HEREDITARY DISORDERS OF HUMAN

Azerbaijan Medical University

Medical biology and genetics department

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Lecture plan:

1. General characteristics of genetic disorders
2. Classification of genetic disorders
3. Genetic metabolic disorders
4. Inherited disorders (by type of inheritance): autosomal-dominant, autosomal-recessive, X-linked dominant inheritance, X-linked recessive inheritance, Y-linked inheritance
5. Chromosome disorders: structural and numerical aberrations
6. Mitochondrial disorders
7. Multifactorial disorders
8. Imprinting disorders

General characteristics of genetic disorders

- A **genetic disorder** is a genetic problem caused by one or more abnormalities formed in the genome. Most genetic disorders are quite rare and affect one person in every several disease thousands or millions.
- Genetic disorders may be hereditary or non-hereditary, meaning that they are passed down from the parents' genes. However, in some genetic disorders, defects may be caused by new mutations or changes to the DNA.

Classification of genetic disorders

- **Chromosomal disorders**

  - Whole or part of a chromosome is missing or duplicated. These are large enough to be seen on a standard karyotype.

  Examples: Trisomy 21, Cri-du-chat, Turner, Kleinfelter

- Microdeletion or microduplication

  - Part of a chromosome is missing or duplicated. These are often too small to be seen on a standard karyotype

  Examples: DiGeorge syndrome, Prader-Willi syndrome (deletion type), Smith-Magenis syndrome, Williams syndrome

- **Single gene disorders**

  - A mutation on a single gene. May be autosomal dominant, autosomal recessive, X-linked.

  Examples: Cystic fibrosis, Duchene muscular dystrophy, Marfan syndrome, Sickle cell anemia

- **Triplet repeat disorders**

  - Exceeding the number of normal trinucleotide repeats in genes. The normal number varies depending on the gene.

  - Examples: Fragile X, Huntington's disease

Classification of genetic disorders

- **Epigenetic disorders**

  - The genetic sequence is not changed, but the expression of the DNA is altered

  Examples: Angleman, Beckwith-Wiedemann syndrome, Prader-Willi (methylation or isodisomy type)

- **Multifactorial disorders**

  - Combination of genetics and environment

  Examples: isolated congenital heart defects, cleft lip and palate, pyloric stenosis

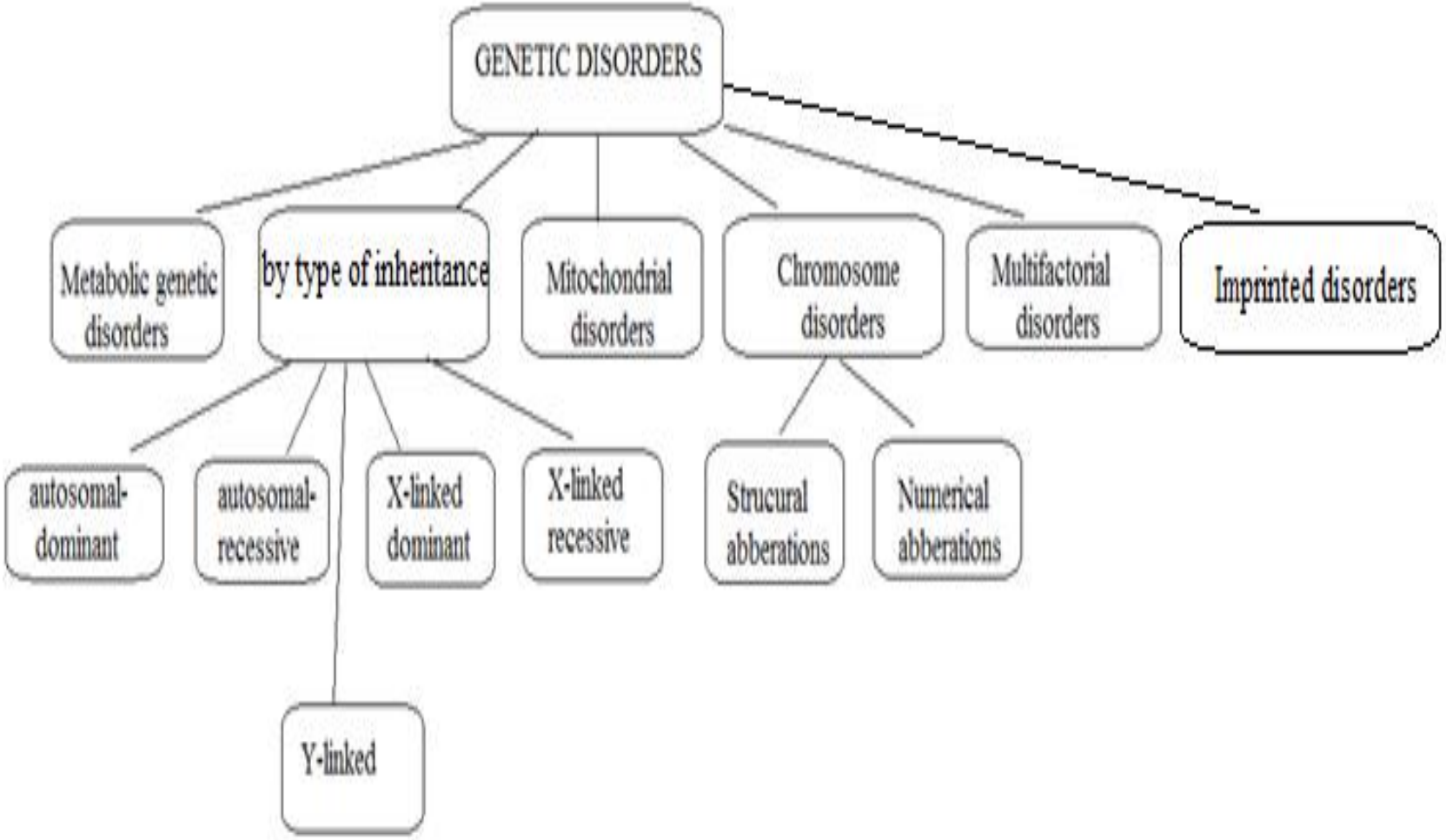
- **Miscellaneous**

  - Not otherwise categorized, and also includes:
  - Associations or non-random association of anomies without a known genetic basis,

  Example is CHARGE association

  - Disruptions or morphological defect of a previously normal organ, example is amniotic bands
  - Sequences or one malformation leads to other malformation, example is Pierre-Robin sequence

Classification of genetic disorders



Genetic metabolic disorders

- A **genetic metabolic disorder** can happen when abnormal chemical reactions in the body alter the normal metabolic process. It can also be defined as inherited single gene anomaly, most of which are autosomal recessive.
- Genetic metabolic disorders are one cause of metabolic disorders, and occur when a defective gene causes an enzyme deficiency.

Genetic metabolic disorders

- Some of the more common and important genetic metabolic disorders include:
- **Lysosomal storage disorders**: Lysosomes are spaces inside cells that break down waste products of metabolism. Various enzyme deficiencies inside lysosomes can result in buildup of toxic substances.
- **Maple syrup urine disease**: Deficiency of an enzyme called BCKD (branched-chain ketoaciduria) causes buildup of amino acids in the body. Nerve damage results, and the urine smells like syrup.
- **Phenylketonuria** (PKU): Deficiency of the enzyme PAH (phenylalanine hydroxylase) results in high levels of phenylalanine in the blood. Intellectual disability results if the condition is not recognized.
- **Glycogen storage diseases**: Problems with sugar storage lead to low blood sugar levels, muscle pain, and weakness.
- **Mitochondrial disorders**: Problems inside mitochondria, the powerhouses of cells, lead to muscle damage.
- **Friedreich ataxia**: Problems related to a protein called frataxin cause nerve damage and often heart problems. Inability to walk usually results by young adulthood.
- **Peroxisomal disorders**: Similar to lysosomes, peroxisomes are tiny spaces filled with enzymes inside cells. Poor enzyme function inside peroxisomes can lead to buildup of toxic products of metabolism.
- **Metal metabolism disorders:** Levels of trace metals in the blood are controlled by special proteins. Inherited metabolic disorders can result in protein malfunction and toxic accumulation of metal in the body.

Genetic metabolic disorders

- The symptoms of genetic metabolic disorders vary widely depending on the metabolism problem present. Some symptoms of inherited metabolic disorders include:

  -Lethargy

  -Poor appetite

  -Abdominal pain

  -Vomiting

  -Weight loss

  -Jaundice

  -Failure to gain weight or grow

  -Developmental delay

  -Seizures

  -Coma

  -Abnormal odour of urine, breath, sweat, or saliva.

Genetic metabolic disorders

- **Galactosemia** is a genetic metabolic disease that affect an individual's ability to convert of galactose to glucose.
- Lactose in food is broken down by the enzyme lactase into glucose and galactose. In individuals with galactosemia, the enzymes needed for further metabolism of galactose (Galactokinase and galactose-1-phosphate uridyltransferase) are severely diminished or missing entirely, leading to toxic levels of galactose or galactose 1-phosphate (depending of which enzyme is missing) in various tissues as in the case of classic galactosemia, resulting in hepatomegaly (an enlarged liver), cirrhosis, kidney failure, cataracts, vomiting, seizure, low blood sugar (hypoglycemia), lethargy, brain damage, and ovarian failure.

Genetic metabolic disorders

Galactosemia (GAL)

- GAL is a condition in which the body is unable to process galactose, the sugar present in milk. Accumulation of excessive galactose in the body can cause many problems, including liver damage, brain damage and cataracts.

Genetic metabolic disorders

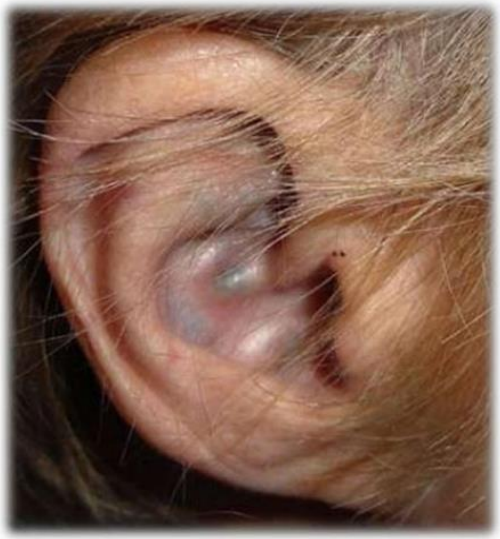
- **Alkaptonuria** (black urine disease, black bone disease, or alcaptonuria) is inherited genetic metabolic disorder in which the body cannot process the amino acids phenylalanine and tyrosine, which occur in protein. It is caused by a mutation in the HGD gene for the enzyme homogentisate 1,2-dioxygenase.

Genetic metabolic disorders

SYMPTOMS

- Urine in an infant's diaper may darken and can turn almost black after several hours. However, many persons with this condition may not know they have it until mid-adulthood (around age 40), when joint and other problems occur.
- Arthritis (especially of the spine) that gets worse over time
- Darkening of the ear
- Dark spots on the white of the eye (sclera) and cornea

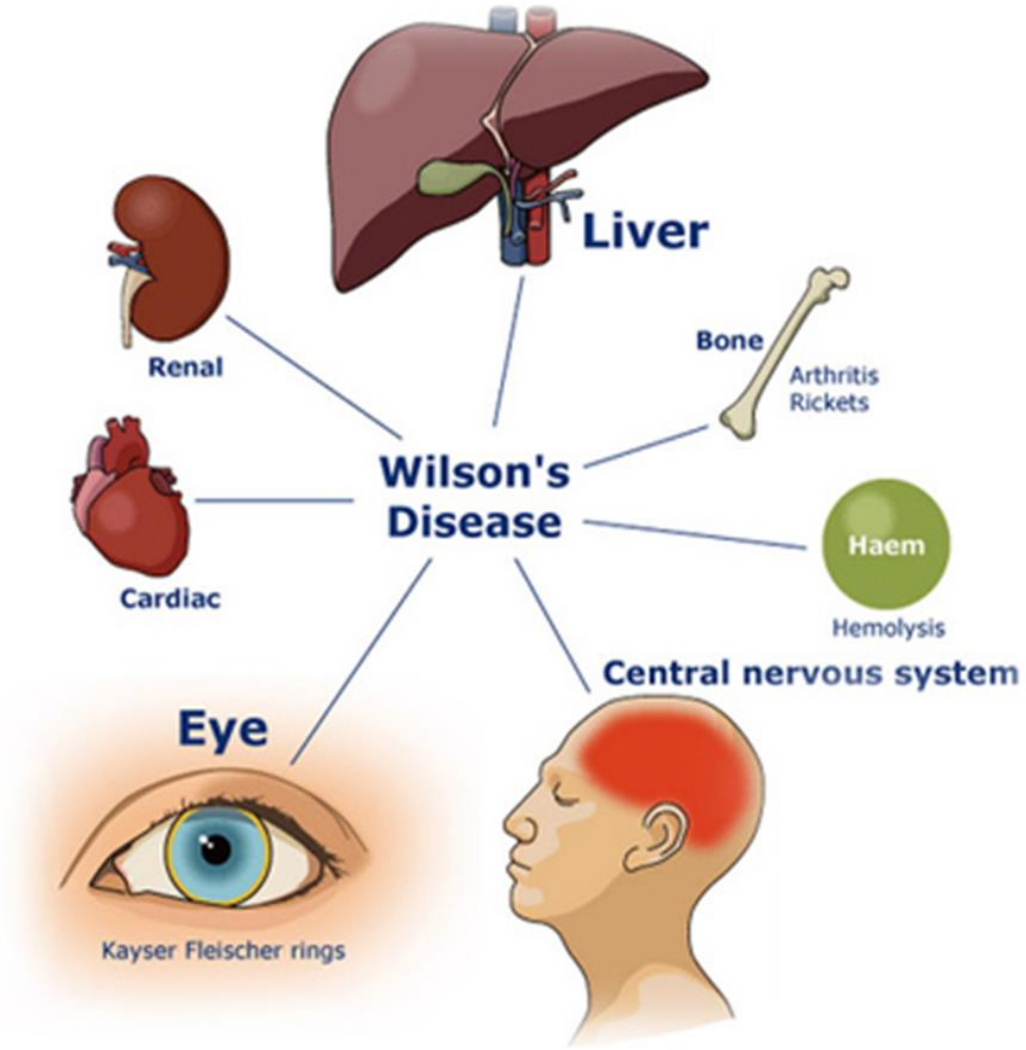
Genetic metabolic disorders

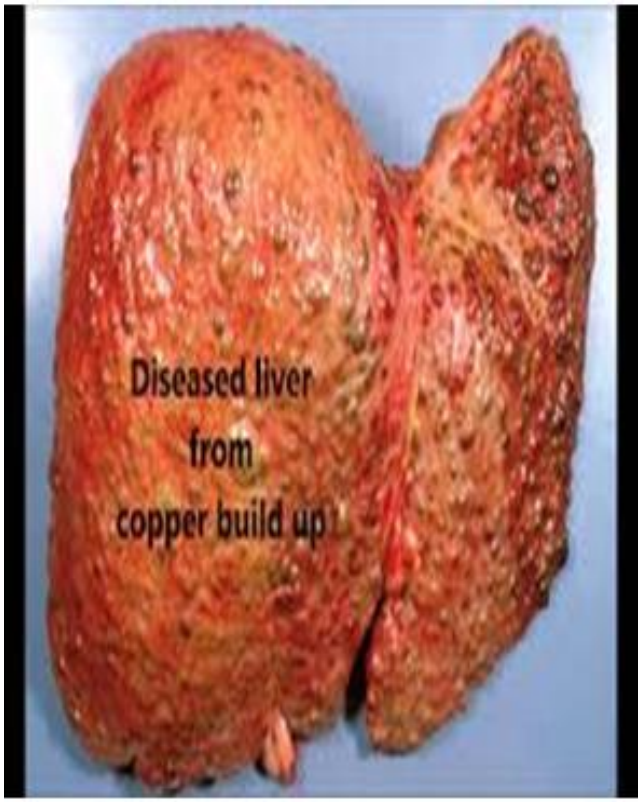


Genetic metabolic disorders

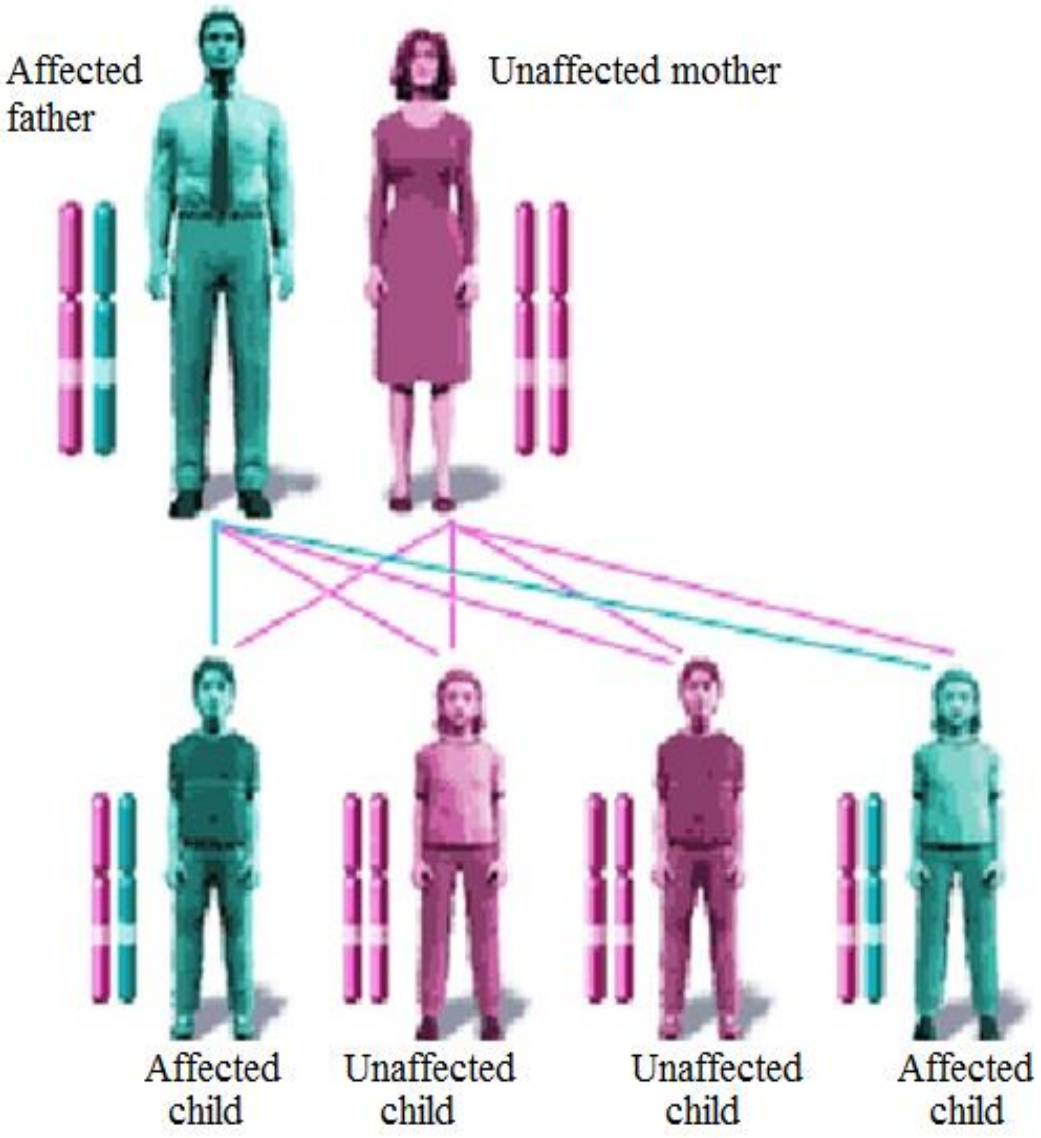
- **Wilson's disease** is a genetic metabolic disorder in which copper builds up in the body. Symptoms are typically related to the brain and liver.
- Liver related symptoms include vomiting, weakness, fluid build up in the abdomen, swelling of the legs, yellowish skin, and itchiness.
- Brain related symptoms include tremors, muscle stiffness, trouble speaking, personality changes, anxiety, and seeing or hearing things that others do not.
- Wilson's disease is an autosomal recessive condition due to a mutation in the Wilson disease protein (ATP7B) gene.

Genetic metabolic disorders





Autosomal-dominant disorders



- The mutated gene is dominant and presents in one parent.
- The children have a 50% chance of being affected.

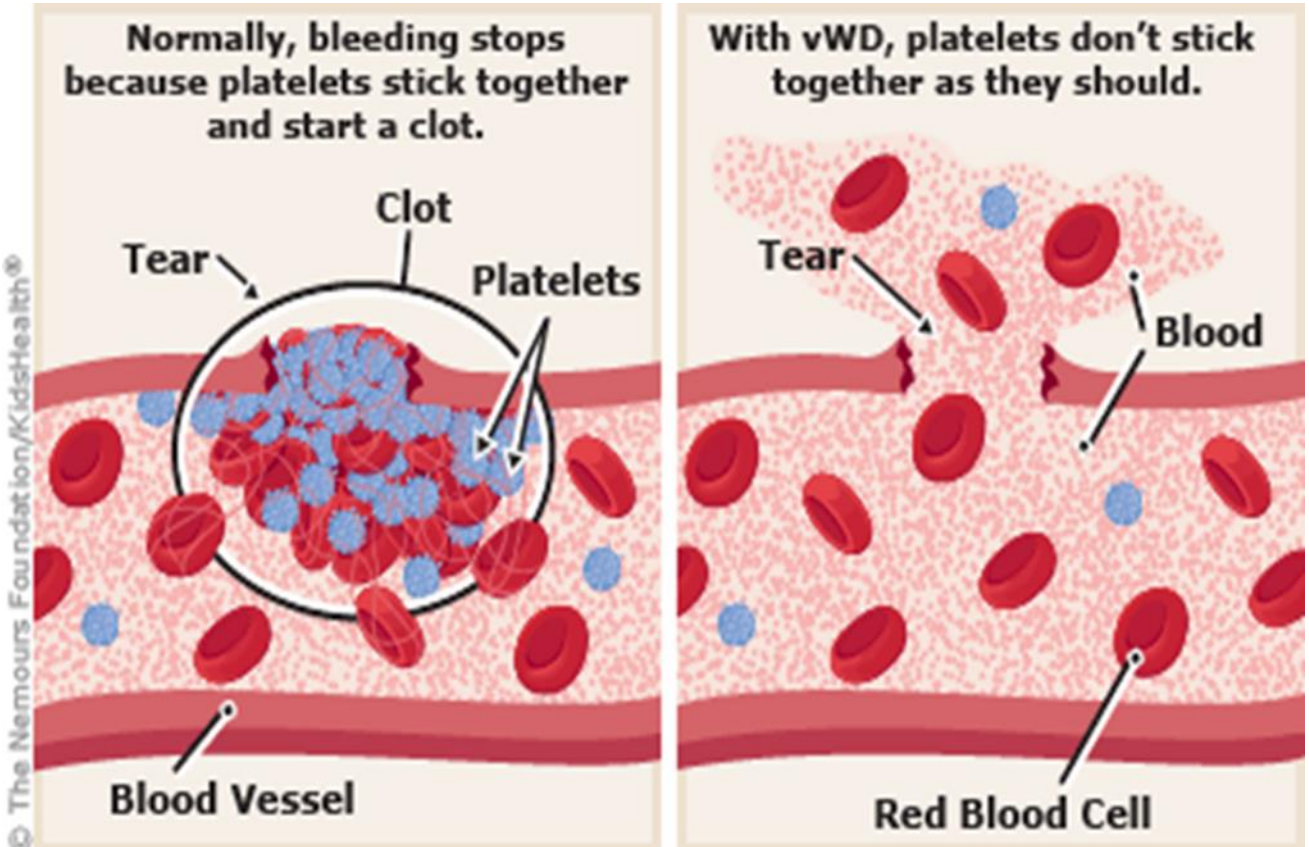
Autosomal-dominant disorders

- **Von Willebrand disease** is a lifelong bleeding disorder in which blood doesn't clot well. It takes its name from Dr. Erik von Willebrand, who first described the condition in 1926.
- Most people with the disease are born with it, though its warning signs may not show up for years.
- Von Willebrand disease is the most common inherited bleeding disorder, affecting about 1% of the population.

Autosomal-dominant disorders

Symptoms:

- Excessive bleeding from an injury or after surgery or dental work
- Nosebleeds that don't stop within 10 minutes
- Heavy or long menstrual bleeding
- Blood in urine or stool
- Easy bruising or lumpy bruises



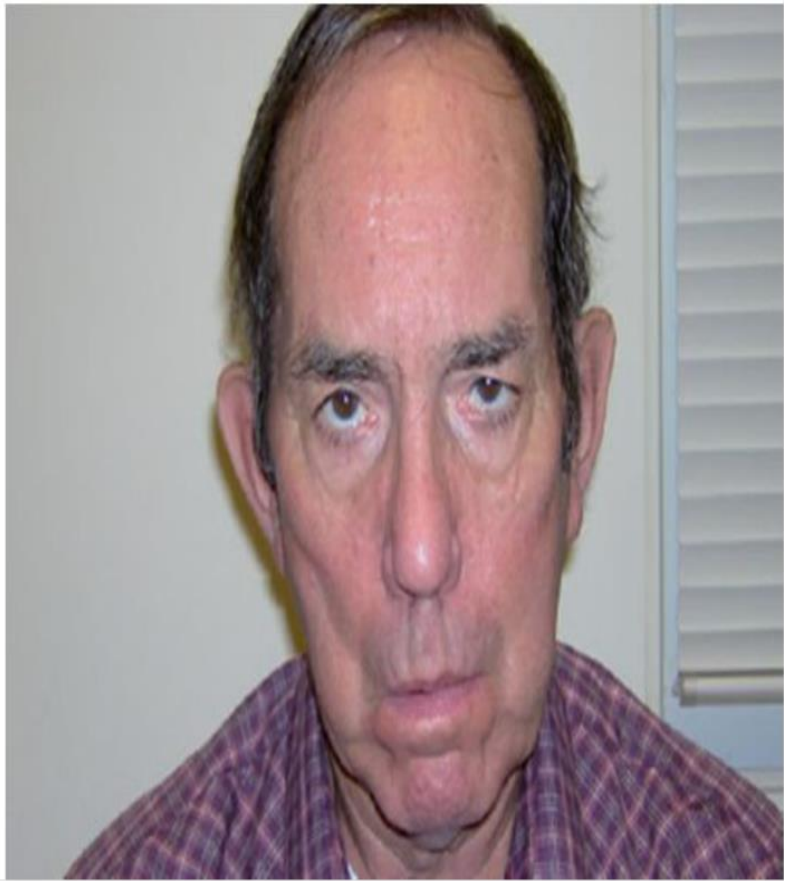
Autosomal-dominant disorders

- **Myotonic dystrophy** is characterized by progressive muscle wasting and weakness. People with this disorder often have prolonged muscle contractions (myotonia) and are not able to relax certain muscles after use. For example, a person may have difficulty releasing their grip on a doorknob or handle. Also, affected people may have slurred speech or temporary locking of their jaw.

Autosomal-dominant disorders

Symptoms:

- cataract formation,
- hypogonadism,
- frontal balding,
- cardiac disorders.



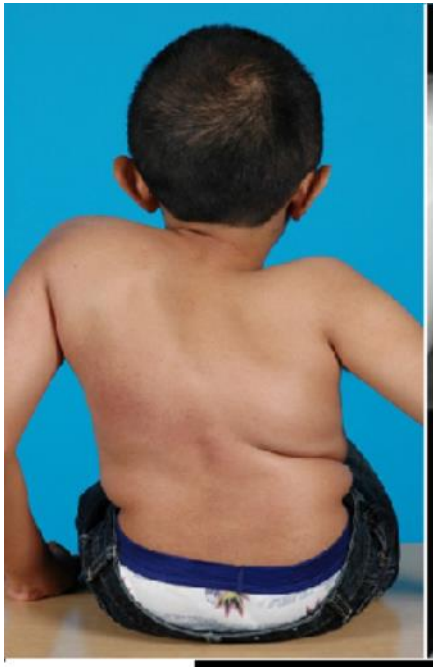
Autosomal-dominant disorders

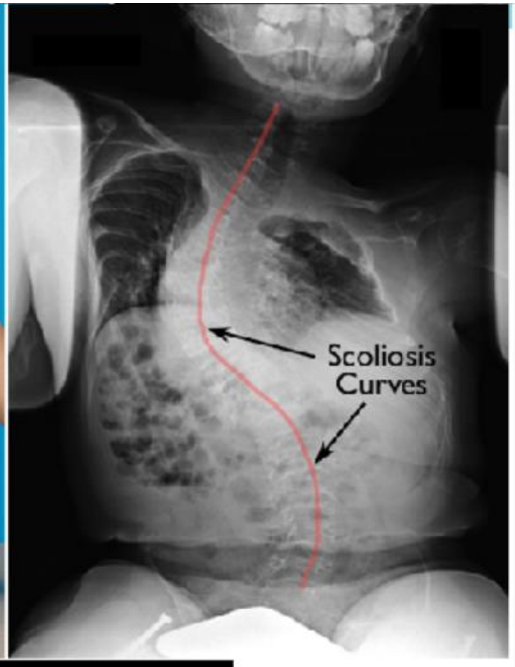
- **Osteogenesis imperfecta** (OI), also known as brittle bone disease, is a group of genetic disorders that mainly affect the bones. It results in bones that break easily.
- The majority of cases of OI (possibly 85-90 %) are caused by a mutation in a gene coding for collagen (collagen is the major protein of the body's connective tissue).

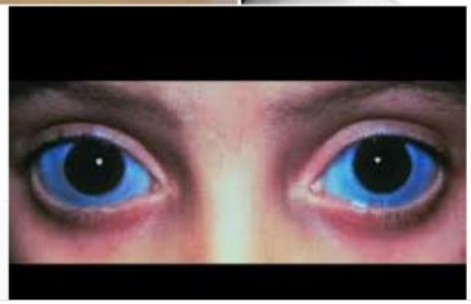
Autosomal-dominant disorders

Symptoms:

- Bones that break easily,
- Blue tinge to the whites of the eye,
- Short height,
- Loose joints,
- Hearing loss.







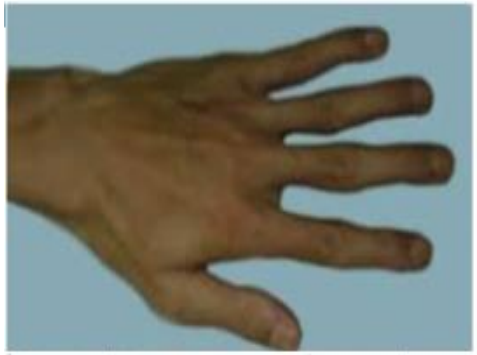
Autosomal-dominant disorders

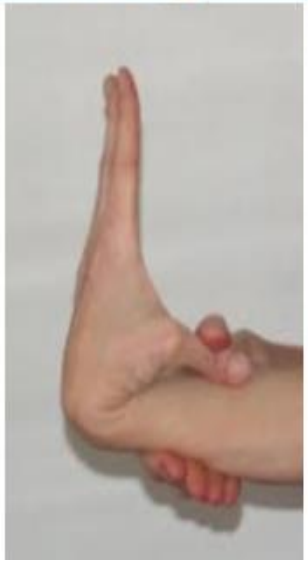
- **Marfan syndrome** is a genetic disorder that affects the body's connective tissue.
- Connective tissue is made up of proteins. The protein that plays a role in Marfan syndrome is called fibrillin-1. Marfan syndrome is caused by mutation in the gene that tells the body how to make fibrillin-1.

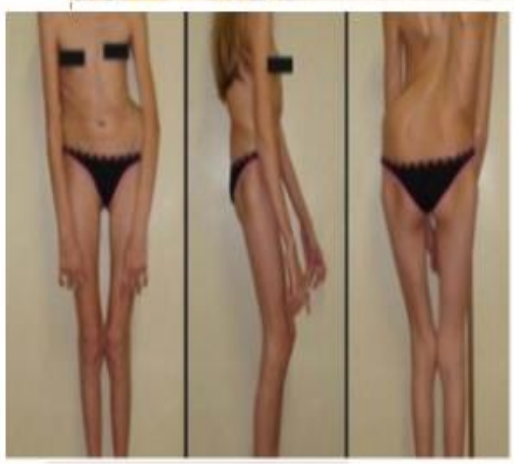
Autosomal-dominant disorders

Symptoms:

- - Long arms, legs and fingers
- - Tall and thin body type
- - Curved spine
- - Chest sinks in or sticks out
- - Flexible joints
- - Flat feet
- - Crowded teeth
- - Stretch marks on the skin that are not related to weight gain or loss







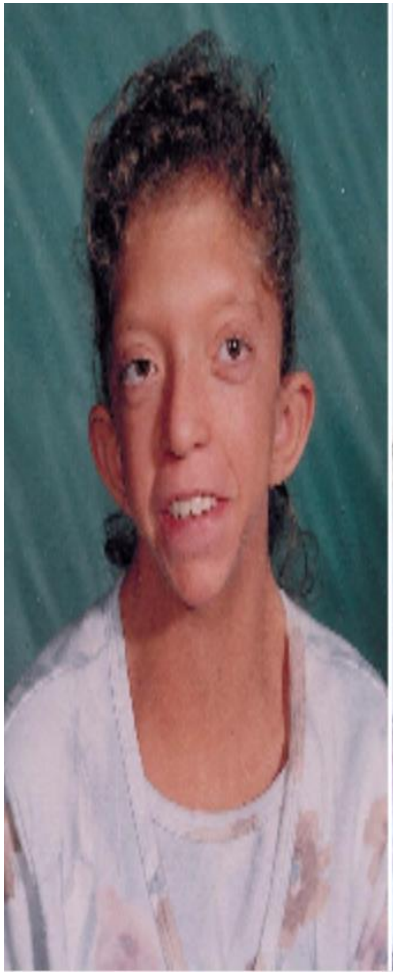
Autosomal-dominant disorders

- **Noonan syndrome** is a relatively common autosomal dominant congenital disorder and is named after Jacqueline Noonan, a pediatric cardiologist. It is referred to as the male version of Turner's syndrome; however, the genetic causes of Noonan syndrome and Turner syndrome are distinct and both males and females are affected.

Autosomal-dominant disorders

Symptoms:

- congenital heart defect (typically pulmonary valve stenosis with dysplastic pulmonary valve also atrial septal defect and hypertrophic cardiomyopathy),
- short stature, learning problems,
- impaired blood clotting,
- a characteristic configuration of facial features including a webbed neck and a flat nose bridge.



Autosomal-dominant disorders

- **Huntington's disease**, also known as Huntington's chorea, is an inherited disorder that results in death of brain cells.
- Symptoms of Huntington's disease most commonly become noticeable between the ages of 35 and 44 years, but they can begin at any age from infancy to old age.

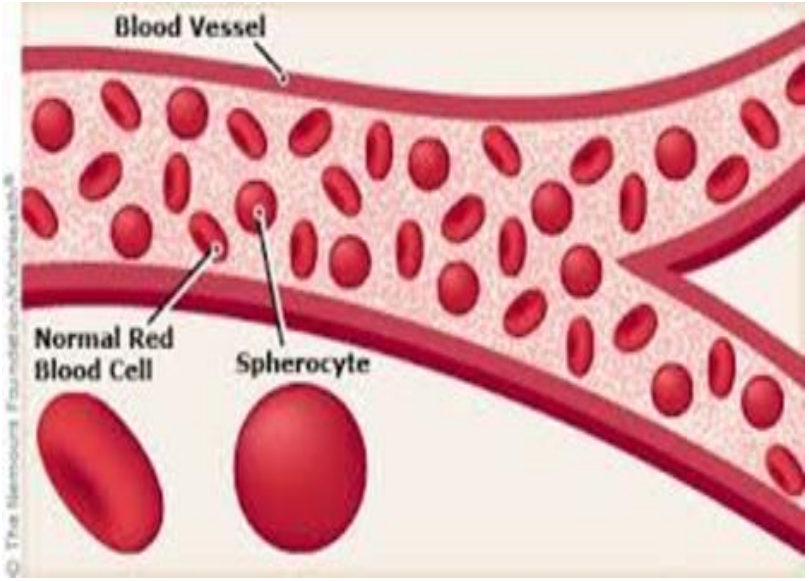
Autosomal-dominant disorders

Symptoms:

- Personality changes, mood swings and depression
- Forgetfulness and impaired judgment
- Unsteady gait and involuntary movements (chorea)
- Slurred speech, difficulty in swallowing and significant weight loss

Autosomal-dominant disorders

- **Hereditary spherocytosis** (also known as Minkowski–Chauffard syndrome) is an autosomal dominant abnormality of erythrocytes. The disorder is caused by mutations in genes relating to membrane proteins that allow for the erythrocytes to change shape. The abnormal erythrocytes are sphere-shaped (spherocytosis) rather than the normal biconcave disk shaped.
- As a result of this shape change, the red cells lose their ability to circulate freely through narrow capillaries in the body. The resulting spherocytes become trapped in the spleen as they course through the sinuses, and the red cells are engulfed by macrophages.
- Symptoms: shortage of red blood cells (anemia), yellowing of the eyes and skin (jaundice), enlarged spleen (splenomegaly).

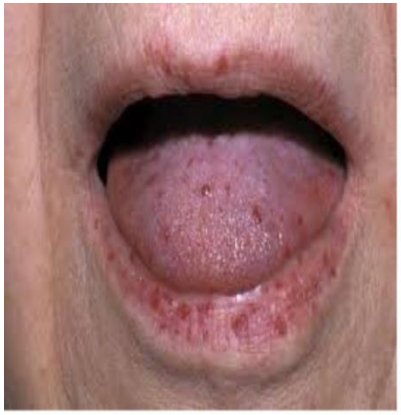


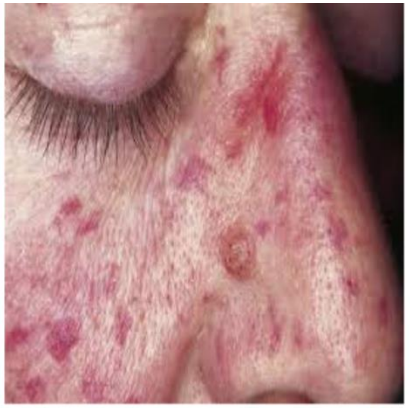
Autosomal-dominant disorders

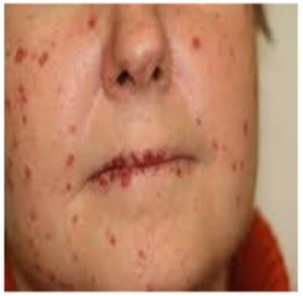
- **Hereditary hemorrhagic telangiectasia** (HHT), also known as Osler–Weber–Rendu syndrome, is a rare autosomal dominant genetic disorder that leads to abnormal blood vessel formation in the skin, mucous membranes, and often in organs such as the lungs, liver, and brain.
- People with HHT have a faulty gene, which is usually inherited from one of their parents. This gene normally provides instructions for making certain proteins found in the lining of the blood vessels. In HHT, the gene can't produce this protein, or the protein it produces is abnormal.

Autosomal-dominant disorders

- In HHT some arterial vessels flow directly into veins rather than into the capillaries. These abnormalities are called arteriovenous malformations. When they occur in vessels near the surface of the skin, where they are visible as red markings, they are known as telangiectases

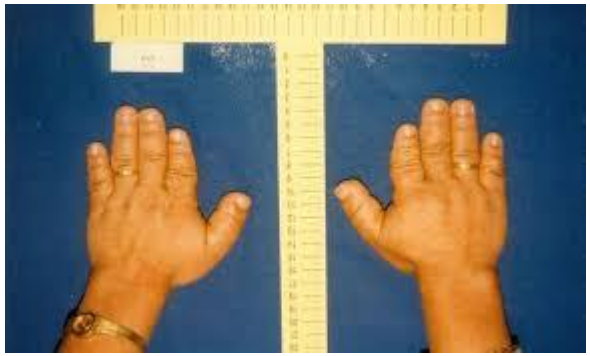




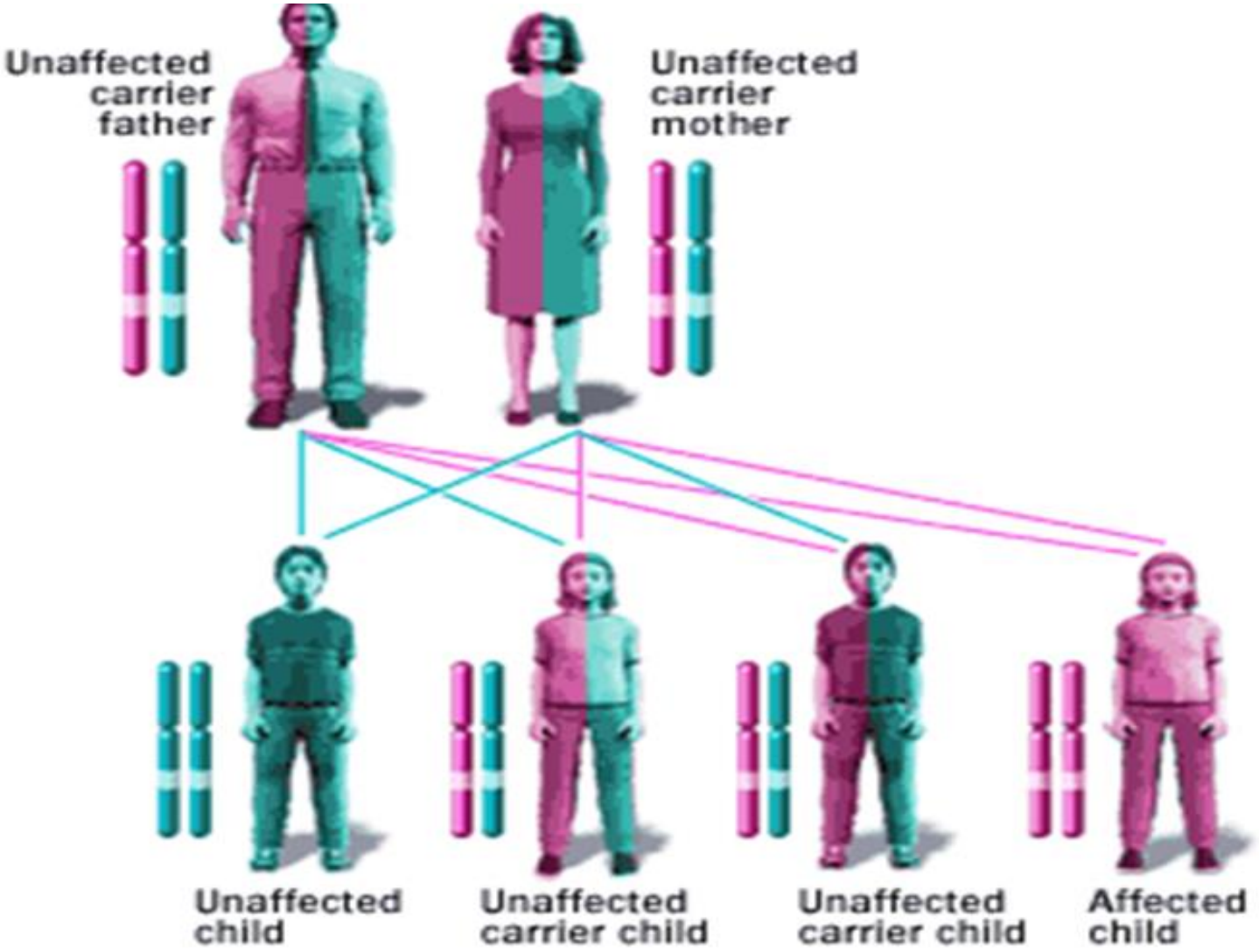


Autosomal-dominant disorders

- **Brachydactyly** is a medical term which literally means "shortness of the fingers and toes" (digits). It can also occur with other anomalies as part of many congenital syndromes.
- Brachydactyly can also be a signal that one will be at risk for heart problems as they age.
- In some cases, it's possible that brachydactyly is caused by exposure to medications that the mother takes during pregnancy. It may also be caused by blood flow problems to the hand and feet, especially in developing babies.



Autosomal-recessive disorders



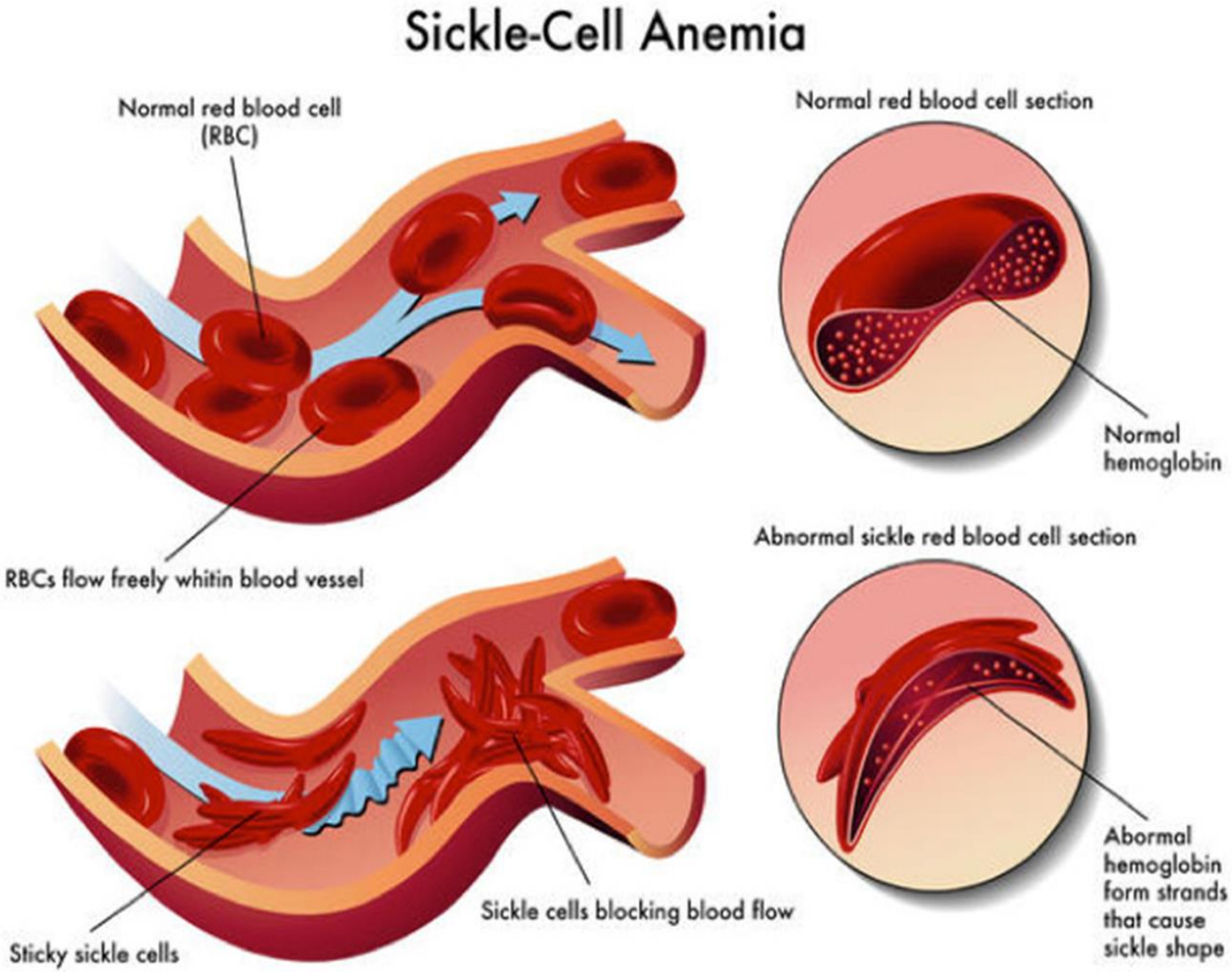
Autosomal-recessive disorders

- **Phenylketonuria**, PKU is an inherited disorder that increases the levels of a substance called phenylalanine in the blood.
- It is due to mutations in the phenylalanine hydroxylase (PAH) gene which results in low levels of the enzyme phenylalanine hydroxylase. The PAH gene is located on chromosome 12 in the bands 12q22-q24.1
- If PKU is not treated, phenylalanine can build up to harmful levels in the body, causing intellectual disability and other serious health problems.

Autosomal-recessive disorders

- **Sickle-cell anaemia** (SCA) results in an abnormality in the oxygen-carrying protein haemoglobin (hemoglobin S) found in red blood cells. This leads to a rigid, sickle-like shape under certain circumstances. Problems in sickle cell disease typically begin around 5 to 6 months of age.
- Normally, humans have haemoglobin A, which consists of two alpha and two beta chains, haemoglobin A2, which consists of two alpha and two delta chains, and haemoglobin F, consisting of two alpha and two gamma chains in their bodies. Out of these three types, haemoglobin F dominates until about 6 weeks of age. Afterwards, haemoglobin A dominates throughout life. In people diagnosed with sickle cell disease, at least one of the β-globin subunits in hemoglobin A is replaced with what's known as hemoglobin S.
- A number of health problems may develop, such as attacks of pain ("sickle-cell crisis"), anemia, swelling in the hands and feet, bacterial infections, and stroke.

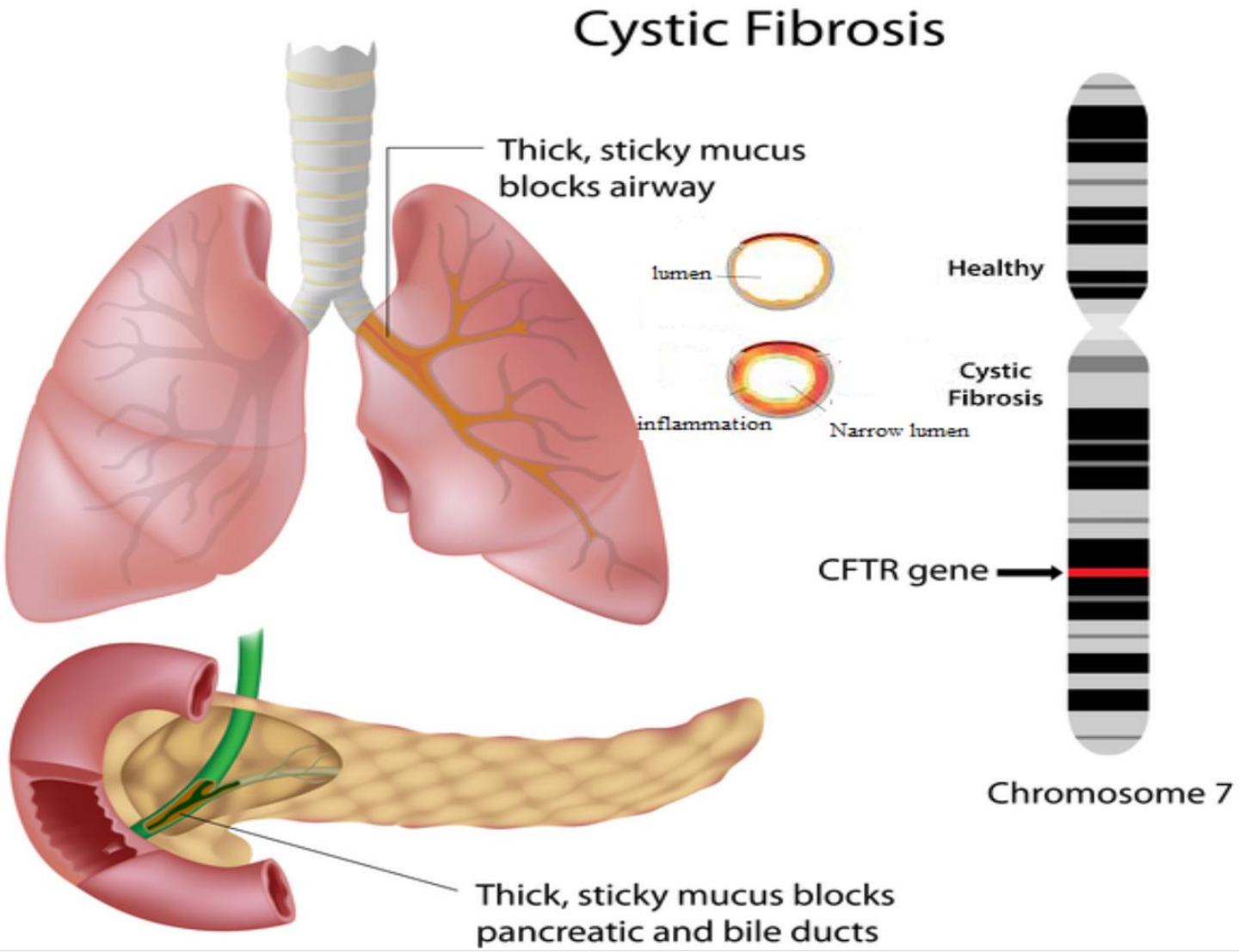
Autosomal-recessive disorders



Autosomal-recessive disorders

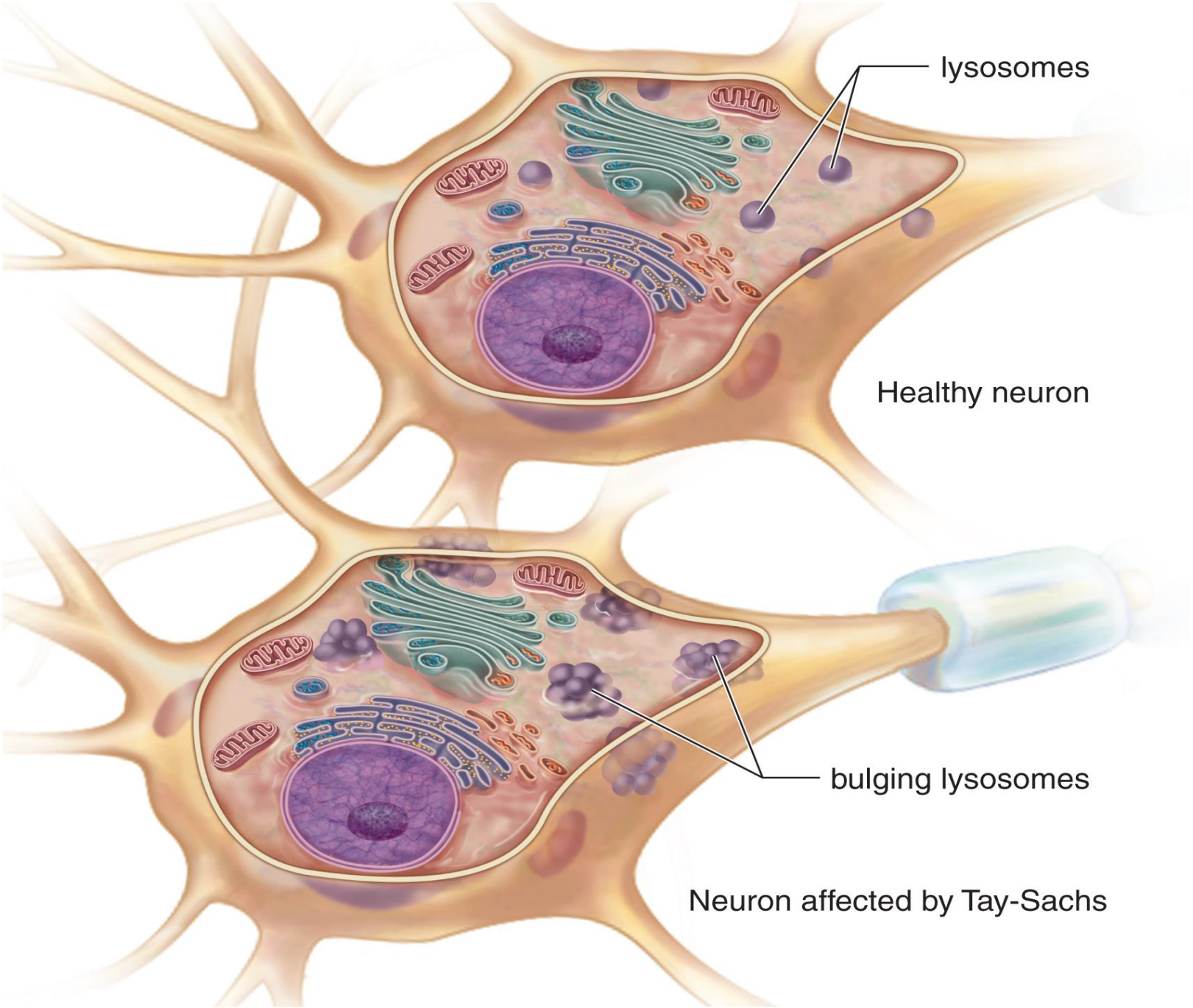
- **Mucoviscidosis, another name for cystic fibrosis**, is a genetic disorder that affects mostly the lungs, but also the pancreas, liver, kidneys, and intestine.
- It is caused by the presence of mutations in both copies of the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein.
- When CFTR is not functional, secretions which are usually thin instead become thick. This abnormal mucus can clog the airways, leading to severe problems with breathing and bacterial infections in the lungs.

Autosomal-recessive disorders



Autosomal-recessive disorders

- **Tay-Sachs disease** is a rare disorder in which deficiency of an enzyme (hexosaminidase A) results in excessive accumulation of certain fats (lipids) known as gangliosides in the brain and nerve cells. This abnormal accumulation of gangliosides leads to progressive dysfunction of the central nervous system.
- This disorder is categorized as a lysosomal storage disease. Lysosomes are the major digestive units in cells. When an enzyme like hexosaminidase A, which are needed to breakdown certain substances like fats, are missing or ineffective, they build up in the lysosome. This is called abnormal "storage". When too much fatty material builds up in the lysosome, it becomes toxic destroying the cell and damaging surrounding tissue.
- Tay–Sachs disease is caused by a genetic mutation in the HEXA gene on chromosome 15.
- Symptoms include muscle weakness, loss of muscle coordination (ataxia) and other problems with movement, speech problems, and mental illness.



Chromosome disorders

- A **chromosome disorder** results from a change in the number or structure of chromosomes.
- There are two main types of chromosomal abnormality which can occur during meiosis and fertilization: numerical aberrations and structural aberrations.

Chromosome disorders

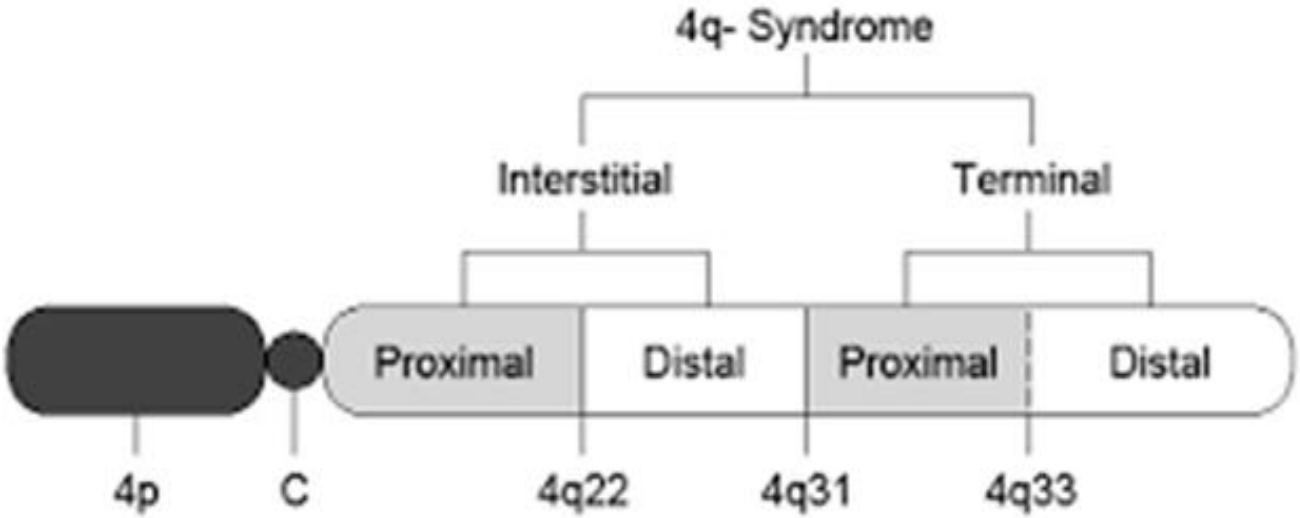
- **Structural abnormalities:** These occur due to a loss or genetic material, or a rearrangement in the location of the genetic material.
- Structural abnormalities include: deletions, duplications, inversions, ring formations, and translocations.

Chromosome disorders

- **Wolf–Hirschhorn syndrome**, is a chromosomal deletion syndrome resulting from a partial deletion from the short arm of chromosome 4 (del(4p16.3)). Features include a distinct craniofacial phenotype and intellectual disability.
- The most common characteristics include a distinct craniofacial phenotype (microcephaly), growth restriction, intellectual disability, muscle hypotonia, seizures, and congenital heart defects. Less common characteristics include renal anomalies and deafness.

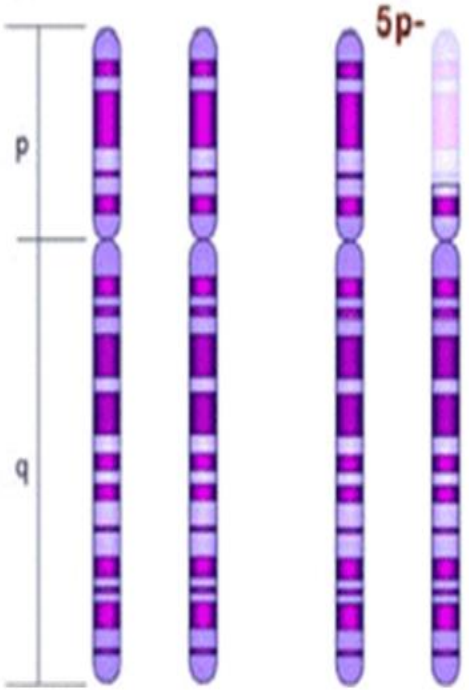
Chromosome disorders

- **Chromosome 4, monosomy distal 4q** is a rare chromosomal disorder in which there is deletion of a portion of the 4th chromosome.
- Characteristic features include growth deficiency after birth (postnatal growth retardation), varying degrees of mental retardation, malformations of the skull and facial (craniofacial) region, structural heart defects, abnormalities of the hands and feet, and other physical findings.
- Chromosome 4, monosomy distal 4q usually appears to result from spontaneous mutations during embryonic development.



Chromosome disorders

- **Cri du chat syndrome** is due to a partial deletion of the short arm of chromosome 5 ("5p monosomy"). The syndrome gets its name from the characteristic cry of affected infants, which is similar to that of a meowing kitten, due to problems with the larynx and nervous system. About one third of children lose the cry by age of 2 years.



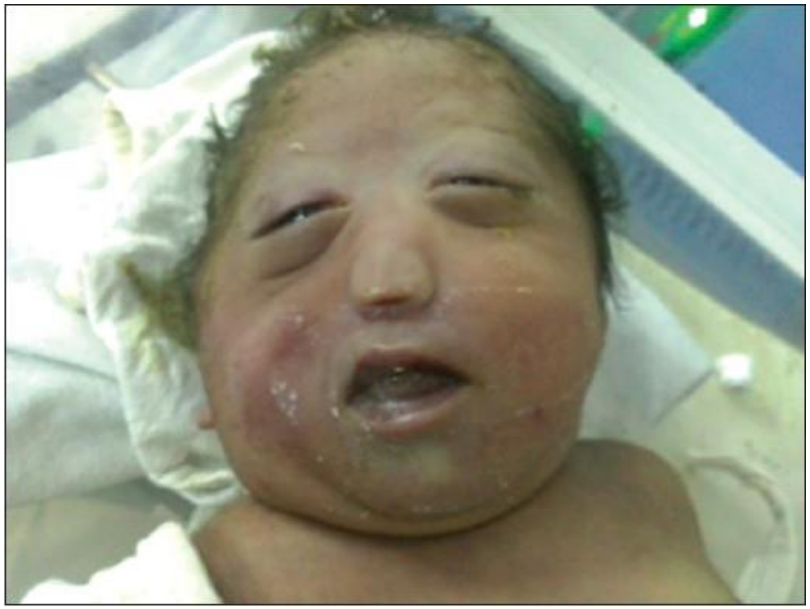
Chromosome disorders

Other symptoms of cri-du-chat syndrome may include:

- -feeding problems because of difficulty in swallowing and sucking;
- -low birth weight and poor growth;
- -severe cognitive, speech and motor disabilities;
- -behavioral problems such as hyperactivity, aggression, outbursts and repetitive movements;
- -unusual facial features, which may change over time;
- -excessive drooling;
- -small head (microcephaly) and jaw (micrognathism);
- -widely-spaced eyes (hypertelorism);
- -skin tags in front of eyes.

Chromosome disorders

- **Chromosome 18, monosomy 18p** is a rare chromosomal disorder in which all or part of the short arm (p) of chromosome 18 is deleted.
- The disorder is typically characterized by short stature, variable degrees of mental retardation, speech delays, malformations of the skull and facial (craniofacial) region, and additional physical abnormalities.



Chromosome disorders

- **Monosomy 18q** is a partial deletion of the long arm of chromosome 18 characterized by highly variable phenotype, most commonly including hypotonia, developmental delay, short stature, growth hormone deficiency, hearing loss and external ear anomalies, intellectual disability, palatal defects, dysmorphic facial features, skeletal anomalies (foot deformities, tapering fingers, scoliosis) and mood disorders.

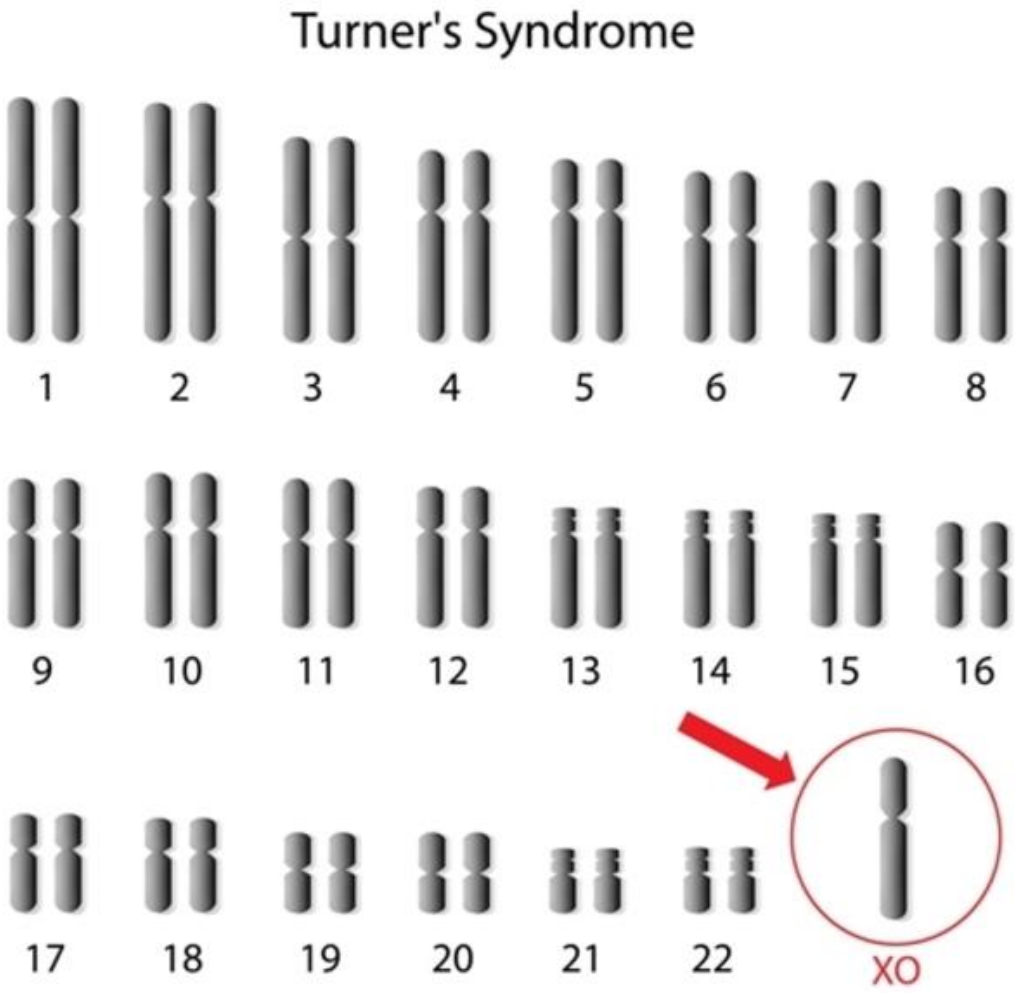
Chromosome disorders

- **Numerical aberrations**: These are usually caused by a failure of chromosome division, which results in cells with an extra chromosome or a deficiency in chromosomes.
- Numerical chromosomal aberrations result from errors in chromosome segregations during cell division.
- Common types of numerical aberrations are: triploidy, trisomy, monosomy and mosaicism.

Chromosome disorders

- **Turner syndrome, also known 45,X, or 45,X0,** is a genetic monosomy condition in which a female is completely missing an X chromosome.
- Symptoms: short and webbed neck, low-set ears, low hairline at the back of the neck, short stature, and swollen hands and feet are seen at birth.
- Typically, they develop menstrual periods and breasts only with hormone treatment, and are unable to have children. Heart defects, diabetes, and low thyroid hormone occur more frequently. Most people with Turner syndrome have normal intelligence. Many have troubles with spatial visualization that may be needed for mathematics.
- Vision and hearing problems occur more often.

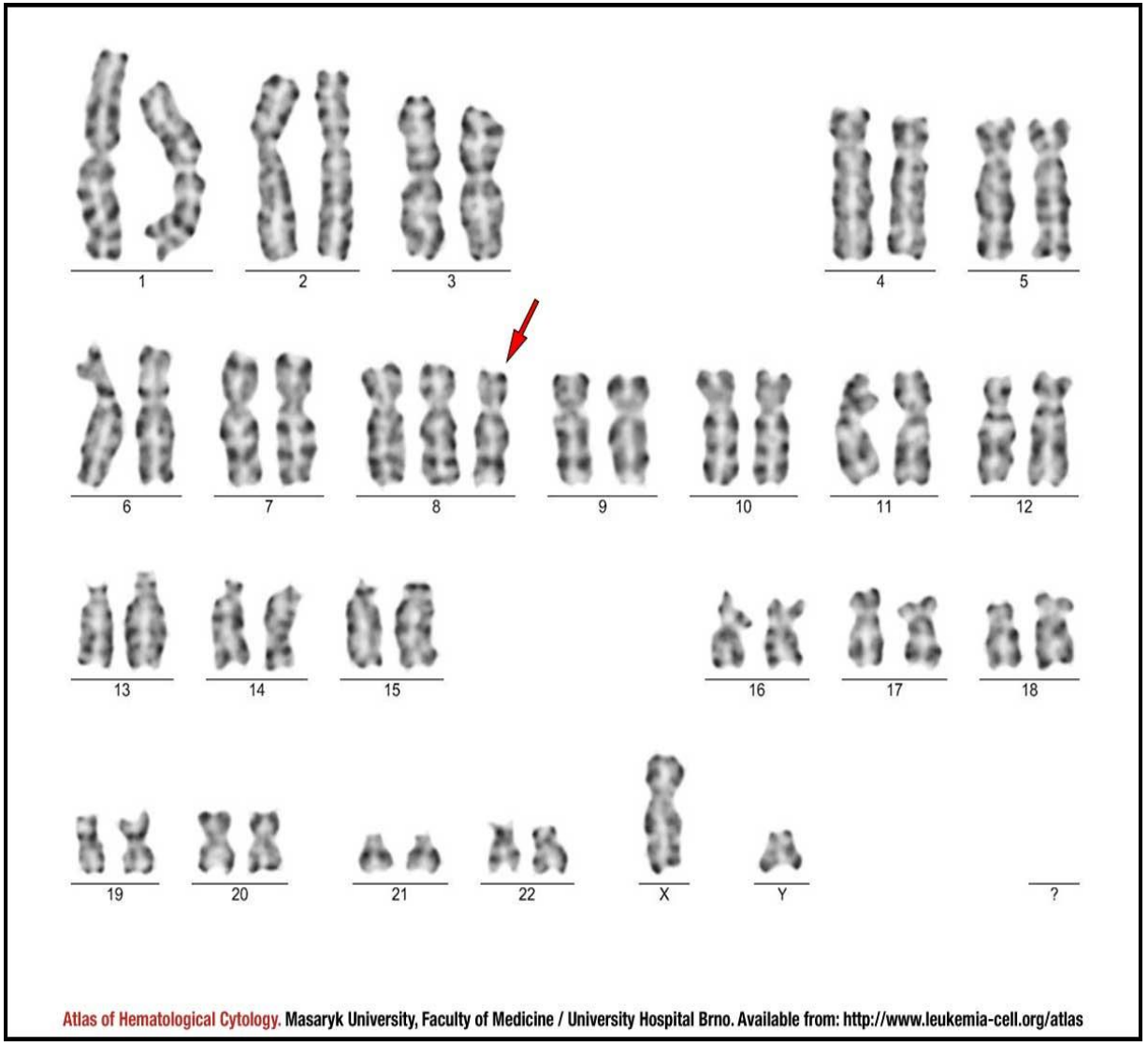
Chromosome disorders

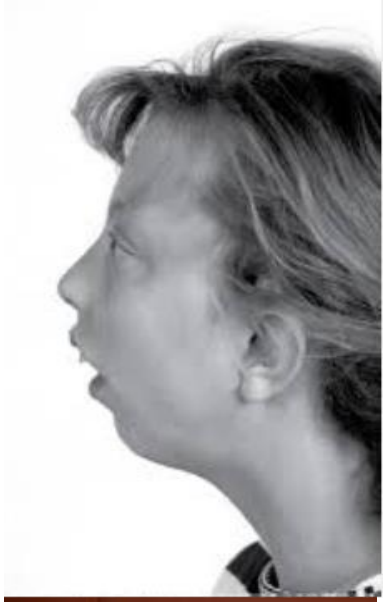


Chromosome disorders

- **Trisomy 8, also known as Warkany syndrome** is a human chromosomal disorder caused by having three copies (trisomy) of chromosome 8. It can appear with or without mosaicism.
- Complete trisomy 8 causes severe effects on the developing fetus and can be a cause of miscarriage.
- Trisomy 8 mosaicism is less severe and individuals with a low proportion of affected cells may exhibit a comparatively mild range of physical abnormalities and developmental delay. Common abnormalities of individuals include mental retardation, variable growth patterns which can result in either abnormally short or tall stature, an expressionless face, and many musculoskeletal, visceral, and eye abnormalities, as well as other anomalies.

Chromosome disorders

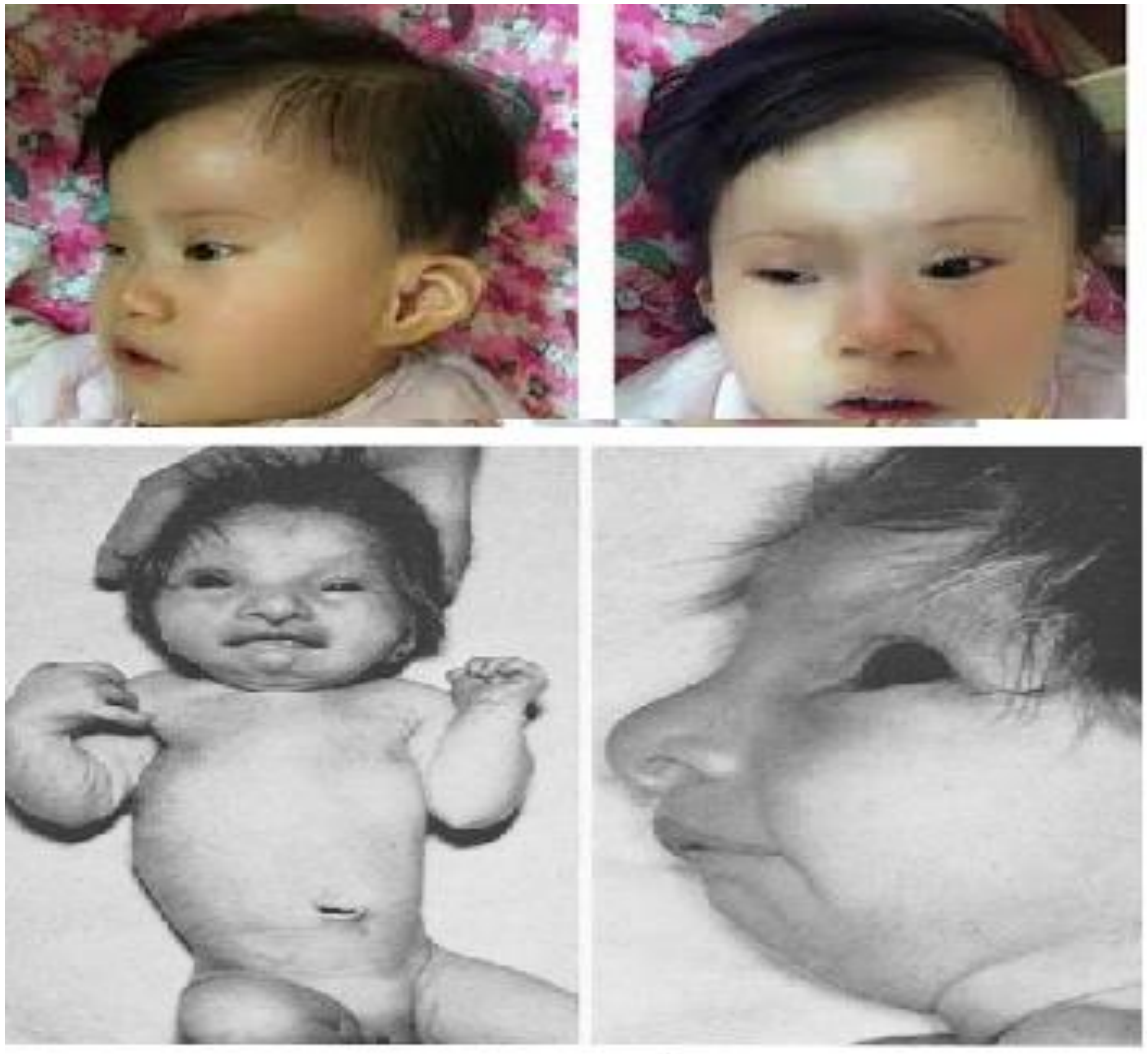




Chromosome disorders

- **Trisomy 9** is a rare chromosome disorder with high neonatal mortality. It is often seen in mosaic form. Most patients who survive are severely mentally retarded. The main features of this syndrome are "bulbous" nose, dislocated limbs, and other anomalies of skeletal, cardiac, genitourinary, and central nervous system. Most patients have developmental and cognitive impairment.

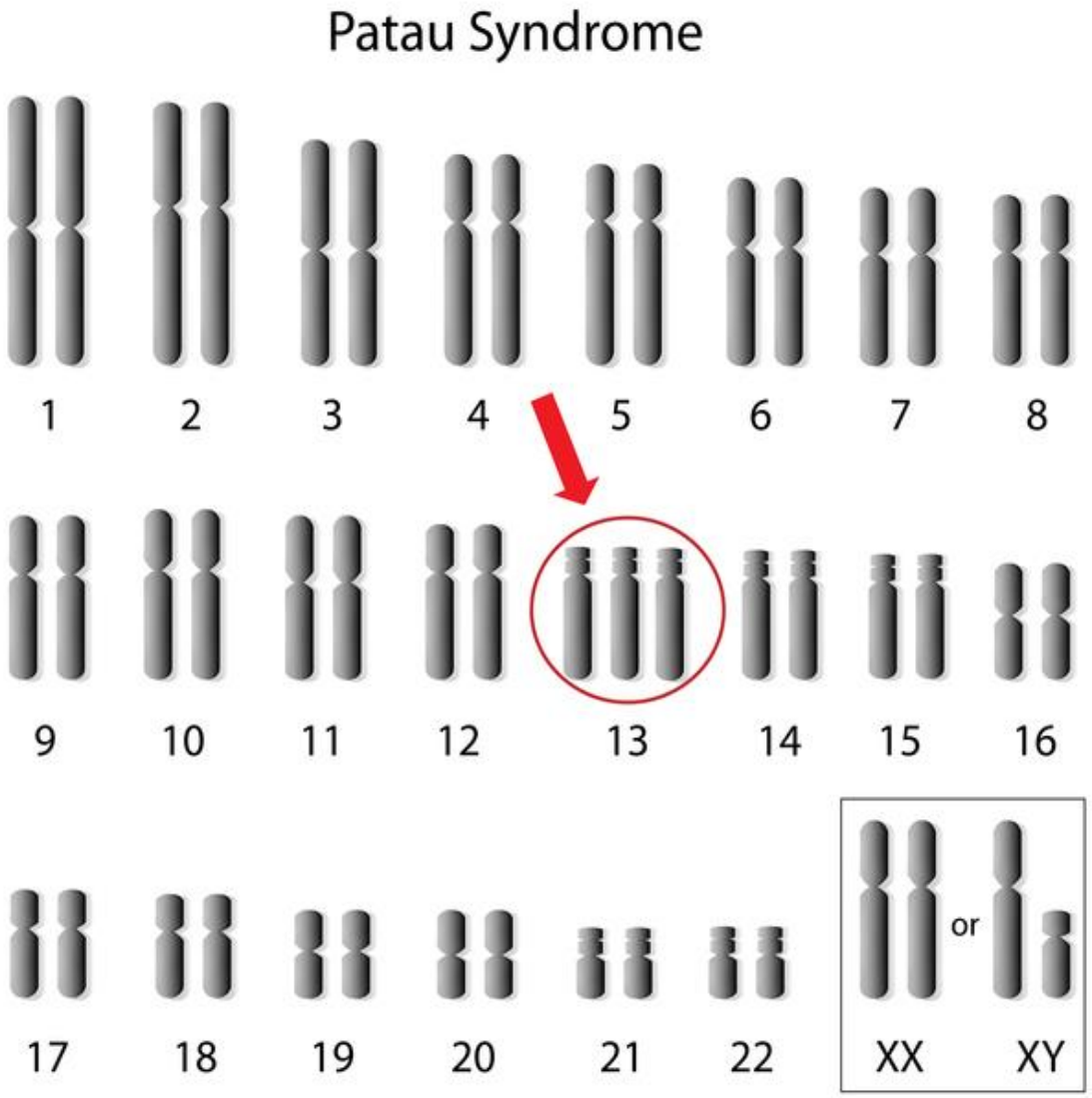
Chromosome disorders

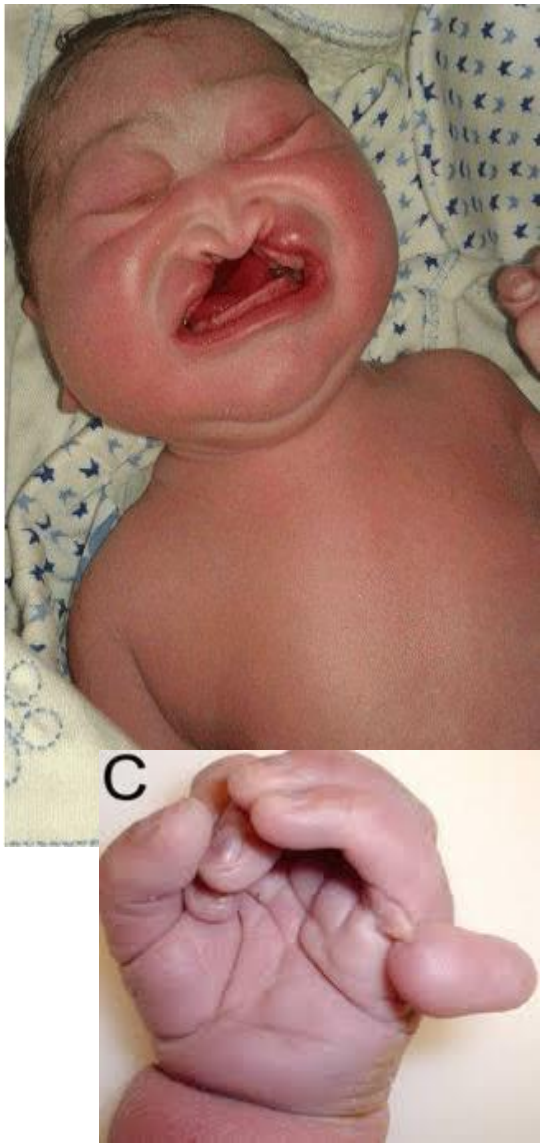


Chromosome disorders

- **Patau syndrome**, or **trisomy 13** is a syndrome caused by a chromosomal abnormality, in which some or all of the cells of the body contain extra genetic material from chromosome 13.
- The extra genetic material disrupts normal development, causing multiple and complex organ defects: intellectual disability, microcephaly, eye defects, spinal defect, polydactyly, low-set ears, overlapping of fingers over thumb, cleft palate, kidney defects, heart defects.
- Patau syndrome is the result of trisomy 13, meaning each cell in the body has three copies of chromosome 13 instead of the usual two. A small percentage of cases occur when only some of the body's cells have an extra copy; such cases are called mosaic Patau.

Chromosome disorders

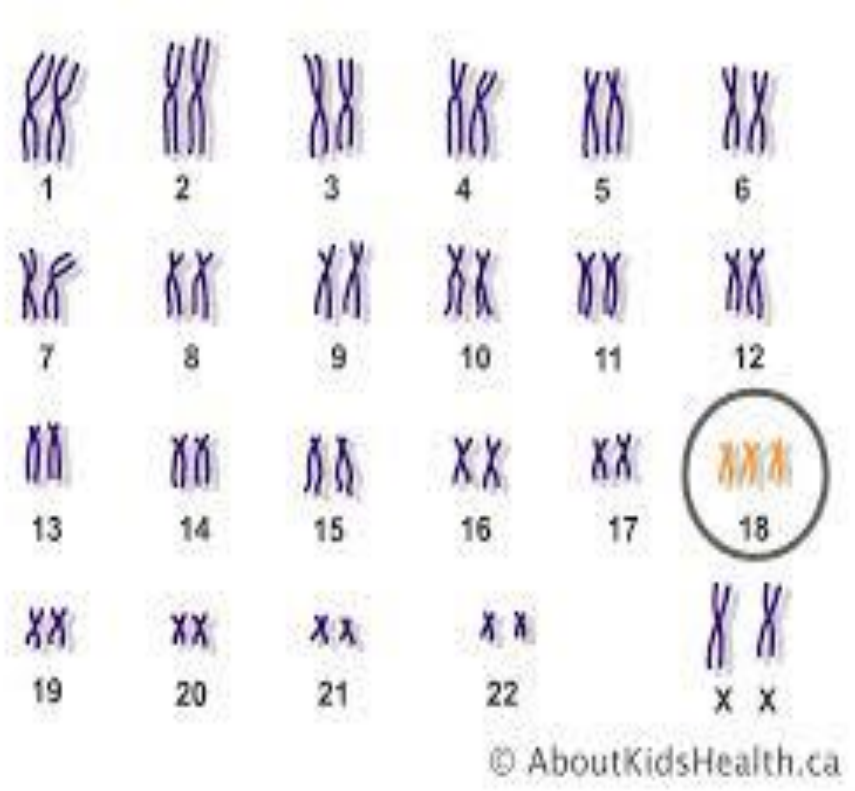


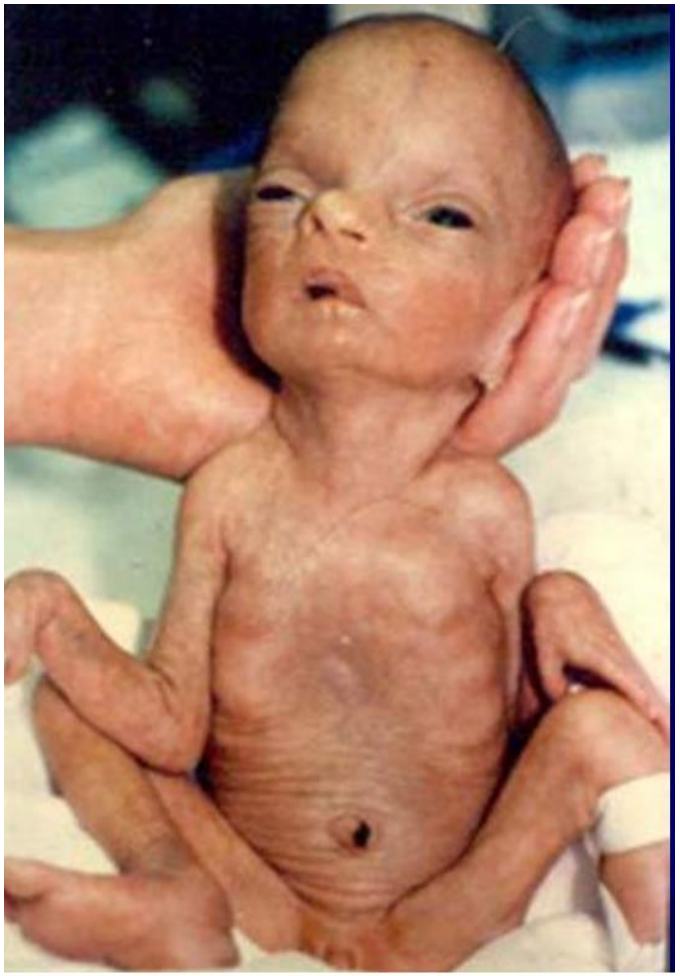


Chromosome disorders

- **Edwards syndrome**, also known as **trisomy 18**, is a genetic disorder caused by a third copy of all or part of chromosome 18 (mosaic trisomy 18 is the extra chromosome 18 is only in some of the baby's cells). This form of trisomy 18 is also rare. Many parts of the body are affected. Babies are often born small and have heart defects. Other features include a small head, small jaw, clenched fists with overlapping fingers, and severe intellectual disability.
- Trisomy 18 is caused by a meiotic nondisjunction event. With nondisjunction, a gamete (sperm or egg cell) is produced with an extra copy of chromosome 18; the gamete thus has 24 chromosomes. When combined with a normal gamete from the other parent, the embryo has 47 chromosomes, with three copies of chromosome 18.

Chromosome disorders



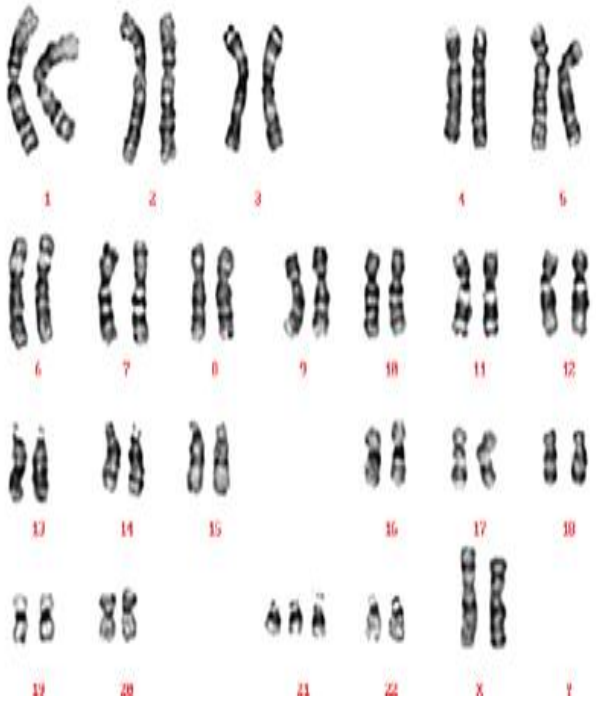


Chromosome disorders

- **Down syndrome** also known as **trisomy 21,** is a genetic disorder caused by the presence of all or part of a third copy of chromosome 21.
- Trisomy 21 is caused by a failure of the 21st chromosome to separate during egg or sperm development (nondisjunction). As a result, a sperm or egg cell is produced with an extra copy of chromosome 21; this cell thus has 24 chromosomes. When combined with a normal cell from the other parent, the baby has 47 chromosomes, with three copies of chromosome 21.

Chromosome disorders

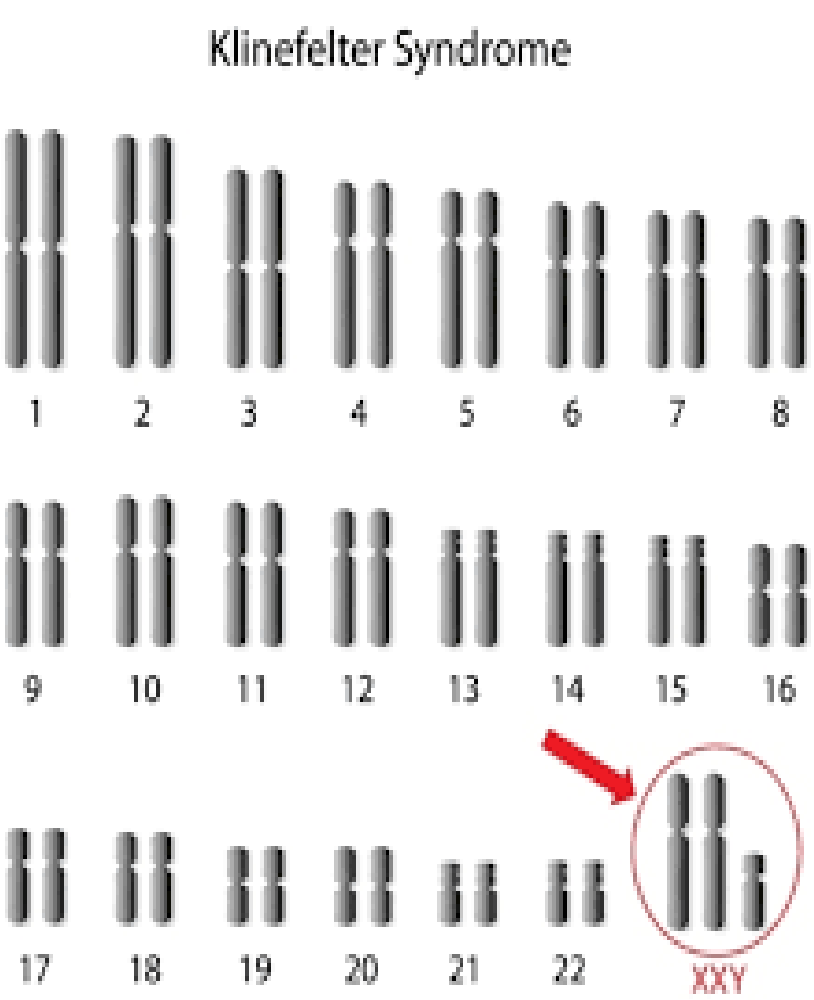
- Symptoms: mental impairment 99%, abnormal teeth60%, stunted growth 90%, slanted eyes 60%, shortened hands 60%, increased skin on back of neck 80%, short neck 60%, low muscle tone 80%, flat head 75%, abnormal outer ears 70%, congenital heart disease 40%, flattened nose 68% separation of first and second fingers 68%.

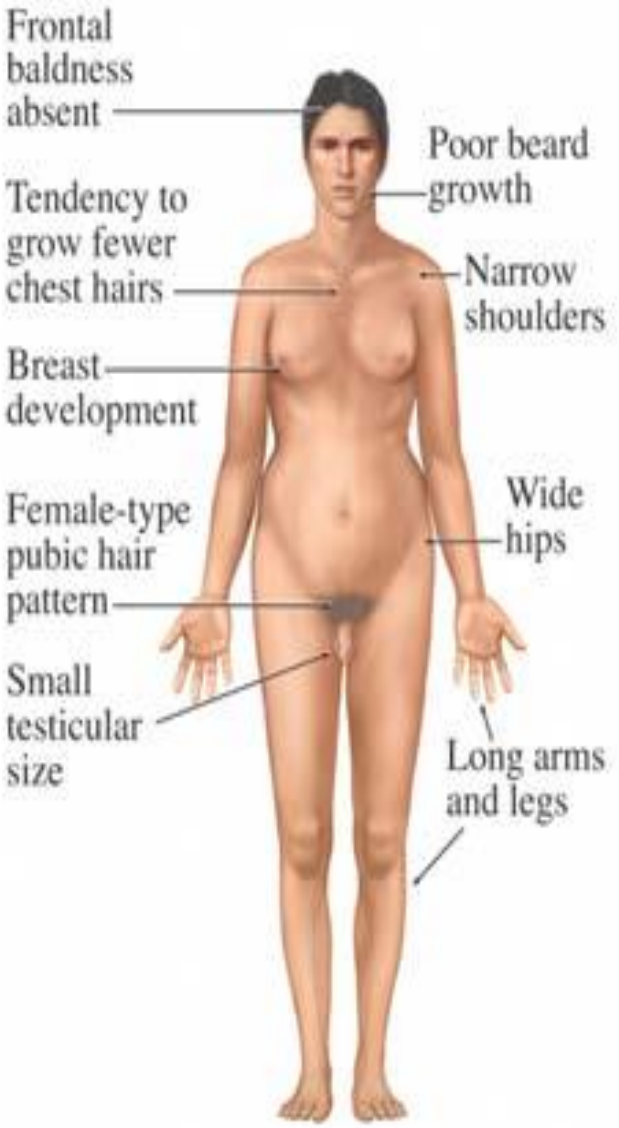


Chromosome disorders

- **Klinefelter syndrome,** also known as 47,XXY or XXY, is the set of symptoms that result from two or more X chromosomes in males.
- The primary features are infertility and small testicles. Sometimes, symptoms are more prominent and may include weaker muscles, greater height, poor coordination, less body hair, breast growth, and less interest in sex. Often it is only at puberty that these symptoms are noticed. Intelligence is usually normal; however, reading difficulties and problems with speech are more common.

Chromosome disorders

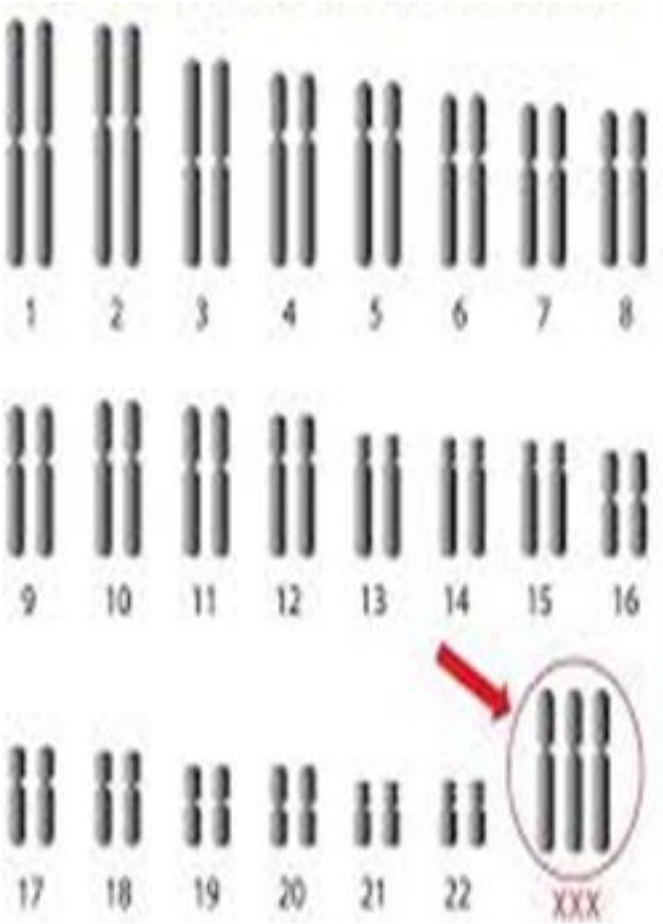




Chromosome disorders

- **Triple X syndrome, also known as trisomy X and 47,XXX,** is characterized by the presence of an extra X chromosome in each cell of a female. Those affected are often taller than average. Usually there are no other physical differences and normal fertility. Occasionally there are learning difficulties, decreased muscle tone, seizures, or kidney problems. A person with triple X syndrome have two Barr bodies in each cell.

Chromosome disorders



Chromosome disorders

- **XYY syndrome, also as known as YY syndrome, 47 XYY, Jacobs syndrome**, is a rare chromosomal disorder that affects males. It is caused by the presence of an extra Y chromosome. Affected individuals are usually very tall. Many experience severe acne during adolescence. Additional symptoms may include learning disabilities and behavioral problems such as impulsivity. Intelligence is usually in the normal range.

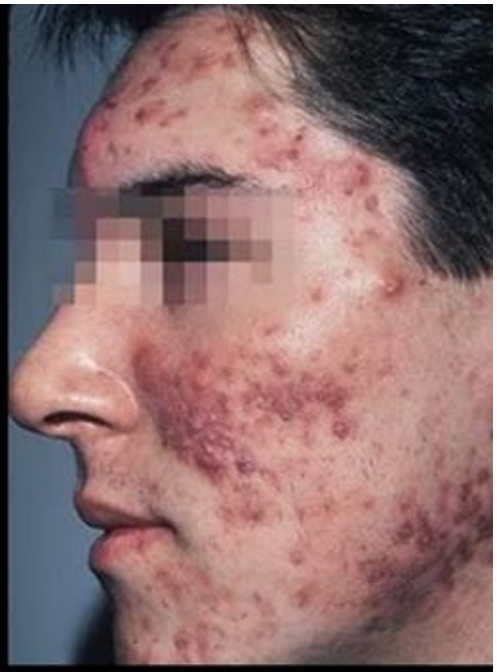
Chromosome disorders

- 47,XYY is not inherited, but usually occurs as a random event during the formation of sperm cells. An incident in chromosome separation during anaphase II (of meiosis II) called nondisjunction can result in sperm cells with an extra copy of the Y-chromosome.
- In some cases, the addition of an extra Y-chromosome results from nondisjunction during cell division during a post-zygotic mitosis in early embryonic development. This can produce 46,XY/47,XYY mosaics.

Chromosome disorders

XYY syndrome

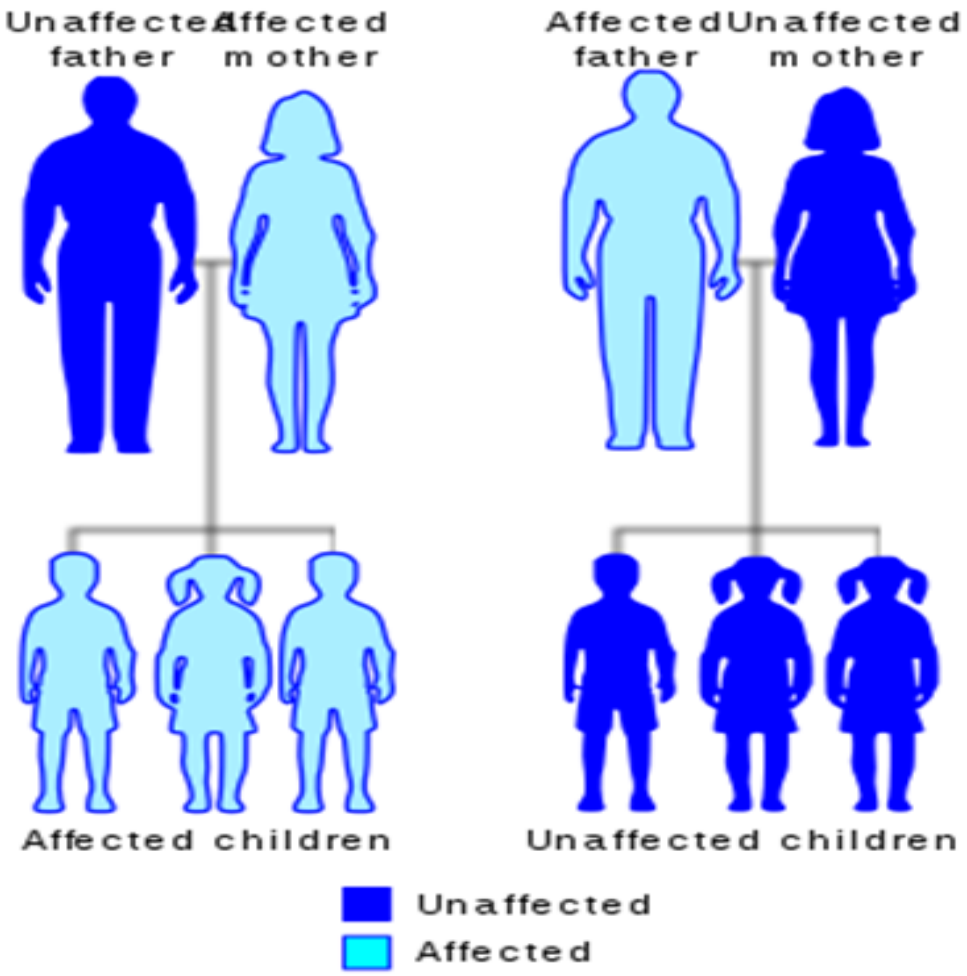
- Supermales
- Tall above 6 feet
- Act normal
- Produce HIGH levels of testosterone
- Puberty- slender, severe acne, poorly coordinated
- Fertile



Mitochondrial disorders

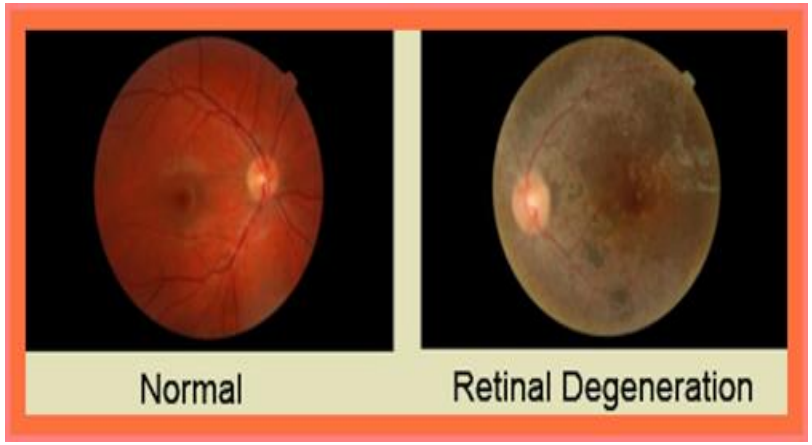
- Mitochondrial disorders are chronic (long-term), genetic, often inherited disorders that occur when mitochondria fail to produce enough energy for the body to function properly. Mitochondrial disorders can be present at birth, but can also occur at any age.
- Mitochondrial dysfunction occurs when the mitochondria do not work as well as they should due to another disorder or condition. Many conditions can lead to secondary mitochondrial dysfunction and affect other diseases, including Alzheimer's disease, muscular dystrophy, Lou Gehrig's disease, diabetes and cancer. Individuals with secondary mitochondrial dysfunction do not have primary genetic mitochondrial disease and do not need to be concerned about the ongoing development or worsening of symptoms.
- Mitochondrial disorders caused by mutations in the mitochondrial DNA are exclusively inherited from mothers. If this is the way a mitochondrial disorder was inherited, there is a 100% chance that each child in the family will inherit a mitochondrial disease.

Mitochondrial disorders



Mitochondrial disorders

- **Leber's hereditary optic neuropathy (LHON)** is a severe mitochondrial optic neuropathy disease leading to central vision loss in both eyes.1–5 People living with LHON will often find it impossible to read, drive or recognize faces.
- LHON is caused by mutations in the MT-ND1, MT-ND4, MT-ND4L, and MT-ND6 genes in mitochondria. When such mutations are present, nerve cells in the retina at the back of the eye do not have enough energy to work properly (retinal ganglion cell dysfunction), leading to the characteristic loss of vision.

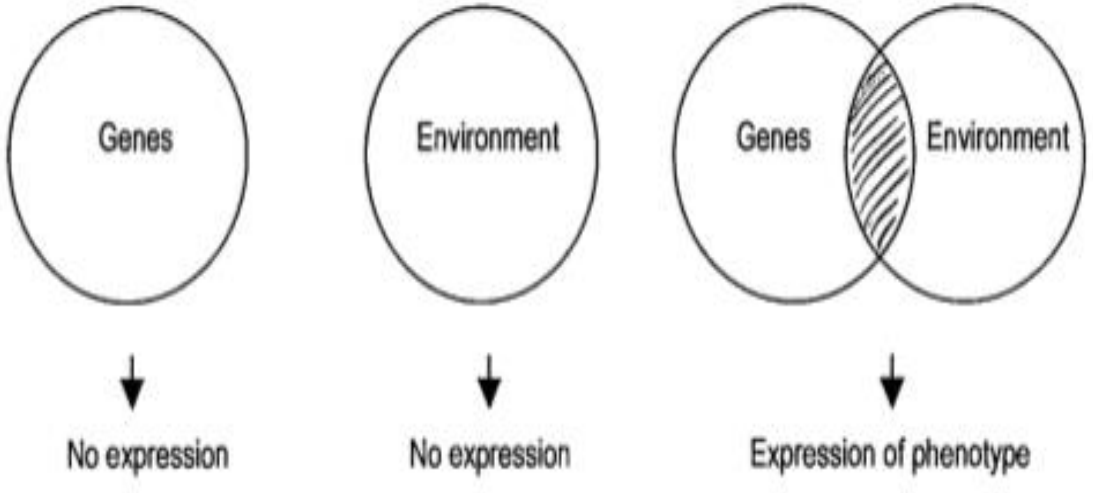


Multifactorial disorders

- **Multifactorial disorders** are caused by a combination of "external environmental factors" (bad habits, lifestyle, professional activity, and others) and genetic predisposition (in result occur mutations in multiple genes). The presence of a genetic predisposition to the disease will not necessarily lead to the development of this disease. However, in the presence of unfavorable factors of the "external environment", a person with a hereditary predisposition has a much greater probability of getting sick than people who do not have such a predisposition.

Multifactorial disorders

- The most common multifactorial diseases include: rheumatoid arthritis, coronary heart disease, hypertension and peptic ulcer disease, cirrhosis, diabetes mellitus, bronchial asthma, psoriasis, schizophrenia, etc.



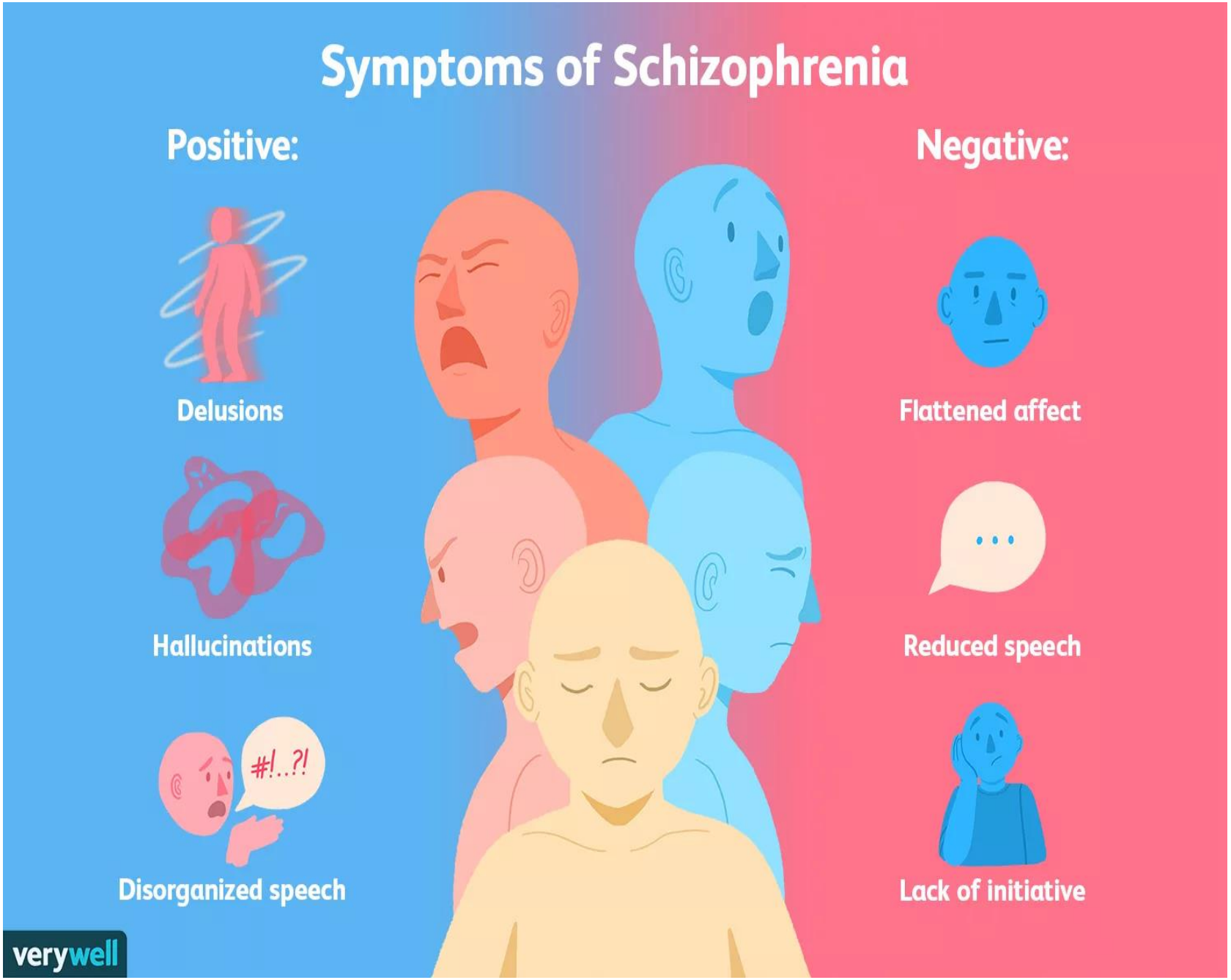
Multifactorial disorders

- **Schizophrenia** is a mental disorder characterized by abnormal behavior, strange speech, and a decreased ability to understand reality. The causes of schizophrenia include environmental and genetic factors. Possible environmental factors include being raised in a city, marijuana use during adolescence, certain infections, the age of a person's parents, and poor nutrition during pregnancy.
- Schizophrenia most commonly strikes between the ages of 16 and 30, and males tend to show symptoms at a slightly younger age than females.

Schizophrenia

The symptoms are classified into four categories:

- Positive symptoms - also known as psychotic symptoms. For example, delusions and hallucinations.
- Negative symptoms - these refer to elements that are taken away from the individual. For example, absence of facial expressions or lack of motivation.
- Cognitive symptoms - these affect the person's thought processes. They may be positive or negative symptoms, for example, poor concentration is a negative symptom.
- Emotional symptoms - these are usually negative symptoms, such as blunted emotions.


Symptoms of Schizophrenia
Positive:
Delusions
Hallucinations
#!..?!
Disorganized speech
Negative:
Flattened affect
Reduced speech
Lack of initiative
verywell

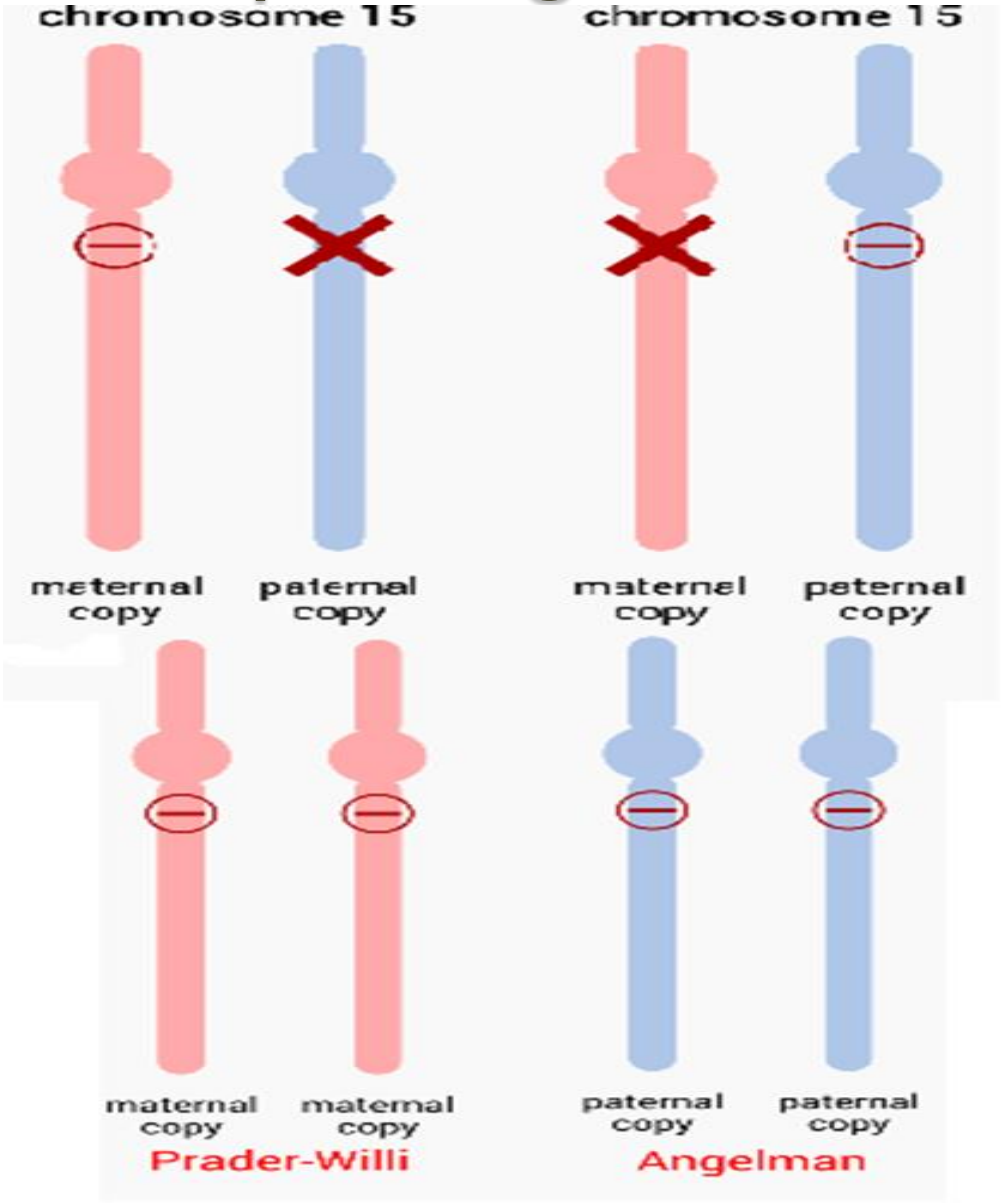
Imprinting disorders

- Imprinted genes are expressed from one parental allele only. Some imprinted genes are critical regulators of growth and development, and thus disruption of their normal monoallelic expression causes congenital imprinting disorders, with clinical features impacting growth, development, behaviour and metabolism.
- A classic example of imprinting disorders is the hereditary Prader-Willy and Angelman syndromes, the main clinical manifestations of which are mental retardation of varying severity in combination with deep neurological disorders.

Imprinting disorders

- The most common cause of Prader-Willy and Angelman syndromes is microdeletion of a critical region of chromosome 15. Prader – Willi syndrome develops when a child inherits a deletion from his father, and the same deletion received from the mother becomes the cause of Angelman syndrome. Thus, the occurrence of two hereditary syndromes, clinically different, is determined by those from which of the parents the chromosomal damage was received.
- Normally, human inherit 1 copy of each chromosome pair from mother, and the other copy of the chromosome pair from father. **Uniparental disomy** (UPD) refers to the situation in which 2 copies of a chromosome come from the same parent, instead of 1 copy coming from the mother, and 1 copy coming from the father. Angelman syndrome (AS) and Prader-Willi syndrome (PWS) are examples of disorders that can be caused by uniparental disomy.

Imprinting disorders



Imprinting disorders

- People with Angelman syndrome (AS) have an unusual facial appearance, short stature, severe intellectual disability with a lack of speech, stiff arm movements, and a spastic, uncoordinated walk. They may have seizures and often have inappropriate outbursts of laughter.
- Angelman syndrome can result when a baby inherits both copies of chromosome 15 from the father (rather than 1 from the mother, and 1 from the father).
- AS can also occur, even when chromosome 15 is inherited normally—1 chromosome coming from each parent. If that section of the mother's chromosome 15 is deleted, only the father's section will be present, allowing AS symptoms to occur. This deletion of a section of the maternally inherited chromosome is the most common cause of AS.

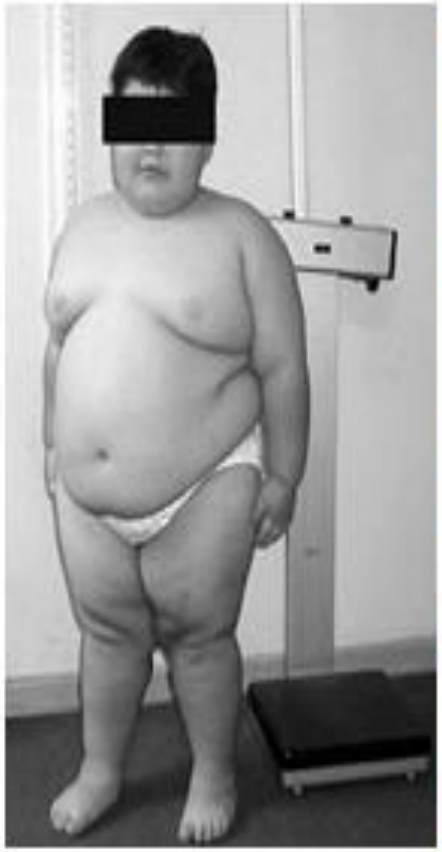
Imprinting disorders: Angelman syndrome

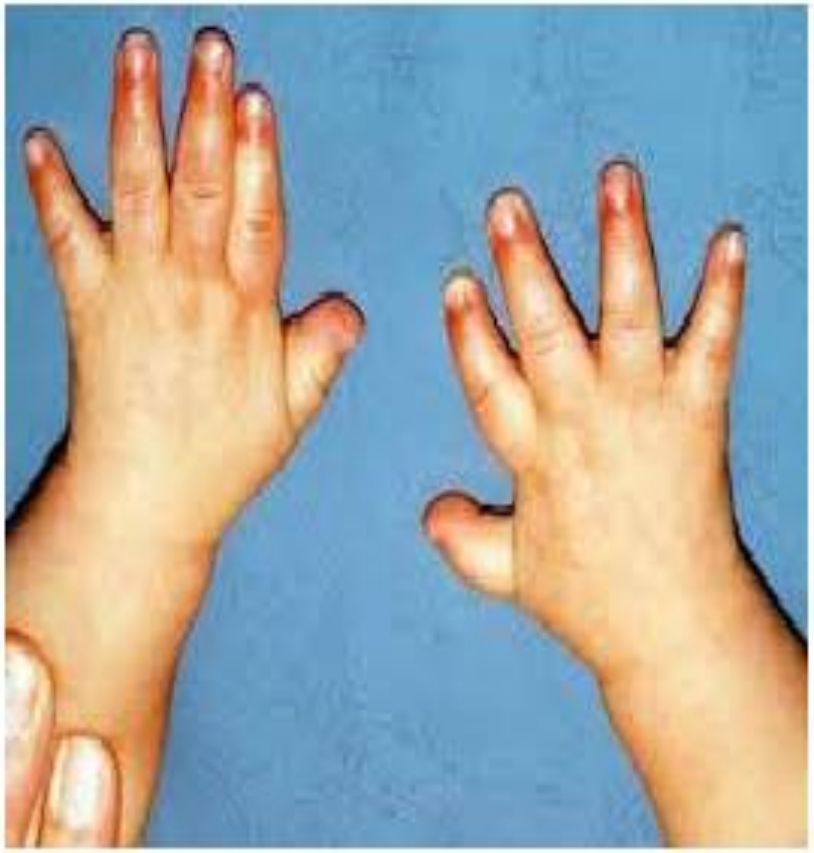
Imprinting disorders

- **Prader-Willi syndrome** (PWS) is result when a baby inherits both copies of a section of chromosome 15 from the mother. As with Angelman syndrome, PWS can also occur, even if chromosome 15 is inherited normally. If that section of the father's chromosome 15 is deleted, only the mother's section will be present, allowing PWS symptoms to occur. This latter development happens in 74% of PWS cases.

- Babies born with PWS have poor muscle tone and a weak cry. They initially are slow feeders and appear undernourished. The feeding problems improve after infancy. Typically, between 2 to 4 years of age, the child becomes obsessed with food and is unable to control his or her appetite. The overeating often results in rapid weight gain, obesity, and type 2 diabetes. People with PWS have short stature, small hands and feet, and intellectual disability.

Imprinting disorders: Prader-Willi syndrome





THANK YOU FOR ATTENTION