HUMAN BLOOD GROUP

- International Society of Blood Transfusion has recently recognized 33 blood group systems.
- Apart from ABO and Rhesus system, many other types of antigens have been noticed on the red cell membranes.
- The knowledge on blood group system is necessary to approach blood group-linked diseases which are still at the stage of research.
- The term "blood group" refers to the entire blood group system comprising red blood cell (RBC) antigens whose specificity is controlled by a series of genes which can be allelic or linked very closely on the same chromosome.
- "Blood type" refers to a specific pattern of reaction to testing antisera within a given system.
- Over a period of time, our understanding on blood groups has evolved to encompass not only transfusion-related problems but also specific disease association with RBC surface antigens.
- Karl Landsteiner has been credited for the discovery of ABO blood group system in 1900. His extensive research on serology based on simple but strong scientific reasoning led to identification of major blood groups such as O, A, and B types, compatibility testing, and subsequent transfusion practices.
- He was awarded Noble Prize in 1930 for this discovery.

- His obituary lists an immense contribution of more than 346 publications.
- Later, Jan Jansky described classification of human blood groups of four types.

BLOOD GROUPS

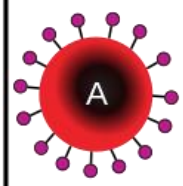
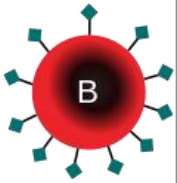
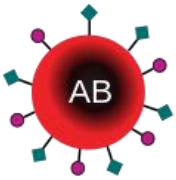
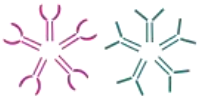
- At present, 33 blood group systems representing over 300 antigens are listed by the International Society of Blood Transfusion.
- Most of them have been cloned and sequenced.
- The antigens can be integral proteins where polymorphisms lie in the variation of amino acid sequence (e.g., rhesus [Rh], Kell), glycoproteins or glycolipids (e.g., ABO).

Blood group systems

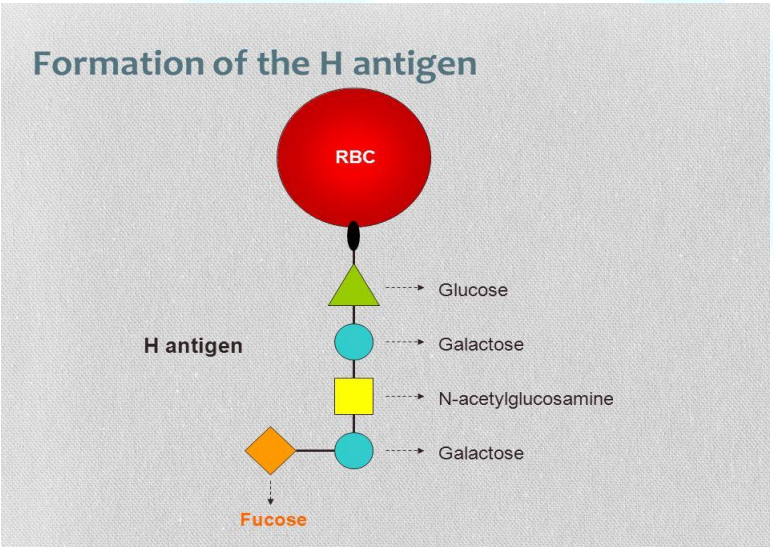
➢ ABO system

Blood type	Genotype	
A	I^A, I^O I^A, I^A	AO AA
B	I^B, I^O I^B, I^B	BO BB
AB	I^A, I^B	AB
O	$I^O I^O$	OO

- Among the 33 systems, ABO remains the most important in transfusion and transplantation since any person above the age of 6 months possess clinically significant anti-A and/or anti-B antibodies in their serum.
- Blood group A contains antibody against blood group B in serum and vice-versa, while blood group O contains no A/B antigen but both their antibodies in serum.

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	A antigen	B antigen	 A and B antigens	None

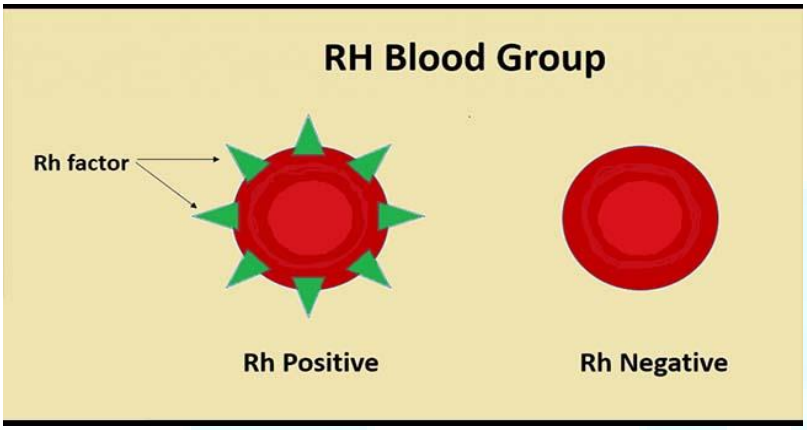
- H-antigen



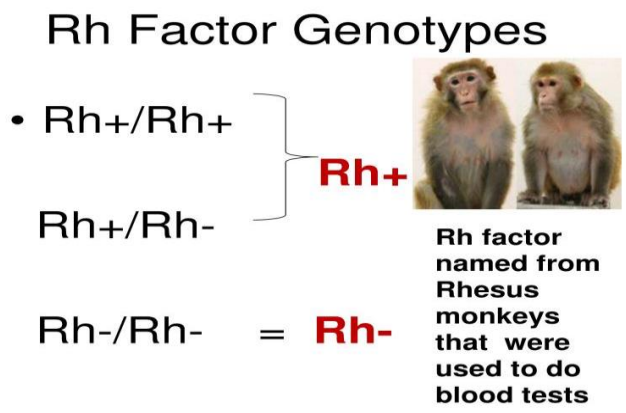
- H-antigen is the precursor to the ABO blood group antigens.
- It is present in all RBCs irrespective of the ABO system.
- Persons with the rare Bombay phenotype are homozygous for the H gene (HH), do not express H-antigen on their RBCs.

- As H-antigen acts as precursor, its absence means the absence of antigen A and B.
- However, the individuals produce isoantibodies to H-antigen as well as to antigens A and B.

➢ Rhesus system



- Rhesus-system is the second most important blood group system after ABO.
- Currently, the Rh-system consists of 50 defined blood group antigens out of which only five are important.
- RBC surface of an individual may or may not have a Rh factor or immunogenic D-antigen.



- Accordingly, the status is indicated as either Rh-positive (D-antigen present) or Rh-negative (D-antigen absent).
- In contrast to the ABO system, anti-Rh antibodies are, normally, not present in the blood of individuals with D-negative RBCs, unless the circulatory system of these individuals has been exposed to D-positive RBCs.
- These immune antibodies are immunoglobulin G (IgG) in nature and hence, can cross the placenta.
- Prophylaxis is given against Rh immunization using anti-D Ig for pregnant Rh-negative mothers who have given birth to Rh-positive child.

➢ MNS antigen system

Population	Genotype			Allele freqs	
	MM	MN	NN	f(M)	f(N)
Eskimo	0.835	0.156	0.009	0.913	0.087
Australian	0.024	0.304	0.672	0.176	0.824
Egyptian	0.278	0.489	0.233	0.523	0.477
German	0.297	0.507	0.196	0.550	0.450
Chinese	0.332	0.486	0.182	0.575	0.425
Nigerian	0.301	0.495	0.204	0.548	0.452

- MNS antigen system, first described by Landsteiner and Levine in 1927 is based on two genes: Glycophorin A and Glycophorin B.
- The blood group is under control of an autosomal locus on chromosome 4 and also under control of a pair of co-dominant alleles LM and LN.
- Anti-M and anti-N antibodies are usually IgM types and rarely, associated with transfusion reactions.

➢ Lutheran system

- Lutheran system comprised of four pairs of allelic antigens representing single amino acid substitution in the Lutheran glycoprotein at chromosome 19.
- Antibodies against this blood group are rare and generally not considered clinically significant.

➢ Kell system

- These erythrocyte antigens are the third most potent immunogenic antigen after ABO and Rh system, and are defined by an immune antibody, anti-K.

- It was first noticed in the serum of Mrs. Kellacher.
- She reacted to the erythrocytes of her newborn infant resulting in hemolytic reactions.
- Since then 25 Kell antigens have been discovered.
- Anti-K antibody causes severe hemolytic disease of the fetus and newborn (HDFN) and haemolytic transfusion reactions (HTR).

➢ Duffy system

- Duffy-antigen was first isolated in a patient called Duffy who had haemophilia.
- It is also known as Fy glycoprotein and is present in the surface of RBCs.
- It is a nonspecific receptor for several chemokines and acts as a receptor for human malarial parasite, Plamodium vivax.
- Antigens Fya and Fyb on the Duffy glycoprotein can result in four possible phenotypes, namely Fy(a+b−), Fy(a+b+), Fy(a−b+), and Fy(a−b−). The antibodies are IgG subtypes and can cause HTR.

➢ Kidd system

- Kidd antigen (known as Jk antigen) is a glycoprotein, present on the membrane of RBCs and acts as a urea transporter in RBCs and renal endothelial cells.
- Kidd antibodies are rare but can cause severe transfusion reactions.
- These antigens are defined by reactions to an antibody designated as anti-Jka, discovered in the serum of Mrs. Kidd who delivered a baby with HDFN.
- Jka was the first antigen to be discovered by Kidd blood group system, subsequently, two other antigens Jkb and Jk3 were found

- Agarwal et al. carried out a study on automated analysis of blood groups in north Indian donor population and observed that the common blood groups in order of frequency were B, O, A, and AB; 94.4% being Rh-positive.
- In minor blood groups, the most commonly appearing phenotypes were Le (a−b−) for Lewis, Fy(a+b+) for Duffy, Jk(a+b+) for Kidd, and M+N+ for MNS system.

IMPORTANCE OF BLOOD GROUPS

Structural lesions of red blood cell

- Of the 33 blood group system antigens, five are defined by their carbohydrate structures (ABO, H, P1Pk, I, GLOB); two are obtained from the plasma (LE, CH/RG).
- The remaining 23 are characterized by the protein sequence of the RBC membrane protein, five major proteins (DI, Rh, RhAG, MNS, GE, and CO) among them are expressed at higher levels and function as membrane transporters, whereas the functional importance of rest of 17 antigens is unknown.
- The proposed function of other antigens are mostly receptor/ligand signaling, enzymatic activity, and glycocalyx formation.
- The null phenotype of the system, however, shows no immune system abnormalities when compared with mice except for a blunted neutrophil response on exposure to bacterial lipopolysaccharide.
- Similarly, Knops blood group antigen has been associated with complement receptor 1 and Cromer system with decay acceleration factor.
- Nevertheless, the clinical function of the null phenotypes of these blood groups still remains to be elucidated .

Blood groups and disease association

- The ABO blood groups have a profound influence on haemostasis.
- They exert major quantitative effects on plasma levels of von Willebrand factor and factor VIII.
- Increased association of myocardial infarction, ischemic stroke, and venous thromboembolism is seen with blood groups A and AB possibly through functional ABO glycol transferases modulation of thrombosis.
- A higher risk of cerebral venous thrombosis has been reported in non-O groups.
- Significant association of ABO groups with the prevalence of preeclampsia has been reported, where AB group was found to be associated with an increased risk of 2.1-folds.
- Preliminary studies suggested an association of ABO system with malignancies.
- A positive correlation has been shown between blood group A with chronic hepatitis-B infection and pancreatic cancer; and blood group B with ovarian cancer.
- Protection against falciparum malaria can be achieved with group O by reducing rosette formation.
- Blood group O increases the severity of infection in Vibrio cholerae strains (O1 El Tor and O139).

BLOOD REQUISITION

- After the decision to transfuse blood is taken the next step should be to order a requisition during which the following steps need to be remembered.
    i. Blood grouping and cross-matching
        - The most fatal of all transfusion-related reaction is ABO incompatibility causing complement-mediated intravascular hemolysis.
        - Hence, correct blood grouping and typing, and cross-checking with the blood requisition form is of utmost importance.

- ABO typing is carried out by testing RBCs for the A and B antigens and the serum for the A and B antibodies before transfusion.
- The next step involves Rh typing with only 15% of the population being Rh-negative.

ii. Cross-matching

- Cross-matching involves mixing of donor RBCs with the recipient serum to detect fatal reactions.
- It has three phases in which the first phase (1-5 min) involves detection of ABO incompatibility and detection of antibody against MN, P, and Lewis systems.
- The second phase (30-45 min in albumin and 10-20 min in low ionic salt solution) involves incubation of first phase reactants at 37°C for detection of incomplete antibodies of Rh system.
- The third phase consists of the addition of antiglobulin sera to the incubated second phase reactants to detect incomplete antibodies of Rh, Kidd, Kell and Duffy.
- Among the three phases, the first two phases are more important as they detect those involved in fatal HTR. The total time taken for all the three phases is in between 45 and 60 min.

iii. Antibody screening

- Here, commercially prepared RBCs with all the antigens, which direct production of antibodies causing hemolytic reactions, are mixed with the recipient's serum to detect the presence of those very antibodies.
- It is also carried out with the donor's serum.

CHANGING PRACTICES IN BLOOD GROUPING

- There are controversies regarding the best method for procurement of blood during elective and emergency situations:

  (a) It can be done by routinely asking for grouping and cross-matching in elective surgical patients. Many scientific articles disputed the relevance of preoperative arrangement of blood in surgeries where blood loss is not anticipated to be significant.

  (b) Blood may be ordered without full set of investigations. ABO-Rh typing alone results in a 99.8% chance of a compatible transfusion. Antibody screening increases this safety margin up to 99.94%, and an additional cross-match further increases the compatibility to 99.95%. In absence of cross-matching, there is a possibility of missing the antigens on donor cells, but in clinical practice, they are of less importance. Hence, "screening and typing" alone should be carried out. Other methods include "type and partial cross-match," which includes the immediate phase of cross-match; "type and uncross match," for those recipients who have never been transfused before, the chance of detection of antibody with each cross-match is 1:1000; "type O Rh-negative uncross match," it is performed in emergency situation when the time for these procedures is limited. In the latter condition, type O Rh-negative packed RBCs, that is, the universal donor can be used as they will have a negligible amount of hemolytic anti-A/anti-B antibodies against the recipient RBCs.

CURRENT TRENDS AND FUTURE AREAS OF RESEARCH

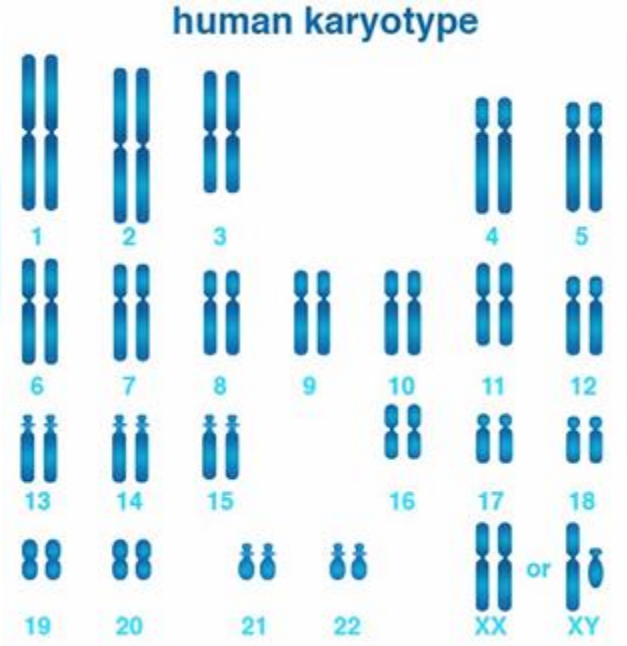
- Three main antigen-modulation strategies have been proposed to prevent immune recognition of incompatible RBCs and to avoid haemolytic reactions due to alloimmunization.
- The first approach relies on enzymatic conversion of specific blood group antigens, that is, manipulation of the ABO system.
- Goldstein and Lenny achieved a remarkable milestone with the development of technology named "enzyme converted group O-RBC (ECO-RBC) concept" where the B antigen is replaced with O using galactosidase.

- This treatment leaves fewer than 2000 antigenic sites per RBC without affecting membrane deformability, gas exchange, or expression of the RhD, C and E, MNS, Lewis, Kell, Lutheran, Duffy, and Kidd blood group systems as their antigenicity do not depend on the terminal galactose residues.
- In contrast with the B antigen, enzymatic conversion of A antigen was difficult due to existence of two Type-A blood group structures (A2 and A1).
- Two new enzymes, N-acetylgalactosaminidase and a-galactosidase have been identified for removal of antigens A and B, respectively; and tested for their ability to generate ECO-RBCs from A1, A2, B, or AB donor units.
- The enzyme conversion strategy has also been proposed to resolve ABO incompatibility issues in the field of organ transplantation.
- The second approach is to mask antigens by treatment of RBCs with polyethylene glycol; also known as the stealth RBC concept.
- The third approach involves in vitro production of RBCs with a predefined antigenic profile from genetically manipulated stem cells. Such cells could be used for the generation of "universal-donor" RBCs.

HUMAN KARYOTYPE

- Karyograms are images of real chromosomes
- Each eukaryotic species has its nuclear genome divided among a number of chromosomes that is characteristic of that species.
- For example, a haploid human nucleus (i.e. sperm or egg) normally has 23 chromosomes (n=23), and a diploid human nucleus has 23 pairs of chromosomes (2n=46).
- A karyotype is the complete set of chromosomes of an individual.

- The cell was in metaphase so each of the 46 structures is a replicated chromosome even though it is hard to see the two sister chromatids for each chromosome at this resolution.
- As expected there are 46 chromosomes. Note that the chromosomes have different lengths.
- In fact, human chromosomes were named based upon this feature.
- Our largest chromosome is called 1, our next longest is 2, and so on.
- By convention the chromosomes are arranged into the pattern and the resulting image is called a karyogram.



- A karyogram allows a geneticist to determine a person's karyotype - ***a written description of their chromosomes including anything out of the ordinary***.
- Various stains and fluorescent dyes are used to produce characteristic banding patterns to distinguish all 23 chromosomes.

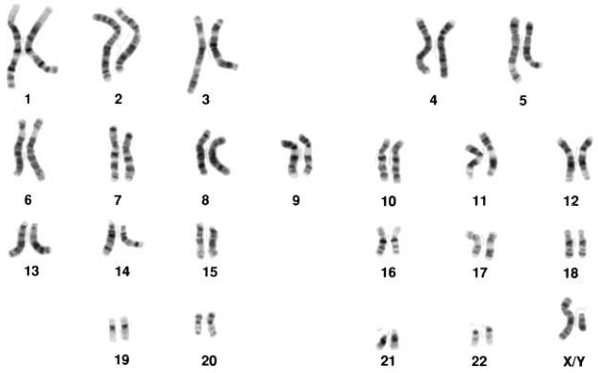
- The number of chromosomes varies between species, but there appears to be very little correlation between chromosome number and either the complexity of an organism or its total amount genomic DNA.

Autosomes and Sex Chromosomes

- In humans males have one of each while females have two X chromosomes.
- Autosomes are those chromosomes present in the same number in males and females while sex chromosomes are those that are not.
- When sex chromosomes were first discovered their function was unknown and the name X was used to indicate this mystery.
- The next ones were named Y, then Z, and then W.
- The combination of sex chromosomes within a species is associated with either male or female individuals.
- In mammals, fruit flies, and some flowering plants embryos, those with two X chromosomes develop into females while those with an X and a Y become males.
- In birds, moths, and butterflies males are ZZ and females are ZW. Because sex chromosomes have arisen multiple times during evolution the molecular mechanism(s) through which they determine sex differs among those organisms.
- For example, although humans and Drosophila both have X and Y sex chromosomes, they have different mechanisms for determining sex .
- In mammals, the sex chromosomes evolved just after the divergence of the monotreme lineage from the lineage that led to placental and marsupial mammals.
- Thus nearly every mammal species uses the same sex determination system.
- During embryogenesis the gonads will develop into either ovaries or testes.
- A gene present only on the Y chromosome called TDF encodes a protein that makes the gonads mature into testes.
- XX embryos do not have this gene and their gonads mature into ovaries instead (default).

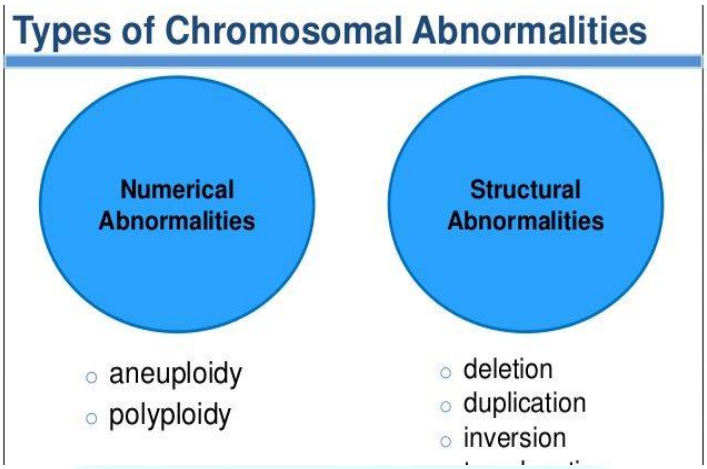
- Once formed the testes produce sex hormones that direct the rest of the developing embryo to become male, while the ovaries make different sex hormones that promote female development.
- The testes and ovaries are also the organs where gametes (sperm or eggs) are produced.
- In those individuals with two of the same chromosome (i.e. homogametic sexes: XX females and ZZ males) the chromosomes pair and segregate during meiosis I the same as autosomes do.
- During meiosis in XY males or ZW females (heterogametic sexes) the sex chromosomes pair with each other .
- In mammals the consequence of this is that all egg cells will carry an X chromosome while the sperm cells will carry either an X or a Y chromosome.
- Half of the offspring will receive two X chromosomes and become female while half will receive an X and a Y and become male.

Chromosomal abnormalities



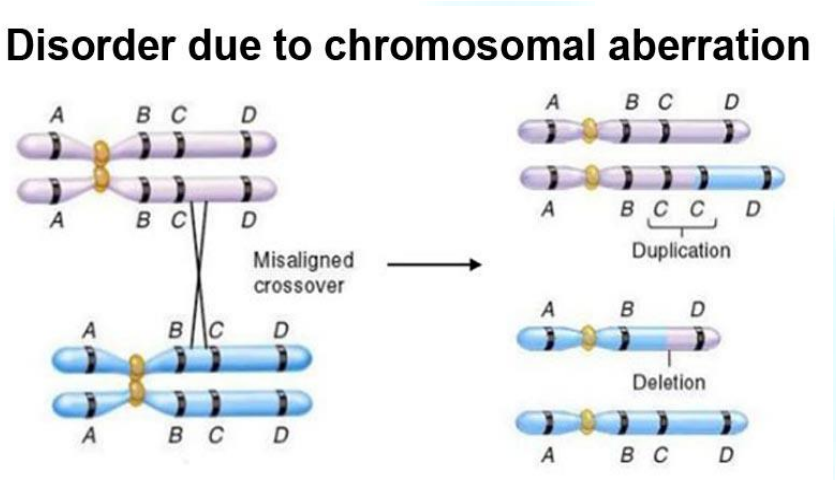
Normal Karyotype

- Analysis of karyotypes can identify chromosomal abnormalities, including aneuploidy, which is the addition or subtraction of a chromosome from a pair of homologs.

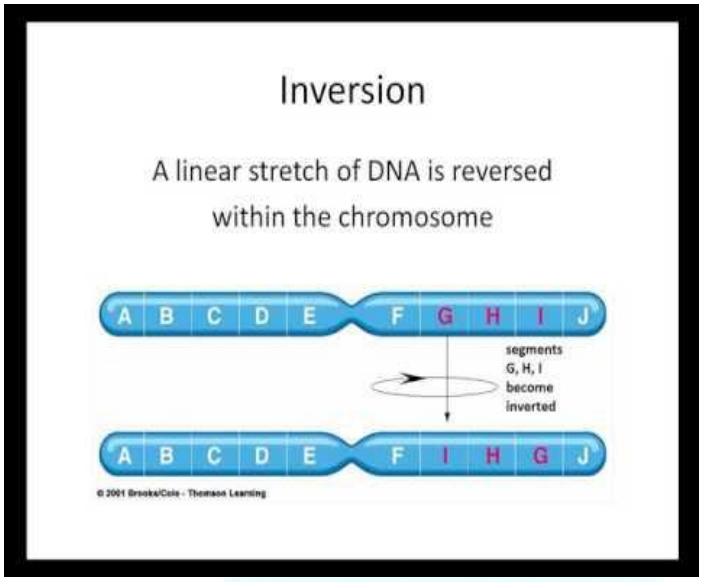


- More specifically, the absence of one member of a pair of homologous chromosomes is called monosomy (only one remains).
- On the other hand, in a trisomy, there are three, rather than two (disomy), homologs of a particular chromosome.
- Different types of aneuploidy are sometimes represented symbolically; if 2n symbolizes the normal number of chromosomes in a cell, then 2n-1 indicates monosomy and 2n+1 represents trisomy.
- The addition or loss of a whole chromosome is a mutation, a change in the genotype of a cell or organism.
- The most familiar human aneuploidy is trisomy-21 (i.e. three copies of chromosome 21), which is one cause of Down syndrome.
- Most (but not all) other human aneuploidies are lethal at an early stage of embryonic development.
- Note that aneuploidy usually affects only one set of homologs within a karyotype, and is therefore distinct from polyploidy, in which the entire chromosome set is duplicated (see below).

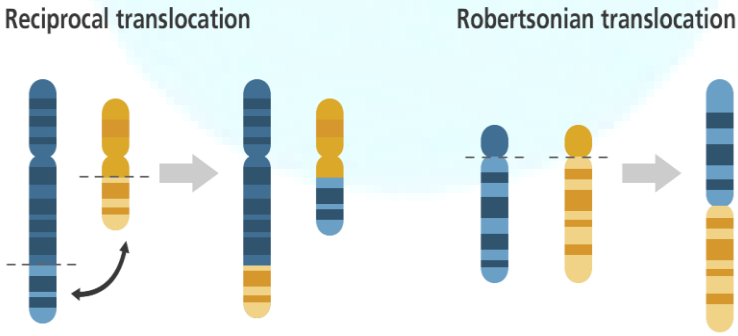
- Aneuploidy is almost always deleterious, whereas polyploidy appears to be beneficial in some organisms, particularly many species of food plants.
- Aneuploidy can arise due to a non-disjunction event, which is the failure of at least one pair of chromosomes or chromatids to segregate during mitosis or meiosis. Non-disjunction will generate gametes with extra and missing chromosomes.
- Structural defects in chromosomes are another type of abnormality that can be detected in karyotypes .



- These defects include deletions, duplications, and inversions, which all involve changes in a segment of a single chromosome.



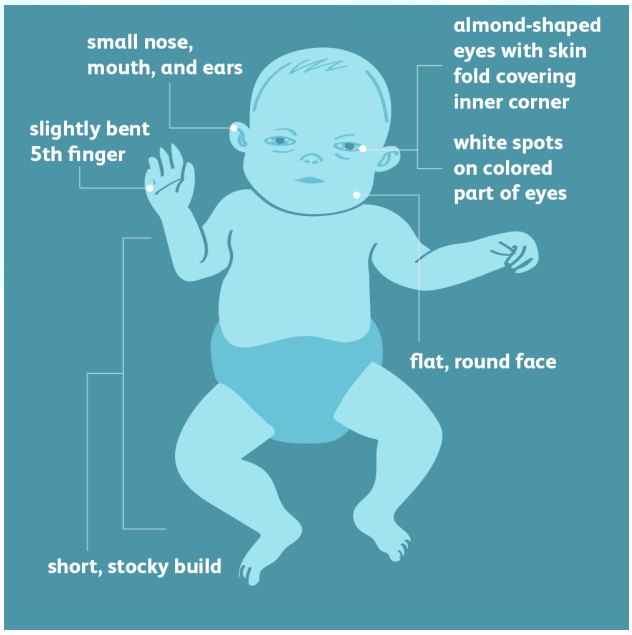
- Insertions and translocations involve two non-homologous chromosomes.
- In an insertion, DNA from one chromosome is moved to a non-homologous chromosome in a unidirectional manner.
- In a translocation, the transfer of chromosomal segments is bidirectional and reciprocal – a reciprocal translocation.



Syndrome Caused Due To Chromosomal Abberations

Down Syndrome

- Down syndrome is a genetic disorder.
- Most babies are born with 23 pairs of chromosomes within each cell for a total of 46.
- A chromosome is a structure that contains genes, which are made up of your DNA.
- Genes determine how you form and develop growing in the womb and after birth.
- The majority of babies with Down syndrome are born with an extra copy of chromosome 21, with three copies of the chromosome instead of the usual two.



There are three types of Down syndrome. They are:

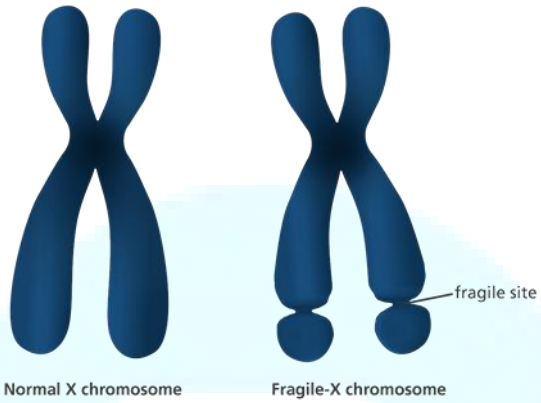
- **Trisomy 21**:
  - The term "trisomy" means having an extra copy of a chromosome.
  - The most common type of Down syndrome, trisomy 21, occurs when a developing baby has three copies of chromosome 21 in every cell instead of the typical two copies. This type makes up 95% of the cases.
- **Translocation**:
  - In this type of Down syndrome, there is an extra full or partial amount of chromosome 21 attached to another chromosome.
  - Translocation accounts for 4% of the cases.
- **Mosaicism**:
  - In the rarest type (only 1%) of Down syndrome, some cells contain the usual 46 chromosomes, and some contain 47.
  - The extra chromosome in these cases is chromosome 21.

Fragile X syndrome

- Fragile X syndrome is the leading cause of inherited intellectual disabilities like autism.
- There are behavioral, physical, intellectual and mental health symptoms.
- Females have milder symptoms than males. FXS is not life-threatening and although there is no cure, medication and therapy can help manage the symptoms.
- Fragile X syndrome (FXS), also known as Martin-Bell syndrome, is an inherited condition that causes developmental delays, intellectual disabilities, learning and behavioral issues, physical

abnormalities, anxiety, attention-deficit/hyperactivity disorder and/or autism spectrum disorder, among other problems.

- It's the most common form of inherited intellectual and developmental disability (IDD).

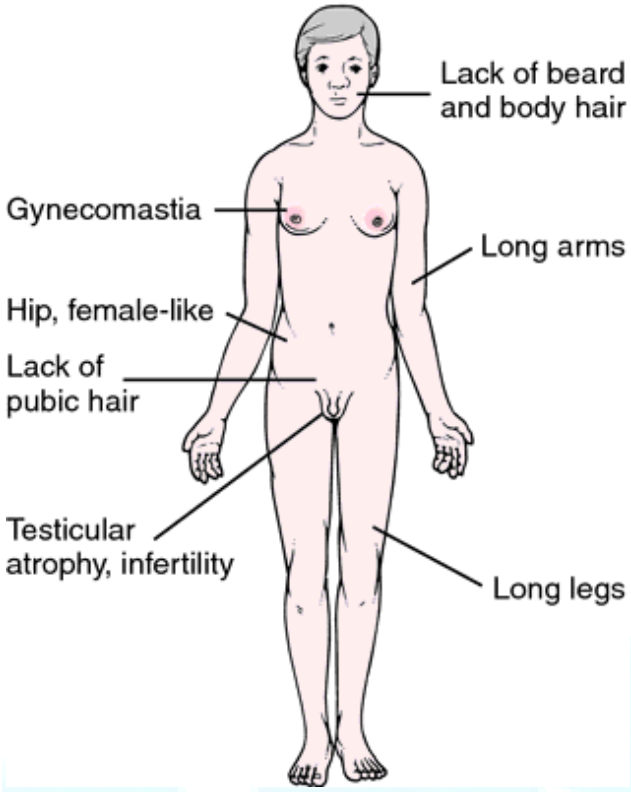


- FXS is named fragile X syndrome because, when looked at through a microscope, part of the X chromosome looks "broken" or "fragile."
- FXS is one of three syndromes in the fragile X family. The other two syndromes are

    1. Fragile X-associated tremor/ataxia syndrome (FXTAS). Symptoms include balance problems, shaky hands, unstable mood, memory loss, cognitive problems and numbness in the hands and feet.
    2. Fragile X-associated primary ovarian insufficiency (FXPOI). Symptoms include reduced fertility, infertility, missing or unpredictable menstrual periods and premature menopause.

Klinefelter syndrome

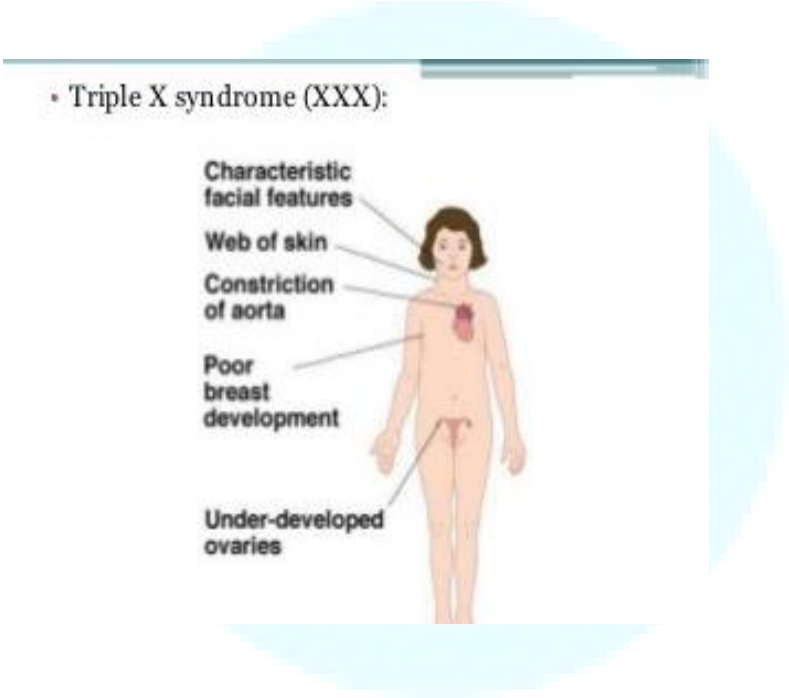
- Klinefelter syndrome is a common genetic condition where a male is born with an extra X chromosome.
- Typically, a male has one X and one Y chromosome.
- People with Klinefelter syndrome can experience breast growth, breast cancer, osteoporosis, infertility and learning difficulties.
- Treatment typically involves physical and emotional therapy, as well as hormone replacement.
- A typical male has a total of 46 chromosomes (packages of DNA) – one copy of an X chromosome and one copy of the Y chromosome (46, XY).
- A typical girl has two copies of the X chromosome (46, XX).
- There are a number of different conditions where an individual may have more or less than the expected X or Y chromosomes.
- Klinefelter syndrome (KS) is a genetic condition where there's an extra X chromosome present in a male's genetic code.
- Instead of having a total of 46 chromosomes, they have 47 — with two copies of the X chromosome and one copy of the Y chromosome (47,XXY).
- There are some forms (called mosaic) where only some (not all) of the person's cells have this change (other cells can either have the typical 46 XY, or can have another abnormality).



- Klinefelter syndrome is a congenital condition, which means it's present from the time of birth.
- There are certain tests that can be done during the mother's pregnancy that can diagnose it before birth, however more often it's diagnosed later in life.
- If not found before birth, it can sometimes be diagnosed because the baby has a smaller penis than expected, or later in the teenage years if puberty doesn't start or progress as expected.
- Many males may not be diagnosed at all, or only when experiencing fertility challenges later in life (if they're having a difficult time getting pregnant with their partner).
- In most cases, the differences in their puberty and/or fertility are because the testicles have early "failure" and cannot make enough testosterone and/or sperm.

- This results in these individuals needing testosterone replacement and testing for fertility.
- People with Klinefelter syndrome are also more likely to develop certain conditions that are part what is known as metabolic syndrome.

Triple X syndrome

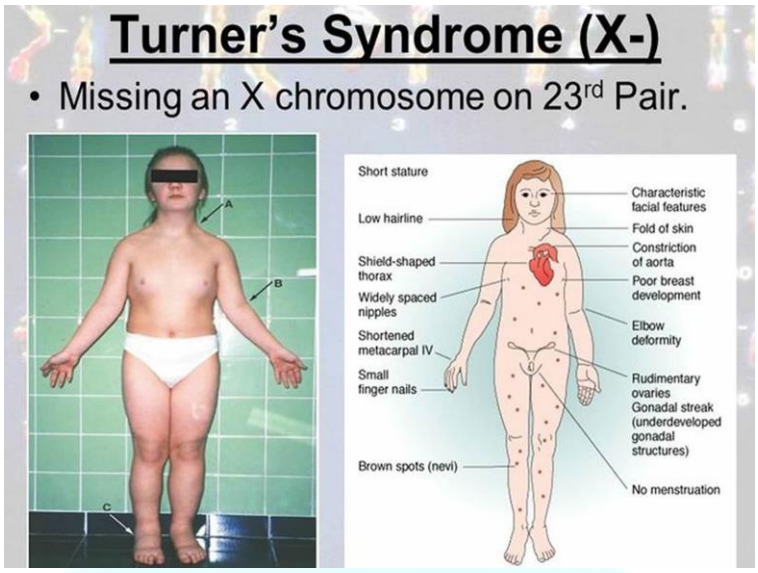


- Triple X syndrome is a genetic condition where a female is born with an extra X chromosome.
- This condition only happens in females.
- It can be passed down from a parent or happen spontaneously.
- Females with triple X syndrome may have no symptoms and not know they have the condition, or their symptoms could include being usually tall and fertility issues.
- There's no cure for triple X syndrome.

- Triple X syndrome is a rare genetic condition that affects only females.
- It can also be referred to as trisomy X syndrome or 47,XXX.
- A trisomy is a genetic condition in which there are three copies of a chromosome.
- Males and females are usually born with 46 chromosomes total, arranged in 23 pairs.
- One copy of each chromosome in the pair comes from the mother, and the other copy in the pair comes from the father.
- The 23rd chromosome pair is known as the sex chromosomes. Normally, females have two X chromosomes, while males have one X chromosome and one Y chromosome.
- Triple X syndrome happens when a female is born with an extra X chromosome, and therefore has a total of 47 chromosomes.
- For some girls and women with triple X syndrome, all of their cells contain three X chromosomes.
- In other females with triple X syndrome, some cells have three X chromosomes while other have the usual two X chromosomes — this is referred to as mosaicism.
- The degree of mosaicism (the number of cells with three X chromosomes) may vary from a small percentage to close to 100%.

Turner syndrome

- Turner syndrome is a genetic disorder affecting girls and women.
- The cause of Turner syndrome is a completely or partially missing X chromosome.



- Turner syndrome symptoms include short stature and lack of breast development and periods.
- Treatment for Turner syndrome may include hormone therapy.
- Turner syndrome (TS), sometimes referred to as congenital ovarian hypoplasia syndrome, is a genetic disorder.
- It is the most common sex chromosomal abnormality affecting girls and women.
- More specifically, it's a problem with one of the two X chromosomes -- the thread-like structures inside cells that are made of DNA.
- We get our DNA from our parents and it is the DNA that contains the specific instructions that make each living creature unique!
- Turner syndrome is a congenital condition, meaning it's something a person is born with.
- Each of us is born with two chromosomes. If you're female, you were born with two X chromosomes.

- If you're a male, you are born with one X and one Y chromosome.
- Turner Syndrome occurs when one of the X chromosomes is missing, either partially or completely.
- Turner syndrome often causes short stature, typically noticeable by age 5.
- It usually doesn’t affect intelligence but can lead to developmental delays especially with calculations and memory.Heart problems are common, too.
- While TS can somewhat shorten life expectancy, screening for and treating known related conditions helps protect health.

GENETIC COUNSELING

- Genetic counseling gives you information about how genetic conditions might affect you or your family.

- The genetic counselor or other healthcare professional will collect your personal and family health history.
- They can use this information to determine how likely it is that you or your family member has a genetic condition.
- Based on this information, the genetic counselor can help you decide whether a genetic test might be right for you or your relative.
- Based on your personal and family health history, your doctor can refer you for genetic counseling.
- There are different stages in your life when you might be referred for genetic counseling:

➢ Planning for Pregnancy:

  - Genetic counseling before you become pregnant can address concerns about factors that might affect your baby during infancy or childhood or your ability to become pregnant, including
  - Genetic conditions that run in your family or your partner's family History of infertility, multiple miscarriages, or stillbirth
  - Previous pregnancy or child affected by a birth defect or genetic condition Assisted Reproductive Technology (ART) options

➢ During Pregnancy:

  - Genetic counseling while you are pregnant can address certain tests that may be done during your pregnancy, any detected problems, or conditions that might affect your baby during infancy or childhood, including
  - History of infertility, multiple miscarriages, or stillbirth
  - Previous pregnancy or child affected by a birth defect or genetic condition
  - Abnormal test results, such as a blood test, ultrasound, Chorionic Villus Sampling (CVS), or amniocentesis
  - Maternal infections, such as Cytomegalovirus (CMV), and other exposures such as medicines, drugs, chemicals, and x-rays
  - Genetic screening that is recommended for all pregnant women, which includes cystic fibrosis, sickle cell disease, and any conditions that run in your family or your partner's family

➢ Caring for Children:

- Genetic counseling can address concerns if your child is showing signs and symptoms of a disorder that might be genetic, including
- Abnormal newborn screening results
- Birth defects
- Intellectual disability or developmental disabilities
- Autism spectrum disorders (ASD)
- Vision or hearing problems

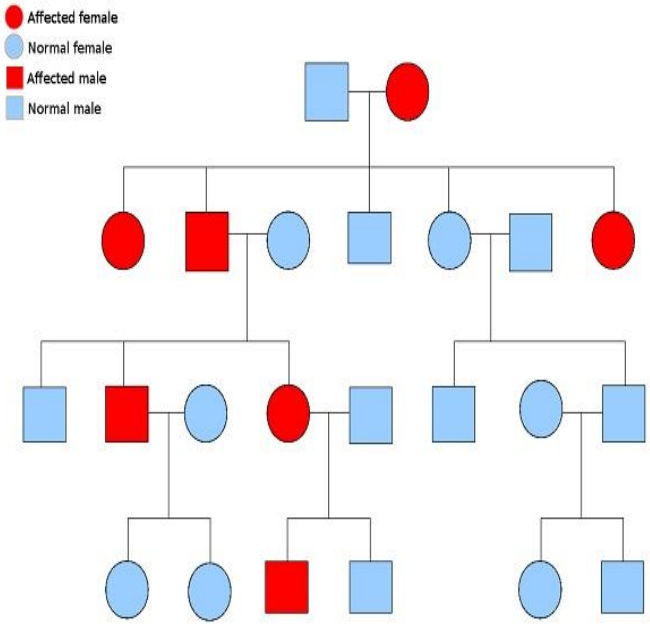
➢ Managing Your Health:

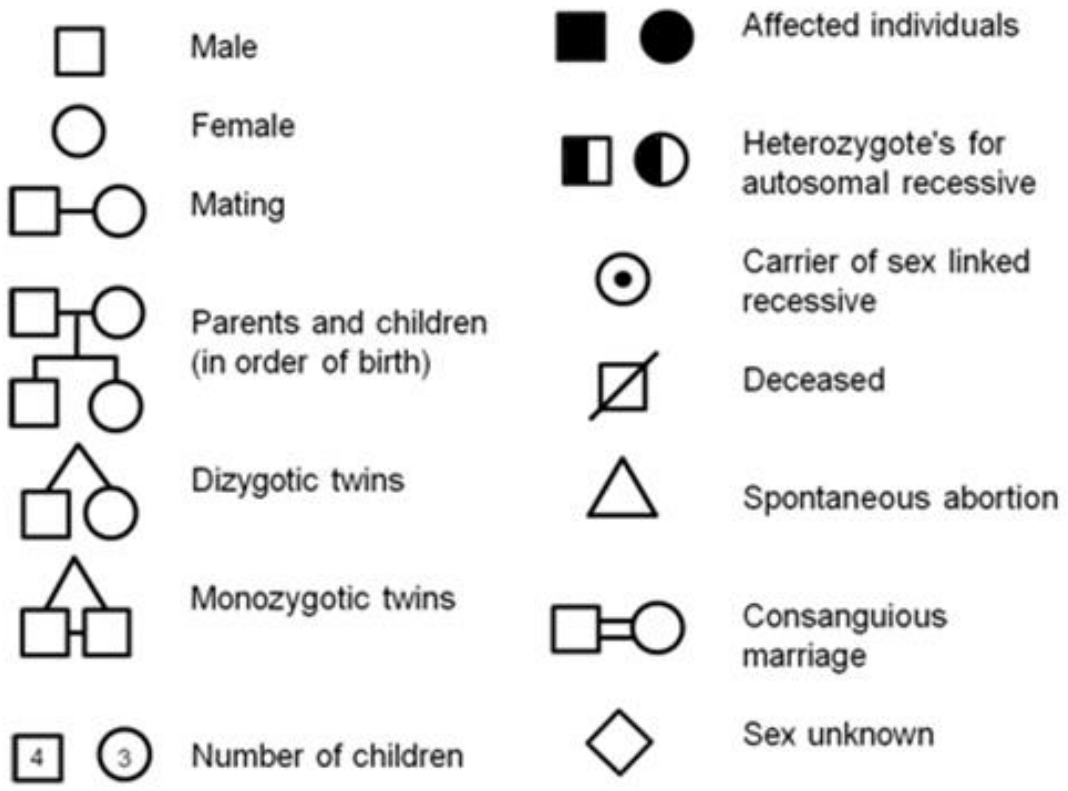
- Genetic counseling for adults includes specialty areas such as cardiovascular, psychiatric, and cancer.
- Genetic counseling can be helpful if you have symptoms of a condition or have a family history of a condition that makes you more likely to be affected with that condition, including
- Hereditary breast and ovarian cancer (HBOC) syndrome
- Lynch syndrome (hereditary colorectal and other cancers)
- Familial hypercholesterolemia
- Muscular dystrophy and other muscle diseases
- Inherited movement disorders such as Huntington's disease
- Inherited blood disorders such as sickle cell disease

- Following your genetic counseling session, you might decide to have genetic testing.
- Genetic counseling after testing can help you better understand your test results and treatment options, help you deal with emotional concerns, and refer you to other healthcare providers and advocacy and support groups.

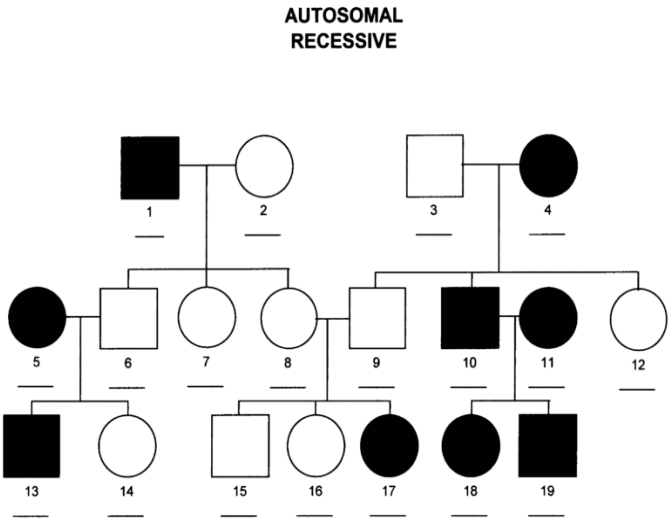
PEDIGREE ANALYSIS

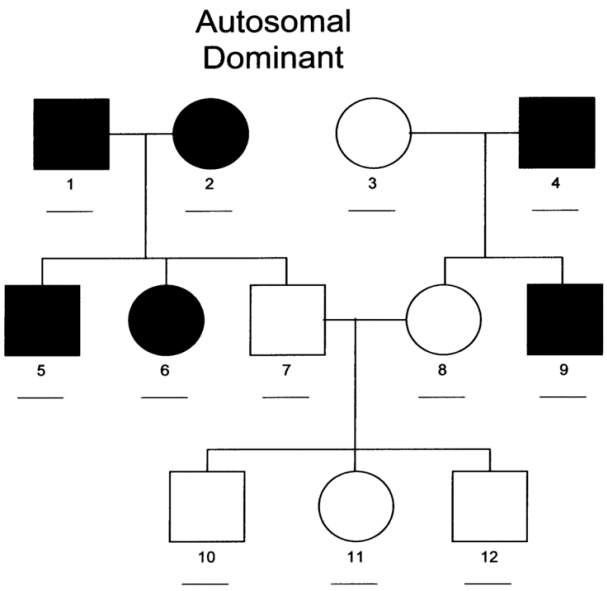
- Pedigree charts are diagrams that show the phenotypes and/or genotypes for a particular organism and its ancestors.





- Geneticists use a standardized set of symbols to represent an individual's sex, family relationships and phenotype.
- While commonly used in human families to track genetic diseases, they can be used for any species and any inherited trait.
- These diagrams are used to determine the mode of inheritance of a particular disease or trait, and to predict the probability of its appearance among offspring.





- Pedigree analysis is therefore an important tool in both basic research and genetic counseling.
- Each pedigree chart represents all of the available information about the inheritance of a single trait (most often a disease) within a family.

- The pedigree chart is therefore drawn using factual information, but there is always some possibility of errors in this information, especially when relying on family members' recollections or even clinical diagnoses.
- In real pedigrees, further complications can arise due to incomplete penetrance (including age of onset) and variable expressivity of disease alleles, but for the examples presented in this book, we will presume complete accuracy of the pedigrees.
- A pedigree may be drawn when trying to determine the nature of a newly discovered disease, or when an individual with a family history of a disease wants to know the probability of passing the disease on to their children.
- In either case, a tree is drawn, with circles to represent females, and squares to represent males.
- Matings are drawn as a line joining a male and female, while a consanguineous mating (closely related is two lines.
- The affected individual that brings the family to the attention of a geneticist is called the proband (or propositus).
- If an individual is known to have symptoms of the disease (affected), the symbol is filled in.
- Sometimes a half-filled in symbol is used to indicate a known carrier of a disease; this is someone who does not have any symptoms of the disease, but who passed the disease on to subsequent generations because they are a heterozygote.
- Note that when a pedigree is constructed, it is often unknown whether a particular individual is a carrier or not, so not all carriers are always explicitly indicated in a pedigree.