In Brief

Turner Syndrome

Tracy Milbrandt, MD,
Ellen Thomas, CGC,
Southern Illinois University School of Medicine
Springfield, IL

Author Disclosure

Dr Milbrandt and Ms Thomas have disclosed no financial relationships relevant to this article. This commentary does not contain discussion of unapproved/investigative use of a commercial product/device.

Frias JL, Davenport M; American Academy of Pediatrics, Committee on Genetics and Section on Endocrinology. Health supervision for children with Turner syndrome. *Pediatrics.* 2003;111(3):692–702

Bondy CA; The Turner Syndrome Consensus Study Group. Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. *J Clin Endocrinol Metab.* 2007;92(1):10–25

Hjerrild BE, Havmand Mortensen K, Gravholt CH. Turner syndrome and clinical treatment. *Br Med Bull.* 2008;86:77–93

Davenport M. Moving toward an understanding of hormone replacement therapy in adolescent girls. *Ann N Y Acad Sci.* 2008;1135:126–137

Devernay M, Ecosse E, Coste J, Carel J. Determinants of medical care for young women with Turner syndrome. *J Clin Endocrinol Metab.* 2009;94(9):3408–3413

Dr Henry H. Turner first described Turner syndrome in 1938 in a published report describing a series of patients with infantilism, webbing of the neck, and cubitus valgus. Turner syndrome is the most common sex-chromosome abnormality in females. The condition affects approximately 1 in 2,500 live-born females and requires a chromosomal analysis for definitive diagnosis. Multiple karyotypes (eg, 45,X monosomy, 45,X/46,XX mosaicism, and structurally abnormal X) have been identified that are associated with variable presentations along the Turner syndrome phenotype spectrum. Girls with 45,X monosomy typically have the most severe phenotype.

Most prenatally detected cases of Turner syndrome are diagnosed as a result of amniocentesis or chorionic villus sampling performed for other reasons. Prenatal ultrasonography revealing thickening of the nuchal folds, cystic hygroma, renal anomalies, or left-sided heart anomalies also may increase prenatal suspicion for Turner syndrome.

In the neonatal period, a diagnosis may be suggestive by the presence of congenital lymphedema, presenting as swelling of the hands or feet or the appearance of a webbed neck and low hairline. Other evidence of abnormal development of lymphatic channels can give the appearance of a shield chest with inverted and widely spaced nipples. Deformity of the ears, nail dysplasia, cubitus valgus, short metacarpals, and micrognathia with high palate also may be noted.

It is typical to see intrauterine growth retardation, decreased growth rates during infancy and childhood, and an absent pubertal growth spurt in girls with Turner syndrome. In some instances, growth retardation may be the only clinical manifestation of Turner syndrome in infancy and early childhood. Untreated women with Turner syndrome have an ultimate height of approximately 143 cm, which is 20 cm less than the mean in the female population.

Growth hormone therapy has been proven to increase adult height, and its use in girls with Turner syndrome is considered standard of care. However, there are no established guidelines as to when to initiate therapy. To achieve the potential of reaching normal adult height, it is recommended that human growth hormone therapy should be started as soon as decreasing height percentiles are noted.

Left-sided cardiovascular abnormalities are the most serious clinical manifestations associated with Turner syndrome. Aortic valvular disease occurs in 20% to 30% of females born with Turner syndrome, and coarctation occurs in 3% to 10%. Other cardiovascular manifestations include an increased risk of aortic dissection, electrocardiographic abnormalities, and hypertension.

Current recommendations suggest that all patients at the time of diagnosis have a baseline evaluation performed by a cardiologist familiar with Turner syndrome. This evaluation should include a thorough clinical examination, 4 extremity blood pressures, electrocardiography, echocardiography (infants and younger girls), or echocardiography and magnetic resonance imaging (older girls and adult women). Magnetic resonance imaging is recommended for patients old enough to not require sedation to better image the aortic valve leaflets, in addition to the distal aortic arch and descending aorta, or in younger patients if echocardiography does not visualize these areas adequately.

Renal anomalies are found in approximately 30% to 50% of females

born with Turner syndrome. The most common anomaly is a horseshoe kidney, followed by vascular abnormalities. It is recommended that renal ultrasonography be performed at the time of diagnosis.

The ovaries in females who have Turner syndrome are described as streak gonads, consisting of connective tissue and few if any follicles. Premature ovarian failure begins during fetal life in females with Turner syndrome. Serum levels of follicle-stimulating hormone and luteinizing hormone are elevated and estradiol levels are low. Essentially, all girls with Turner syndrome will require estrogen therapy to induce and maintain sexual development. Newer guidelines recommend beginning hormone replacement therapy between ages 12 and 13 years if there is no indication of spontaneous puberty by that time.

Intelligence usually is normal in these patients; however, there may be problems with nonverbal skills that can present as educational deficits in mathematics, visual-spatial reasoning, and executive functioning. There is also a higher incidence of attention-deficit/hyperactivity disorder noted in girls with Turner syndrome. Educational intervention directed at these concerns may offer an improved educational outcome. To that end, current recommendations are to provide an educational and psychosocial evaluation at the time of school entry.

More detailed evidence-based clinical practice guidelines provide recommendations for periodic screening for other associated clinical manifestations. Females with Turner syndrome are at higher risk for a variety of autoimmune disorders, including hypothyroidism and celiac disease. Otolaryngologic and audiology examinations are recommended every 1 to 5 years because of the increased risk of sensorineural hearing loss. Strabismus and hyperopia both occur in 25% to 35% of children with Turner syndrome, and monitoring for these conditions should be performed.

In older girls, levels of fasting lipids, glucose, and liver enzymes should be evaluated annually because of a higher risk of abnormalities in females born with Turner syndrome. Ongoing monitoring of skeletal issues, including evaluation for hip dislocation, scoliosis, and kyphosis, should take place. Craniofacial skeletal features common in Turner syndrome can predispose patients to dental malocclusion, and tooth development and anatomy can be abnormal.

The spectrum of clinical manifestations associated with Turner syndrome can make diagnosis and management difficult. Continued research and updated guidelines will continue to improve our ability to care for these patients. Additional information garnered in adult populations of women with Turner syndrome also reinforces the need for appropriate transitioning of care, as with other childhood chronic diseases, with monitoring during the entire span of life.

Comment: Turner syndrome is an excellent example of a genetic disorder that is manifest through multiple phenotypes. Variability of presentation leads to variability in time of diagnosis throughout the lifespan, from prenatal ultrasonography through adulthood. Because prenatal diagnosis is now common and feasible, balanced genetic counseling is prudent to provide parents with information about the broad phenotypic spectrum that may be manifest and the available treatment regimens.

Both growth hormone and hormone replacement therapy are essential to induce appropriate growth velocity and pubertal development. Identification of aortic arch and aortic valve involvement with potential risk of aortic dissection is essential for appropriate counseling to determine pregnancy risk and risk to rigorous athletes.

Clinical practice guidelines are available to provide the highest quality and most comprehensive care possible. Special attention to effective transitions to adult medicine is essential because the clinical conditions require lifelong surveillance and treatment. This condition provides an example of how the pediatrician must help to establish a medical home for these patients to orchestrate their care and must work with centers that have an expertise in Turner syndrome in providing a multidisciplinary approach to treatment.

Janet Serwint, MD
Consulting Editor, *In Brief*

Answer Key for September 2013 Issue:
***Salmonella* Infections:** 1. D; 2. D; 3. A; 4. D; 5. B.
Contraception for Adolescents: 1. B; 2. A; 3. A; 4. C; 5. E.
Thermal Burn Injuries: 1. D; 2. C; 3. E; 4. D; 5. D.