

Nutrition and Health: New Imperatives for Clinical and Public Health

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Nutrition and health is undergoing a major shift. Nutrition science which underpins nutrition and health is at a watershed. The way in which this watershed will affect both public health and clinical work will be enormous.

One of the most interesting phenomena of this century has been the marked improvement in life expectancy — undoubtedly attributable to improved availability and quality of food. It is interesting to know that today the Asia-Pacific region, Japan, Hong Kong, Australia and New Zealand have amongst the world's greatest life expectancies. Hong Kong is perhaps the most remarkable of all, because it has achieved this status very quickly and in an urban setting, which shows that urbanisation, with all of its problems, is not necessarily alien to improvement in life expectancy or, perhaps, to an associated relative absence of morbidity.

There is a reconceptualisation of the nutritional pathogenesis of disease taking place and one of its highlights is that we now know a number of nutritional determinants of gene expression; molecular nutrition is very much on the move. There is also great interest in how the nutritional status of the mother affects fetal and childhood development, beginning with conception[1-5]. At the other end of the line, longevity is increasing and there is increasing evidence that it is possible to compress morbidity towards the end of life through lifestyle modifications[4] and that, as we

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live longer, we need our food to be as safe as possible for that period of our lives as well. The safety we seek is microbiological, chemical and nutritional.

1. DILEMMAS CONFRONTING NUTRITION AND HEALTH

There are a number of interesting and important dilemmas confronting nutrition and health. The first of these is that increased longevity in communities is associated with a paradoxical increase in a number of diseases, even from an age-adjusted point of view. It is also associated with a generally abundant and varied diet, with its own advantages and disadvantages.

The second dilemma is that obesity and its complications are becoming endemic as we live longer. The increase in prevalence of overweight and obesity combined (BMI greater than 25 kg.m²), in Australia, judging from the National Heart Foundation and National Nutrition Surveys of 1983 and then, most recently, of 1995, is dramatic to say the least[7,8]. In 1995, the prevalence of combined overweight and obesity amongst middle-aged Australian men was over 70% and for women, it was in excess of 50%. Around the world, in some industrialised countries, the prevalence of BMI over 30 is now of the order of 20%, notably in North America, the Middle East and Eastern Europe.

Another dilemma is that we have regarded increased stature as an important signal of nutritional adequacy. Much of the focus on childhood nutrition is to achieve maximal stature, but there is an emergent literature which despite saying that cardio-protection and longevity are conferred by increased stature, also finds that increased stature may confer increased risk of certain cancers in later life, especially breast cancer in women, so that we need to work out optimal growth[9,10].

Fourthly, there is the concept of a dietary "best practice". The globalisation of this idea, which may or may not be correct, is beginning to run counter to the quest for retention of food cultures, for biodiversity and sustainability.

Fifthly, nutrition in early life and its later life consequences is now to the fore. The Barker hypothesis is well known to most of us by now[1-5]. It has to do with maternal nutritional deprivation, low birth weight and growth retardation in the first year of life as precursors of chronic non-communicable diseases like obesity, especially abdominal obesity, non-insulin dependent diabetes and macrovascular disease. The mechanisms through nutritional modulation of foetal gene expression are becoming clearer.

Also, for early childhood rearing, we have interesting data because of registries of both adoption and twins who may be identical or non-identical and adopted or not adopted. The Swedish Twin Registry is such a registry and a landmark study has been published by Heller and others entitled "Genetic and environmental influences on serum lipid levels in twins"[10-11], but there is more to it than its title suggests, because what the paper shows is that lipoprotein status over the age of 50 is dependent on early childhood rearing, and not, as might have been thought, on genes alone, or even later life environment. This is particularly evident for HDL cholesterol concentrations where something must operate in early life to alter gene expression, and this could conceivably operate at the family or community level. There has, therefore, probably been an overstatement of what was genetic from basic twin studies which did not have the advantage of adoptive analysis, relevant to a number of factors, nutritional and other lifestyle, which operate in early life.

An important dataset shedding light on the consequences of early development, measured as growth, is the Boyd Orr Cohort Study which is now managed at the Rowett Laboratories in Aberdeen and began in the early 1930s. One of the papers from this work published in 1998 identifies a linkage between stature, energy intake and cancer risk[4]. Then, there is the Dundee Infant Feeding Study by Andrea Wilson and co-workers which shows that breast feeding, or the lack of it, is a determinant, at a median age of 7.2 years, of percentage body fatness, which in turn, from Finnish data, is a determinant of adult obesity and the "insulin resistance syndrome[12]. The Dundee study shows that if solids are introduced before 15 weeks there is increased body fatness 7 years later. Further, of particular interest from a nutritional point of view, is that the probability of childhood respiratory illness, including asthma depends on the number of weeks of breast feeding, being protective[13]. The search for factors which might be increasing the problem of childhood asthma might thus be provided a clue. Not only do these studies emphasise the importance of breast milk, but provide a stimulus to understand the limitations of dairy products and their components, and the prospects of humanized cow's milk.

2. EMERGENT UNDERSTANDING OF FOOD-HEALTH RELATIONSHIP

Some of the dilemmas identified raise our interest in a broader spectrum of food-health relationship. Most nutrition concern this century has been about micronutrient deficiency and also protein and energy deficiency. Food deprivation has led to impaired growth and development, maternal and childhood mortality. Protein and energy

malnutrition (PEM) and its sequelae, especially immunodeficiency and infection, and various micronutrient deficiencies still account along with PEM for most of the nutritionally-related diseases in the world and, with infection, the two most important disease patterns in the world, which encompass iron, iodine, vitamin A, vitamin D, zinc and folate deficiency disorders. Perhaps not entirely nutritional, but the frail aged constitute one of the important new world health problems contributed to by food deprivation, and also by physical inactivity[14].

Foodborne illness has not received a great deal of attention in industrialised countries and is thought to be principally a problem of the developing world, but is attracting a great deal of attention all the way around the world as a food safety issue. Foodborne illness in nutrition is much more than microbial contamination or inadequate hygiene. There is interest at the moment in how a healthy intestinal microflora might be maintained by the ingestion of live bacteria (probiotics) and, perhaps even more importantly, by their dietary substrates (prebiotics), which are ingredients in foods like oligosaccharides and are able to stimulate a favourable flora in the colon. There is also renewed interest in food antimicrobials, not the ones that are antibiotic contaminants, but the host of factors in food which are antimicrobials and, interestingly, many located in herbs and spices[15]. Individual susceptibility to food borne illness in relation to nutritional status is also an important issue.

If one were to take just one area of food safety as an example of the growing complexity in the thinking about food and health and how one might handle it from a public health point of view, the question could be asked how might one eat meat safely, given some of the concerns about microbial contamination on the one hand and about chronic non-communicable disease on the other. Firstly, one can say that preference for low fat meat is a way of contributing to less chronic non-communicable disease. Cooking is a way of ensuring microbiological safety, although the entire business of bovine spongiform encephalopathy (BSE) is an issue which we have not adequately understood as yet, but sets some interesting scenarios for food borne disease. Recent data in the UK suggest that there may be spontaneous advent rates for BSE of something like one per million of a cattle herd, making it possible for unaffected herds in Australia to be infected unless there is good herd management practice, a prototype of new ways in which we have to think about managing the meat supply. There is a clearer definition now of those components of meat which contribute to increased risk of large bowel cancer, in particular those derived from creatinine, the heterocyclic amines, and an even greater interest in how their content in meat might be minimised by cooking with compounds in food which might reduce the formation of these. Increasingly, it is recognised that flavonoids derived from fruit and vegetables can reduce their formation; therefore,

it is not just a matter of meat and whether it is cooked or not, but how it is cooked.

Another issue is about meat and the world food supply. There is a growing awareness that it is not only for health reasons that the UK Committee on Medical Aspects of Food (COMA) and the World Cancer Fund have proposed preferred ranges of meat intake somewhere between 80 and 130 g per day. On environmental grounds alone one might prefer to have meat as a condiment and for most of the world to have a little meat rather than a few people a lot. One might also reduce the impact of fat from one source by varying the source and by co-ingesting fat, from meat or elsewhere, with fruit and vegetables. Energy excess reflected in obesity and its sequelae is one of the world's major health problems. One concept which helps to understand the obesity problem is that of food energy density or energy per unit mass of food (kcal or kJ per gram of food) and, along with it, food component (which means more than nutrient and includes other components in food which are biologically active), density expressed as mass per unit energy (for example, mg of nutrient or food component per 1000 kJ), a measure of nutrition quality. It has been of great interest as to the extent to which fat itself or energy density, or both, contribute to overeating. There is evidence now that both are important and a particular rather clever study by Saltzman and colleagues found that energy intake over a few days of randomization to low fat or high fat is indeed associated with an energy intake which is higher when fat intake is greater than 40% of energy intake opposed to 20%, so in that range one seeks a preferred fat intake[16]. There is no doubt that saturated fat, including that from meat, contributes to the development of macrovascular disease. The earliest trials to change blood cholesterol did so by changing the polyunsaturated and saturated fat intake ratio. However, there is re-thinking now about whether all saturated fat is equally hazardous for macrovascular disease and the answer is that it is not. This is partly because of not only the chain length of fat but also because of food factors which might or might not be present with the fat depending on how refined or unrefined it is. This rather broad range of considerations about meat and health requires a level of risk assessment and management at the policy and individual level, not previously articulated.

The polyunsaturated fatty acids, which are essential fatty acids, have been systematically increasing in established market economics (EME) for the last 30 years principally through increasing intake of n-6 fatty acids like linoleic acid, from margarine and cooking oils. There is little doubt that their introduction has contributed to overall health, especially cardiovascular health, but in recent times, questions have been raised about the upper limit of acceptable intake of these fatty acids[17]. There is now a body of evidence, including our own[18,19], which

suggests that in Australia and the US, many people may have reached the upper limit of acceptable intake of this kind of fatty acids and, with it, developed an increased severity and extent of coronary atherosclerosis. So as with all food changes (and this has been the most major change in fat intake quality in the history of the human species), ultimately we must ask how much is enough?

For n-3 fatty acids, on the other hand, there is increasing evidence that most populations around the world are not having enough; but, since most of it comes in its preferred form from fish with few land plants as an alternative, this is a challenge to the environment, in particular to the world seafood supply, now that we are getting increasingly clear that two or three meals of fish a week is a preferred level of intake. The mechanisms whereby n-3 fatty acids enhance health are fairly well known, but one of the most exciting for cardiovascular disease is the increasing evidence that enriching cardiac muscle membranes with n-3 fatty acids decreases arrhythmia and proneness to sudden death. What then might be a safe approach to fat in the human diet becomes a complicated issue, whether it is saturated, monounsaturated or polyunsaturated, n-3, n-6 or trans-fatty acid that one is talking about. If you look at all the evidence, somewhere between 20 and 25% of energy intake coming from fat is probably the safest, but the fat ought to come from a variety of sources and not just one; otherwise we will be forever asking, should we have rapeseed (canola), should we have butter, this or that. The answer can be that a variety of fat sources is to be preferred and for a good deal of it, to be unrefined from nuts, seeds and grains, or from primary food commodities like low fat milk or dairy products and lean meat; when refined, oils are safer than solid fats because they do not require hydrogenation or re-esterification to novel triglycerides. Fat should also be part of a varied food intake because of the other components of food which might protect fat from being detrimental, for example, if one has the antioxidants of fruit and vegetables as one eats fat, then there is some evidence that endothelial damage will be less[20].

There are complex food component considerations in problems like osteoporosis and certain cancers and probably for most nutritionally-related health problems. There is very interesting data from a multicentre European osteoporosis study which show that the least prevalence of osteoporosis is in Italy, where the lowest calcium intake applies, and highest, in Poland, where calcium intake is amongst the highest[21]. Calcium is certainly not the whole story in so far as nutrition and osteoporosis is concerned, and a growing number of food factors, along with physical activity and substance abuse, are now recognised as important in bone health.

Emergent food-health relationships are several, but one has to do with food and food patterns, and we are understanding more and more

that chronic non-communicable diseases have to do with the measured variety of food[22–25], energy and food component densities, frequency of intake and to how much fruit and vegetables we have[26–28]. Jenkins published important work to show that meal patterns — nibbling more favourable than gorging, were important in determining a number of risk factors for macrovascular disease, including insulin resistance[29].

Nibbling is to be preferred provided one does not have fatty nibbles. We now understand more and more that a food-based and even a cuisine-based approach to health is more helpful than nutrients in food choice. There are some fairly health protective cuisines, including some indigenous, the Far Eastern, Japanese, Chinese, Mediterranean, Greek, Italian and Scandinavian. Perhaps what is happening is that we are getting together a new integral cuisine. In our studies of nutrition and ageing around the world, called the Food Habits in Later Life Study, coordinated through the International Union of Nutrition Sciences, we have had an opportunity to look at cuisines and survival[30]. For Greeks, diet score as an index of the traditional Greek form of the Mediterranean diet even in people over the age of 70 predicts survival[10].

We have applied the same index in other communities, Greeks in Melbourne, people of Anglo-Celtic ancestry in Melbourne, and found similar outcomes.

One of the most important companions to nutrition is physical activity — aerobic, for strength and for balance; walking, gardening and Tai-chi are examples of available and affordable ways to undertake these forms of physical activity. Studies on walking show it contributes to increased life expectancy[31]. Fries has shown a compression of morbidity towards the end of longer life expectancies in runners as opposed to community controls and according to age mean disability scores; the gains might be 15 or 20 years in reduced morbidity simply by being physically active. This is a very important consideration. Exercise training improves the value of food or nutritional supplementation, even for the frail aged[32]. For other dimensions of health, nutrition itself counts, but physical activity studies remind us that when we go the nutritional way, we also need to go the exercise way. The physical activity-food linkage operates by better regulation of appetite, by maintenance of lean mass and basal metabolic rate (BMR) and by increasing energy throughout so that we can eat more and get away with it without getting fat. It also has to do with the availability of food components, as the more we eat the more we are able to have food of varied origin. As it increases strength, it also increases well-being and improves attitudes to eating[33].

3. PHYTOCHEMICAL DEFICIENCY

One of the most exciting developments that we might now think about is phytochemical deficiency[34]. One of the models for this line of thinking has been the understanding that the hormone-like properties of food which reside in isoflavones and lignans can reduce the expression of menopause[35–37]. Phytochemical deficiency may also, in part, be the basis of neoplastic disease[38]. One might also say this about some aspects of ageing, given the antioxidant and oxidation theory of ageing, and likewise, foodborne illness.

There are many chemical families of phytochemicals — salicylates, polyphenols, monoterpenes, carotenoids, indoles, allyl thiosulfates. Particular compounds attracting interest are Epigallocatechin gallate (EGCG) from green tea; the flavonoid quercetin from onion, apples and tea, the focus of the European Zutphen study as coronary heart disease protectants; the isoflavones, genistein and daidzein from soy in menopause; limonene from citrus, a monoterpene in cancer prevention; and the carotenoid lycopene from tomatoes in prostate cancer prevention. As far as neoplastic disease is concerned, just take one type like isoflavones — they might be antioxidant, anti-angiogenic, reducing tumour growth from metastases, gene regulators, cell signal modulators, apoptosis inducers; and, in case of indoles from cruciferous vegetables, induce catabolism of mutagens. If one just takes one type of cancer, say prostate cancer, amongst many, there is now emerging evidence that lycopene from tomatoes, isoflavones from soy, EGCG from green tea, and vitamin E might be protective and, perhaps, for prostate size, β -sitosterol which acts as a 5- α reductase inhibitor. Vitamin E is a more traditional nutrient (although there is renewed interest in its isoforms), but even in prostate cancer, there is an interest in food components and how they might give us a new insight into food-health relationship. There is a growing body of evidence for lycopene in respect of other tumours as well, like the data from Comstock in relation to the pancreas[39], but the only tumour in these data not associated with increased intake for protection was melanoma. Attention was drawn to flavonoids from the Zutphen Elderly Study for coronary heart disease and myocardial infarction where increased intake was associated with reduced CHD risk; these flavonoids come from a variety of foods, which indicates that we need to think about berries, mushrooms and tea for which there is growing evidence that they may reduce cardiovascular mortality. For black tea, Wales is an exception so far as cardioprotection goes.

Micronutrients are also being revisited in relation to cardiovascular disease for folate, B₆ and B₁₂, by way of homocysteine; and for vitamin K as well. For example, the form of vitamin K in cheese, cardiovascular

system (CVS) menaquinone, may support the formation of unique proteins in CVS and the vasculature. There are also zoochemicals, not regarded as nutrients from animal derived foods, of growing health interest.

4. HEALTH CLAIMS ABOUT FOOD AND EVIDENCE

Many developments are affecting us from education and regulatory points of view. An active example is the development of new or novel foods or of functional foods, food designed or repositioned to deal with particular health problems or to be preventive. Whether one likes it or not, the nutrition and medical professions will be involved in this area because it will affect our practice and our patients. Several countries now have a regulatory framework for health claims and Australia is evaluating a pilot health claim, for folate in the prevention of neural tube defect (ANZFA home page: www.health.gov.au/anzfa/ANZFA), as a prelude to the progressive development of health claims on foods. There is a lot of controversy about how useful this will be, but most think there is enough evidence to proceed. My own view is that the health claim approach will probably only be useful for 5 or 10 years and that we will then be looking at another approach, based on nutrition informatics. In the meanwhile, we are going to be looking for the evidence. Epidemiology has set the scene for us and clinical trials are also helpful, but clinical trials in the nutrition and health area are sometimes, not possible. One can rarely make these trials double-blinded and they are extremely expensive. The Australian Polyps Prevention Project in which the combination of increased dietary fibre and reduced fat intake can protect against recurrence of large adenoma polyps (>10 mm), cost us about 1½ million dollars; it went on for four years and we only studied three nutrients (β -carotene, dietary fibre and fat)[40]. There is no way in which we can cover all of the relevant nutritional variables or issues without a multi-billion dollar programme and a considerable number of subjects. This is just not feasible and my view is that we have to be increasingly involved in modelling studies of the human diet in which we predict outcomes, as engineers and astronomers do, and which nutrition and medicine are going to have to do as well.

We have come a long way from being foragers and hunter-gatherers to subsistence agriculturalists and pastoralists, to urban dwellers and, now the informatics revolution is pressing hard on food choice for consumers. We are at the beginning of an era of "informatics driven food choice" that has great implications for consumers. The food regulatory and environment agencies are endeavouring to keep pace with these changes and a new regime of health claims and nutrition informatics is

unquestionably on the immediate horizon. In both the preventive nutrition and nutrition management domains of health, functional and formula foods are on the ascendancy, at the expense of basic commodities, established recipes and traditional eating patterns, which we will need to document quickly in relation to health. There is much public and professional re-learning and re-skilling required for food security and safety, let alone health advantage.

5. HEALTH PROTECTIVE FOODS

Much health protective food is reflected in dietary guidelines. Fruit and vegetables are unquestionably protective against almost all cancers that have any nutritional basis. Legumes like soy look to be particularly important in Asian diets, protecting against certain cancers like breast and prostate, and against osteoporosis. There is good data over many years that whole grain cereals is health protective. Fish is also a protective food and so is lean meat as a condiment. Very much on the agenda are herbs and spices. Health protective beverages include water, tea, low fat milk and wine made from grapes, but fermented food and beverages themselves are undergoing re-scrutiny in nutrition science.

With food and health, there is going to be an active consideration of biodiversity and through the food variety we can encourage the maintenance of biodiversity. This is obviously of great international and regional concern as wonderful ecosystems are under serious threat. And so we can promote the message of the Australian Nutrition Foundation which is to achieve optimal health through food variety and physical activity.

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Nutrition Research

Current Scenario and Future Trends

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