Obesity Declared a Disease

A consensus panel says losing weight is not just a matter of vanity—it is a matter of health

A National Institutes of Health consensus panel on the health implications of obesity has concluded that obesity is a potential killer. It is like high blood pressure in that there is no threshold of overweight where the ill effects begin. Any degree of overweight, even 5 or 10 pounds, may be hazardous to health. And everyone who is 20 percent or more overweight—the usual definition of obese—should make every effort to reduce, the panel said.

Although the medical community has long considered morbid obesity to be related to poor health, it has not until now determined whether more moderate degrees of overweight are risky, according to panel chairman Jules Hirsch of Rockefeller University.

Edward Huth, who is editor of the *Annals of Internal Medicine*, likened the obesity report to the surgeon general's report on smoking of about 25 years ago and remarked that he hopes this report will have the same sort of effect. Like smoking, he said, obesity is extremely difficult to treat, its ill effects do not extend to everyone with the condition, and its biological effects are long delayed.

But although the panel was definite in its statements, the data it relied on in drawing its conclusions were soft, to say the least. Studies contradicted each other, particularly in the area of obesity and heart disease. No one study stood out as definitive or even particularly convincing as compared to others. "We don't have a 'capstone' consensus," says Hirsch, referring to the recent panel that considered cholesterol and heart disease and cited repeatedly a recent study by the National Heart, Lung and Blood Institute. "It is based more on a feeling for the data."

One indicator of the panel's "feeling for the data" is its decision, originally, to stress treatment for those who are 40 percent or more above their desirable weights. After presenting this conclusion to the consensus conference audience, the panel was persuaded to change its recommendation so that those who are 20 percent or more above their desirable weights be treated.

The panel was swayed by a multitude of studies concluding that the obese are prone to a wide variety of diseases, including hypertension, adult-onset diabetes, hypercholesterolemia, hypertriglyceridemia, heart disease, cancer, gall stones, arthritis, and gout. They also tend to have shorter life-spans, according to insurance industry data.

People who are obese, for example, are three times more likely to have high blood pressure. Among the young obese, who are 20 to 44 years old, the prevalence of hypertension is five times greater than it is among nonobese people of the same ages. More than twice as many of these young obese people have hypercholesterolemia than their normal weight peers. Nearly three times as many obese as normal weight people have diabetes. Highly obese men, who are at least 40 percent above their desirable weights, have higher mortality rates from cancers of the colon, rectum, and prostate. Highly obese women have higher mortality rates from cancers of the gallbladder, biliary passages, breast (among postmenopausal women), and endometrium. Markedly obese women are more than five times as likely to develop endometrial cancer as women of normal weight. However, says Hirsch, "the evidence is very good" that when obese people lose weight, their risk for these adverse health effects declines accordingly.

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The panel found it difficult to compare the risk of obesity to other factors, such as smoking, hypertension, and hypercholesterolemia. But Per Bjorntorp of the University of Göteborg in Sweden says that his group has analyzed Swedish data to answer this question. What they did was compare the mortality rates of the upper quintile of obese people to the mortality rates of the lowest quintiles. That gave them a measurement of the risk of obesity. Then they did the same for hypertension, hypercholesterolemia, and smoking. By this sort of measurement, Bjorntorp says, obesity is a risk factor of the same order as hypertension, hypercholesterolemia, and smoking.

In order to advise people to lose weight, the medical community must know what weights people should strive for, and here there is some confusion. The most frequently used tables are compiled by the Metropolitan Life Insurance Company and are "desirable" weights by height as based on mortality data. These are the weights at which people live longest. But there are two versions of the height-weight tables. One, first published in 1959, gives lower weights than the revised Metropolitan Life table published in 1983. The desirable weights for the shortest men in the 1983 table are 12 pounds heavier than in the 1959 table, and the desirable weights for the shortest women are 14 pounds higher in the 1983 tables. The panel suggests using the 1983 table except for patients who already have disorders such as diabetes or hypertension which are aggravated by excess weight.

However, with such variations in desirable weights and with large ranges of desirable weights even within a table, the panel runs into some difficulties when it says that even 5 or 10 pounds of excess fat is hazardous. For example, according to the 1983 table, a woman who is 5 feet 3 inches tall can weigh anywhere from 111 to 148 pounds—a 37 pound range.

Children, as well as adults, should reduce if they are overweight, the panel said. But with children there is an even more difficult problem. It is hard to determine children's ideal weights because they are still growing and so might normally go through periods when their weight fluctuates and their growth spurts and slows. Although obese children are at risk for being obese as adults, most fat children grow up to be of normal weight. For that reason, says Hirsch, the panel tempered its recommendation that overweight children diet with a note of "concern that excessive zeal or misplaced treatment may do more harm than good."

Although the panel recommended that all overweight people reduce, it also mentioned new evidence that particular subgroups of the obese may be at greater risk than others. Those who tend to accumulate their fat in their abdomens rather than in their hips and buttocks

seem to be more prone to the illnesses associated with obesity. Why this is so is "far from answered," Hirsch says, but, he remarks, "a number of labs are finding that fat cells behave differently in different parts of the body." In particular, fat cells in the abdomen seem to be metabolically more active.

The number of obese people in the United States shows no signs of diminishing. In fact, according to Theodore Van Itallie of Columbia University College of Physicians and Surgeons, there is a virtual epidemic of obesity among middle-aged black women. Sixty percent of black women between the ages of 45 and 55 are obese, as compared to 30 percent of white women in the same age range and 26 percent of the U.S. population as a whole.

Why obesity should be so prevalent among black women is unclear, but Albert Stunkart of the University of Pennsylvania School of Medicine points out that poor people are more likely to be overweight. He finds that obesity is six times more common among members of the lowest socioeconomic class as among those of the highest class and so the large numbers of obese black women may reflect the fact that these women are more likely to be poor. Stunkart and Van Itallie speculate that the incidence of obesity is kept down among more affluent people by the very strong social pressures against being fat. Such pressure does not exist among poorer people, Stunkart says.

Although the panel did not address the question of how people should lose weight, it did note that dieting is a big business in the United States and that, obviously, there are no easy answers to weight loss. In 1983 alone, Hirsch says, there were 1 billion tablets of phenylpropanolamine sold over the counter specifically as appetite suppressants. The cost of those pills is more than $150 million, and that is just one drug. More than 1 million people a week are treated in weight loss clubs such as Weight Watchers, according to Stunkart. Obesity, says Hirsch, "is a health problem that affects nearly everybody."

But even though there is no foolproof way to reduce and even though those who do lose weight frequently gain it back, the panel still feels that it is essential that overweight people make the effort to get their weight down to normal. "So much of the talk about obesity relates to vanity. We found that there are multiple health hazards at what to me are surprisingly low levels of obesity," Hirsch says. "Obesity, therefore, is a disease."—**GINA KOLATA**

Fish to Bacterium Gene Transfer

Although natural gene transfer from prokaryotes to eukaryotes is well known, and includes, for instance, the insertion into plant cells of plasmid fragments by *Agrobacterium tumefaciens* in the formation of crown gall disease, examples of the reverse transfer have remained uncertain at best. One putative such case that has been debated for some years concerns the enzyme copper/zinc superoxide dismutase in *Photobacterium leiognathi*, the gene for which has been suggested to have derived from ponyfish, with which the bacterium has a close symbiotic relationship (*1*). Rigorous analysis of the primary, secondary, and tertiary structure of the *P. leiognathi* enzyme now supports very strongly the idea of natural transfer for the origin of the bacterial gene, according to Oxford University researchers Joe Bannister and Michael Parker (*2*).

Superoxide dismutase scavenges the superoxide radical O_2^-, and therefore forms an important line of defense against this highly toxic species. The enzyme is a metalloprotein: in higher eukaryotes it contains copper and zinc, in some prokaryotes and mitochondria of eukaryotes the metal is manganese, while iron is usually present in other prokaryotes. This neat pattern was ruffled somewhat by the discovery that iron superoxide dismutase is to be found in three plant families—Gingkoaceae, Nymphaeaceae, and Cruciferae—out of a total of 43 surveyed, which observation has been interpreted to imply three separate gene transfers from bacteria to the plants. The presence of the solidly eukaryotic copper/zinc enzyme in *P. leiognathi* was again inferred to be the result of gene transfer, this time from eukaryote to prokaryote. The only other known example of a bacterium containing this enzyme—*Caulobacter crescentus*—presents a mystery as, unlike *P. leiognathi*, this organism does not regularly consort with eukaryotic organisms.

Photobacterium leiognathi, a light-producing bacterium, colonizes the luminescent organ of ponyfish, thus providing an intimacy that might permit natural gene transfer. The demonstration in 1981 that the amino acid composition of the copper/zinc enzyme from host and symbiont are much closer than either is to that of the swordfish seemed to confirm this contingency (*3*). Elucidation of the bacterial enzyme's amino acid sequence in 1983, however, revealed that it had little direct identity with several eukaryotic comparisons, and the idea of natural gene transfer fell into disfavor (*4*).

In spite of this, Bannister decided to pursue the issue further and, with Parker, embarked on an in-depth structural analysis. It turns out that although direct identity is in the region of 25 percent or so, when constraints on mutation are taken into account a figure for weighted sequence similarity of 44 percent is obtained, which is much more indicative of a homologous relationship. In spite of the differences in primary structure, the *P. leiognathi* enzyme yields a secondary structure prediction closely similar to that from eukaryotes. Studies on the crystal structure of the bovine enzyme (the only one for which such information is available) shows the tertiary structure to be comprised of eight antiparallel β-strands that form a flattened cylinder plus three external loops. The question was, could the features of the bacterial enzyme be "squeezed" into a comparable three-dimensional configuration, using computerized model building? Again, although some modification was necessary, there was an impressive conservation of overall structure.

Bannister and Parker point out that although convergent evolution in terms of function in the biochemical realm is common, as in many of the oxygen-binding proteins for example, convergence on structure is not. The structural similarities they see between the bacterial and eukaryotic enzymes in this case, they conclude, strongly indicate, if not prove, homology.—**ROGER LEWIN**

References

1. R. Lewin, *Science* **217**, 42 (1982).
2. J. V. Bannister and M. W. Parker, *Proc. Natl. Acad. Sci. U.S.A.* **82**, 149 (1985).
3. J. P. Martin and I. Fridovich, *J. Biol. Chem.* **256**, 6080 (1981).
4. G. J. Steffens *et al.*, *Hoppe-Seyler's Z. Physiol. Chem.* **364**, 675 (1983).