

although typically milder than is seen in affected males. This subsarcolemmal protein attaches to the sarcolemmal membrane overlying the A and M bands of the myofibrils and consists of four distinct regions or domains: the amino terminus contains 250 amino acids and is related to the N-actin binding site of β -actinin; the second domain is the largest, with 2,800 amino acids, and contains many repeats, giving it a characteristic rod shape; a third, cysteine-rich domain is related to the carboxyl-terminus of β -actinin; and the final carboxyl-terminal domain of 400 amino acids is unique to dystrophin and to a dystrophin-related protein encoded by chromosome 6. If the mother of an affected male has normal CK levels, it is unlikely that her daughter can be identified as a carrier by measuring CK. Muscle biopsy of suspected female carriers can detect an additional 10% in whom serum CK is not elevated; a specific genetic diagnosis using polymerase chain reaction (PCR) on peripheral blood is definitive. Approximately 40% of female carriers may be at risk of developing cardiomyopathy or fibrosis (as has been seen by cardiac imaging of carrier females), even in the absence of skeletal muscle weakness. Prepubertal females who are carriers of the dystrophy also have increased serum CK values, with highest levels at 8–12 yr of age. The molecular defects in the dystrophinopathies vary and include intragenic deletions, duplications, or point mutations of nucleotides. These symptomatic females are explained by the Lyon hypothesis, in which the normal X chromosome becomes inactivated and the one with the gene deletion is active (see Chapter 97). The full clinical picture of DMD has occurred in several females with Turner syndrome in whom the single X chromosome must have had the Xp21 gene deletion. This gene contains .79 exons of coding sequence and 2.5 Mb of DNA