

Walter Willett, MD, DrPH, discusses current concepts of nutritional management

Concepts and Controversies on Diet: Stop Recommending Low-Fat Diets!

By Walter C Willett, MD, DrPH

History of Dietary Recommendations

I will provide an overview of what is increasingly being seen as an optimally healthy diet and will then focus on how nutritionists and physicians can help control the problems of obesity and overweight—problems which are engulfing this country and the world.

The Food Guide Pyramid

The major means of communicating advice about nutrition to the general public is the US Department of Agriculture's Food Guide Pyramid. The main message of the dietary pyramid is that all fats are bad and that we should try to minimize their use in our diet. Because most calories in the US diet are derived from fats and carbohydrates, adhering to a low-fat diet implies eating large amounts of carbohydrates. Carbohydrates form the base of the Food Guide Pyramid and we are told to eat as many as 11 servings of starch per day. The pyramid includes potatoes as a vegetable, so we may consume as many as 13 servings of starch per day. Is that amount really healthful for us? When pressed, representatives of the Department of Agriculture acknowledge that no evidence exists supporting inclusion of large amounts of starch in a healthful diet. Indeed, information that has accumulated during the past decade may indi-

cate that consuming large amounts of starch can contribute to health problems—particularly when we refer to starchy foods such as potatoes, white bread, white rice, white pasta, bagels, and other refined starches.

Fat: Facts and Fallacies

Thirty years ago, the Keys et al¹ and Hegsted et al² equations provided the basis for dietary guidance in the United States. These equations resulted from meta-analyses of many carefully controlled feeding studies that evaluated the way in which total serum cholesterol level was affected by replacing dietary carbohydrates with different types of fat. We learned that saturated fat has a positive coefficient: The more saturated fat in the diet, the higher the serum cholesterol level. However, polyunsaturated fat has a negative coefficient: The more polyunsaturated fat in the diet, the lower the serum cholesterol level. Thus, the concept conveyed by the 1992 Food Guide Pyramid—that all types of fat are unhealthy—is inconsistent with what we have known for more than 30 years.

After publication of the Keys and Hegsted equations, the main dietary recommendation during the 1960s and 1970s was to replace saturated fat with polyunsaturated fat; as a result, polyunsaturated fat intake in the US doubled. Retrospect suggests

that this dietary change was the dominant contributor to the 50% decline in coronary event mortality during the same period. In the early 1980s, the message subtly shifted from “replace saturated fat with polyunsaturated fat” to “remove all fat from the diet.” Exactly how this shift happened is unclear, but a segment of the nutrition community believed that messages about different types of fat in the diet were too complex and that promoting reduction of total dietary fat made more sense. However, no evidence showed that the message of “remove all fat from the diet” was easier for people to understand or practice.

By the 1990s, published information from the American Heart Association strongly advised use of nonfat products,³ a recommendation which marked the beginning of the big, national crusade against dietary fat. We were supposed to avoid foods such as regular yogurt, margarine, and butter because they were high in fat; instead, we were supposed to eat nonfat yogurt, butter-flavored granules, nonfat salad dressing, and fat-free cookies and crackers, even though these substitutes typically had just as many calories as the products we were supposed to avoid. Were these substitutes really better for us? Important findings from a population study in Holland by Mensink and Katan⁴ have been replicated many



Walter C Willett, MD, DrPH, is a professor at the Harvard School of Public Health. He is also a co-investigator of the Nurses' Health Study I and the principal investigator of The Nurses' Health Study II. Dr Willett is author of the nationally best-selling book, "Eat, Drink and be Healthy: The Harvard Medical School Guide to Healthy Eating." E-mail: walterwillett@channing.harvard.edu.

Weight Management and Obesity Symposium

times.⁵ Those authors studied the effect on serum cholesterol and triglycerides in people who had been eating a typical “Western” diet (about 40% of total calories from fat) when they replaced 10% of calories from saturated fat with calories either from olive oil (mostly monounsaturated fat) or from complex carbohydrates. The strategy of replacing fat calories with carbohydrate calories is consistent with the advice from the American Heart Association. A similar decrease in total serum cholesterol was seen in people on both replacement diets; if anything, replacement of saturated fat calories by monounsaturated fat calories reduced total serum cholesterol slightly more than did replacement by carbohydrate calories. However, the most important differential effect was in high-density lipoprotein cholesterol (HDL-C, the “good cholesterol”) level. As carbohydrates in the diet increased, serum HDL-C level decreased; however, as saturated fat was replaced by monounsaturated fat, serum HDL-C level remained stable. In addition, increased dietary carbohydrates resulted in increased fasting serum triglycerides. The higher monounsaturated fat diet was apparently healthier than the low-fat, high-carbohydrate diet because although both reduced total serum cholesterol, the higher monounsaturated fat diet resulted in better serum HDL-C and triglyceride levels.

Understanding Trans Fatty Acids

The story on dietary fat has become a bit more complex with the realization that trans fatty acids (trans fats) are also important. Trans fats are extremely prevalent in processed foods. Trans fats are created from polyunsaturated fats during the partial hydrogenation process that

converts liquid vegetable oil, soybean oil, or corn oil into solid fats such as margarine or shortening (Crisco); cis-isomers are transformed to trans-isomers, a change that causes the molecules to straighten and organize into a solid. In addition, omega-3 fatty acids are destroyed during partial hydrogenation, a reaction that creates a product with a longer shelf life (important to the food industry) but with less nutritional value.

For a long time, we believed that fat was fat, and that the form of dietary fat didn't really matter. But in the 1970s, we became concerned that the partial hydrogenation process may be transforming an essential fatty acid that has important biologic function into a molecule that may have very different biologic function. Mensink and Katan et al⁶ studied the effect on serum cholesterol level after people replaced 10% of their dietary calories from monounsaturated fat with calories from either trans fat or saturated fat and found less of an increase in total serum cholesterol level with replacement by trans fat. For a number of years, the food industry used these results deceptively by saying that because trans fats reduced total serum cholesterol level relative to saturated fats, trans fats should be used regularly in our food supply. This message was erroneous, because although increased dietary trans fat or saturated fat similarly increases LDL-C cholesterol level, trans fat also causes undesirable decreases in HDL-C level.

In a meta-analysis of studies on the effect of various dietary fats on blood lipids (eg, total cholesterol: HDL-C

ratio),⁷ the negative effect of dietary trans fat was about twice that of saturated fat on a calorie-for-calorie basis. We now also know that dietary trans fats have additional adverse effects, including increased serum triglyceride⁷ and lipoprotein(a)⁸ levels and adverse effects on endothelial function.⁹

Findings from The Nurses' Health Studies

Although this discussion has focused on the effects of trans fat and other types of dietary fat on blood lipid levels, researchers now know that many other mechanisms can potentially mediate an effect of diet on risk of heart disease. These mechanisms include systemic or local inflammation, hypertension, homocysteine, and prooxidant and antioxidant processes. Now, researchers are recognizing the important role mediated by the threshold for ventricular fibrillation.

If we consider only the effect of diet on blood lipids, we could be misled about how the dietary factor influences the risk of heart disease—which is, of course, what we are ultimately concerned about.

Ideally, researchers could conduct a series of large randomized trials comparing different types of dietary fat in different amounts and proportions to assess the effects on risk of coronary heart disease. However, this type of study requires large numbers of people, long follow-up periods, and strict dietary compliance; consequently, few such studies exist. An alternative strategy for a prospective study would be one in which dietary and health data were collected from large numbers

... the negative effect of dietary trans fat was about twice that of saturated fat on a calorie-for-calorie basis.

of people over time, with regular updates as participants' diets changed; this study would measure and control for potentially confounding variables, such as smoking and physical activity. My colleagues and I planned and are conducting three such studies. In 1976, Frank Spizer established The Nurses' Health Study,¹⁰ in which 121,000 female nurses participated. In 1989, The

Nurses' Health Study II¹⁰ began with more than 116,000 of the next generation of female nurses enrolled. Because both of these studies included women only, we began the Health Professionals Follow-Up Study in 1986 and enrolled 52,000 men.¹¹ These studies are unique, not only because of their large size but also because we periodically reevaluate diet—a very important factor because people gradually change their diet. These studies track participants' diet and assess risk of cancer, cardiovascular disease, and other major health conditions.

In The Nurses' Health Study, we evaluated levels of different types of dietary fat and associated risk of heart disease (after controlling for other variables) after 14 years of follow-up.¹² On the basis of about 1000 incident cases of coronary heart disease, the deleterious effect of trans fats on blood lipids would have predicted that trans fat was clearly the worst type of dietary fat.

Risk of coronary heart disease increased only slightly with increases in dietary saturated fat compared with increase in dietary carbohy-

drates. This result is not surprising because replacing calories from saturated fat with calories from carbohydrate does not alter the serum

HDL-C level. In contrast, replacing calories from carbohydrate with calories from saturated fat increases levels of total serum cholesterol, LDL-C, and HDL-C, so the ratio does not change. Just substituting saturated fat calories for carbohydrate calories does not have much effect on coronary heart disease.

To substantially decrease risk of heart disease, we have to replace calories from the "bad" fats—trans fat or saturated fat—with calories from the "good" fats—monounsaturated or polyunsaturated fat—or from some proportion of both. In our studies, level of total dietary fat was not related to risk of heart disease, because most women ate some bad fats and some good fats. The key association was in the balance of types of fat in the diet. Women with a high proportion of trans fat to polyunsaturated fat in the diet had up to three times the risk of heart disease compared with women with a high proportion of polyunsaturated fat to trans fat in the diet. Why did some women have high levels of trans fat and low levels of polyunsaturated fat in their diet? The sad fact is that nutritional messages told women that they should eat margarine instead of butter, Crisco, or vegetable shortening because margarine was lower in saturated fat. Although some of the women were perhaps eating unhealthful foods, such as donuts or fast-food hamburgers, these women primarily were doing what they had

been told was good for them. During the late 1970s and early 1980s, most physicians were telling people to use margarine instead of butter; but at that time, almost all the margarines were less healthful than butter. Fortunately, with publication of results of studies about trans fat, some margarines are now manufactured that are free of trans fats.

Polyunsaturated Fats: About Omega-3 Fatty Acids

Polyunsaturated fats can be divided into two main classes, omega-6 and omega-3 polyunsaturated fats.

A growing body of compelling evidence indicates that omega-3 fatty acids have antiarrhythmic properties. One of the most conclusive studies, the large, randomized GISSI trial¹³ conducted in Italy, showed that people with a previous myocardial infarction (MI) episode who ingested fish oil (in capsule form) had moderately reduced risk of recurrent cardiovascular disease compared with that of patients with previous MI who took placebo. In this study, the benefits of fish oil related specifically to prevention of sudden death, presumably caused by arrhythmia. The Physicians' Health Study¹⁴ evaluated risk of heart disease in 18,000 men and found no relation between serum omega-3 fatty acid level and total incidence of heart disease. However, when Albert and her colleagues categorized incident events of heart disease as sudden death versus all other events, they found strong inverse relation between serum level of omega-3 fatty acids and risk of sudden death. Men with the highest serum levels of omega-3 fatty acids had about 80% lower risk of sudden death.¹⁴

In our studies, level of total dietary fat was not related to risk of heart disease, because most women ate some bad fats and some good fats.

Weight Management and Obesity Symposium

Primary dietary sources of omega-3 fatty acids include fish oil, plant oil, and walnuts.

Fish Oil

The most popular source of dietary omega-3 fatty acids is fish oil. Fatty fish, such as mackerel, lake trout, herring, sardines, and albacore tuna contain high levels of omega-3 in the forms of eicosapentaenoic and docosahexaenoic acid.

Plant Oil

Despite fish oil's popularity as a source of omega-3 fatty acids, the greatest quantity of omega-3 fatty acids in our food supply is found in plant oil. About 10% of the fat in canola oil, 7% of the fat in soybean oil, 5% to 10% of the fat in walnuts, and 50% of the fat in flaxseed oil is omega-3 fatty acid, specifically alpha-linolenic acid.

The most important source of omega-3 fatty acid in the diet of participants in The Nurses' Health Study was oil-and-vinegar, full-fat salad dressing, because most dressings were made with either soybean oil or canola oil. Salad dressings are not hydrogenated; if they were, they would be of solid consistency in the refrigerator. We found a 50% lower risk of fatal coronary heart disease among women who ate full-fat salad dressing most days of the week compared with women who rarely ate full-fat salad dressing.¹⁵ Unfortunately, because the American Heart Association and others have been telling people to avoid full-fat salad dressing, many people could have died thinking they were making the healthier choice by using fat-free dressing.

Nuts

Another misinformed nutritional message was to avoid eating nuts, because nuts are high in fat. Nut

consumption by participants in The Nurses' Health Study decreased by about 50% after 1980 because women were doing what they were told was healthful. However, incidence of myocardial infarction was about 30% lower in women who ate nuts almost daily compared with that of women who rarely ate nuts.¹⁶ This result is expected, because the fat in nuts is almost all unsaturated. A number of carefully controlled feeding studies concluded that if you consume more nuts, you improve your blood lipids. And in all of these studies, people who consumed more nuts did not weigh more, because nuts satisfied their hunger. These studies provide evidence that you do not get fat just because you eat high-fat products.

To summarize, coronary heart disease rates can be dramatically reduced by nutritional means, but this benefit will not be achieved by replacing saturated fat with carbohydrate.

Is Dietary Change After Myocardial Infarction Too Late?

The good news is that definite benefit results from dietary change after a coronary event. In the Lyon Diet Heart Study,¹⁷ conducted in France, people who had already had an MI were randomized to either the experimental diet (what they called a Mediterranean-type, high alpha-linolenic-acid diet) or the control diet. The experimental diet consisted of high quantities of fruits and vegetables, low amounts of red meat, low amounts of trans fat and saturated fat, and moderate amounts of whole grains. This diet also had substantially increased amount of omega-3 fatty acids in the form of canola oil (10% alpha-linolenic acid). The control diet was the American Heart Association diet.

The results were dramatic: far better survival on the experimental diet with about 70% reduction in recurrent coronary heart disease and coronary heart disease mortality. The benefit showed up within months of changing to the experimental diet. A confirmation study¹⁸ was done in India, where similar dietary changes were made using mustard oil (the genetic precursor of canola oil) as the source of omega-3 fatty acids. These researchers also observed a dramatic reduction in recurrent coronary heart disease in participants after a short time on what they called an Indo-Mediterranean diet, which had Indian seasonings but nutritionally was similar to the Mediterranean diet used in the Lyon Heart Study.

So it's not too late to make dietary improvements after a heart attack.

Dietary Fat and Cancer

Although recommending low-fat diets may not decrease coronary heart disease, if a high percentage of calories from fat in the diet has other deleterious effects, we still might reasonably recommend low-fat diets.

Breast Cancer

Breast cancer was thought to be related to high-fat diets. This hypothesis was derived, to a large extent, from comparison of fat intake and breast cancer rates between Western and Asian countries. Because of many differences between Western and traditional Asian diets and lifestyle, great potential exists for confounding factors in these international comparisons. For that reason, the relation between

... coronary heart disease rates can be dramatically reduced by nutritional means, but this benefit will not be achieved by replacing saturated fat with carbohydrate.

... we found a 30% lower risk of coronary heart disease with higher intake of cereal fiber but not with fruits or vegetables.

total fat intake and breast cancer risk was a primary study objective in the Nurses' Health Study and was the primary justification for funding the dietary component of the Nurses' Health Study. On the basis of about 3000 women in whom breast cancer developed during 14 years of follow-up, we did not find any support for an important relation between fat total intake and breast cancer.¹⁹ Over a wide range of fat intake, no hint was found of a positive association with breast cancer. In fact, the trend was inversely statistically significant in that the highest breast cancer rates were in the women who had the lowest total fat intake.

Colon Cancer

For colon cancer, we saw a somewhat different result. Although no association existed between level of animal fat intake and risk of breast cancer, such an association was seen for risk of colon cancer. With more detailed examination, however, this association appeared to result entirely from red meat consumption data, particularly of processed red meat. Although we are not sure of the cause, the fat in red meat does not appear to increase risk of colon cancer.²⁰

In summary, after examining many different outcomes within The Nurses' Health Study and our cohort of men as well, we did not see any disease that is clearly related to total intake of fat.

Fruits, Vegetables, Alcohol, and Folic Acid

Many aspects of diet besides fat and type of fat clearly influence the risk of coronary heart disease. Our study demonstrated an inverse relation between consumption of

fruits and vegetables and risk of coronary heart disease. Probably many components of fruits and vegetables contribute to this reduction in risk. One probable component is potassium, because potassium does lower blood pressure—a major risk factor for coronary heart disease.

One component of fruits and vegetables that does seem important is folic acid. Level of homocysteine in the blood is now fairly well established as an independent risk factor for coronary heart disease.²¹ Despite a small genetic contribution, blood level of homocysteine is primarily determined by the amount of folic acid in the diet.

Reducing the homocystine blood level is fairly easy. For example, when we look at folic acid and coronary heart disease, we see a benefit as well as a strong interaction with alcohol. Dr Arthur Klatsky (KP Northern California), using data from Kaiser Permanente,²² provided some of the first good evidence that regular, moderate consumption of alcohol reduces risk of coronary heart disease compared with not drinking at all. A moderate drinker has the very beneficial effect of having more folic acid in the diet. Women who had the highest amount of folic acid and were moderate drinkers had about one fourth the risk of coronary heart disease compared with women who were nondrinkers and had low amounts of folic acid in the diet. Almost every time we look at folic acid, we see interaction with alcohol.

How can we increase our folic acid level? It's very simple: just take a multiple vitamin. Although a good diet is also certainly important because you get other benefits from fruits and vegetables, absorption of folic acid from fruits and vegetables is somewhat inconsistent. Without

some sort of supplementation, you can't be certain that you are getting adequate folic acid.

Carbohydrates: About Glycemic Index and Glycemic Load

Carbohydrate intake has been a fairly neglected area until recently—a surprising fact because carbohydrate accounts for most calories in most diets. Part of the reason for this neglect has been the "party line" from the American Diabetes Association, which says that all carbohydrates are the same. I believe that the evidence clearly shows that all carbohydrates are not the same.

Until recently, when we talked about the importance of different kinds of carbohydrates, we talked about high-fiber, whole-grain types of carbohydrates. The fiber content of grains does appear important. We published an article²³ that showed no relation between fiber intake and colon cancer, and this finding has been reproduced in a number of other studies as well.^{25,25} In The Nurses' Health Study and the Health Professionals Follow-Up study, we found a 30% lower risk of coronary heart disease with higher intake of cereal fiber but not with fruits or vegetables.²⁶ This finding has been reproduced in about a dozen epidemiologic studies.

Glycemic Index

However, more than just the fiber content of cereal products and carbohydrates may need to be considered; glycemic index may also be important. During the last few years, the evidence has become convincing that coronary heart disease benefit is not conveyed solely by high-fiber carbohydrates but also by low-glycemic-index carbohydrates. High-glycemic-index carbohydrates could be, for example, bagels. This

Weight Management and Obesity Symposium

is what happens if you sneak off and have your bagel: you very rapidly break down that refined starch into glucose in the stomach. That glucose is very rapidly absorbed, and your blood sugar increases sharply, or “spikes.” Of course, the body does not want high blood sugar so the pancreas pumps out a big blast of insulin, and the blood sugar comes crashing down. Often, then, by three or four hours after eating refined starch, people are a bit hypoglycemic relative to the fasting level of glucose.

This reaction has several potentially adverse consequences. First, this rapid decline in blood sugar makes you feel hungry and you want to run for the refrigerator. That’s great if the refrigerator is a mile away, but, it’s usually not. Despite what Kenneth H Cooper, MD, MPH, (founder Cooper Aerobics Center; author of *Aerobics*) would like, the refrigerator is often just in the next room or around the corner—just all too easy to get more calories into our environment. Second, these high levels of glucose and insulin appear related to the adverse metabolic response we talked about earlier—to low HDL-C and high triglycerides that would predict higher risk of coronary heart disease. Third, high demand over the years for insulin—and for high amounts of insulin—may well lead to pancreatic exhaustion and risk of Type II diabetes.

In contrast, when you have low-glycemic-index carbohydrate, such as a coarsely ground whole-grain muffin, whole-grain pasta, or an apple, that kind of carbohydrate is absorbed less rapidly. The rise in blood glucose and in insulin is less, and you don’t get that midmorning depression in glucose level. You’re less likely to get hungry before the next meal with low-glycemic-index

carbohydrates, as has been shown in short-term studies.

Glycemic Load

Using data from The Nurses’ Health Study, we computed what we call glycemic load (the amount of carbohydrate available times its glycemic index), because glycemic load will most specifically relate to elevation in blood glucose. The glycemic index has been misused by some people, and popular books on this topic tell you to avoid carrots because the carbohydrate in carrots has a high glycemic index. However, because carrots have such a small amount of carbohydrate, blood glucose level won’t rise much no matter what the glycemic index is. You must eat about a pound-and-a-half of carrots to consume the 50 g of carbohydrate used to test for glycemic index. So, the amount of carbohydrate and its quality (as is reflected in the glycemic index) is what we used to calculate glycemic load: the amount of carbohydrate multiplied by its glycemic index.

Glycemic Load and Disease Risk

Risk of Type II diabetes increases with higher glycemic load or higher glycemic index and lower cereal fiber in the diet. Women in The Nurses’ Health Study with a high-glycemic-load, low-cereal-fiber diet had about 2.5-fold increased risk of diabetes compared with women who had a low-glycemic-load, high-cereal-fiber diet.²⁷ And we’ve reproduced this finding in the Health Professionals Follow-Up Study²⁸ and, more recently (although we haven’t published it yet), in The Nurses’ Health Study II as well. So how did these women get that high-glycemic-load, low-cereal-fiber diet? Well, they were following the Food Guide Pyramid. They were load-

ing up on carbohydrate—they may have had the bagel for breakfast in the morning or maybe a bagel and jam. That’s the best thing—fat-free, right? Isn’t that supposed to be the paradigm of a healthful breakfast? For lunch, they may have had some pasta with fat-free sauce on it and come home for dinner and had a baked potato—also what we were told is a virtuous thing to have, with no fat on it and fat-free salad dressing. And they might have had some fat-free yogurt for dessert, which has a lot of sugar, and maybe even a fat-free cookie, which is high in sugar, and they might have felt very good about all of that. But they were putting themselves at high risk for Type II diabetes in the process, even though they were doing what they were told—and that’s particularly tragic. It’s hard enough to get people to follow advice, but when we misguide them—then that’s a real tragedy.

Looking at coronary heart disease incidence among participants in The Nurses’ Health Study was interesting, because we saw an interaction between glycemic load and body mass index (BMI).²⁹ Participants who were really lean did not experience much adverse effect from a high-glycemic-load diet. However, women who were of average or above-average BMI almost doubled their risk of coronary heart disease by eating a high-glycemic-load diet compared with eating a low-glycemic-load diet. This interaction explains why traditional Asian countries can live on high amounts of rice in the diet and not have adverse problems. They are very lean and physically active and have extremely low prevalence of insulin resistance. Gerald Reaven at Stanford University demonstrated this interaction first in a carefully controlled feeding study³⁰ in which

he replaced monounsaturated fat with carbohydrate and overall saw depressed HDL-C and elevated triglycerides with a higher-carbohydrate diet. But that adverse metabolic change was far worse if women had an underlying degree of insulin resistance. Insulin resistance, which is mainly in our population because of our overweight and inactivity,

... the possibility exists that high carbohydrate intake, particularly of highly refined carbohydrates and sugars ... may also have contributed to the problem of overweight for metabolic reasons ...

greatly exacerbates the adverse metabolic response to a high-carbohydrate diet. Again, if you're very lean and active and have low insulin resistance, you can tolerate the higher-glycemic-load diet, but if you're overweight and have more insulin resistance, you cannot tolerate the high glycemic load so well. Ironically, if people go to see a dietitian in most institutions—maybe not here, but in most places—the

first thing they're told is "You've got to go on a low-fat, high-complex-carbohydrate diet." These are the very people who metabolically cannot tolerate that kind of diet. And we've seen in the Nurses' Health Study confirmation of Gerald Reaven's findings—that there's a much worse adverse metabolic picture among women on a high-glycemic-load, low-fat diet if they're overweight.

Overweight, Obesity, and Disease Risk

I'll summarize some of the adverse consequences of higher BMI that we found in the Nurses' Health Study and in the Health Professionals Follow-Up Study. Very strong associations exist between BMI and adverse health outcomes. The worst, of course, is Type II diabetes, the dis-

ease most closely linked with being overweight. Someone who has a BMI of 23 has four times the risk of Type II diabetes compared with a person with a BMI of less than 21, and a BMI of 25 is considered within the range of healthy weight. Thus, many people who are considered within the healthy weight range are far from their optimal weight. People in the mid or upper range of overweight also have a two- to three-fold increased risk of coronary heart disease, gallstones, and hypertension. Of course, during the last three years, we've come to appreciate many other consequences of overweight besides those of more classic cardiovascular disease and diabetes. We analyzed incidence of breast cancer in postmenopausal women in The Nurses' Health Study.³¹ For a while, we had trouble understanding the results until we stratified women by their use of hormone replacement therapy. All women who were using hormone replacement therapy were at elevated risk of breast cancer, regardless of BMI. However, among women who never used hormone replacement therapy, about a two-fold higher risk of breast cancer existed for women who had gained 20 kilograms or more since they were 18 years old compared with women who had maintained stable weight during their adult lives. What this shows is that the major effect of being overweight is mediated by elevated estrogens. For example, women who are obese have about three times the blood level of estradiol compared with that of lean women. Taking a hormone replacement pill did not, in fact, further elevate breast cancer risk among the women who were most overweight. Addition of progesterone changes that picture; progesterone has substantial addi-

tional adverse effects on breast cancer risk above and beyond the estrogen alone.

What Diet Can We Recommend?

One of the concerns to us was that if we looked at the changes over time in the United States—a big upturn in obesity occurred starting around the late 1970s and early 1980s. Until that time, prevalence of obesity was still an important problem, but the prevalence was rather flat and not increasing. But then the rates skyrocketed up. Interest shifted about that time from removing certain types of fat to removing all fats from the diet.

Just until the last two years or so, the "party line" in the nutrition community was that it's only fat calories that count, and that really goes along with the official dietary pyramid. I've had colleagues who said you can't get fat from eating carbohydrates—that you only get fat by eating fat in the diet. Farmers have known for thousands of years that is not true. How do you make the fattened lamb or fattened anything? You put the animals in a pen so they don't run around and get physical activity, and you feed them grain—even whole grain—and they get fat. And this sad story appears to apply to people—not just lambs. Unfortunately, we probably have collectively as a nutrition community contributed to the overweight problem—perhaps because people were given the impression that they could eat all the carbohydrates they wanted to—that you could have your box of fat-free cookies and it wouldn't make you fat. I think this picture has changed in the last couple of years: recognition that total calories count has evolved. But the possibility exists that high carbohydrate intake,

Weight Management and Obesity Symposium

particularly of highly refined carbohydrates and sugars (as the dominant form of carbohydrate in the US diet) may also have contributed to the problem of overweight for metabolic reasons, which I discussed when describing the glycemic index.

A tremendous debate has begun, which I'm sure everyone is familiar with, about what type of diet best helps with weight loss and management. This question should ideally be settled by randomized trials: it's not impossible and not nearly as difficult to do randomized trials looking at weight as those studying incidence of coronary heart disease. For heart disease, you may need tens of thousands of people; you need perhaps 100 or 200 people for a reasonable study of dietary effects on body weight. This topic may also have been misinterpreted, because most of the randomized trials done until recently used only short follow-up periods, a few weeks or a few months, from which you can get quite misled. Clearly, long-term weight control is most important. People lose weight on almost any diet in the short term; the real challenge is to maintain weight loss and weight control.

We analyzed³² results of a series of randomized trials that examined the effect of diets with lower levels of dietary fat as a percentage of total calorie intake and that lasted one year or more. Our analysis showed no weight benefit accrued after one year or more. Although a number of studies showed some modest decrease in body weight during the first few months, weight either stabilized or was regained by 12 to 18 months. It's very clear that low-fat diets are really not effective, on average, for long-term weight control. Some people can go on a low-fat

The Atkins Diet

Many are troubled by this diet because it usually contains the recommendation to eat all the red meat and butter and cheese you want. But a handful of studies have been published recently indicating that people on that type of diet are able to lose more weight and control their weight better than people on a low-fat diet, a finding which adds important evidence that a low-fat, high-carbohydrate diet makes it difficult for many people to control their weight. Weight reduction, if somebody is overweight, is so important and so beneficial that reducing weight can counter the adverse effects of eating large amounts of saturated fat in the diet.

Thus, it's important to pay attention to these studies and to learn from them, even though I wouldn't recommend long-term high intake of animal fat to anybody. If it's true (and it probably is true) that substantially decreasing carbohydrate intake can make it easier to control total calories, you can have a very-low-carbohydrate diet and have it be a healthful diet at the same time if—instead of red meat and butter—you consume salmon, nuts, olive oil, and plenty of salad. That combination is a good diet that's low in carbohydrates and may be useful for many people. For most people, a Mediterranean-type diet such as I've suggested, which includes modest amounts of whole-grain forms of carbohydrate, will probably be most acceptable and beneficial in the long run. But more long-term studies of the effects of various diets on weight control are clearly needed.

diet and have enough willpower to lose weight, but randomized studies show that most people do not lose weight on low-fat diets.

These findings are surprising, because most of these studies were seriously biased in favor of the low-fat group. In most of the studies, the control group got no intervention, and the low-fat-diet group got intensive, state-of-the-art intervention with monitoring of food intake, keeping diaries, weighing food, group support, and lots of counseling. Still, they didn't do any better than the control group. Evidence suggests that just intensive monitoring and attention to diet can help people lose a few pounds, so this result was surprising.

On the basis of a small meta-analysis (restricted to the four studies that had similar-intensity intervention in both groups), low-fat diets did worse. A study by McManus et al³³ had similar-intensity intervention for both groups.

One group, on what was called "high-fat" but probably better called "moderate-fat," ate a diet with 35% of total calorie intake from fat, a Mediterranean-type, healthful diet. This diet included low amounts of red meat, lots of whole grains, lots of vegetables, and the fat was from nuts, olive oil, and salad dressing. The "low-fat" group ate a diet with 20% of calories from fat, an American Heart Association type of diet. What researchers saw was a paradigm for what's happened in the United States. In the first six months, similar weight loss occurred in both groups, but the people on the low-fat diet just couldn't adhere to this diet; they dropped out at a very high rate. When researchers brought these participants back in to weigh them, they had regained much of the weight. But the people on the higher-fat, Mediterranean-type diet had about twice the weight loss by 18 months compared with loss in

the low-fat group, and these people felt satisfied. Their diet was something they could live with, and they didn't feel deprived.

Conclusion

To emphasize the tremendous potential of dietary intervention and lifestyle, I'll summarize with a look at how much disease could be prevented. As Dr Cooper emphasized, not smoking is important and we saw that BMI is important and that activity, even fairly modest activity, is important. We defined a good diet by using a score based on low trans fat, high polyunsaturated fat, low glycemic load, high cereal fiber, fish twice a week or more, and high folic acid. We also defined moderate drinking as five or more grams of alcohol per week. That's about a half a drink, so it's a very modest amount of alcohol that seems to be beneficial.

During 14 years of follow-up to The Nurses' Health Study, we found that had participants followed this very moderate, very achievable set of behaviors, they could have avoided more than 80% of cases of coronary heart disease, 92% of cases of Type II diabetes, and 71% of cases of colon cancer.

The Food Guide Pyramid does not provide people with good dietary advice because the guide ignores type of fat, form of carbohydrate, and source of protein in the diet—all of which can make an enormous difference to health. ❖

Acknowledgment

Support for much of the research described was provided by the National Institutes of Health.

References

1. Keys A, Anderson JT, Grande F. Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet.

- Metabolism 1965 Jul;14(7):776-87.
2. Hegsted DM, McGandy RB, Myers ML, et al. Quantitative effects of dietary fat on serum cholesterol in man. *Am J Clin Nutr* 1965 Nov;17:281-95.
3. Krauss RM, Deckelbaum RJ, Ernst N, et al. Dietary guidelines for healthy American adults. A statement for health professionals from the Nutrition Committee, American Heart Association. *Circulation* 1996 Oct 1;94(7):1795-800.
4. Mensink RP, Katan MB. Effect of a diet enriched with monounsaturated or polyunsaturated fatty acids on levels of low-density and high-density lipoprotein cholesterol in healthy women and men. *N Engl J Med* 1989 Aug 17;321(7):436-41.
5. Mensink RP, Zock PL, Kester AD, et al. Effects of dietary fatty acids and carbohydrates on the ration of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* 2003 May;77(5):1146-55.
6. Mensink RP, Katan MB. Effect of dietary trans-fatty acids on high-density and low-density lipoprotein cholesterol levels in healthy subjects. *N Eng J Med* 1990 Aug 16;323(7):439-45.
7. Katan MB, Zock PL, Mensink RP. Effects of fats and fatty acids on blood lipids in humans: an overview. *Am J Clin Nutr* 1994 Dec;60(6 Suppl):1017S-1022S.
8. Katan MB, Mensink R, Van Tol A, et al. Dietary trans-fatty acids and their impact on plasma lipoproteins. *Can J Cardiol* 1995 Oct;11 Suppl G:36G-38G.
9. de Roos NM, Bots ML, Katan MB. Replacement of dietary saturated fatty acids by trans-fatty acids lowers serum HDL cholesterol and impairs endothelial function in healthy men and women. *Arterioscler Thromb Vasc Biol* 2001 Jul;21(7):1233-7.
10. Welcome to the home page of the Nurses' Health Study at Brigham and Women's Hospital [Web site]. Available from: www.channing.harvard.edu/nhs/ (accessed June 5, 2003).
11. Harvard School of Public Health. Health Professionals Follow-Up Study [Web site]. Available from: www.hsph.harvard.edu/hpfs/ (accessed June 5, 2003).
12. Hu FB, Stampfer MJ, Manson JE, et al. Trends in the incidence of coronary heart disease and changes in diet and lifestyle in women. *N Engl J Med* 2000 Aug 24;343(8):530-7.
13. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. *Lancet* 1999 Aug 7;354(9177):447-55.
14. Albert CM, Campos H, Stampfer MJ, et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *N Engl J Med* 2002 Apr 11;346(15):1113-8.
15. Hu FB, Stampfer MJ, Manson JE, et al. Dietary intake of alpha-linolenic acid and risk of fatal ischemic heart disease among women. *Am J Clin Nutr* 1999 May;69(5):890-7.
16. Hu FB, Stampfer MJ, Manson JE, et al. Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. *BMJ* 1998 Nov 14;317(7169):1341-5.
17. de Lorgeril M, Salen P, Martin JL, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation* 1999 Feb 16;99(6):779-85.
18. Singh RB, Niaz MA, Sharma JP, et al. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian experiment of infarct survival—4. *Cardiovasc Drugs Ther* 1997 Jul;11(3):485-91.
19. Holmes MD, Hunter DJ, Colditz GA, et al. Association of dietary intake of fat and fatty acids with risk of breast cancer. *JAMA* 1999 Mar 10;281(10):914-20.
20. Willett WC, Stampfer MJ, Colditz GA, et al. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N Engl J Med* 1990 Dec 13;323(24):1664-72.
21. Ford ES, Smith SJ, Stroup DF, et al. Homocyst(e)ine and cardiovascular disease: a systematic review of the evidence with special emphasis on

Weight Management and Obesity Symposium

- case-control studies and nested case-control studies. *Int J Epidemiol* 2002 Feb;31(1):59-70.
22. Klatsky AL. Moderate drinking and reduced risk of heart disease. *Alcohol Res Health* 1999;23(1):15-23.
 23. Fuchs CS, Giovannucci EL, Colditz GA, et al. Dietary fiber and the risk of colorectal cancer and adenoma in women. *N Engl J Med* 1999 Jan 21;340(3):169-76.
 24. Albers DS, Martinez ME, Roe DJ, et al. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. Phoenix Colon Cancer Prevention Physicians' Network. *N Engl J Med* 2000 Apr 20;342(16):1156-62.
 25. Terry P, Giovannucci E, Michels KB, et al. Fruit, vegetables, dietary fiber, and risk of colorectal cancer. *J Natl Cancer Inst* 2001 Apr 4;93(7):525-33.
 26. Wolk A, Manson JE, Stampfer MJ, et al. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. *JAMA* 1999 Jun 2;281(21):1998-2004.
 27. Salmeron J, Manson JE, Stampfer MJ, et al. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. *JAMA* 1997 Feb 12;277(6):472-7.
 28. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes Care* 1997 Apr;20(4):545-50.
 29. Liu S, Willett WC, Stampfer MJ, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr* 2000 Jun;71(6):1455-61.
 30. Reaven GM. Diet and Syndrome X. *Curr Atheroscler Rep* 2000 Nov;2(6):503-7.
 31. Huang Z, Hankinson SE, Colditz GA, et al. Dual effects of weight and weight gain on breast cancer risk. *JAMA* 1997 Nov 5;278(17):1407-11.
 32. Willett WC, Leibel RL. Dietary fat is not a major determinant of body fat. *Am J Med* 2002 Dec 30;113 Suppl 9B:47S-59S.
 33. McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low-fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord* 2001 Oct;25(10):1503-11.

Our Ambitions

To wrest from nature the secrets, which have perplexed philosophers in all ages, to track to their sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of disease—these are our ambitions.

Sir William Osler, 1849-1919, physician, professor of medicine, and author