Biology for Engineers and Other Non-Biologists
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Week- 04
Lecture - 18
Mendelian Genetics: Pedigree Analysis

Welcome to the next lecture on Mendelian genetics. We have been talking about the use of Mendelian principles to analyse inheritance especially toward prediction of the occurrence of a (certain) of some inherited disease in an offspring, so that the parents would be able to handle it better.

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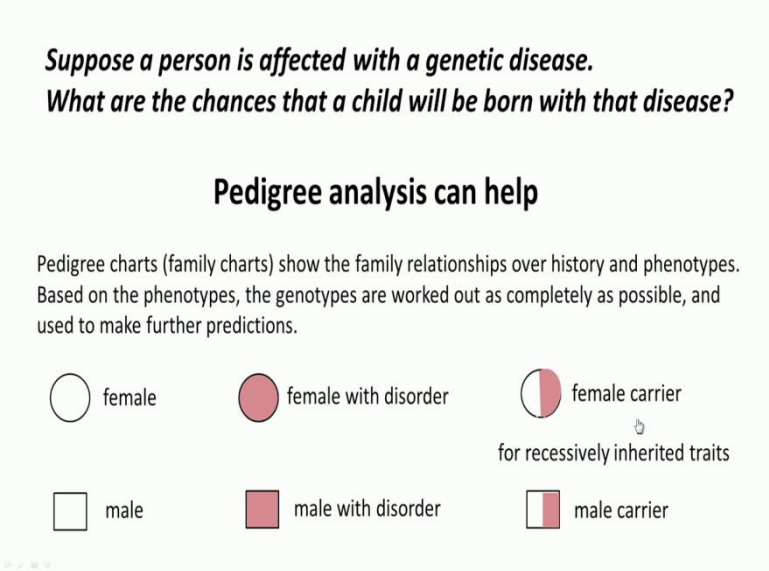

Let us look at a person affected with a genetic disease. Suppose a person is affected with genetic disease. What are the chances that the child will be born with that disease? That is a question that we are going to ask now, okay? In this lecture this is what we are going to see the various possibilities of that happen. To do this, something called a pedigree analysis can help. Pedigree charts or family charts show the family relationships over history and phenotypes characters, characteristics.

So based on the phenotypes the characters the observable characters, the genotypes are worked out as completely as possible and used to make further predictions, okay? We cannot go and do experiments with humans and therefore we need to use all the information that is available in terms of observable characters and draw our conclusions. Of course if it is if somebody's genotype can be tested, just by taking some part of the saliva or some blood and

so on and so forth, that can be done. That is that is acceptable to most and that can be used to help in the analysis.

However in many of these cases it may not be even be possible because maybe the grandparents and the previous generations have passed on and therefore the analysis of the phenotypes and the guests of the genotypes are used to get as complete (inf) an information on the genotype as possible and thereby make further predictions. We will see a couple of examples of those.

For that you have a certain terminology, if we have a circle it means a female, if you have a square it means a male. These are standard terminologies for Pedigree analysis. If you have a filled square it means that the female has the disorder, the disorder is apparent; if it is a filled square it is a male with the disorder. If it is a half-filled circle then something called a female carrier, it will become clearer, if the person does not show the disease with (the) person carries a part one allele which can cause the disease.

And this is true for recessively inherited traits, you know, if both need to be small, let us say small P small P for a decease to manifest, then if it is capital P small P then this becomes a carrier, right? The small P is still there, that can be passed on to the next generation although because of the capital P this disease may not manifest in this particular person in the carrier. That is what the carrier means. The disease is not manifest but the person has a potential to pass on the allele to cause the disease in (s) in the offspring, or in the offspring's offspring.

And this is a male carrier. So circle is a female, square is a male, it is filled than the person is showing the disorder, if it is partly filled then the person is a carrier, okay? These 2 can be (s) you know, filled in or these 2 can be decided just by observations and records, rest this requires a genetic analysis or a disgenetic possibilities which we can deduce with surety.

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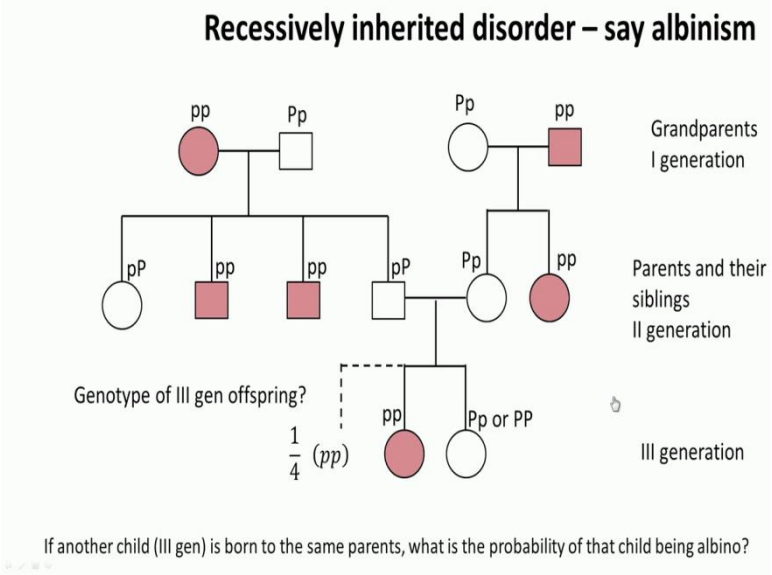

Let us take the case of a recessively inherited disorder, okay, which is what would be natural to think if it is both small then the person has the disease, that is not always the case but (in) let us, let us that for the time being, that is what would be that is what one would expect given the background that we have been through.

Albinism, you know the person with (w) who has light coloured skin patches, skin patches or sometimes even the entire body that is albinism, okay? That is recessively inherited disorder. Let us say that this is a family that we are considering. A female who has albinism marries a male without albinism and they have children. A female without albinism, a male with albinism, a male with albinism and a male without albinism, and these 2 marry and they produce 2 children, a female without albinism and a female with albinism, okay?

Then these 2 marry, these are 2 different families, their children (t) the 2 among their children, each one a child from each family marries the other and they have children. So far the observations are one has albinism, is a female with albinism and another is a female without albinism and this is the grandparents generation, first generation terminology, this is the parents and their siblings, okay, the second generation and this is the third generation that we are currently (c) concerned with this is what it is and this is the (pet) family tree on which we are going to do pedigree analysis.

If we are interested in finding the following, if another child in the third generation, in this generation is born to the same parents, what is the probability of that child being an albino, okay? Here itself is I mean, by now it is not very surprising, but to see here this person is not

affected with albinism, this person is not affected with albinism, whereas the offspring of that those parents is affected with albinism. That is because it comes from the grandparents, okay? Now that we know Mendelian inheritance, we know how this can happen, the recessive possibility (skip) it is skipped here where it is manifested in the third generation.

Let us go back to the (an) let us go to the analysis now. This is the way the various linkages in the family are shown and the various phenotypes are shown according to according to our code, the generally accepted code. If we look at obvious genotypes, this is a male with albinism therefore it has to be small P small P, or anything with an albinism has to be small P small P because it is a recessively inherited disorder.

So let us start here small P small P, small P small P. This one should also be small people small P, that we can fill in for everything. Whereas here the person does not have (the) it's a female who does not have albinism, okay, whereas this parent has both small P alleles and since one allele comes from each parent, definitely one of the alleles has to be P. And since this person is not showing albinism allele has to be capital P. If the other allele had been a small P then this person would have also been affected.

Similarly, this person is from this parent therefore must have inherited a small P, and this, the other allele must have been a capital P from the other parent, okay? With this, and taking a look at this, this father (the) or the grandfather should have had at least one capital P and one small P. Only then these kind of possibilities would exist, right? (Otherwise) if both had been capital P then these 2 people would not have had albinism, the (cap) both the other allele would have been capital P and as long as one allele was capital then the disease would not have been manifested here. And since it has manifest here and also it has not manifest here this person must have had capital P, small P, okay? This is the analysis.

Similarly we can do an analysis here. This is small P small P definitely, this is (cap) and this is small P small P. These both are affected and this must have been capital P because this person does not have the disease and therefore it is quite easy to see why this must (al) must have also been capital P small P because the person does not have the disease. Now this is heterozygous, this is also heterozygous, it is a cross between heterozygous parents and what is their probability that this person, whether male or female would have the disease.

It would be one fourth the probability you know these (are) these are heterozygous cross, therefore capital P capital P, capital P small P, small P capital P and small P small P are the

possibilities, therefore one fourth is the (probability) probability that it will be small P small P, result in the child being albino. We could also ask what would be the genotype of the third generation offspring which is these 2 and quite easy to see it has to be either capital P small P or capital P (spa) capital P, both can arise. We cannot rule that out from just this observation that the person is not an albino. The person could be a carrier, okay? Whereas here it is very clear that it has to be small P small P, okay?

So this is lot of information that we can gather just by looking at what the the various relationships between people and their observed characters. And we have guessed the genotypes based on or deduced the genotypes that is the best way to say it, deduced the genotypes, given that albinism is a recessively inherited disorder, okay? Now, some of you might have been wondering why did I keep harping on recessively inherited, okay. You (can) you could think how else could the disorder be inherited. It so happens that a disorder could be a dominantly inherited disorder too.

And Huntington's disease which is so prevalent in the US is actually a dominantly inherited disorder which means if one allele is capital then the person has the disorder which also means that most of the population is homozygous recessive, okay? Both are small small, right, only then will the population not have (will) will the person not have the Huntington's disease. If one of them is capital then the person definitely has the disease that can also happen. At the same time the dominant allele is not the one that is found the majority of people, okay? This could also happen, we will not get into how it happens and so on so forth. If you are interested you can go and read later chapters of your textbook, it does talk about that.

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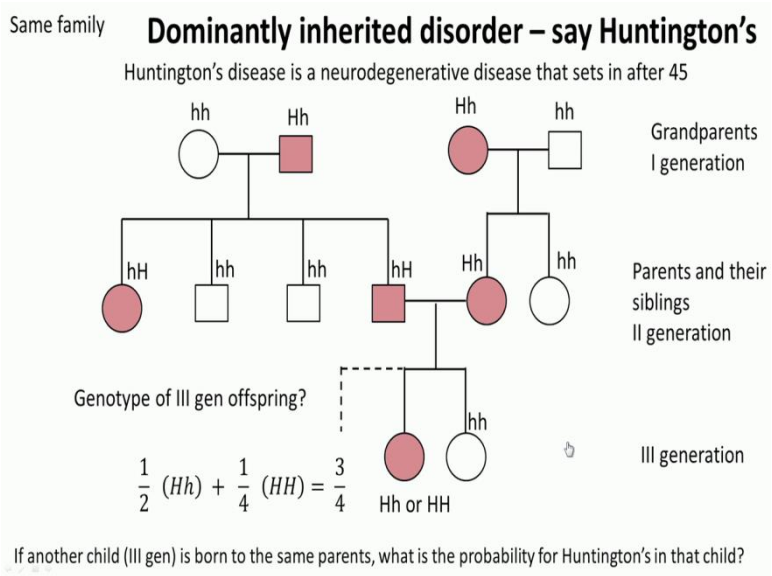

But for now, basic goes let us look at what happens if you have a dominantly inherited disorder and let us do a pedigree analysis for the very same family, okay? It is the same family so this is what was, right? And these things refer to the Huntington's disorder. By the way Huntington's disease or a disorder is a neurodegenerative disease that sets in after 45, okay? So it is sometimes a little difficult for the people and they could actually have their genes genotype tested to say whether they (are) to see whether they have Huntington's disease.

If they have Huntington's disease then it is badly degenerative disease that sets in after 45 and its bad life after that. So it is it has a lot of ramifications social and cultural and so (on) social essentially and of course health wise and the fact that you could be sitting on a ticking time bomb. So it is one such disorder which is predominantly found in the US not much in India. Here this shows the family members who have Huntington's disease by a shaded square or a circle, okay, a shaded square is (an) an affected male and the shaded circle is affected female, okay?

Now let us do the analysis here, the same way that we did analysis for a recessively inherited disorder which was albinism, it was an example of that. Same question if (a) another child is born to the same parents what is the probability for Huntington's in that child, okay? This is more serious than albinism, albinism is merely looks and maybe it it makes the person prone to cancer and so on, skin cancer but it is not as dangerous as this, okay, but it has a social angle to it so that could also be considered in point putting off.

Very clearly this has to be both smalls for the person not to show the disease, (s) both small here and both small here that can be very easily guessed, deduced. Since this person is showing the disease and this is both recessive, it has to be at least one dominant for the person to show the disease and therefore (it) this has to be (s s) small H and capital H. This is also got to be small H capital H same parents, and because this is small H capital H the only way this can result is if this is capital H small H. This cannot be capital H capital H, otherwise these 2 people would have also had the disease.

Similarly this would be small H small H, no disease. This one would also be small H small H, no disease. This has to be capital H capital H with the disease because this has resulted in one small H coming from here therefore at least one is a small, the other one has to be capital for it to show the disease, therefore it is capital H (smca) small H, and by the same argument this is capital H small H.

And what is the probability that this person will (have) will have Huntington's, you can work at the probabilities here. Either if one of (the) either if it is heterozygous dominant or homozygous dominant the person will show the disease, so it is a very high three fourth or a 75% probability that the (sib) that the child, born to the same parents will have Huntington's disease, Huntington's gene which will develop into a disease at around 45 or so.

And genotype of the third-generation offspring is capital, small H (cap) small H here and if you work out the details here we will not be sure. It would either be this and this or this and this or this and this. Therefore it is either capital H small H or capital H capital H. (One) at least one has to be capital because the person is showing the disease. Okay, these kind of questions can be answered and the parents can be alerted to these possibilities, the people can themselves be alerted to these possibilities.

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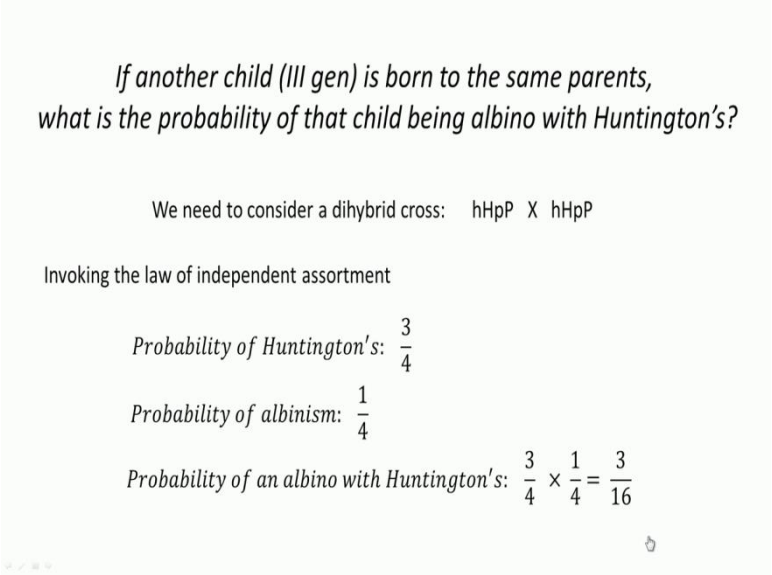

Now let us look at both of them together, okay, and use probabilities here. If another child of the third-generation these want to the same parents, what is the probability of that child being an albino with Huntington's? Okay? Albino is 1 characteristics, Huntington is another (character) character, they are independently inherited according to Mendelian principles and to come up with the probability we need to consider a dihybrid cross in which albino character and Huntington's character (is c) are considered. If we do that (invo) invoking law of independent assortment, the probability of Huntington's is three fourth; the probability of albinism is one fourth according to the various combinations here.

Therefore, the probability of an albino with Huntington's, okay, both are independently inherited independent assortment, three fourth into one fourth (prob) multiplication rule, 3 by 16, okay, so this is the probability. So you can work out various different things with these probabilities and the law of independent assortment.

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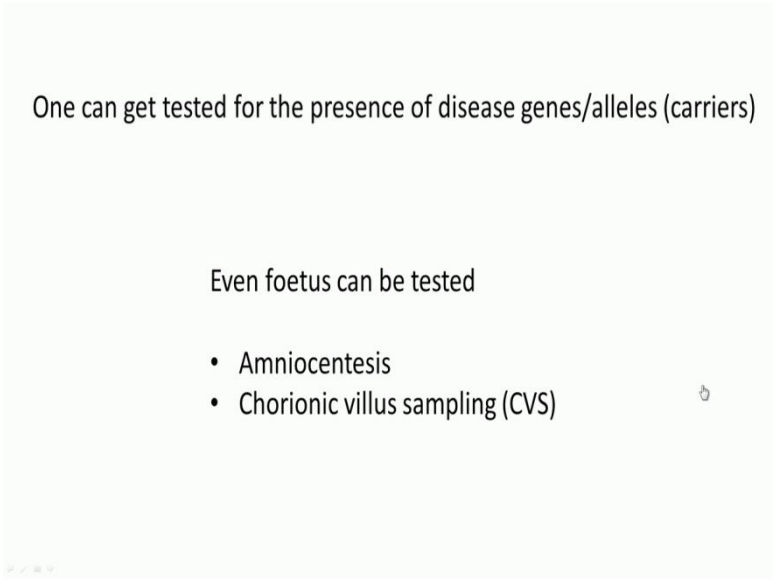

One can get tested for the presence of disease genes and alleles whether you are a (ca) a carrier or not. If you have the disease you know that your genotype could be a certain way, if you do not have the disease you would like to know whether you are a carrier, whether you are going to pass it on to the next generation, one can do that. Even foetuses can be tested through (p) procedures called amniocentesis or chorionic villus sampling called CVS. These 2 are done, especially for disease kind of a situation and so on, okay?

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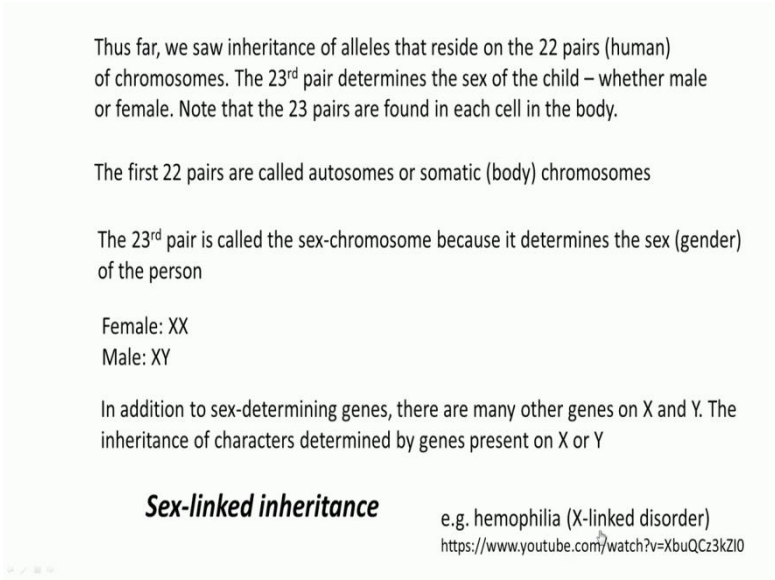

Whatever we have seen so far is valid for a certain kind of inheritance. It is for the inheritance of alleles that reside on the 22 pairs of human chromosomes. The 23rd pair, XY if you recall, determines the sex of the child, okay, whether it is a male or a female. And the 23

pairs are found in each cell in each body, that that you already know. Whatever we have seen so far is valid if the allele sits on the first 22 chromosomes, not the 23rd. If it is, if it sits on the sex chromosomes then things are going to be different and let us see how the things become different if the allele sits on the sex chromosome.

The first 22 pairs are actually called autosomes or somatic chromosomes, somatic for body, somatic chromosomes. And the 23rd pair is called the sex chromosome because it determines sex of the person. Now, gender I think in this lecture we would use interchangeably with sex but in actual terms gender has a social connotation and sex has a biological connotation but (we) we could use this, or I could use this interchangeably in this lecture. The female has an XX sex chromosome occurrence and the male has a XY sex chromosome occurrence.

In addition to sex determining genes there are many other genes that are present on X and Y (and) the inheritance of characters determined by the genes present in X and Y is what is called sex linked inheritance. If it is sex linked inheritance the probabilities would be different from what we have seen if they had been autosomal inheritance.

An example of sex linked inheritance is haemophilia, haemophilia is an inability to inability of the blood to clot and if that happens then the person has a wound then the person continues to bleed. If it is outside there is a way of handling it but if it happens inside then it can be dangerous, the person can bleed to that for no fault. And that condition is actually called haemophilia.

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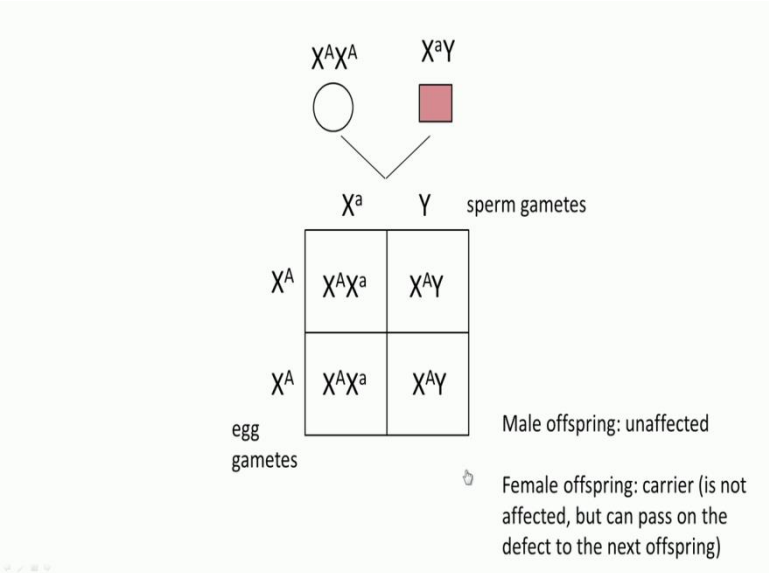

You can take a look at this youtube video, it is a female it is XX and let us say that the person as A and A (pheno) A and A genotype there, we are using a superscript to determine the genotype, that is associated with the X chromosome. Since it is a male it has to be X and X and Y, since the male is affected it is a (capi) it is a small A. The gametes from a cross between these 2 would result in Xa Y, X small A, Y, and capital A capital A the gametes are XAXA from the eggs and the sperm gametes are Xa Y. And a panelled square from this kind of a cross would result in capital A small A, capital A, capital A small A and capital A.

And as you can see the, if there is a Y, the offspring is going to be a male, both these are males and both these have the capital A on their X chromosome so therefore they are unaffected. The female offspring, these 2 they are again unaffected because they have at least one capital A, but they are carriers they have the other small A, right? Therefore female offspring is a carrier, is not affected but can pass on to the (it can) pass on the defect to the next offspring, this we have already seen, okay, this is the way it happens. The probabilities would be different if you calculate, it is (deter) it is dependent on the sex of the person, sex of the offspring.

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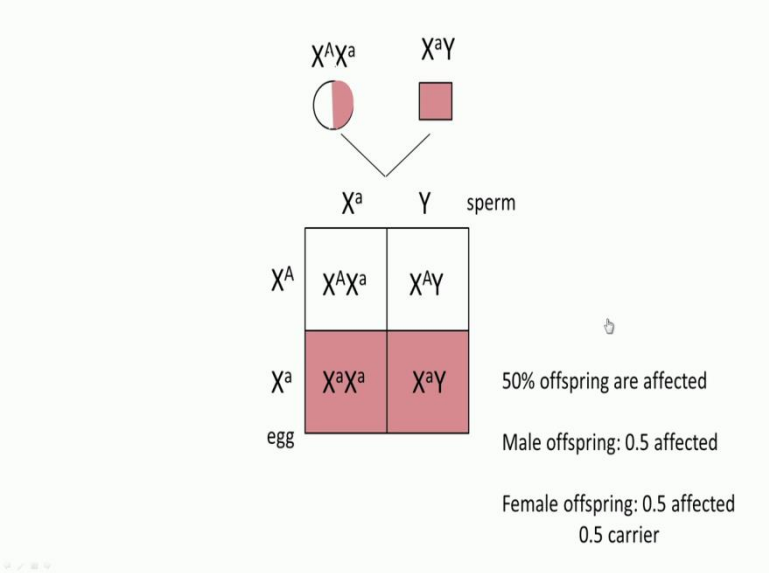

Now let us say, it is a cross between a carrier and an affected male, carrier female and an affected male. If we work out the panelled square, it is going to be something like this. The one female and one male are going to be affected, okay? Therefore 50% of the offspring are affected this shaded ones are the affected ones, 50% of the offspring are affected. The male offspring this and this are males, male offspring (again) again 50% affected and female offspring, 50% affected and 50% are carriers.

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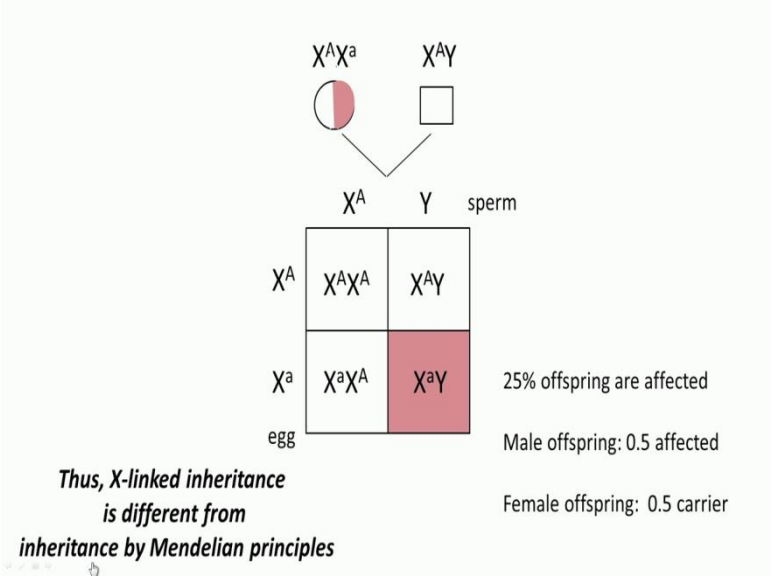

Another example between a carrier female and an affected male; in this case only 25% of the offspring are affected, it happens to be a male because the small A comes here, the Y does not have anything, the (male) if you consider the male offspring alone, 50% are affected. If you consider the female offspring alone, no female offspring is affected but 50% are carriers which are these, okay? So if the allele (rests) lies on the X chromosome then the probabilities are going to be different from that we found with autosomal disorders or the alleles that reside on autosomal chromosomes.

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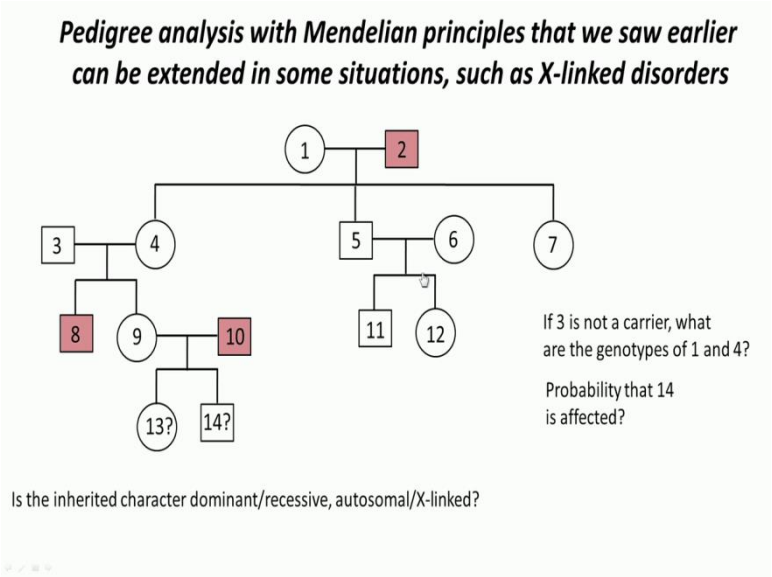

Thus X linked inheritance is different from inheritance by Mendelian principles. Pedigree analysis with Mendelian principles that we saw earlier can be extended in some situations,

such as (ec la) X linked disorders, okay, to a certain extent. This is one such possibility that have shown here, what I would say is why do not you work this out we have already been at it for about 30 minutes or so, a long lecture; why do not you work this out with whatever we have learnt in this particular class and when we begin the next class I will begin by solving this, okay, there are these question marks here, this is what we need to find whether these are affected or not that is a question these are various numbers that are given for our reference the other representations are the normal representations and these 3 are affected.

You would like to find out what kind of a disorder it is it ya these are the questions; is it, is the inherited character dominant or recessive, autosomal or X linked; that is the first question. If 3 is not a carrier, if this is given, what are the genotypes of 1 and 4? That is what you are asked to find. The probability that 14 is affected is what you are asked to find, okay? What do not you work this out and then when we meet you can check the solution with the solution that I will provide in the next lecture. See you then.