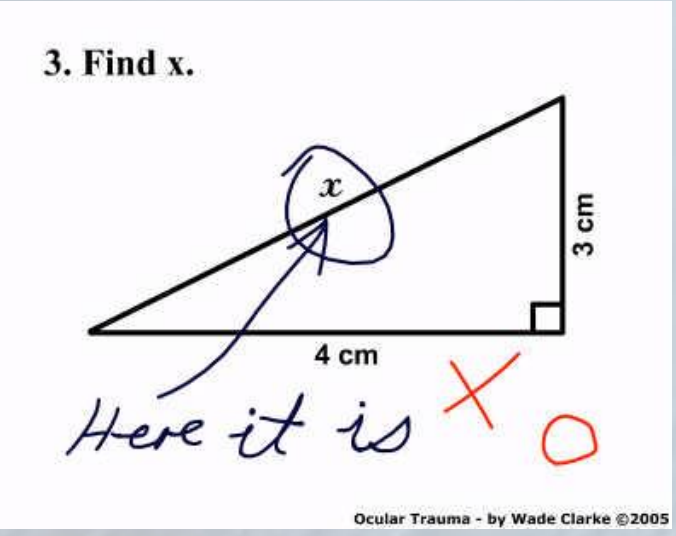
# Turner Syndrome

Discovered by Henry Turner in 1938, this genetic disease reduces the quality of life in those that are affected.

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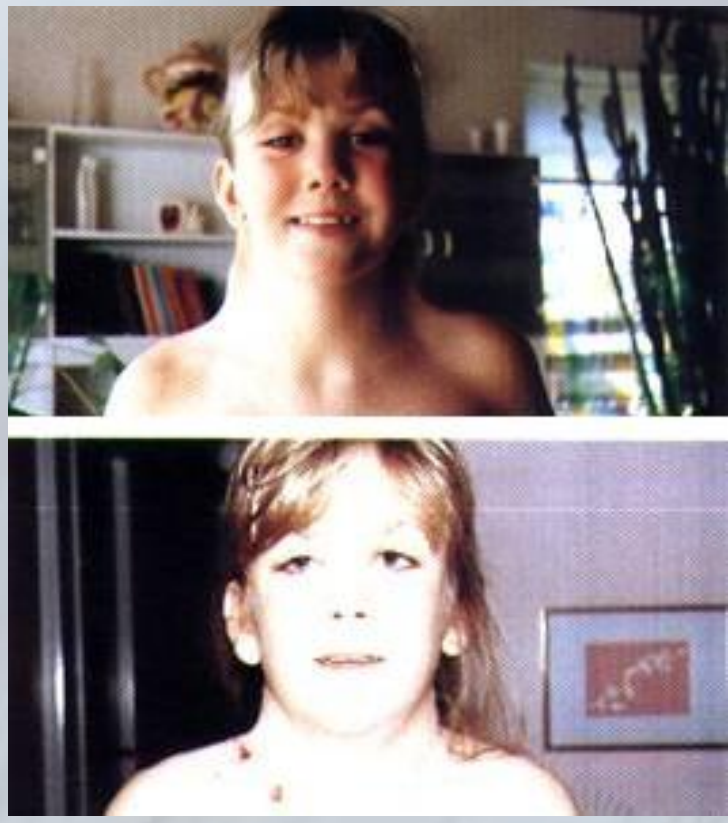
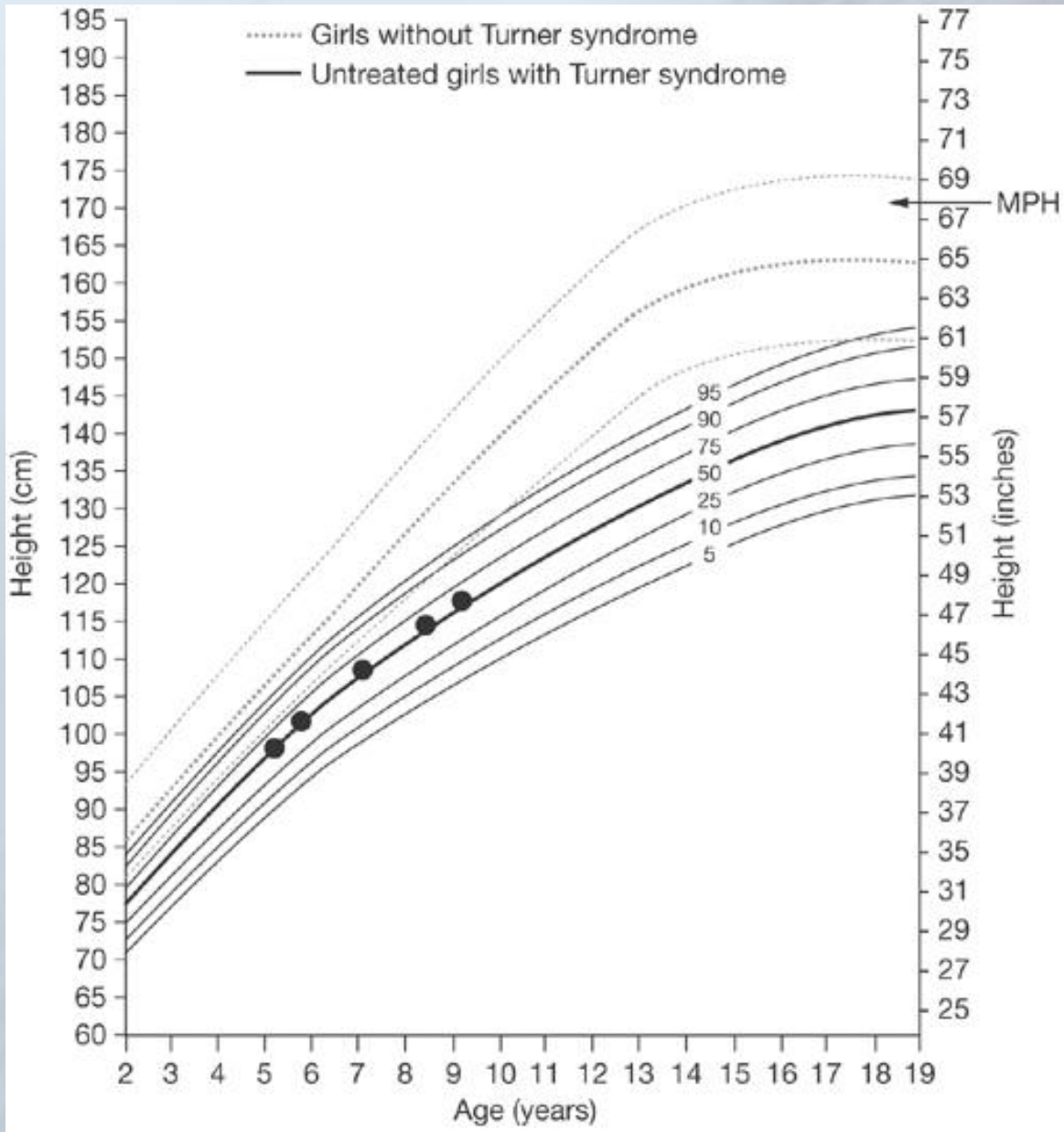
# Physiology

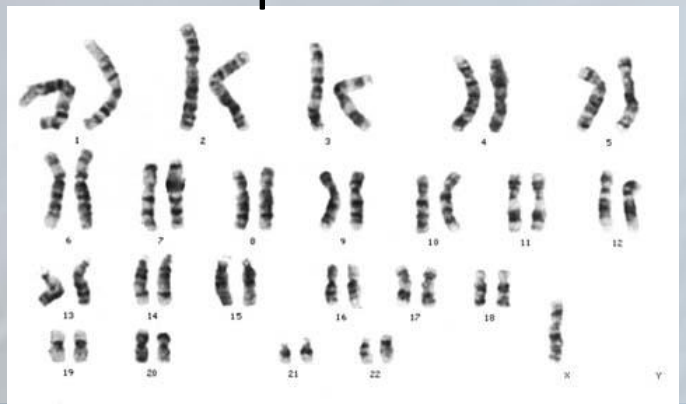
- Usually a result of a nondisjunction, a spontaneous mutation. In rare cases, it is hereditary.
- Onset is from birth.
- Range of severity.
- Turner syndrome has many symptoms. The symptoms in all Turner patients are short stature, sterility, and ovarian dysgenesis.
- Other common symptoms include difficulty with spatial recognition, nonverbal memory, and attention, heart and renal complications, and facial deformities.

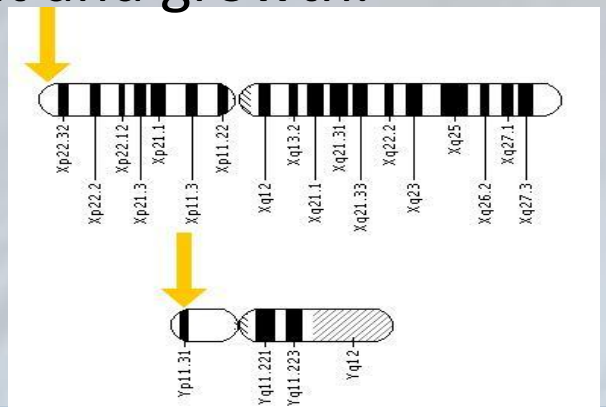



Girls without Turner syndrome
Untreated girls with Turner syndrome
MPH
95
90
75
50
25
10
5
Height (cm)
Height (inches)
Age (years)
195 190 185 180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60
77 75 73 71 69 67 65 63 61 59 57 55 53 51 49 47 45 43 41 39 37 35 31 29 27 25
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

# Molecular Cause

- No inheritance pattern. Due to nondisjunction, a spontaneous event.
- Targeted molecule: X chromosome.
- Nature of lesion: X chromosome is partially and entirely missing
- Karyotype of amniotic fluid or white blood cell: 45, XO
- Missing the X chromosome results in missing genes. Missing genes results in haploinsufficiency, or the condition when there is an insufficient gene product.
- Not all the genes on the X chromosome are known. One known gene is SHOX (short stature homeobox), a gene that is important in bone development and growth.





# Treatments

- Must be constantly monitored.
- To treat problems targeting endocrine system, the most common method is to give the affected individuals the hormones they lack.
  - To reduced height, Turner patients are given growth hormone supplements until their they turn 15. This results, on average, a gain of 10 cm.
  - After the age of 15, Turner patients are treated with estrogen and progesterone therapy.
  - Limit: Affected individual may not responds to the hormones and may fail to grow or develop sexually.
- To treat heart and renal complications, you need an organ transplant. Heart complications is detected by an echocardiography and renal ultrasound detects kidney problems.
  - Limit: Like any surgery, this procedure can fail and will kill the individual.
- To treat sterility, a fertilized egg is implanted into the affected individual. Because the uterus and vagina are still functional, the woman can still undergo a normal pregnancy and delivery.
- Today's clinical studies focus on trying to understand more about Turner syndrome. For examples, one study tries to understand the effect of growth hormone on height while another tries to find the genes that results in each Turner syndrome symptom.

# Proposed Cure

- Impossible to add an X chromosome to each cell in an affected individual.
- Part 1: Deactivate Xist (X-inactive specific transcript)
  - Xist is responsible for the inactivation of the X chromosome in normal females, which is done for dosage compensation. However, in Turner patients, Xist is still active and will inactivate parts of the remaining X chromosome, resulting in haploinsufficiency.
  - Use something similar to MBD1 (Methyl-CpG binding domain protein 1). MBD1 causes methylation by binding to the DNA. By doing so, it can shut down a gene and prevent it from being expressed.
  - Another way is to use Tsix antisense, the RNA complementary to the Xist gene. This RNA negatively regulates Xist, a function discovered after studying cells with Tsix knocked out.
- Part 2: Add more inducers
  - Inducers start transcription
  - Required to know what each gene on the X chromosome does and what induces their transcription. This can only be done after more information is known about the X chromosome. To find this out, a scientist should test various substances on DNA.
- This treatment will be delivered through injection. If it is taken orally, then the proteins will be denatured by the stomach acids. Also, because proteins do not last forever, frequent injections must be done to ensure that the genes are upregulated all the time.

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