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Pathobiology of Obesity Adipose tissue evolved as a solution to the challenge of the intermittent availability of food. At times when food is plentiful, excess calories are converted to triglycerides and efficiently stored in the unilocular lipid droplets that occupy most of the volume of fat cells. When needed, the triglyceride is rapidly broken down to free fatty acids and glycerol, which provide an energy source to other sites throughout the body. However, in environments where food is abundant and when indi viduals tend to be sedentary, the chronic excess of energy intake over expenditure leads to obesity. The risks of developing obesity under those circumstances and of

developing the illnesses associated with obesity vary greatly between individuals, with that variation having a strong genetic basis. ■ ■DEFINITION OF OBESITY AND OVERWEIGHT Obesity is defined as a state of excess adipose tissue mass that adversely affects health. The direct measurement of fat mass is not something that is readily undertaken in routine clinical practice, so a proxy mea sure, the body mass index (BMI), is generally used. This is calculated as weight/height2 (in kg/m2) (Fig. 413-1). BMI-based definitions of obesity and overweight have been established based on associations with certain morbidities and excess mortality. These definitions have been based largely on studies of predominantly white, Western popula tions, and there is growing evidence that the relationship between BMI and adverse outcomes is different in people from other ethnic groups, usually in the direction of worse health outcomes being seen at lower levels of BMI. The World Health Organization (WHO) defines a BMI of 30 kg/m2 as the cutoff point for obesity, while individuals with values between 25 and 30 kg/m2 are classified as overweight. For individuals with a very muscular body habitus, the BMI may overestimate the

Body Mass Index (weight in kg/height in meters squared) Pathobiology of Obesity CHAPTER 413 Underweight <18.5 Normal weight 18.5–24.9 Overweight 25–29.9 Obese

> 30.0 FIGURE 413-1 Definitions of overweight and obesity. The World Health Organization defines obesity based on body mass index (BMI), which is calculated as weight in kilograms divided by the height in meters squared.
> amount of body fat. For any given BMI, women will generally have a higher percentage of body fat than men. The extent to which different adipose depots expand in response to chronic overnutrition varies markedly between people. In general, females store more fat in subcutaneous tissues, especially on buttocks, thighs, and upper arms, whereas men are more prone to store fat in intraabdominal and truncal subcutaneous sites. A simple measure of fat distribution is provided by a measurement of the waist-to-hip ratio. Independent of the degree of obesity, a waist-to-hip ratio >0.9 in women and >1.0 in men is associated with adverse health outcomes such as type 2 diabetes and dyslipidemia. ■ ■EPIDEMIOLOGY The annual National Health and Nutrition Examination Survey (NHANES) provides an ongoing record of the prevalence of obesity in the United States. In 2017–2018, 42.4% of U.S. adults aged ≥20 years old had obesity with no significant differences in prevalence by age group. Non-Hispanic black people had the highest prevalence of obesity at 49.6%, followed by Hispanic (44.8%), non-Hispanic white (42.2%), and non-Hispanic Asian (17.4%) people. In the United States, Asians repre sent a highly heterogeneous group encompassing both East and South Asia as well as a substantial Filipino community. The risks of obesity and its complications may differ greatly between people from different parts of Asia; in general, the prevalence of obesity is somewhat higher in women than in men, with black women having the highest preva lence at 56.9%. There has been a marked increase in the prevalence of obesity over time. For example, between 1976 and 1980, the NHANES survey reported a prevalence of 14.5%, indicating a near threefold increase over the past 40 years. This trend is seen globally. According to the WHO, obesity has nearly tripled worldwide since 1975. In 2016, >1.9 billion

> adults aged ≥18 years old were overweight. Of these, >650 million were obese; 39% of adults aged ≥18 years old were overweight in 2016, and 13% were obese. Most of the world’s population lives in countries where over weight and obesity kills more people than underweight. During this time, one of the most striking changes has been in the prevalence of obesity in children. In children, the relationship between BMI and body fat varies considerably with age and with pubertal maturation; however, when adjusted for age and sex, BMI is a reason able proxy for fat mass. Using age- and sex-specific BMI cutoffs (over weight ≥91st percentile; obesity ≥99th percentile), in 2019, the WHO estimated that 38 million children under the age of 5 were overweight or obese, and in 2016, they reported that 340 million children and adolescents aged 5–19 were overweight or obese. ■ ■PHYSIOLOGIC REGULATION OF ENERGY BALANCE Discussions about obesity so frequently focus on the issues of personal choice or the obesogenic environment that it can be easy to forget that

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