Bioengineering: An Interface with Biology and Medicine

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Lecture – 21
Chromosomal Basis of Inheritance

Welcome to MOOC-NPTEL course on bioengineering and interface with biology and medicine. In todays class we will study Mendelian genetics in more detail. We will discuss the chromosomal basis of inheritance and we will find out what are the heritable factors involved as defined by the Mendelian.

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I must say that you know Mendel made huge contributions for identifying that there are certain factors heritable factors which transmit from one to next generation. But you know quite long time people did not know that what those factors are and then you know also people did not have too much information about whether those factors you know in which manner then inherited. So, few scientists started making more investigation.

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And one scientist who had made a huge contribution the area is Morgan and I will talk about some of his experiments.

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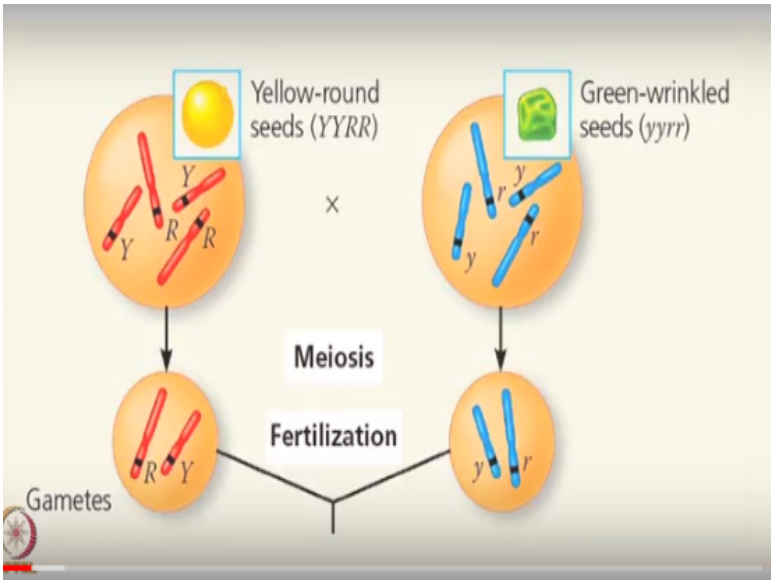

But before you know kind of what we are going to talk is are the genes for the pea property which we are talking are they present on the chromosomes and do this segregate as a part of the divisions miotic divisions the way we have been studying the meiosis process right? so in this case here we have yellow and round and we have green and wrinkled seeds as a part of meiosis these gametes are separated.

And if these gametes contain the genes those genes which are giving the property like you know yellow and round seed or you know wrinkled seed. So, are they also getting segregated part of the divisions which are happening. So, genes are located on the chromosomes and what are the behavior of these chromosomes during the meiosis process and whether Mendels law which had we have talked about the segregation.

And independent assortment in also valid as a part of this chromosomal basis of separation little complex slide but you know one could start thinking and refreshing yourself about.

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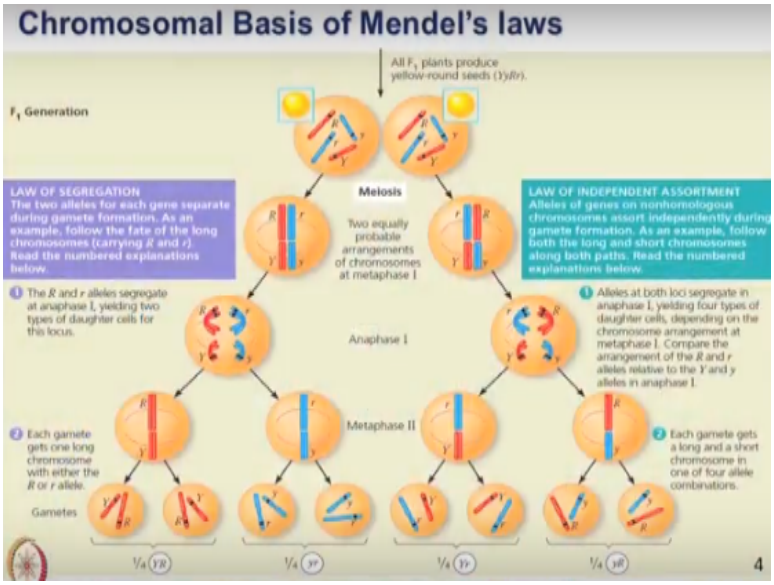

Meiotic cell division so as a part of law of segregation the two alleles for each of these genes will separate during the gamete formation which you can follow the same what we have done in the meiotic process and the law of independent assortment it means alleles of genes on non-homologous chromosomes could assort independently during the gamete formation. So, it is very well color coded here.

In the red and blue showing that in all your R and a r alleles for the same gene properties how in the Meiotic process they are getting segregated. So, these are the kinds of assumptions made thinking about whether what mental health discussed whether that has any basis at the chromosomal level.

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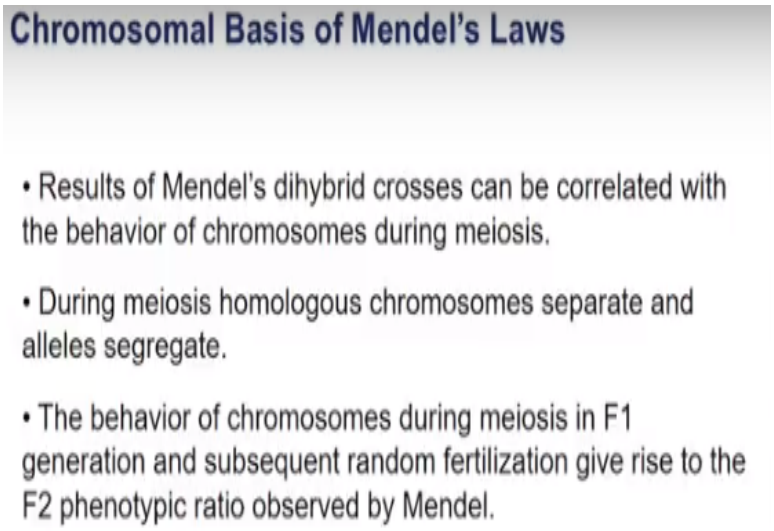

So, far what we talked is essentially Mendels dihybrid crosses one could correlate also at the looking at the behavior of the chromosomes during meiosis. During meiosis these homologous chromosomes they get segregated and therefore alleles also get segregated the behavior of chromosomes in Meiosis process of the F1 generation as well as after the fertilization in the F2 generation could be observed by what Mendel had already shown in his process.

So, while these are some assumptions but there are no experimental evidence that how one could prove this.

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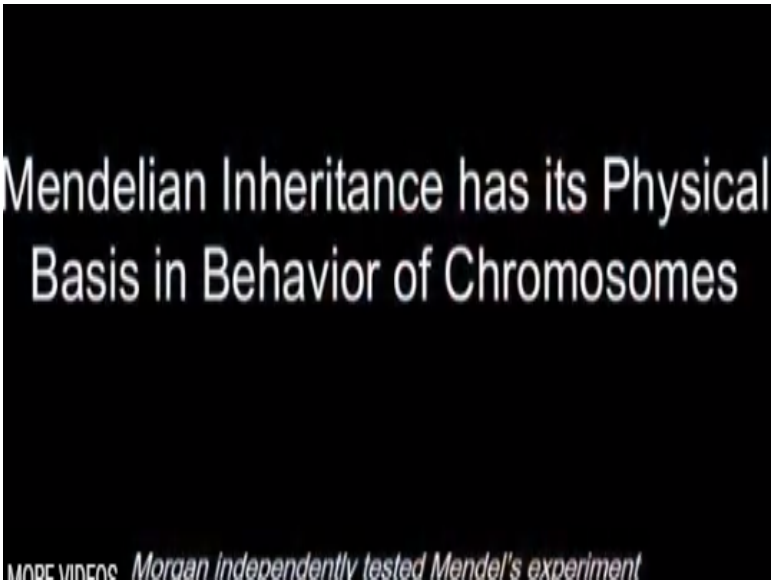

And this is an area where I must say that another scientists who made huge contribution is Dr Morgan who has studied the Mendelian inheritance and what are its physical basis at the chromosomal level.

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So, this is scientists for whom we are talking Thomas Hunt Morgan Columbia university and he selected a model system which is drosophila or the fruit fly. So, far we have been talking mainly about pea plants and but at some point, I had mentioned to you that many people like to work on drosophila. Because again you know it comes in many properties you can grow and grow them very fast, I am sure you have seen drosophila you know sometime on the banana peel.

You know you will see those small flies with you know with red eyes and people make these you know cultures of these particular drosophila stocks they make this is showing you here you know a lot of labs which works in the genetics and developmental biology area. They have the stocks of the drosophila strains and these drosophila you can make mutations in different genes and you can keep doing.

And keep growing those which can be very handy for doing lots of experiments and testing your hypothesis. So, what is shown here you know you have small tubes, and, in those tubes, you are having banana essential nutrients on which these flies can grow, and people will store them and

made them and make sure that you know they are maintained well for doing autogenic experiments.

So, this is what where we are right now but at that point in 19th century Morgan you know he started working on drosophila and thought about looking at Mendelian genetics at the fly level. So, let us see what kind of experiments he did finally he provided evidences that chromosomes are indeed the location of Mendels heritable factors. So, I have you know there is no suspense on that I already made the conclusion.

But now let us see the experimental system and what kinds of things he did so no nomenclature of the things that we have been discussing from the pea plant will slightly change.

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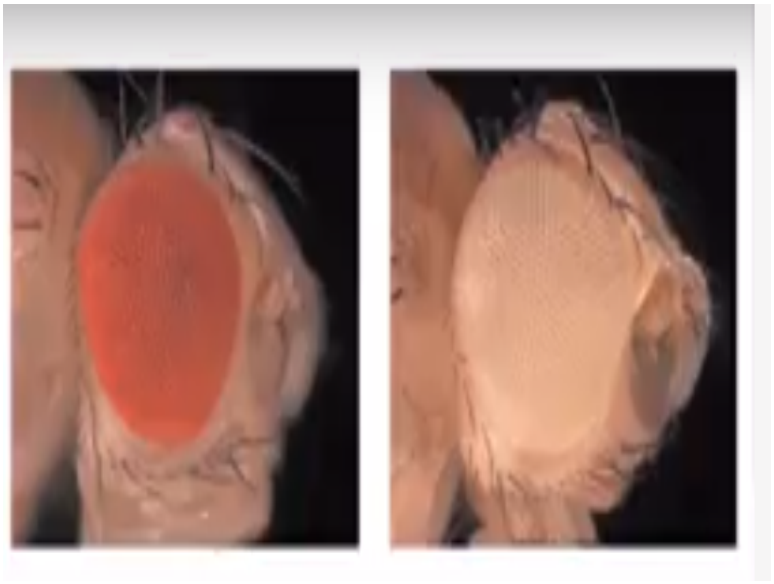

Here we are talking about phenotypes of drosophila some characteristics of these are commonly found for example red eyes that is wild type character and if a deviation of that is found that is known as mutant type behavior. So, if this particular eye is white eye which is not commonly found in drosophila that is mutant type behavior whereas the red eye is commonly found normal phenotype that is wild type.

So, I am sure now you are familiar with the wild type and the mutant terminologies.

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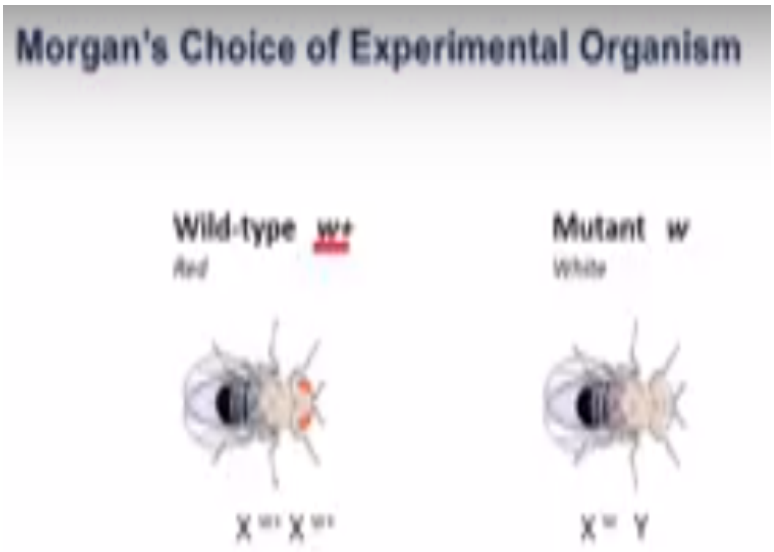

Let us look at some of the how you can denote them so far, we are talking about in the pea plant context you know only simple nomenclatures knowledge add a little complexity here when we say wild type you are denoting with a +sign and when you are a mutant then there is no plus sign. We are also showing here male and female chromosomes, so this is a male drosophila so XY chromosomes and X is having the blue a suffix on that are super equipped on that.

So, that is a mutant behavior, or this particular thing is a XX a female both contain the W+ W+ that is a wild type which will give the red eye pattern. Keep this in mind I think there are some process which we have to do which now we have to use these kind of nomenclature. So, if in a given cross of some point, we will talk to you about a given property it is wild type and the newton behavior.

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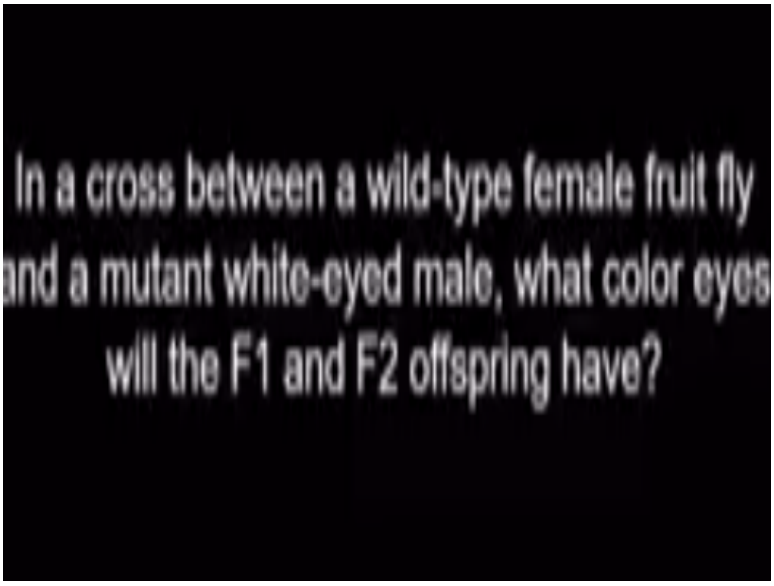

You can denote those with + or without + so now let us see what kind of cross Morgan did.

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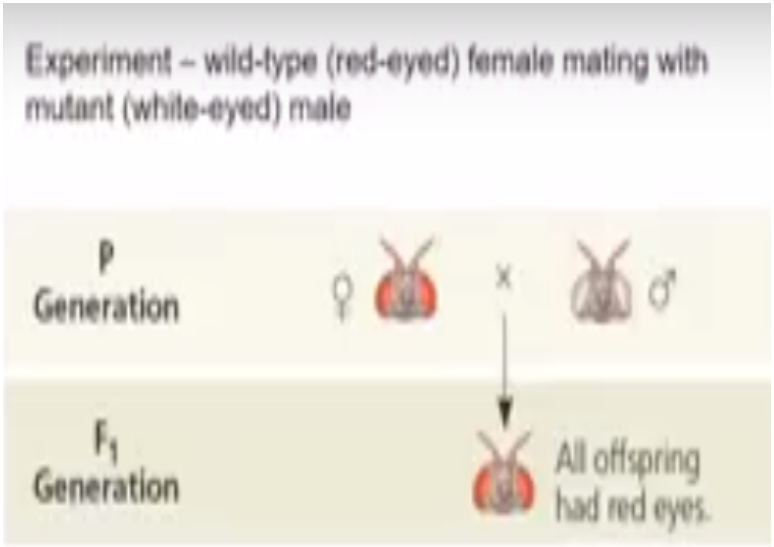

So, he took this wild type female fruit fly as well as mutant white eyed male fruit fly and then observed their progenies in F1 and F2 generation. So, in this case the female is red eyed here a and males is white eyed in the parent generation. In the F1 generation all the off springs they showed red eye just imagine what Mendels experimental were right? so purple was the dominant and now that were shown in all the F1 generation.

Something similar he also seen now he wanted to follow this particular cross in the F2 generation and I would ask all of you know to start thinking and start making this kind of cross.

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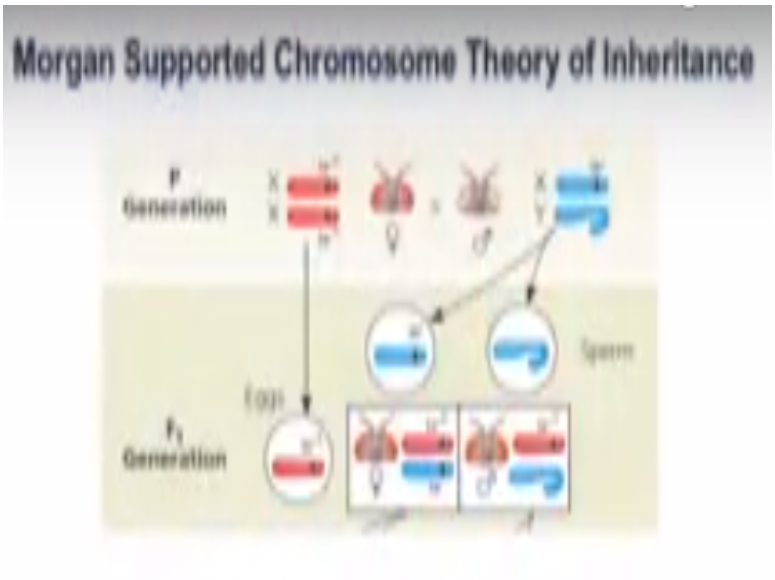

So, let us start doing that alright so we have the, so you have to know now start making X and Y chromosomes and then also you have to denote what is a wild type and what is mutant right then only you can say that off springs how many are male and female and what are their characteristics?

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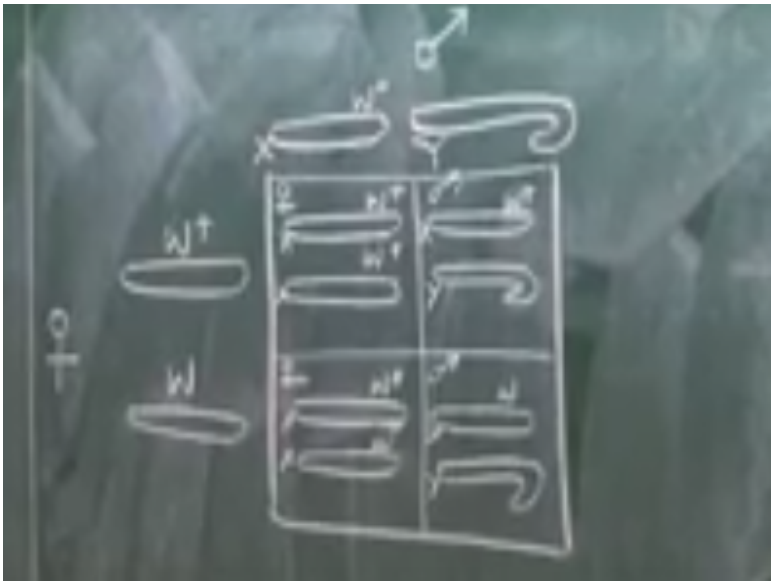

So, let us try out simple the same Punnett square. So, let us draw only for F2 generation so Y chromosome and we have this X chromosome which is having W+. All of you are doing that right I ill come and see your results alright. I am sure it is not very difficult for you to do the

crosses, but you have to assume that you have to know the terminology you have to know how genetic process can be done in different type of properties which we already described.

Alright I am sure all of you have done your cross by now. So, what is the phenotypic ratio? we are looking at one property which is a red eye versus white eye white eye is a mutant property and red eye is the white eye and these signs are for male and female which also important to draw those. It is not so difficult right because you have done already this kind of crosses for Mendalian genetics in the pea and at time three stone were very simply defined.

"Professor - student conversation starts" Yes yeah good observation that whether we have no gene on the y chromosome and that is I think right observation that what Morgan also proved here that certain genes they are only carried on a specific type of either X chromosome or Y chromosome. "**Professor - student conversation ends"** So, some properties are linked to specific sex chromosomes they are not present in both the chromosomes.

And therefore and this observation did not come beforehand it came only after this cross. So, now if you realize we have only one white eye male right which is the mutant eye. So, because he also observed 3 is to 1 ratio 3 other flies where red eyed 2 of them female and one male. But one of the white eyed male it was he was observing only male. So, based on that when he made this process, he realized that the segregation is happening.

But there is some sort of link to the chromosomal basis of that probably the these genes are located on some specific chromosomes X chromosome or Y chromosome and that is why they are seeing this mutant behavior is coming only in the male type here. So, I think it was important and genetics that you should make good observations for a given cross and then use all the properties label properly and then probably you cannot make any mistake.

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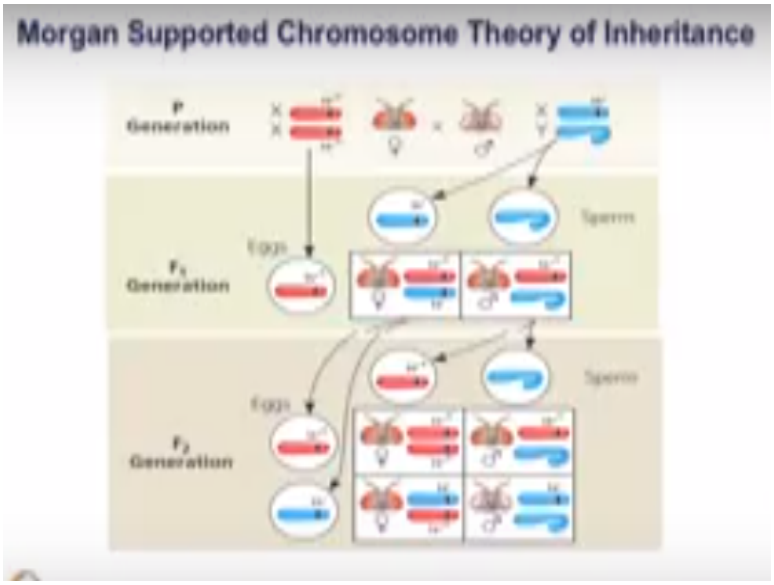

So, this is kind of cross we just talked a we have these gametes from the sperm W+ and the Y chromosome here from the X we have W+ and W and now if you are making this crosses you have only one white eyed male you have remaining 3 flies which are all red eyed. **"Professor - student conversation starts"** Yes what is the ratio 3:1 or 1:1:1:1 so phenotype wise 3 are red eyed phenotype if you look at of the 4 it is 3:1"**Professor - student conversation ends"**.

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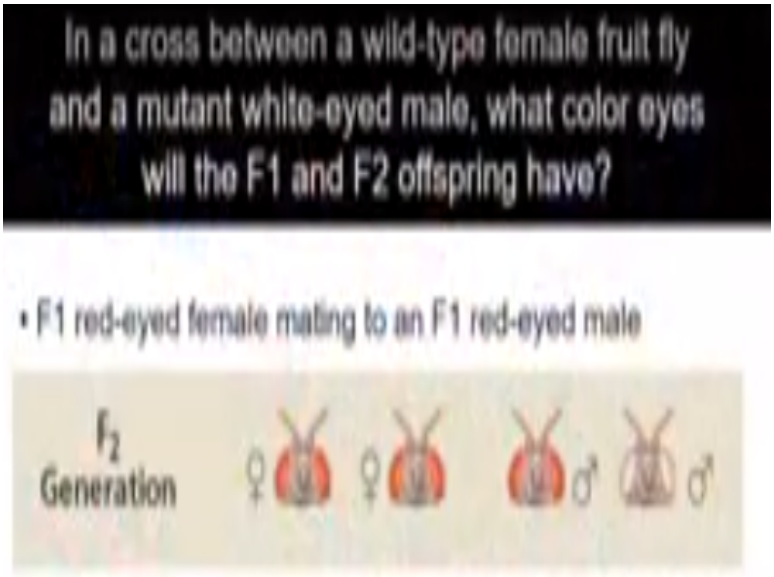

Alright so what we just discussed the cross the main points of this cross are that they are mutant or the white eyed trait that is recessive as compared to the wild type of the red eye trait which is W+ in the recessive trait white eye was expressed only in the male in the F2 generation. I think

you had rightly have observed this and that led Morgan to conclude that eye color gene is located on the X chromosome and not on the Y chromosome.

So, Y get segregating it is some specificity that where these genes are located.

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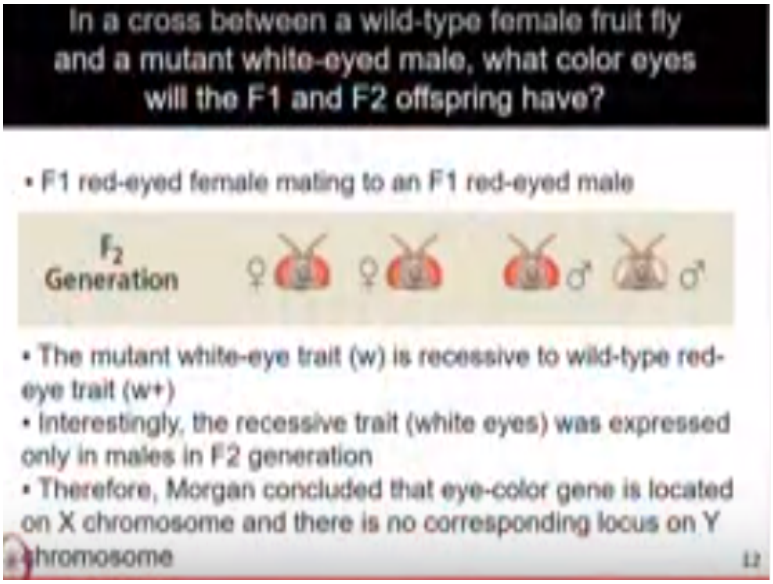

So, conclusions from the experiment is we saw the evidence that chromosomes are indeed the locations of what Mendel had defined those heritable factors. So, Mendel was only able to say that you know there are some factors which are transmitting from one to the next generation. Morgan will also able to show that there are some chromosomal basis to them. **"Professor - student conversation starts"** what is the genotypic ratio?

Alright so genotypic ratio you can say in the female what is genotypic ratio in the male what is genotypic ratio and overall genotypic ratio of all the off springs. So, in that way it can be you can say that you know among the female there is a genotypic ratio among the male there is a genotypic ratio among all of the four what in the phenotypic ratio or even you can split into male and female and you can put in the ratio fall. "**Professor - student conversation ends."**

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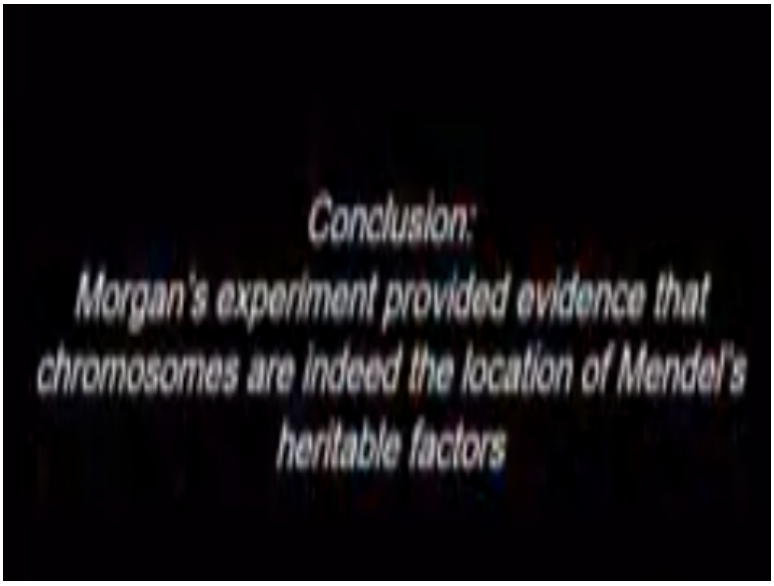

So, if you think about the human and the chromosomal basis of sex in human.

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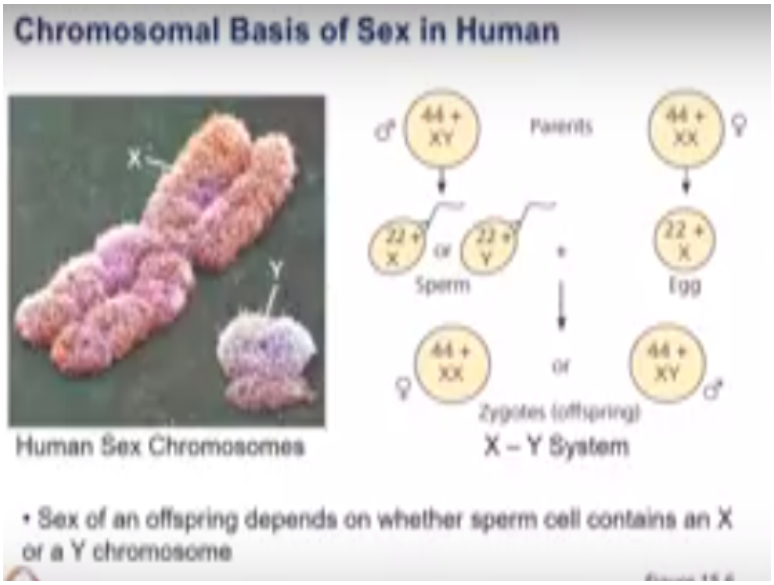

We have 44 pair of the 44 autosomes and XY chromosomes are there. So, these 22+X or 22+Y part of the sperm. And 22+X part of the egg this is known as XY system where X and Y chromosomes and the various genes which are linked to them are getting segregated. So, the sex of a child actually depends on whether the sperm contains X or the Y chromosome because egg will always carry X chromosome only.

So, the sex of child will be derived from the sperm whether it is coming from X or the Y.

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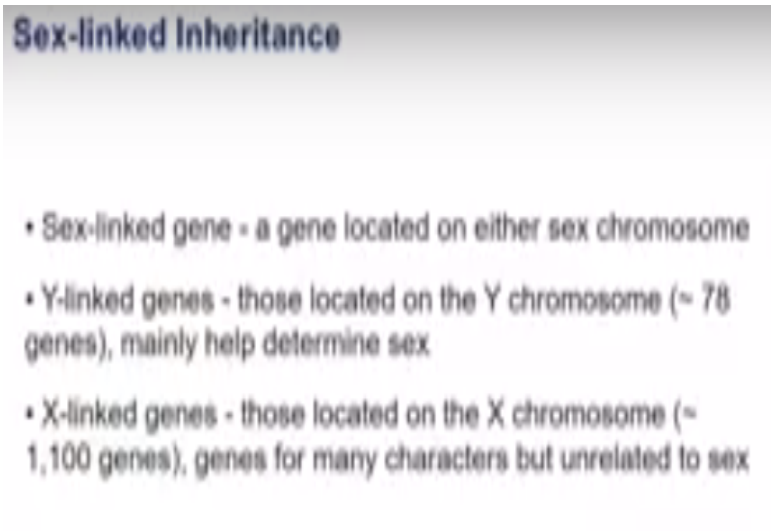

So, there are many sex linked genes which are only found on the X chromosome or the Y chromosomes and the way linked genes are actually much smaller in number only around 78 genes have been found on the Y chromosomes. Whereas on the X chromosome almost 1100 genes are there. So, lot of properties are only uniquely present on the X chromosome or the Y chromosome and they will follow that pattern coming from these chromosomes.

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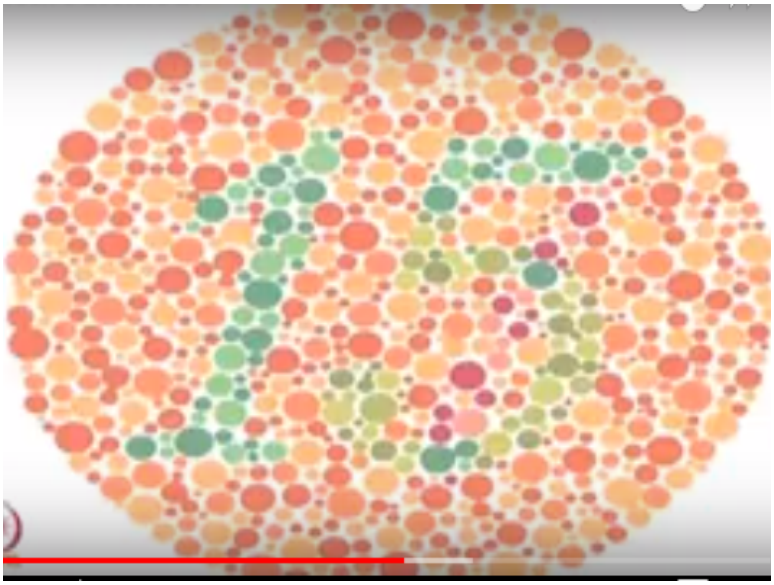

If you look at this circle can you read something in that? How many people cannot read? cannot read how many people cannot read. Alright so well if in case you are not able to read, I think you should pay closer attention to this and you should go for some tests you might be not able to

distinguish the colors so easily. And this is you know reality because for many of the exams especially for the railways military etc.

They also test for your color blindness can you distinguish the colors clearly?

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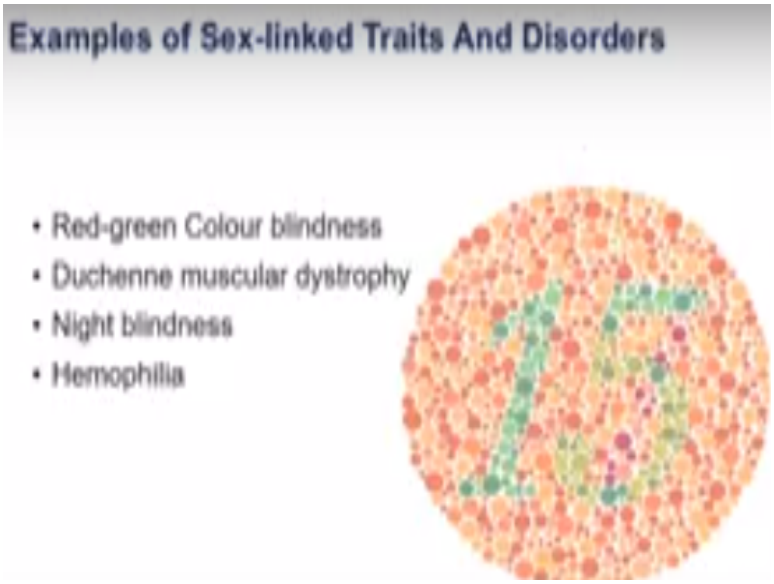

So, many of the disorders which are sex linked includes red green color blindness a muscle dystrophy you have night blindness and hemophilia. So, many of these diseases are a bit on the transmission of X linked massive traits especially for the red green color blindness. So, let us think about the red green color blindness which is much more apparent case.

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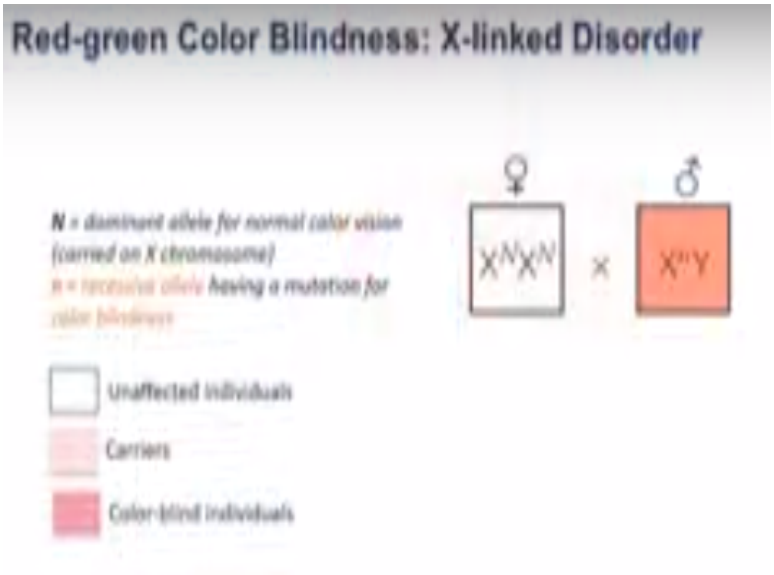

Let us think about again some of the ways to denote the conditions. Please pay attention to the slide a lot of question that are going to be based on this. So, for a color blindness to happen this gene is going to be on the recessive allele which were denoting from the n. If an individual is unaffected or normally normal vision, then we are showing from the this white square if it is carrier, we are showing them the light shade.

If colorblind from the dark shade so this case let us think about female and male a cross is happening. In this case it is normal when we have normal phenotype it means N and N right on both the chromosomes and if it is carrying the recessive allele which is n then only have the disorder. So, if I am just showing you this what did this cross is you know between what type of male and female

"Professor - student conversation starts" Male is color blind and female is unaffected alright, so female is unaffected, and male is color blind alright. Now let us take second situation in this case what will happen female is carrier and male is unaffected male is unaffected and female is there is the third situation female is carrier and male is color blind. "**Professor - student conversation ends."**

Alright so I am hoping that you know in addition to looking at the colors you are also paying attention here that whenever there is a small n which is recessive allele is here with the male it is only it has to be only one on the X chromosome. So, it is always getting colorblind now in the female even if it is present in one copy then it is still it only carrier it is not showing the full effect right.

Now let us try to take these conditions and then do the crosses and see what will be the fate of these off springs coming from these crosses. Please start doing that.

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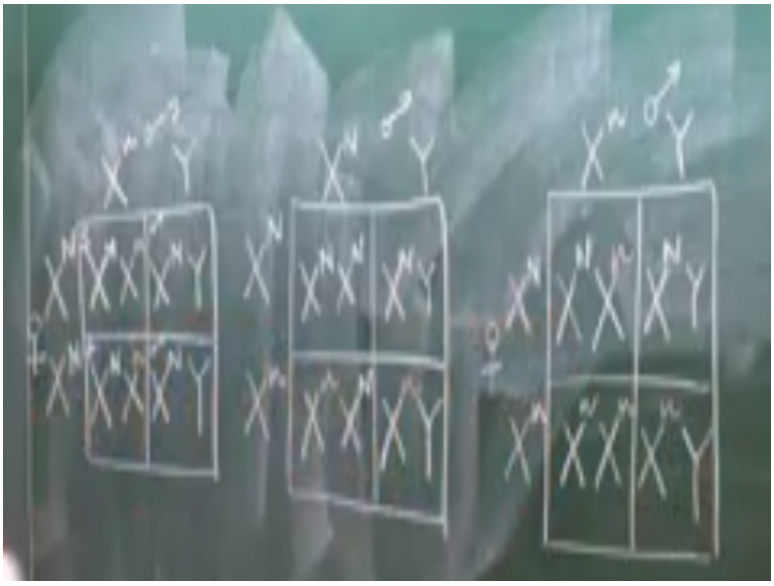

So, that is the first situation we had talked second one is that we have male which is normal, and female is carrier third cross we have male colorblind female is the carrier. Alright all of also you should write based on the XXXY which are male and female. Alright so I am sure all you have done the crosses as well. So, you have to now do this crosses and give me the answers for each of the cross what will be the progenies look like.

And when the questions will be asked you will be given a situation when the you know when a cross happens and the kind of child which are born 50 percent of them are carrier and 50 percent of normal what could be the genotype of the parents for then you have to go backwards. So, let us s go one at a time the first cross is everybody trying now is everybody comfortable how about this side?

Okay so let us think about you know different crosses which we have done.

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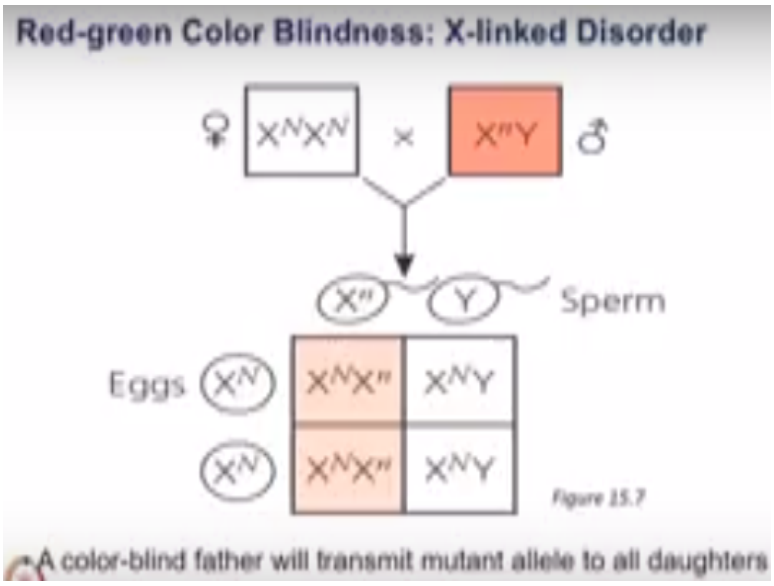

So, the first situation is when we have a color blind male and we have the normal female from this the progeny which are born of them 50% of them are carrier okay. You will not see apparent of any change in the phenotype but the 50% of the child are actually going to be carrier. So, if colorblind father is going to transmit these alleles to their daughter. It is only transmitting, and it is not going to be apparent in the next generation.

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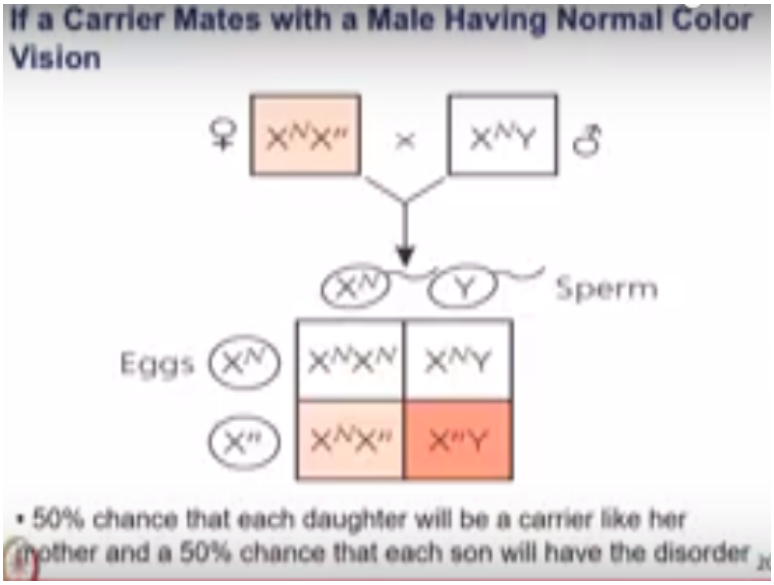

Second situation the second across we have the female which is carrier and male is normal in this case out of the 4 progeny there is a probability that one of the male child will be color blind and one of the female will be the carrier.

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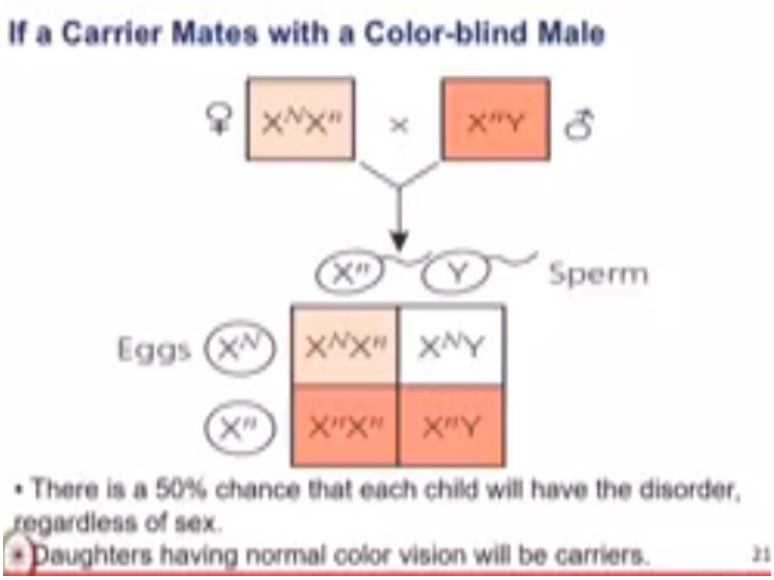

Now let us think about the third situation when we have a color blind father and mother is a carrier in this situation you have 50% child who are going to be colorblind and 25% of them will be carrier so many times if a family has the history of carrying these kinds of disorders. So, it is a good idea for them to do genetic testing or get genome counseling before marriages. Because you want to know that you know what could be the fate of those small genes.

And whether they will be apparent in the progeny and therefore many people make those kinds of choices. In this case if let us imagine here in this case even if the father is actually color blind but as long as mother is totally normal and not carrier then the progenies will not have any effect but if this is a third situation is there you know the father is colorblind and they are not doing any genetic testing they are marrying with anybody.

And then act of female it also carrier then the possibility is there you know most of the child will be either colorblind or they will be carrier. So, these are reality hand many times when these genetic disorders happen people do these genetic testing to ensure that they can avoid this situation okay? so these things can be just done in the same kind of mathematical probabilities the way you read many mathematics questions.

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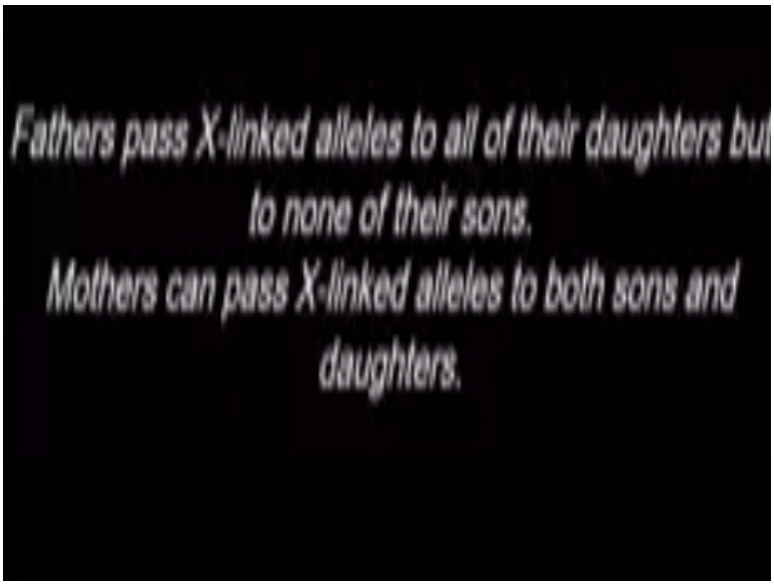

So, conclusions from these crosses are their fathers pass X linked alleles to all of their daughters but none to their sons and this female these child these daughters they are actually carriers that are going to carry from the that generation to the next generation. Mothers can pass the X linked genes and alleles to both the son and daughters.

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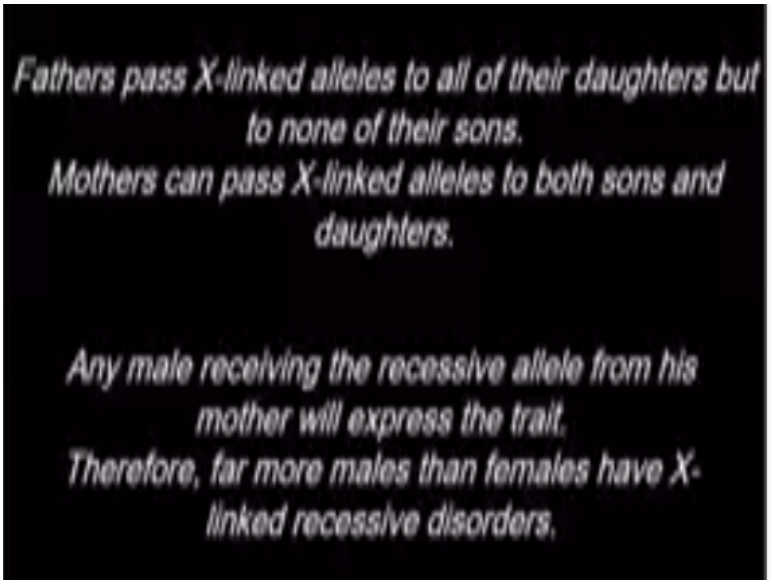

Any male which receives the recessive allele from the mother will express the trait sometimes I will just give you this kind of statement and I will ask you to show this is true or false by doing the cross the small which I showed you are very simple, but it becomes difficult when you are having just given a statement and you have to derive the causes on that. So, I am hoping that you know from this exercise you are getting more comfortable now.

And you should be very easily able to derive your crosses now. So for more males than females actually have X linked recessive disorders.

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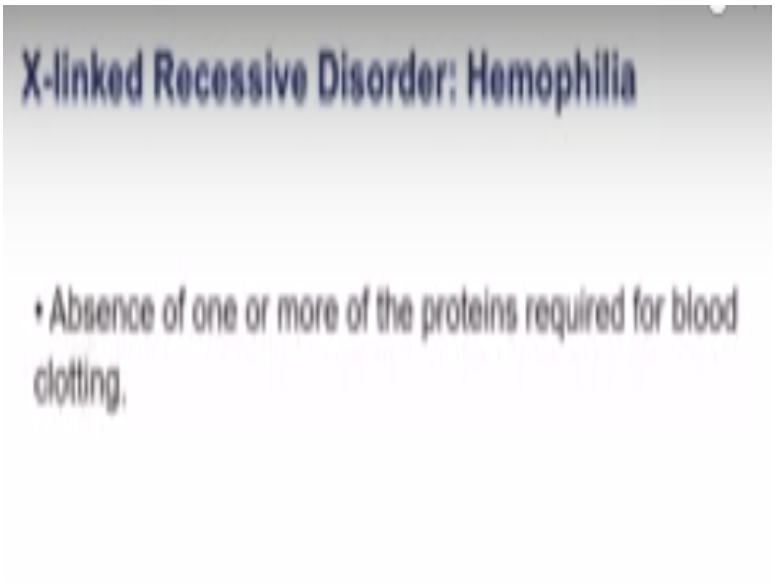

So, absence of one or more of the proteins which is involved in doing the blood clotting is not found in this particular disease condition and therefore there is excessive blood loss happens from their own sides. In fact, now nowadays because of all our advancement understanding of doing genetic engineering and protein research it is not possible that we have those clotting factors which in the purified form present which could be injected in the individuals.

And try to overcome this deficiency but of course that time it was much more serious issue.

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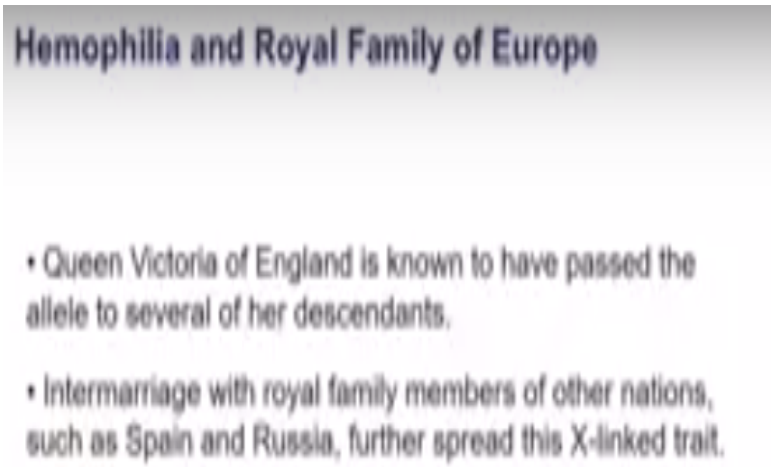

And what was more interesting that you know people started queen's family in Victorias family that many of their descendants were actually passing these traits. So, many of the royal family children were carrying these alleles and therefore some of them started showing these symptoms and then it became more apparent that its not only one child which is having problems there are not many from that family who are having these issues.

Because the inter marriages were from the very small group of individuals from Spain and Russia etc. But this was you know definitely one of the very interesting fact it was happening in royal families that became much more apparent and everybody started not noticing this problem and that time some scientists published a study on hemophilia and then they you know this thing became much more like a case study.

For all the scientific community to find out what has happened in the royal family and how the genes are getting inherited okay. So, the conclusion is that you may now overcome some of these deficiencies because we have understanding of how to synthesize these proteins and the clotting factors which could be injected in the individual and that may prevent the blood loss.

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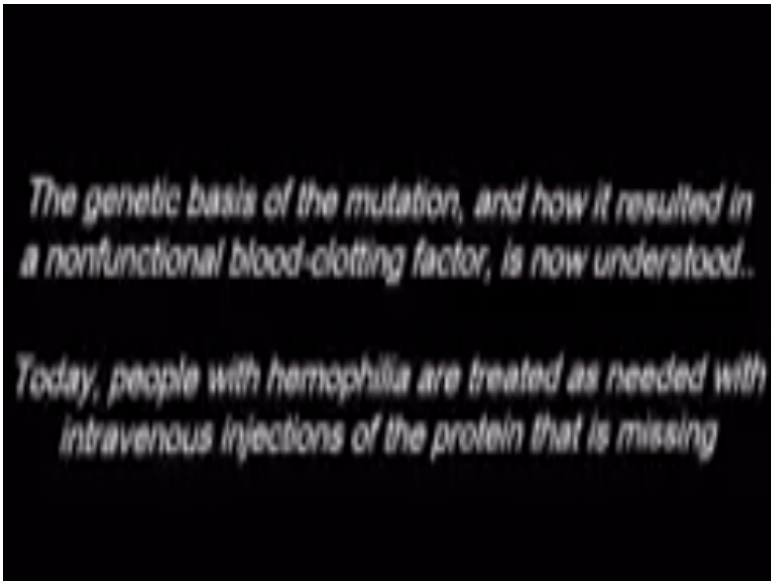

But nevertheless understanding the genetic basis is very crucial and these kinds of genetic counseling per say can actually help us to avoid many of these kind of miss happenings

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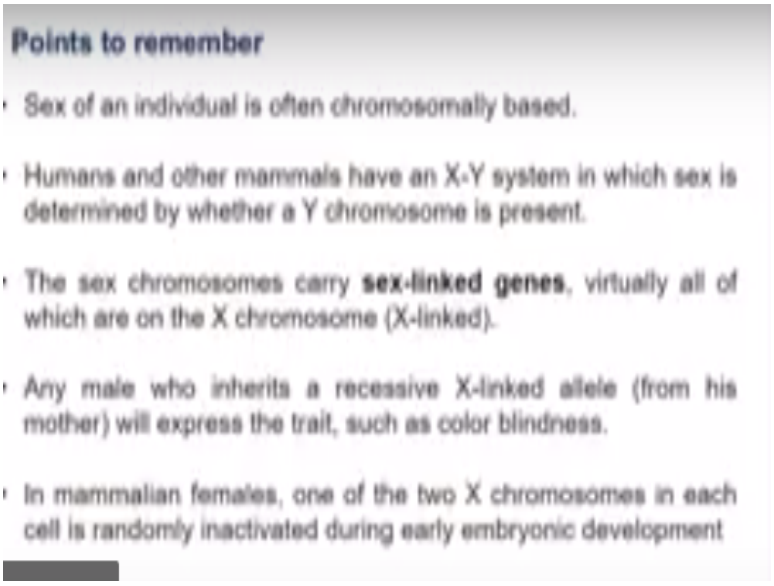

So, by now you are familiar with chromosomal basis of inheritance.

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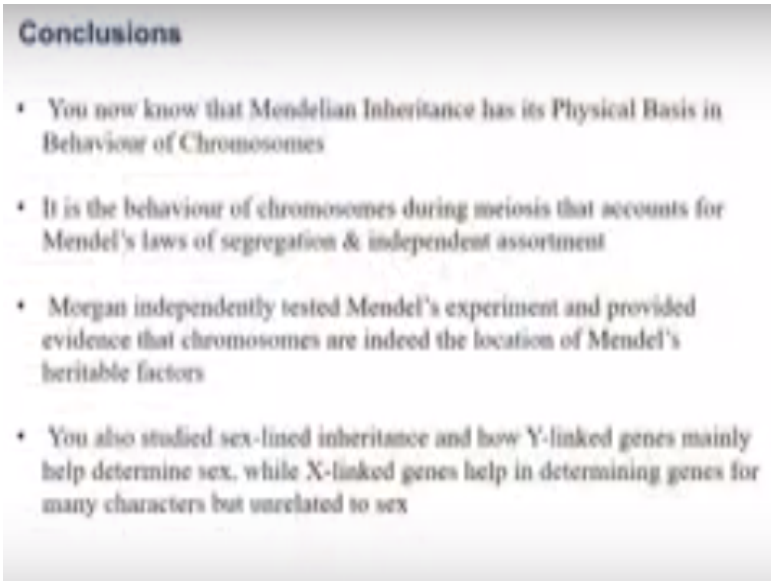

You now know that Mendelian inheritance has its physical basis in behavior of chromosomes. It is a behavior of chromosomes during meiosis that accounts for Mendels law of segregation and independent assortment Morgan independently tested Mendels experiment and provided evidence that chromosomes are indeed the location of Mendels heritable factors.

You also studied sex linked inheritance and how Y linked genes mainly help determine sex. While X linked gene help in determining genes for many characteristics but unrelated to the sex. In the next class we will study genetic recombination and linkage which is very important in determining the inheritance of characters. See you in the next class. Thank you.