Cell and Molecular Biology
Prof. Vishal Trivedi
Department of Biosciences and Bioengineering
Indian Institute of Technology, Guwahati
Week 07
Concepts of Genetics (Part 1)
Lecture - 27
Law of Inheritance (Part 3)

Hello, everyone. This is Dr. Vishal Trivedi from the Department of Bioengineering, IIT Guwahati. And in this particular module, we are trying to understand how the genetic information is flowing from one generation to the next generation. In this context, so far, what we have discussed is the law of inheritance. So in that context, we have discussed Mendel's first law of dominance.

Then we also discussed Mendel's second law. And in the previous lecture, we also discussed Mendel's third law. Mendel's first law is mostly related to the genetics of the inheritance of a single gene, whereas in the previous lecture we also discussed the inheritance of two genes or polygenic situations. So far, what we have discussed is that the factors which the term Mendel has pointed to are responsible for carrying genetic information from one generation to the next generation.

So there are instances where the external factors, which are not part of the genetic material, are also influencing the phenotype, and there are many cases where people actually have identical genotypes but show different types of phenotypes depending on the external factors. Now, it's these external factors; the influence of external factors on the phenotypic characters is a very, very interesting topic to understand. Right. So in today's lecture, we are initially going to discuss how the external factors are controlling or regulating the phenotypic characters. And then, subsequent to that, we are briefly going to discuss sex determination.

We are also going to discuss genetic disorders. So, let's start today's lecture. So the first thing we would like to understand is how the external factors, which are not part of the cell and not part of the DNA, the genetic material, are also influencing the genetic factors or the phenotypic outcomes. Until the people who are following Mendelian genetics understand the concept that the genotype actually governs the phenotype. Then there was the concept of the twins, right? So people have found that the twin's brother, right? If there are twins, one is in the X condition, and the other is in the Y condition.

And if they continue to grow in those different conditions, what we found is that these two particular individuals, which are genotypically identical, actually have a lot of

variations in their phenotype. And then people have started discussing how these kinds of changes are happening, and all these genetic changes or all these phenotypic changes are actually part of epigenetics, so the C.H. Waddington, the person, coined the term epigenetics in the year 1940 to describe how environmental influences on developmental events can affect the phenotype of an individual. This is a very, very interesting observation that I have just given you an example of, right? If you have a twin, right? And suppose you have zygotic twins, for example, not Siamese twins.

So if you have zygotic twins, and if you keep one twin in hot weather, for example, and the other one in cold weather, what you see here is that at the end, phenotypically they are actually going to be different. So this kind of change affects the DNA because, if these are zygotic twins, the DNA or genetic material is the same. But the guy who is staying in the hot weather and the guy who is staying in the cold weather are actually phenotypically very, very different. Different in terms of many aspects, and not only that, this is the environmental influence, whereas there are other factors that are also influencing the overall phenotype. So it's not like they are very different in terms of skin color, only right? They are also different in terms of their metabolism.

They are also very different in terms of many other phenotypic characters. Now, how did all this start? This started with the study of genetics in the year 1871, leading to the development of a field called genetics, and then epigenetics, which was termed in 1942. In 1948, DNA modifications were discovered. So one of the modifications was that the DNA is getting methylated. Then in the year 1951, the Barbara M.

Thiglin talk actually discovered the nature of the mutable locus, right? And then, you know, DNA methylation and gene switching were discovered in the year 1975. And then in the year 1984, the role of the paternal and maternal genomes was discovered in development. And then we also started doing a lot of experiments where they are actually cloning and doing all these kinds of experiments. As a result of that, in the year 1996, Dolly was discovered, having been cloned. And then, subsequent to that, people have also studied topics related to the histones.

So remember when we were discussing the genetic material of the organisms and how the packaging is happening and all that, we discussed that the histone is very, very important. And histones are actually controlling the packaging of the DNA, right? So if you control the packaging of the DNA, although the two individuals will have the same genetic material, their expression status is going to change because you are actually changing the histones by making different types of modifications. So what are the different types of traits that are related to epigenetics? So epigenetic traits are stable, mitotically and meiotically heritable phenotypes that result from changes in gene

expression without alterations to the DNA sequence. This is a very interesting topic. Basically, what you have is, for example, you are going to have the epigenetic tags.

You are going to have the epigenetic sequences, and you are going to have the epigenetic tags on the female eggs and these tags on the sperm. And then, when they are actually going to join, they are going to form the eggs, right? And they are actually going to form the embryo. So that's how the epigenetic tags from the male and the female are actually going to come together. And that's how they are actually going to result in phenotypic changes, you know, because the reproductive cells are going to grow and give you complete organisms. Since these epigenetic tags are responding to environmental factors, they are actually going to produce different types of individuals.

Epigenetics is the study of the way in which epigenetic traits are altering the cells and the tissue-specific patterns of gene expression, so basically, epigenetics. The study is how the DNA, the information from the DNA, is actually going to be utilized for the production of the protein. So basically, it is not changing the DNA, but it is changing the protein. And remember that the protein is actually the final molecule that is going to be responsible for providing the phenotype, right? So, if you alter the protein, if you reduce the amount of protein, if you increase the amount of protein, that's how you are actually going to change the phenotype, right? And all of that is being done by the many types of epigenetic traits and characters. So how does the regulation of epigenetics work? So the gene expression uses the reversible modification of the DNA and the chromatin structure to mediate the interaction of the genome with a variety of environmental factors and generate changes in the pattern of gene expression in response to these factors.

So remember that epigenetics is a very big topic, and epigenetic regulation is also very important, and you actually have different types of mechanisms through which you can modify the DNA, do the DNA packaging, and so on. So epigenetic regulation is itself a very, very important topic, and in this particular lecture, what we are trying to do is introduce you to the topic so that if you find it more interesting, you will be able to study it, right? Then there is the concept of the epigenomes. So the epigenetic state of a cell, the organism has one genome, and the genome can be modified in diverse cell types at different times to produce many epigenomes. Remember that the genome of an organism is the same, right? Whether it is the genome present in the liver, whether the genome is present in the brain, whether the genome is present in our eyes, tongues, and so on, right? Or the genome that is present in the pancreas and so on. But you see that the protein production from all these organisms or all these organs is very, very, very different, right? And all of that is being done because the genome is being modified in a different way, and that's how it is producing the epigenome, which means the genome is being modified by the epigenetic factors.

And that's how it is actually going to change. Now, what is the epigenome? So, the epigenome is actually the way in which the normal genome is altered, and that's how it is referred to as the epigenome. So, there are, you know, different types of alterations. Alteration is when you are actually going to have the epigenetic repressors, or you are actually going to have the epigenetic activators or the remodelers. Right? Epigenetic repressors are actually going to downregulate the expression of certain genes, so it will actually reduce the amount of that particular protein, whereas in the case of epigenetic activators or remodelers, it is actually going to increase.

The amount of that particular protein. And you know that when we were discussing polygenic inheritance, what we said is that it is not a single gene that is actually going to regulate a particular type of phenotype. Sometimes what phenotype you observe is regulated by multiple genes, right? And when multiple genes are producing the actual phenotype, it is the summation of the effects of the individual proteins. Right. A classical example is skin color.

Right. So skin is being controlled not by one gene. Right. Skin is controlled by multiple genes. And if multiple genes are responsible for skin color, what you can do is actually modulate the production of these proteins. And that's how you can have the different shades of a particular skin.

Right. So you can have the, you know, no color. Right. So then it's going to be very white skin. If you have the expression of all the genes, then it's going to be black skin.

Right. So all the epigenetic alterations are encoded within the genome, and that's how they are actually going to be carried from one generation to the next. and that's how it is actually going to be responsible for you know the final outcomes, although there's no change in the DNA content Now, talking about the epigenetic alterations, the epigenetic information or epigenome can be transmitted to the daughter cells via mitosis and to future generations via meiosis. Remember, all these epigenetic tags are going to be carried in a particular family, and that epigenetic tag will be passed from one generation to the next. Depending on the environmental factors, these epigenetic tags are actually going to be expressed more or less. As a result, you might see that some of the people who are staying in one genetic environmental condition versus another environmental condition will experience alterations in phenotypic changes.

So there are three major mechanisms that have actually been responsible for the epigenetic outcomes. First is the reversible modification of DNA by the addition or removal of a methyl group. So this means there will be methylation, right? And so if

there is methylation of the DNA at the different sites, methylation is going to modulate gene expression. Right. And there is a developed mechanism through which methylation is actually going to change gene expression.

And when there is a change in gene expression, it is actually going to change the amount of protein that is going to be produced. And as a result, you are actually going to show one phenotype versus the second phenotype. The same is true for the eye color as well. Right? So if the amount of protein is actually going to decide what color grade you are going to exhibit in your eyes. Then the second is the alteration of the chromatin by the addition or removal of chemical groups to the histone proteins.

So, remember that the histones are packed with the DNA by a positive-negative interaction. So, histones are positively charged proteins. These are histones, right? When we were discussing the nucleosome, we discussed it at that time. Right. So histones are actually going to cover the DNA.

Right? And this DNA, which is present on the histone core, will not be allowed to participate in any of the downstream reactions, such as replication, transcription, and so on. So if you are actually going to make the epigenetic changes to these histone proteins, they will lose their positive charge. Right. For example, if you do the stylization, it is actually going to impart the negative charges.

Right. So if you do the acetylation, basically, you are actually going to reduce the effective positive charges. You are actually going to bring more negative charges to the histone proteins. And as a result of that, the DNA that has been rolled onto this is going to be more freely available for participation in the different types of reactions. For example, it is going to participate in the transcription. And as a result of this, this portion of DNA, which has not been bound to the histone, will actually be transcribed better.

And that's how it is actually going to provide you with the protein corresponding to this region. And because of this protein, it is actually going to result in the phenotypic changes. Then you are actually going to have the third aspect, where you are going to have a regulation of gene expression by the known coding messenger RNA, or the mRNA. Right. So these are some of the three mechanisms that people have proposed for the observed epigenetic changes in the particular organism.

And what is the role of these epigenetic changes? So they are actually going to have a role in the imprinting. They are also playing a role in the development of cancers. They are also playing a role in the behavior of an organism, and they're also going to change the environmental genome interactions, right? Moving on to the next topic, which is the

sex determination in the organism. So sex determination has always been controlled by the sex chromosomes, right? So sexual reproduction is the formation of offspring that are genetically distinct from their parents, most often two parents contribute genes to their offspring, right? Among the few periods, sexual reproduction consists of two processes that lead to the alteration of haploid and diploid cells. Meiosis reduces the haploid gamete, and fertilization produces the diploid zygote.

The term "sex" refers to the sexual phenotype. Most organisms have only two sexual phenotypes: the male and the female. The fundamental difference between males and females is the gamete size. The male produces the small gamete, which is called sperm in the case of humans, and the female produces the relatively large gamete, which is called egg. The mechanism by which sex is established is sex determination.

So you have different types of mechanisms. You have the XX/XY sex determinations. The mechanism of sex determination is, in a grasshopper, studied by Mackling and is one of the simplest mechanisms of chromosomal sex determination. It's called XXXO system. In this system, the females have two X chromosomes and the males possess a single X chromosome, XO.

There's no O chromosome. The letter O signifies the absence of a sex chromosome. In meiosis in females, the two X chromosomes pair and then separate, with one X chromosome entering each haploid. So basically, you have the female, you have the male; the female is XX and the male is XY, right? And in males, the single X chromosome segregates during meiosis to half the cells, and the other half has no X chromosome, right? So basically, it is going to give you the two gametes. One is X, the other one is X, and in this case, you're going to have the two gametes.

One is X. The other one is actually going to be O, which means minus. Right. So there will be XO.

Right. Now, when there is fertilization. So if X is going with X, then it is going to produce XX. If the X is going with the X, it is going to produce the XX. Right? And if the X is going with O, then it is going to produce the XO. And with this one too, you are going to produce the XO, right? So, because the male produces two different sex chromosomes, they are said to be the heterogametic sex. Females, when we produce a gamete, are full with respect to the sex chromosomes and the homogametic sex.

So, in the X-X exosystem, the sex of an individual is therefore determined by which type of male gamete fertilizes the egg. X-bearings form units with the X-bearing to produce the XX digot, which then develops into a female, right? So, remember that if the XX is

formed, then it is going to be female. XO is being formed, so it is going to be male, right? So, if the sperm lacking the X chromosome and the X bearing the X produce the exozygote, then it is going to develop into the female. Then the second way of characterizing is the XX and XY. So, this is the most popular one, which is actually happening in many types of organisms, including humans, right? So where you are actually going to have the females, females are actually going to have XX and the males are actually going to have XY.

So this is the female, right? And this is going to be male, right? And one after the meiosis, you are actually going to produce the eggs, which are going to have X, or you are going to produce the sperm, which is going to be either X, or you are going to produce the sperm, so this is going to be an egg. This is going to be sperm. And when there is fertilization, if you are producing XX or you are producing XY. Right. So you basically have two eggs, and if the X is combining with X, you're going to have XX.

If X is combining with Y, then you're going to have XY. If X is combining with X, you're going to have XX. And if X is combining with Y, you're going to have XY. Now, this XX is going to be female. And the XY is going to be male, right? So here again, the male is actually going to decide the sex of the offspring, right? So the female is homogametic, and the male is heterogametic. Male is the heterogametic, so it is going to have XY; female is going to be XX, right? And ultimately, it is going to be that humans, like Drosophila, have XXXY determination.

But in humans, the presence of a gene on the Y chromosome must determine maleness. Right. And this is what we have; we are going to study further where we are going to talk about the Y-linked characters and so on. Right. Then the sex chromosomes do not segregate properly in meiosis or mitosis, illustrating the importance of the Y chromosome in human sex determination.

The XY determinations are not truly homologous. They do pair and segregate into different cells in meiosis. Now, this is what it's showing here. In the parent generation, you have the XY and the XX, which will be male and female when they undergo meiosis. Then it is going to form the gametes: gametes containing X, gametes containing Y, or gametes containing XX. And then there will be a fertilization that is going to produce either the XX or the XY.

And that's how the inheritance of a sex in an organism with XY chromosomes results in an equal number of male and female offspring. Then we have a third system; the third system is ZZ and ZW. So in this particular system, the female is heterogametic, which means the ZW is actually for the female and ZZ is actually for the male.

Right. And the male is homogametic. So to prevent confusion with the XS and XY systems, the sex chromosomes in these systems are labeled as Z and Y, but the chromosomes do not resemble ZS and WS, right? So female, In this system are ZW. After meiosis, half of the eggs have a Z and the other half actually have a W. Males are actually ZZ, right? So all sperms contain only the Z chromosomes, and the sperm in birds, moths, some amphibians, and fish. Then we also have sex determination in honeybees, which is a haplodiploid system. So in some insects like Hynometra, there are no sex chromosomes; instead, the sex is based on the number of chromosome sets found in the nucleus of each cell.

So males develop from the unfertilized eggs and females develop from the fertilized eggs. The cells of the male Hynometra possess only a single set of chromosomes, right? That means they are haploid. Whereas the cells of the female process the two sets of chromosomes, which means they are going to be fertilized and are diploid. So the haploid-diploid method of sex determination produces some odd genetic relationships. When both parents are diploid, siblings on average have half their genes in common because they have a 50% chance of receiving the same alleles from each parent.

In these insects, the male produces sperm by mitosis, so all offspring receive the same set of paternal genes, right? So, there will be no diversity, and there will be no deviations. They deployed female-produced eggs by normal meiosis. Therefore, the sisters have a 50% chance of receiving the same allele from their mother and a 100% chance of receiving the same allele from their father. The average relationship among the females is 75%. Brothers have a 50% chance of receiving the same copy of each of their mother's two alleles at any particular locus, so their average heterozygosity is only 50%.

The greater genetic relatedness among female siblings in insects with haploid-diploid sex determination may contribute to the high degree of social cooperation that exists among the females of these insects. So this is exactly what is shown here, right? Once we discuss the epigenetic contributions to genetic variations, we will talk about sex determination. Now let's move to the next topic, which is whether there will be an alteration in the DNA; if so, it will result in different types of disorders.

Right. Some of the disorders could be related to genetics. Right. Some of the alterations may not be noticed because they may not be causing significant changes to the phenotype and so on. So let's talk about a genetic disorder. So we have two different types of genetic disorders: the genetic disorders where a particular type of chromosome is altered and disorders that follow Mendelian inheritance. So the first trait is X-linked recessive.

So these X-linked recessive traits have a distinct pattern of inheritance. They actually appear more frequently in males because males need to inherit only a single copy of the allele to display the trait. Whereas the female must inherit two copies of the allele, one from each parent, to be affected. So this is actually a characteristic of the X-linked recessive traits, right, where the males are going to be affected even if they are actually getting one copy of the X chromosome, whereas the females are only affected if they are getting the affected X from both parents, right? So it is actually going to be more of a problem for the male. So all the X-linked recessive traits would be a problem for males rather than females. So even if the males are getting one X chromosome where this particular trait is present, they are actually going to exhibit the particular disease.

So this is what is shown here: if you have the female, where the female is actually a carrier, it is actually carrying the gene. But having only one X means, you know, getting the wrong information. The other X is perfectly fine. So it is actually going to be a career. When this is going to mate with the normal male, the normal male will be like this.

Right. And then they are actually going to produce the male. And the male is only going to have one X chromosome, which is from the female side. So it is a carrier. And that's how it is actually going to have the X and Y. As soon as they have the one X. Which is from the affected gene, carrying the affected gene; it is going to show you the disease, actually.

Right. So wherever there are, whereas in the case of females, it's only going to show the problem when this particular male is also going to go for sexual reproduction with the carrier females or with the affected females. Right. Only then is it actually going to show you that this is what is shown here. So actually, these traits appear more often in males and are not passed from father to son. So it doesn't go from father to son, actually, because from the father to the son, the son is going to get the X from the mother, not from the father.

It's only going to get the Y character. And daughters are also not going to get it as long as the mother does not have the affected X chromosome. So if only the mother is a carrier of this particular trait and the father has the disease, then there is a chance that the sons and daughters will also inherit the excellent characteristics. One classical example is hemophilia. So the X-linked recessive trait in Haemophilia is Haemophilia A, also called the classical Haemophilia. And in this particular disease, there will be an absence of the protein necessary for the blood to clot.

So remember, there's a cascade of reactions that is required for blood clotting. And one of the proteins is missing, and that has been responsible for the development of

hemophilia. So the factor eight is located at the tip of the long arm of the X chromosome. So, hemophilia A is an X-linked recessive disorder. People with Haemophilia A bleed excessively; even small cuts and bruises can be life-threatening.

Then we have another disease that is called color blindness. So color blindness is also an X-linked recessive trait, and it is a type of color blindness, right? So when the human eye color is perceived in light-sensing cones that link, each cone contains one set of three pigments, right? So you have the light-absorbing pigments and so on, right? And humans actually detect only three colors: red, green, and blue. But the brain mixes the signals from the different cones to create a wide spectrum of colors that we perceive. So these are actually the basic colors, right? And each of these pigments is encoded by a separate locus. The locus for the blue pigment is found on chromosome number seven.

And for the green and the red, it is close to the X chromosome. So the most common type of human red blood color blindness is caused by the defect of the red and green pigment, and we will refer to this condition as red-green color blindness. Because the red and green pigments are coded for in a region very close to the X chromosome. So, mutations that produce defective color vision are generally recessive, and because the genes coding for the red and green pigments can be located on the X chromosome, they actually follow the X-linked recessive characteristics. So this is what is shown here.

You have normal vision, normal vision, and color vision for the female. Then you have a color-blind male. And when they come together, there will be fertilization in the first generations. And then you are going to have the normal color vision females, who actually carry the X chromosomes even from the father. Whereas in this case, the normal color vision male is going to color, right? So, a male with normal color vision, actually.

So the red-green color blindness is inherited through X-linked recessive traits in humans. So, the normal female and the color-blind male, actually. So in the reciprocal cross between a colorblind woman and a man with normal color vision, the woman produced only XC-bearing gametes. The man produces the gametes, which are the X and Y chromosomes. And men inherited the X chromosomes from their mother, because both of the mother's X chromosomes bear the XC allele. And all the male offspring will be colorblind, right? So, in contrast, the female inherited X chromosome from both parents, thus the female offspring of this reciprocal cross will be heterozygous and will have normal vision.

So, females are colorblind only when the colorblind alleles have been inherited from both parents, and that is very, very important. So, X-linked characters are mostly a problem for males rather than females. Then we have the X-linked dominant traits. So X-

linked dominant traits appear in males and females, although they often affect more females than males. So, like X-linked recessive traits, the male inherits X-linked dominant traits only from his mother; the trait is not passed from father to son, right? A female, on the other hand, inherits an X chromosome from both her mother and her father, so she can receive X-linked traits from either parent.

Each child with an X-linked dominant trait must have an affected parent, unless the child possesses a new mutation or genes. X-linked dominant traits do not skip generations. Affected men pass the traits on to all their daughters and none of their sons, as seen in the children of 1-1, right? In contrast, the affected woman passes the traits on to half of her son and half of her daughter, as seen, right? So this is exactly what is shown here, right? So this is the affected male, and this is the female, and then there will be a second generation; all the females are actually going to be affected, and so on. Right, so excellent dominant traits affect both males and females, and males must have an affected mother.

Right, then we have another disease which is called hypophosphatemia. Hypophosphatemia is a disease. So it's an X-linked dominant trait, where you have the hypophosphatemia, also called familial vitamin D resistant rickets. People with these traits have features that superficially resemble those produced by rickets, such as bone deformities, stiff spines and joints, bowed legs, and mild growth deficiencies. This disorder is resistant to treatment with the vitamin D that normally cures rickets. So, X-linked hypophosphatemia results from defective transport of phosphate, especially in the cells of the kidney. People with this disorder excrete large amounts of phosphate in their urine, resulting in low levels of phosphate in the blood and reduced deposition of the mineral into the bone.

As is common with the X-linked dominant trait, males with hypophosphatemia are often more severely affected than females. Then we have the Y-linked traits. A trait resulting from a mutant gene that is carried on the Y chromosome but has no counterpart on the X is called the Y-linked or holandric traits, right? Such traits should be easily recognizable because every son of an affected male is expected to have the trait. So the female should never express it, right? Only the males are affected, and the trait is passed from father to son.

So this is the pedigree of the Y-linked characters. So if the father is affected, it is going to transmit everything to the son. Right? All the time. Right? So it's going to go into the son only because it is a trait that is present on the Y chromosome, and the Y chromosome is only present in males. One such example is the hairy air, right? A possible example of Y-linked inheritance is the hairy air trait in which the bristle hair of a typical land grows from the ear.

This trade is common in that part of India, and some other populations also exhibit it. Although the trade show is a father-to-son inheritance, there's no doubt that it is a complex phenotype. Many of the collective pedigree can be interpreted in other ways, such as autosomal inheritance. Then we have the autosomal recessive traits. So autosomal recessive traits normally appear with equal frequency in both sexes and appear only when a person inherits two alleles for the trait, one from each parent.

And if the trait is uncommon, most individuals carrying the alleles are heterozygous and unaffected. Consequently, the traits appear to skip a generation. Frequently, a receptive allele may be passed down for a number of generations without the trait appearing in a pedigree, right? So this is an example of recessive traits, right? So where are you, you know, the female, actually getting affected, right? And a male is being affected. So auto-level recessive traits normally appear with an equal frequency in both sectors, and it seems to skip a generation. So remember that in this generation, it is affecting, skipping the first cousins, and then skipping again, right? One such example is sickle cell anemia, right? So, sickle cell anemia is a genetic disease affecting hemoglobin, the oxygen-carrying protein.

So sickle cell anemia was first described in the year 1910. And this is a condition of low oxygen tension. Red blood cells in people who have the disease lose their characteristic disc shape and assume the shape of a sickle. This is sickle cell anemia, right? So these are the disc-shaped RBCs when they convert to the sickle cell phenotype. The sickle red eyes are fragile and break easily, resulting in anemia. Sickle cells are not as flexible as normal cells, and they tend to clog capillaries rather than squeeze through them.

And as a result, blood circulation is impaired and tissue becomes deprived of oxygen. So these are just details of sickle cell anemia, where you actually have mutations in the hemoglobin structure. As a result of that, it is actually going to change the morphology of the RBCs. Then the second is thalassemia. So thalassemia is an inherited disease characterized by faulty synthesis of hemoglobin.

The name is derived from the Greek word thalassa. which means the C and thalassemia consist of a group of disorders that may range from a barely detected abnormality of blood to a severe or fatal anemia. So, adult hemoglobin is composed of two alpha and two beta chains, right? There are two copies of hemoglobin alpha genes, HbA1 and HbA2, which encode the alpha chain, and both genes are located on chromosome number 16. The hemoglobin beta chain encodes the beta chain, and it is located on chromosome number 11. In alpha thalassemia, there is a deficiency of the alpha chain and an excessive amount of the beta chain, which binds oxygen poorly, leading to a low concentration of

oxygen in the tissues, which is called hypoxia.

Whereas in the case of beta thalassemia, there is a lack of beta chains. So basically, there will be, you know, an underproduction of the alpha chain or the beta chain. Then the second disease is called phenylketonuria. Phenylketonuria is an inherited error of metabolism caused by a deficiency in the enzyme phenylalanine hydroxylase. Loss of this enzyme results in mental retardation, organ damage, and unusual posture and can result in a case of maternal PQ. Classical phenylketonuria is an autosomal recessive disorder caused by mutations in both alleles of the gene for phenylalanine hydroxylase found on chromosome 12.

So, in some cases, the mutations in this particular gene result in the mild form of phenylketonuria, which is called hyperphenylalaninemia, right? Both diseases are the result of a variety of mutations in the pH locus in cases where a patient is heterozygous for the two mutations of the pH. Then we also have the autosomal dominant traits. So autosomal dominant traits appear in both sexes with equal frequency, and both sexes are capable of transmitting their traits to their offspring. Every person with the dominant traits must inherit the alleles from at least one parent, whereas the autosomal dominant traits do not escape degeneration. Then one of the classical examples is hypercholesterolemia, right? So the one trait usually considered to be autosomal dominant is familial hypercholesterolemia, an inherited disease in which the blood cholesterol is greatly elevated, owing to a defect in cholesterol transport, right? So cholesterol transport is an essential component in which cholesterol is transported from the blood to the liver, and that's how it is stored, or the cholesterol is transported from the blood to the depot tissues, right? So, because cholesterol is a lipid, it is not readily soluble in the blood.

As a result, it is being formed as they understand the LDL particles and all that. Therefore, it has been transported for the body in a small soluble particle, which is called the lipoprotein or LDL. And the LDL particles consist of a core lipid surrounded by a shell of charged phospholipid and protein that dissolve easily into the blood. One of the principal lipoproteins is the LDL or low-density lipoprotein. So when the LDL molecule reaches the cell, it attaches to the LDL receptor and then it is taken up, right? This is what we discussed when we were talking about the transport of the material into the cell, right? And then, you're also going to have, you know, hypercholesterolemia because there will be a problem with the alterations in, you know, the uptake, actually.

So there will be a problem in the gene that will code for the LDL receptor. Then the second series of the genetic disorder is where you are actually going to have the problem on the chromosome, right? So, chromosomal aberrations, right? So the changes in the

genome involve the part of the chromosome where the chromosome or the whole chromosome is being, you know, altered, right? So chromosomal aberrations or chromosome mutations. So it is of two types: structural alterations and numerical alterations. In the structural alterations, there will be a change in a specific part of the chromosome. So it could be duplications, deletions, inversions, or translocations. So, what is a duplication? So duplication, chromosome duplication is a mutation in which part of the chromosome has been doubled.

Consider a chromosome with a segment A, B, C, D, E, F in which they represent the centromere, right? And then there will be a tandem duplication. There will be a displaced duplication, and there will be a reverse duplication. So in a duplication, in a tandem duplication, the duplication might include the E of sigma. So this is actually going to have them. This segment, right? Giving rise to a chromosome with a segment like A, B, C, D, E, F, G, right? So this actually gets doubled, right? And because of that, you are going to have a chromosome like this, and this is actually the syndromia, right? Then we have the displaced duplication.

So, if the displaced duplication is located some distance from the original segment, either on the same chromosome or a different one, then it is called a displaced duplication. For example, there will be A, B, C, D, EF, GH, and then EF at the end of the particular chromosome. So then there will be a displaced application, and then you have a reverse duplication. Reverse duplication means that EF is actually going to present as FE. So in a duplication, it can either be in the same orientation as the same signal or, as in the preceding examples, be inverted, right? For example, A, B, C, D, E, F, and then F, E, and G.

So, when the duplication is inverted, it is called a reverse duplication. Then we have a deletion. The deletion could result in the loss of a segment of genetic material. And this is called deletion. So it could be terminal deletions, or it could be intercalary deletions. So in a terminal, deletions like A, B, C, D, E, F, G, the G is going to be deleted.

So this is going to be your mutated chromosome. And then you have inter-curly deletions. So you are going to have the ABCDEF, and in between, there will be a deletion. So it is actually going to have the ABCDEFG, right? Then we have the inversions. So it is another chromosomal abnormality in which the order of a gene in a chromosome segment is reversed by an angle of 180 degrees. So remember that we have the genes which are being placed onto the chromosome.

Remember that the chromosome has a centromere, and then you have a chromosome like this. So, genes are placed like this. Genes are placed like this. and they are actually in

order. So remember that if the order is A, B, C, D, E, F, G, H, due to the abbreviation, the sequence of genes becomes A, B, C, D, G, F, E, and H.

There is an alteration here. So it could be a pericentric inversion. So in the pericentric inversion, the inverted segment of the chromosome contains the centromere. Sometimes it is responsible for the evolution of organisms. For example, you have a, b, c, d, e, f, g; then it becomes a, e, right? So it means you know this one comes here and this one goes here, and then you have a, d, c, v, f, g. So if you have a pericentric inversion, then the things will go from here to here, and as a result, it is going to have complete changes.

Then we have the pericentric inversion. So in the parasitic inversion, the inverted segment of the chromosome does not have a centromere. So, for example, A, B, C, D, E, F, and G.

Then you have A, B, C, and D. And here there is the gene. So, actually, this pigment is getting flipped. So it is going to be flipped like this. And because of that, the genes that are present on this side will come to this side, and the genes that are present on this side will come to this side. So that will be called a parasitic inversion.

Then you have a translocation. So this is a kind of chromosomal abnormality in which the interchange of chromosome segments occurs. So, it could be a reciprocal translocation. So when the translocation occurs between the two non-homologous chromosomes, it is called a reciprocal translocation or the illegitimate crossover. In a heterozygous translocation, one member of each pair of chromosomes is normal and the other member has the interchange segment. Then there is the non-reciprocal translocation.

So in a non-reciprocal translocation, the genetic material moves from one chromosome to another without any reciprocal change. So, for example, if you have two non-homologous chromosomes like AB-C, D, E, F, G, and MN-OPQRS, and if there is a non-reciprocal movement, then there will be some movement of the molecule between A, B, C, D, and G. So you basically have the EF, which is moved from this chromosome to this chromosome, and as a result of this, this chromosome changed to AB-CDG, and this one is going to change to MN-OPEFQRS, right? Then we have the Robustian translocation. So the long arm of the two epicenters becomes joined to form a single common centromere through a translocation.

So this is an example of the Robustian translocation. Then we also have the numerical chromosomal variations. So where the number of chromosomes is actually being changed. So it is also known as the alteration in the number of chromosomes from the

deployed state, which is called numerical chromosomal alterations. This is also known as ploidy. So if there is a change in the number of individual chromosomes, it will be called aneuploidy, or if there is a change in the number of chromosome sets, it will be called polyploidy. So in aneuploidy, aneuploidy can be caused by the loss of the centromere, preventing the spindle fibers from attaching, or the small chromosome generated by the Robertsonian translocation may be lost during mitosis and meiosis.

And the third aneuploidy may arise because of the failure of a homologous chromosome to segregate or separate during meiosis or mitosis. Aneuploidy has two types. Hypoploidy and hyperploidy. So in hypoploidy, a decrease of one or two chromosomes from the diploid set is described as hypoploidy. So there are two types of hypoploidy: monosomy and nullisomy. So monosomy is due to the loss of a chromosome from the diploid set, for example, 2N-1, right? Remember that all the chromosomes are present as the 2N number, correct? So if there is a loss of one chromosome, then it will be 2N-1, and that will be a part of monosomy.

Whereas nullisomy is a condition in which a pair of homologous chromosomes is absent, which means 2n minus 2. So basically it will still be 2n, but there is a loss of two molecules, right, instead of one molecule. So here there will be one chromosome that will remain unpaired, whereas in this case both chromosomes are being removed, so it is actually not going to have any chromosome that remains unpaired.

Then we have the hyperploidy. So hyperploidy is the addition of one or two chromosomes in a diploid set. So it results in hyperploidy. So it could be trisomy, it could be tetrasomy, it could be Turner syndrome, and it could be cliffhanger syndrome, right? And the most common is the autosomal aneuploidy, which is a trisomy of 21, also called Down syndrome. Then we have polyploidy, right? So the addition of one or two correct sets of chromosomes to the diploid state as well as to the polyploidy. And it is commonly noticed in the plants and rarely in the animals. There are two kinds: autopolyploidy and allopolyploidy.

So the autopolyploidy, the addition of one or more haploid sets of its own genome in the organism, results in autopolyploidy. For example, the watermelon, grape, and bananas are autotriploid, whereas the apple is autotetraploid. Then you have allopolyploidy, where an increase in one or more haploid sets of chromosomes from two different species results in allopolyploidy. Then titicale is the first man-made cereal. It is obtained by crossing a wheat, Triticums, and a rice cereal, right? The F1 hybrid is sterile; then the chromosome number is doubled using colchicine and becomes hexaploid. So, there are many examples; there are many diseases, the important diseases that are happening because of these chromosomal numerical alterations, such as the downstream norms, as well as the

different types of chromosomal problems.

Okay, so what we have discussed is the epigenetic effect of environmental factors on the alteration of the phenotypic characteristics of organisms. So we discussed the mechanism, how the epigenetic sites are carried from one generation to the next, and that's how these epigenetic effects continue and are carried out from generation to generation. And there are three different types of mechanisms that have been responsible for the epigenetic mechanism, one of which is where you are actually, you know, altering the DNA by doing the methylation. The second is that you are actually changing the DNA packaging. And the third, where you are actually using the small non-coding messenger RNAs, is. Now, this epigenetic control is very, very important, and it has actually been used by organisms to adapt to different types of environmental factors or conditions.

Apart from that, we also discuss the sex chromosomes. We have discussed the sex determinations in the different types of organisms. So we have discussed the XX and XO types of sex determination. Then we also discuss the XX and XY types of sex determination and so on. And lastly, we have also discussed the different types of genetic disorders. So we discuss genetic disorders due to the different types of chromosomally linked genetic disorders.

So we discussed the X-linked chromosomal genetic disorders and Y-linked chromosomal genetic disorders. And then lastly, we have also discussed how the genetic disorder arises when there is a change in the number of chromosomes present in a particular organism. So with this brief discussion about the different types of principles and the rules required for carrying the information from one generation to the next and how we can use this information to understand the phenotypic characters going from one generation to the next. I would like to conclude my lecture here. In our subsequent lecture, we will discuss some more aspects related to this particular topic. Thank you.