Medical Progress

Obesity
Part I—Pathogenesis

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Obesity—defined by a body mass index above 30 kg per m^2—is a major problem for affluent nations. Its prevalence is higher in North America than in Europe—between 9% and 12% of the population. Reduced energy expenditure from exercise or metabolism or both may be an important contributory factor in the development of obesity because of a failure to reduce food intake sufficiently to maintain energy balance. A high ratio of abdominal circumference relative to gluteal circumference carries a twofold or greater risk of heart attack, stroke, hypertension, diabetes mellitus, gallbladder disease, and death. The effect of increased quantities of abdominal fat is greater than that of a similar increase in total body fat on the risks of ill health associated with obesity. Genetic factors appear to contribute about 25% to its etiology.

(Bray GA, Gray DS: Obesity. Part I—Pathogenesis. West J Med 1988 Oct; 149:429-441)

The importance of obesity as a health problem can be highlighted by four statistics. Based on the changes in levels of cholesterol, glucose, blood pressure, and uric acid associated with spontaneous changes in body weight, Kannel and Gordon have estimated that "if everyone were at optimal weight there would be 25% less coronary heart disease and 35% less congestive failure and brain infarction."[1] If persons with diabetes mellitus who are obese were to attain normal weight and ameliorate their diabetes, the annual reduction in cost from hemodialysis for renal failure might be $200 million per year. Waaler has indicated that if body mass of the population became normal, this would produce a "total reduction [in mortality] of 15% corresponding to 3 years of added life expectancy."[2] Finally, Hannon and Lohman[3] have calculated the total amount of fossil fuel that would be equivalent to the food calories saved by overweight persons reducing to an optimal weight. Their calculations went as follows: adult Americans carry an excess of 2.3 billion pounds of fat. If these calories were used for daily metabolic needs, the reduced intake of food would be the equivalent of 1 to 3 billion gallons of gasoline. Such a saving in energy would supply more than the electrical demands for residences in Boston, Chicago, San Francisco, and Washington, DC.

Definition and Measurement of Body Fat and Its Distribution

If obesity can be this important, then we need to have a clear definition of the factors that produce this problem and its attendant risks. "Overweight" is an increase of body weight above some arbitrary standard defined in relation to height. To be obese, on the other hand, means to have an abnormally high proportion of body fat. To determine whether a person is obese or simply overweight because of increased muscle mass—as found in athletes—one needs techniques and standards for quantitating body fat. Several approaches to this problem are listed in Table 1, which also includes an estimate of the cost, ease of use, and accuracy of these methods.

Direct Analysis of Body Composition

Analyzing cadavers has provided basic information about body composition.[4] Water is the main component, accounting for about 60% to 65% of body weight.[5] Adipose tissue accounts for about 28% of body weight in men and 40% in women. When the mass of fat tissue is subtracted from total weight, the percentage of other components is similar in men and women.[4] Because direct carcass analysis cannot be done under normal circumstances, investigators have used indirect methods for measuring body composition and estimating the percentage of fat.

Indirect Analysis of Body Composition

Visual. A superficial analysis of fatness may be done by self-examination or through a visual inspection by another person. Increased bulging of skin folds or excessive roundness suggests in most instances increased fatness. Although such observations provide a good individual guide, they are not quantitative. One solution to this problem is the assignment of body types using photographs of persons without clothes.[6] With this technique, called somatotyping, the degree of endomorphy (roundness), mesomorphy (muscularity), and ectomorphy (leanness) can be given numeric values.

Anthropometric. Anthropometric measurements include height and weight; circumference of the chest, waist, hips, or extremities; diameter of the iliac crest, greater trochanters, or acromioclavicular joints; and skin-fold thickness (Table 1). Of these, the most widely used are height and weight, from which relative weight can be calculated. Relative weight is the actual body weight divided by a standard or "desirable" weight based on height. Thus, a man who is 178

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TABLE 1.—*Methods of Estimating Body Fat and Its Distribution*

Method	Cost	Ease of Use	Accuracy	Measures Regional Fat
Height and weight	$	Easy	High	No
Skin folds	$	Easy	Low	Yes
Circumferences	$	Easy	Moderate	Yes
Density				
Immersion	$$	Moderate	High	No
Plethysmograph	$$$	Difficult	High	No
Heavy water				
Tritiated	$$	Moderate	High	No
Deuterium oxide, or heavy oxygen	$$	Moderate	High	No
Potassium isotope (^{40}K)	$$$	Difficult	High	No
Conductivity, total body electrical	$$$	Moderate	High	No
Bioelectric impedance	$$	Easy	High	No
Fat-soluble gas	$$	Difficult	High	No
Computed tomography	$$$$	Difficult	High	Yes
Ultrasonography	$$$	Moderate	Moderate	Yes
Neutron activation	$$$$	Difficult	High	No
Magnetic resonance	$$$$	Difficult	High	Yes

$=low cost, $$=moderate cost, $$$=high cost, $$$$=very high cost

TABLE 2.—*Body Weights in Kilograms According to Height and Body Mass Index**†*

Height, cm	Body Mass Index, kg/m²													
	19.0	20.0	21.0	22.0	23.0	24.0	25.0	26.0	27.0	28.0	29.0	30.0	35.0	40.0
	Body Weight, kg													
140.0	37.2	39.2	41.2	43.1	45.1	47.0	49.0	51.0	52.9	54.9	56.8	58.8	68.6	78.4
142.0	38.3	40.3	42.3	44.4	46.4	48.4	50.4	52.4	54.4	56.5	58.5	60.5	70.6	80.7
144.0	39.4	41.5	43.5	45.6	47.7	49.8	51.8	53.9	56.0	58.1	60.1	62.2	72.6	82.9
146.0	40.5	42.6	44.8	46.9	49.0	51.2	53.3	55.4	57.6	59.7	61.8	63.9	74.6	85.3
148.0	41.6	43.8	46.0	48.2	50.4	52.6	54.8	57.0	59.1	61.3	63.5	65.7	76.7	87.6
150.0	42.8	45.0	47.3	49.5	51.8	54.0	56.3	58.5	60.8	63.0	65.3	67.5	78.8	90.0
152.0	43.9	46.2	48.5	50.8	53.1	55.4	57.8	60.1	62.4	64.7	67.0	69.3	80.9	92.4
154.0	45.1	47.4	49.8	52.2	54.5	56.9	59.3	61.7	64.0	66.4	68.8	71.1	83.0	94.9
156.0	46.2	48.7	51.1	53.5	56.0	58.4	60.8	63.3	65.7	68.1	70.6	73.0	85.2	97.3
158.0	47.4	49.9	52.4	54.9	57.4	59.9	62.4	64.9	67.4	69.9	72.4	74.9	87.4	99.9
160.0	48.6	51.2	53.8	56.3	58.9	61.4	64.0	66.6	69.1	71.7	74.2	76.8	89.6	102.4
162.0	49.9	52.5	55.1	57.7	60.4	63.0	65.6	68.2	70.9	73.5	76.1	78.7	91.9	105.0
164.0	51.1	53.8	56.5	59.2	61.9	64.6	67.2	69.9	72.6	75.3	78.0	80.7	94.1	107.6
166.0	52.4	55.1	57.9	60.6	63.4	66.1	68.9	71.6	74.4	77.2	79.9	82.7	96.4	110.2
168.0	53.6	56.4	59.3	62.1	64.9	67.7	70.6	73.4	76.2	79.0	81.8	84.7	98.8	112.9
170.0	54.9	57.8	60.7	63.6	66.5	69.4	72.3	75.1	78.0	80.9	83.8	86.7	101.2	115.6
172.0	56.2	59.2	62.1	65.1	68.0	71.0	74.0	76.9	79.9	82.8	85.8	88.8	103.5	118.3
174.0	57.5	60.6	63.6	66.6	69.6	72.7	75.7	78.7	81.7	84.8	87.8	90.8	106.0	121.1
176.0	58.9	62.0	65.0	68.1	71.2	74.3	77.4	80.5	83.6	86.7	89.8	92.9	108.4	123.9
178.0	60.2	63.4	66.5	69.7	72.9	76.0	79.2	82.4	85.5	88.7	91.9	95.1	110.9	126.7
180.0	61.6	64.8	68.0	71.3	74.5	77.8	81.0	84.2	87.5	90.7	94.0	97.2	113.4	129.6
182.0	62.9	66.2	69.6	72.9	76.2	79.5	82.8	86.1	89.4	92.7	96.1	99.4	115.9	132.5
184.0	64.3	67.7	71.1	74.5	77.9	81.3	84.6	88.0	91.4	94.8	98.2	101.6	118.5	135.4
186.0	65.7	69.2	72.7	76.1	79.6	83.0	86.5	89.9	93.4	96.9	100.3	103.8	121.1	138.4
188.0	67.2	70.7	74.2	77.8	81.3	84.8	88.4	91.9	95.4	99.0	102.5	106.0	123.7	141.4
190.0	68.6	72.2	75.8	79.4	83.0	86.6	90.3	93.9	97.5	101.1	104.7	108.3	126.4	144.4
192.0	70.0	73.7	77.4	81.1	84.8	88.5	92.2	95.8	99.5	103.2	106.9	110.6	129.0	147.5
194.0	71.5	75.3	79.0	82.8	86.6	90.3	94.1	97.9	101.6	105.4	109.1	112.9	131.7	150.5
196.0	73.0	76.8	80.7	84.5	88.4	92.2	96.0	99.9	103.7	107.6	111.4	115.2	134.5	153.7
198.0	74.5	78.4	82.3	86.2	90.2	94.1	98.0	101.9	105.9	109.8	113.7	117.6	137.2	156.8
200.0	76.0	80.0	84.0	88.0	92.0	96.0	100.0	104.0	108.0	112.0	116.0	120.0	140.0	160.0

*Each entry gives the body weight in kilograms (kg) for a person of a given height and body mass index.
†Desirable body mass index range in relation to age (from Bray[7]).

Age Group, yr	Body Mass Index, kg/m²
19-24	19-24
25-34	20-25
35-44	21-26
45-54	22-27
55-64	23-28
65+	24-29

cm tall (5′8″) and weighs 82 kg (180 lb) would have a desirable weight of 69.4 kg (153 lb) and a relative weight of 1.18 (82/69.4 = 1.18) or 118% of desirable weight.

The tables of desirable weight provided by the Metropolitan Life Insurance Company have received the widest use. They are divided into three subgroups based on frame size. No direct measures of frame size were made, however, when these data were collected. The upper and lower frame sizes appear to be the upper and lower quarters (quartiles) of the population, with the medium frame representing the middle two quarters. The newest tables, published in 1983, provide a higher weight range than the older tables, and there has been a reluctance on the part of many to use the newer life insurance tables.

Weight and height can also be related by various ratios. These include wt/ht, ht/$(wt)^{1/3}$ (Ponderal index), or wt/$(ht)^P$. When P=2 in this latter expression, wt/$(ht)^2$ is called the body mass or Quetelet index (kg per m^2). The correlation of these indices with body fat measured from body density ranges between 0.7 and 0.8.[6] Because the body mass or Quetelet index has the best correlation with body fat, it is preferred. Tables 2 and 3 show the body mass indices for various height and weight categories.

The desirable range of body weights for each height appears to increase slightly with age.[7] These ranges are listed in Tables 2 and 3. The body mass or Quetelet index can also be used to assess the magnitude of potential health risks associated with being overweight, and it may be used as a guide to therapy.

The degree of body fat or obesity measured with the use of specially designed calipers can be assessed from the thickness of skin folds. Regression equations are available that calculate the amount of body fat from skin-fold thicknesses measured at several sites.[8] One difficulty with skin-fold measurements is that the equations used to estimate body fat are related to age, sex, and ethnic background. Body fat increases with age even though the sum of the skin folds remains constant.[9] This implies that the accumulation of fat with age occurs in large part at sites other than subcutaneous ones. There are also sex and ethnic differences in the distribution of body fat.

The ratio of waist or abdominal circumference to the hip or gluteal circumference provides an index of the regional distribution of body fat and has proved valuable as a guide to health risks. A nomogram for obtaining the abdominal-gluteal ratio (android-gynoid ratio) or waist-hips ratio is shown in Figure 1. The circumference of the waist is measured at the narrowest area above the umbilicus; the hip circumference is at the maximal gluteal protrusion. Abdominal fat (high android-gynoid ratio) is characteristic of men and is referred to as android or upper body obesity. Fat on the hips is typical for women and is referred to as gynoid or lower body fat distribution. The percentile values for these for men and women in relation to age are shown in Figure 2. Persons with values above the 10th percentile are at high risk for adverse health consequences, as we will discuss in more detail later.

Isotopic or chemical measurement of body compartments. A more quantitative approach to measuring body composition is to use one of several dilutional techniques. The most direct method is with fat-soluble agents, such as cyclopropane or krypton, whose distribution can be related to total fat (Table 1). The equilibration time is long, however, and special equipment is needed, thus making this method expensive. The second approach is to calculate body fat from measuring body water using tritiated water (^3H_2O), deuterated water (D_2O), or water with heavy oxygen ($H_2{}^{18}O$),[5,10] all of which equilibrate with body water. Lean body mass is

TABLE 3.—*Body Weights in Pounds According to Height and Body Mass Index**†*

Height, in	Body Mass Index, kg/m²													
	19.0	20.0	21.0	22.0	23.0	24.0	25.0	26.0	27.0	28.0	29.0	30.0	35.0	40.0
	Body Weight, lb													
58.0	90.7	95.5	100.3	105.0	109.8	114.6	119.4	124.1	128.9	133.7	138.5	143.2	167.1	191.0
59.0	93.9	98.8	103.8	108.7	113.6	118.6	123.5	128.5	133.4	138.3	143.3	148.2	172.9	197.6
60.0	97.1	102.2	107.3	112.4	117.5	122.6	127.7	132.9	138.0	143.1	148.2	153.3	178.8	204.4
61.0	100.3	105.6	110.9	116.2	121.5	126.8	132.0	137.3	142.6	147.9	153.2	158.4	184.8	211.3
62.0	103.7	109.1	114.6	120.0	125.5	130.9	136.4	141.9	147.3	152.8	158.2	163.7	191.0	218.2
63.0	107.0	112.7	118.3	123.9	129.6	135.2	140.8	146.5	152.1	157.7	163.4	169.0	197.2	225.3
64.0	110.5	116.3	122.1	127.9	133.7	139.5	145.3	151.2	157.0	162.8	168.6	174.4	203.5	232.5
65.0	113.9	119.9	125.9	131.9	137.9	143.9	149.9	155.9	161.9	167.9	173.9	179.9	209.9	239.9
66.0	117.5	123.7	129.8	136.0	142.2	148.4	154.6	160.8	166.9	173.1	179.3	185.5	216.4	247.3
67.0	121.1	127.4	133.8	140.2	146.5	152.9	159.3	165.7	172.0	178.4	184.8	191.1	223.0	254.9
68.0	124.7	131.3	137.8	144.4	151.0	157.5	164.1	170.6	177.2	183.8	190.3	196.9	229.7	262.5
69.0	128.4	135.2	141.9	148.7	155.4	162.2	168.9	175.7	182.5	189.2	196.0	202.7	236.5	270.3
70.0	132.1	139.1	146.1	153.0	160.0	166.9	173.9	180.8	187.8	194.7	201.7	208.6	243.4	278.2
71.0	135.9	143.1	150.3	157.4	164.6	171.7	178.9	186.0	193.2	200.3	207.5	214.6	250.4	286.2
72.0	139.8	147.2	154.5	161.9	169.2	176.6	183.9	191.3	198.7	206.0	213.4	220.7	257.5	294.3
73.0	143.7	151.3	158.8	166.4	174.0	181.5	189.1	196.7	204.2	211.8	219.3	226.9	264.7	302.5
74.0	147.7	155.4	163.2	171.0	178.8	186.5	194.3	202.1	209.9	217.6	225.4	233.2	272.0	310.9
75.0	151.7	159.7	167.7	175.6	183.6	191.6	199.6	207.6	215.6	223.5	231.5	239.5	279.4	319.4
76.0	155.8	164.0	172.2	180.4	188.6	196.8	205.0	213.2	221.4	229.5	237.7	245.9	286.9	327.9

*Each entry gives the body weight in pounds (lb) for a person of a given height and body mass index.
†Desirable body mass index range in relation to age (from Bray[7]).

Age Group, yr	Body Mass Index, kg/m²	Age Group, yr	Body Mass Index, kg/m²
19-24	19-24	45-54	22-27
25-34	20-25	55-64	23-28
35-44	21-26	65+	24-29

usually assumed to be 72% water, although this assumption may be in error in children and in very obese persons, since the water content of the non-fat part of adipose tissue is 85%. Body "cell mass" can also be quantitated by measuring the amount of the naturally occurring isotope of potassium (^{40}K) in the body (Table 1). For this measurement, the lean body mass is usually assumed to contain 63 mEq of K^+ per kg.[10] Once lean body mass has been determined, body fat can be calculated as follows:

body fat = (body weight) − (lean body mass)

Body density and body volume. Measuring the body density provides a quantitative technique for measuring body fat and fat-free mass. Density is determined from the weight of the body in and out of water using Archimedes' principle.[5,8] In this procedure, a person is weighed both underwater and out of water, and the residual volume of the lungs is determined. With this information, it is possible to fractionate the body into its fat and nonfat components, assuming a density for fat of 0.9 grams per cm^3. This technique is relatively easy if appropriate facilities are available, but it remains primarily a research method.

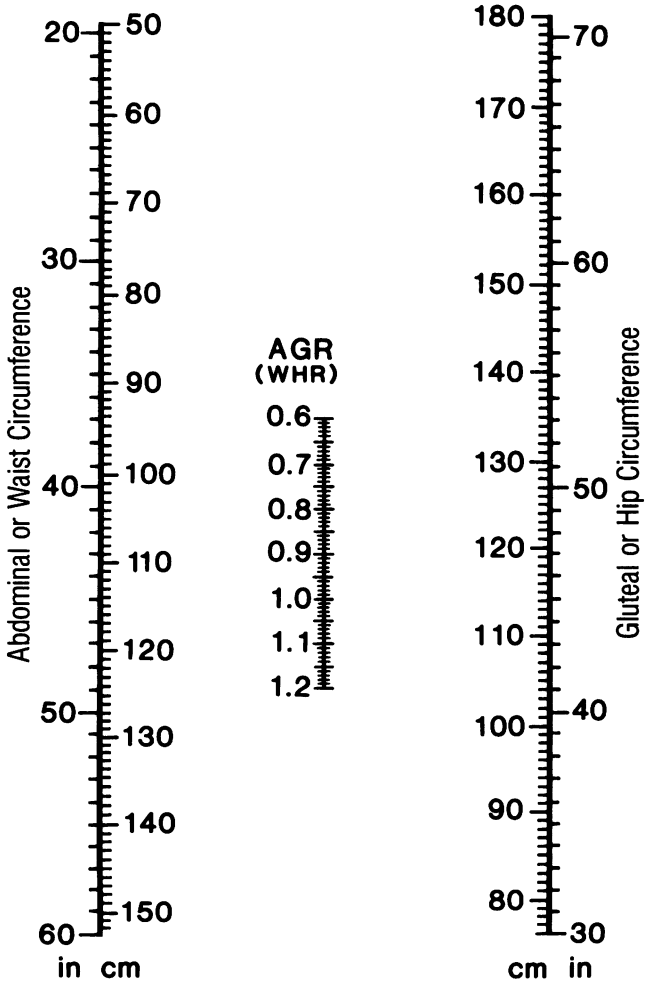

Figure 1.—The abdominal (waist) to gluteal (hips) ratio (AGR) can be determined by placing a straight edge between the column for waist circumference and the column for hip circumference and reading the ratio from the point where this straight edge crosses the AGR or waist-hips ratio (WHR) line. The waist or abdominal circumference is the smallest circumference below the rib cage and above the umbilicus, and the hips or gluteal circumference is taken as the largest circumference at the posterior extension of the buttocks.

Other. Ultrasound waves applied to the skin will be reflected by the fat, muscle, and other tissues and can provide a measure of fat thickness.[11] Electromagnetic conductivity or total body electrical conductivity can also be used to quantitate lean and fat tissue because of differences in their ability to conduct electromagnetic waves.[12] A relatively inexpensive instrument for measuring body fat uses bioelectric impedance analysis. Electrodes are applied to an arm and leg and the impedance (reciprocal of conductance) is measured. Because impedance is related to the aqueous portion of the body, formulas can be developed to estimate the percentage of fat in the body. These formulas provide good estimates of the percentage of body fat in normal weight persons,[13] but the validation in obese subjects is less adequate. Computed tomographic scans and magnetic resonance imaging provide pictures from which the thickness of fat can be determined. The advantage of the computed tomographic scan is that it provides quantitative estimates of regional fat and can give a

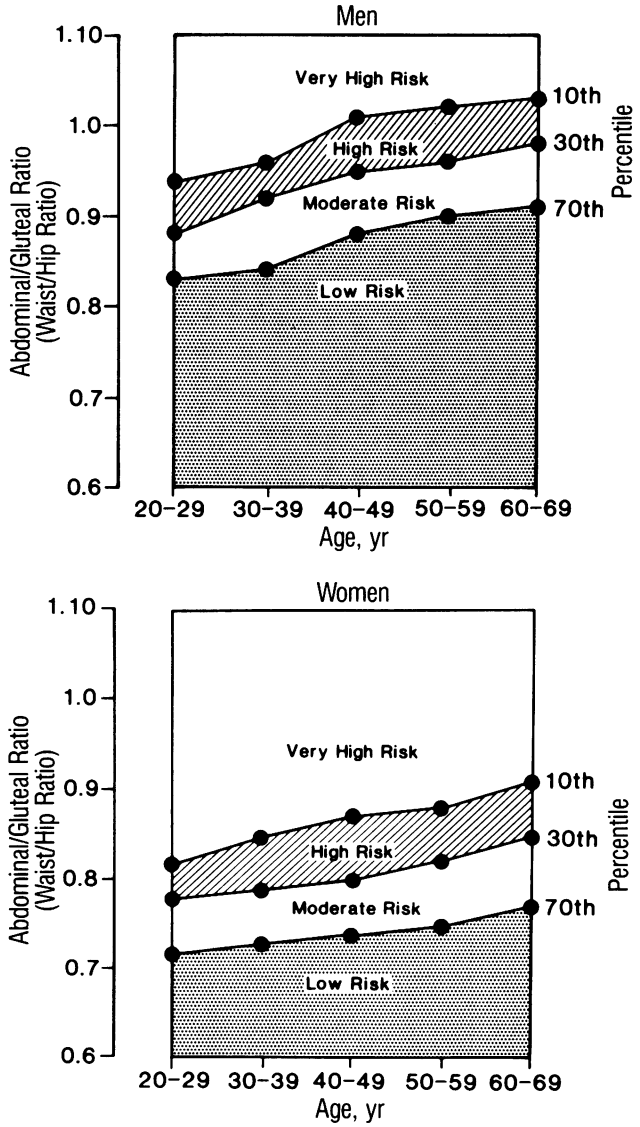

Figure 2.—The percentiles for the ratio of abdominal circumference to gluteal circumference (ratio of waist to hips) are shown for men **(top panel)** and women **(bottom panel)** by age groups. The relative risk for these percentiles is indicated based on the available information. (Plotted from tabular data in the Canadian Standardized Test of Fitness, Third Edition 1986 [available from Fitness and Amateur Sport Canada, 365 Laurier Ave W, Ottawa, Ontario K1A OX6].)

ratio of intra-abdominal to extra-abdominal fat.[14] Because fat distribution and possibly the relative amount of intra-abdominal to subcutaneous fat relate to the health risks of obesity, this technique may become more widely used. Its disadvantages, however, are that there is radiation exposure during the measurement and the equipment is expensive (Table 1). Finally, neutron activation of the whole body can be used to identify chemical components by their emission spectra.[15]

Using one or more of these techniques, the major components of the body can be determined. The proportions of fat and nonfat components for a normal (70 kg) and obese (100 kg) man and a corresponding woman are shown in Figure 3. The extra 30 kg of weight is assumed to be two-thirds fat, which adds a little more than half to body weight but increases energy stored as fat by 200%.

In summary, body fat can be estimated in many ways, but the most accurate methods are not widely available or are expensive. From a practical point of view, three methods are most useful. Measurements of height and weight, preferably expressed as the body mass index, provide an estimate of degree of overweight. Measuring impedance may also prove useful in estimating total fat. For regional fat distribution, the use of the circumference at the abdomen or waist and the gluteus or hips has been useful, but measuring skin folds on the trunk and extremities—particularly the subscapular skin fold—would also appear to be useful.

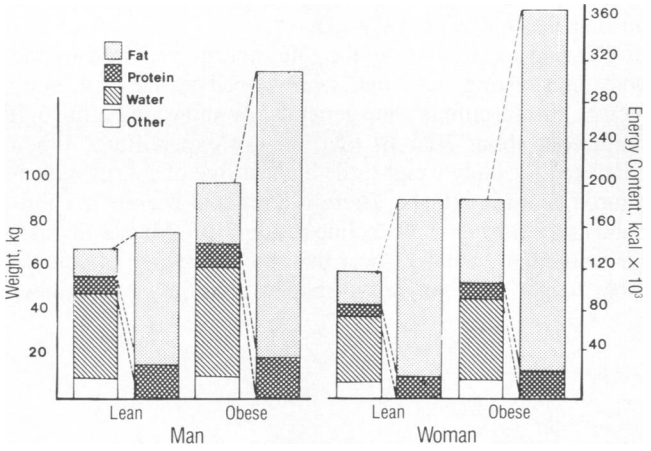

Figure 3.—The percentage of fat, protein, water, and other components for a normal 70-kg man and a 55-kg woman is shown at the left of each group, along with the data for an obese person who is 30 kg heavier in the middle. The contribution of fat and protein to body energy stores is indicated in the bars to the right.

Prevalence of Obesity

A number of factors influence body fat, including age, sex, race, and physical activity. At birth the human body contains about 12% fat, a content that is higher than in any other mammal except the whale. During the newborn period, the body fat content rises rapidly to reach a peak of about 25% at 6 months of age and then declines to 15% to 18% in the prepubertal years. At puberty there is a notable increase in the percentage of fat in girls and a notable decrease in boys. By age 18 boys have about 15% to 18% body fat and girls, 20% to 25%. The amount of body fat increases in both sexes after puberty and during adult life rises to between 30% and 40% of body weight. Between ages 20 and 50, the fat content in men approximately doubles and that in women increases by about 50%. Total body weight, however, rises by only 10% to 15%. The increased fat is accounted for in part by an increase in body weight and in part by a reduction in lean body mass.[5]

The composition of the body is also influenced by the level of physical activity.[16] During physical training, body fat usually decreases and lean tissue increases. After training ends, however, this process is reversed. These shifts between body fat and lean tissue can occur without any changes in body weight, but if regular activity is maintained throughout adult life, the increase in body fat that usually occurs even when body weight is stable may be prevented.

Racial differences in body weight (Figure 4) may exist, but it is often difficult to separate racial from environmental factors. Socioeconomic conditions, however, clearly play an important role in the development of obesity. Excess body weight is 7 to 12 times more frequent in women from lower social classes than in women from the upper social classes.[17] Among men, social class has a much smaller relationship to being overweight.

The patterns of body weight in men and women are changing. Data obtained at the time of evaluation for military service show that men inducted into the army in the 1950s were heavier than men of the same height drafted in 1943. The 1943 inductees were in turn heavier than those inducted in 1918.[5] The Framingham study shows similar changes for men but suggests that women may not be getting fatter.[1]

Using the body mass index, it is possible to compare the

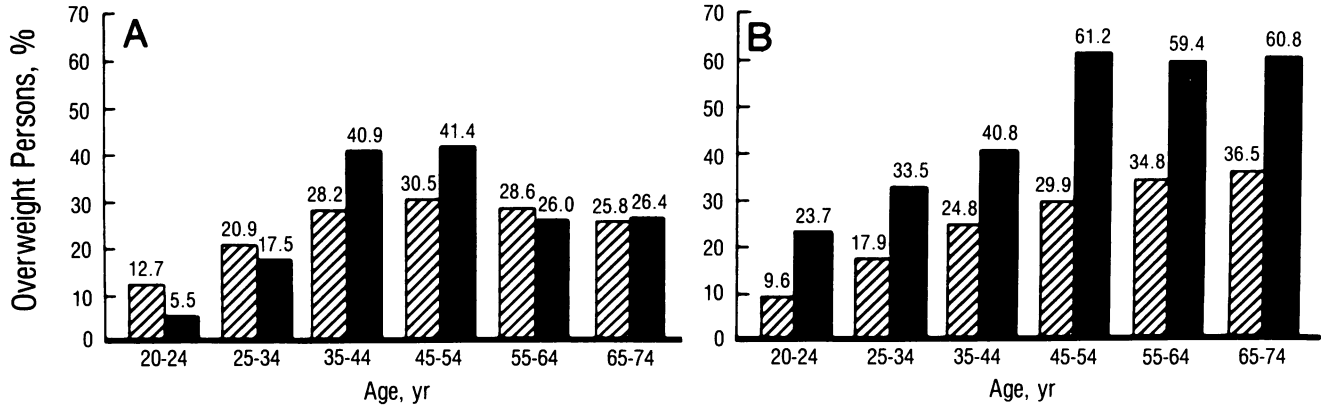

Figure 4.—Data from the National Center for Health Statistics show the percentage of overweight men **(A)** and women **(B)** by age and race using the 85th percentile of weights for height of 20- to 24-year-olds as the upper limits for weight (from Van Itallie[18]). The crosshatched bars show percentages for whites, the solid bars those for blacks.

TABLE 4.—*Percentage of Overweight and Obese Persons in Several Affluent Countries**

	Age, yr	Overweight, %		Obese, %	
		Men	Women	Men	Women
United States	20-74	31	24	12	12
Canada	20-69	40	28	9	12
Great Britain	16-65	34	24	6	8
The Netherlands	20+	34	24	4	6
Australia	25-64	34	24	7	7

*Adapted from Bray.[19]

prevalence of obesity in several countries (Table 4).[18,19] The prevalence of persons with a body mass index of 25 to 30 kg per m^2 is almost identical in all populations. The higher percentage of men in the range of 25 to 30 kg per m^2 results from the fact that the median body mass index for women is 22 kg per m^2, whereas for men it is 25 kg per m^2. The prevalence of those with a body mass index above 30 kg per m^2 is, however, higher in both the United States and Canada than in Great Britain, the Netherlands, or Australia. There are at least three possible explanations for this. First, the higher proportion of automobiles in North America might substantially reduce energy expenditure. Second, there might be differences in quantity or quality of dietary intake. Third, higher rates of smoking might explain the lower rates of obesity outside North America. Obesity is also prevalent in many other populations, suggesting its worldwide importance.[20]

Pathogenesis of Obesity

Nutrient Imbalance

Food intake. Obesity is a problem of nutrient imbalance—more foodstuffs are stored as fat than are used for energy and metabolism. Do the obese eat more than lean subjects? Three general techniques have been used to obtain information about the energy intake of humans. These include the use of nutritional histories and records of food eaten, observing and measuring food choices in natural settings, and measuring food intake in a laboratory setting, with experimental changes in the nature of the food or the eating situation. Most surveys suggest that energy intake is significantly lower in the overweight than in those of normal weight.[21] One concern with these observations is the reliability of the study when the data are based on self-reports. Repeat dietary histories on obese patients during a three-month period showed an apparent underreporting of intake in the initial interview.[22] It may be that the accuracy of reporting becomes less reliable as excess weight increases.

In direct observations of food intake, obese persons chose or ate larger meals than did lean persons. In a variety of studies on food choice, Stunkard and Kaplan found relative uniformity in the size of meals chosen in natural settings.[23] The caloric content of the meals was strongly affected by the eating site, and there was great variability in the amount of food chosen at each site. Thus, the major influence on how much people chose to eat was where they ate. Eating in a cafeteria led to eating more food. A recent naturalistic study by Stunkard and Waxman indicated that obese adolescent boys ate more than did their lean siblings at school but not at home.[24]

Adjusting caloric intake to changes in the caloric concentration of the food eaten has produced a nearly uniform pattern in several laboratory studies. Obese persons failed to compensate for changes in caloric concentration as well as normal weight persons did.[25]

Energy requirements generally decline with age, and we would anticipate that food intake would show a corresponding decrease.[5] The values for caloric intake from three surveys are presented in Figure 5. The peak values occur in the second decade of life, followed by a gradual decline in successive decades for both sexes. Thus, the increase in body weight and body fat with age cannot be attributed to an increased nutrient intake but rather to a relatively greater reduction in energy expenditure.

In summary, objective measurements on obese subjects tend to support the conclusion that they choose and eat more food and often do so more rapidly than normal weight subjects. The data also suggest that retrospective observations of food intake may be biased on the low side, particularly in the obese. External environmental influences, such as lighting and noises, may modify the quantity and the quality of food eaten by obese persons more than it does in lean ones. Finally, increasing fatness with age appears to result from a greater reduction in energy expenditure because food intake also declines with age.

Energy expenditure. Total energy expenditure can be measured by a variety of methods.[5,26] Although some differences in terminology exist, the partition of energy expenditure can be shown as in Figure 6.

Resting metabolism is the total energy required by the body in a resting state and is influenced by age, sex, body weight, drugs, climate, and genetics. As shown in Figure 6, it represents about 70% of total energy expenditure. When corrected for body weight, the highest rate of energy expenditure occurs in infants. There is a gradual decline in childhood and a further slow decline in adult life. Metabolic rates for women are usually lower than those for men of comparable height and weight, primarily because of the higher

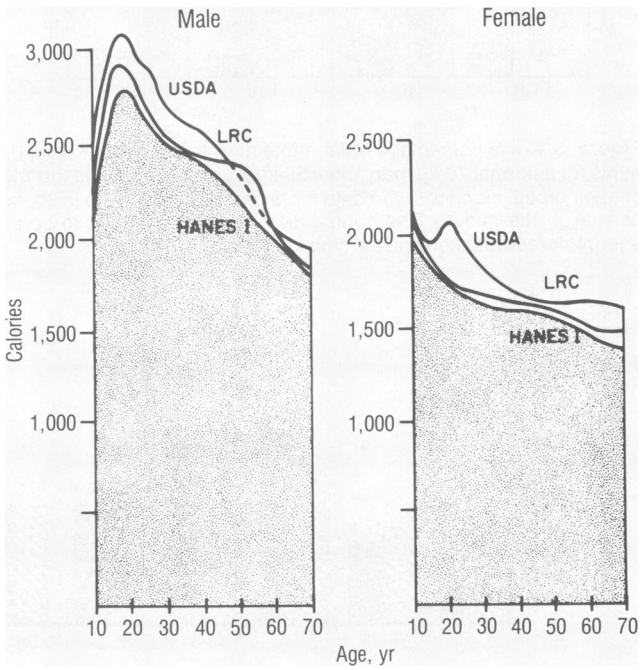

Figure 5.—Data from three studies of food intake in relation to age are plotted for men and women (from Bray[26]). HANES 1 = Health and Nutrition Examination Survey, LRC = Lipid Research Clinics, USDA = US Department of Agriculture

body fat content of women. The resting metabolic rate has the best relationship to fat-free body mass, but it is also closely related to surface area and total body weight because heat loss is related to the surface area of the skin. As body weight or lean body mass increases, there is a rise in the metabolic rate.[27-29] Figure 7 shows the 24-hour energy expenditure in relation to body weight. As weight rises, the energy expenditure also rises at a rate of about 22 kcal per kg of body weight.

Energy expenditure, even for persons with the same lean body mass or surface area, age, and sex, may vary as much as 20%. Thus, if the mean resting expenditure is 1,000 kcal per day^{-1}, then two persons of normal weight could differ by 400 kcal per day^{-1} (1,200 versus 800 kcal per day^{-1}).

In a careful study of the resting metabolic rate among family members, Bogardus and colleagues[29] showed that metabolic rate clustered in families. If one person was below the median for energy use, other members of the family also tended to be below the median. In longitudinal studies, these

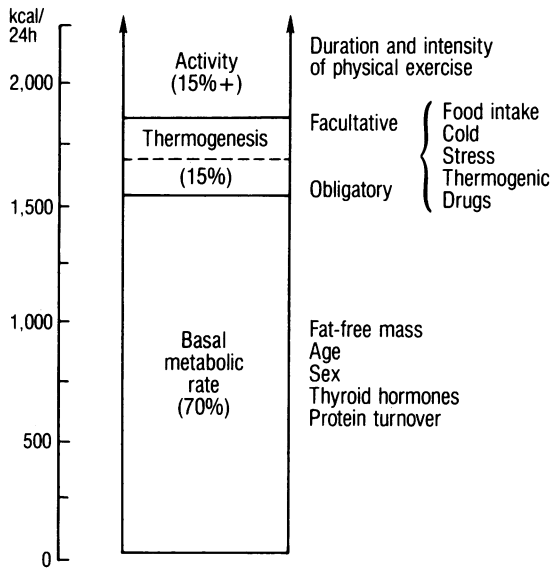

Figure 6.—The energy partition into basal energy needs, thermogenesis, and activity are estimated based on a 2,500-kcal-per-day requirement. The upper end is open, indicating that activity is variable and can be increased for a normal weight person. This usually involves about 30% of the total daily energy expenditure, however.

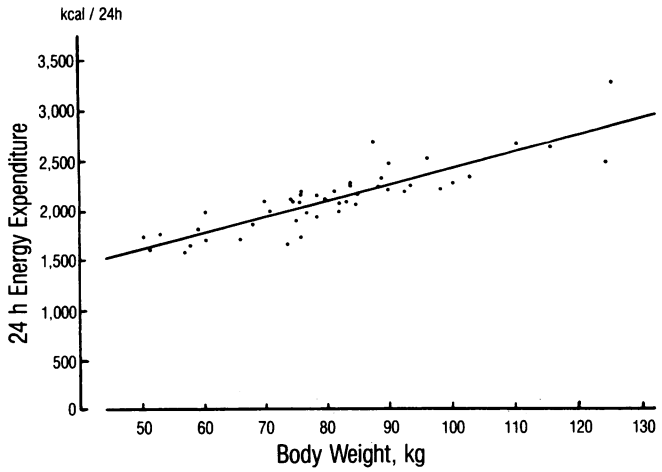

Figure 7.—As body weight rises, the metabolic rate increases. The slope of this relationship is approximately a 24-hour energy expenditure = (750 kcal) + (15 kcal per kg) (from Jequier and Schutz[27]).

same workers have found suggestive evidence that weight gain is more likely in those with lower metabolic rates in relation to lean body mass.[30]

The resting metabolic rate, then, is closely related to body weight, lean body mass, and body surface area. Obese persons tend to have an expanded lean body mass and thus greater resting metabolic rates than lean persons of similar heights. A low resting metabolic rate in relation to lean body mass may be a predictor for the onset of obesity.

Physical activity. There are two approaches to studying the relationship of physical activity to obesity. In the laboratory, the treadmill and the cycle ergometer have been the main tools used to examine the efficiency of exercising muscle in obese subjects. Lean persons before and after weight gain and notably obese persons have both been studied by bicycle ergometry.[26] The resting level of energy expenditure in massively obese subjects weighing in excess of 140 kg (285 lb) was twice that of lean subjects. In each group the efficiency for coupling energy production to muscular contraction was 30%. Moreover, the efficiency of coupling metabolism to muscular contraction remained the same following substantial weight gain in normal weight subjects.[26] We thus conclude that there is no evidence to indicate an abnormality in the metabolic coupling of substrate metabolism to the contraction of muscular tissue in moderately or massively obese persons.

The second approach to studying energy expenditures is that of naturalistic observation. Obese persons are often observed to be less active than those of normal weight, as documented by several techniques. When given a choice of an escalator or stairs, for example, the obese were more likely to take the escalator.[31]

A lower level of spontaneous movement does not necessarily imply reduced energy expenditure, however, since an overweight person uses more energy for any given movement.[26] In one approach to this problem, Waxman and Stunkard related movement to energy expenditure and found that obese boys expended more energy on the playground but similar amounts inside the home when compared with lean siblings.[32] It is thus not possible to conclude that spending less time in physical activity results in a reduction of energy expenditure. In normal weight persons, graded increases in physical activity have been reported to increase food intake. In the obese, however, changing the level of physical activity has much less effect on food intake.[33] There is, therefore, no evidence to implicate a decrease in energy expenditure because of physical inactivity in the pathogenesis of obesity.

Thermogenic effects of food. When food is eaten, the metabolic rate rises and then returns toward normal. This process requires several hours, and during this time the increase in energy expenditure can approximate 10% to 15% of the total caloric value of the food eaten. One explanation for this thermogenic response to a meal is that it results from enhanced activity of the sympathetic nervous system and its effect on brown adipose tissue.[34] If this is correct, then a reduction in sympathetic activity of obese subjects compared with lean ones may provide a mechanism for enhanced metabolic efficiency that might allow calories to be stored rather than burned. Although brown adipose tissue is important in rodents, its importance in adult humans has not yet been shown.[35]

The concept that an altered thermic response to food may serve as a mechanism for the storage of extra calories *in*

human obesity is intriguing and controversial.[36] Some investigators have found a difference between obese and lean persons in the energy produced following a meal; others, however, have found no such difference. The discrepancy may lie in the size of the meal eaten, in the techniques of recording, in the meal's palatability,[37] and in whether subjects had abnormal glucose tolerance. Golay and co-workers examined 55 subjects with varying degrees of obesity and impaired glucose tolerance, including those with diabetes mellitus.[38] The increment in energy expenditure was significantly lower in obese persons without diabetes and those with impaired glucose tolerance than in the normal volunteers.[38] In turn, the obese persons with diabetes had a smaller response than those of normal weight or obese persons without diabetes. There was a negative correlation between the degree of thermic response and circulating insulin.[38] These data suggest that there is an impairment in the thermic response to a meal in obese persons and that one mechanism associated with this change is the cephalic phase secretory response of the pancreatic system for releasing insulin.

Adipose Tissue

More than 90% of body energy is stored as triglyceride in adipose tissue. Protein and glycogen provide important but smaller quantities of energy. Adipose tissue has two principal functions: the synthesis and storage of fatty acids in triacylglycerols and the release of fatty acids as a source of metabolic fuel. Triglyceride is stored in fat cells that differ in size between one region of the body and another. There may be important regional differences in the total number of fat cells, and this number appears to vary in different types of obesity.[39]

The storage of fat in the first months of life occurs primarily by an increase in the size of already existing fat cells. By the end of the first year, fat cell size has nearly doubled, with little change in the total number,[40] both in children who become obese and in those who do not. In children who are lean, the size of the fat cells decreases after the first year of life. Obese children, on the other hand, retain throughout childhood the large fat cells that developed during the first year of life. Fat cells multiply in number throughout the growing years in a process that usually stops in adolescence. The number of fat cells in obese children increases more rapidly than that in lean children, reaching adult levels by 10 to 12 years of age.[40] Current evidence suggests that, after puberty, acute changes in body fat stores occur primarily by an increase in the size of adipocytes that already exist, with little or no change in the total number. Severe weight loss is likewise accomplished primarily by a reduction in the size of extant fat cells. Recent evidence suggests, however, that the number of fat cells may change in adult life.[41] A steady increase in body fat, on the one hand, may lead to an increase in the number of fat cells; conversely, a prolonged reduction in body fat may possibly lead to a decrease in the number of fat cells.[41]

Knowing the size, number, and distribution of fat cells may be useful in classifying obesity and in estimating the prognosis with different forms of therapy.[42] Substantially overweight persons almost always have hypercellular fat organs, whereas those with modest degrees of overweight may be hypercellular but are much more likely to have only an increase in fat cell size or hypertrophic obesity. The duration of weight loss that follows successful dietary treatment is shorter and the rate at which weight is regained is more rapid in persons with hypercellular obesity compared with those with hypertrophic obesity.[42]

Health Risks Associated With Obesity

Total Body Fat and Risk of Mortality

The risk of mortality from obesity can be evaluated only in prospective studies. Studies involving more than 750,000 subjects each, by the life insurance industry,[43,44] the American Cancer Society,[45] and one involving nearly the entire population of Norway[2] have yielded similar results that have been confirmed by numerous smaller, prospective evaluations of cardiac risk factors. This overall relationship is shown in Figure 8, which shows relative mortality rates for various deviations of body mass index.[45] The data show a J- or U-shaped curve, with the lowest mortality for both men and women occurring among persons somewhat below the average body mass index.[46] Deviations above and below this are associated with an increase in mortality risk. The effect on life expectancy of small deviations in weight, however, is small, and there is a wide range around the average body mass index in which it is impossible to discern any increase in mortality. At an index of 30 kg per m^2, the mortality has already increased, and above 40 kg per m^2 the curve becomes steep. It is also apparent that mortality increases when the body mass index falls to values below the minimum mortality level. A 1983 study examining mortality during 16 years of follow-up in 2,381 men and women in Scotland sheds further light on this point.[47] While mortality from lung cancer increased with decreasing fatness, mortality from cardiovascular disease increased with increasing fatness. Findings similar to these have led to the concept that the two limits of the U-shaped relationship between fatness or relative weight and mortality are due to different causes of death. Thus, some digestive and respiratory tract diseases compose the low-weight deaths, whereas cardiovascular diseases, diabetes, and gallbladder disease make up the high-weight causes of death.

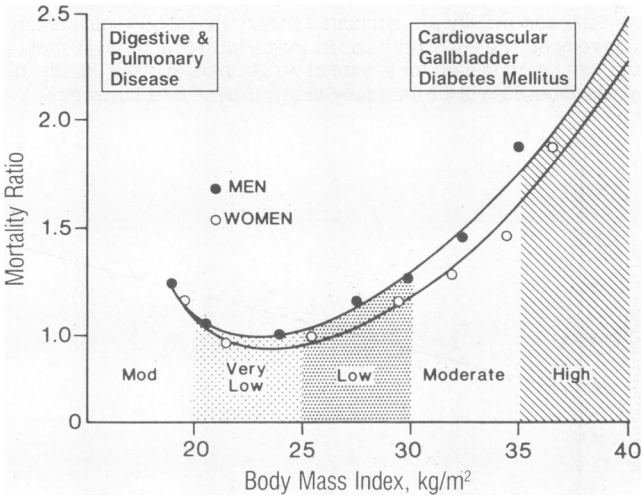

Figure 8.—Data from the American Cancer Society study have been plotted for men and women to show the relationship of body mass index to overall mortality risk. At a body mass index below 20 kg per m^2 and above 30 kg per m^2, there is an increase in relative mortality. The major causes for this increased mortality are listed, along with a division of body mass index groupings into various levels of risk (adapted from Lew and Garfinkel[45]).

Body Fat Distribution and Health Risks

One of the most important developments in understanding the health risks associated with obesity has been realizing the important role of body fat distribution. There are two types of fat distribution: the abdominal, android, upper body, or male type; and the gynoid, lower body, or female type. The former has a higher ratio of abdominal to gluteal circumference (android to gynoid ratio or waist-to-hip ratio). As early as the 1950s, Vague suggested that a preponderance of abdominal fat increases the risk for diabetes and cardiovascular disease.[48] Five prospective studies have examined the relation of fat distribution to morbidity and mortality.[49-53] Whether the ratio of abdominal to gluteal circumference, the subscapular skin fold, or a combination of skin folds was used as the indicator of abdominal fat, all five studies found a clear-cut and significant increase in the risk of death or an increased risk of diabetes mellitus, hypertension, or stroke. Fat distribution was a more important risk factor for morbidity and mortality than overweight or obesity per se and had a relative risk ratio of two or more. This is shown in data from a prospective study of residents of Gothenberg, Sweden (Figure 9). The data for waist-to-hips ratio divided into fifths of the population (quintiles) showed a much greater chance of remaining free of myocardial infarction and of long-term survival in the quintile with the lowest waist-to-hips ratio compared with the quintile with the highest waist-to-hips ratio.[49] This effect was independent of total fatness.

In addition to the prospective data described here, cross-sectional studies have also clearly shown an increased prevalence of glucose intolerance, insulin resistance, elevated blood pressure, and elevated blood lipid levels in both men and women with increased abdominal fat.[54,55] It has been suggested that the abdominal or android fat pattern may represent an increase in the size or number of more metabolically active intra-abdominal fat cells. These fat cells release free fatty acids directly into the portal circulation, which might interfere with insulin clearance in the liver and thus affect various metabolic processes. It is interesting to note in this context that a recent study from Japan used abdominal computed tomographic scanning of fat distribution to separate intra-abdominal or visceral fat from subcutaneous fat and thus defined a visceral-subcutaneous fat ratio. The visceral-subcutaneous ratio is correlated inversely with glucose tolerance.[56]

Obesity and Organ Function

Cardiovascular system. The relation of hypertension to obesity has been widely recognized. It is important to use a large enough cuff to measure the blood pressure in obese persons because a cuff that does not encircle 75% of the arm may artificially elevate the blood pressure.[57] Even with the limitations in the techniques of measuring blood pressure by indirect auscultation, however, the available data almost uniformly indicate the important relationship between body weight and blood pressure and between fat distribution and blood pressure (Figure 10).[58,59] The increased blood pres-

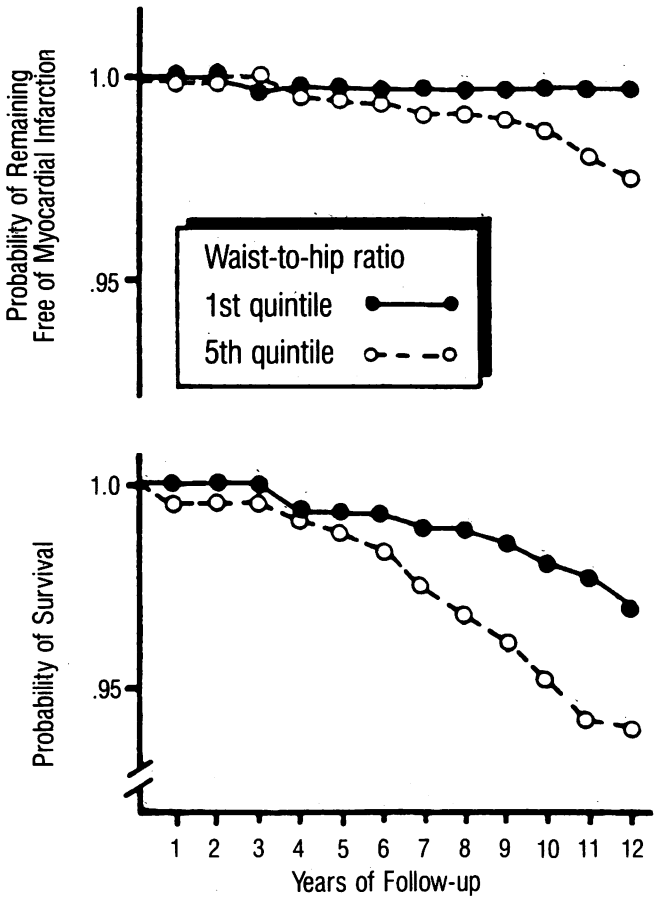

Figure 9.—These data show cumulative mortality in relation to abdominal (waist) to gluteal (hips) circumference ratio. They are from a prospective study of women in Gothenberg, Sweden, who were followed for 12 years (from Lapidus et al[49]).

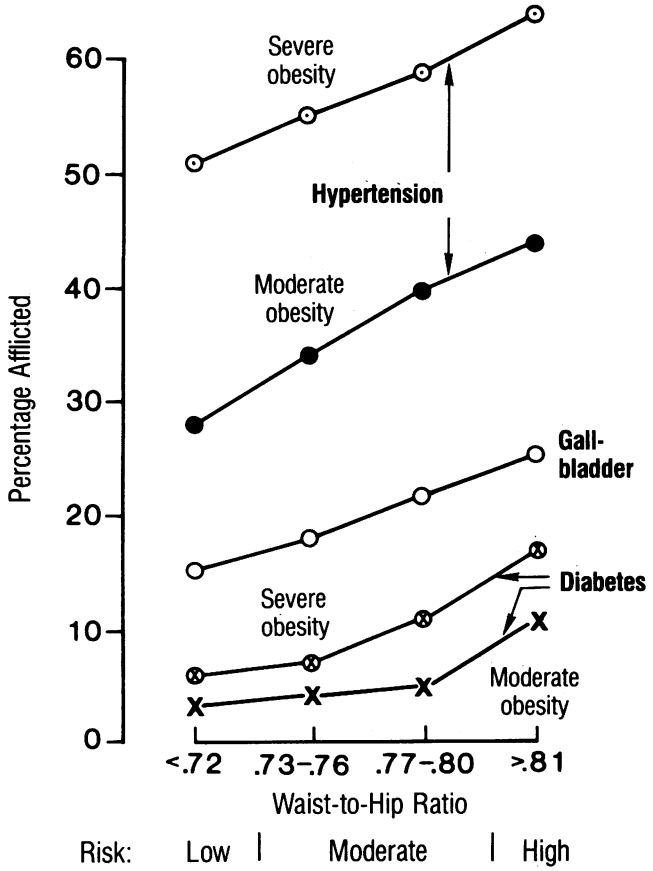

Figure 10.—These data show the relationship of abdominal (waist) to gluteal (hips) circumference ratio to various risks of obesity (from Hartz et al[59]).

sure probably results from increased peripheral arteriolar resistance. A reduction in blood pressure usually follows weight loss.[60] Obesity also increases the work of the heart, even if the blood pressure is normal. A cardiomyopathy of obesity has been reported with an associated congestive heart failure.

Diabetes mellitus. Obesity appears to stimulate the development of diabetes mellitus, and weight loss appears to reduce the risk of this disease.[61,62] Drenick followed a group of obese men, none of whom initially had diabetes.[61] During the six years of follow-up, the percentage of those with overt diabetes increased steadily to more than 40%. An additional 40% showed impaired glucose tolerance, meaning that during the six years of follow-up, more than 80% of the group showed a deterioration in glucose tolerance. The risk of diabetes is worsened with increased abdominal fat (Figure 10). With weight loss, glucose tolerance improves, insulin secretion falls, and insulin resistance is reduced.[63]

Gallbladder disease. The association of obesity with gallbladder disease has been documented in several studies.[59] Obese women between 20 and 30 years of age had a sixfold increase in the risk of gallbladder disease developing compared with normal weight women. By age 60 nearly a third of obese women can expect to have gallbladder disease.[59] The relationship to fat distribution is also evident (Figure 10). Increased cholesterol production with obesity results in increased biliary excretion of cholesterol, producing a bile that is more saturated in cholesterol, thus increasing the risk of gallstone disease in obesity.

Pulmonary function. Measurements of pulmonary function are generally normal in most obese persons.[64,65] Only with massive obesity are decreased reserve volumes and lowered arterial oxygen saturation obvious. The most important pulmonary problem in obese patients is the uncommon pickwickian or obesity-hypoventilation syndrome, which occurs mainly in the massively obese. There is a growing body of literature that suggests that the symptoms of this syndrome may result largely from sleep apnea.[64] With time, hypoxemia is followed by hypercapnia, which eventually leads to cor pulmonale.[64] Patients with the pickwickian or obesity-hypoventilation syndrome may require intensive care in a hospital to treat respiratory or cardiac failure.

Endocrine and metabolic changes. The basal concentration of growth hormone is normal or reduced in obese persons, and there is a negative correlation between body mass index and the integrated concentration of growth hormone obtained by frequent sampling over a 24-hour period.[66] The induction of hypoglycemia with insulin normally stimulates a rise in the level of growth hormone, but in obese patients this response is reduced.[5]

Nutrition appears to be more important than body weight itself in determining the circulating concentration of triiodothyronine (T_3).[67] During fasting or severe caloric restriction, total thyroxine (T_4) levels remain normal, but the serum concentration of total T_3 falls and that of reverse T_3 increases. In contrast to starvation, overnutrition is associated with a rise in serum T_3 and a fall in reverse T_3 values[67] in both obese and lean subjects.

The diurnal rhythm of cortisol is preserved in patients with simple obesity,[5,68] but the afternoon values may be above normal. There is a small, significant, negative correlation of cortisol with the percentage of overweight in women but not in men. Administering 1 mg of dexamethasone at midnight followed by measuring plasma cortisol or urinary free cortisol levels the next morning is the best screening test to separate a diagnosis of obesity from that of Cushing's syndrome. Obese patients whose cortisol levels are not suppressed with this test are a small group for whom more complex procedures are needed to exclude the possibility of Cushing's syndrome.

In obese men, the concentration of testosterone in plasma is decreased.[68] This reduction in the total testosterone level is accompanied by a reduction in the level of sex hormone-binding globin, resulting in a normal level of free testosterone in moderately obese men.[69] In massively obese men, however, there may also be a decrease in the free testosterone level as well.

In obese girls, the onset of menarche frequently occurs at a younger age than in normal weight girls.[5] The observation that menstruation is initiated when body weight reaches a critical mass provides one explanation for this phenomenon. As the rate of growth accelerates in late childhood, the entrance into this critical weight range initiates the pubertal process. Because obese girls grow faster and enter this critical mass at a younger age than normal ones, menstruation usually starts at an earlier age. Obese women often show less regularity of menstrual cycles and a greater frequency of menstrual abnormalities. In one study, 43% of 100 women with menstrual disorders were overweight.[70]

Does Weight Loss Improve Health?

Both insurance companies[43,44] and the Framingham study[71] have provided data that suggest that weight reduction may be beneficial to health. In both men and women who successfully lose and maintain a lower weight, mortality was reduced to within the normal limits based on sex and age according to life insurance statistics. Data from the Framingham study showed that a 10% reduction in relative weight for men was associated with a fall in serum glucose levels of 2.5 mg per dl, a fall in serum cholesterol levels of 11.3 mg per dl, a fall in the systolic blood pressure of 6.6 mm of mercury, and a fall in serum uric acid levels of 0.33 mg per dl.[71] For each 10% reduction in the body weight of men, these data predict that there would be an anticipated 20% decrease in the incidence of coronary artery disease.

Clinical Types of Obesity

Genetic Factors

In human obesity, genetic factors manifest themselves in two ways. First, there is a group of rare or dysmorphic forms of obesity in which genetic factors are of prime importance. Second, there is a genetic substrate upon which environmental factors interact in the development of obesity.

The dysmorphic forms of obesity are listed in Table 5, and while obesity is only of moderate degree in most, it may be pronounced in a few. These forms of obesity are transmitted by both recessive and dominant modes of inheritance. The Prader-Willi syndrome is associated in about half of persons with a translocation or a deletion of chromosome 15. For a more detailed discussion of dysmorphic obesity, the reader may consult other sources.[72]

Although studies show that obesity runs in families, they do not critically separate environmental from genetic factors.[5] This can only be done in studies of adopted children and twins. Using the Danish registry, Stunkard and colleagues examined 800 adoptees.[73] There was no relationship

between the body mass index in the adoptive parents and their children. On the other hand, the body mass index of the biologic parents increased with increasing weight of the children. These data suggest that inheritance plays an important role in the risk of obesity developing and are consistent with most studies of the adopted.[74]

The most definitive evidence for genetic versus environmental factors in obesity comes from examining body weight in twins.[75,76] Monozygotic twins have identical genetic material, whereas dizygotic twins have the genetic diversity of brothers and sisters but the closeness of monozygotic twins. Evaluating these groups of twins, along with other siblings and more distant relatives, should make it possible to separate nature from nurture. Using the body mass index as the criterion for obesity, Stunkard and associates compared 1,983 male monozygotic and 2,104 male dizygotic twins.[75] Monozygotic twins had higher correlations between body weights than the dizygotic twins, and calculations of the heritability for obesity suggested that nearly two thirds of the variation in body weight could be attributed to genetic factors.

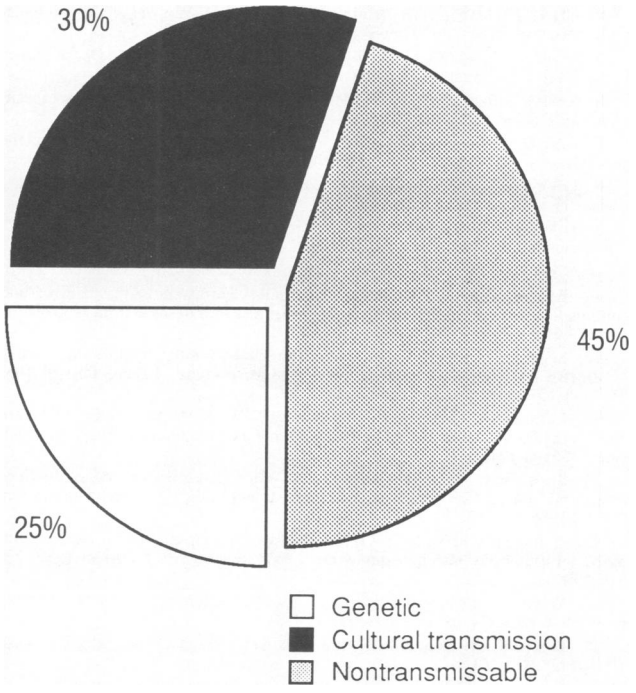

Figure 11.—The genetic and nongenetic transmission of body fat, fat mass, and extremity-to-trunk skin-fold ratio measurements are shown (from Bouchard et al[76]).

Bouchard and co-workers have examined the skin folds and total body fat in various groups with differing degrees of genetic relationships, including monozygotic and dizygotic twins.[76] Adopted siblings have a low order of correlation, but biologic siblings showed a higher one. As might be expected, this was highest among the monozygotic twins. Biologic siblings had a lower order of correlation for all of the variables than did dizygotic twins, although they all had the same genetic variation, suggesting that there was an environmental influence operative in the dizygotic twins that was absent in the biologic siblings. The genetic and nongenetic components for body fat and body mass index are shown in Figure 11.

In summary, single and polygenic inheritance are both involved in the transmission of obesity. Genetic factors may be of less importance than environmental ones in the determination of body fat and its distribution.

Classifying Obesity

Obesity can be classified in at least three ways: by the anatomic characteristics and regional distribution of adipose tissue; by etiologic causes; and by the age at onset.

Anatomic. The anatomic classification is based on the number of adipocytes. In many who become obese in childhood, the number of adipocytes may be increased twofold to fourfold. People with increased numbers of fat cells are classified as having hypercellular obesity, which is distinguished from other forms of obesity in which the total number of adipocytes remains normal but the size of individual fat cells is increased. In general, all obesity is associated with an increase in the size of adipocytes, but only selected forms have an increase in the total number of such fat cells.

Obesity may also be classified according to body fat distribution. As mentioned, both men and women with abdominal or android obesity have an increased risk of cardiovascular disease, hypertension, and diabetes. On the other hand, gluteal or gynoid obesity appears to have a much lower risk.

Etiologic. There are a number of causes of obesity. Endocrine diseases may cause obesity, but they are rare. Moreover, with endocrine diseases the increase in fat is usually

TABLE 5.—*Syndromes of Obesity, Hypogonadism, and Mental Retardation*

Syndrome	*Mental Retardation*	*Inheritance*	*Stature*	*Obesity Type and Onset*	*Craniofacial Features*	*Limbs*	*Reproductive Status*	*Other*
Prader-Willi	Mild to moderate	Sporadic—2/3 have defective chromosome 15 (q:1.2)	Short	Generalized, moderate, severe; onset: 1-3 yr	Narrow bifrontal diameter, almond-shaped eyes, strabismus, V-shaped mouth, high arched palate	Small hands and feet; hypotonia	Primary hypogonadism	Enamel hypoplasia
Bardet-Biedl	Mild to moderate	Autosomal recessive	Normal, infrequently short	Generalized; early onset: 1-2 yr	Not distinctive	Polydactyly	Primary hypogonadism	...
Alström	None	Autosomal recessive	Normal, infrequently short	Truncal; early onset: 2-5 yr	Not distinctive	No abnormalities	Hypogonadism in males only	...
Cohen	Mild	Probably autosomal recessive	Short or tall	Truncal; midchildhood, age 5	High nasal bridge, arched palate, open mouth, short philtrum	Hypotonia; narrow hands and feet	Normal gonadal function or hypogonadotrophic hypogonadism	...
Carpenter's	Mild	Autosomal recessive	Normal	Truncal, gluteal	Acrocephaly, flat nasal bridge, high arched palate	Polydactyly, syndactyly, genu valgum	Secondary hypogonadism	...

small. Hyperinsulinism, produced by islet cell tumors or by injecting excess quantities of insulin, produces an increased food intake and increased fat storage, but the magnitude of this effect is small. A somewhat more substantial obesity occurs with the increased cortisol secretion in Cushing's syndrome. Obesity may also occur with hypothyroidism. Finally, aberrations in the distribution of body fat are also noted with hypogonadism.

Hypothalamic obesity is a rare syndrome in humans[77] but can be regularly produced in animals by an injury to the ventromedial region of the hypothalamus. This region is responsible for integrating information about energy stores and regulating the function of the autonomic nervous system. Hypothalamic obesity has been reported in humans under a variety of circumstances, the major factors being trauma, malignancy, and inflammatory disease. Symptoms and signs that accompany the syndrome include those related to changes in intracranial pressure (headache and diminished vision due to papilledema), manifestations of endocrine alterations (amenorrhea, impotence, diabetes insipidus, and thyroid or adrenal insufficiency), and a variety of neurologic and physiologic derangements (including convulsions, coma, somnolence, and hypothermia or hyperthermia). Treatment of the syndrome requires treating the underlying disease and giving appropriate endocrine support.

Physical inactivity plays an important role in the development of obesity. Gross obesity in rats can be produced by severely restricting their activity. In a modern affluent society, energy-sparing devices that reduce energy expenditure may enhance the tendency to become fat.

Diet is a third etiologic factor in obesity. This is particularly prominent in experimental animals but may also play a role in the development of obesity in humans. When rodents eat a high fat diet, drink sucrose-containing solutions, or eat a cafeteria type of diet, most strains are unable to appropriately regulate energy balance, and they ingest more energy than is needed for maintaining weight. The excess energy is accumulated as fat, and the animals become obese to varying degrees. Whether the rising fat consumption, the high intake of sugar-sweetened beverages observed in most Western nations, and the increase in corpulence in these same societies are manifestations of a similar phenomenon remains to be proved.

By age of onset. Progressive childhood obesity is a hypercellular form of obesity[5] that develops early in life; persons afflicted with this disorder show a continuing weight gain thereafter. At present, none of the forms of obesity, including progressive childhood obesity, can be detected at birth. Birth weights of children who become obese are in general not different from the birth weights of those whose childhood weights are normal. The critical periods for the appearance of progressive childhood obesity are in the first two years of life and again between ages 4 and 11. The most serious form begins in this latter period and may progress thereafter. Obesity that begins in childhood is usually hypercellular and may be resistant to therapy. Adult-onset obesity tends to be hypertrophic and features large fat cells.

The base of information about obesity has expanded dramatically in the past decade. New methods have been developed to document the degree of obesity, which have provided better evidence of the prevalence of this widespread problem. The importance of fat distribution as a risk to health has added a new dimension to the problem. It is now clear that increased abdominal fat can be as much as or more of a health risk than smoking, hypertension, or high levels of blood cholesterol. Along with this growth in knowledge has come an improved understanding of the mechanism underlying obesity. The possible roles of the sympathetic nervous system and of brown adipose tissue are two examples. The possibility that white fat cells may both increase and decrease in number during adult life needs to be reckoned with. Finally, we seem to be on the verge of new methods of treatment. The treatment of obesity will be discussed by us in the next issue of the journal.

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