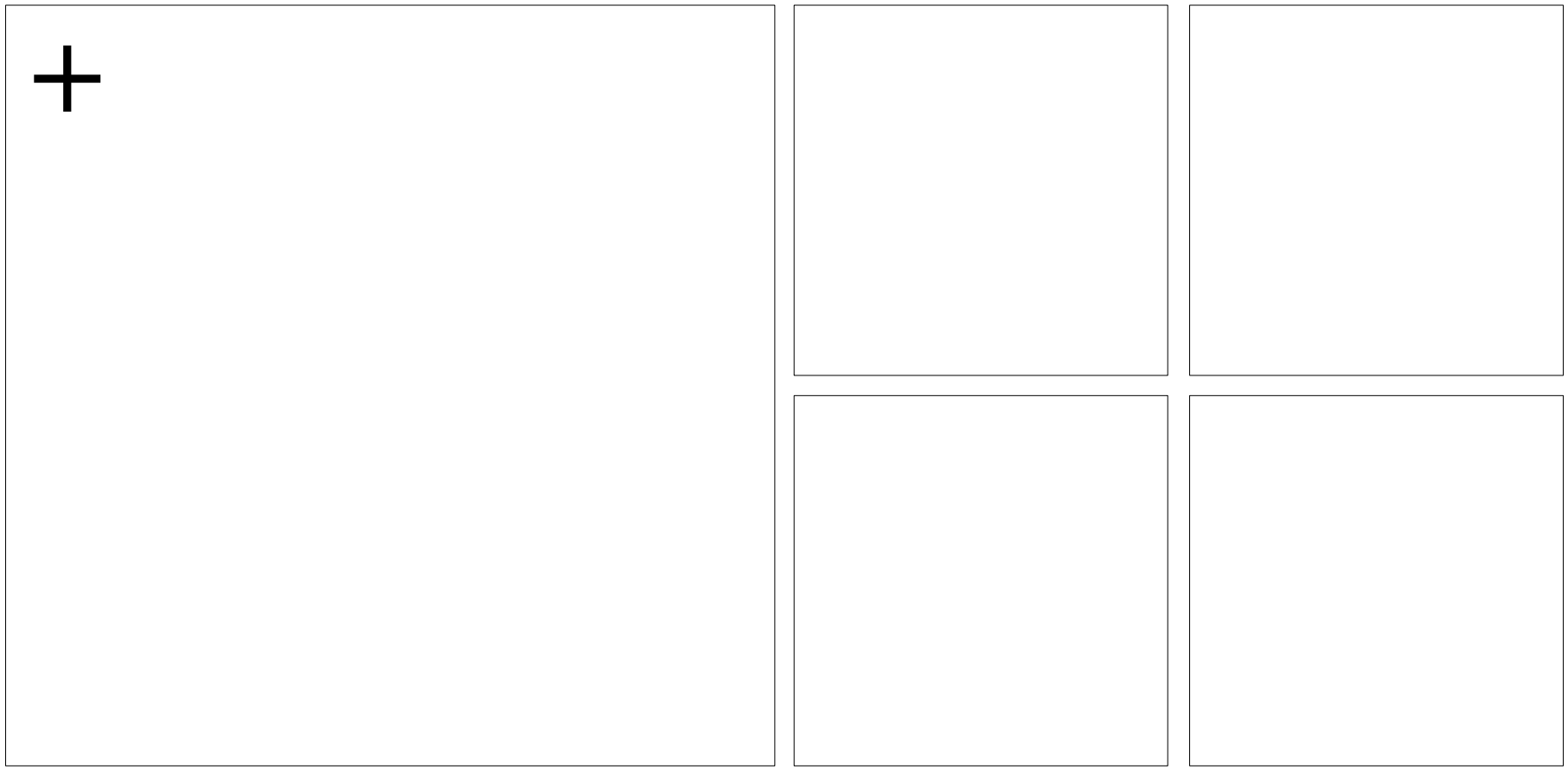


GENETIC DISORDERS

Genetic Disorders

- A genetic disorder is an abnormality in an individual's DNA. Abnormalities can range from a small mutation in a single gene to the addition or subtraction of an entire chromosome.

Possible Genetic Disorders

- Missing part of a chromosome
- Missing an entire chromosome or having an extra chromosome.
- Autosomal recessive
- Autosomal dominant
- X-linked recessive
- X-linked dominant

Missing Part of a Chromosome

- Williams Syndrome
- A rare genetic disorder that affects a child's growth, physical appearance, and cognitive development.

What is Missing?

- Genetic material from chromosome 7, including the gene for the creation of elastin. This protein product gives blood vessels the stretchiness and strength required to withstand a lifetime of use.

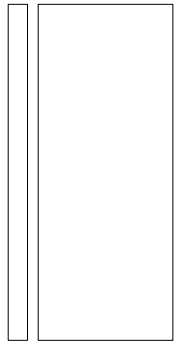
When Does it Happen?

- During meiosis, a deletion is caused by a break in the DNA molecule that makes up a chromosome. 25 genes are affected by this deletion.

Are the Parents Affected?

- No, the break is in the sperm or egg cell. No cells in the parents' body contains the break.

What are the Symptoms?

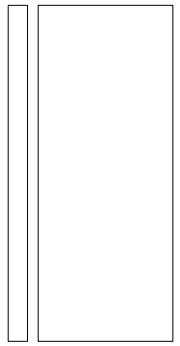


- Mental disabilities, heart defects, and unusual facial features (small upturned nose, wide mouth, full lips, small chin, widely spaced teeth).

Other Symptoms

- Low birth weight, failure to gain weight appropriately, kidney abnormalities, and low muscle tone.
- Characteristic behaviors, such as hypersensitivity to loud noises and an overly outgoing personality.

Is There a Cure?



- No, suggestions include avoidance of extra calcium and vitamin D, as well as treating high levels of blood calcium.

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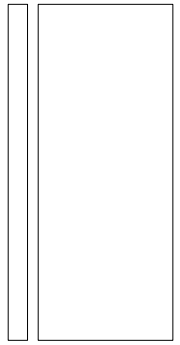
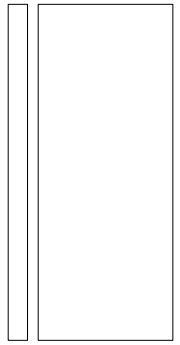
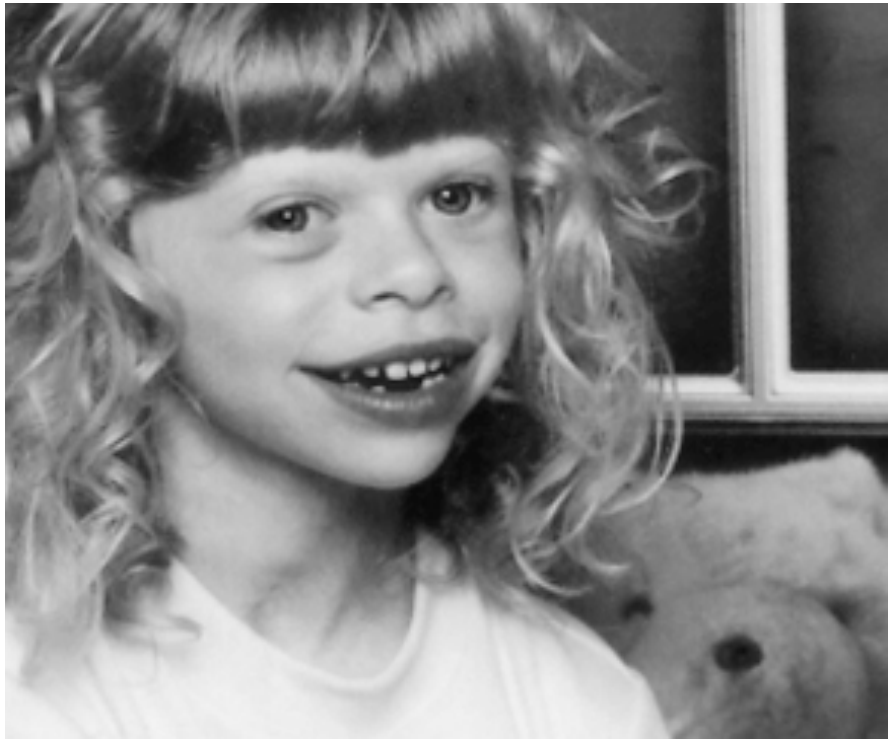


- Blood vessel narrowing can be a significant health problem. Physical therapy is helpful to patients with joint stiffness and low muscle tone. Developmental and speech therapy can also help children and increase the success of their social interactions.

What are the Odds?



- About 1 in 7500 live births will have Williams Syndrome.
- It is considered a microdeletion because less than 5 million bases are deleted.



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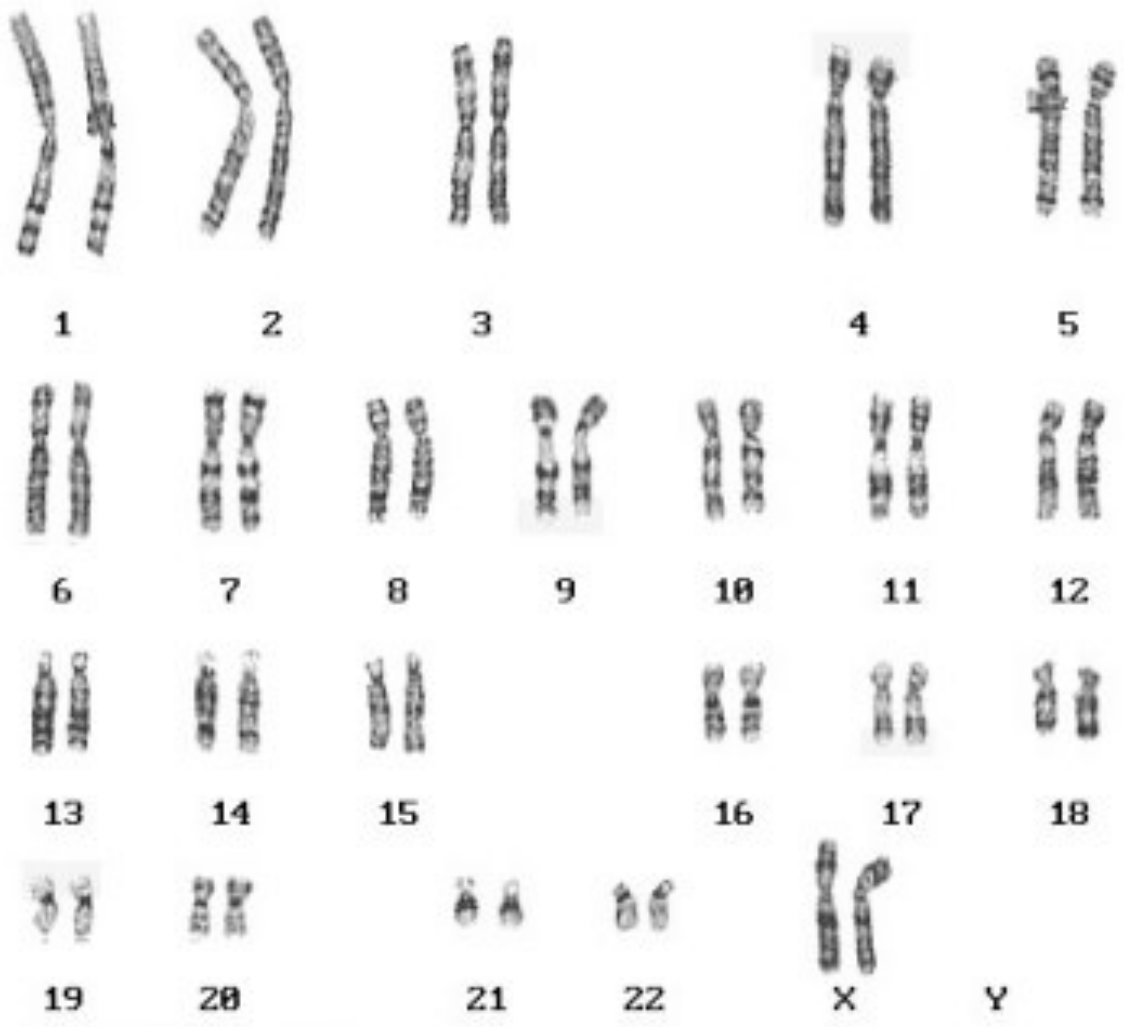
How is Chromosome Number Affected?

- Chromosome numbers can be higher or lower than normal because of a mistake during meiosis called non-disjunction. Here the chromosomes fail to separate resulting in sperm or egg cells with too many or too few chromosomes. Examples include; Turner's Syndrome, Klinefelter's Syndrome and Down's Syndrome to name a few.

Karyotype

- A karyotype is a picture that allows us to see the number and appearance of chromosomes in the nucleus of a eukaryote cell. The term is also used for the complete set of chromosomes in a species, or an individual organism.

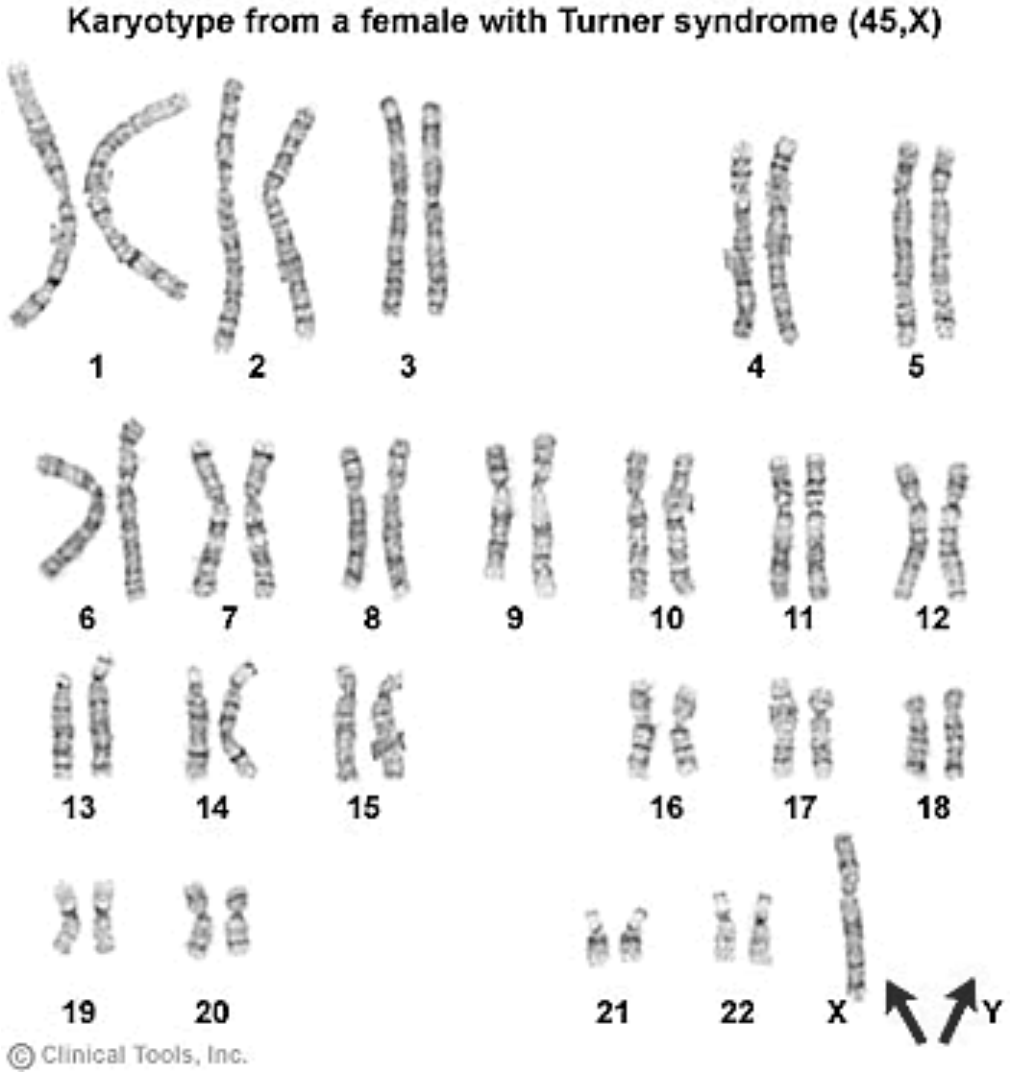
Normal Karyotype



+ Missing an Entire Chromosome

- Turner's Syndrome
- Characterized by a missing or incomplete X chromosome. The genes affected are involved in growth and sexual development, which is why girls with the disorder are shorter than normal and have abnormal sexual characteristics.

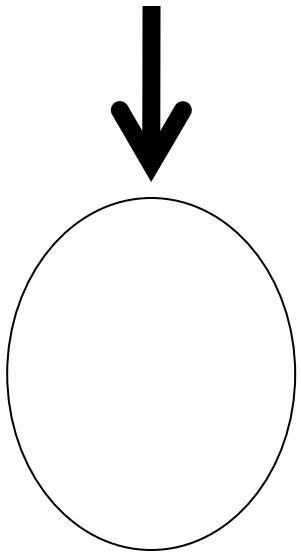
Turner's Karyotype



How Do You Get Turner's Syndrome

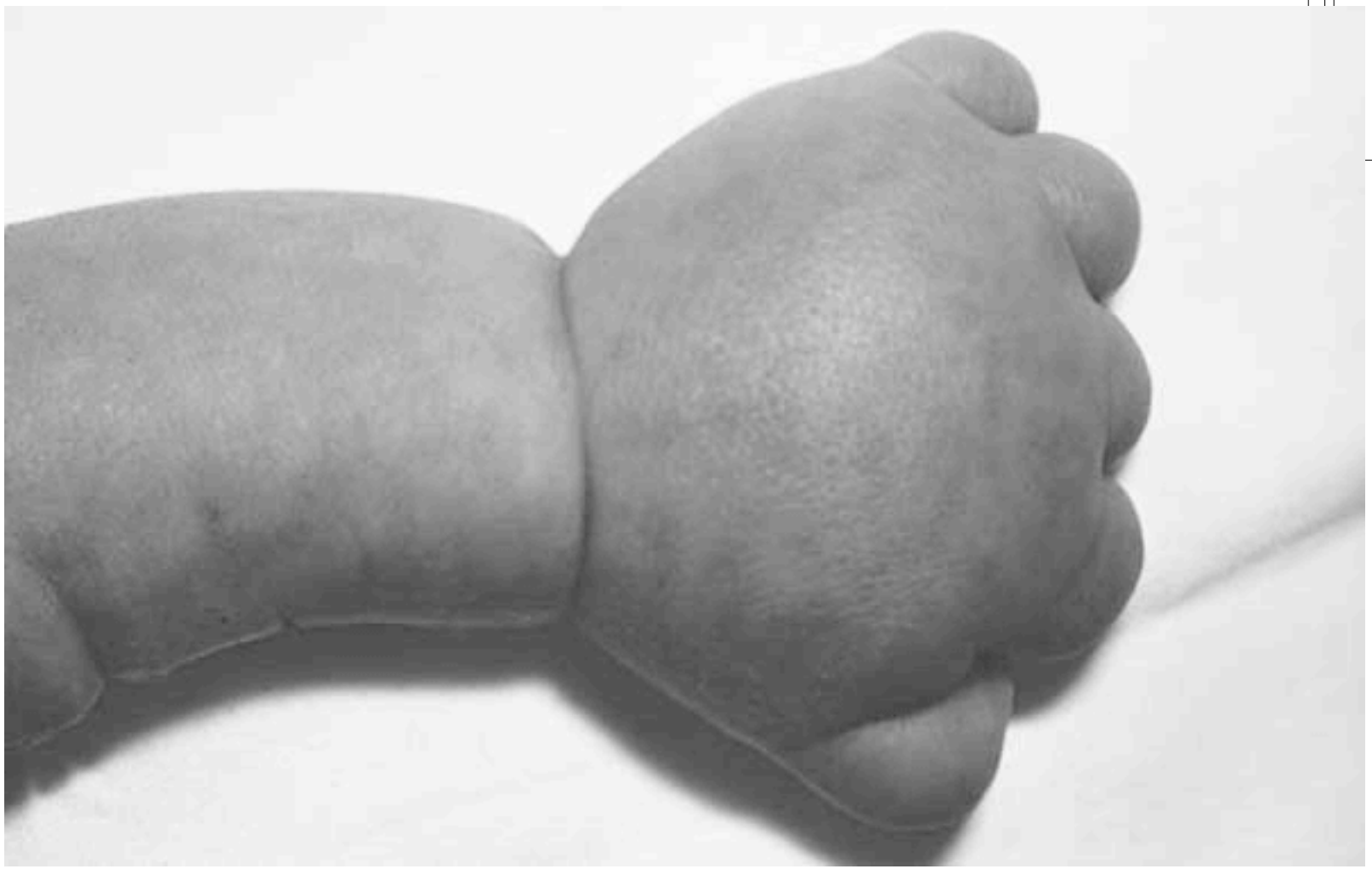
- Normally, females inherit one X chromosome from their mother and one X chromosome from their father. But females who have Turner's syndrome are missing one of their X chromosomes. This happened because of non-disjunction during meiosis.

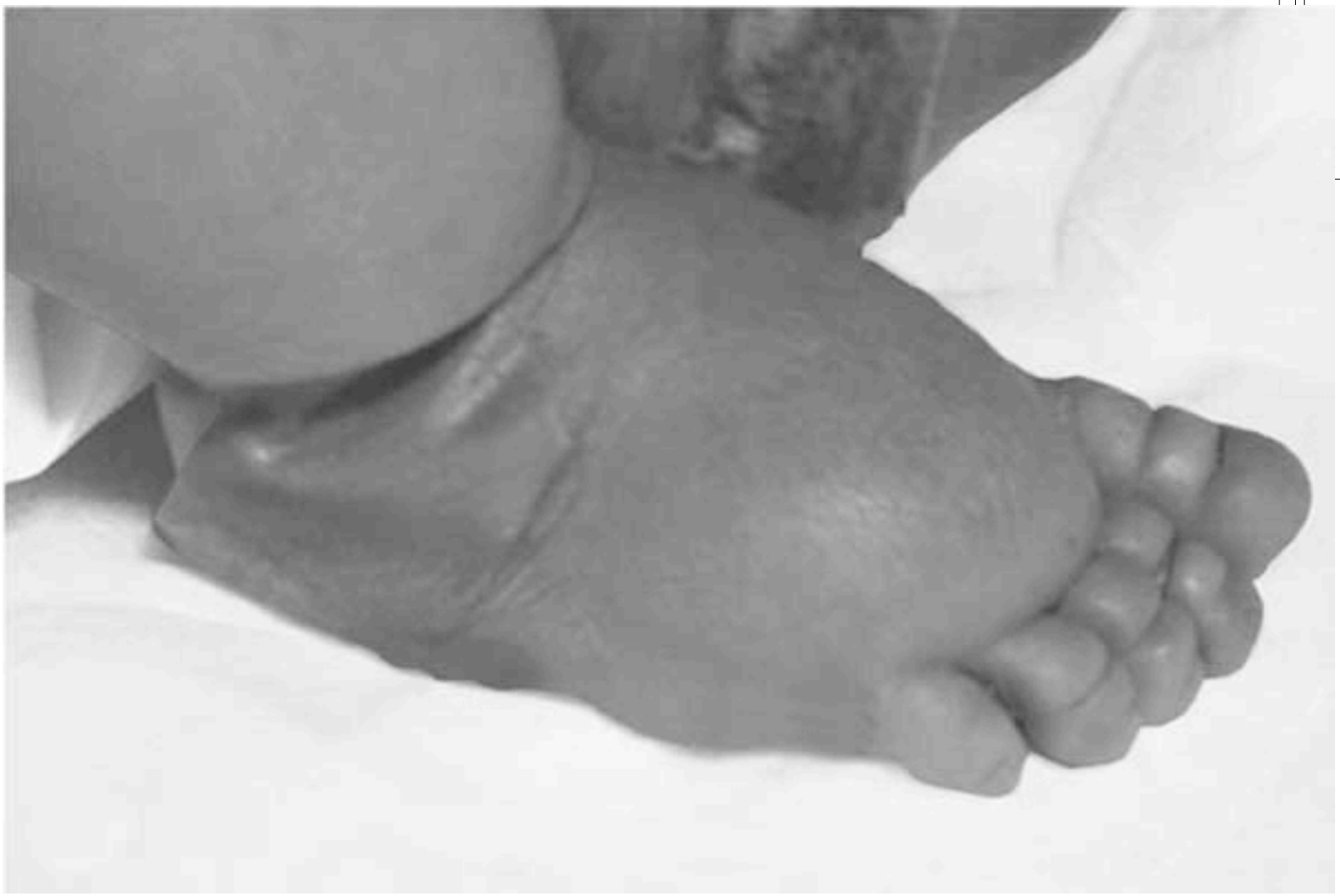
How it Happens



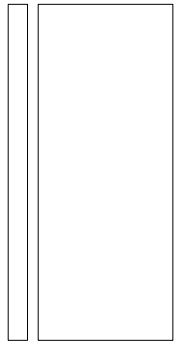
How is it Diagnosed?

- About half of the cases are diagnosed within the first few months of a girl's life by the characteristic physical symptoms (swelling of the hands and feet, or a heart defect). Other patients are diagnosed in adolescence because they fail to grow normally or go through puberty.





Do the Parents Have Turner's



- The abnormality is not inherited from an affected parent (not passed down from parent to child) because women with Turner syndrome are usually sterile and cannot have children.

What Causes the Physical Characteristics?

- One of the missing genes on the X chromosome is the SHOX gene, which is responsible for long bone growth, which causes the short stature. Other missing genes regulate ovarian development, which influences sexual characteristics.

Treatment

- Hormone replacement therapy is the best way to treat this disorder. Teenagers are treated with growth hormone to help them reach a normal height and sex hormones to bring on secondary sex characteristics.

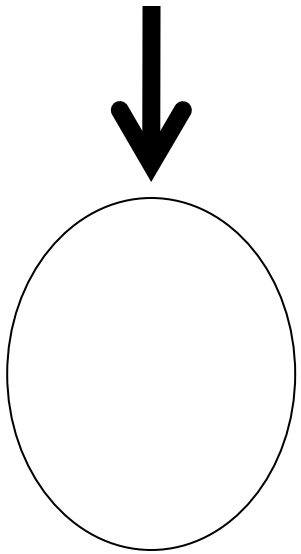
Facts and Odds

- Turner's Syndrome affects 60,000 females in the United States. This disorder is seen in 1 of every 2000 to 2500 babies born.
- In 75-80% of cases, the single X chromosome comes from the mother's egg; the father's sperm that fertilizes the egg is missing its sex chromosome.

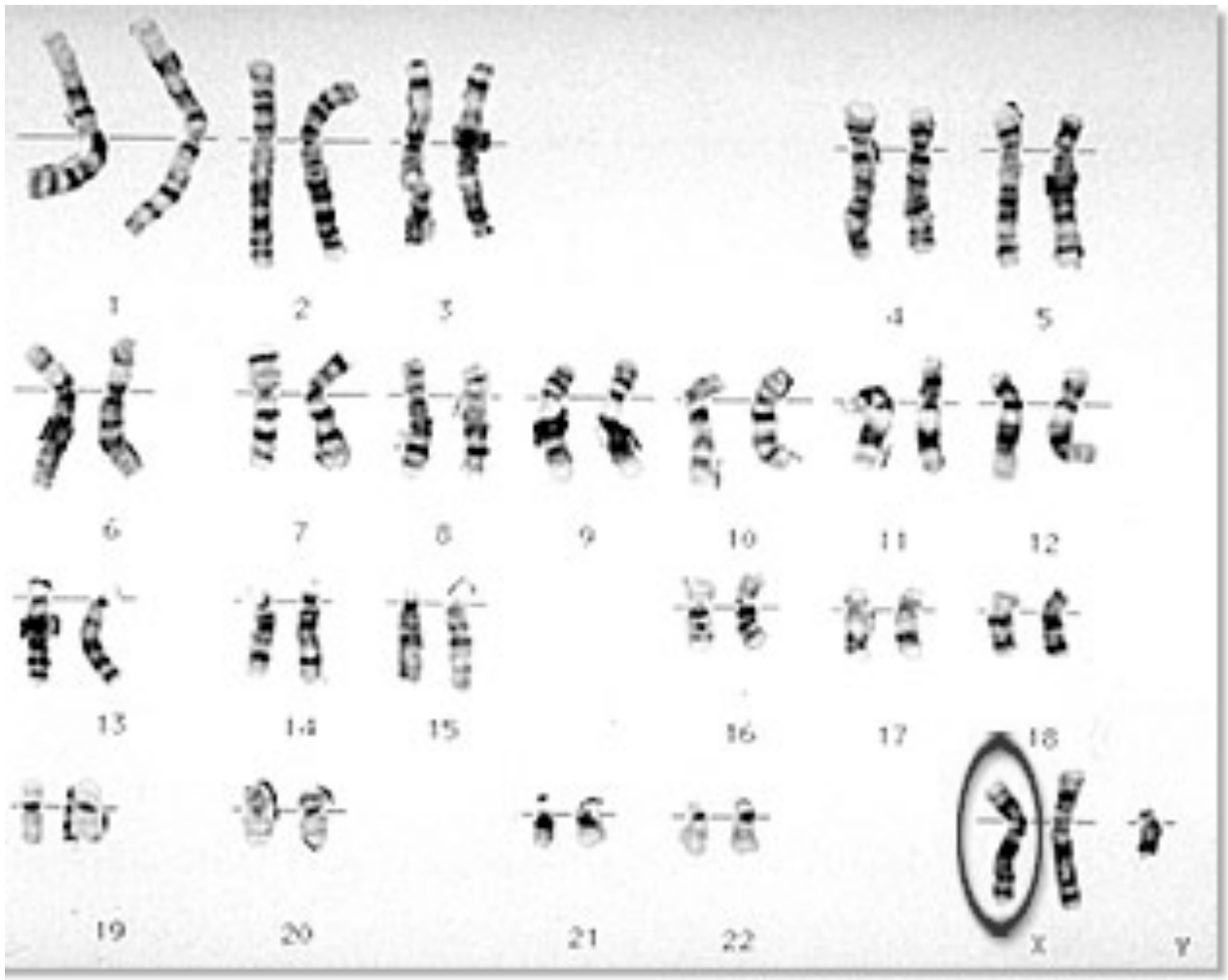
An Extra Entire Chromosome

- Klinefelter's Syndrome
- Affects only males. Males normally have an X chromosome and a Y chromosome (XY). But males who have Klinefelter's syndrome have an extra X chromosome (XXY), giving them a total of 47 instead of the normal 46 chromosomes.

How it Happens



Klinefelter's Karyotype



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Physical Characteristics

- They develop as males with subtle characteristics that become apparent during puberty. They are often tall and usually don't develop secondary sex characteristics, such as facial hair or underarm and pubic hair. The extra X chromosome primarily affects the testes, which produce sperm and the male hormone testosterone.

Symptoms

- Many people with this disorder have no idea they have it until they hit puberty or try to have children. At puberty, men with this syndrome often develop more breast tissue than normal, have a less muscular body, and grow very little facial or body hair.

+

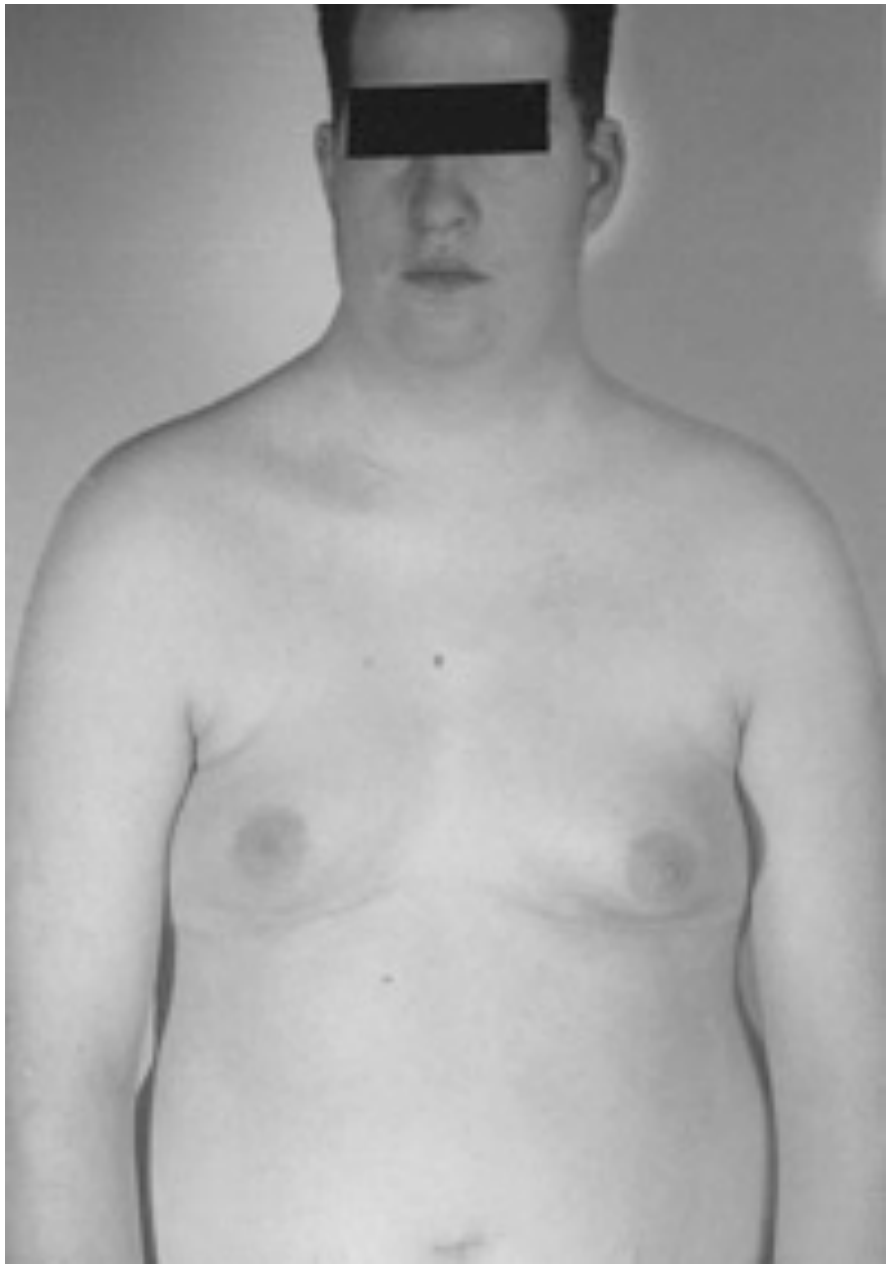
- When men with Klinefelter's syndrome try to have children, most discover that they are sterile because they cannot produce sperm. Learning disabilities (not categorized as mental retardation) are also a common problem for them.

Treatment

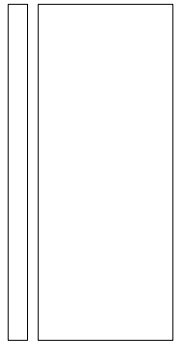
- Hormone replacement therapy where testosterone injections replace the hormone that would normally be produced by the testes. Synthetic testosterone works like natural testosterone - it builds muscle and increases hair growth.

What are the Odds?

- Klinefelter's Syndrome is one of the most common genetic abnormalities. It affects between 1 in about 1,000 males.

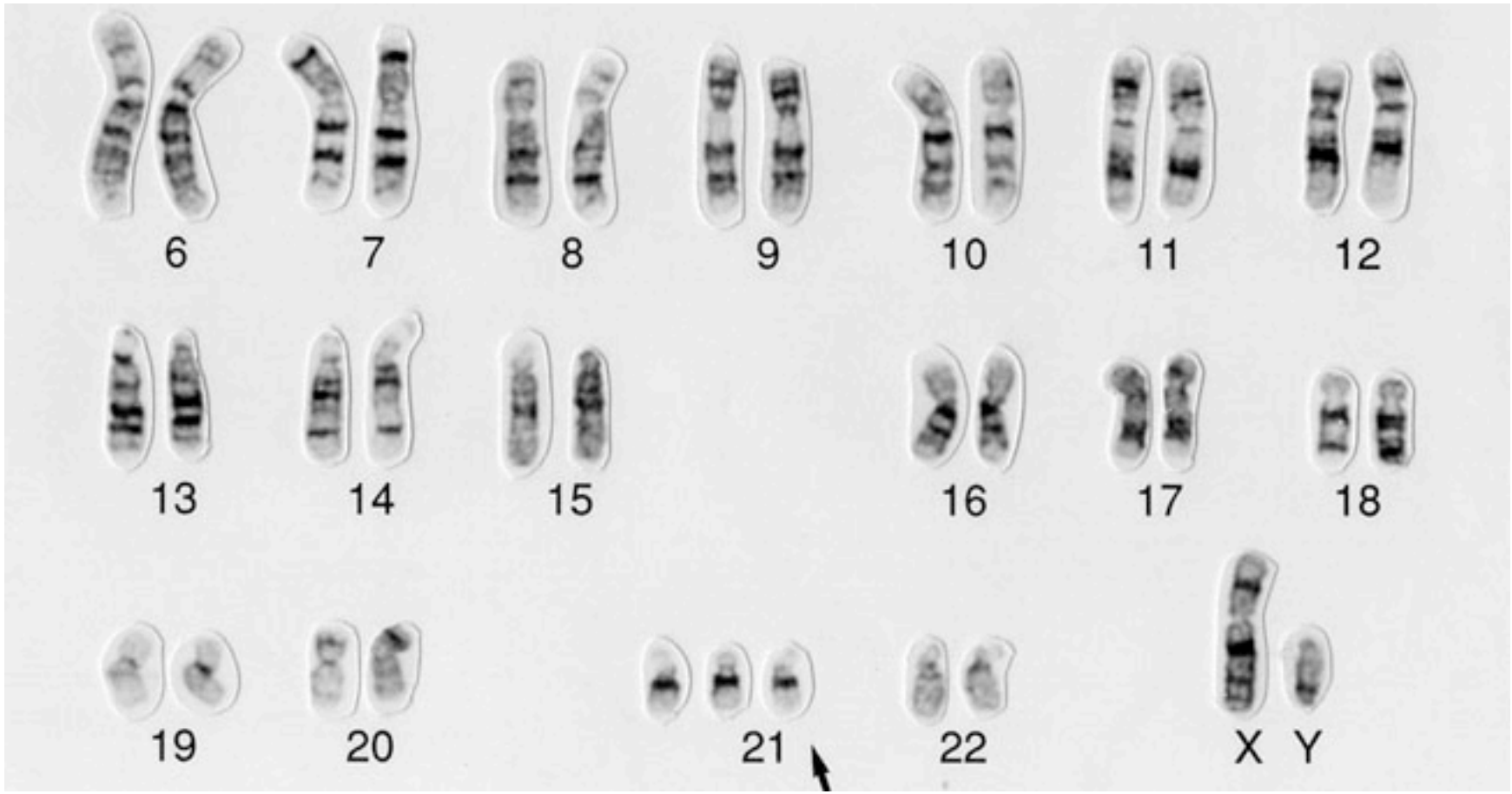


An Extra Entire Chromosome



- Down's Syndrome
- Down syndrome is a developmental disorder caused by an extra copy of chromosome 21 (which is why the disorder is also called "trisomy 21").

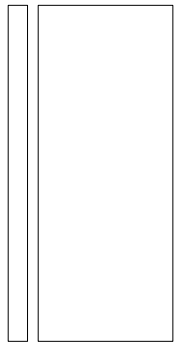
Down's Karyotype



How does it Happen?

- A pair of number 21 chromosomes fails to separate during the formation of an egg (or sperm), this is referred to as nondisjunction. When that egg unites with a normal sperm to form an embryo, that embryo ends up with three copies of chromosome 21 instead of the normal two.

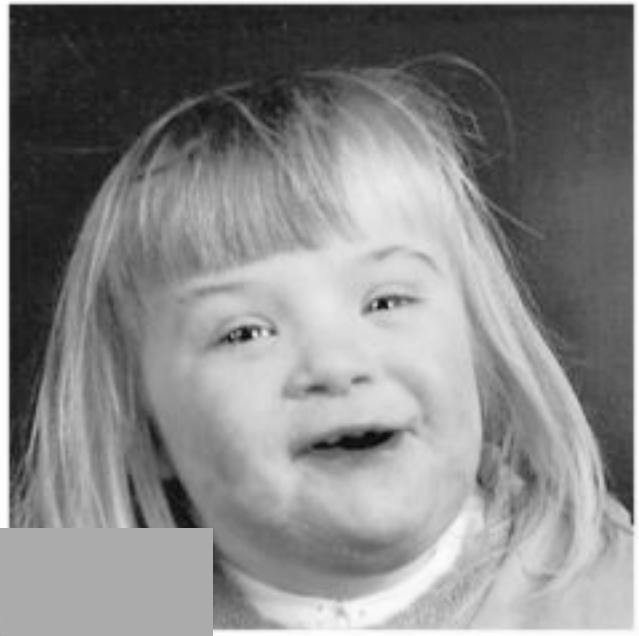
Is This Mistake in Every Cell?

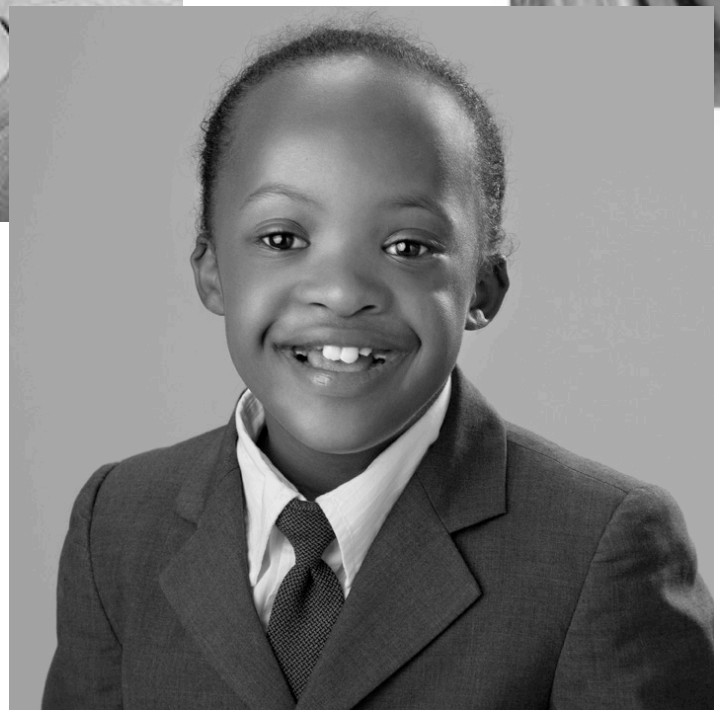


- Yes, every cell with the exception of the gametes is affected.

What are the Symptoms?

- Very distinct facial features: a flat face, a small broad nose, abnormally shaped ears, a large tongue, and upward slanting eyes with small folds of skin in the corners.





Other Medical Risks

- Increased risk of developing a number of medically significant problems: respiratory infections, gastrointestinal tract obstruction (blocked digestive tract), leukemia, heart defects, hearing loss, hypothyroidism, and various eye abnormalities. They also exhibit moderate to severe mental retardation.

Treatment

- No cure exists for Down syndrome. But physical therapy and/or speech therapy can help people with the disorder develop more normally.

What are the Odds

- Down syndrome is the most common genetic disorder caused by a chromosomal abnormality. It affects 1 in about 1,000 babies.

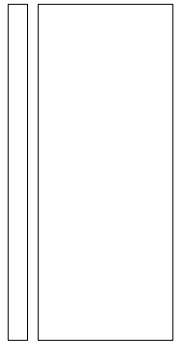
Are the Odds Affected by Age?

- Down syndrome can occur in people of all races and economic levels. Older women have an increased chance of having a child with Down syndrome. A 35-year-old woman has about a one in 350 chance of conceiving a child with Down syndrome, and this chance increases gradually to one in 100 by age 40. At age 45 the incidence becomes approximately one in 30

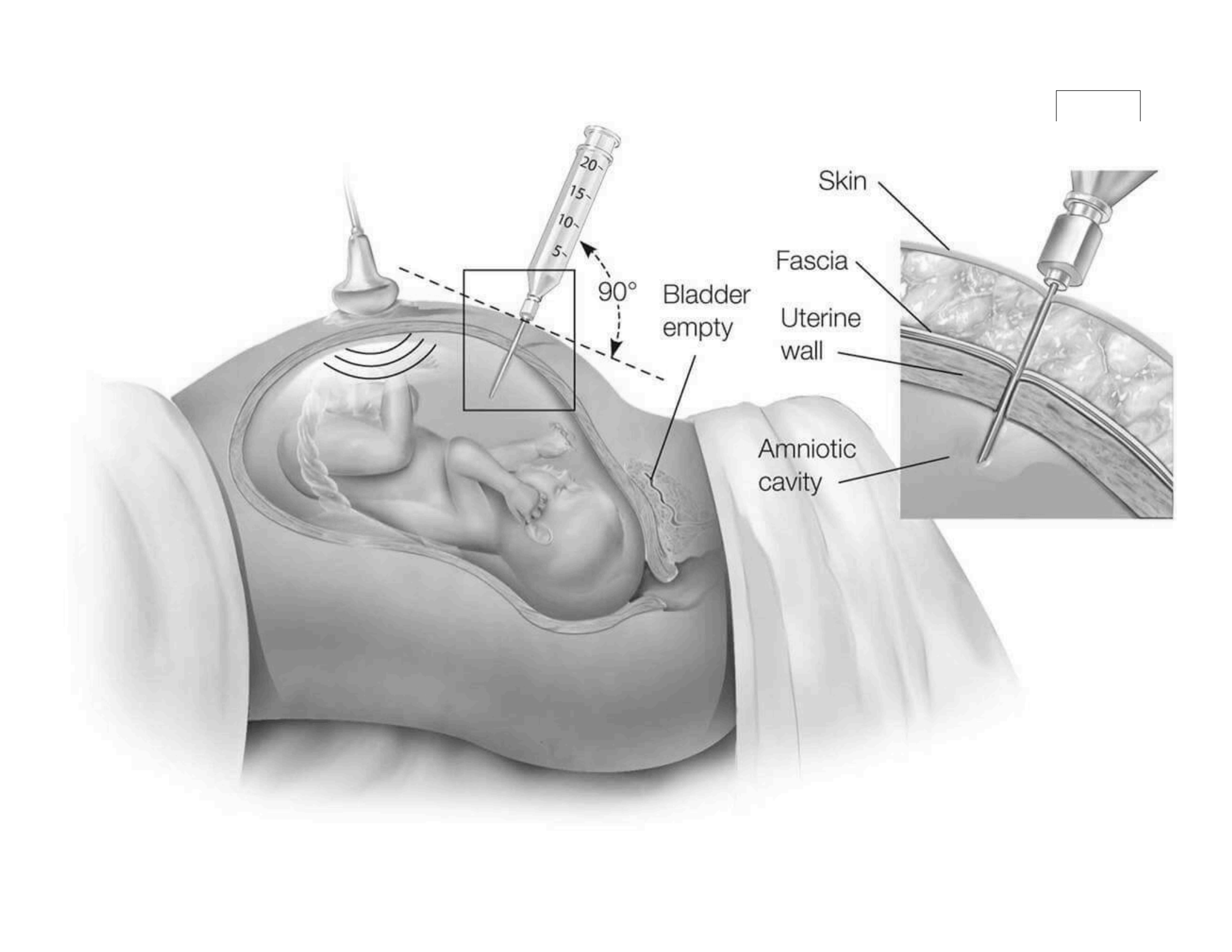
Can Down's Be Passed Down?

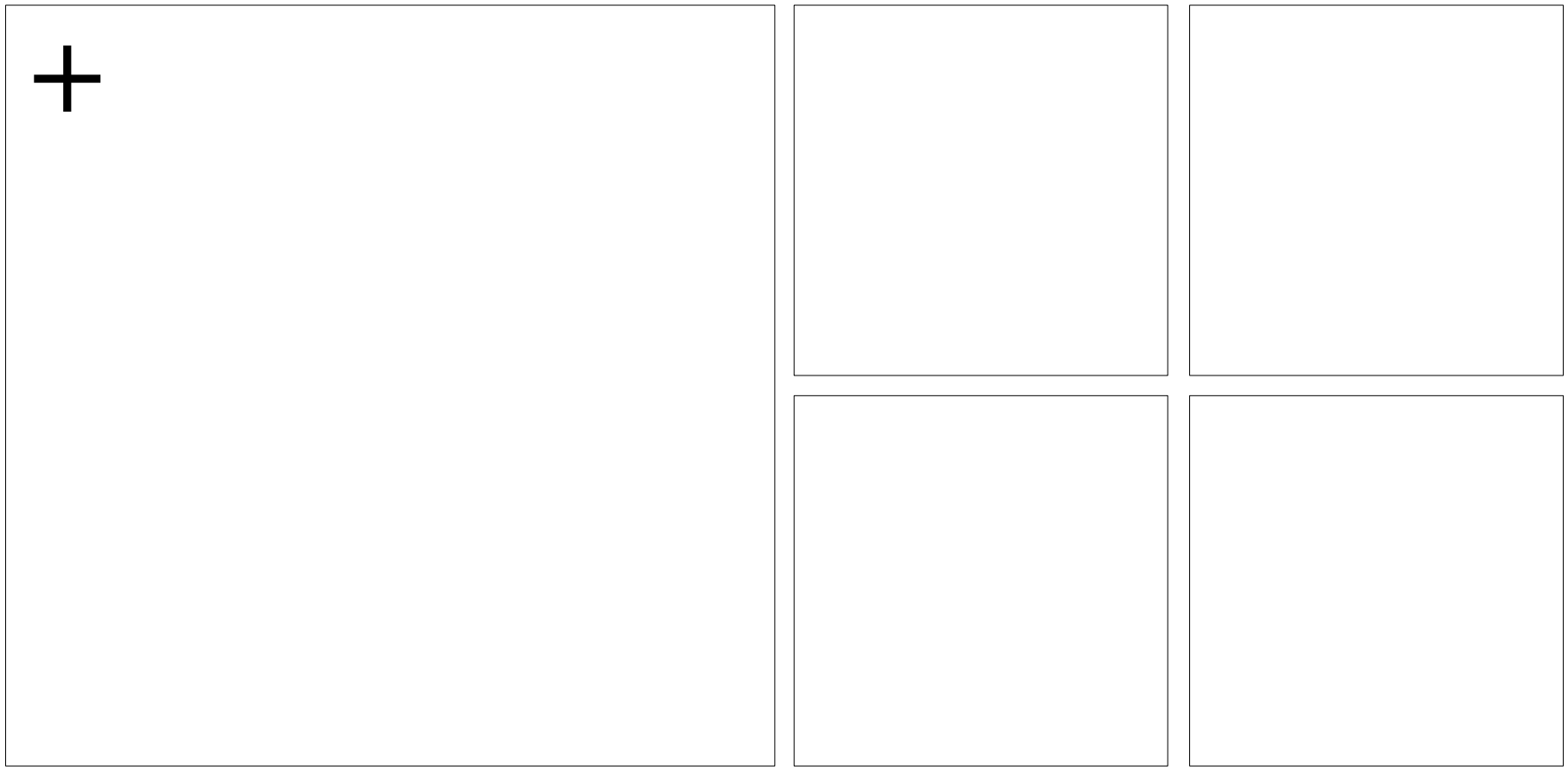
- If one or both partners have Down's Syndrome the rate of fertility is greatly reduced but there is a small chance they can have a child. The chance of a child having Down's syndrome is very high.
- If one parent has Down's Syndrome the chance of having a child affected goes down to between 35-50%.

Diagnosis in the Womb



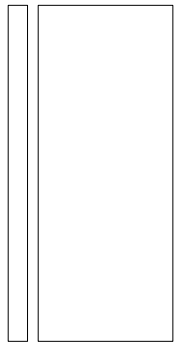
- Non-Invasive-Ultrasounds allow the doctor to examine the fetus in the womb for the physical signs of Down syndrome.
- Invasive-An amniocentesis can be done, which is a sample of mom's amniotic fluid is removed and the child's cells can be analyzed.


20
15
10
5
90°
Bladder empty
Skin
Fascia
Uterine wall
Amniotic cavity



Autosomal Disorders

Autosomal Disorders



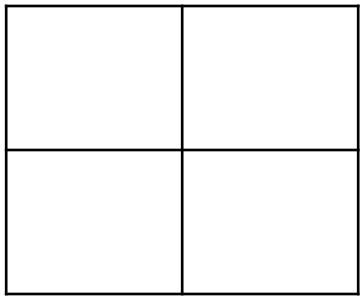
- These are chromosomal disorders affecting genes on the autosomal chromosomes (1-22)
- These can be dominant or recessive.

Autosomal Recessive Disorders

- You have 2 copies of each chromosome, 1 from mom and 1 from dad. If 1 chromosome is affected with a recessive disorder, the normal copy prevails and you are considered a carrier for the disorder. You DO NOT show any signs of the disorder. Males and females are equally affected.

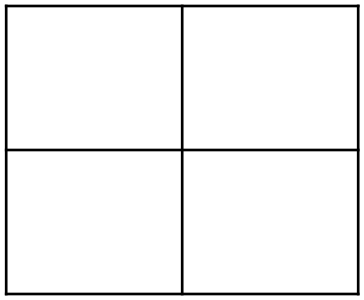
Odds of Passing Down the Disorder

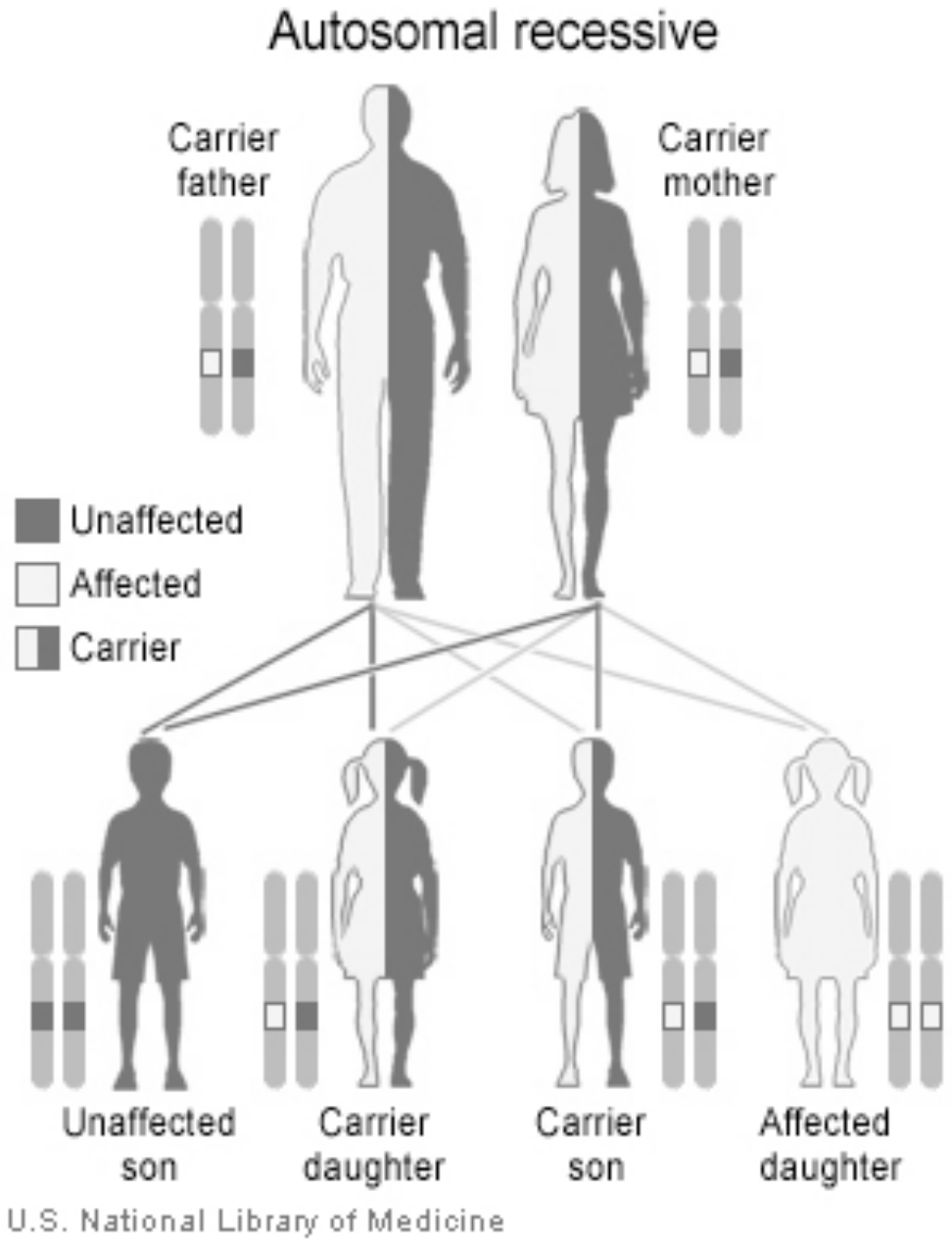
- If one parent is unaffected and the other parent is a carrier, the odds are 0% for the child to have the disorder.
- G is a normal copy and g is a affected copy.



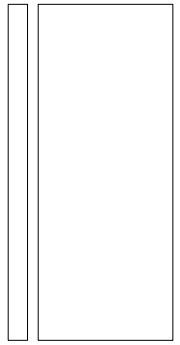
Odds of Passing Down the Disorder

- If both parents are carriers, the odds are 25% for the child to have the disorder.
- G is a normal copy and g is a affected copy.

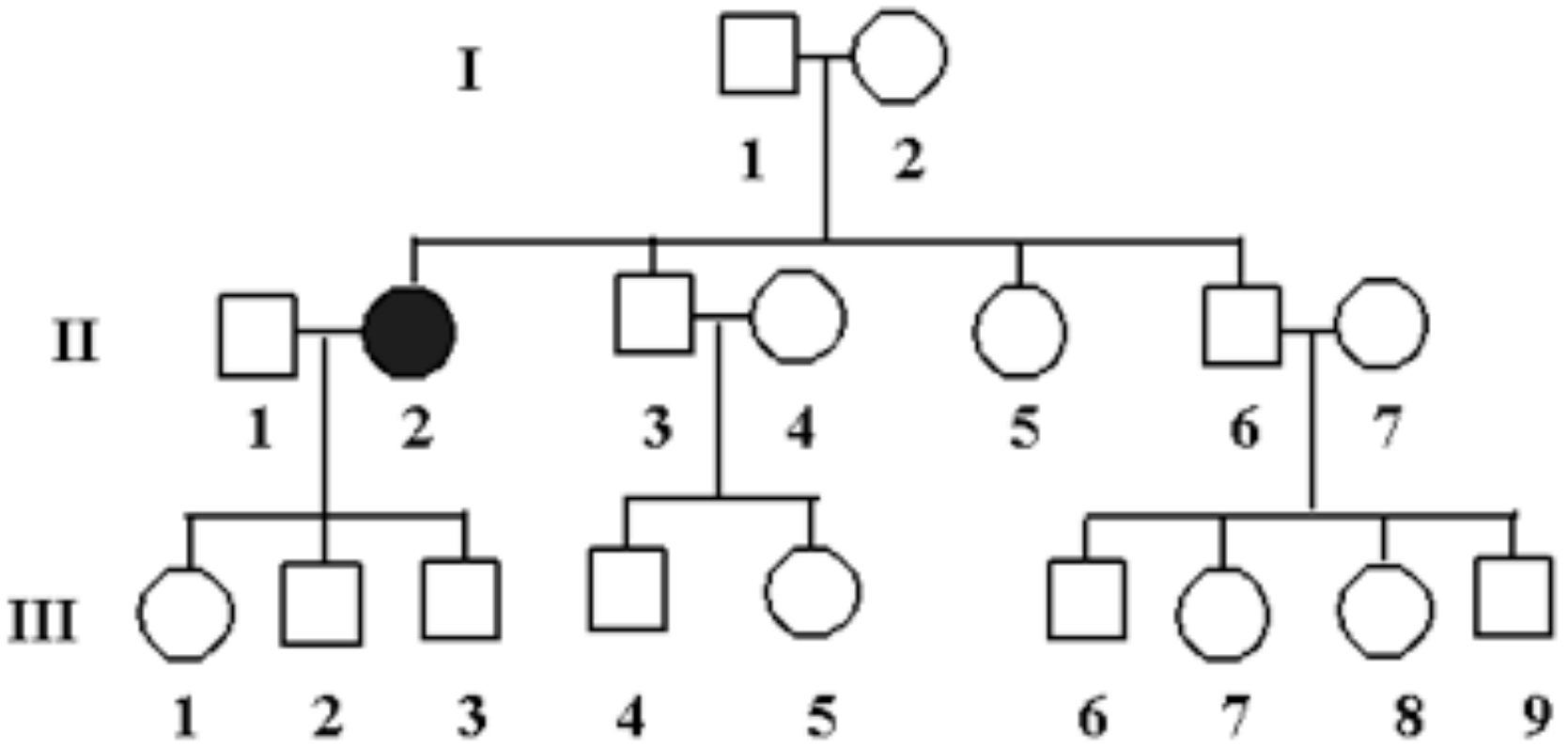



Autosomal recessive
Carrier father
Carrier mother
Unaffected
Affected
Carrier
Unaffected son
Carrier daughter
Carrier son
Affected daughter
U.S. National Library of Medicine

Surprise



- In the case of both parents being carriers the disorder comes as a total surprise.


I
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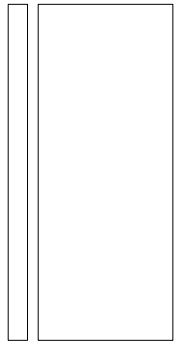
Examples of Autosomal Recessive Disorders

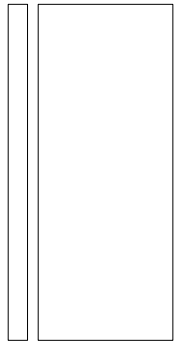


- Cystic Fibrosis
- Tay Sachs
- Sickle Cell Anemia

Sickle Cell Anemia

- Sickle cell disease involves the red blood cells, or hemoglobin, and their ability to carry oxygen.
- Normal hemoglobin cells are smooth, round, and flexible, like the letter "O", so they can move through the vessels in our bodies easily.

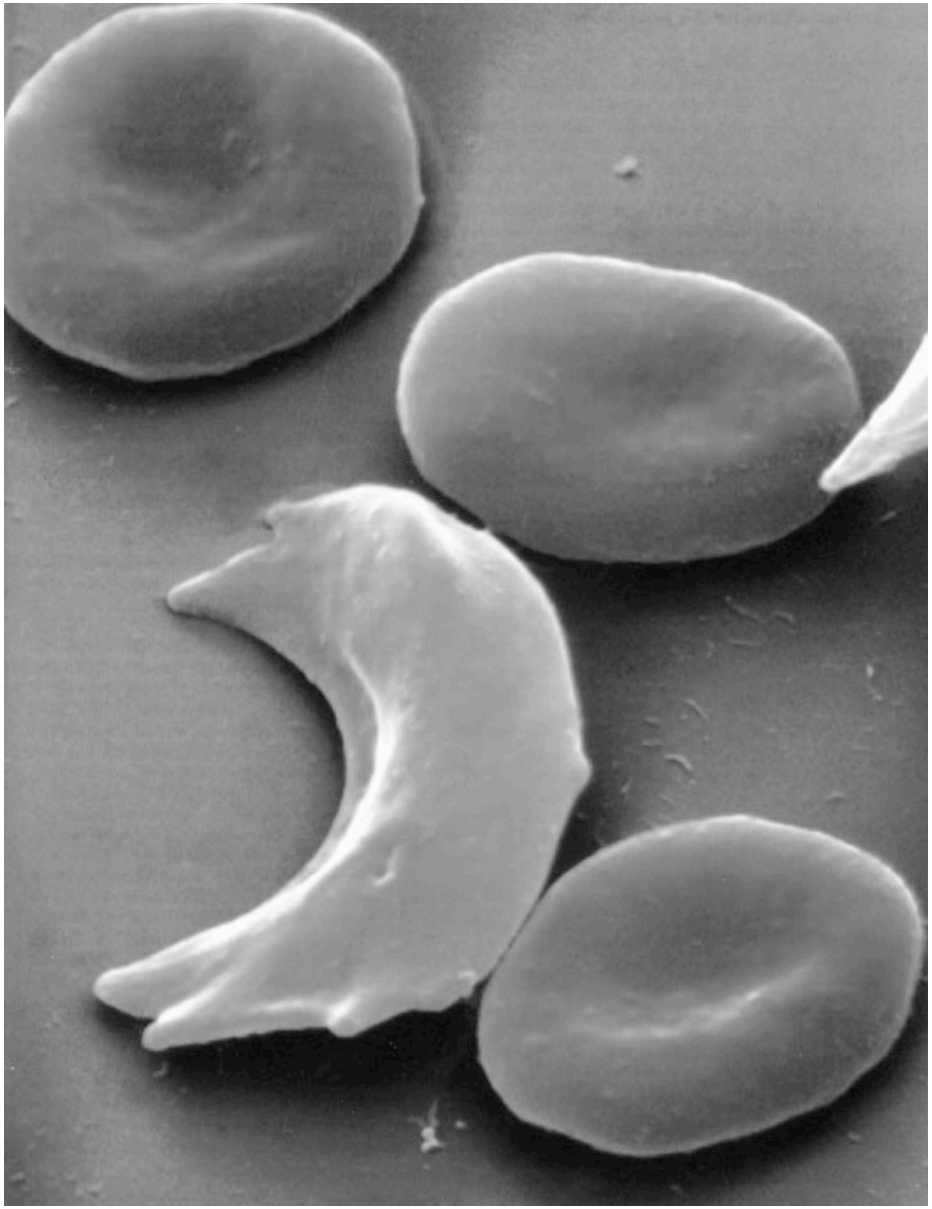
Cause



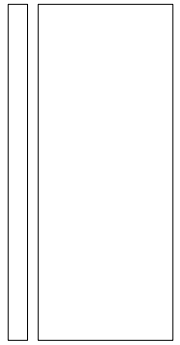
- Amino acid valine replace a glutamic acid which caused the hemoglobin not to fold right and to stick together when oxygen tension is low forming long fibers that distort the shape of the red blood cell.

How is the Shape Affected?

- Sickle cell hemoglobin cells are stiff and sticky, and form into the shape of a sickle, or the letter "C" when they lose their oxygen.



Why is That a Problem?



- These sickle cells tend to cluster together and cannot easily move through the blood vessels. The cluster causes a blockage and stops the movement of healthy, normal oxygen carrying blood. This can be painful.

How Long do the Sickle Cells Live

- About 15 days, whereas normal red blood cells can live up to 120 days. Also, sickle cells risk being destroyed by the spleen because of their shape and stiffness. This is a problem because blood iron will decrease with fewer RBC's.

How is the Spleen Affected

- After repeated blockages, the spleen is very small and does not work properly. Without a functioning spleen, these individuals are more at risk for infections.

Treatment or Cure

- Prompt emergency care for fevers and infections, appropriate vaccinations, penicillin, and management of anemia.
- Bone marrow transplant offers the only potential cure for sickle cell anemia. But, finding a donor is difficult and the procedure has serious risks associated with it, including death.

Who's Affected, Odds and Expectancy

- Sickle cell anemia is one of the most common, inherited single gene disorders in African-Americans.
- About one in 500 African-American babies is born with SC, and about one in 12 African-American people carries the gene for SC.
- Average in males was 60 and in females was 68.

Autosomal Dominant Disorders

- A disorder affecting chromosomes 1-22 where you only need 1 copy of the affected gene to cause the individual to have the disorder.
- In this case one parent will be affected with the disorder and there is a 50% chance the offspring will be affected.

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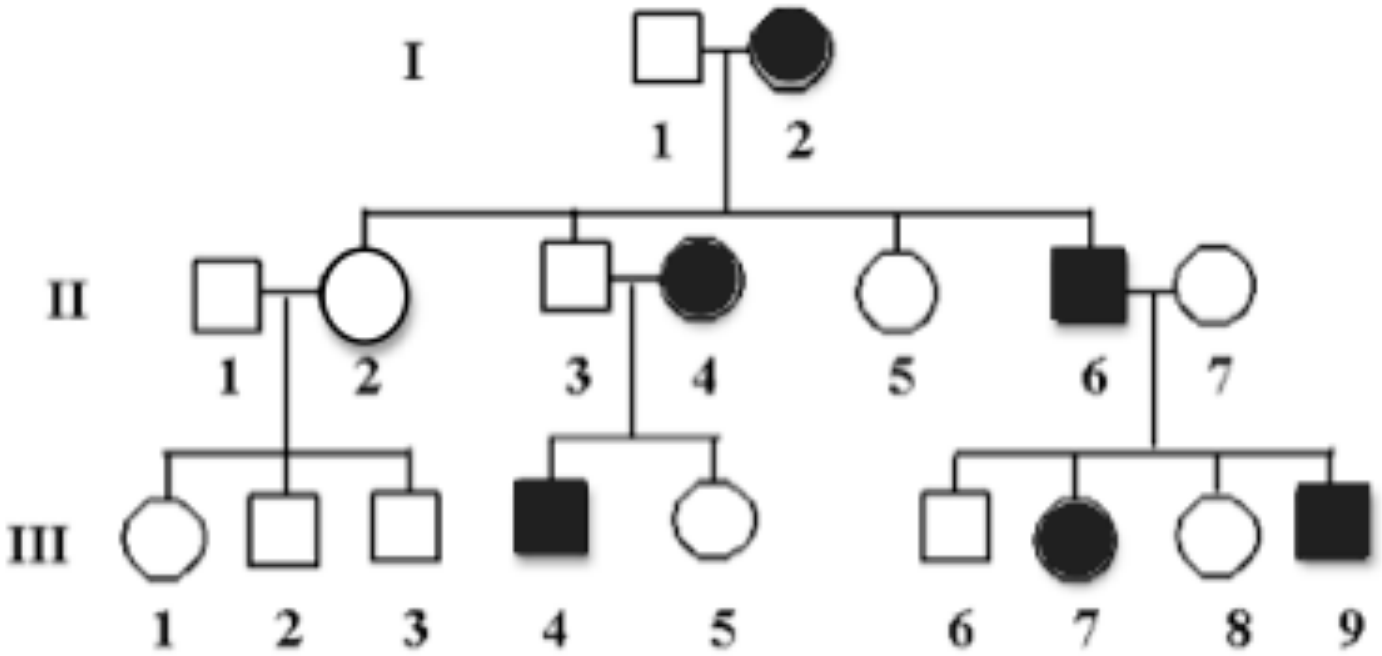
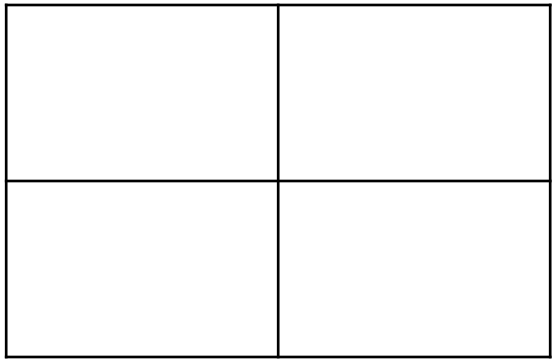
Half of the Offspring are Affected (Males and Females Affected Equally)



Punnet Square

- G=Normal copy
- G=Affected copy



Huntington's Disease

- A genetic defect on chromosome 4. The defect causes a part of DNA, called a CAG repeat, to occur many more times than it is supposed to. The normal repeat is between 10 and 35 times. In Huntington's the repeat is 36-120 times.
- The symptoms develop in a person's mid-30's.

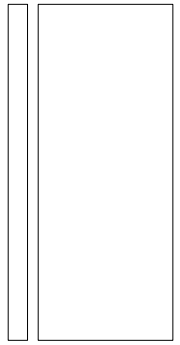
Symptoms

- Behavior changes may occur before movement problems, and can include:
- Antisocial behaviors/Moodiness/Irritability
- Hallucinations
- Restlessness or fidgeting
- Paranoia
- Psychosis

Unusual Movements

- Abnormal and unusual movements include:
- Head turning to shift eye position
- Facial movements, including grimaces
- Slow, uncontrolled movements
- Quick, sudden, sometimes wild jerking movements of the arms, legs, face, and other body parts
- Unsteady gait

Dementia



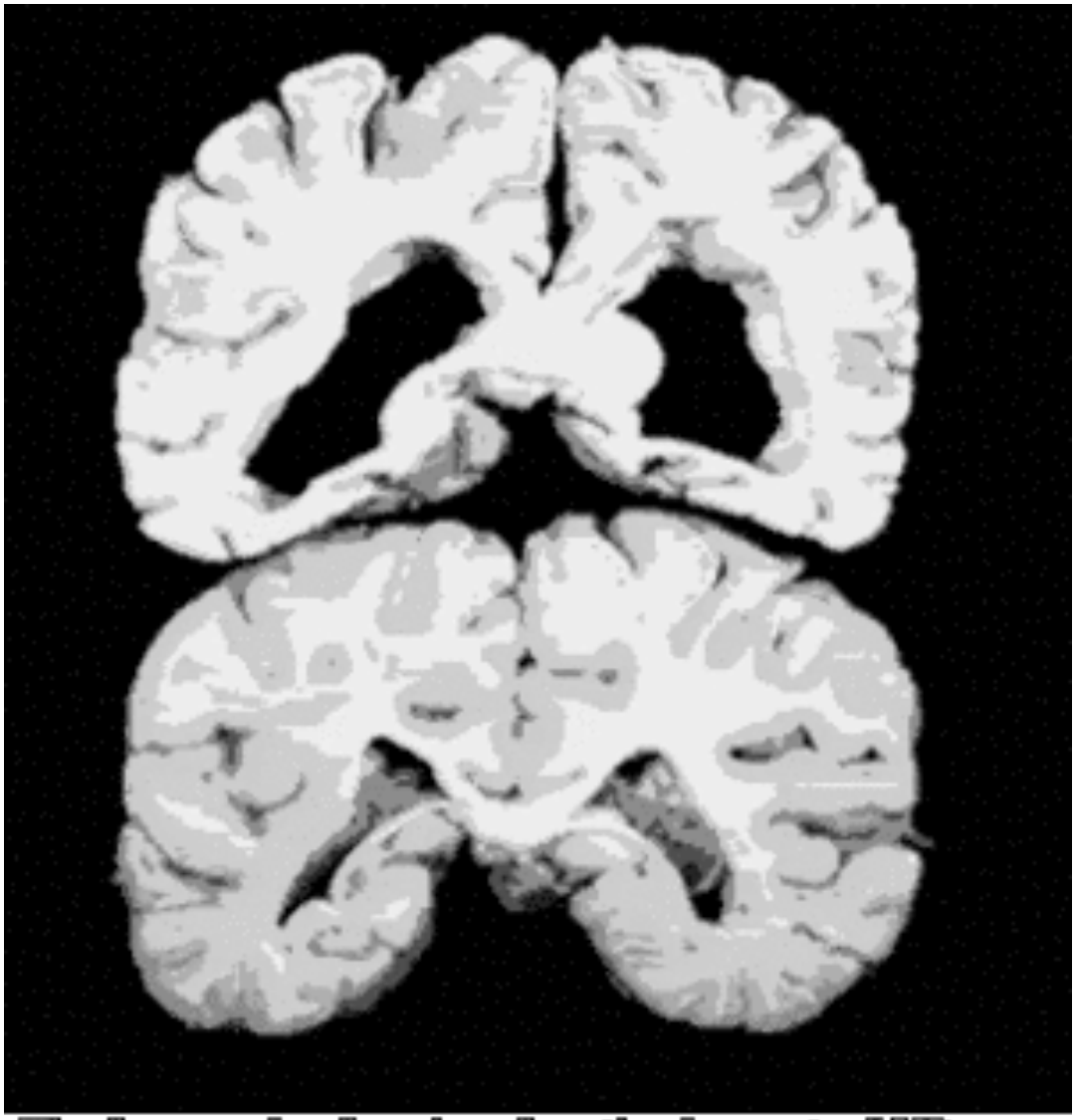
- Loss of memory
- Loss of judgment
- Speech changes
- Personality changes
- Disorientation or confusion

Treatment or Cure

- There is no cure for Huntington's disease, and there is no known way to stop the disease from getting worse. The goal of treatment is to slow down the course of the disease and help the person function for as long and as comfortably as possible.

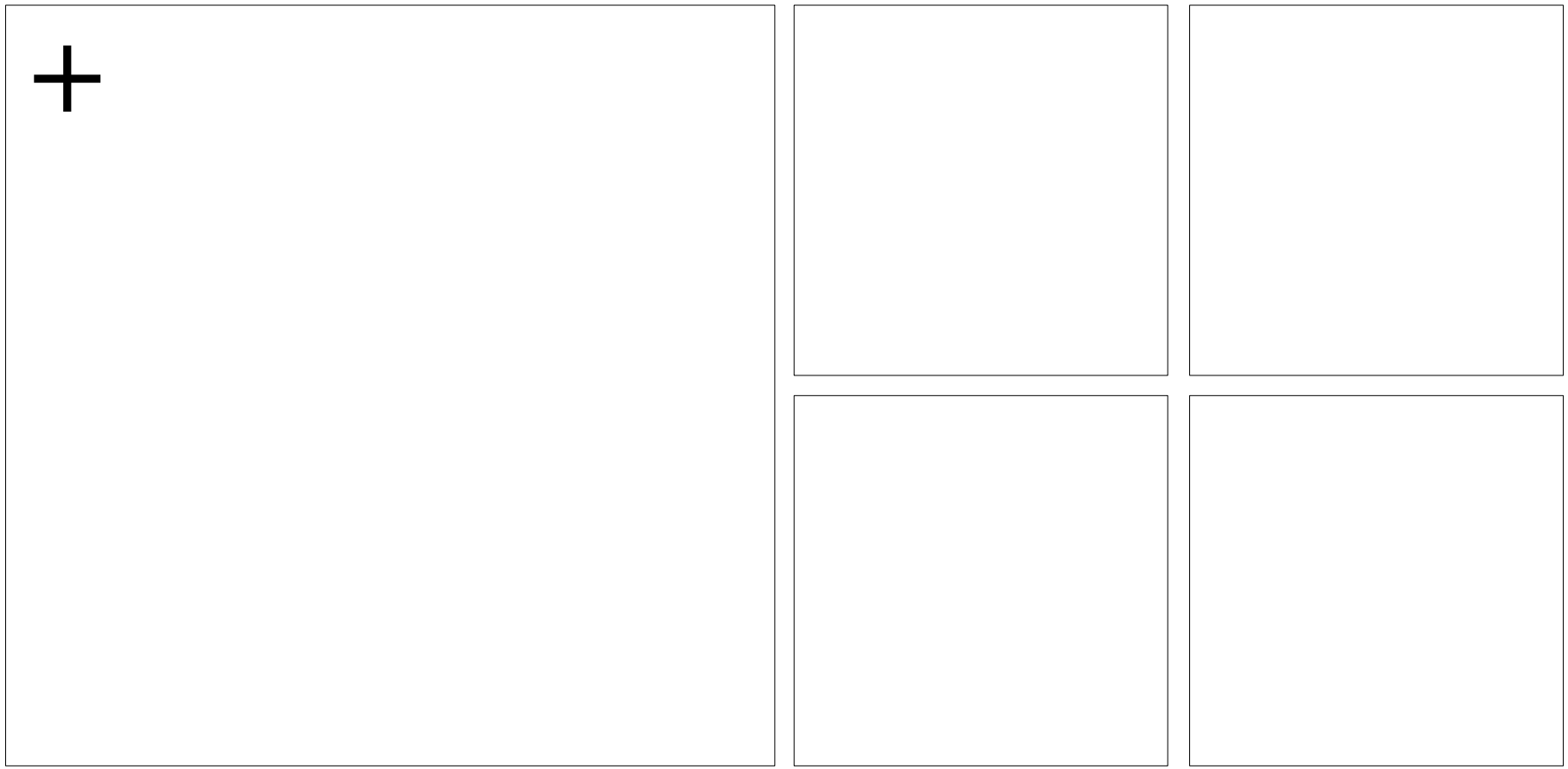
Life Expectancy

- Huntington's disease causes disability that gets worse over time. Persons with this disease usually die within 15 to 20 years. The cause of death is often infection.
- It is important to note that everyone reacts different based on the number of repeats in the CAG sequence.



The human brain, showing the impact of HD on brain structure in the basal ganglia region of a person with HD (top) and a normal brain (bottom).

https://toolbiotk.nsx.edu



X-Linked Disorders

X-Linked Disorders

- X-linked disorders are associated with the X chromosome. If it is recessive and you are female, you are simply a carrier. If it is recessive and you are a male, you have the disorder.
- If it is dominant, it does not matter if you are male or female.

X-Linked Recessive

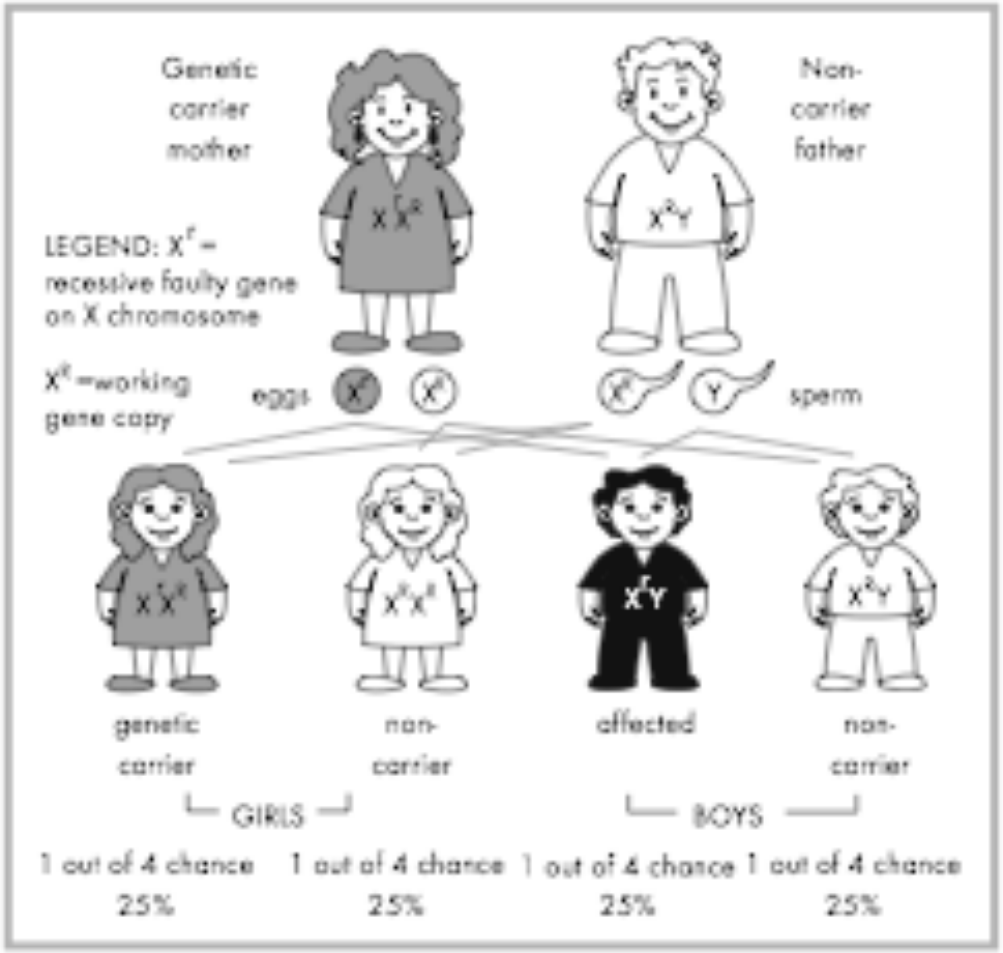
- X-linked diseases usually occur in males. Males have only one X chromosome. If that X chromosome is affected with a disorder it will show up because there is no other X chromosome present.

Odds of Getting an X-Linked Recessive

For a given birth, if the mother is a carrier (only one abnormal X chromosome) and the father is normal:

- 25% chance of a normal boy
- 25% chance of a boy with disease
- 25% chance of a normal girl
- 25% chance of a carrier girl without disease

- **Half of the boys are at risk

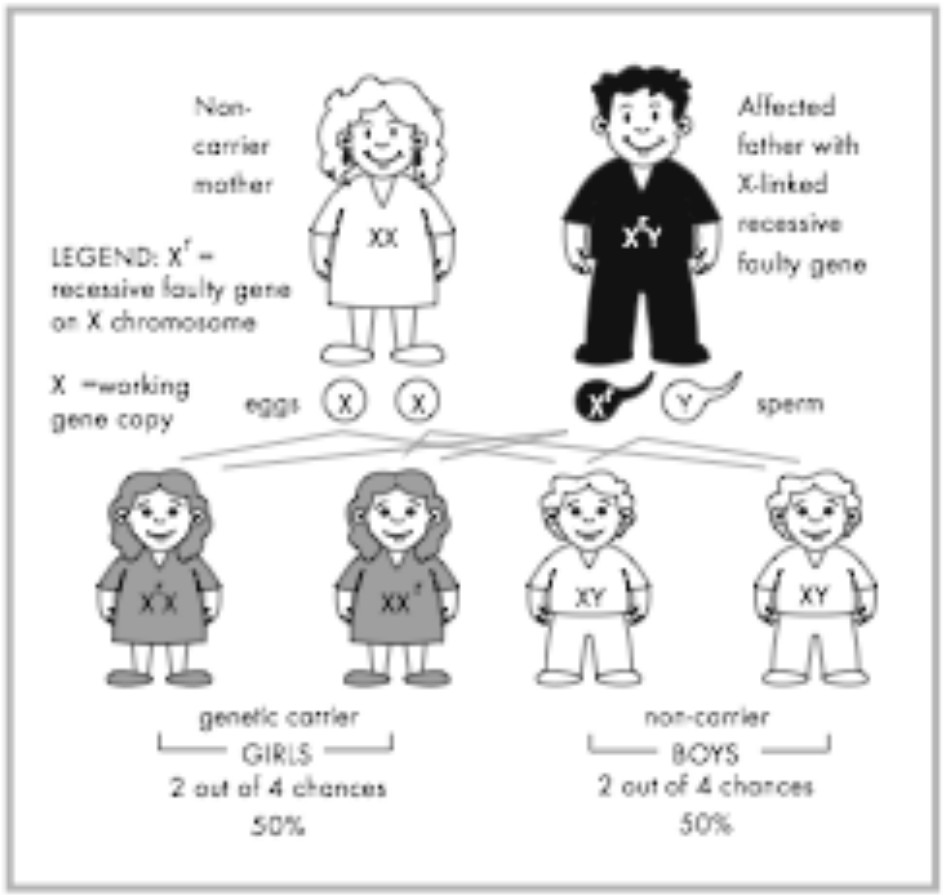

Genetic carrier mother
Non-carrier father
LEGEND: X^r – recessive faulty gene on X chromosome
X^R =working gene copy
eggs
sperm
genetic carrier
non-carrier
affected
non-carrier
GIRLS
BOYS
1 out of 4 chance 25%
1 out of 4 chance 25%
1 out of 4 chance 25%
1 out of 4 chance 25%

Odds of Getting an X-Linked Recessive

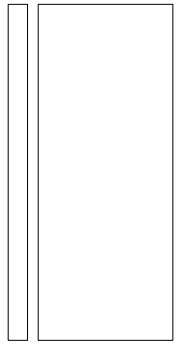
If the father has the disease and the mother is normal:

- 100% chance of a normal boy
- 100% chance of a carrier girl without disease

- **Girls are only CARRIERS


Non-carrier mother
XX
Affected father with X-linked recessive faulty gene
XrY
LEGEND: Xr = recessive faulty gene on X chromosome
X = working gene copy
eggs
X
X
Xr
Y
sperm
XrX
XXr
XY
XY
genetic carrier
GIRLS
2 out of 4 chances
50%
non-carrier
BOYS
2 out of 4 chances
50%

X-Linked Recessive Disorders



- Hemophilia
- Duchenne Muscular Dystrophy

Hemophilia

- When one or more of the blood's clotting factors are missing, there is a higher chance of bleeding.
- The main symptom of hemophilia is bleeding. Mild cases may go unnoticed until later in life, when they occur during surgery or after trauma.

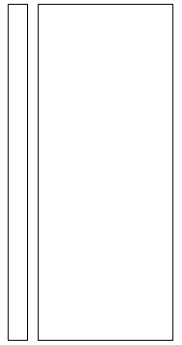
Treatment

- In more severe cases, serious bleeding may occur without any cause. Internal bleeding may occur anywhere. Bleeding into joints is common.
- Standard treatment involves replacing the missing clotting factor.

Life with Hemophilia

- Most people with hemophilia are able to lead relatively normal lives. However, some patients have significant bleeding events, most commonly chronic bleeding into the joint spaces.
- A small percentage of people with hemophilia may die from severe bleeding.

Life Expectancy

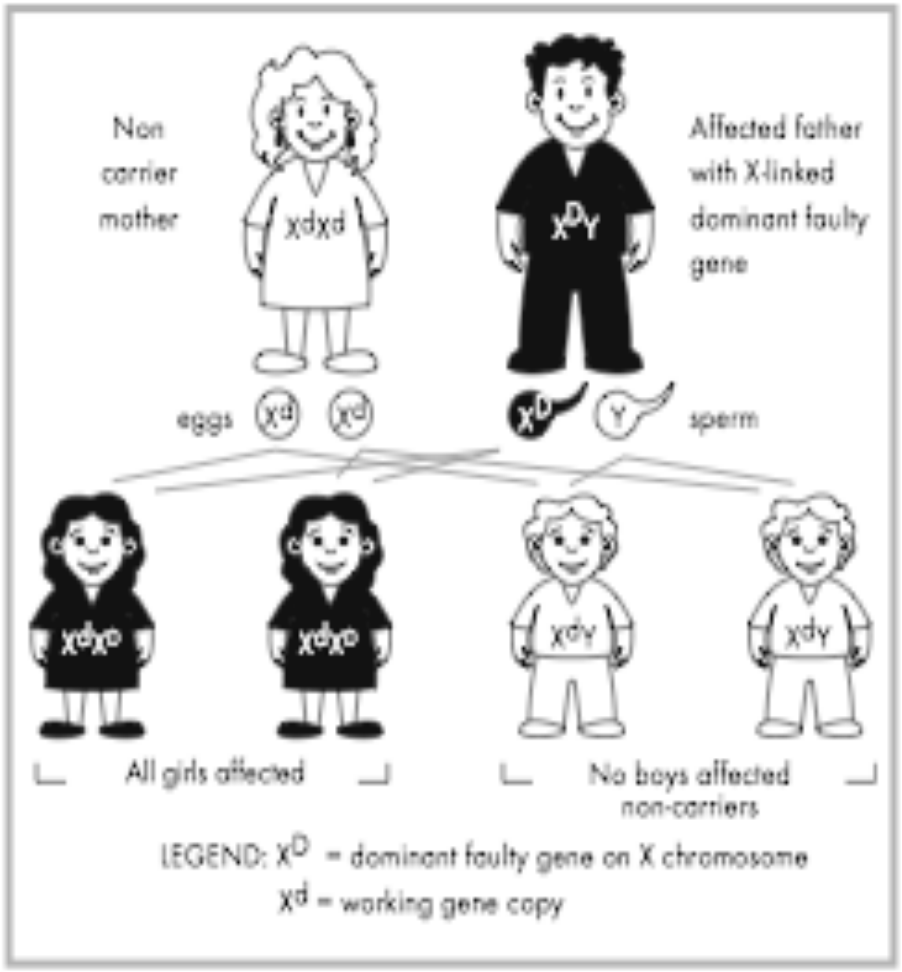


- If you are careful and avoid any major injuries, life can be as close to normal as possible.

X-Linked Dominant Disorders

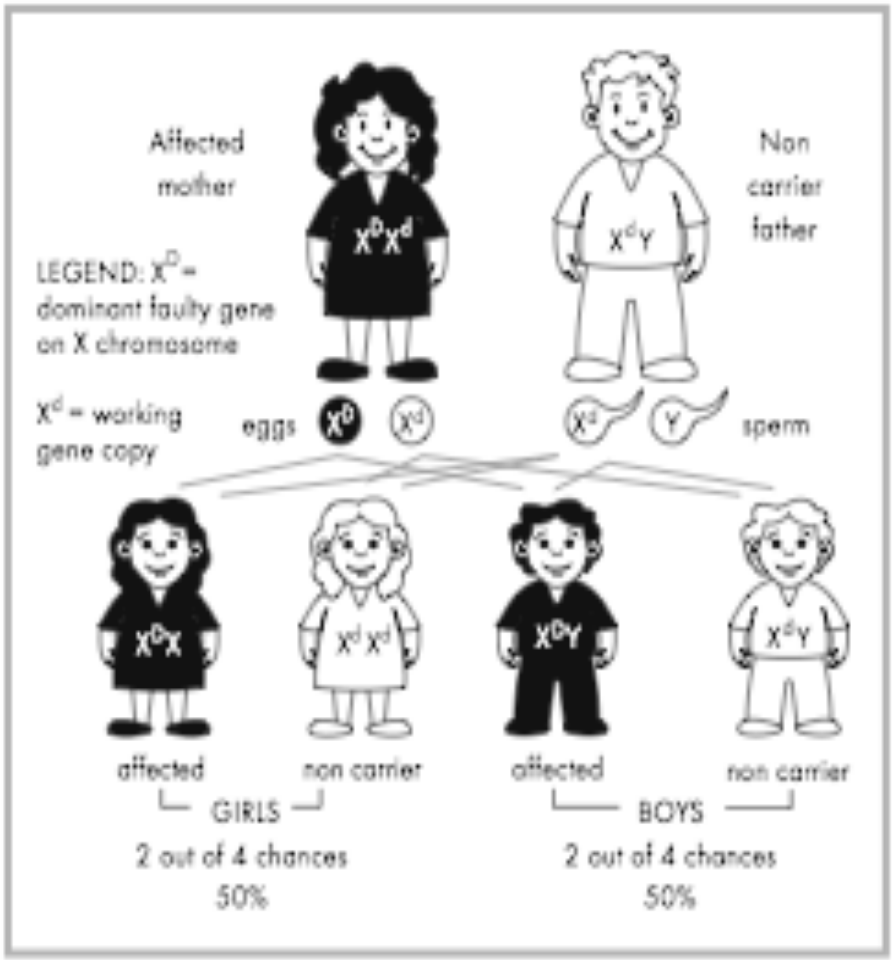
- Dominant inheritance occurs when an abnormal gene from one parent is capable of causing disease, even though a matching gene from the other parent is normal. The abnormal gene dominates the gene pair.

Dad Carries the Affect Gene



- All of his daughters will inherit the disease and none of his sons will have the disease.

Mom Carries the Affected Gene



- Half of all their children (daughters and sons) will inherit the disease tendency.