KEY POINTS

• The current “epidemic” of obesity is the result of increasing disruption between the balance of energy intake and energy expenditure related to the action and interaction of biological and nonbiological causes.
• Animal models are extremely useful in identifying the contributions of genes because they can be subjected to genetic manipulation.
• Studies with monozygotic and dizygotic twins have estimated that body mass index (BMI = kg/m$^2$) is about 70% heritable.
• Use of genetic tools has been beneficial in increasing our understanding of the neurohumoral controls of energy balance.
• Recent advances have begun uncovering many of the genetic–environment interactions that result in obesity.

1. INTRODUCTION

The incidence of obesity and other comorbidities in the US population has increased dramatically during the past two decades. According to the Center for Disease Control, the number of states in the United States that have obesity prevalence rates greater than 15% has increased from none in 1985 and 1990 to 25 states in 1995 and 49 states in 2000 (Fig. 1).

This increase in the prevalence of obesity is the result of increasing disruption between the balance of energy intake and energy expenditure related to the action and interaction of biological and nonbiological causes (1). The regulation of body weight and food intake is a highly complex and redundant homeostatic system set to ensure positive energy balance (2). Its main purpose, prevention of starvation, provides an evolutionary advantage under circumstances of uncertain food supply to assuage the effects of prolonged starvation (3). As a consequence, in an environment of plentiful food, many individuals gain excessive weight (4). Body weight is regulated by interactions of both peripheral and central nervous system mechanisms including drives for palatability and variety and neurohormonal stimulation of centers in the dorso-medial hypothalamus, arcuate nucleus, and nucleus tractus solitarius (5,6).
To understand these aspects, scientists have investigated the role that genetic and environmental factors play in the etiology of this condition. Advances in molecular biology, the development of animal models for genetic manipulation, and the enterprise of the human genome project have greatly contributed to the identification of