Abstract—The prevalence of overweight among children and adolescents has dramatically increased. There may be vulnerable periods for weight gain during childhood and adolescence that also offer opportunities for prevention of overweight. Overweight in children and adolescents can result in a variety of adverse health outcomes, including type 2 diabetes, obstructive sleep apnea, hypertension, dyslipidemia, and the metabolic syndrome. The best approach to this problem is prevention of abnormal weight gain. Several strategies for prevention are presented. In addition, treatment approaches are presented, including behavioral, pharmacological, and surgical treatment. Childhood and adolescent overweight is one of the most important current public health concerns. (Circulation. 2005;111:1999-2012.)

Key Words: AHA Scientific Statements ■ cardiovascular diseases ■ obesity ■ nutrition ■ epidemiology

Cardiovascular disease (CVD) is the leading cause of mortality in the United States and is becoming increasingly important as a cause of mortality worldwide.1 It is increasingly well known that obesity is an important risk factor for CVD in adults.2 For >75 years, height and weight tables developed by the Metropolitan Life Insurance Company have been used to assess risk and assign costs to insurance policies, a visible example of the now well-established expectation that overweight is associated with a shorter life span.3 The prevalence and severity of overweight is increasing in children and adolescents. The short- and long-term association with morbid outcomes raises the level of importance for understanding overweight as a major public health concern for children and adolescents. For children in the United States, overweight is defined using Centers for Disease Control and Prevention (CDC) age- and sex-specific nomograms for body mass index (BMI). These nomograms are based on data acquired from sequential evaluations of representative samples of children in the United States performed during the past 4 decades (the National Health and Nutrition Examination Surveys) but exclude more recent surveys from when the population had shifted to higher BMI.4 The term “obesity” to characterize BMI ≥95th percentile in children and adolescents.4 The term obesity was used in this report in part to more effectively convey the seriousness, urgency, and medical nature of this problem. Thus, the terms overweight and obesity are often used interchangeably in pediatric patients.

This scientific statement examines the pathophysiology and epidemiology of overweight in children and adolescents. We present updated information on the adverse outcomes associated with childhood overweight and discuss approaches for the prevention and treatment of overweight in young individuals.5

Physiology of Overweight
Obesity results from an imbalance between energy intake and energy expenditure. Excesses in adipose tissue mass also can be viewed as a pathological derangement in the feedback between energy intake and expenditure. In modern times, this excess in adipose tissue fuel storage is considered a disease; however, a better way to view obesity may be as a survival

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on February 22, 2005. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0320. To purchase additional reprints: up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 410-528-4121, fax 410-528-4264, or e-mail kgray@lww.com. To make photocopies for personal or educational use, call the Copyright Clearance Center, 978-750-8400.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit http://www.americanheart.org/presenter.jhtml?identifier=3023366.

© 2005 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org

DOI: 10.1161/01.CIR.0000161369.71722.10

1999
advantage that has gone astray. It is important to remember that what is now considered “pathophysiology” was probably advantageous when food was less available and a high level of energy expenditure in the form of physical activity was a way of life.6

The development of adipose tissue in the fetus begins in the mid- to late third trimester of pregnancy. Early in life, the ability of adipose tissue stromal cells to differentiate into triglyceride-filled adipocytes is facilitated; however, the view that the number of adipocytes is unchangeable after birth is historical and not supported by recent observations. Critical periods of adipocyte differentiation may include infant feeding, puberty, after the administration of steroids, and by peroxisome proliferator-activated receptor-λ–mediated adipocyte differentiation in adulthood.7–9 With weight reduction, a decrease in adipocyte volume but not number occurs10; however, after suction lipectomy, the failure of adipocyte volume to change suggests that a new program of adipocyte differentiation becomes operational to return fat mass to baseline.11 Much in the way of additional research is needed to better understand the development and regulation of adipocyte number/volume from fetal to adult life.

Understanding the regulation of energy intake requires differentiating the short-term signals that control hunger, food intake, and satiety, as well as the long-term signals that relate to the defense of energy stores, lean tissue, or both. In short-term regulation, gastrointestinal signals provide important input to the brain. For the most part, hormones released from the stomach and intestine that affect food ingestion are inhibitory.12 One example is the recently identified polypeptide YY3-36, which is produced by the L cells of the small intestine. When YY3-36 is infused into lean or obese subjects, reductions in food intake by ∼30% are seen.13 Ghrelin is an exception. This peptide is produced by the stomach and proximal small intestine, and its release stimulates food intake. Ghrelin declines after a meal and rises before the next meal. Ghrelin is elevated in Prader-Willi syndrome,14 which is a genetic form of obesity accompanied by marked hyperphagia. Ghrelin is dramatically reduced after gastric bypass surgery15; this fall in ghrelin is a potential explanation for the sustained anorexia and long-term benefit of this operation.

Adipose tissue is critically involved in feedback regulation of energy balance by the production of a number of peptide hormones, and leptin and adiponectin are 2 of the most important. The absence of leptin produces massive obesity, and treatment of leptin-deficient individuals reduces food intake and body weight.16 In most obese people, however, leptin has little effect on food intake or body weight.17 Adiponectin is the most abundant hormone from fat cells, increases insulin sensitivity, and appears to be a cytokine that is antiinflammatory.18 To a large extent, the signals directed by leptin and other adipose tissue–derived peptides are integrated in the hindbrain and mid-brain through various signals (monoamines, neuropeptide-Y, agouti-related peptide, α-melanocyte–stimulating hormone), which in turn send efferent signals for food seeking and modulation of function of various organs, including the pancreas and muscle (glycerol 3-phosphate dehydrogenase), and in rodents, brown adipose tissue (uncoupling proteins).19 Metabolism of the adrenal steroid in adipose tissue may provide a mechanism for the increase in visceral fat. When the enzyme 11β-hydroxysteroid dehydrogenase type-1, which converts cortisol to the inactive cortisone in fat cells, is genetically disrupted, mice develop visceral obesity.20 This pathophysiology may also apply to humans.

**Epidemiology of Childhood Overweight**

In the United States, the prevalence of childhood overweight tripled between 1980 and 2000.21 This increase parallels that seen in US adults during the same period and has been the cause of much concern. In Australia, data from 2 national surveys show that the prevalence of overweight almost doubled between 1985 and 1995.22 Increases in childhood overweight or obesity have also been observed in Canada and the United Kingdom, China, Germany, France, and Finland.23

The definition of childhood obesity remains problematic. Almost all definitions use some variant of BMI. BMI is useful for depicting overweight in the population but is an imperfect approximation of excess adiposity.24 BMI in children varies with age. This in itself makes BMI definitions of overweight for children more complex than definitions for adults, which use a single cutoff value for all ages. Definitions of overweight that use BMI-for-age can be based on a number of different standards that all give slightly different results, and all are essentially statistical, not functional definitions. They are useful tools, but they should not be overinterpreted. The 2000 CDC growth charts can be used clinically to track growth over time despite being based on cross-sectional and not longitudinal data.25 The statistical percentiles used to designate overweight (≥95th percentile) and at-risk-for-overweight (85th to 95th percentile) are general guidelines for clinicians and others.26 The 2000 CDC growth charts facilitate the implementation of these cut points. Another international set of reference values is that provided by Cole et al,27 based on data from 6 countries—the United States, Brazil, the Netherlands, Hong Kong, the United Kingdom, and Singapore. Overall, various definitions of childhood overweight are useful for tracking prevalence and trends, but these should not be confused with clinical diagnoses or functional definitions. This may be particularly true of the “at-risk-for-overweight” category, which was originally intended as a way to identify children who needed further clinical investigation.

Examination of historical standards for defining overweight in children from many countries tells us that the distribution of BMI is becoming increasingly skewed.28 The lower part of the distribution has shifted relatively little, whereas the upper part has widened substantially. This finding suggests that many children may be more susceptible (genetically or socially) to influence by the changing environment. Within a variety of developed countries, differences in overweight and overweight trends also occur by social class and by ethnic groups, emphasizing the importance of nongenetic variables.29–31 There is relatively little understanding of these epidemiological variations.
Critical Periods for Abnormal Weight Gain
A life-course approach to chronic disease (e.g., obesity) classifies determinants in several different ways. A critical period refers to a specific period of development when an insult has an enduring effect on the structure or function of organs, tissues, and body systems. If not completely deterministic, these periods are often referred to as sensitive rather than critical. Several models have been advanced to explain which early factors are important in assessing later disease.32 Although some “insults” or events may occur at a particular period of development, they also may accumulate over time. These events may act independently or be correlated through clustering. Intrauterine influences (environmental factors in utero) have emerged as an important area of investigation. Epidemiological studies have demonstrated a direct positive relationship between birth weight and BMI attained in later life.33 Although these data are limited by the lack of information on potential confounders, the observed associations appear to be robust. Possible explanatory mechanisms include lasting changes in proportions of fat and lean body mass, central nervous system appetite control, and pancreatic structure and function. Other data suggest that rapid weight gain during infancy is also associated with obesity later in childhood, potentially reflecting an interaction of genetic and postnatal environmental factors.34 In addition, lower birth weight for gestational age has been associated with later risk for more central deposition of fat, which also confers increased cardiovascular risk.35 This association may be mediated through changes in the hypothalamic pituitary axis, insulin secretion and sensing, or vascular responsiveness. Accumulated research to date suggests that the combination of lower birth weight and higher attained BMI is most strongly associated with later CVD risk.36

Several studies suggest that early rebound of the BMI is associated with an increased risk of higher BMI in adulthood; however, this association may not be independent of the level of BMI in early childhood.36 BMI rebound refers to a period, usually between 4 and 7 years of age, when BMI reaches a nadir and then begins to increase throughout the rest of childhood, adolescence, and young adulthood. A recent study links early rebound of BMI to glucose intolerance and diabetes in adults.37 Other data suggest that BMI at age 7 or 8 is as good a predictor of obesity as age at BMI rebound. If the age at BMI rebound is shown to be related to future obesity, then this could provide a useful tool to help prevent obesity because it would identify children at risk before the development of obesity. Important areas for research include explicating the mechanisms through which early BMI rebound may lead to these sequelae and whether the BMI at the age of rebound is as important a determinant as the age at which the rebound occurs.

Whereas research attention has focused on determinants and correlates of overweight and obesity in childhood and adolescence, fewer data are available on factors that may be protective against excess weight gain. Several studies have demonstrated that breast-feeding is associated with a lower risk of obesity in childhood and adolescence.38 The results are not consistent across studies, with some showing no relationship between breast-feeding and later obesity.39 Potential mechanisms underlying an association between breast-feeding and obesity remain to be clarified. A particular challenge in epidemiological research in this area is accounting for the confounding influence of other behavioral and socioeconomic factors that may underlie both the decision to breast-feed and the risk of later obesity. Given the multiple benefits of breast-feeding that are already known, encouraging breast-feeding for the prevention of obesity carries few risks.

Adolescence, the transitional period that begins with puberty, is marked by dynamic physiological and psychological changes in both boys and girls. Changes that occur in body composition during adolescence have been well characterized and demonstrate sexual divergence. Specifically, in boys, fat-free mass tends to increase, and body fat as a percentage of body weight decreases. In girls, both fat and fat-free mass increase, and fat-free mass as a percentage of body weight decreases.40 In addition to alterations in total and percentage of body fat during adolescence, patterns of fat distribution also change. Mediated in part by hormonal influences, patterns of fat distribution during this developmental period also demonstrate sexual differences. Pronounced centralization of fat stores with increases in subcutaneous fat and visceral fat in the abdominal region occurs in boys; this pattern is similar but less dramatic for girls.41 In addition, fat tends to be deposited peripherally in the breasts, hips, and buttocks in girls during this period. Noteworthy is that the risk of becoming overweight during adolescence appears to be higher among girls than it is among boys. Other observations suggest that up to 80% of overweight adolescents will become obese adults. Adolescence has also been emphasized as a critical period for the development and expression of obesity-related comorbidities in both sexes.42–45

The original critical periods hypothesis suggested that obesity with onset in adolescence is more likely to persist into or exert its health effects in adulthood.46 The data on persistence of childhood obesity to obesity in later life are fairly consistent; however, data on incident obesity are lacking. Specifically, studies of adolescent obesity usually have not included measures earlier in childhood, making it impossible to distinguish between obesity present in adolescence and obesity with onset in adolescence. In addition, the extent to which obesity present or incident during adolescence has enduring effects on the contributors to the metabolic syndrome, either independent of or dependent on central adiposity, remains to be clarified.

Obesity present in adolescence has been shown to be associated with increased overall mortality and specifically with increased risk of CVD and diabetes in adult men and women.47 Controversy exists, however, about whether the increased risks of these diseases are mediated through their effect on adult weight.

Taken together, the available data suggest the need for additional research focused on identifying the factors that contribute to the onset of overweight in childhood and adolescence and factors that contribute to the persistence of overweight beyond these developmental periods. The observed associations of adult obesity and attendant comorbidities with birth weight, rebound of the BMI, and overweight...
TABLE 1.  Adverse Outcomes in Childhood Obesity

<table>
<thead>
<tr>
<th>Metabolic</th>
<th>Type 2 diabetes mellitus</th>
<th>Metabolic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopedic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slipped capital femoral epiphysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blount’s disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor quality of life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudotumor cerebri</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonalcoholic steatohepatitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma (exacerbation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

during adolescence suggest that these periods may be critical for targeting prevention efforts.

Comorbidities Related to Overweight in Youth

Overweight is associated with a number of comorbidities in children. Although the amount of information available about youth is less than that about adults, it is clear that children experience many detrimental effects of overweight similar to adults. Table 1 presents comorbid conditions related to overweight that may present during childhood and adolescence.

Metabolic Syndrome

The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program defined the metabolic syndrome (also known as the insulin-resistance syndrome) as a cluster of traits that include hyperinsulinemia, obesity, hypertension, and hyperlipidemia. It is estimated that 1 million US adolescents meet the ATP III criteria for the metabolic syndrome. The prevalence of the metabolic syndrome in adolescents is 4% overall, but it is 30% to 50% in overweight children. Weiss et al found that each half-unit increase in BMI (converted to a z score) was associated with an ~50% increased risk of metabolic syndrome among overweight children and adolescents.

The metabolic syndrome is believed to be triggered by a combination of genetic factors in combination with environmental factors such as excess calorie intake and reduced levels of physical activity. The primary cause of the syndrome appears to be obesity leading to excess insulin production, which is associated with an increase in blood pressure and dyslipidemia. The effects of increased insulin resistance are multiple and include increased hepatic synthesis of very-low-density lipoprotein, resistance of the action of insulin on lipoprotein lipase in peripheral tissues, enhanced cholesterol synthesis, increased high-density lipoprotein degradation, increased sympathetic activity, proliferation of vascular smooth muscle cells, and increased formation and decreased reduction of plaque. Fat tissue produces adipokines, including leptin, adiponectin, and resistin, in addition to other cytokines (eg, interleukin-6, tumor necrosis factor-α, plasminogen activator inhibitor-1) that are involved in inflammation. Therefore, the pathological consequences of an excessive increase in body fat are broad and involve a number of organ systems.

The metabolic syndrome has a profound effect on CVD risk in youth. Berenson et al evaluated the presence of aortic and coronary atherosclerosis in young individuals who died from accidental causes and found a striking increase in the extent of lesions with obesity and an increasing number of metabolic syndrome risk factors. Data collected by Pankow and colleagues support the claim that the metabolic syndrome has strong associations with CVD risk factors. Although there are limited prospective data evaluating the long-term implications of the metabolic syndrome in youth, the study of Steinberger et al suggests that obesity in youth is associated with hyperinsulinemia, decreased insulin sensitivity, and increased total cholesterol and triglycerides. The correlation between BMI measured at age 13 and BMI measured at age 26 was 0.75 (P=0.0001), whereas the correlation between BMI at age 13 and glucose utilization at age 26 was −0.50 (P=0.0001). Data such as these suggest that risk factors associated with the metabolic syndrome that are precursors of CVD can begin in childhood but track into adulthood.

Whether excess body weight is the cause or the consequence of excess insulin in youth remains unclear; however, prospective data suggest that the most important risk factor for the metabolic syndrome is the rate of increase in BMI in youth.

Type 2 Diabetes Mellitus

Concomitant with the rise in the prevalence of overweight and the metabolic syndrome has been a dramatic increase in type 2 diabetes mellitus in youth. Type 2 diabetes mellitus had been primarily a disease of adulthood; however, type 2 diabetes now occurs in adolescents typically with a BMI >30 kg/m², a level that would be considered obese even by adult standards. The prevalence of type 2 diabetes mellitus in US adolescents, according to NHANES III, is 4.1 in 1000 individuals, more than double the prevalence of type 1 diabetes mellitus (1.7 in 1000 individuals). This is a particular concern with regard to risk for CVD. The National Cholesterol Education Program has identified diabetes in adults as a coronary artery disease risk equivalent. This leads to the recommendation that adults with diabetes receive aggressive therapy including lipid lowering to prevent cardiovascular
morbidity and mortality. It is not currently known whether the level of risk for adolescents with type 2 diabetes mellitus is equivalent to that for adults. It is also not known whether adolescents typically have a prolonged period of asymptomatic hyperglycemia as is often observed in adults. If adolescents with type 2 diabetes mellitus do have risk for CVD that is similar to that in adults, then it means that they may experience adverse cardiovascular outcomes in the third or fourth decade of life if appropriate intervention to lower risk is not provided.

Inflammation
The association of obesity and inflammation is well recognized in adults. Data on this association in youth are also emerging. In general, inflammation occurs through the activation of the mononuclear phagocytes, which leads to the upregulation of interleukin-1, an upstream regulator with many downstream effects. In the liver, upregulation of interleukin-1 leads to an increase in acute-phase reactants, such as C-reactive protein. Inflammation also increases oxidant stresses, common in obesity, in which free radicals are generated in excess of the ability to detoxify them. This may lead to vascular damage over time. Insulin resistance is a proinflammatory condition, increasing tumor necrosis factor-α and other cytokine production. Inflammation may be an important mechanism for the development of medical complications of obesity, including CVD.

Cardiovascular Abnormalities
It is well recognized that CVD causes a substantial proportion of excess mortality in overweight individuals, as first observed in the London Bus Drivers’ study in 1956. What remains less clear is whether obesity is a completely independent risk factor or whether it works through other risk factors. The Muscatine study and the Bogalusa study have convincingly shown that obesity during childhood and adolescence is a determinant of a number of cardiovascular risk factors, including atherogenic dyslipidemia (increased triglycerides, lowered high-density lipoprotein), hypertension, left ventricular hypertrophy, obstructive sleep apnea, and atherosclerosis.

Adult blood pressure is an important risk factor for CVD. Overweight is associated with blood pressure elevation in both children and adults. In the Muscatine and Bogalusa studies, increased BMI consistently has been shown to be associated with higher blood pressure. In the Muscatine study, adult blood pressure was related to the change in BMI from childhood to adulthood. Increased left ventricular mass is a strong independent predictor of coronary heart disease, stroke, and sudden death in adults. Left ventricular hypertrophy has also been related to overweight in children. It has been shown that lean body mass, fat mass, and systolic blood pressure were independently associated with left ventricular mass in children and adolescents. Moreover, in children and adolescents with essential hypertension, elevated BMI was associated with severe left ventricular hypertrophy.

Obstructive sleep apnea is an emerging cardiovascular risk factor in adults. Obstructive sleep apnea is also associated with obesity in children and adults. Amin et al showed that increased BMI was related to an increased risk of obstructive sleep apnea in children and adolescents. They also showed that obstructive sleep apnea was associated with increased left ventricular mass index in a pediatric population.

There has been concern that overweight may contribute to the development of atherosclerosis. In the Bogalusa study, the relationship of antemortem CVD risk factors to the presence of atherosclerotic lesions was evaluated. The researchers found that a higher BMI was associated with more extensive fatty streaks in the coronary arteries in 15- to 24-year-old men and with more extensive raised lesions in 15- to 24- and 25- to 34-year-old men. This effect of BMI was independent and not explained by other CVD risk factors. Berenson et al also demonstrated that the presence of multiple risk factors, including obesity, is associated with an increased risk of atherosclerosis. This may reflect the influence of clustering of risk factors in the metabolic syndrome. Mahoney et al evaluated the presence of coronary artery calcium in young adults who had been studied as children in the Muscatine study. In the age group 29 to 37 years old, the prevalence of coronary artery calcification was 31% in men and 10% in women. The factors that were associated with coronary artery calcium included weight in childhood, BMI in young adulthood, and BMI at the time of the study, with odds ratios ranging from 3.0 to 6.1. In the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study of premature atherosclerosis, BMI >30 kg/m², increased panniculus thickness, and abnormal glucose tolerance were associated with advanced lesions at young ages.

Psychosocial Abnormalities
There is little information about the relationship between psychosocial factors and obesity in youth. The causal pathways by which psychological disturbances exert influence on body weight are unclear, although the association is likely to be complex rather than simple. The best-studied area is depression. In a study by Pine et al, adults who had been diagnosed with clinically defined major depression during their youth had a greater BMI than adults who did not suffer from depression during their youth (26 versus 24 kg/m² at 10 to 15 years of follow-up). Other studies have confirmed the association between depression and subsequent obesity. Goodman et al examined 9374 adolescents in grades 7 to 12 and found that elevated BMI was related to depression at 1 year of follow-up. The depression scores were highest in the children with the greatest increase in BMI. Other studies have supported the premise that psychopathology is associated with obesity in children.

The development of overweight also may be related to subsequent psychosocial difficulties. One of the primary mediators of the psychopathological relations with obesity is compromised peer relationships. Overweight children have fewer friends, and social network mapping suggests that normal-weight children have more relationships with a central network of children, whereas overweight children appear to have more isolated and peripheral relationships. In addition to having fewer friends, being teased about weight is another important mediator of psychosocial distress. Teasing over-
Overweight. Individually oriented prevention approaches that are important and appropriate for children who are already overweight. Population-oriented intervention. Treatment approaches are delivered in specialty care, primary care, and health systems, (downstream approaches) are individually oriented, usually delivered in specialty care, primary care, and health systems, and are more familiar to health professionals than is population-oriented intervention. Treatment interventions (upstream approaches) that have the broadest reach and the lowest intensity of effort focus on children at high risk of becoming overweight and obesity remains an important goal for those studying the pathogenesis and treatment of obesity in both adolescents and adults.

Medical Evaluation of Comorbidities

When an overweight child or adolescent is evaluated for medical reasons, it is important to consider potential comorbidities. A recommended approach to this evaluation is presented in Table 2. This approach should help guide clinicians in identifying medical problems that may require attention in addition to the treatment of overweight.

**Prevention of Overweight**

Potential interventions for obesity in youth span a continuum from preventing the development of obesity to treating established obesity and its complications. Treatment of obese children, discussed in the next section, can be a strategy for preventing adult obesity. Here, obesity prevention refers to avoiding the occurrence of obesity during childhood and adolescence. Obesity prevention includes both population-oriented and individually oriented approaches, with an emphasis on population-oriented approaches. Population approaches focus on environmental and policy change (upstream approaches) that have the broadest reach and the lowest intensity and cost and are critical for reaching the least-advantaged population segments (Figure). Treatment interventions (downstream approaches) are individually oriented, usually delivered in specialty care, primary care, and health systems, and are more familiar to health professionals than is population-oriented intervention. Treatment approaches are important and appropriate for children who are already overweight. Individually oriented prevention approaches that...
Promoting breast-feeding is a promising prevention strategy given its potential protective effect on later obesity and overall benefits for nutrition. Such efforts require more attention to the incentives and barriers that affect rates of breast-feeding by different subgroups within the population, including the social and environmental variables that support or discourage women’s decisions to breast-feed. For example, cultural norms that discourage breast-feeding in public or workplace policies that do not permit women who return to work after childbearing to pump or store breast milk in clean and comfortable circumstances represent significant barriers to the duration of breast-feeding.

**Toddlers**

Early childhood is a time of rapid growth, development, and learning. Reasons to emphasize prevention in early childhood include adipocyte physiology, adiposity rebound, and the limited potential for reversing metabolic changes associated with overweight. Findings from the Healthy Start Preschool Study suggest that a reasonable goal for preschool interventions would be to aim toward weight gains of 2.5 lb/in (1.0 kg/2 cm) of growth. This rate of gain from preschool age (3 to 4 years) onward predicted desirable weight at 8 to 9 years of age, whereas a gain of 5 lb/in (1.8 kg/2 cm) predicted overweight at elementary school age. Strategies to achieve an optimal rate of pounds gained per inch might help families and children acquire the critical life skills to enable them to better balance energy intake (diet) with energy expenditure (physical activity). Goals are to work toward establishing healthy environments at home, at school, and in the community that encourage families and children to practice and maintain the life skills that are conducive to maintaining a healthy weight.

The important role of parenting skills and teacher training in helping young children learn and practice healthful behaviors has increasingly been recognized. Behavior targets include increasing consumption of fruits and vegetables (“5-a-day”), increasing consumption of fiber-containing grain products, switching from full-fat to 1% or fat-free dairy products after 2 years of age, preparing and eating family meals at home, increasing daily physical activity (eg, active play 1 h/d), and limiting sedentary time (eg, watching television ≤2 h/d).

**School-Age Children and Adolescents**

Most efforts to prevent obesity among school-age children and adolescents have been implemented in school settings. There is ample evidence that theory-based interventions that include classroom curricula, physical education curricula, changes in school meals, vending machines, and cafeterias, and after-school programs, can increase physical activity and improve dietary patterns in children and adolescents. Many of these interventions have not successfully changed weight and body fat, however. Further research is needed to evaluate the specific reasons for this lack of change in body weight, including insufficient duration of the intervention and lack of consistent lifestyle changes outside school.

Additional attention paid to applying theoretical models to develop interventions that are more relevant and motivating to children has produced a growing body of theory-based
interventions in schools that have successfully reduced weight gain and obesity. Two successful recent studies emphasized reducing television, videotape/DVD, and video game use.76 These interventions addressed school, family, peer, and cultural influences to maximize program adoption and implementation and to allow a sufficient “dose” of the intervention to be received by the participating schoolchildren. The underlying theoretical models prompted interventions that addressed changes in schools as a whole and administrator and teacher behaviors, in addition to the children’s behaviors themselves. There are also successful examples of physical education interventions that have resulted in reductions in weight and fat gain by replacing the standard physical education curricula with higher-intensity or more motivating activities, specifically endurance training77 and popular dance.78 In contrast, increasing the duration and frequency of the standard physical education curricula alone has not resulted in changes in fitness or body composition.

Exposure to various media may be important in considering population-based prevention efforts. For example, a substantial proportion of the advertising on children’s television promotes food, and there is a direct relationship between television viewing and obesity.79,80 Furthermore, reducing television viewing has reduced weight gain and the prevalence of obesity in experimental trials.76,81 It has been hypothesized that television promotes obesity through the consumption of food while watching television, the consumption of foods advertised on television, or reduced physical activity.79,81,82 Food advertising has become a particularly controversial issue. The Kaiser Family Foundation recently suggested that the relationship between television viewing and overweight in childhood was mediated by the effect of televised food advertising directed at children,83 and the American Psychological Association called for a ban on all televised advertising directed at children <8 years old.84 The conclusions of all of the bodies that reviewed this literature, however, have not been consistent.85 Despite supporting evidence, there is insufficient causal evidence to definitively link advertising directly with childhood obesity.4

Children in Ethnic Minority Populations
The challenge of obesity prevention includes the need to develop tailored strategies that are well matched to the social and cultural contexts of children in ethnic minority populations with a high risk of obesity.86 Eating, activity, and perceptions of weight and health are strongly influenced by cultural norms and culturally influenced attitudes and values. The relevant variables can be considered from programmatic, child, familial, and environmental perspectives that are then each specified along multiple related dimensions such as ethnic identification and related cultural attitudes, beliefs, and values; family and household characteristics; and socioeconomic status variables. Theoretical guidance to inform systematic approaches to developing culturally specific prevention strategies is available but not yet fully used or developed in relation to the specifics of obesity prevention.86

Culturally adapted obesity prevention studies in ethnic minority populations identify strategies that deserve further testing.78,87 Culturally specific programming tends to shift control to the client population and challenges providers to acknowledge their own personal and professional cultural concepts and biases. A fundamental issue is whether the social and familial relationships and cultural practices that define patterns of daily living in the client population are viewed as targets for change, as difficulties to be overcome, or as positive forces that can be leveraged in favor of the programmatic goals. Other important issues are the respective roles of those from inside versus outside the communities of interest and the ability to sustain over the long term programs that are well received and effective in the short term.

Adaptation to ethnically based cultural perspectives is not the only consideration for effective health interventions. As discussed previously, any program should be otherwise theoretically sound. In addition, cultural factors related to obesity prevention are not solely defined along ethnic lines. Cultural variation related to age, generation, and gender is highly relevant to obesity-related norms, attitudes, and practices. The cultural context for obesity prevention also includes mainstream cultural forces such as media that are targeted differently to different demographic groups.

Setting-Specific Approaches
Setting-specific approaches target institutions that provide access to groups of children. Potential childhood obesity prevention settings include schools, Head Start programs, and other centers where preschoolers participate in groups; homes, where preschool children are cared for by parents and other caregivers; healthcare settings, where growth and weight status are routinely monitored; industries that develop television programs and other media, print books, and toys for preschoolers; and community and government programs and policies that affect families with young children. Typical interventions in physical settings are based on individual behavioral theories and designed to enhance motivation and teach behavior-change skills in large groups. In group settings, hands-on experiences with food or activity are often provided on site. Interventions in health care that teach providers effective counseling or deliver additional services can be effective, but there are significant barriers to implementation in such settings. Overall, a strength of setting-specific approaches is the ability to intervene in the setting itself—in other words, to consider the setting as an environment in which policies and practices can be changed to enable targeted behaviors and discourage competing behaviors. The key limitations of setting-specific approaches are that they reach a limited portion of the population and they do not coordinate strategies or messages across settings.

Community-wide approaches include coordinated interventions in multiple settings and may include mass media components. An underlying concept is that behavior-change interventions in multiple sectors, reaching many segments of the population, are needed to create population change. The effectiveness of community-wide interventions is not well established, however.

Environmental and policy approaches are based on the concept that education and motivational interventions will be more effective in social and physical environments where healthful choices are the easier choices. Relevant environ-
TABLE 3. Weight Management and Treatment Goals Based on BMI Percentile and Health Status

<table>
<thead>
<tr>
<th>BMI Status</th>
<th>Classification</th>
<th>Treatment Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;85th percentile</td>
<td>Normal weight for height</td>
<td>Maintain BMI percent to prevent obesity</td>
</tr>
<tr>
<td>85th–95th percentile</td>
<td>At risk for overweight</td>
<td>Maintain BMI with aging to reduce BMI to &lt;85th percentile; if BMI &gt;25 kg/m², weight maintenance</td>
</tr>
<tr>
<td>≥95th percentile</td>
<td>Overweight</td>
<td>Weight maintenance (younger children) or gradual weight loss (adolescents) to reduce BMI percentile</td>
</tr>
<tr>
<td>≥30 kg/m²</td>
<td>Adult obesity cut point</td>
<td>Gradual weight loss (1–2 kg/mo) to achieve healthier BMI</td>
</tr>
<tr>
<td>≥95th percentile and comorbidity present*</td>
<td>Overweight with comorbidity</td>
<td>Gradual weight loss (1–2 kg/mo) to achieve healthier BMI; assess need for additional treatment of associated conditions</td>
</tr>
</tbody>
</table>

See Table 2.


tments include physical (what is available and promoted; eg, food choices in homes, fast food advertisements on television, opportunities for or barriers to physical activity); economic (financial factors; eg, the price of soda versus water, subsidies to sugar farmers); policy (rules; eg, school food service standards, regulations on marketing that targets young children); and sociocultural (attitudes, perceptions, beliefs, and values such as fast food, everyday food, personal responsibility, and the ethos of governments).88

Treatment of Overweight

The principal strategies for the treatment of overweight in children are similar to those for adults (dietary modification and increased physical activity), with treatment goals based on age, severity of obesity, and the results of risk factor assessment. With its emphasis on acute short-term interventions, contemporary healthcare delivery is often not well suited to meet the long-term needs of overweight children and their families. Support for family-based nutrition and behavior-management programs to teach long-term self-management skills is lacking. Guidelines for the treatment of overweight in children are based on age, degree of overweight, and presence of associated comorbidities (Table 3). For children with BMI >85th percentile, there are 3 potential goals for weight management depending on age and the level of BMI: (1) slowed rate of weight gain to achieve BMI maintenance, (2) weight maintenance to improve BMI with increasing height, and/or (3) gradual weight loss at a rate of 1 to 2 kg/mo to improve BMI. Very young children (2 to 4 years old) who are overweight will achieve reductions in BMI percentile by achieving a rate of weight gain <1 kg/2 cm of linear growth. Older children (≥4 years old) who are at risk for overweight (BMI 85th to 95th percentile) or who are overweight (BMI ≥95th percentile) without comorbidities may achieve BMI percentile reductions to <85th percentile with BMI maintenance or more rapidly with weight maintenance during linear growth. Children classified as overweight (BMI ≥95% percentile) with comorbidities require an individualized approach based on the severity of comorbidities and a consideration of the importance of weight loss in conjunction with other treatment modalities. When weight loss is necessary, slow weight loss is recommended for several reasons: (1) The goal is achievable and, with success, provides positive feedback for children who often have low self-esteem, (2) slow weight loss requires a substantial decrease in calorie intake for children who are still growing and who often have been gaining 20 to 40 lb/y, and (3) the diet adapted to meet a gradual weight loss goal is more easily sustained over a long period. Older adolescents who have completed linear growth and have a BMI ≥30 kg/m² require more aggressive weight loss similar to that for adults to reduce their long-term risk.89 Occasionally, physically fit children have increased BMI secondary to increased lean body mass as opposed to fat mass; these children do not need to reduce BMI percentile to the same target goal as children with greater fat mass.

Guiding Principles

Five guiding principles are important for the treatment of overweight. These guiding principles can be summarized as follows:

1. Establish individual treatment goals and approaches based on the child’s age, degree of overweight, and presence of comorbidities.
2. Involve the family or major caregivers in the treatment.
3. Provide assessment and monitoring frequently.
5. Provide recommendations for dietary changes and increases in physical activity that can be implemented within the family environment and that foster optimal health, growth, and development.

Children <85th percentile with no other health risk factors should be screened (weight, height, and BMI percentile calculated and plotted) every year. Identification of risk for overweight before adolescence is encouraged so that health habits can be improved at a stage of increased parental influence and control. Treatment of overweight should rarely be instituted before 2 years of age because of the rapid growth and development that occurs during these early years and lower correlation with overweight in later years. As more is learned about the prevention of overweight, however, the focus on these early years of life may become critical. Importantly, primary care providers should assess diet and activity habits at annual well-child visits; this should be routinely integrated into the overall care plan.

Family involvement is critical in the treatment of childhood overweight. If treatment is initiated when a family is not ready to support the program, then success is unlikely. The treatment planned should also take into consideration long-term management with the continued assessment of the child
for adequate growth and development because overweight is a long-term problem.

**Dietary Management**

Age-specific dietary modification is the cornerstone of treatment. The major goals in dietary management are to provide appropriate calorie intake, provide optimum nutrition for the maintenance of health and normal growth, and to help the child develop and sustain healthful eating habits. The most recent Dietary Reference Intakes recommend a fat intake of 30% to 40% kcal in children 1 to 3 years old, with a reduction to 25% to 35% in children 4 to 18 years old (compared with 20% to 35% in adults); a carbohydrate intake of 45% to 65% kcal in all children and adults; and protein intakes of 5% to 20% kcal in children 1 to 3 years old with gradual increase to 10% to 30% kcal in children 4 to 18 years old (compared with 10% to 35% kcal in adults).90

Assessment begins with an understanding of the child’s dietary pattern before any modifications are imposed. Estimated energy requirements vary throughout childhood and reflect large increments with a range of 570 to 3152 kcal/d for boys and 520 to 2368 kcal for girls from age 3 months to 16 years.84 In addition, caloric needs may vary widely even for children of the same age because of normal differences in size. Thus, individualizing the calorie-intake recommendations and monitoring weight change are essential. Healthcare professionals must help parents or caregivers recognize and prevent overeating. Additional dietary recommendations should include providing adequate nutrition by offering a variety of foods that are low in saturated fat (<10% kcal), total fat (≤30% kcal), and cholesterol (<300 mg/d); promoting age-appropriate serving sizes including ≥5 servings of fruit and vegetables, ≥3 servings of milk or dairy products, and ≥6 servings of whole-grain and grain products per day; consuming adequate amounts of dietary fiber (age in years + 5 g/d). Limiting the intake of salt (<6 g/d) and sugar to follow recommended healthier lifelong dietary habits is also important.91

Because it is difficult for parents to judge calorie intake and energy expenditure on a regular basis, it is necessary to help parents guide the diet and physical activity patterns of their children. Counseling and recommendations must be made within the context of the family’s culture, living environment, and socioeconomic status. Most dietary strategies for weight loss emphasize balance, variety, and adequacy of the overall eating pattern. Appropriate food portion sizes are recommended for children92 at varying ages to guide appropriate intake and are critical in the education process. Dietary recommendations also emphasize reducing the number of meals eaten outside the home, planning for healthy snacks, offering healthier, low-calorie food choices (especially fruit and vegetables), and structuring eating times and places for family meals. Involving children in meal planning, shopping, gardening, and preparation of food has been promoted, along with including all caregivers (including grandparents) in helping the child to adhere to recommended consumption patterns and healthier food choices.

**Physical Activity**

Most reports of successful weight loss and maintenance emphasize the importance of incorporating regular physical activity into treatment programs.89 Children are similar to adults in that regular exercise provides additional health benefits for overweight individuals, including prevention of future risk acquisition, improved insulin sensitivity, blood pressure reduction, and improved socialization through group participation in activities.93 Regular physical activity is critical for the prevention of abnormal weight gain and weight maintenance. The current recommendation for the amount of physical activity is 30 to 60 minutes of regular exercise daily. “Working up a sweat” during the activity suggests adequate effort expended. These recommendations apply to children of normal weight as well as to children who are overweight.

Young children should not and many adolescents will not exercise simply to lose or maintain weight. Recommended activities must be enjoyable and congruent with the child’s and family’s lifestyle and be rewarding independent of the health benefit. Activities such as playing hopscotch, riding bicycles, skating, walking the dog, participating in marching band, jumping rope with friends, dancing, climbing, weight-lifting structured to improve endurance, training during the off-season, and gardening may be more easily integrated into a child or teen’s lifestyle than would be simply recommending participation on organized sports teams (these often do not provide sufficient exercise). A complementary approach is to restrict sedentary free-time activities to <2 h/d.94

Fitness levels vary significantly among overweight individuals. Whereas one child may not be able to walk several blocks without becoming short of breath, another may be adept at playing sports. Other variables also influence the recommendation for a child’s physical activity and exercise program. Some may have easy access to recreational areas and play and exercise equipment, whereas others may not be allowed out of the house for safety reasons. Parental supervision and availability for participation vary greatly and must be considered.

**Pharmacological Treatment**

Data supporting the use of pharmacological therapy for pediatric overweight are limited and inconclusive.95 Sibutramine has been studied in a randomized controlled trial of severe obesity. It has been shown to be efficacious as compared with behavior therapy alone, but it may be associated with side effects including increases in heart rate and blood pressure.96 Orlistat is approved for use in adolescence. The efficacy of orlistat has not been tested extensively in young patients. Orlistat is associated with gastrointestinal side effects and requires fat-soluble vitamin supplementation and monitoring.97,98 For rare genetic and metabolic disorders, pharmacological treatment may be useful. For example, recombinant leptin is useful in hereditary leptin deficiency. Octreotide may be useful in hypothalamic obesity.99 Metformin, used to treat type 2 diabetes mellitus, has been used in insulin-resistant children and adolescents who are overweight, but long-term efficacy and safety are unknown.100
Surgical Treatment
Surgical approaches to treat severe adolescent obesity are being undertaken by several centers.\(^1\)\(^1\) Indications used include a BMI > 40 kg/m\(^2\) and severe associated comorbidities, such as obstructive sleep apnea, type 2 diabetes mellitus, and pseudotumor cerebri. More severe elevation of BMI (> 50 kg/m\(^2\)) may be an indication for surgical treatment in the presence of less severe comorbidities such as hypertension and dyslipidemia, particularly if the degree of overweight hinders performing the activities of daily living. An experienced team approach including comprehensive medical and psychological evaluation is critical both for selection of appropriate candidates and for postoperative care that is sophisticated and often intense.\(^1\)\(^1\) Weight loss goals and reduction of morbidity are often achieved with gastric bypass surgery. The rates of short-term mortality appear to be low, but significant complications can occur. Intermediate and long-term outcomes, including information on malabsorption of critical nutrients, are unknown. Overall, surgical therapy should be reserved for full-grown adolescents with the severest obesity-related morbidity, offered only by experienced multidisciplinary teams, and presented to families with appropriate informed consent procedures.

Healthcare Delivery Systems
Obesity treatment and prevention require a long-term care model.\(^1\)\(^3\) Substantial changes in the current healthcare delivery system are needed to accommodate the needs of long-term weight management for children as they grow. Children are at risk for not receiving appropriate intervention when physical growth and maturation occur simultaneously and when important lifelong nutrition and physical activity habits are formed. Emphasis should be placed on self-management, in which the child and his or her family (rather than the healthcare provider) set the goal. It is important that children and patients in treatment understand the implications of their choices through a problem-solving approach and that strategies be tailored to individual needs. The effectiveness of this long-term care model is also dependent on a comprehensive team approach that targets the individual, the family, and the many environmental influences affecting the child’s behaviors.

Summary
The prevalence and severity of childhood overweight have been increasing dramatically. Childhood overweight is one of our most critical public health problems that threatens to ultimately reverse the favorable trends in cardiovascular morbidity and mortality that have occurred during the past half-century. Immediate action must be initiated to prevent excess weight gain and to treat those children and adolescents who are already overweight. Children and adolescents at risk of developing obesity and its complications must be identified and interventions begun. Strategies must be developed that involve families, the healthcare system, healthcare insurers, government agencies, the school system, the food and entertainment industries, and public health professionals. Support for research on the development and testing of interventions to prevent and treat overweight in young members of our population is needed to provide a strong evidence base for programs and policies.

Acknowledgments
The authors acknowledge William H. Dietz, MD, PhD, who reviewed a draft of the manuscript and provided helpful suggestions for improving it. In addition, the authors acknowledge the participants in the Lloyd J. Filer Conference on Overweight and Its Consequences Beginning in Youth. The information presented by the following speakers was quite useful for the writing group of this scientific statement: Bruce Bistrian, George Bray, Myles Faith, Katherine Flegal, Matthew Gillman, Thomas Inge, Aviva Must, Russell Pate, James Sallis, Julia Steinberger, Nicolas Stettler, Boyd Swinburn, and Jack Yanovski.

### Authors’ Disclosures

<table>
<thead>
<tr>
<th>Writing Group Member Name</th>
<th>Employment</th>
<th>Research Grant/Other Research Support</th>
<th>Speakers Bureau/Honoraria</th>
<th>Stock Ownership</th>
<th>Consultant/Advisory Board</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stephen R. Daniels</td>
<td>Cincinnati Children’s Hospital</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Abbott Laboratories</td>
<td>None</td>
</tr>
<tr>
<td>Donna K. Arnett</td>
<td>University of Alabama-Birmingham</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Robert H. Eckel</td>
<td>University of Colorado Health Sciences Center</td>
<td>Merck Pharmaceutical</td>
<td>Merck Pharmaceutical</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Samuel S. Gidding</td>
<td>Nemours Foundation</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Laura L. Hayman</td>
<td>New York University</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Shirk-i Kumanyika</td>
<td>University of Pennsylvania School of Medicine</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Weight Watchers International</td>
<td>Member, African American Lipid and Cardiovascular Council</td>
</tr>
<tr>
<td>Thomas N. Robinson</td>
<td>Stanford University</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Robert Wood Johnson Foundation; WK Kellogg Foundation</td>
<td>None</td>
</tr>
<tr>
<td>Barbara J. Scott</td>
<td>University of Nevada School of Medicine</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>State of Nevada</td>
<td>None</td>
</tr>
<tr>
<td>Sachiko St. Jeor</td>
<td>University of Nevada School of Medicine</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Council on Women’s Nutrition Solutions; National Cattlemans’ Beef Association</td>
<td>None</td>
</tr>
<tr>
<td>Christine L. Williams</td>
<td>Columbus University</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit.


Overweight in Children and Adolescents: Pathophysiology, Consequences, Prevention, and Treatment

doi: 10.1161/01.CIR.0000161369.71722.10
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/111/15/1999

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/