

Radiotherapy and chemotherapy may reduce ovarian reserve, with effects on both the oocytes and the supporting granulosa cells. New approaches, including ovarian, oocyte, and embryo cryopreservation, should be offered to women of reproductive age prior to gonadotoxic chemotherapy or pelvic radiation treatment. The recognition that early ovarian insufficiency occurs in premutation carriers of the fragile X syndrome is important because of the increased risk of severe intellectual disability in male children with *FMR1* mutations. Thus, follow-up testing should include a karyotype in all POI patients, serum anti-cortisol and 21-hydroxylase antibodies (specific but not sensitive for subsequent adrenal insufficiency), thyroid function and thyroid peroxidase antibodies, *FMR1* premutation screening, and assessment of bone mineral density. Ovarian biopsy is not indicated. Although the number of genetic causes of POI is increasing, routine testing for mutations other than *FMR1* is currently not recommended.

Hypergonadotropic hypogonadism occurs rarely in other disorders, such as mutations in the FSH or LH receptors. Aromatase deficiency and 17 α -hydroxylase deficiency are associated with decreased estrogen and elevated gonadotropins and with hyperandrogenism and hypertension, respectively. Gonadotropin-secreting tumors in women of reproductive age generally present with high, rather than low, estrogen levels and cause ovarian hyperstimulation or dysfunctional bleeding.

TREATMENT

Hypo- and Hypergonadotropic Causes of Amenorrhea

Amenorrhea almost always is associated with chronically low levels of estrogen, whether it is caused by hypogonadotropic hypogonadism or ovarian insufficiency. Development of secondary sexual characteristics requires gradual titration of estradiol replacement with eventual addition of progestin. Hormone replacement with either low-dose estrogen/progesterone regimens or oral contraceptive pills is recommended until the usual age of menopause for bone and cardiovascular protection. In women with