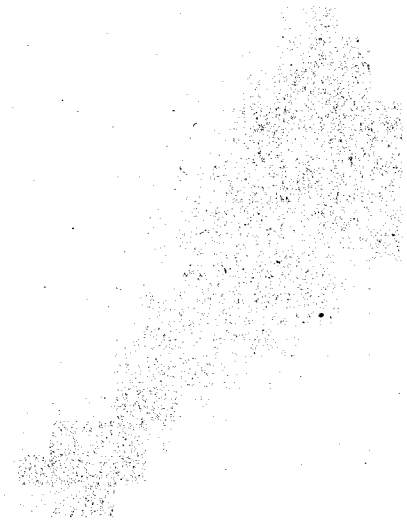

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Functional Foods and Their Impact on Nutrition and Health: Opportunities in the Asia Pacific

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PEOPLE IN ASIA

Countries of the Asian Pacific region have a wide range of nutritional status, with some countries wrestling with problems of undernutrition (like Cambodia, Myanmar, and Papua New Guinea), and others suffering more from health problems associated with overnutrition (such as Australia and Singapore). In between are countries (such as China and Malaysia), where the transition from a closed economy to an open economy takes place, the so-called "diseases of affluence" (obesity, diabetes, cardiovascular disease, osteoporosis, and certain cancers) may coexist with those of "undernutrition" (protein-energy malnutrition, micronutrient deficiency, and food-borne illness). This phenomenon of the double burden of disease is now increasingly common.[1] This requires the application of a

new paradigm, arguably one that more effectively relates the human condition to the environment.[2] There is great potential to address both sets of problems through nutritional means.

KEY PUBLIC HEALTH NUTRITION ISSUES IN THE ASIA PACIFIC REGION

Transitional Health

The emerging nutrition problems in the Asia Pacific region are probably partly explained by the Barker hypothesis, also referred to as the thrifty phenotype hypothesis.[3,4] It is postulated that nutritional transition begins *in utero* where the mother is exposed to nutritional inadequacy. In response to maternal and fetal malnutrition, there are adaptive changes, in order to survive, in fetal organ development. These adaptations may permanently alter adult physiology and metabolism in ways that are beneficial to survival under continued conditions of malnutrition, but detrimental when the food supply is abundant. This fetal "programming" is thought to lead to increased rates of coronary heart disease, hypertension, insulin resistance syndrome, noninsulin-dependent diabetes, obesity, osteoporosis, and some cancers later in life.

Urbanization and its Effects

This social change has a remarkable effect on diet in the developing countries. Urbanization increases labor-force participation of women and it indirectly affects the diet of the family.[5] Whereas the food supply of rural populations comes from its own food production, the food supply of urban populations has to be purchased, and more processed, rather than represent fresh animal products and garden produce.[6]

Changing Demography with an Aging Population

There are increasing numbers of people in communities that age to 70, 80, and beyond. Thus, it is increasingly important to understand the relationship between food and health in later life.

Food Security

Without the ability to stay near the place of food production there is not the same scrutiny of the food supply. People become increasingly dependent on others to produce food and become more vulnerable from a health point of view.

Loss of Traditional Food Culture

One of the great threats to human civilization is that food diversity may progressively diminish.

OPPORTUNITIES FOR FUNCTIONAL FOOD DEVELOPMENT

Thousands of products with supposed health benefits, ranging from the nutritionally beneficial to the fraudulent, are already available in the world market, and the number of products is soaring. Science and technology, agriculture, food manufacture and markets are driven by the belief and actuality that food characteristics are relevant to health.[7]

It is proposed that food-health relationships could be categorized for the purposes of functional food development.[8] The extensive list of general and particular possibilities and roles for foodstuffs (Table 1.1) was presented to and discussed at a Joint FAO/WHO Workshop on Novel Foods in Nutrition Health and Development: Benefits, Risks and Communication.[9] Some of these relationships are pertinent to the key public health issues in the Asia Pacific region.

Food Shortage and Malnutrition

A 1997 report by the International Food Policy Research Institute predicted that by 2010, every 20th person in East Asia is likely to have an insecure food situation.[10] Pervasive poverty rather than food shortage is frequently the underlying cause of hunger, limiting an individual's access to food. Poverty also exacerbates access to education, health care services, and a clean living environment, while malnutrition coupled with a poor education often impairs employment, in turn earning prospects, and ultimately there is less money to buy food.

Table 1.1 Categorizing Food–Health Relationships for the Purposes of Food Product Development (8)

Health Category	Food Characteristics
Disease related to environmental degradation and methods of food production	Eco-sensitive foods (e.g., produced in sustainable ways; biodegradable or edible packaging; identifiable biosecurity for animal-derived foods; nature of genetic material)
Food shortage and PEM (protein-energy malnutrition)	Technologies which minimize postharvest loss, increase shelf life and maintain palatability
Disease related to protein quality, fat quality and micronutrient status	Nutrient-dense foods; fish or its plant or microbial food surrogates
Physical inactivity and health (especially over fatness; also loss of lean mass, particularly muscle)	Food of low energy density and high nutrient density
Phytochemical deficiency disorders including menopause, macular degeneration, osteopenia	Greater emphases on plant-derived foods and their variety
Diseases of changing demography	
• Aging	Anti-aging food, especially ones to delay body compositional change (bone, muscle and fat); loss of sensory function; decline in immune function; proneness to neoplastic disease; decline in cardio-respiratory function; and decline in cognitive function; and anti-inflammatory foods
• Rapid loss of traditional food culture and acquisition of new food cultures	Maintenance of traditional foods in convenient, affordable and recognizable form
New psychosocial stressors and mood change	Food which favorably affects mood
Food-borne illness and the microbiological safety of foods	• Pre- and probiotic foods • Immune system enhancing foods
Illness related to the chemical safety of foods (e.g., pesticide residues)	Regional origin and certification of foods

Biotechnology can greatly advance staples farming, and undoubtedly, the production of functional foods is a ray of hope in the fight against malnutrition. Genetically improved foods with a higher yield and more resistance to diseases and insects have the capacity to alleviate food insecurity and malnutrition in the world's underfed populations. More resources and research need to be directed toward resolving these problems in developing countries.

Food fortification has been a major and integral food-based strategy to eliminate micronutrient deficiencies, especially iodine deficiency disorders, vitamin A deficiency and iron deficiency anaemia, in developing countries and an increasing number of developed countries. Recently, biofortification has been proposed to combat micronutrient malnutrition. Supplying micronutrients to vulnerable populations by using conventional plant breeding and biotechnology is low cost and sustainable. "Golden Rice" is an example of biofortification through gene manipulation to improve nutritional value, vitamin A in particular. Genes from the daffodil and a bacterium were introduced to the rice line to complete the biosynthetic pathway to β-carotene, a provitamin A carotene.[11] The insertion of these genes into rice to express β-carotene was necessary because parts of the pathway had been lost, although the downstream parts of the pathway were still expressed. The resultant transgenic rice line synthesizes enough β-carotene in the endosperm to meet part of the vitamin A requirements of people dependent on rice as a primary food staple.

At the same time, the rediscovery of hundreds of natural "yellow" rice cultivars, which may have the missing genes, has encouraged the study and propagation of rice varieties that can be used as natural food sources of provitamin A carotenoids.[12] Production of added value grains of this type is likely to be their provision of a wider array of carotenoids with wider health benefits than the prevention of vitamin A deficiency.[13] As grains richer in other micronutrients, like iron and zinc, are identified in seed banks and libraries and in traditional communities, the prospects of safe and effective biofortification in the food supply would increase.[14]

Overweight and Obesity

At the other end of the malnutrition scale, obesity threatens to become the leading cause of chronic disease in the world. The health consequences of obesity are well known. For more than a decade, dietary guidelines advising a reduced fat intake to no more than approximately 30% of total calories have been issued in developed countries. This triggered a proliferation of low-fat, fat-reduced, and fat-free food products targeted for consumers seeking a more healthy diet.

However, the role these foods have to play on a population basis is less clear. In many countries, total fat consumption as a percentage of calories has slightly declined on a population basis, while total calorie intake has risen, along with the prevalence of obesity.[15] There are too few prospective studies to conclude that dietary fat plays a role in the development of obesity. Epidemiological analysis of nutrient intake and obesity provide inconclusive results that high fat/low carbohydrate diets lead to the development of obesity.[16]

Body fatness may be altered by a number of food factors; they are either physico-chemical or chemical, with mechanisms of action that alter energy or food intake, energy expenditure, or the deposition of fat in various anatomical sites. Food factors could alter energy intake by suppressing or stimulating appetite, or by interfering with or enhancing absorption or utilization of energy (Figure 1.1). Simply using a wide range of foods, rather than bland food, can stimulate appetite without excessive energy consumption, and it can be associated with lower body fat, provided that the foods have low energy density.[17] This can be achieved by changes in the organoleptic properties of food, this being the taste, smell, and texture, and even the sound of chewing, which influence food intake. In addition, there may be various anorectic properties of food, operating in the central nervous system at cortical or subcortical levels, notably at the level of the hypothalamus and pituitary. Examples of compounds in food with such properties include xanthines (caffeine in tea and coffee, and theobromine in cocoa), and small peptides with opioid activity derived from gluten, β-casein, and compounds found in coffee

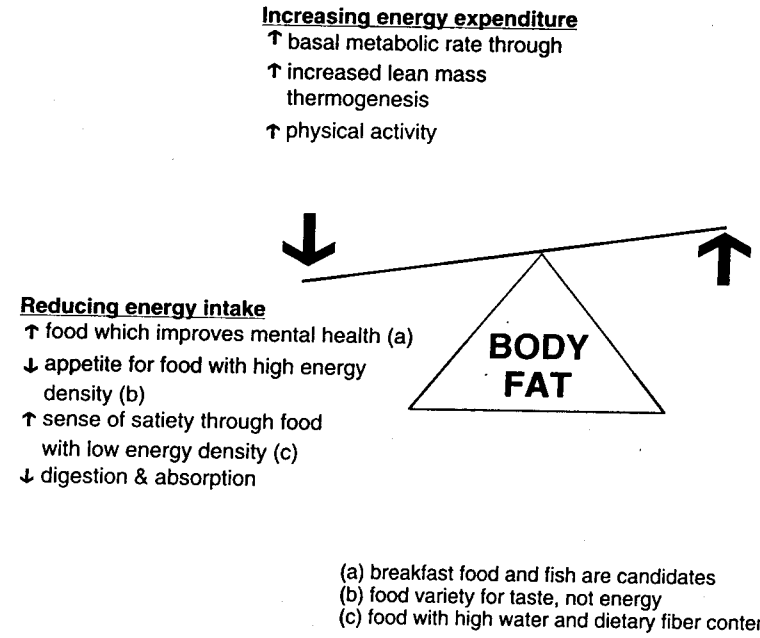

Figure 1.1 Ways for food factors to alter energy balance safely.

with roasting or brewing.[18] Supplementation with garlic (*Allium sativum*) for 12 weeks was found to reduce fat and carbohydrate intakes in mild or moderate hypercholesterolemia.[19] The choice of food may also affect energy expenditure.

Food could potentially affect basal metabolic rate, thermogenesis, and physical activity (not only exercise, but also fidgeting, gesture, and other self-paced activity). Certainly one component of energy expenditure can be attributed directly to food; this is the difference in thermic response to various foods which may, in part, offer a basis for preference in macronutrient choice, with fat being least and protein most wasteful of energy in this respect. Capsaicin found in chilli (*Capsicum frutescens*) or red pepper (*Capsicum annuum*) may increase thermogenicity, principally by way of effects on the vasculature,[20,21] and consumption of red pepper has recently

been reported to decrease energy intake as well.[22] While caffeine has the potential to reduce energy intake, it also stimulates the central nervous system and cardiac function, resulting in an increase in spontaneous activity and consequently energy expenditure. Additionally, caffeine is known to enhance physical performance, so that food and beverages containing it may, in this way, increase energy expenditure (Figure 1.1); this may be more in evidence when the food provides liberal carbohydrate for glycogen stores in muscle and liver. The combination of red pepper and caffeine in foods is now attracting attention in relation to energy balance.[23] Precaution should, however, be taken with the ingestion of large doses of caffeine present in certain foods and diet pills, as it can induce cardiac arrhythmia.[24]

It is generally agreed that fat intake is a significant factor in allowing energy imbalance. In addition, reduction in fat intake together with total energy intake can favorably influence body fat. The best indicator of energy balance in humans is the measure of body storage fat. But not only is the total amount of body fat important for human health, so too is the distribution of body fat. An increase in the polyunsaturated (principally *n*-6) and saturated fat ratio in serum phospholipids in overweight men has been found to predict a decrease in body mass index,[25] and *n*-3 fatty acids are less prone than other fat to increase truncal fatness in rodents.[26]

Phytochemical Deficiency Disorders

The use of plants for health promotion has been known in food cultural folklore for many centuries. However, only a limited number of biologically active compounds, known as phytochemicals, have been identified in plant food. For most of these compounds, their mechanisms of action are not clearly understood, and sometimes it has been difficult to reproduce their therapuetic benefits. In the mid-1980s, the link between coronary heart disease and diet focused exclusively on the lipid hypothesis or the theory that high blood lipids were a significant risk factor in cardiovascular disease (CVD) morbidity and mortality.

A considerable number of epidemiological studies in recent decades suggest that the high consumption of fruit and vegetables (as a collective term), or in some studies, of specific vegetables, is associated with low morbidity and mortality from CVD and certain cancers.[27–29] New analytical technology and advances in molecular biology have identified phytochemical components of popular foods used in health promotion that may explain traditional health benefits and help quantify their effects. A problem in considering the place of phytochemicals in human health is that they are numerous, alongside a few known essential nutrients, and, therefore, their net interactive effect ultimately requires a study of food itself and food patterns,[30] or that the intake of food components be subjected to sophisticated mathematical modeling. However, the advent of advanced informatics may help resolve this dilemma[31].

While evidence continues to emerge showing that the intake of certain foods and their constituents can have profound physiological effects, including the potential to prevent or delay the onset of chronic diseases such as CVD and certain types of cancer, the role of specific food phytochemicals in the prevention and/or treatment of health conditions is rapidly unfolding.[32] Compounds found in fruits and vegetables, such as polyphenols in fruits, isoflavones in the legume soy and β-carotene in vegetables, have been considered to be the responsible active compounds. However, several intervention studies have shown that ingestion of some of these isolated compounds, in tablet or capsule form, cannot confer similar health benefits to those observed with the intact food from which they come.[33–35] Studies of intact foods on health outcomes, like those with whole grains on diabetes and CVD, support these findings.[36–38] The similar dichotomy between ingredient-based phytochemical-rich foods and the administration of isolated phytochemicals is illustrated by the field of phytoestrogens and menopause. It was demonstrated in the late 1980s that certain foodstuffs (soy flour, flaxseed, and red clover as sprouts) could exhibit estrogenic effects including improving vaginal health and decreasing pituitary follicle stimulating hormone production in postmenopausal women.[39]

Thereafter, there have been those who have favored food ingredient-based studies and applications, especially bone health and breast cancer protection, to women's health[40–42] and those who have pursued a more nutraceutical or pharmaceutical approach.[43,44] The risk–benefit ratio in each case is quite different, with more checks and balances on intake in the phytochemical-rich food ingredient approaches than with encapsulated phytochemicals.

When particular bodily functions or disease processes are considered alongside the phytochemical or other nonnutrient food components, which may modulate them, the potential for making better use of basic food commodities and of relevant functional foods becomes apparent. The nutritional trend is increasingly shifting to use protective foods to prevent and manage diseases rather than to depend on exclusion of detrimental items. This may equally be the focus of prevention and management of phytochemical deficiency.

Disease of Changing Demography

Aging

There is a worldwide increase in the proportion of people in the older age groups. It is predicted that by the year 2020 people over 65 years in some countries, such as Japan, will comprise nearly one-quarter of the population. Socioeconomic progress and advances in medical care have apparently underpinned this increase in longevity, but it is also likely that it has been facilitated, in part, through food availability and quality. With the help of micronutrients, phytochemicals, and probably other compounds, it is hoped that people will live longer and remain healthier.

Although aging appears to be an inevitable, natural process programmed into the genes, many of the changes are partly the result of lifestyle or environmental factors. As people grow older, a decline in muscle mass and increase in body fat tends to occur. A major contributor to these changes is the increasingly sedentary nature of lifestyle. Appropriate health promotion strategies that encourage desirable food habits and other lifestyle factors need to be implemented to maximize the quality of life for elderly populations and reduce the cost of health care.

Particular food patterns have not only been able to predict overall mortality,[30] favorable patterns have also been shown to reduce mortality. Studies have shown that consuming a wide variety of foods, especially plant foods,[45] and having a proportionately higher intake of plant foods relative to animal foods is associated with longevity.[30,46,47]

Loss of Traditional Food Culture

Economic development together with recent technological innovation and modern marketing techniques have modified dietary preferences, and consequently, led to major changes in the composition of diet. There was a shift toward high fat, refined carbohydrate, and low fiber diets. The accelerating factors for the rapid transition include globalization, e.g., exposure to the global mass media, shift in occupational structure including the trend from labor-intensive occupations and leisure time activities toward more capital-intensive, less strenuous work and leisure. The globalization of human diet is very much a combined outcome of cultural sensory preferences coupled with the greater availability of cheap fats in the global economy and rapid social changes in the lower-income world. As people move into cities, their food supplies change, and therefore, so do their diets and body composition. Traditional staples are often more expensive in urban areas than in rural areas, whereas processed foods are less expensive. This favors the consumption of new processed foods. The shift from traditional staples to processed foods in urban areas is also strongly enhanced by the advocacy of western culture through mass media, commercial marketing and through other channels related to globalization.

Food acculturation normally occurs when a population has migrated and established itself amongst a majority food culture, and consequently, the loss of traditional food culture.

An example can be seen from the Asian migration to Australia. There has been a decrease in energy expenditures, an increase in food energy density (through increased fat and sugary drink consumption), and a decrease in certain health protective foods (lentils, soy, green leaf vegetables) and beverages (tea), amongst Asians in Australia. However, food acculturation with migration is generally bidirectional. The process of "Asianification" of Australian eating patterns has been evident through fresh food markets and groceries, restaurants, and the development of household cooking skills. The great advantage of Asian migration to Australia, for the majority population, has been the increased diet diversification, most of which has been with rice, soy, green leafy and root vegetables, and various "exotic fruits."[48]

Depression and Mood Change

The World Health Organization (WHO) estimates that depression is one of the major single causes of disability worldwide. Loss of appetite and loss of interest in surroundings and social relationships occur in depression. The risk of being depressed is rising rapidly in developed countries, for reasons that are unknown. There is a growing body of evidence to suggest that *n*–3 fatty acids may play an important role in the etiology of depression.[49–51] The variation in the prevalence of depression found in different countries appears to relate to fish consumption.[52] For example, in Japan the prevalence is 0.12%, whereas in New Zealand the prevalence is 5.8%; fish consumption is 67 and 18 kg per person per year, respectively.

Several nutritional factors appear to be associated with mood. Carbohydrates have been shown to influence brain serotonin levels, and in individuals under emotional stress like depression, a preference for sweet simple carbohydrates has been demonstrated. One particularly striking observation is that total long-chain polyunsaturated fatty acid levels in plasma are positively related to cerebrospinal fluid 5-hydroxyindolactic acid, the main metabolite of serotonin, a neurotransmitter involved in mood control.[53]

Immunodeficiency

Nutritional immunoenhancement is relevant to chronic infectious conditions that are characterized by multiple nutrient deficiencies. In some situations like inadequate food or nutrient intake, excessive nutrient loss or increased nutrient demand, immunodeficiency may be reversible by nutritional means, to the extent that it has been nutritionally caused.[54,55] However, impairment of immune function can be caused not only by deficiencies of various nutrients, but also by imbalances of nutrients, such as iron excess and changes in the ratios of *n*-3 to *n*-6 fatty acids.[56,57] There are many potential therapeutic applications of specific nutrients for immune defence. The *n*-3 fatty acids are of interest as anti-inflammatory agents, acting at least partly by influencing leukotriene and prostaglandin balance.

Another area of nutritional immunoenhancement would be fermented foods. The link between fermented foods and longevity received interest over a century ago, and the idea of beneficial gut microflora was introduced. Fermented milks and yogurts are consumed worldwide and research has shown them to be associated with various physiological benefits such as regulation of intestinal peristalsis and alleviation of the symptoms of lactose intolerance. Study of the organisms contained in fermented foods led to the concept of probiotics, which can be defined as a live microbial food ingredient that, when consumed in sufficient quantities, exerts health benefits on the host beyond basic nutrition.[58] Probiotic therapy has been implicated in enhancing the colonization resistance of the gut microflora against intestinal pathogens such as *Helicobacter pylori*, *Salmonella sp.*, *Clostrolidium difficile* and rotavirus infection, gut and systemic immunity, as well as colonocyte nutrition from the lumen. However, there is still divided opinion about the general effectiveness of lactic acid bacteria in promoting human health. Differences in strains, dose, model systems, and stringency of data interpretation have led to some of the inconsistencies in conclusions. In the meantime, although research support is lacking for many claims about live bacterial culture-induced promotion of intestinal

and human health, products containing such cultures are marketed successfully worldwide.

HEALTH CLAIMS AND SAFETY CONSIDERATIONS

The social, food, nutrition and biomedical sciences allow for increasingly rational product development to fit consumers' health needs. The development of new food products brings with it elements of the unknown and therefore risk. However, when it comes to foodstuffs and beverages, it is expected that the risk will be negligible. Monitoring and surveillance is a requisite of any community that is exposed to products launched for purported physiological or health reasons.[59]

In order to optimize the risk–benefit relationships of functional foods with definable health properties, the following approach has been recommended by a Joint WHO/FAO Working Group on Novel Foods in Nutrition Health and Development: Benefits, Risks and Communication, and published in the Metung Report.[60]

1. Consider the health outcome in question
2. Select a plant food or foods, which confer these characteristics, preferably with an established food cultural base
3. Formulate a food for trial
4. Carry out a risk evaluation
5. Conduct a food trial using biomarkers and/or health outcomes
6. Develop an appropriate monitoring and surveillance strategy
7. Seek regulatory approach as novel food for safety
8. Formulate a food-based educational and informational framework, with or without health claims (depending on regulatory regime)

In all cases, affordability and sustainability should be considered. These considerations will be increasingly important as food novelty and related health opportunities become more evidence.

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