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B.A AND B.SC SEMESTER IV PAPER- 7

TOPIC- RECESSIVE INHERITANCE in MAN – SOME EXAMPLES

The patterns, in which Mendelian traits appear or transmitted in families, are called modes of inheritance. On the basis of chromosome where genes are located, you can find two types of inheritance - autosomal i.e. located on autosomes; and sex-chromosomal i.e. located on sex chromosomes, X or Y. Both autosomal and sex chromosomal inheritance may be subdivided as dominant or recessive inheritance on the basis of expression of alleles. However in respect of Y chromosome, there is no such subdivision like that described earlier. Hence, we have five modes of inheritance — autosomal recessive inheritance, autosomal dominant inheritance, X-linked recessive inheritance, X-linked dominant inheritance and Y-linked inheritance.

Mendel's observation of two different expressions of an inherited trait in a single locus (e.g. short or tall in respect of pea plant) narrates the facts that a gene can exist in alternate forms, usually called allele. An individual having two identical alleles is called homozygous, whereas the one with two different alleles is called heterozygous. Hence an individual may be homozygous either by two dominant alleles or two recessive alleles.

The allele that masks the effect of the other allele is called dominant (specifically completely dominant) and the masked one is called recessive. Whether the trait is dominant or recessive mostly depends upon the particular nature of the phenotype. Sometimes the heterozygous behave like an intermediate or a mix between homozygous dominant and homozygous recessive. Recessive disorders, in many cases, tend to be more severe or lethal and produce symptoms at an earlier age than dominant disorders.

If the genetic basis of a trait is known one can predict the outcomes of crosses. These are Punnett square method, forked line method and probability method. The ratios predicted from Mendel's law, apply to a new allele combination to each newly conceived offspring i.e. 50% chance of inheriting the allele, no matter what was the previous combination. You can compare the situation with tossing of coins; for first one the possibility of its being the head (or tail) is 50%. The same is true for second or any subsequent tossing. Therefore, if there is a 25% chance for a recessive disorder and first child is affected, there is no guaranty that next three will not be affected. The best way to calculate the probability of inherited traits was invented by Reginald Punnett and is called Punnett square. This is a simple graphical way to calculate all potential combinations of genotype for each time. You can start the same by drawing a grid of perpendicular lines. Now put the genotype of one parent across the top and other one down the left side. At last you can fill all the boxes by copying row and column letters (alleles).

AUTOSOMAL RECESSIVE INHERITANCE

Genes are inherited from our biological parents in specific ways. One of the basic patterns of inheritance of our genes is called autosomal recessive inheritance. Autosomal recessive inheritance means that the gene is located on one of the

autosomes (chromosome pairs 1 through 22). This means that males and females are equally affected. "Recessive" means that two copies of the gene are necessary to have the trait, one inherited from the mother, and one from the father. A person who has only one recessive gene is said to be a "carrier" for the trait or disease, but they do not have any health problems from "carrying" one copy of the gene. Most people do not know they carry a recessive gene for a disease until they have a child with the disease. Once parents have had a child with a recessive trait or disease, there is a one out of four, or 25 percent chance, with each subsequent pregnancy, for another child to be born with the same trait or disorder. This means that there is a three out of four, or 75 percent chance, for another child to not have the trait or disease.

The birth of a child with a recessive condition is often a total surprise to a family, since in most cases, there is no previous family history of a recessive condition. Many autosomal recessive conditions occur this way. As mentioned above, a person who "carries" one copy of an autosomal recessive gene is usually not aware they carry the gene, because they do not show any signs of the disease or condition. It is estimated that all people carry about five or more recessive genes that cause genetic diseases or conditions. Usually a person does not know they carry a recessive gene unless they have the disease in their family, or if they have had an affected child.

To have an autosomal recessive disorder, you inherit two mutated genes, one from each parent. These disorders are usually passed on by two carriers. Their health is rarely affected, but they have one mutated gene (recessive gene) and one normal gene (dominant gene) for the condition. With each pregnancy, two carriers have a 25 percent chance of having an unaffected child with two normal genes (left), a 50 percent chance of having an unaffected child who is also a carrier

(middle), and a 25 percent chance of having an affected child with two recessive genes (right).

Some important characteristic features are:

• Occurrence and transmission is not influenced by sex;.

• Traits can express only in homozygous condition;

• In a pedigree you can find the trait only in siblings, not in their parents;

• On average ¼ th of the sibs of the proband are affected;

• In the instance of a rare disease, affected individuals have normal parents;

• Ratio of affected, carrier and non-affected is 1:2:1 (in sibs); and

• Parents of an affected child, in many cases, are close blood relatives.

Results from each of the six possible crosses are summarized in Table 1

Autosomal Recessive inheritance

Parents	**Offspring**
One parent homozygous Normal Other parent homozygous Normal	All the offspring will be homozygous Normal
One parent homozygous Normal Other parent heterozygous Normal (Carrier)	50% probability that offspring will be homozygous normal 50% probability that offspring will be heterozygous normal (Carrier)
One parent heterozygous Normal (Carrier) Other parent heterozygous Normal (Carrier)	25% probability that offspring will be homozygous normal 50% probability that offspring will be heterozygous normal (Carrier) 25% probability that offspring will be Affected
One parent homozygous Normal	All the offspring will be heterozygous

Other parent affected	normal (Carrier)
One parent heterozygous Normal (Carrier) Other parent affected	50% probability that offspring will be heterozygous normal (Carrier) 50% probability that offspring will be Affected
One parent affected Other parent affected	All the offspring will be affected

Examples of AUTOSOMAL RECESSIVE include:- cystic fibrosis, sickle cell anemia, and Tay-Sachs disease.

Cystic fibrosis (CF) - Cystic fibrosis is one of the most common inherited single gene disorders in Caucasians. About one in 3,000 Caucasian babies is born with CF and about one in 25 Caucasians of northern European descent carries the gene for CF. People with CF secrete abnormal body fluids, including unusual sweat and a thick mucus which prevents the body from properly cleansing the lungs. The mucus interrupts the function of vital organs and leads to chronic infections. Classic CF also involves the pancreas and causes decreased absorption of essential nutrients. Life expectancy has improved, but, ultimately, death most often occurs from respiratory failure. Other people with variants of CF may have only lung involvement, sinusitis, or infertility.

Sickle cell anemia (SC)- Sickle cell anemia is one of the most common, inherited single gene disorders in African-Americans. About one in 500 African-American babies is born with SC, and about one in 12 African-American people carries the gene for SC. Sickle cell disease involves the red blood cells, or hemoglobin, and their ability to carry oxygen. Normal hemoglobin cells are smooth, round, and flexible, like the letter "O," so they can move through the vessels in our bodies

easily. Sickle cell hemoglobin cells are stiff and sticky, and form into the shape of a sickle, or the letter "C" when they lose their oxygen. These sickle cells tend to cluster together and cannot easily move through the blood vessels. The cluster causes a blockage and stops the movement of healthy, normal oxygen carrying blood. This blockage is what causes the painful and damaging complications of sickle cell disease. Sickle cells only live for about 15 days, whereas normal hemoglobin cells can live up to 120 days. Also, sickle cells risk being destroyed by the spleen because of their shape and stiffness. The spleen is an organ that helps filter the blood of infections. Sickled cells get "stuck" in this filter and die. Due to the decreased number of hemoglobin cells circulating in the body, a person with sickle cell is chronically anemic. The spleen also suffers damage from the sickled cells blocking healthy oxygen carrying cells. After repeated blockages, the spleen is very small and does not work properly. Without a functioning spleen, these individuals are more at risk for infections. Infants and young children are at risk for life-threatening infections. Treatment includes prompt emergency care for fevers and infections, appropriate vaccinations, penicillin, and management of anemia.

Tay-Sachs diseaseTay- Sachs disease is a fatal disorder in children (usually by age 5) that causes a progressive degeneration of the central nervous system. It is caused by the absence of an enzyme called hexosaminidase A (or hex A). Without hex A, a fatty substance builds up on the nerve cells in the body, particularly the brain. The process begins early in pregnancy when the baby is developing, but is not apparent until several months after the birth. To date, there is no cure for Tay-Sachs. Dr. Tay and Dr. Sachs, who originally described this condition, noted that most Tay-Sachs babies were usually of eastern European Jewish origin. About one in 30 persons of Ashkenazi Jewish ancestry carries the Tay-Sachs gene.