Detecting Genetic Conditions: Via Paper Karyotyping

Activity exploring human karyotypes, syndromes, and Mendelian genetics

Age
Grades 6-12

Content Areas
- Karyotypes
- Anomalies

Time
45 minutes

Objectives
- Students will become familiar with karyotypes and their role when diagnosing genetic disorders in individuals.
- Students will create a karyotype of a random individual and diagnose the disorder.
- Students will discuss genetic testing and the ethical issues that can arise.

Contact
SMILE Program
SMILEinfo@oregonstate.edu
Activity Authors
Genetic4.osu@gmail.com

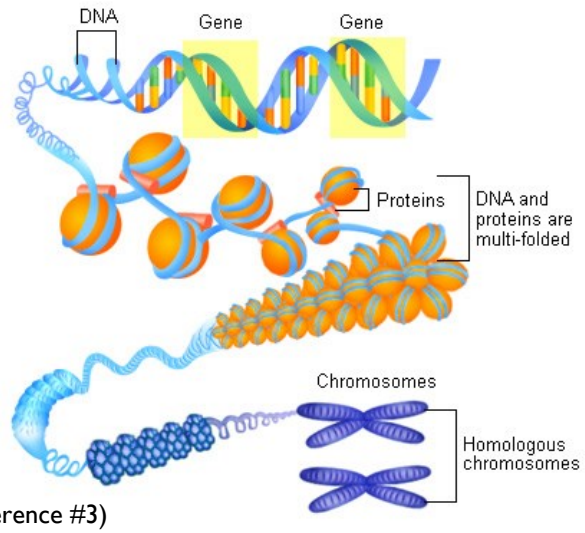
Teacher's Handout

Description:

In this activity, students will learn what a **karyotype** is and will assemble a karyotype by matching corresponding sister chromatids. After the students are finished matching chromatids, they will analyze the karyotype and diagnose a genetic disorder. Once each small group has completed their diagnosis, they will engage in a number of discussion questions. These questions are meant to encourage the students to think about how genetic anomalies arise and about the ethics of direct-to-consumer testing.

Using this Activity:

This activity is done in pairs or small groups. An introduction to the background of karyotypes should be given before the karyotype activity begins. Then hand out a small baggy with the skeleton and pre-cut chromatids to each pair/group. You can choose to pre-cut the chromatids or have the students cut them out before the activity. Keep in mind that cutting takes a significant amount of time. There are six different karyotypes with different disorders that you can hand out to your classroom. Refer to the Genetic Disorder Key section for detailed descriptions and the completed karyotypes.



(Reference #3)

Background:

Occasionally, chromosomes can be lost or misplaced during the formation of gametes in meiosis or cell division in mitosis. Non-disjunctions (see glossary) or translocations that occur due to these changes can result in miscarriage or lack of fertilization. One in 150 live births that occur have some type of chromosomal abnormality (1). It is important to note that in most cases, these chromosomal abnormalities are not the result of genetic inheritance but are simply abnormal events in meiosis or mitosis.

Some abnormalities associated with chromosome structure and number can be visibly seen by a *karyotype* (see glossary). Karyotypes are used in genetic counseling for potential parents as well as for diagnosis when an anomaly is suspected. A person's biological sex is in most cases directly evident in their karyotype. Over 400,000 karyotype analyses are performed each year in the U.S and Canada (2).

In order to create a karyotype, chromosomes from a cell are stained and photographed in the metaphase of mitosis in order to visualize the replicated and condensed chromosomes under a microscope. The photograph is then enlarged and the homologous chromosomes are paired and arranged in order by size (except the sex chromosomes which are by convention displayed last). The tests are generally performed from a blood sample, but any tissue containing cells in the correct phase of mitosis can be used.

Glossary

Autosomal Chromosomes: All chromosomes other than the sex chromosomes.

Chromatid: each of the two threadlike strands into which a chromosome divides longitudinally during cell division. Each contains a double helix of DNA.

Gene: A hereditary unit that is transferred from parent to offspring to help determine the characteristics of the offspring.

Genome: The complete set of genes present in an organism.

Karyotype: The number and visual appearance of chromosomes present in the nuclei of a cell.

Mosaicism: The condition of being composed of two or more genetically different types of cells.

Mutation: A change in the nucleotide sequence of an organism's DNA or in the DNA or RNA of a virus.

Nondisjunction: Failure of chromosomes to separate and move to opposite poles of the division spindle. It results in the loss or gain of a chromosome.

Sex Chromosomes: A chromosome responsible for determining the sex of an individual.

Sister chromatid: refers to either of the two identical copies (**chromatids**) formed by the replication of a single chromosome, with both copies joined together by a common centromere.

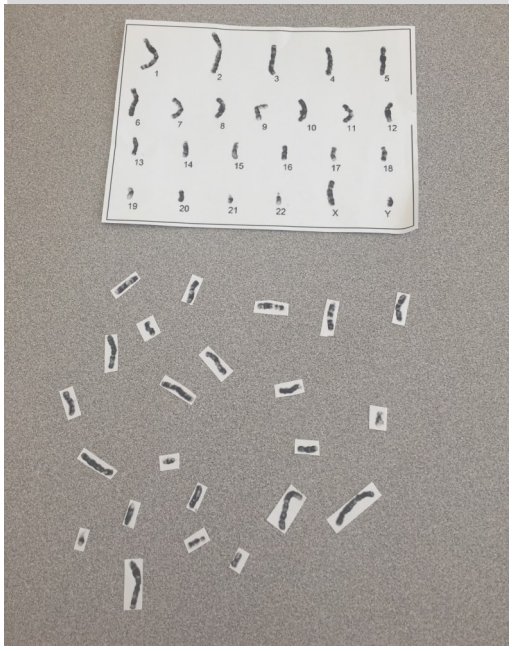
Translocation: An abbreviation in chromosome structure resulting from an attachment of a chromosomal fragment to a nonhomologous chromosome.

Trisomy: a condition in which an extra copy of a chromosome is present in the cell nuclei, causing developmental abnormalities.

(Reference #6)

Materials

- Glue/tape
- Scissors
- Incomplete karyotype worksheet



Directions:

1. Find a partner and take a plastic bag containing chromosomes from a karyotype with an unknown genetic disorder.

2. Using scissors, cut out all the chromosomes that are not labeled. Find its match on the karyotype skeleton labeled 1-23. (hint: Don't throw away extra chromosomes! They could be the key evidence for the presence of a genetic disorder!)

3. Continue step 2 until you and your partner are confident that all of the chromosomes are matched up. Proceed to glue or tape the pairs to the worksheet.

4. Observe the karyotype. Is there an extra chromosome where there shouldn't be? Is one arm of a chromosome noticeably shorter than the other one in its pair? Flip to the back of this document to find a list of common genetic disorders to identify the one in your worksheet.

Student Questions after completing activity:

1. **What chromosomal abnormality is displayed in the karyotype you received? How do you know?**

2. **How can you determine if your paper karyotype is male or female?**

(look at the last two chromosomes) (XX=genetic Female) (XY= genetic Male)

3. **What type of mutation occurs in this particular anomaly? Where in the genome does it occur?**

Discussion question for worksheets:

1. In the paper karyotype activity, you were able to clearly see the chromosomal abnormalities, but other common disorders or illnesses such as migraines, obesity, and diabetes are thought to be genetically inherited to varying degrees. Why do you think the scientific community is unable to pinpoint a specific, universal genetic the cause of migraines, obesity, and diabetes in an affected karyotype?

2. A new company offers genetic testing and claims it can find out if you will get diabetes or high blood pressure for $1000. Does this sound like a good deal to you? Do you think this is likely to be reliable test? Would you want to get tested? Why or why not?

3. What other factors can affect the potential of someone being predisposed to a genetic abnormality?

4. Assuming that you tested positive for a future serious health condition, do you feel that your health insurance company should have knowledge of this and be able to raise the rates of your health insurance based on these results? Why or why not?

Notes for teachers on discussion above:

-After many years, the 1st draft of a human genome was sequenced in 2003, but because of the size and vastness of the genome, many more years of work will be required to understand the specific biological function of the sequences and genes that make up the genome.

-Because of the Affordable Care Act (2010), insurance companies can no longer deny coverage to a person with a pre-existing health condition, but genetic testing to assess an individual's predisposition to a disease could possibly be used by insurance companies in the future to determine the price of one's rates.

-Although there has been extensive research on identifying cancer associated alleles in genes such as *BRCA1, TP53*, and *PTEN,* and genetic tests for such alleles are commercially available, when a person chooses to perform these tests, it is essential that the person speaks with a genetic counselor, doctor, or other health care professional trained in genetics, in order to fully understand the results.

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-Genetic testing can have several possible results: positive, negative, true negative, uninformative negative, false negative, variant of unknown significance, or benign polymorphism (see complete definitions below). Although testing can be done on specific cancer associated genes such as *BRCA1, TP53,* and *PTEN,* scientists have yet to identify specific genes that cause diabetes, but have only been able to identify genetic risk factors. However, it is important that the students understand that if they test positively for a risk factor for diabetes, it does not necessarily mean they will develop diabetes; rather , it mean they have a higher probability for developing diabetes.

Box 1: Positive & Negative Test Results

A "positive test result" means that the laboratory found a specific genetic alteration (or mutation) that is associated with a hereditary cancer syndrome. A positive result may:

-Confirm the diagnosis of a hereditary cancer syndrome

-Indicate an increased risk of developing certain cancer(s) in the future

-Show that someone carries a particular genetic change that does not increase their own risk of cancer but that may increase the risk in their children if they also inherit an altered copy from their other parent (that is, if the child inherits two copies of the abnormal gene, one from their mother and one from their father).

-Suggest a need for further testing

-Provide important information that can help other family members make decisions about their own health care.

A "negative test result" means that the laboratory did not find the specific alteration that the test was designed to detect. This result is most useful when working with a family in which the specific, disease-causing genetic alteration is already known to be present. In such a case, a negative result can show that the tested family member has not inherited the mutation that is present in their family and that this person therefore does not have the inherited cancer syndrome tested for, does not have an increased genetic risk of developing cancer, or is not a carrier of a mutation that increases cancer risk. Such a test result is called a "true negative." A true negative result does not mean that there is no cancer risk, but rather that the risk is probably the same as the cancer risk in the general population.

G. H. Reference, "What do the results of genetic tests mean?," *Genetics Home Reference*. [Online]. Available: https://ghr.nlm.nih.gov/primer/testing/interpretingresults.

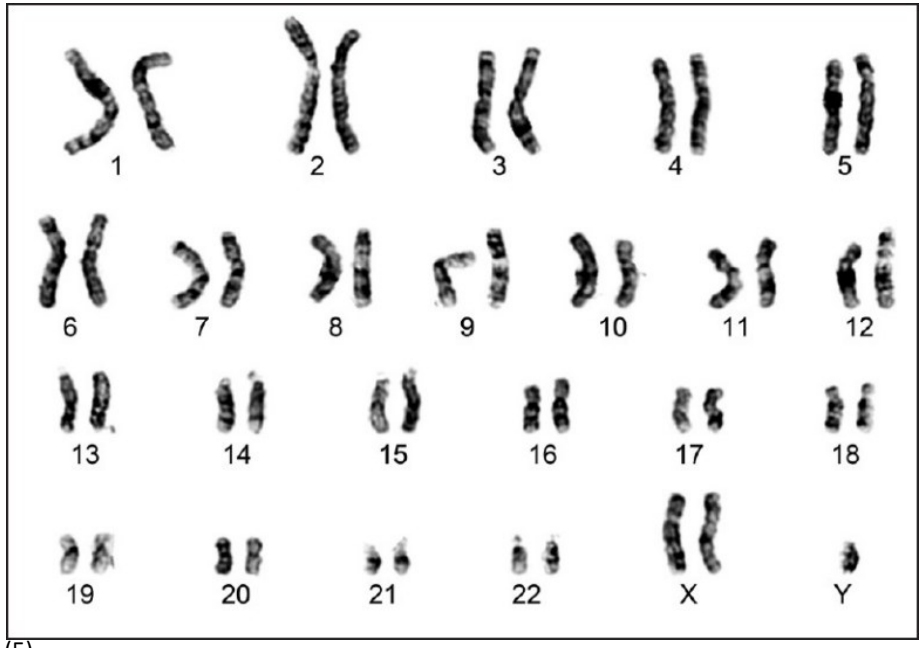
When a person has a strong family history of cancer but the family has not been found to have a known mutation associated with a hereditary cancer syndrome, a negative test result is classified as an "uninformative negative" (that is, does not provide useful information). It is not possible to tell whether someone has a harmful gene mutation that was not detected by the particular test used (a "false negative") or whether the person truly has no cancer-predisposing genetic alterations in that gene. It is also possible for a person to have a mutation in a gene other than the gene that was tested.

If genetic testing shows a change that has not been previously associated with cancer in other people, the person's test result may report "variant of unknown significance," or VUS. This result may be interpreted as "ambiguous" (uncertain), which is to say that the information does not help in making health care decisions.

If the test reveals a genetic change that is common in the general population among people without cancer, the change is called a polymorphism. Everyone has commonly occurring genetic variations (polymorphisms) that are not associated with any increased risk of disease

Karyotype Key

Klinefelter Syndrome (XXY)



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What is it?

47, XXY is a genetic condition that is caused when a person has two X chromosomes and one Y chromosome. A typical male has one X and one Y chromosome and a typical female has two X chromosomes. A small proportion of XXY individuals will develop as intersex (between male and female) or female.

How do people get it?

XXY is caused by a nondisjunction. A nondisjunction occurs during meiosis I or meiosis II which results in gametes with either too many or too few chromosomes. Specifically, Klinefelter syndrome occurs in meiosis II where one pair of sister chromatids did not separate during anaphase II.

What are the characteristics?

The XXY chromosome primarily affects sexual development. Testosterone levels are lower than normal as well as sexual organs do not fully develop. Puberty may be accelerated or halted. As adults, most all XXY males are infertile. Children and adults may be taller than average, with proportionally longer arms and legs. They also may have less-muscular bodies, wider, narrower shoulders, or minor to moderate learning disabilities.

How is it diagnosed?

Physical characteristics or most commonly, infertility via analysis of a person's karyotype. This may also be diagnosed during a woman's pregnancy if amniotic fluid or placenta is tested for chromosomal abnormalities but 75% of XXY individuals are never diagnosed.

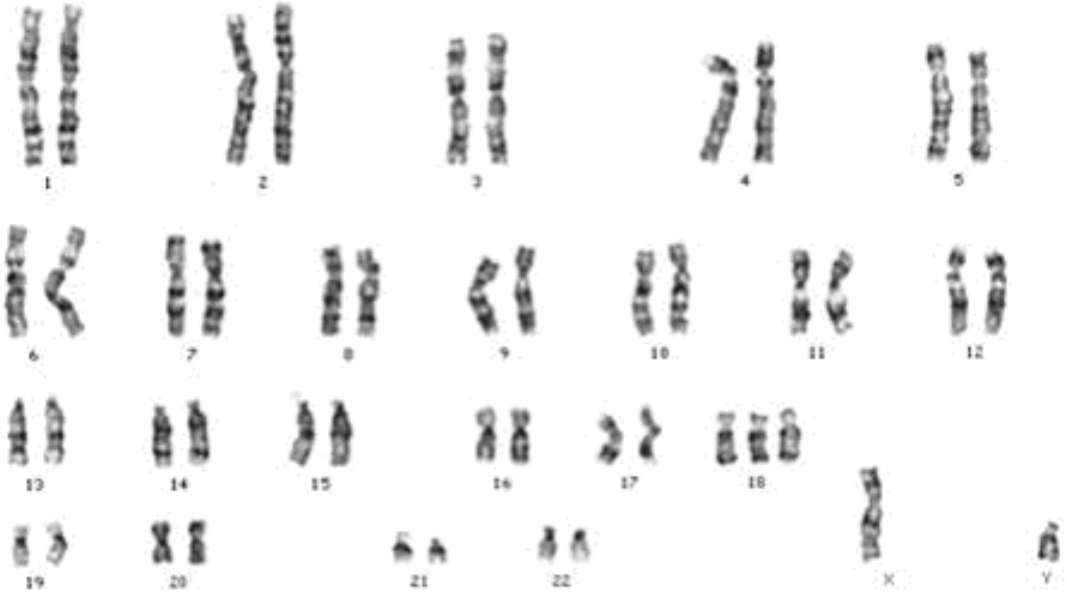
Treatments?

Hormone treatments can be given if desired.

For more information : http://learn.genetics.utah.edu/content/disorders/chromosomal/

Karyotype Key

Edwards Syndrome



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What is it?

Edwards syndrome occurs when an individual has an extra chromosome 18. A Trisomy 18 error occurs in about 1 out of every 2500 pregnancies in the United States and 1 in 6,000 live births.

How do people get it?

There are three types of Edwards Syndrome: nondisjunction (Trisomy 18), translocation, and mosaicism. The most common cause is nondisjunction (95% of cases), where there is an error in cell division. Edwards Syndrome is caused by a error in cell division, known as meiotic nondisjunction. Trisomy is not inherited and is a random occurrence that takes place during cell division.

What are the characteristics?

Characteristics of Trisomy 18 include heart defects, kidney problems, small head, and severe developmental delays.

How is it diagnosed?

Diagnostic tests can be performed in utero during the first or second trimester of a pregnancy. Karyotyping of the baby's DNA can be performed.

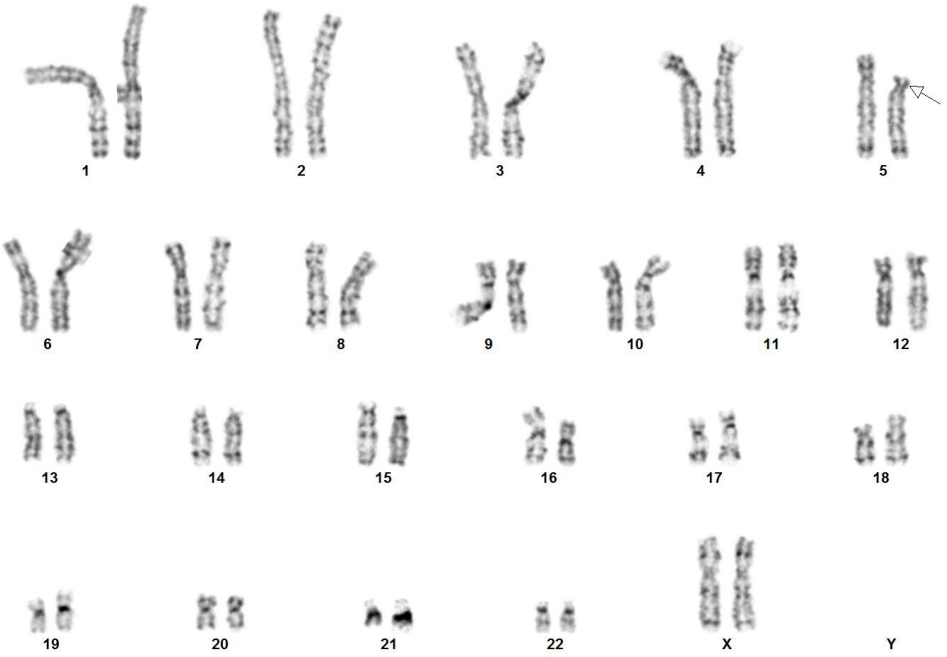
Treatments?

There is no available treatment for Edwards Syndrome. There is a high mortality rate for children with Trisomy 18 before or shortly after birth.

For more information: http://www.learningaboutelectronics.com/Articles/Edwards-syndrome-trisomy-18.php.

Karyotype Key

Cri-du-chat



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What is it?

Cri-du-cat Syndrome (5p minus) is a rare chromosomal condition that happens when a portion of small arm of chromosome 5 is missing.

How do people get it?

Cri-du-chat is caused by a deletion of the short (p) arm of chromosome 5. It occurs in an estimate 1 in 20,000 newborns. Studies show that larger deletions tend to result in more severe disabilities to the infants. Most cases of Cri-du-chat are not inherited. It most often occurs due to a random error in reproductive cell development.

What are the characteristics?

Common characteristics include a distinctive cry that resembles a cat (in infants), delayed intellectual development, slow or incomplete development of motor skills, small head size, diminished muscle tone, wide side eyes, a small jaw, etc.

How is it diagnosed?

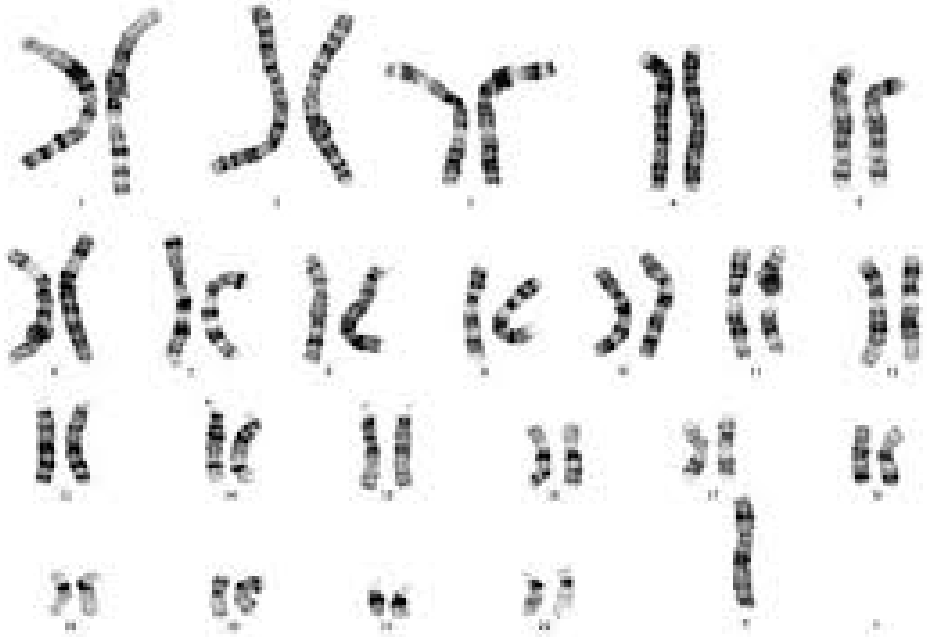
Genetic tests such as amniocentesis or CVS can be performed before birth to diagnosis Cri-du-cat. After birth, it can be diagnosed within the first few days of birth.

Treatments?

Drug therapy, surgery, and rehabilitation may be utilized to manage the syndrome.

Karyotype Key

Turner Syndrome (XO)



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What is it?

A genetic condition that results from a missing or incomplete X chromosome and only affects females.

How do people get it?

It is caused by a chromosome change where only one X chromosome is created. Turner Syndrome is in most cases not inherited; in fact, in most cases, a female with the syndrome will be the first and only person affected in the family.

What are the characteristics?

Characteristics of the disorder include short stature, infertility, heart defects, and delayed puberty.

How is it diagnosed?

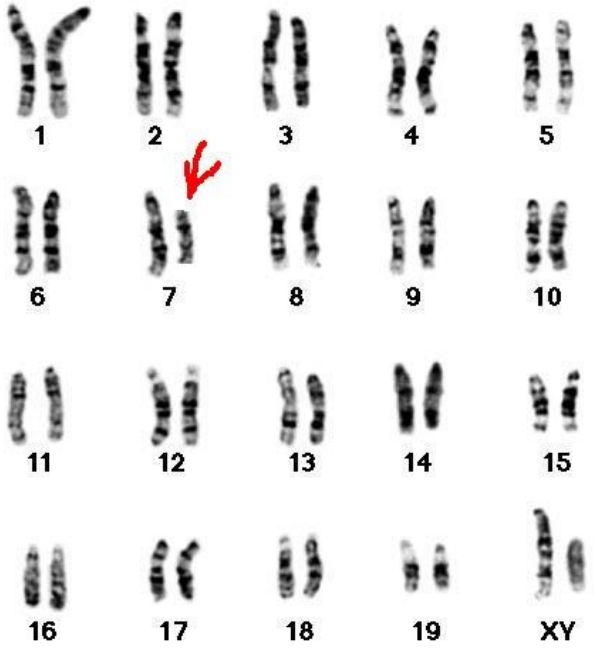
A female with TS can be diagnosed *in utero* with an amniotic fluid test or at any point in their life using a karyotype.

Treatments?

Hormone therapy and ongoing medical care can be utilized to manage the disorder, specifically for growth and development.

Karyotype Key

Williams Syndrome



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What is it?

Williams syndrome is a developmental disorder. It affects many functions of the body including intellectual ability, personality characteristics, distinct facial features, and problems with the heart and blood vessels.

How do people get it?

Williams syndrome is caused by the deletion of genetic materials from region 11.23 chromosome 7. This results in the loss of one of the two copies for the 25-26 genes.

What are the characteristics?

Those with Williams Syndrome have highly social personalities, an affinity for music, specific types of cardiovascular disease, attention deficit disorder, and broad foreheads. Though they can have difficulty with visual-spatial tasks, they often excel at tasks that involve spoken language.

How is it diagnosed?

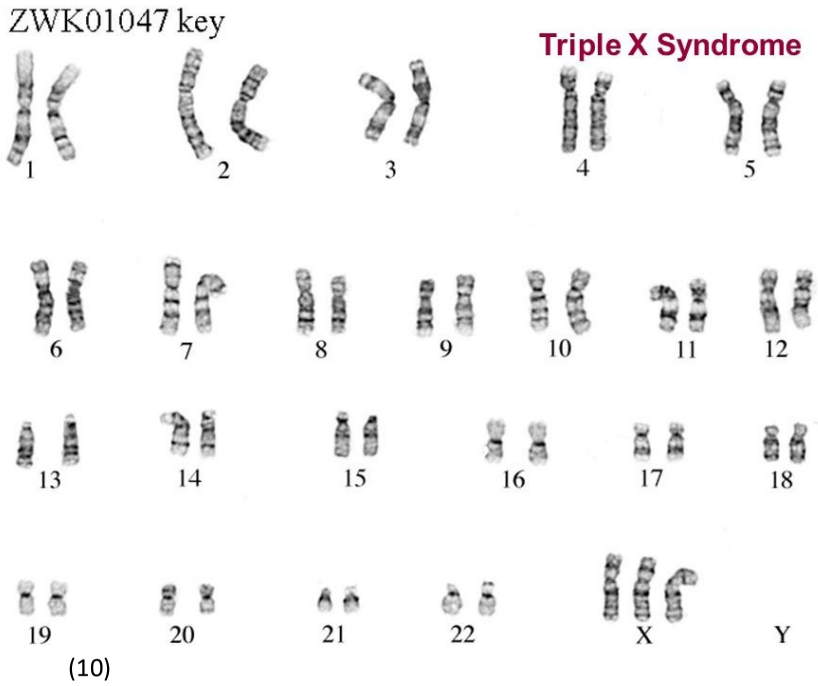
The main diagnosis for Williams Syndrome is the detection of the gene deletion in the critical region of chromosome 7 that surrounds the elastin gene. Fluorescent *in situ* hybridization can detect the deletion.

Treatments?

Early intervention programs and special education programs can provide individualized care and counseling for those with Williams Syndrome. Diet modification and drug therapy can alleviate the symptoms of the cardiovascular problems that accompany the ailment.

Karyotype Key

Triple X Syndrome (XXX)



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What is it?

Triple X syndrome is characterized by the presence of an additional X chromosome in each of a female's cells. It occurs in approximately 1 in 1,000 newborn girls, making it the most common female chromosomal abnormality.

How do people get it?

It results from an extra copy of the X chromosome.

What are the characteristics?

There are typically no extreme physical features/ailments that accompany XXX. It is, however, associated with an increased risk of learning disabilities, tall stature, and a delay in speech and language skills.

How is it diagnosed?

Tissue placental sampling are used during the prenatal period. After birth, a karyotype can be examined.

Treatments?

Early intervention therapies including psychological evaluations to support emotional development. If sexual development or fertility problems arise, hormone therapy is an option.

Resources

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Authors

Demi Butler, Emma Cushing, Morgan McCarthy, & Lexi Wilson.