151, and the incidence of carrier boys is 1 in 468 worldwide (National Fragile X Foundation, 2012a).

The syndrome is caused by an abnormal gene on the lower end of the long arm of the X chromosome. Chromosome analysis may demonstrate a **fragile site** (a region that fails to condense during mitosis and is characterized by a nonstaining gap or narrowing) in the cells of affected males and females and in carrier females. This fragile site has been determined to be caused by a gene mutation that results in excessive repeats of nucleotide in a specific DNA segment of the X chromosome. The number of repeats in a normal individual is between 6 and 50. An individual with 50 to 200 base-pair repeats is said to have a **permutation** and is therefore a carrier. When passed from a parent to a child, these base-pair repeats can expand from 200 or more, which is termed a **full mutation**. This expansion occurs only when a carrier mother passes the mutation to her offspring; it does not occur when a carrier father passes the mutation to his daughters.

The inheritance pattern has been termed **X-linked dominant with reduced penetrance**. This is in distinct contrast to the classic X-linked recessive pattern in which all carrier females are normal, all affected males have symptoms of the disorder, and no males are carriers. Consequently, genetic counseling of affected families is more complex than that for families with a classic X-linked disorder, such as hemophilia. Both affected sexes are capable of transmitting the fragile X disorder. Prenatal diagnosis of the fragile X gene mutation is possible with direct DNA testing in a family with an established history using amniocentesis or chorionic villus sampling (National Fragile X Foundation, 2012b). The FMR1 mutation testing is highly accurate and is being researched regarding the incorporation into the newborn universal screening program (Abrams, Cronister, Brown, et al, 2012; Bagni, Tassone, Neri, et al, 2012; Finucane, Abrams, Cronister, et al, 2012; Hagerman, Berry-Kravis, Kaufmann, et al, 2009; Skinner, Choudhury, Sideris, et al, 2011).

Clinical Manifestations

The classic trend of physical findings in adult men with FXS consists of a long face with a prominent jaw (prognathism); large, protruding ears; and large testes (macroorchidism). In prepubertal