Diet and chronic degenerative diseases: perspectives from China[1-3]

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ABSTRACT A comprehensive ecologic survey of dietary, life-style, and mortality characteristics of 65 counties in rural China showed that diets are substantially richer in foods of plant origin when compared with diets consumed in the more industrialized, Western societies. Mean intakes of animal protein (about one-tenth of the mean intake in the United States as energy percent), total fat (14.5% of energy), and dietary fiber (33.3 g/d) reflected a substantial preference for foods of plant origin. Mean plasma cholesterol concentration, at ≈3.23–3.49 mmol/L, corresponds to this dietary life-style. The principal hypothesis under investigation in this paper is that chronic degenerative diseases are prevented by an aggregate effect of nutrients and nutrient-intake amounts that are commonly supplied by foods of plant origin. The breadth and consistency of evidence for this hypothesis was investigated with multiple intake-biomarker-disease associations, which were appropriately adjusted. There appears to be no threshold of plant-food enrichment or minimization of fat intake beyond which further disease prevention does not occur. These findings suggest that even small intakes of foods of animal origin are associated with significant increases in plasma cholesterol concentrations, which are associated, in turn, with significant increases in chronic degenerative disease mortality rates. *Am J Clin Nutr* 1994;59(suppl):1153S–61S.

KEY WORDS Diet, lifestyle, animal protein, fiber, plasma cholesterol, disease

Introduction

During the past decade a large number of organizations, particularly in Western industrialized countries, have recommended a modest decrease in the average consumption of dietary fat to a level of ≈ 30% of energy (from ≈37–38% of energy) to prevent chronic degenerative diseases. This is to be achieved, in large measure, by using low-fat foods (eg, low-fat dairy foods), leaner cuts of meat (eg, poultry and fish instead of beef, pork, or lamb), and less added fat (1–4). Increased consumption of vegetables, fruits, and cereal grain products has also been recommended, but no particular target amounts have been specified.

The 30% of energy target level chosen for the dietary fat intake recommendation through various dietary guideline deliberations has generally been based on estimates of what consumers might be willing to accept (1–5). This is illustrated by the 1982 report of the National Academy of Sciences Committee on Diet, Nutrition, and Cancer (DNC) (1), which admittedly chose this level of intake for practical reasons, not because of scientific evidence available at that time. This committee concluded (in its executive summary) that "the scientific data do not provide a strong basis for establishing fat intake at precisely 30% of total calories. Indeed, the data could be used to justify an even greater reduction." A further assumption was made that a dietary fat level of 30% of energy could be fairly easily achieved without significantly altering traditional dietary patterns, whereas increasingly lower levels of fat intake would require increasingly greater exchange of foods of animal origin with foods of plant origin. Although authors of later dietary guideline reports restate the 30% of energy figure, they appear somewhat less impressed with its precision by suggesting it as an upper level of intake (3, 4).

Between these two recommendations, either to decrease the intake of dietary fat or to increase the intake of fruits, vegetables, and cereals, the recommendation for dietary fat reduction appears to have received greater emphasis during the past 10 y, particularly if the principal hypotheses under investigation in certain large-scale human studies are any indication (6–8). For example, in the feasibility studies for the Women's Health Trial, the principal advice given to the experimental subjects focused on how to reduce fat intake, and at the end of the 2–3-y trial, these participants succeeded in doing so essentially without altering their aggregate consumption of vegetables, grains, and legumes (as a percent of total energy intake) (7).

The fruit-vegetable-cereal recommendation appears to have received less attention even though these foods contain virtually all of the individual constituents known to prevent chronic degenerative diseases. Several factors might be responsible for this inattention. First, numerous investigators have expressed concerns that consumers may not wish to significantly change their diets, particularly if the changes entailed an exchange of foods of animal origin with foods of plant origin (7, 9, 10). Second, many observers have long been concerned that a diet that becomes too vegetarian may be nutritionally imbalanced (11–16), with some imbalances allegedly serious in nature (17). Third, relevant food-industry groups whose product sales could be adversely affected by a specific dietary recommendation distribute

much self-serving public information. Last, the recommendation to increase the consumption of vegetables, fruits, and grains has not been quantitatively specified in dietary guideline reports, which may infer that, perhaps subliminally, the reports' authors are less certain of the evidence for making this recommendation.

The belief that consumers will not be willing to accept significant substitution of foods of animal origin with foods of plant origin has been used to justify the investigation of the disease-prevention properties of individual nutrients and other constituents in plant foods. It has been said that "prescription" (for individual nutrient supplements) may be more acceptable than "proscription" (against the consumption of undesirable foods) (9). These plant constituents, often called chemopreventive compounds, now number several hundred to a few thousand depending on the criteria of classification (Herbert Pierson, James Duke, and Christopher Beecher, personal communication, 1993). Chemopreventive compounds are being tested in several dozen human intervention trials in the hope that some may prove useful as nutrient supplements (9, 18–20).

These two strategies of subtracting a small amount of fat or adding individual nutrient supplements to a relatively unmodified diet may be too simplistic, too modest, too likely to result in tradeoffs of disease prevalence, or may be too likely to divert attention from the whole diet approach that is favored by the major diet-disease expert panels (1, 3, 4). It is ironic that contemporary disease-prevention strategies of modifying the intakes of single nutrients (or even of "designer foods"), mostly for cancer prevention, were not intended by the DNC, which wrote the seminal report on this topic (1). Furthermore, the 1988 *Surgeon General's Report on Nutrition and Health* (3) and a 1989 report by the National Research Council, Diet and Health, (4) concluded that the total diet was the key determinant of the diet-disease relationship.

The 1982 DNC report explicitly states in its executive summary that the disease-prevention benefits of the vegetable-fruit-cereal food groups did not apply to nutrient supplements. Although a very large number of human intervention trials have been mounted nonetheless to test nutrient supplements and substantial research money is being spent for this purpose, several virtually unanswerable questions about nutrient supplements will undoubtedly remain for the foreseeable future (9, 18–20). It will take time before nutrient supplements can be reliably and efficaciously used in the marketplace. Who should and who should not use these materials? Will it be acceptable to continue consuming a high-risk diet, especially when the individual does not know which undetectable disease he or she wishes to avoid because of this diet? What will be the dose, and is there an upper limit? For how long should dosing continue? To what extent will the intake of one nutrient supplement counterbalance the effects of another, perhaps decreasing the risk for one disease but increasing the risk for another?

If these highly focused but nutritionally simplistic strategies to prevent chronic degenerative diseases prove to be without sufficient merit, then the only reasonable dietary alternative is to make significant, perhaps substantial, whole-diet changes, especially by exchanging foods of animal origin with foods of plant origin. This would simultaneously increase the consumption of vegetables, fruits, and cereals, and decrease total fat intake, assuming that added fat is kept to a minimum, thus satisfying the recommendations called for by these expert panel reports. This whole-diet option has been most appealing to me ever since I served on the 1982 DNC. Implicit in each of the diet-disease expert panel reports is the hypothesis that comprehensive dietary change will cause comprehensive disease prevention through a simultaneous increase in the intakes of desirable constituents found in foods of plant origin and a decrease in the intakes of undesirable constituents found in foods of animal origin (1, 3, 4).

Another dietary option for the prevention of chronic degenerative diseases is to reduce total energy intake, essentially reducing the intake of a high-risk diet (21–23). This suggestion has been primarily based on the ability of energetically restricted diets, even diets of the high-fat type (22), to inhibit chemically induced tumor development in experimental animals (22, 24) and also on the observed associations between some degenerative diseases and excessive body weight (and, presumably, excess energy intake) (23). However, energy restriction by humans is not a practical option for disease prevention, at least not the degree of energy restriction required for experimental animals, for three reasons. First, humans are relatively unable to sustain energy-intake restriction for long periods of time (25, 26). Second, some observations of decreased tumor development in experimental animals (27) and of decreased cancer prevalence in humans (28) have been associated with the greater energy intake that occurs during low-fat, low-protein diets. Last, humans are able to lose body weight, and presumably to reduce cancer and heart disease risks, merely by consuming energy-dilute diets (29–32). This lack of a simple direct relationship between cancer risk and total energy intake was the reason the 1982 DNC failed to make a recommendation on energy intake, concluding that "neither the epidemiological nor the experimental studies permit a clear interpretation of the specific effect of caloric intake on the risk of cancer."

Although the DNC thought that a proper intervention trial to test the disease-prevention effects of a whole diet would be exceedingly difficult, if not impossible, to undertake, it was clear to the committee that a rational investigation of the hypothesis was needed. If the whole-diet effect is the most significant disease-causing effect, then appropriate methods of experimental investigation must be sought so that the whole-diet effect can be described until it is adequately understood. It was, therefore, fortuitous that we were presented with an opportunity to investigate the whole-diet effect by our colleagues in the People's Republic of China. In 1981 Chinese investigators published a cancer atlas, based on data that had been retrospectively collected for the period of 1973–1975 from ≈ 2400 of their counties (> 800 million people). This atlas showed remarkable geographic differences in mortality rates. The atlas included about a dozen different cancer sites and was based on age-adjusted data for each sex. An investigation of the chief dietary and lifestyle correlates of these unusual cancer-mortality rates was highly promising because of the assumption that most individuals would exhibit stable residence patterns, would consume only the locally produced food, and would consume mostly the same kinds of food over their lifetimes.

Junshi Chen, deputy director of the Institute of Nutrition and Food Hygiene, which is part of the Chinese Academy of Preventive Medicine, and his staff directed a nationwide survey in 1983–1984 of dietary and lifestyle characteristics in 65 rural counties, two villages per county. The Chinese Academy of Preventive Medicine provided the services of their provincial health teams for the actual conduct of the survey in the field. The dietary and lifestyle data obtained from this 1983–1984 survey were

combined with the previously recorded 1973–1975 mortality rates (33) for about four dozen different kinds of diseases, including about a dozen different kinds of cancer and several types of cardiovascular and communicable diseases. The original data from these combined surveys, representing 367 dietary, lifestyle, and mortality characteristics, were published in early 1991 (28). Several investigators have undertaken subsequent interpretations of these data by examining various specific cause-and-effect hypotheses and the present paper reviews a relevant selection of their publications.

Dietary and biochemical characteristics for most nutrients were recorded during the survey to examine diet-disease hypotheses from comprehensive vantage points. Chinese people's intakes of fat, dietary fiber, protein, and several micronutrients were markedly different from the intakes of people in industrialized countries. Moreover, average intakes of these constituents in China were well beyond the intake ranges recommended by the relatively modest dietary guidelines of Western countries (1, 3, 4). Thus, if Western countries were to choose the whole-diet option to implement dietary guidelines, essentially toward greater vegetarianism, then interpretation of these data from China could help us predict what to expect in Western countries.

Before presenting the initial results of this massive data set, I should make two comments on the applicability of ecologic data from rural China to an American setting. First, this study is ecological and includes 6500 individuals residing in 130 villages. Thus according to widely held assumptions, any inferences concerning cause-and-effect relationships should be considered to be hypothetical only, with validation to be provided by intervention or prospective analytic studies on individuals. However, this limitation of interpretation includes an assumption that does not apply to the main hypothesis under investigation in this study. In other ecological studies, hypotheses under investigation are almost always narrowly, and mostly inappropriately, focused on single causes (eg, single foods, nutrients, and carcinogens) and single effects (single diseases), often when inferences about simple cause-and-effect relationships should not be made. This study in rural China, in contrast, includes a very large number of variables that allow investigation of a much more comprehensive hypothesis, one that can be examined from multiple vantage points. The main hypothesis to be considered states that the nutritional characteristics of a diet rich in plant foods reduces the risk of a comprehensive group of chronic degenerative diseases. For example, rather than focusing on the very narrow hypothesis that dietary fat is the principal cause of breast cancer, there is an opportunity in this study to analyze separate, but multiple, other nutrient and food intakes (eg, various fiber, complex carbohydrate, and protein intakes) that may be causal in this disease. In addition, the metabolic, anthropometric, and physiologic consequences of these nutrient intakes (eg, various circulating hormones, menarche or menopausal characteristics, and body size) can be included in the analytic models of interpretation.

With this approach, it becomes possible to go beyond our general understanding of putative but narrow associations of a single disease with a single intake or single biomarker, and to consider, instead, a constellation of various related intakes and biomarkers that are characteristic of a plant-rich diet. It also becomes possible to investigate the relevance of the same evidence for diseases other than chronic degenerative diseases that are hypothesized to have similar underlying nutritional causes. If there is internal consistency among the various diet-disease associations within

such a data set, particularly if the evidence, both separately and collectively, is biologically plausible, then multifaceted causal inferences become more substantial and robust. Thus, the comprehensiveness of this study in rural China provides an analytical dimension that is very different from other ecological studies and that lends more than usual credence to causal inferences.

A second general comment on comparing residents of rural China with residents of highly industrialized societies is that it may not be appropriate to extrapolate diet-disease relationships across cultures. Some observers, for example, are concerned that unless genetic differences are documented and taken into consideration, comparisons of one culture with another may not be appropriate. Undoubtedly, it is true that there are unique genetic or genetic-like differences in nutritional and chronic-disease responses among individuals, but this fact does not negate the role that diet and other environmental factors may play in modulating the expression of these genetic differences. The more relevant concern should be about how much control dietary and lifestyle factors can have over the expression of genetic predisposition. The most persuasive evidence of the "nurturing" effect of diet and nutrition on disease prevalence, when compared with the "naturing" effect of genetic background, may be found in the hundreds, if not thousands, of reports on populations that adopt new dietary practices either over relatively short times when they migrate to new cultures (ie, migrant studies) or over somewhat longer times when they remain within their cultural settings (ie, time-trend studies). Chronic-disease occurrence, in both instances, closely follows dietary change, regardless of whether or not individuals had a genetic predisposition for such diseases.

This paper summarizes a relevant selection of previously published findings from the survey in rural China. These findings may predict the kind of changes to be expected if Western societies were to alter their dietary habits by a substantial replacement of foods of animal origin with foods of plant origin.

Procedures and methods

Survey design and other methods and procedures were described in detail by Chen et al (28). A multistage random-sampling scheme was used to select survey subjects. Sixty-five mostly rural Chinese counties were initially selected to represent the full range of mortality rates for seven of the most prevalent cancers. These counties, geographically scattered across the country, were situated in 24 of 27 provinces and autonomous regions in China. To assess within-county data concordance, data from two randomly selected communes in each county were compared. Twenty-five adults were randomly selected from each production brigade, which is an administrative subunit of a commune, to yield a total of 100 adults for each county. The subjects were evenly distributed across 5-y age groups from 35 to 64 y (50 males and 50 females), thus giving 6500 subjects for the entire survey. Each survey subject was asked to donate blood and to complete a questionnaire. In addition, urine samples were collected from subjects in one of the two communes in each county, and individual body weights and heights were measured.

Fasting venous blood was drawn from each subject between 0600 and 1200 and separated into plasma and red blood cells by centrifugation. Plasma samples, pooled by commune, age, and sex, were used to measure a large number of biochemical markers of nutritional, viral, and hormonal status.

Food consumption data were obtained from a 3-d survey of household diets by weighing all food in the household before the 3-d survey, food purchased during the 3-d period, and food remaining at the end of the 3-d period. This procedure of food weighing provided an estimate of total food consumption per household for a wide variety of the most commonly consumed foods.

The food consumed in each household over three d was divided by the total number of person days, then multiplied by an appropriate coefficient to adjust for the age, sex, and physical activity levels of household members. These calculations yielded for each food item a standardized daily intake per "reference man" (a man weighing 65 kg, aged 18–45 y, undertaking light physical activity). Estimated intakes of a variety of micro- and macronutrients were calculated using the Chinese food composition tables (34). This estimation method has been validated against direct weighing of individual food intakes in five of the survey counties (Hu J, Zhao X, Parpia B, Chen J, and Campbell TC, personal communication, 1993).

Mortality rates were obtained for a variety of diseases as recorded in the nationwide survey of causes of death in 1973–1975 (33). All rates were standardized for age by calculating the cumulative rate per 1000 subjects by 65 y of age (28). A cumulative rate of 30 for a specific disease, for example, would mean that 3% of the population would die of that disease by the age of 65 y.

Summary of findings

To illustrate the sharp differences in dietary practices between rural China and the United States, a few comparable dietary and biochemical characteristics, previously published by Chen et al (28), are shown in **Table 1**.

These characteristics, which include only a few of those available, demonstrate a sharp difference in the composition of diets in the United States and rural China (urban dwellers and herdspeople of northwestern China were not included in this comparison). Excepting the much higher fat intake of urban dwellers and the herdspeople of northwestern China, dietary fat content in rural China is far below that in the United States. County means in China span a range of 6–24% of energy. This is primarily achieved through a marked decrease in the intake of foods of animal origin, a marked increase in the intake of foods of plant origin, and addition of very little dietary fat. For example, the proportion of total protein in China as animal protein is 10.8%, whereas in the United States it is 69% (28; Zhao X, Campbell TC, Parpia B, Chen J, personal communication, 1992) (data not shown). Note also the much lower intake of retinol in China, found exclusively in animal foods (particularly organ meats and dairy foods, which are rarely, if ever, consumed in most of China). There are also higher intakes of plant food constituents such as vitamin C, dietary fiber, and soluble carbohydrate. Average intakes of dietary fiber and fat in China go substantially beyond the recommended changes advocated by the Western dietary guidelines of 30% of energy for fat, and 25–35 g/d for dietary fiber (37). Mean county intakes of dietary fiber in China were as high as 76.6 g/d.

Energy intake, when adjusted for body weight, is more than 30% higher in China than in the United States (38). In spite of this increased energy consumption, obesity is much less common

TABLE 1
Comparison of selected population characteristics of rural China with the United States[1]

	China	United States
Anthropometry		
Body weight (kg)		
Males	55	77.2
Females	49	69.5
Body height (cm)		
Males	164	173
Females	154	163
Blood constituents		
Plasma cholesterol (mmol/L)[2]	3.75	5.48
	(2.59–4.91)	(4.01–7.09)
Plasma iron (μmol/L)		
Males	(13.1–44.2)	(10.7–26.9)
Females	(11.5–26.1)	(9.0–23.3)
Hemoglobin (g/L)	(110–160)	(140–170)
Females	(100–150)	(120–150)
Intakes[3]		
Total protein (g/d)	64.1	91
Dietary fiber (g/d)	33.3	11.1
Fat (% of energy)	14.5	38.8
Soluble carbohydrates (g/d)	473	245
Energy (kJ/d)	11 080	9912
Iron (mg/d)	34.4	18.4
Retinol (RE/d)	27.8	990
Vitamin C (mg/d)	140	73

[1] $\bar{x}$ ("normal" range). Adapted from reference 28.
[2] Values adjusted up 15% from measured values because of a possible methodological underestimate (Zhao X, Campbell TC, Parpia B, Chen J, personal communication, 1992).
[3] Means of intakes are given for "reference man." Data for China are for a "reference man" who is an adult male of 65-kg body wt who undertakes light physical work. Data for the United States are for an individual adult male (ref 35) whose average body weight is 77.2 kg (ref 36). Both intakes are consumption at the household level, not disappearance data.

in China. For example, average body mass indexes (in kg/m^2) for adult males are 20.5 in China and 25.8 in the United States (38), a difference made all the more remarkable by the fact that the Chinese data are standardized for a reference adult male who undertakes "very light physical activity" (ie, office type work). There may be two factors that contribute to the lower frequency of obesity in China; 1) greater physical activity, which causes greater energy expenditure, and 2) routine consumption of a less energy-dense diet, although the relative contributions of these two factors cannot be estimated at this time.

Although the physical activity of each individual in the survey was defined by one of five activity levels, the relationship between energy intake and energy expenditure from physical activity has not yet been fully analyzed. From casual observation, however, we believe that physical activity in most Chinese people, even office workers, is performed more regularly than in the United States, in part because of their extensive use of bicycles for transportation to and from work.

The much greater leanness, ie, weight-for-height, of Chinese adults is consistent with numerous and long-known observations of Western vegetarians, especially vegans, when compared with

Western omnivores (39–44). Unfortunately, most of these studies did not control for the contribution of physical activity to this leanness, thus the relative proportions of leanness due to diet and to physical activity cannot not be ascertained. However, Hardinge and Stare (39), who investigated adult "pure" vegetarians (vegans), ovolactovegetarians, and omnivores, found that vegans were considerably more lean, even after controlling for energy intake and physical activity. The extent to which diets that are low in fat, in energy density, and in foods of animal origin independently contribute to body leanness, apart from the contributions of physical activity, remains unclear in spite of much research investigation. Recently, Levitsky and his colleagues (31, 32), following the work of others (29, 30), elegantly showed that switching from a high-fat diet to a modestly low-fat diet did not result in energy-intake compensation but resulted in less total energy intake and lower body weight. This effect of a low-fat diet, when coupled with the greater energy expenditure required for lipogenesis following consumption of a high-carbohydrate as opposed to a high fat-diet, could account for some of the lower body weight observed in Chinese subjects, particularly those who eat very-low-fat diets (45, 46). In view of these interpretations, the higher energy intake among the Chinese when compared with Americans is all the more remarkable, because a low-fat diet, according to Levitsky's group (31, 32) and others (29, 30), should result in less energy intake. Either the energy intake observed in this study is due to a substantial effect of physical activity on energy expenditure or, perhaps at this level of very-low-fat intake (6–24% of energy), the observed intake is due to a significant elevation of diet-induced thermogenesis, which is often observed at the modestly low fat ($\approx$20% of energy) intakes used by these investigators (47).

Attained adult height in the Chinese appears to have increased quite dramatically since 1953, according to a comparison of data from the survey with data from the World Bank (48). Between 1953 and 1982, male height-for-age increased an average of 3.2 cm/decade, a rate which surpasses the increase in Europe in the 20th century and is about equal to the increase in Japan since 1950. A recent interpretation of these data showed that attained height was highly correlated with the intake of plant protein, but not with the intake of animal protein (although this was probably because of a statistical insensitivity because the intake of animal protein was low) (Zhao X, Campbell TC, Parpia B, Chen J, personal communication, 1992). This finding of greater attained height during the past several decades in China may be the result both of improved public health conditions, which result in lower growth stunting in earlier childhood, and of improved nutrition. It particularly emphasizes the idea that greater body height can be obtained in less industrialized countries if plant-rich diets that are adequate in amount, quality, and variety are consumed. In other words, attained body height need not be compromised in those who consume a diet rich in foods of plant origin but sparing in foods of animal origin. For example, vegetarian children and adolescents who consume a nutritionally balanced diet grow at least as tall, if not taller, than nonvegetarian children (49), while maintaining lower weight for height (50).

Plasma cholesterol concentrations in rural China, as measured at the time of the survey, were substantially below those in the United States, although the values in China may have been underestimated by $\approx$10–15% because of the sample assay procedures used (28). If 15% is added to the observed mean concentration of 3.28 mmol/L to give 3.78 mmol/L, this compares with

values of 4.01–4.14 mmol/L obtained for Guangzhou rural workers by Tao et al (51). However, this underestimate is likely to not be important for consideration of the associations of plasma cholesterol concentration with other experimental variables because between-village, within-county cholesterol means were highly correlated ($r = 0.77$, $P < 0.001$), thus indicating consistency of error.

Several previous studies have indicated a positive relationship between blood cholesterol concentrations and prevalence of coronary heart disease in populations with traditionally high cholesterol concentrations (52–54). However, there have been persistent reports that cholesterol concentrations below $\approx$4.66–4.91 mmol/L are associated with increasing numbers of deaths from other causes, particularly colon cancer (55–57). Some of these observations have been ascribed to a depressing effect of clinically undetected disease on cholesterol concentrations (54, 58, 59). The data from the survey in China, comprised of mortality rates for a wide variety of diseases and cholesterol concentrations well below 5.17 mmol/L, offered an opportunity to examine the relationship between disease and very-low blood cholesterol concentrations, and thus to determine whether there is a threshold cholesterol concentration below which no further decrease in mortality rates are observed (28). To date, these cholesterol relationships have been studied both for diseases in the aggregate and for single diseases.

Of the various diseases in China, we observed that there was geographic clustering of two disease groups, one associated with poverty, the second with affluence (Table 2) (60). The chief correlate of the diseases of affluence was plasma cholesterol concentration ($P < 0.01$). In turn, plasma cholesterol concentration was associated with the intake of meat and total fat and inversely associated with the intake of legumes and certain fiber fractions.

TABLE 2
Self-clustered disease groups[1]

Diseases of poverty
Pneumonia (16)
Intestinal obstructions (12)
Peptic ulcer (13)
Other digestive disorders (17)
Nephritis (12)
Pulmonary tuberculosis (10)
Infectious diseases other than tuberculosis (17)
Parasitic diseases other than schistosomiasis (10)
Eclampsia (13)
Rheumatic heart disease (13)
Metabolic and endocrine disease other than diabetes (10)
Diseases of pregnancy and birth other than eclampsia (15)
Diseases of affluence
Stomach cancer (5)
Liver cancer (10)
Colon cancer (9)
Lung cancer (16)
Breast cancer (1)
Leukemia (15)
Diabetes (2)
Coronary heart disease (1)
Brain cancer, ages 0–14 years (13)

[1] Numbers in parentheses indicate the number of correlations that are statistically significant ($P < 0.05$) from a total of 20 comparisons between diseases. Adapted from reference 60.

These associations were analogous to correlations obtained for Western populations at much higher blood cholesterol concentrations. This finding is considered rather remarkable in view of the low plasma cholesterol concentration and the low dietary intake of its chief determinants, thus suggesting the absence of a threshold. Thus, in China, only small intakes of meat and very modest elevations of dietary fat are associated with increases in plasma cholesterol, which is associated in turn with the emergence of diseases that typically occur in Western countries.

In-depth investigations of the chief correlates of liver (61) and breast cancers (62) also were revealing. In the case of liver cancer, which is very common in many parts of China, the main correlates of the disease were plasma cholesterol ($P < 0.01$) and chronic infection with the hepatitis B virus (HBV) ($P < 0.001$). Aflatoxin, which is widely regarded as a cause of human liver cancer (63), was not related to liver cancer ($r = -0.17$). This unusual finding suggested that the combination of chronic HBV infection in addition to the consumption of only small amounts of dietary determinants of plasma cholesterol are capable of causing liver cancer, essentially without modification by aflatoxin as a carcinogen. We believe that this negative effect of aflatoxin should be taken seriously because this human study is the most comprehensive study on aflatoxin relationships ever undertaken, being more statistically sensitive than all other studies combined, and it is in accord with a long series of experimental animal studies in our laboratory that provide biological plausibility (27, 64, 65).

Plasma cholesterol concentration was associated directly with all-cancer mortality rates measured in this study. Most notably, these associations were statistically significant for eight different cancers, including colon cancer ($P < 0.01$ for males and $P < 0.001$ for females) (55, 56, 66). In a brief overview of the relationship of plasma cholesterol with aggregate cancer rates, expressed as cumulative mortality from cancer by age 65 y in the absence of other causes of death, Peto et al (67) observed that "there was no evidence that those [counties] with particularly low plasma cholesterol concentrations had high cancer rates." Indeed, when compared with cholesterol concentrations in Britain, these data suggested that at these much lower concentrations of plasma cholesterol in China, if anything, ". . . the opposite trend [ie, high cholesterol, high cancer] was indicated." Thus, these results suggest that there is no threshold between the dietary determinants of plasma cholesterol and cancer mortality rates and that a common nutritional basis, indicated by elevated plasma cholesterol, may exist for most if not all cancers.

As already mentioned, fat intake in rural China is exceptionally low when compared with Western experience (Table 1). In addition to its correlation with plasma cholesterol, fat intake was also correlated, weakly but significantly ($P < 0.05$), with breast cancer (62). However, Chinese women, when compared with British women for example, exhibited later age at menarche, earlier age at menopause, greater parity, earlier age at first birth, and lower circulating concentrations of estrogen, all of which favor a reduction in breast cancer risk (68).

Intakes of 14 complex carbohydrate and fiber fractions were obtained in this study to determine whether particular fiber fractions were associated with particular diseases, especially cancers of the large bowel. Average dietary fiber intake in China was about three times higher than average US intake, with one county mean being as high as 77 g/d (28). So far we have prepared only a brief report of these data (69). However, based on an overview

of the univariate correlations, colon and rectal cancer mortality rates were consistently inversely correlated with all fiber and complex carbohydrate fractions except for pectin, which showed no correlation (28). These relationships, although consistent, appeared rather weak because only rhamnose-containing complex carbohydrate intakes reached statistical significance for cancer of the colon ($r = 0.33$, $P < 0.05$). It appears, then, that within the range of 7–77 g fiber/d, where mean intakes of 29 of the 65 counties were above the upper US recommendation limit of 30–35 g fiber/d (37), there is evidence of a weak inverse relationship between cancer of the large bowel and the intake of multiple complex carbohydrate and dietary fiber fractions.

Although there is substantial evidence that an increased intake of dietary fiber is associated with a lower risk of certain chronic degenerative diseases, many observers have expressed concern that excessive dietary fiber consumption may inhibit, through gastrointestinal chelation, the absorption of several minerals including zinc, calcium, manganese, selenium, copper, and iron ((16, 70–72) and reviewed by Freeland-Graves, 73). Among these minerals, the inhibition of iron absorption may be of the most concern (72). According to a recent review by Scrimshaw (72), "Iron deficiency is the most prevalent nutritional deficiency in the world today." Scrimshaw goes on to say that "poor absorption from the predominantly vegetarian diets of most people in developing countries is a primary cause of iron deficiency." To address this concern, also expressed earlier by others (70, 74, 75), an upper intake of 35 g/d was recommended by the National Cancer Institute (37). In addition to dietary fiber, there are several other substances associated with high-fiber diets that are hypothesized to be inhibitors of mineral absorption, including phytates, polyphenols, tannins, oxalates, calcium, and phosphate (reviewed by Dwyer, 16). It is reasoned that these substances collectively account for the low absorption of the nonheme iron found in foods of plant origin when compared with the absorption of heme iron, exclusively found in foods of animal origin. Based on these considerations, assessment of iron status in China was therefore of considerable interest. The Chinese have very low, almost negligible intake of the more readily absorbed heme iron as well as very high intakes of the numerous iron chelation constituents, especially the tannin found in tea, a beverage widely used in China (76).

Iron intake in China was surprisingly high, averaging ≈ 37 g/d, especially when compared with a US intake of $\approx 18–19$ g/d (28). Also, $\geq 95\%$ of the mean iron intake is in the nonheme form. Iron status was measured by using six indexes: hemoglobin concentrations for 6500 individuals, 65 county mean iron intakes calculated from the household survey of food intake, mean iron intakes derived from direct analysis of food samples collected at each survey site, and 130 village means of plasma pools of ferritin, iron-binding capacity, and iron. Multiple measures have been suggested to be a more discriminating method of assessing iron status (77–79), although these data represent, except for the individual hemoglobin values, either county or village means. Data quality was judged to be very good because the biochemical indicators of iron status (hemoglobin, plasma ferritin, and plasma iron-binding capacity) demonstrated highly significant self-correlations ($P < 0.001$) within county and between sexes.

An analysis of the iron status data was undertaken by Beard et al (80; Beard JL, Wang G, Chen J, Campbell TC, Smith SM, and Tobin B, personal communication, 1992) who concluded that "iron status is not compromised by a mainly vegetarian Chinese

diet" and that there was "no suggestion that iron deficiency is a causal factor of anemia in this population" (Beard et al, personal communication, 1992). The fact that these results were obtained for individuals who consumed large amounts of tea polyphenols along with intakes of dietary fiber in excess of the upper recommended limits of intake in the United States, makes the suggestion that iron status is not compromised by high-fiber diets all the more impressive (37). In fact, in China, dietary fiber content of foods is highly correlated with their iron content ($r = 0.70$, $P < 0.001$). These data suggest that iron status was not compromised by iron-chelating materials in foods and beverages nor by the overwhelming preponderance of the less absorbable nonheme iron, at least not in adults. Apparently, these hypothetical deficits are more than offset by the very high intakes of iron, along with the consumption of other dietary factors that favor iron absorption and utilization (eg, ascorbic acid and citric acid). Perhaps, also, adaptation to these high fiber intakes minimizes any effect on mineral absorption (81–83). This lack of effect in China of fiber intake on iron status would be in agreement with the results of several studies that showed no particular mineral deficiencies in Western vegetarians, as recently reviewed by Kelsay et al (84) and Freeland-Graves (73). Although certain biomarkers of mineral status in vegetarians, such as serum ferritin (85), are occasionally found to be low, these values are almost always considered low when compared with nonvegetarian reference values that may, in fact, be undesirably high.

These are but a few of the possible data combinations available in this study that might be used to investigate the consequences of major dietary change. Many more manuscripts using the data of Chen et al (28) are presently underway and an additional summary of findings using the survey data is published elsewhere (86).

The findings from this survey in China might be considered rather provocative because they suggest that substantial decreases in intakes of dietary fat and animal protein and substantial increases in dietary fiber and other complex carbohydrates should result in continuing reductions in plasma cholesterol and the associated chronic degenerative diseases. Moreover, there seems to be no evidence thus far from these data to indicate that if risks for these diseases were reduced there would be compensatory increases in other adverse health effects, as long as food choice is varied, of good quality, and adequate in amount. Therefore, simultaneous and substantial modification of all dietary factors that beneficially modify various neoplastic and cardiovascular diseases may be necessary to obtain significant reductions in these diseases. These modifications can be obtained most readily and comprehensively by consumption of a diet rich in foods of plant origin, and, to ensure a comprehensive effect for all relevant diseases, a generous variety of products ought to be used. ☒

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