## 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 or set of chromosomes.

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### 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. More than 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 contain 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.

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.

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

- 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.

Missing an Entire Chromosome

- 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

- 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.

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

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 500 and 1 in 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.

### 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.

### 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 out of every 800 to 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 conceive 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%.

### Other Trisomy Disorders

- Down syndrome is really the only trisomy compatible with life. Only two other trisomies have been observed in babies born alive (trisomies 13 and 18), but babies born with these trisomies have only a 5% chance of surviving longer than one year.
- In 90% of Trisomy 21 cases, the additional chromosome comes from the mother's egg rather than the father's sperm.

### 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 good 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 does not have the bad gene and the other parent is a carrier, the odds are 0% for the child to have the disorder.
- G is a good copy and g is a bad copy.

Surprise

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

Examples of Autosomal Recessive Disorders

- Cystic Fibrosis
- Tay Sachs
- Sickle Cell Anemia

Cystic Fibrosis

- Affects mainly northern European and Jewish cultures.
- The odds are 1 in 2500 births with about 1 in 25 northern Europeans being carriers.

What is the Cause?

- A single amino acid deletion at position 508 in the amino acid chain of CFTR on chromosome 7. This prevents the enzyme that breaks down the mucous around the lungs from appearing at cell surface.
What is Affected

- A person secretes abnormal body fluids, including unusual sweat and a thick mucus which prevents the body from properly cleansing the lungs. The mucus interrupts the function of vital organs and leads to chronic infections.

Treatment or Cure?

- There is no cure. This mutation occurs in every cell in the body.
- Treatment includes awareness and antibiotic treatments as well as removing the sticky mucous from the lungs.
- In extreme cases a lung transplant may be needed.

Life Expectancy

- Life expectancy has improved, but, ultimately, death most often occurs from respiratory failure.
- The average life expectancy is mid 30’s, but some people have reached their late 40’s.

Tay Sach’s

- It is a fatal disorder that causes a progressive degeneration of the central nervous system. It is caused by a defect of the HEXA gene on chromosome 15. This gene produces an enzyme that helps break down a fatty substance in nerve cells. Mutations in the HEXA gene disrupt activity of the enzyme, resulting in a toxic accumulation of lipids in the brain and spinal cord.

Life Expectancy and Affected

- The expectancy is about 5 years.
- People of European Jewish origin. About one in 30 persons of Ashkenazi Jewish ancestry carries the Tay Sachs gene.
<table>
<thead>
<tr>
<th>Cure or Treatment</th>
<th>Sickle Cell Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>➤ There is no cure.</td>
<td>➤ Sickle cell disease involves the red blood cells, or hemoglobin, and their ability to carry oxygen.</td>
</tr>
<tr>
<td>➤ As for treatment, diet is important.</td>
<td>➤ Normal hemoglobin cells are smooth, round, and flexible, like the letter &quot;O&quot;, so they can move through the vessels in our bodies easily.</td>
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<th>Cause</th>
<th>Why is That a Problem?</th>
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<tbody>
<tr>
<td>➤ 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.</td>
<td>➤ 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.</td>
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<tr>
<th>How is the Shape Affected?</th>
<th>How is the Spleen Affected</th>
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<tbody>
<tr>
<td>➤ Sickle cell hemoglobin cells are stiff and sticky, and form into the shape of a sickle, or the letter &quot;C&quot; when they lose their oxygen.</td>
<td>➤ 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.</td>
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<tr>
<th>Treatment or Cure</th>
<th>How Long do the Sickle Cells Live</th>
</tr>
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<tr>
<td>➤ Prompt emergency care for fevers and infections, appropriate vaccinations, penicillin, and management of anemia.</td>
<td>➤ 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.</td>
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<tr>
<td>➤ 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.</td>
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</table>
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.

Punnett Square

- G=Good copy
- g=Bad 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.

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

Symptoms

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

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.

**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.

**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**

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**
**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.

**Duchenne Muscular Dystrophy**

- It is an X-linked inherited disorder that involves rapidly-worsening muscle weakness.
- Symptoms usually appear before age 6 and may appear as early as infancy. They may include:
  - Fatigue
  - Mental retardation (possible, but does not worsen over time)

**Muscle weakness**

- Frequent falls
- Rapidly worsening weakness
- Progressive difficulty walking
- Ability to walk may be lost by age 12
- By age 10, the person may need braces for walking. By age 12, most patients are confined to a wheelchair.

**Life Expectancy**

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

- There is no known cure for Duchenne muscular dystrophy. Treatment aims to control symptoms to maximize quality of life. Gene therapy may become available in the future.
- It is a quickly worsening disability. Death usually occurs by age 25, typically from lung disorders.

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.

Rett Syndrome

- It is a neurological disorder seen almost exclusively in females.
- Onset is between 6-18 months. Life expectancy is about 40 years.
- Starts by losing speech and hand skills they had acquired. Most children develop seizures, repetitive hand movements, irregular breathing and motor-control problems.* A slowing of the rate of head growth also becomes apparent.