAs. Analysis of such sensors would yield assessment superior to the biochemical makers. Development of novel nutritional therapeutics for complex nutrient-linked diseases may thus be facilitated (Peltonen et al., 2001). Genome investigation in micro-organisms should reveal molecular mechanisms, underlying particular nutrient requirements, including the homeostatic sensors employed by microbial system. Such new molecular evidence may guide nutri-therapeutic designs in unexplained diseases. Genetics may help identifying select proportion of individuals who will optimally benefit from drug treatments, such as cholesterol lowering agents, and help avoiding undue medication in the rest. Phytochemical’s role in health, beyond that of the 45+ assigned essential nutrients, needs definition as one of the important goals of post genomic sequencing era. Current methods of agriculture, changes in environment and soil, length of time elapsing between picking and consumption of foods, variety of processing, all are seen as mutilating the beneficence of food. Interactions of such and genetically modified foods call for similar studies in present time.

4. Nutrigenomic Application to Infection and Personalised Nutrition

Nutrient status profoundly influences overall health and immune function of the host, as well as pathogenicity of invading microbes. Diet deficient in selenium was found to permit non-virulent invading microbes turn virulent (Beck, 2007). Further explorations in the line bear significant promise for disease prevention. Nutrigenomics would provide new insights to interaction of emerging risk factors with nutrient system, and causal link between diet and disease.

Optimal nutrition has to address basal nutritional needs as well as individual-specific nutritional status and genotypic needs, constituting personalized nutrition. Integration of extremely varied data sources would be needed to offer products for personalized nutrition. Genes decide the direction and perhaps, the limits of biological events which occur amid specific biotic and abiotic environment existing at the time. The assumed view of reality of the investigators also bears on the investigations in such context. Genomic investigations in isolation also suffer disconnect with real life conditions. Practical significance of many genomic findings therefore faces difficulty for application. Biological systems display variety of regulatory mechanisms, almost redundant and universal tendency to homeostasis. Adaption of cell and organ systems to states of deficit or excess of nutrients is well known. Despite genotypic and phenotypic trait, systems of an individual function under influence of multiple genes and confounding factors of the micro and macro environments. Observed genomic reality therefore has to find true sense in functional consequence at organism level. Challenge of personalized nutrition implies understanding interactions within the individual as well as between individual and the dynamic environment. The challenge of do-ability exists at both experimental and application in social world levels. Approach to ease the situation involves classifying categories of individuals. In practice personalized dietetics is aimed at risk groups in population (Booker et al., 1999). Limited individual variations are allowed in such categorization. Besides, categories may be based on diseases, symptoms, geography, gender and age. These can also be based on single nucleotide polymorphism (SNP) or phenotypic markers. In cognizance of hierarchical food resourcing, suggestion is also to consider social, political and ethical dimensions for categorization (Penders, 2007).

5. Difficulties to Address

Any ideation of single molecules, working in isolation of food, violates the food synergy concept. Reductionist researches focus on partial pathways to
facilitate mechanistic understanding. Epidemiologic studies support the virtue of whole food system, integrating a lifetime of intake for long term health of humans. Randomised controlled trials in dietetics suffer from impracticalities for reference controls and blinding. Thus, balanced convergence of evidence from diverse approaches of research may draw relevant inferences. Defining of functional foods for weight reduction, exemplifies this (Choudhary et al., 2012). In children, micronutrient malnutrition causes stunted growth and may be accompanied by metabolic maladaptations that increase the risk of later life obesity and related diseases. In adults, deficiencies in key micronutrients may promote oxidative stress. Folate deficiency may increase the risk of heart disease. Zinc deficiency is exacerbated by diabetes and further worsens the glucose transport. Low fruit and vegetable consumption increases additional risk of cardiovascular diseases and cancer by variety of mechanisms. Epigenetics promises attractive tool to preventive nutrition in paediatric developmental diseases as well as to delay aging associated processes including cancer. In broad range of diseases as type 2 diabetes, obesity, inflammation, neurodegeneration etc, epigenetics is opening avenues for use of nutrients and bioactive food components for maintaining health and preventing disease through modifiable mechanisms (Choi et al., 2010).

As of now, most fundamental questions about diet-health interactions await adequate quantitative answers. Molecular evidence combined with epidemiologic data on diet-disease-risk relation may, in some cases, obviate need for randomised controlled trials. Pooled analyses of case control and cohort studies on diet disease relationship are very helpful in defining dose-effect relations. Amid climatic change and agricultural practices causing alterations in food constituents and rampant adulterations, much interest is aroused in functional foods, which bear characteristic for health enhancements in one or more respects. Nutrient metabolites have also come under research focus for serving vital roles (Menon et al., 1984). Greater diversity of consumed food is known to associate with greater health adjusted life expectancy readily seen in Australians (Mathers et al., 2003). As climate changes forecast dramatic changes in food patterns, new foods would need to be developed in new ways. Impact of environmental pollution on nutritional biochemistry is brought in focus by obesogenic consequence of endocrine disruptors widely prevailing in environment, which exhibit alarming low dose impacts (Teng-Peronard et al., 2011; Vandenberg et al., 2012). Growing spate of chronic diseases with inflammatory component particularly claims consideration in selection of foods in days to come. Advent of molecular sciences has helped to reveal biologically crucial potentials of food items neither to believed as inert and unimportant. New explanations for nutritional distortion and diseases and new ways of managing them would continue to emerge with modulatory perspectives of nutrition in various pathologies. Biotechnology would endeavour to make alternative food analogues, but simultaneous development of food based strategies for their use must be conceived to avert consequences of food dyssnergy. Food fortification and processing will similarly have to be conscious of the phenomenon.

Homeostasis is natural defence against short term perturbations in nutritional biology but long term inactivity or aberrant dietary pattern gradually erodes homeostatic mechanisms increasing body fat and other health risks. Imbalance between prenatal and postnatal nutrition may distort homeostatic limits and low birth weight babies have propensity to suffer diabetes and hypertension in later life (Lithell et al., 1996; Philips, 1996). Under-nutrition in adults too lowers homeostatic capability exemplified by higher health risk in people of Asian origin than their Western counter parts at same level of BMI or waist circumference (Seidell et.al 2001).
Ultimately, optimal intake of specific dietary factors will continue impacting health policy and education. Sustained generation of evidences and their objective interpretation shall remain time tested approach with employment of new technology as knowledge to resolve issues of molecular homeostasis in human nutrition.

6. Conflict of interest

There are no conflicts of interests among authors.

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