SSBP Syndrome Sheets

Turner Syndrome

First description

Henry Turner first described Turner syndrome in 1938, but it was not until 20 years later that the genetic basis of the syndrome was discovered. The syndrome affects about 4 per 10,000 live female births. About 50% of clinically identified cases of Turner syndrome are associated with a single X chromosome (X-monosomy, XO), and affected females therefore have 45 rather than the usual 46 intact chromosomes. Typical females have two completely intact X-chromosomes. Typical males have one X-chromosome and a Y chromosome which contains the male-sex determining gene. To develop typically, females need to express some critical genetic material from both their intact X-chromosomes in just the right amount, not too little and not too much.

Genetics and molecular biology

Because Turner syndrome females typically have just one sex chromosome in all the cells of their body, the Turner syndrome phenotype (the physical and mental features that are characteristic of the syndrome) arises because there is too little genetic material from genes that are normally expressed from both X- chromosomes. Some of the features are caused directly by that insufficiency, and some are secondary to early degeneration of the ovaries and the consequent oestrogen insufficiency which leads to immature secondary sexual characteristics. Surprisingly, we know rather little about which genes on the X-chromosome are needed in two copies for typical development. To date, the only gene that is clearly linked to the syndromic features is called SHOX, and it is responsible for the limited growth in stature.

Turner syndrome is usually associated with just one intact X-chromosome, and the second X-chromosome is missing altogether in cells throughout the body. In ~70% of X-monosomy, the missing X chromosome came from the father. Typical females inherit one X-chromosome from their father, and one from their mother. In just less than half of clinically identified females with Turner syndrome there is more than one chromosomal rearrangement. One X-chromosome is intact but there is a second X-chromosome too, but that second X is incomplete, and can be structurally very unusual so that it does not function properly. To complicate matters further, about half of all females with Turner syndrome have a mixture of cell-types in their body, and we call this ‘mosaicism’. Females with a mixture of X-monosomic cells (45,X) and typical female cells (46,XX) are likely to have mild features of the syndrome and may not even be diagnosed unless they are investigated genetically, for instance because of infertility.

Physical features and natural history

There are many possible physical characteristics of the syndrome, but none is invariable. The condition may be detected at birth, suspected because of a transient edema (tissue swelling) of the lower legs and feet. It rapidly clears up, and if not recognised at the time the diagnosis may not be made until middle childhood. The usual reason for further investigations is growth delay.

Specific characteristics include a narrow, high-arched palate, which is associated with severe feeding difficulties in infancy. These are not only due to the palatal problem but also to oromotor

immaturity. There are low-set ears, a low hairline, and occasionally a webbed neck (this latter feature being much rarer than textbook descriptions would suggest). The eyes may show strabismus (a squint) and a slight ptosis (droopy eyelids). The chest is typically broad, with widely spaced breasts. When standing with arms at the side, the lower arms typically turn out at the elbows (described as a wide carrying-angle).

Some form of cardiac abnormality occurs in approximately one-third of Turners patients. Problems are primarily left-sided and may include coarctation of the aorta and bicuspid aortic valve. Individuals with Turner syndrome are also at higher risk for hypertension and should receive an echocardiogram or MRI to evaluate the heart at the time of diagnosis regardless of age.
Other common problems include renal anomalies (30%) associated with an increased risk of urinary tract infections and hypertension. Hypothyroidism is associated with an autoimmune thyroiditis. One of the most serious, but often overlooked, complications is recurrent otitis media, exacerbated by anatomical anomalies of the Eustachian tube. This is extremely common, and occurs in up to 80%. The onset is later than in typical children, between 4-15 years of age. Aggressive treatment of infections is appropriate. The majority (50-90%) of women with Turner syndrome will also develop early sensorineural (nerve) hearing loss, with gradual deterioration from childhood. They may require hearing aids earlier than the general population.

Because of the small stature, which is almost invariable relative to the height of the parents, it has become usual to treat with human growth hormone. The average stature after treatment is increased by a few centimeters, although the condition is not associated with growth hormone insufficiency and high doses are needed to achieve any significant benefit. There is no evidence that treatment with growth hormone benefits psychosocial adjustment, although it may improve self-esteem.

Behavioural and psychiatric characteristics

Social integration is usually good until adolescence. The normal adolescent growth spurt does not come along as expected, and secondary sexual characteristics do not appear. Most girls with Turner syndrome mature under the influence of endocrinological management (oestrogen supplementation). Physical immaturity can be associated with difficulties integrating with a typical peer group during early adolescence. Associated behavioural immaturity may be encouraged because such girls are ‘babied’ by others.

Social difficulties usually begin in adolescence. The most important contributory influence is a lack of social confidence. For reasons that are likely to be a combination of genetic and hormonal deficiencies, development of the ‘social brain’ is impaired. At least one in three girls begins to experience social difficulties during the teenage years. Forming and maintaining peer relationships becomes more problematic than it was at primary school, because girls’ social relationshiops become more complex during adolescence. Social difficulties can persist until adulthood. Many women with Turner syndrome find it hard to function effectively in complex social or work environments where they are expected to communicate with lots of adults. A substantial minority choose to take jobs focused on child-care (especially nursery nursing) in the UK.

Many females with Turner syndrome have poor self-esteem, especially in later life. Social anxiety and lack of confidence is made worse by difficulties establishing satisfactory social relationships.

Their social problems are compounded by the onset of associated hearing loss.

Turner syndrome is associated with life-long social adjustment problems, but these are not directly caused by short stature or infertility. They will not be resolved by growth-hormone treatment, although this may have other benefits. There is an increasing acknowledgement among Turner syndrome support groups and clinicians responsible for their care that the symptoms of a mild autism spectrum disorder (ASD) are common and that it is the social communication difficulties inherent in the condition that impact most strongly on friendships and family relationships. Females who are missing a fully functioning second X-chromosome are at increased risk of failing fully to understand other people's social cues and responding appropriately. They may also be rather rigid and resistant to change or new experiences.

Neuropsychological characteristics

Almost all females with the syndrome have normal verbal intelligence. About 80% have relatively poor visuospatial memory (in the lower 33% of ability relative to the general population). This can have practical consequences, such as a tendency to lose one's way in unfamiliar environments. Some motor skills may be impaired; clumsiness is typical, especially in fine motor tasks. Very poor arithmetical abilities, found in the majority, reflect slow processing speeds and a fundamental conceptual problem with comprehending numerical magnitude (e.g. being able quickly to recognise that 9 is half as big again as 6).

Socio-perceptual processing is impaired to some extent in at least one third, with difficulties remembering faces or differentiating facial expressions of emotion. Socio-cognitive anomalies in Turner syndrome extend to deficits in mentalizing abilities. In common with females who are on the autism spectrum, girls with Turner syndrome attempt to compensate for their social deficits from early childhood. They develop superficially good and engaging social skills, which are learned from imitation, but may become associated with social disinhibition. Poor attention is typical during early and middle childhood, leading to the appearance of attention deficit hyperactivity disorder. This often resolves spontaneously by adolescence. On the other hand, social naivety persists and puts many affected women at risk of exploitation.

Available guidelines for behavioural assessment/treatment/management

Gravholt C.H., et al.,, Clinical practice guidelines for the care of girls and women with Turner syndrome: Proceedings from the 2023 Aarhus International Turner Syndrome Meeting, European Journal of Endocrinology, Volume 190, Issue 6, June 2024, Pages G53–G151, https://doi.org/10.1093/ejendo/lvae050Gravholt C.H.(2009) "Turner – know your body!" Editor – Published by Novo-Nordisk. Available as a free web-publication http://np.netpublicator.com/netpublication/n75088268

Useful websites/associations for more information

Turner syndrome support society (UK): http://www.tss.org.uk/
National Institute of Child Health and Human Development (USA): http://turners.nichd.nih.gov/

Updated in 2025 by David Skuse and Jeanne Wolstencroft

References

1. Cardoso G., Daly R., Haq N.A., Hanton L., Rubinow D.R., Bondy C.A., Schmidt P. (2004) Current and lifetime psychiatric illness in women with Turner syndrome. Gynecol Endocrinol 19(6), 313-9.
2. Gravholt, C. H., Andersen, N. H., Conway, G. S., Dekkers, O. M., Geffner, M. E., Klein, K. O., ... & Backeljauw, P. F. (2017). Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. European journal of endocrinology, 177(3), G1-G70.
3. Jacobs P., Dalton P., James R., Mosse K., Power M., Robinson D., Skuse D. (1997) Turner syndrome: a cytogenetic and molecular study. Ann Hum Genet 61(Pt 6), Nov; 471-83.
4. Kuntsi J., Skuse D., Elgar K., Morris E., Turner C. (2000) Ring-X chromosomes: their cognitive and behavioural phenotype. Ann Hum Genet 64(Pt 4), Jul, 295-305.
5. Skuse, D. (2009) Psychological and Psychiatric Aspects of Turner Syndrome (in) Turner-Know Your Body! Novo-Nordisk, pp 200-217.
6. Wolstencroft, J., & Skuse, D. (2019). Social skills and relationships in Turner syndrome. Current opinion in psychiatry, 32(2), 85-91.
7. Wolstencroft, J., Kerry, E., Denyer, H., Watkins, A., Mandy., & Skuse, D. (2021). New approaches to social skills training: Blended group interventions for girls with social communication difficulties. Autism Research. https://doi.org/10.1002/aur.2495

Updated in 2025 by David Skuse and Jeanne Wolstencroft