

# Sex Chromosome Abnormalities

## Turner Syndrome

Turner syndrome occurs in 1/2500 live births. It is caused by a partial or complete absence of one of the X chromosomes in a female. A single X chromosome is the most common cause of miscarriage. It is believed 99% of all 45,X conceptions result in miscarriage. The fetuses are often severely hydropic (Figure 1).

When a baby is born with Turner syndrome there are often few features. One feature that can be noted during the newborn period is puffy hands and puffy feet (Figure 3). Broad chest can also be an early sign. The majority of females have normal intelligence. There are some deficits in visual special abilities.

Most females with Turner syndrome present at age 5-6 with short stature. Features include short stature, webbing of the neck, shield chest, shortened 4<sup>th</sup> metacarpal and madelung deformity of the forearm. There is also a risk of renal anomalies including horseshoe kidneys.

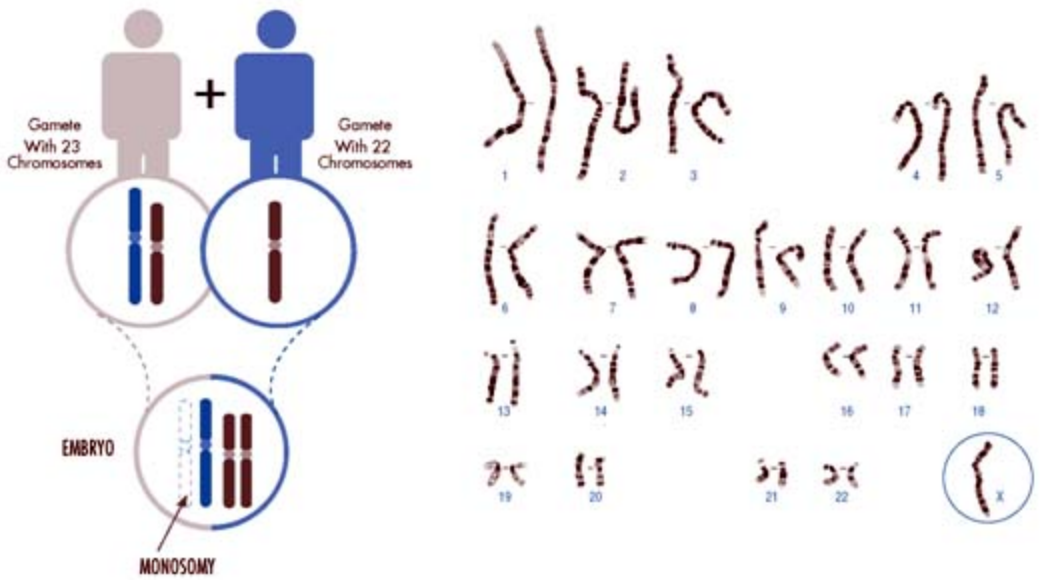
Adolescent girls with Turner syndrome often have failure of puberty, absence of spontaneous breast development and primary amenorrhea.

Approximately 60% of females with Turner syndrome have a single X chromosome in all cells analyzed (Figure 2). Twenty percent are mosaic in which some of their cells have 2 X chromosomes while some have a single X. A small percentage of females with Turner syndrome have a part of one X chromosome in a ring formation. These females are at risk of developmental delay.



Figure 1.

Monosomy X - Turner Syndrome 45,X



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Figure 2.



Figure 3.

Patients with Turner syndrome are at increased risk for a number of medical issues including renal anomalies (most common horseshoe kidneys), hearing impairment, and congenital heart defects. Anticipatory guidance should include a baseline hearing evaluation, renal ultrasound and cardiovascular physical exam. Echocardiogram if there are any concerns.

Growth Hormone: Short stature can be treated with Growth hormone. Most patients with Turner syndrome have low levels of growth hormone. The hormones are often started around age 5-6 until early adolescence.

Sexual development. The majority of patients with Turner syndrome **do not** undergo spontaneous puberty. Secondary sex characteristics can be achieved with the administration of steroids. Monthly cycling of the uterine lining is achieved by the administration of estrogen/progesterone in birth control pills. Females with Turner syndrome have “streak ovaries”. Therefore they cannot conceive a pregnancy. Pregnancy can occur using donor egg and hormone support. Some females with Turner syndrome do undergo spontaneous puberty. Premature ovarian failure is common.

A 7 year old female presents for a school physical. She is noted to be below the 5th percentile for height, 25% for weight. She is doing well in school. The mother is 5'3”, father is 5'9”. The patient has 1 brother age 9. He is on the 50% for height. Her younger sister is 4. She is the same height as the patient.

On physical exam she was noted to have a low hairline, wide spaced nipples.

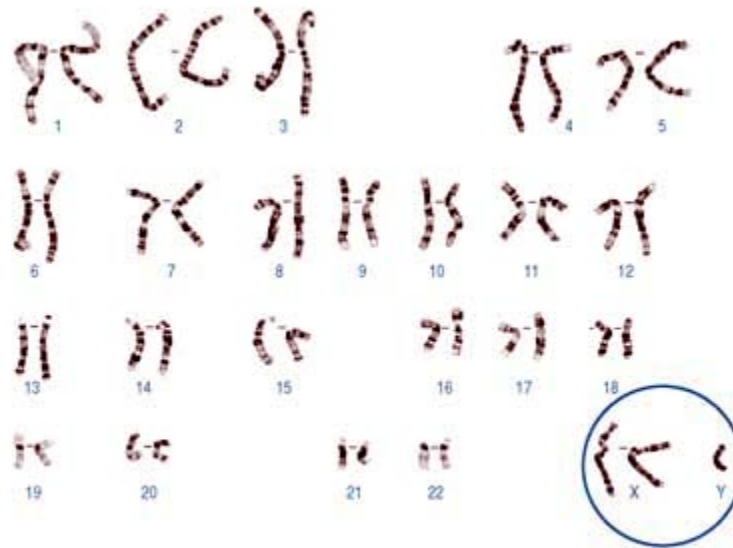
1. What would be the best first study to perform on this patient?
2. Is there a risk of this disorder to her siblings?

Blood chromosomes indicate 45, X. What is the best medical management?

## **Klinefelter Syndrome**

Klinefelter syndrome is caused by the addition of an X chromosome. Normally, males have 46 chromosomes with one X and 1 Y chromosome. In the case of Klinefelter syndrome, the male has 2 X chromosomes and 1 Y chromosome (Figure 1). The presence of a Y chromosome is necessary for an individual to be male. The X chromosome carries more genetic information than is present on the Y chromosome. To prevent females from having additional genetic information the majority of one of the X chromosomes is inactivated. While the majority of this additional X chromosome is inactivated, there are pseudoautosomal genes which remain active on the inactivated X chromosome. In Klinefelter syndrome, it is this additional genetic information that is believed to result in the medical problems and clinical features. Clinical features in Klinefelter syndrome include tall stature, gynecomastia and small testicles post puberty and azoospermia. In general males have lower IQ's than their siblings (10-15 points).

## Klinefelter Syndrome Karyotype - 47,XXY



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Figure 1.

### Case 1

A tall thin 14 year-old boy has not yet shown any signs of puberty. His mother reports he was delayed in speech development. He is below average student. He always has done less well in school than his siblings. He is very shy and teachers report his behavior to be immature. On physical exam he has gynecomastia, long limbs and decreased upper/lower segment ratio. His testes and penis are small and there is no evidence of pubertal development.

1. What is your diagnosis?
2. How would you confirm this diagnosis?

### Case 2

A 16 year old female present with primary amenorrhea. She has no secondary sex characteristics. On physical exam her height is below the fifth percentile. She has a widening carrying angle and wide spaced nipples (Tanner 2).

1. What is a possible diagnosis
2. What testing is recommended

## Reference Material

Klinefelter syndrome: E medicine: <http://emedicine.medscape.com/article/945649-overview>

Family Support Organizations

Turner Syndrome Support Organization: <http://www.turnersyndrome.org/>

Klinefelter Syndrome Support Organization: <http://klinefeltersyndrome.org/>