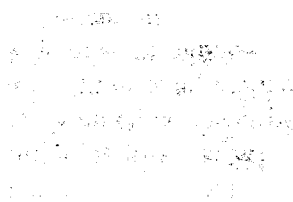


New Directions in Food–Health Research

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ABSTRACT

In Australia, research in nutritional science has begun to explore the relationship between food and health from new perspectives. Ethnic and cultural factors are being recognized for their importance in influencing diet quality and metabolic responses to diet. Rather than considering the impact of isolated, recognized nutrients on health, the roles of non-nutrients in foods, such as estrogenic compounds, and of the overall variety in the diet, are being examined for effects on health. Similarly, new metabolic end-points, such as body-fat distribution, are being related to chronic diseases. These and other

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considerations form the basis for exploring relationships between food and health in entirely new ways.

Introduction

A growing cohort of medical nutrition scientists from my region of the world is beginning to change the way we think about food and health. It has been said that the future of the world is in the Asia-Pacific region. In Australia, one has a sense that the region is indeed very dynamic. An interesting book by two Australians, Reg Little and Warren Reed, about the ideologies that operate in Asia, and the influence they are having and will have on everything from health-care systems to economies, underscores what inevitably will be a major shift in the understanding and application of food-health knowledge as well. I will present some insight into the interests that we have in the Monash University Department of Medicine, and describe some of the research we are doing that has to do with new ways of thinking about food and health.

In a department of internal medicine, it has been uncommon for nutrition to be a major research or clinical interest. I had the Foundation Chair of Human Nutrition at Deakin University, and am now the Chair of Medicine at the Monash Medical Centre. In this way, Monash University and one of its major teaching hospitals, the Monash Medical Centre, have developed a lead interest in nutrition. In less than 6 years, in almost every area of internal medicine, from gastroenterology and respiratory medicine to cardiology and neurology, there has been a rekindling of interest in clinical nutrition. It is a turning point in internal medicine, at least in Australia, evident in various universities. It is my wish that this will happen throughout the Asia-Pacific region as well, and young medical graduates will help us achieve this.

In order for this to work, we first have to address some of the weaknesses of nutrition, and they are its fundamental methodologies.

Methodologies

The first is the methodology of food intake—being able to measure better what people eat. There will never be a gold standard, but understanding the limitations, finding new ways of describing food intake mathematically, and not simply reducing it to nutrient intake are some of the more important considerations. Pivotal, however, is the need to take our understanding of food beyond nutrients, by better food chemistry. We have decided, therefore, that in our department of internal medicine, we should have an interest in food chemistry.

Another area of great importance in terms of nutritional methodology is body composition. With a state-of-the-art body-composition laboratory, we are encouraging clinicians to track their patients in terms of body compartments, to understand what is happening to lean and fat mass, body water, and bone, and for it to be part of usual clinical decision-making. In our body-composition laboratory, we have *in vivo* neutron-activation analysis for total body nitrogen; a whole-body counter for K-40 (the naturally occurring radioisotope for potassium and therefore cell mass); and methods for measuring electrical conductivity, bone density by DEXA (dual-energy x-ray absorptiometry) and ultrasound, and body water using deuterium oxide. The ability to measure energy expenditure over an extended period of time with doubly labeled water and, in non-steady-state conditions, from minute to minute by microprocessor-controlled indirect calorimetry is increasingly valuable in patient assessment.

These improved methodologies are giving a degree of confidence to people in nutrition that other disciplines have already achieved. It also lifts the standing and the standards of the discipline of clinical and public health nutrition. It is the nature of Western medicine that when one has methods for measurement, the discipline attracts more interest and support. For measurement one needs procedures and related skills. Young medical graduates are encouraged by such disciplines, and can then explore the broader nutrition or health issues.

Chronic Noncommunicable Disease

From a nutritional point of view, our interests are principally in chronic noncommunicable disease, namely macrovascular disease, obesity, diabetes, osteoporosis. But, inevitably, we have an interest in transitional nutritional problems in the Asia-Pacific region: transitional between undernutrition and overnutrition. This is a somewhat simplistic view, because many of the problems of “overnutrition” will ultimately be seen to be problems of “food-component deficits.”

Ethnicity and Health

Some of our cross-cultural studies of food–health relationships are the most telling and are unraveling some fascinating questions. In a study of representative samples of both Caucasians and Asians living in Melbourne, we have found differences in *Helicobacter pylori* infestation rates, with higher rates in Chinese Melburnians and Japanese than in their Caucasian counterparts, that relate to food practices. Chopstick use is one of the more important predictors of infestation rates, modulated in turn by some foods that may then alter the propensity for peptic ulcer development or recurrence. In turn, we have developed a joint interest with the Australian Commonwealth Scientific Industrial Research Organization (CSIRO) in probiotic agents that could be included in new food products. These might reduce the overall problem of peptic ulceration in the community. This is an example of how countries such as Australia and the United States, with their ethnic diversity and successive waves of immigration, can take advantage of studying different food cultures, and what they mean for health. A newer view of food–health relationships is emerging from this kind of inquiry.

Nutrition and the Aged

The International Union of Nutrition Sciences Committee on Nutrition and the Aged is studying communities of elderly people that are very disparate around the world. At its recent workshop at the Tufts Center for Nutrition and Aging in Boston, in conjunction with the United Nations University, we brought together the first eight or so community studies (about 1500 representatively sampled individuals) to learn about the particular food-health relationships in elderly people. This project is conjoint with the European nutrition studies, known as Seneca, studies from northern China conducted by the Institute for Preventive Medicine in Beijing, and some other cross-cultural studies in the Antipodes.

Nutritional Risk for Macrovascular Disease

Let us consider some specific food-health relationships. A few years ago there was a cover story in *Time* magazine (Australia) about cholesterol (March 26, 1984). A plate of eggs and bacon was depicted on the cover to summarize the prevailing idea. This was a somewhat simplistic notion that dietary fat, represented by the bacon, and dietary cholesterol, characteristically in eggs, are all there is to say about food and coronary heart disease. The interplay between those variables alone is, of course, important, but other food factors have been somewhat neglected.

The food-intake aspect of the Ireland-Boston study of Kushi et al. was very interesting. It looked first at the relative risk of death from coronary heart disease over 20 years in accordance with the Keys and Hegsted scores. These scores were developed in metabolic studies in which the various combinations of cholesterol, saturated fat, and polyunsaturated fat intake could be expressed in one mathematical equation to predict serum cholesterol concentration. Instead of looking at lipoproteins, their important study looked at the way in which these dietary fat scores predicted death from coronary heart disease. What they found was not a linear inverse relationship between increasing score and coronary mortality, but

a J shape. But when all plant foods—expressed as grams of fiber per 1000 calories ingested—were examined, there was a fairly linear relationship; the more plant food eaten, the lower the relative risk of coronary mortality. And the vegetable score alone did much the same thing. The range of risk over which plant food operates from 1.0 down to about 0.5, is not trivial in biological terms, and is the same order of magnitude as the change seen with the fat scores of Hegsted and Keys. By and large, nutritionists have missed this point. Of course, it does not necessarily mean cause and effect, but it does mean that the predictive power is there. It is very tantalizing. Now we can begin to ask, “what about the nutrient and non-nutrient components of plant foods?” In 1985, when the Ireland–Boston study was published, we were thinking about dietary fiber and coronary heart disease. But there are many other compounds in food that are of biological interest and that could be relevant to the pathogenesis of coronary heart disease. It just so happened that the mode of thinking at the time was concentrated on fiber, so the data were expressed in terms of fiber.

Non-Nutrients of Biological Importance

Another example of how things in food, other than those that are our present frame of reference, could be important is the achievement of a given estrogen status. Neilsen and colleagues in the U.S. Department of Agriculture in North Dakota have been interested in trace elements and osteoporosis. Boron is not regarded as an essential trace element and has been of “fringe interest.” However, Neilsen and co-workers have shown in postmenopausal women that the levels of boron obtainable from fruits and vegetables, about 3 mg/day, are enough, interactively with magnesium intake, to change endogenous estrogen status, as measured by serum estradiol. Boron, particularly at low magnesium intakes, decreases urinary calcium excretion. So here is a factor in food that is not regarded as a nutrient, and yet is of biological relevance in terms of one of the major chronic diseases, osteoporosis.

There are also compounds in food that themselves have estrogenic properties. Exogenous estrogens are found principally in plant-derived foods (phytoestrogens) but these compounds can also be eaten by animals and are found in meat, milk, and other dairy products. People in animal production have known about this since the 1920s. One of the most seminal papers on the matter was that of Eric Underwood, a great Australian scientist. In the late 1940s he published a paper showing that reproductive function in sheep could be affected by the clover on which they grazed, and he found that estrogenic compounds were responsible.

There are families of such compounds in plants, the coumestans, flavonoids, and lignans. We have studied the effects of sprouts, soya flour, and linseed supplements as sources of these compounds in postmenopausal women. They have various potencies, but generally, they are weakly estrogenic compounds, so they are potentially competitive with endogenous steroids. For 2 weeks at a time we gave to postmenopausal women, who of course are estrogen-deficient, different putative sources of estrogens: soya flour, clover sprouts, or linseed, which they could incorporate into, eat with, or sprinkle on their food. We observed an improvement in vaginal cell cytology that was partially equivalent to hormone replacement therapy (HRT), and at the same time we saw suppression of the gonadotropin FSH (follicle stimulating hormone) but not LH (leutinizing hormone). Thus, there can be a change in the hypothalamic-pituitary-gonadal axis with foods in as little as 2 weeks. It is now reasonable to think that food may modulate the expression of the menopause.

Recently, Professor Hin-Peng Lee from Singapore showed that the foods most protective against breast cancer for Chinese women in Singapore are soya products such as tofu. These are good sources of weakly estrogenic compounds which compete with endogenous estrogens. In fact, their level of estrogenicity is almost the same as that of tamoxifen. Tamoxifen is actually pro-estrogenic at the vagina but anti-estrogenic at the breast. What is very interesting about these compounds is that they have a hierarchy of estrogenic effects. At some sites—for example, the bone—we do not know exactly what they do, although recent evidence indicates that

tamoxifen protects against bone loss and coronary heart disease risk. Whereas it might be thought that estrogen-sensitive breast tissue would be at cancer risk with these compounds, the breast might be protected from estrogen excess. The data of Lee would be consistent with the observations we have made in postmenopausal women.

Bioassays show us where estrogenic compounds might be in food. However, there are so many compounds that it is difficult to measure them. Also, because some are activated and others are deactivated in the liver, measuring them in peripheral blood does not tell the whole story. Some, or their metabolic products, are found in adult human urine. Vegetarians excrete more in urine than do nonvegetarians. The human species is exposed to a wide range of intakes of these compounds, which may accompany between a little to 50% of energy intake, depending on food culture. In effect, they are part of human physiology and the pathophysiology of postmenopausal women.

These observations are very profound, and may be important not only for women, but also for men. For example, the incidence and mortality from prostatic cancer are lower in Asian men than in Caucasian men in Melbourne.

Food Variety

The number 1 dietary guideline in almost all developed countries is to encourage eating a greater variety of foods every day. But the only scientific evidence in its favor has been that, if one calculates essential nutrient intake, the narrower the variety, the less likely is an adequate intake of essential nutrients. The argument can also be made that adverse factors in food, e.g., toxicants, would be diluted out with variety. Beyond that, there has been virtually no testing of hypotheses that relate to whether increased food variety might decrease, say, macrovascular disease, osteoporosis, diabetes, or whatever the major health concern is that the dietary guidelines are meant to address.

And why is that? It has become “nutritional parenthood” to espouse such views, even beliefs, without evidence. One of the problems is that we have not had mathematical ways of measuring variety. Even now we do not have good ways, but we have developed some scores based on various premises. For example, if a food is biologically distinct in the plant or animal world, then it would constitute a separate kind of food from the point of view of variety, and it would score, in a hypothetical scoring system. We have done this with various time bases—a week, a month, and a year. If this food was eaten 10 times a week it would not provide more points than if had been eaten once a week.

Let us take meat as an example. Broadly speaking, meat could be from a ruminant like a sheep or cattle, which has a biology and fat composition different from those of a monogastric animal like a pig. Meals from these two sources could thus be regarded as biologically distinct. This is the way we have created scores. We find in cross-sectional studies, using noninvasive indices of atherosclerotic disease in the carotid, femoral, and posterior tibial arteries, that as food variety increases, arterial characteristics are healthier. More recent prospective studies show that is possible to influence favorably arterial-wall characteristics within 12 months via diet.

We have found that in diabetes, with greater food variety not only are arterial-wall characteristics better, but so is glycemic status. This is quite a shift in nutritional thinking for people with diabetes.

Beyond Metabolic End-Points

As we change food intake, it is important to have outcome measures that go beyond the biochemical variables of glycemic status, lipoprotein status, and so on, which, of course, we do need in clinical practice as we manage people with diabetes or lipid disorders. But it is better if what we measure is nearer to morbidity and mortality.

Using noninvasive techniques to assess arteries, we have considered how important fish consumption is in apparent health and in diabetes. With aortofemoral compliance, healthy people who eat fish have a compliance of about 1. If they do not eat fish, it is less; once they are diabetic, it is less again if they eat fish; and if they are diabetic and do not eat fish, it is about half what it is in the reference population. This is without other confounders (tobacco, hypertension) in the “healthy” or diabetic groups or groups of nonsmoking, nonhypertensive individuals. Here is a way in which we potentially can look at food indices and a health outcome, i.e., for arteries. It is this kind of methodology that is needed to look at the relationship between food and health.

Body Fat and Its Distribution: Cross-Cultural Lessons

We have quite a major study of over 500 representative Chinese in Melbourne. Melbourne is ethnically very diverse, as are most American cities, and some of the larger communities are Chinese and Greek, both of which we have studied. Since the population at large is undergoing a change toward increased fatness, we have taken a particular interest in body fat among Chinese. We are interested not only in total fat, represented by body-mass index (BMI), but also fat distribution, represented by waist-hip ratio (WHR). One or both of these could affect cardiovascular risk via blood pressure, serum lipoproteins, glycemic status, or some other pathway, and in turn morbidity and mortality. It has to be acknowledged that these risks might not be equally adverse for all cultural groups. Nevertheless, both total body fat (BMI) and fat distribution (WHR) in men and women in Melbourne Chinese affect risk for these diseases.

What in this community affects BMI and waist-hip ratio? We do not yet know a lot about the determinants of distribution of body fat. We know there are gender differences. We think it is interesting that WHR seems to be undergoing a very significant

change in the Chinese population within an apparently acceptable range of BMI of 20–25 kg/m². We think it may account for more of the cardiovascular risk change in this community than if we were to measure only BMI and maybe changes in BMI. Gender, age, physical activity, and smoking are known to affect adversely distribution of body fat. We can add to this menopause, at least for Chinese women. What about foods and beverages? To what extent could particular foods and beverages affect the distribution of body fat? Alcohol is most frequently regarded as adverse for WHR, but even that is probably worth a closer look. Preliminary observations in the general Melbourne population suggest a high dependence on cigarettes for this health effect.

We have measured food variety in the Chinese population in Melbourne in two ways: the biological variety to which I have referred and “product variety.” We said, “If you have, for example, a wheat-flour-based product that could be used in various ways, e.g., in bread, breakfast cereal, or in cake, or if you have an extruded flour as opposed to a nonextruded flour, then it is possible that each could confer either biological advantage or disadvantage.” If we described this concept mathematically, could it have predictive power for a health outcome? In other words, if the variety of food products increased, which is a matter of some interest and concern in urbanized societies, then what would that do to health?

First, we found that an increase in biological variety had a favorable effect on systolic blood pressure, serum cholesterol, and triglycerides, but not on HDL cholesterol or the HDL-LDL ratio. Also, the more the variety, the less abdominal fat people had, and the lower the fasting blood glucose, one of the indices of glycemic status. As product variety increased, there was an even lower waist-hip ratio. It was something we had not expected. We have looked at a number of confounders, and only “acculturation” exceeds the importance of variety (see below).

We are extending these observations to Chinese beyond Melbourne. We are studying several communities in southern China, Sinhui, Meixian, and Santou, each with a different culinary tradition, including Cantonese, Hakka, and Teochew.

Melbourne Chinese are less fat than the reference population as judged by BMI distributions. Although their mean BMI is less than 25 kg/m², Melbourne Chinese have higher BMIs than their counterparts in China. Most of these Melbourne Chinese are first-generation Chinese.

We see a dissociation between distribution of fatness, especially in women, and BMI. This provides an opportunity for us to look at aspects of food culture that might account for this dissociation. The food factors that determine total fatness might not be the same as those that determine the distribution of fatness. For example, phytoestrogen containing soya products might decrease abdominal fatness but not total fatness. If this is the case, it might provide opportunities to change fat distribution specifically and safely. It may even provide opportunities for new food products targeted at this health problem. Moreover, in traditional Chinese medicine, it is a paradigm to think about new ways of linking food and pharmaceuticals.

We then looked at the degree of acculturation—the degree of movement—toward the majority food culture of Chinese in Australia by what we call a “Food Acculturation Index,” which simply represents the difference between an Australian food score and a Chinese food score. There are various ways one can do this, but this represents mathematically a shift toward the majority food culture.

What we found was that, controlling for numerous other variables, food acculturation is perhaps the single most important factor determining BMI and WHR. The *r*-value is still low, but among the variables this is one of the most important. Much to our surprise, the more acculturated Melbourne Chinese are, the better their WHR, and for women, the better their total fatness. When we talk about diversification of the diet, we are also talking, by and large, about acculturation. This may not apply for all groups coming to Australia, but it does seem that the Chinese pick and choose food in a way that tends to take advantage of both cultures.

Food Acculturation

It is of value to health educators and planners to understand the process of food acculturation. To take an example: Chinese tend to replace the morning rice meal with breakfast cereals or toast. Strikingly, they substitute Chinese tea with cola beverages. While in Chicago in a restaurant serving northern Chinese food, we observed that Chinese diners were having their rice with a can of diet cola instead of Chinese tea. This is very similar to what we have found in Melbourne Chinese, who mainly come from the Southern part of China. There is something about Chinese food culture that seems to encourage these sorts of substitutions.

What is the process of dietary acculturation in Asia? And what are the factors determining it? And to what extent is it affecting food intake? When we see that we are actually observing different food factors operate on distribution of fat as opposed to total fatness, and how biologically important this might be, new and interesting hypotheses open up for us.

The Future of Food, Nutrition, and Health Science

There is a need and a growing interest to study the human diet with respect to health outcomes other than those to which we have so far been attuned. Much of nutrition inquiry in the West, in the post-vitamin-discovery era, has been directed toward macrovascular disease, management of such problems as diabetes, and trying to solve the epidemic of obesity. There remain major areas of human health that need to be addressed from a nutritional point of view—not peptic ulcer in the sense that we used milk drips to manage it, but areas that call for fundamentally different ways of thinking, such as nutrition and upper intestinal microflora, or food patterns that influence the expression of the menopause. Whereas many would suggest that we have found out what we need to know about diet and chronic disease, we are only just beginning to do so. As we describe what we eat in more complete mathematical

terms, link nutrition and gene expression, combine work on nutrition and aging, develop "functional foods," and take account of ecological considerations in food choice, we are poised for a very interesting decade, looking at food-health relationships in altogether new ways.

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Nutrition **in the** **'90s**

Current Controversies and Analysis

Volume 2

edited by

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*The NutraSweet Company
Deerfield, Illinois*

Marcel Dekker, Inc.

New York • Basel • Hong Kong

ISBN: 0-8247-9212-2

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Marcel Dekker, Inc.

270 Madison Avenue, New York, New York 10016

Current printing (last digit):

10 9 8 7 6 5 4 3 2 1

PRINTED IN THE UNITED STATES OF AMERICA