Nutrition and Chronic Disease: Lessons from the Developing and Developed World

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Preceding papers in this symposium will have made the case that the very rapid demographic and nutrition transition affecting many emergent countries is precipitating a ‘double burden’ of disease. This double burden – the unfinished agenda of infectious diseases and the emergent agenda of chronic diseases – is a major threat to the development of nations. The fact that developed nations have previously travelled down this road of abundant, low-cost, highly refined, energy-dense diets combined with sedentary lifestyles, leading to fat gain and its associated morbidities, should hold lessons that could be used to slow the growing pandemic of noncommunicable diseases. Conversely, knowledge gleaned from studying the rapid dynamics of change in developing countries may help us to understand causal pathways with potentially important lessons for affluent societies. What are these lessons, and can we learn them fast enough to have a meaningful impact on global public health?

The issue of genetic variation clearly needs to be addressed when drawing comparisons between nations. There is strong evidence that Africans and South Asians are more prone to diabetes, and global mapping of diabetes susceptibility variants do show a concentration of such alleles in these regions. Africans and African-Americans are more prone to hypertension than Caucasians, and the search for the causal alleles is starting to reveal major findings; though the etiology remains largely unknown. The wide diversity of disease phenotypes (i.e. subvariants of hypertension and insulin resistance/diabetes) especially in populations of African origin is also helping to map pathways of disease causality through genome-wide and phenome-wide association studies. The putative existence of thrifty genes is frequently invoked to explain the rapid transition towards obesity in urban Africans and South Asians, yet some of the known obesity-pre-disposing gene variants are less common in these populations. It is also a misconception to suggest that areas associated with recent famines and
food shortages (i.e. Africa and the Indian subcontinent) would have been under greater pressure to select thrifty genes. Historically, all populations worldwide have been under gene selection driven by famine.

Epigenetic variations are currently viewed as likely mediators of the known associations between early-life nutritional exposures and later disease – the DOHAD thesis. This topic represents another good example of where research in rapidly developing nations can have global implications. Some of the first proof-of-principle studies in humans are demonstrating that alterations in nutrients involved in maternal methyl-donor supply (choline, betaine, methionine, folate, vitamins B\textsubscript{2}, B\textsubscript{6} and B\textsubscript{12}) do affect methylation patterns of the offspring. Such studies are often more tractable in populations with naturally low intake levels. The phenotypic and health implications of these changes are far from being understood, but a key emergent message is that different dietary practices can lead to a range of imbalances in methyl-donor metabolic cycles and that there will not be a single solution to optimizing such diets. For instance, B\textsubscript{12} deficiency (especially against a background of folate repletion) appears to be a major issue in rural Indians but not in rural Africans.

Irrespective of the epigenetic mediators of early-life programming, there is still much to be learnt about the mechanisms by which early-life nutritional exposures affect later disease risk. The compression of the timeframe in which emerging societies are being exposed to affluent diets and lifestyles offers special opportunities to interrogate these mechanisms further, and considerable research is in progress concerning the long-term effects of nutritional deficits and excess as an individual passes through the various phases of the nutrient supply chain (histiotrophic, placental, mammary, weaning and through to adult diet). Matriline (and possibly patriline) influences on the capacity of such processes offer the opportunity for intergenerational effects on chronic disease outcomes, and these are also easier to study in rapidly transitioning societies, but with lessons applicable globally.

The ultimate aim of all such research is to inform public health interventions that can reduce the penetrance of chronic diseases for future generations. Whether such interventions can be effective against the inherent propensity for gluttony and sloth in human populations remains to be seen.