

autism. The somatic mutations in male germ cells that enhance the proliferation of germ cells could lead to within-testis expansion of mutant clonal lines, thus favoring the propagation of germ cells carrying these pathogenic mutations and increasing the risk of mutations in the offspring of older fathers (the “selfish spermatogonial selection” hypothesis).

APPROACH TO THE PATIENT

Androgen Deficiency

Hypogonadism is often characterized by decreased sex drive, reduced frequency of sexual activity, inability to maintain erections, reduced beard growth, loss of muscle mass, decreased testicular size, and gynecomastia. Erectile dysfunction and androgen deficiency are two distinct clinical disorders that can coexist in middle-aged and older men. Some, but not all, patients with erectile dysfunction have testosterone deficiency. Thus, it is useful to evaluate men presenting with erectile dysfunction for androgen deficiency. Except when extreme, these clinical features of androgen deficiency may be difficult to distinguish from changes that occur with normal aging. Moreover, androgen deficiency may develop gradually. When symptoms or clinical features suggest possible androgen deficiency, the laboratory evaluation is initiated by the measurement of total testosterone in a fasting specimen, preferably in the morning using a reliable assay, such as LC-MS/MS that has been calibrated to an international testosterone standard ([Fig. 391-7](#)). A consistently low total testosterone level below the lower limit of the normal male range, measured by an LC-MS/MS assay in a CDC-certified laboratory, in association with symptoms, is evidence of testosterone deficiency. An early-morning testosterone level >400 ng/dL makes the diagnosis of androgen deficiency unlikely. In men with testosterone levels between 200 and 400 ng/dL, the total testosterone level should be repeated, and a free testosterone level should be measured. In older men and in patients with other clinical states that are associated with alterations in SHBG levels, a direct measurement