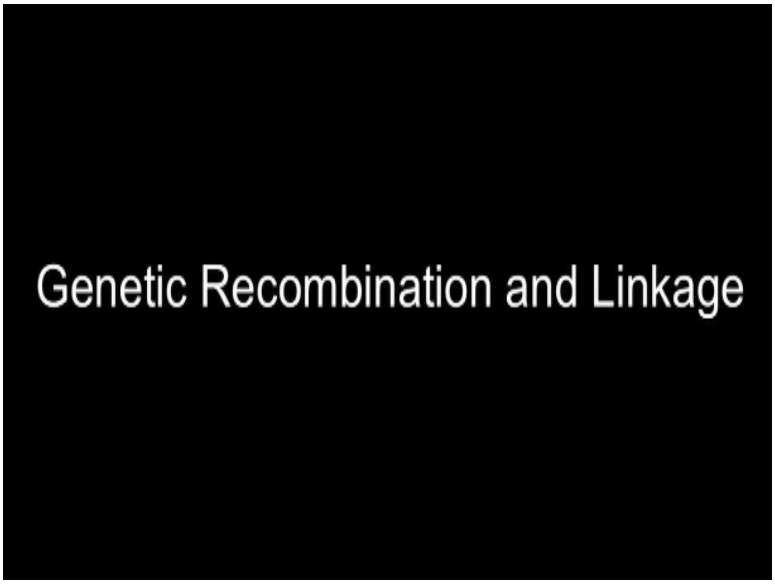
Bioengineering: An Interface with Biology and Medicine

Prof. Sanjeeva Srivastava
Department of Biosciences and Bioengineering
Indian Institute of Technology - Bombay

Lecture – 22
Linkage, Chromosomal Disorders

Welcome to MOOC–NPTEL course on bioengineering and interface with biology and engineers. In todays class we will study genetic recombination and linkage the production of off springs with combination of traits that differ from those found in either parental generations.

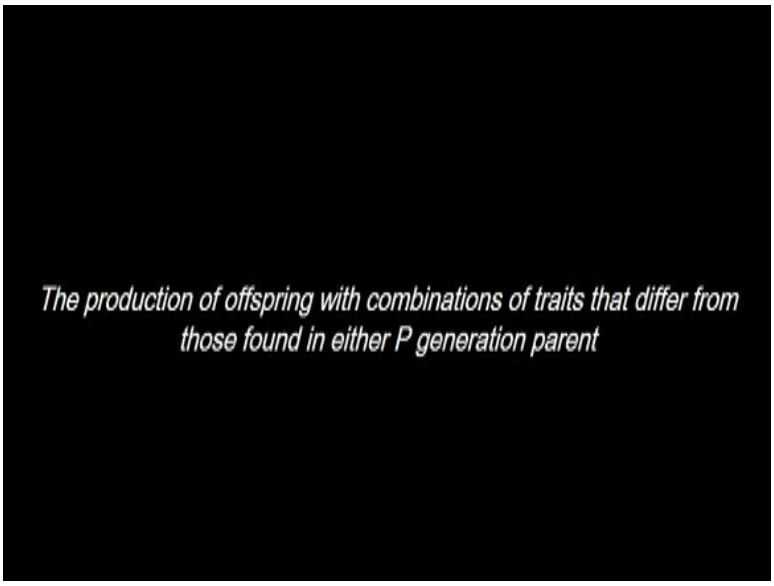
(Refer Slide Time: 00:35)



Morgan in addition to making contribution for understanding the chromosomal basis of the inheritance he was also making many interesting fundamental observations. If you not think about going back to meiosis at some point, we have said that you know the genes get recombined and that is what gives lot of uniqueness among the progenies right among the child you see lot of differences because the genes get recombined.

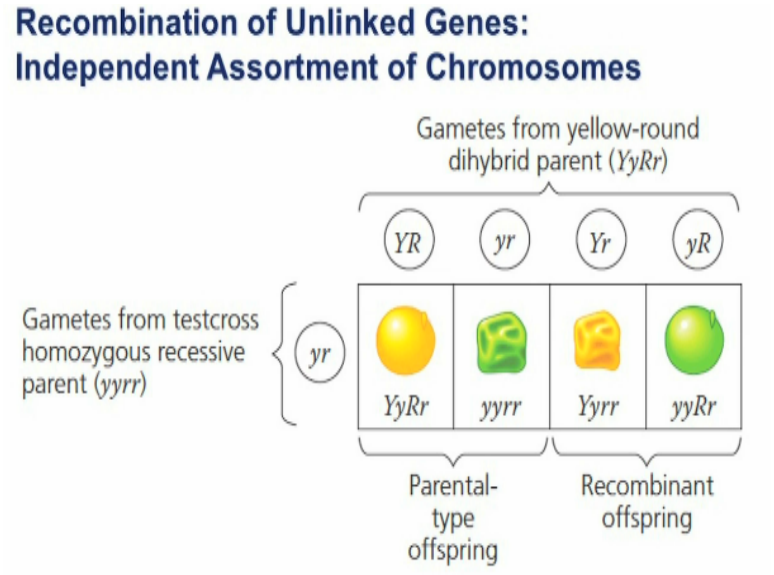
So, he was observing this that whether the genes recombination event happened or there are some genes which are very closely linked to each other and they are not getting recombined.

(Refer Slide Time: 01:20)



So, the production of off springs with combination of traits which differs from the parents whether those are you know passing together or they are getting segregated.

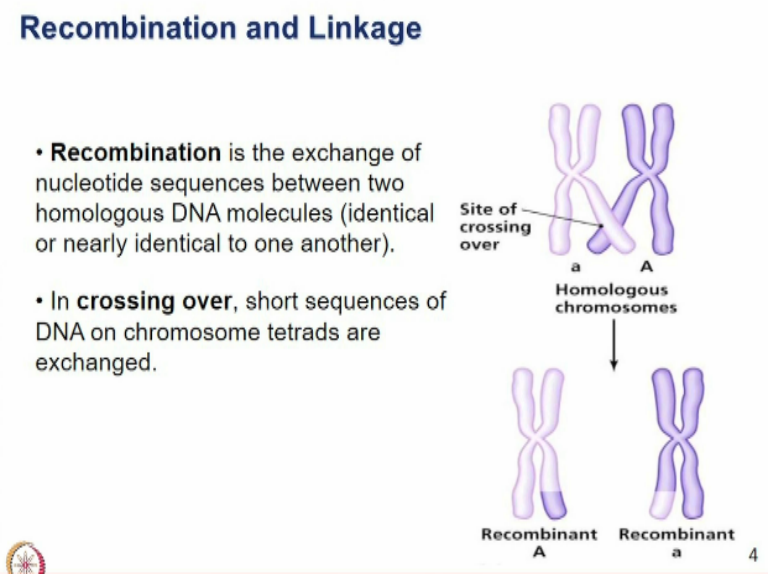
(Refer Slide Time: 01:29)



So think about the classical Mendel thing first and then we come to Morgan. So, in Mendelian experiment we have seen this parental type off springs and then when we did this dihybrid cross, we also saw some recombinant off springs appeared > Recombinant means some new type of features appeared along with the original combination of the characters. So, two non-parental phenotypes were also seen in the off springs.

And these are known as recombinant types or recombinance.

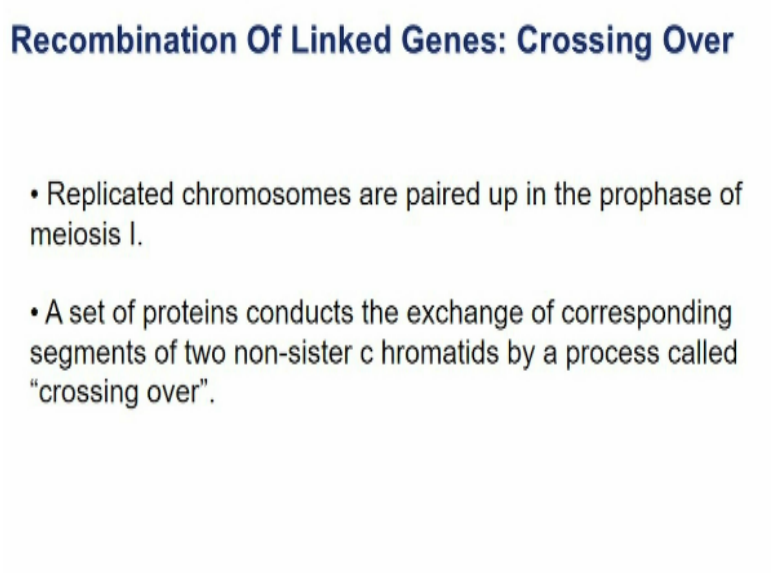
(Refer Slide Time: 02:01)



So, if you remember from the meiosis image these chromosomes are exchanging a small segment of it at a site which is known as crossing over. So, from this part from the male and female gametes they are certain change you know that is interchange is happening. And now you can see the recombinant A recombinant small a this part is actually transferred. So, all the genes which are part of this one has now come in this chromosome.

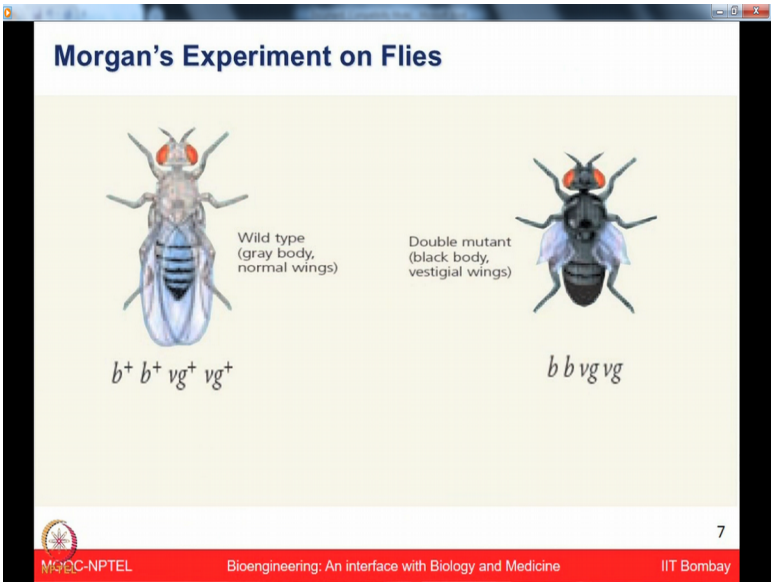
And all genes from this part has come to this chromosome. So, this is kind of concept which we have briefly a seen in the meiosis part and when Morgan was trying to investigate this in much more detail. So, just you know refresh you in recombination is an event when these genes are getting recombined and they are getting an exchange from these two chromosomes and at a site. which is known as crossing over site.

(Refer Slide Time: 02:57)



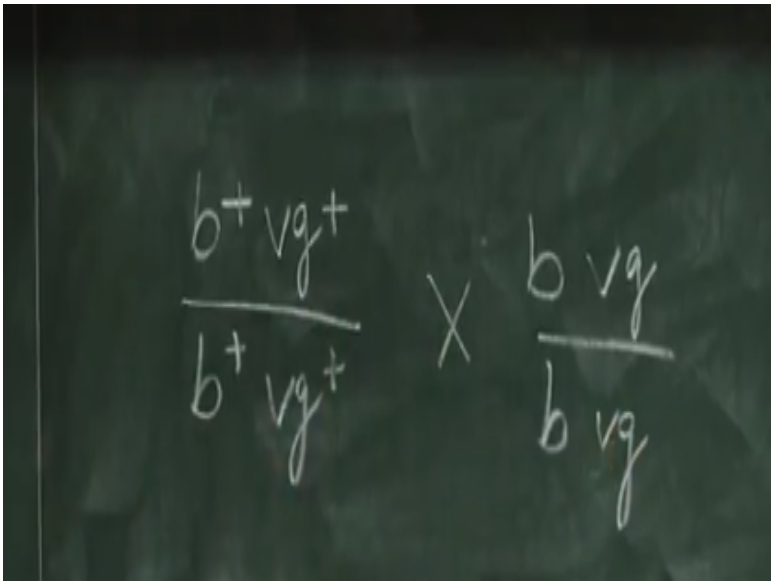
Alright yeah, this part we have talked in the meiosis prophase 1 just to be precise and we have seen that you know a set of proteins are getting exchanged a part of it which we see a crossing over event. So, how does if the genes are linked or they are far apart how that does that information can be transmitted from the one to next generation? And Morgan was always using the fruit fly as a model system and he wanted to study these investigational also in the fruit fly.

(Refer Slide Time: 03:30)



So, lets now increase little bit more information from the fruit fly experiment. And in this case now we have two different types of fruit flies one is wild type which is having the gray body and the normal wings. And second is double mutant which is black body and the vestigial wings.

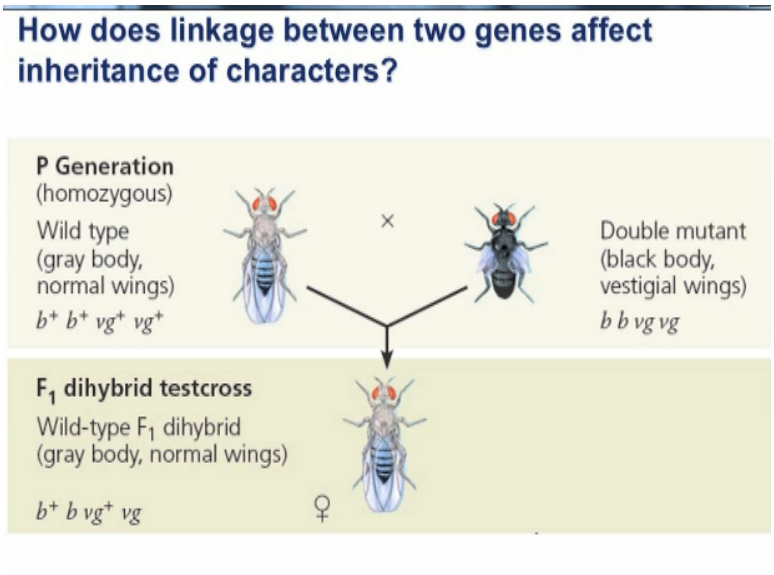
(Refer Slide Time: 03:52)



Just to simplify this part if you make these kinds of crosses or two properties like this that if we are saying wild type it means it is + right. And we are showing the both the chromosomes so b+ and vg+ / b+ vg+ and we are doing a cross with double mutant. So, what is shown here you know b+ b+ it is showing on the both the chromosomes right. So, this is how the cross should ideally look like.

And so now if you take this situation that you have wild type with two features.

(Refer Slide Time: 04:31)

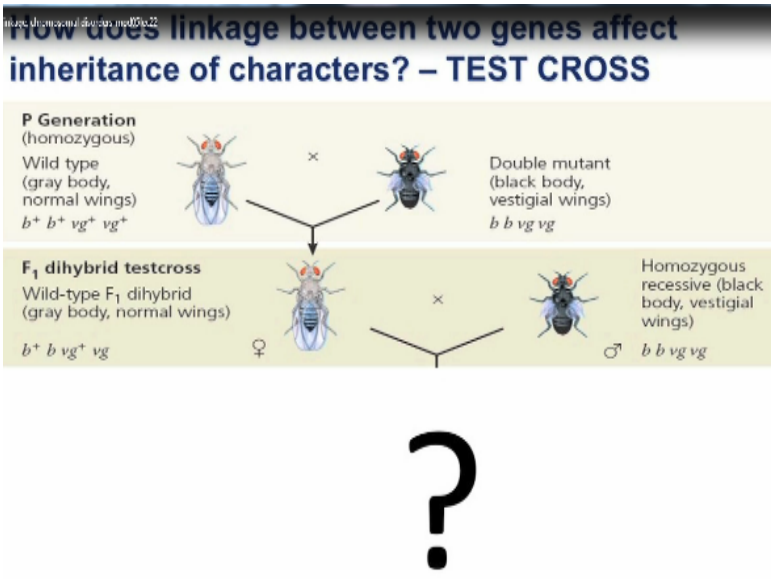


And what you are looking at studying two genes and are they linked to each other or are they going to you know separate in the process of recombination. Now in the f1 dihybrid cross all of

them are looking like the same the wild type feature what we had and now if you want to test cross from this think about Mendelian test cross. So, what would you do the cross now if you want to do test cross f1 whatever the phenotype shown here.

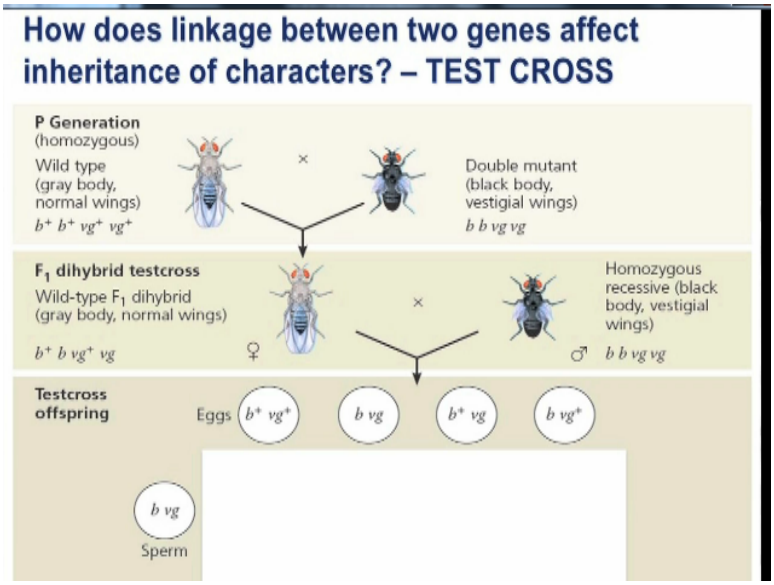
This f1 you want to do a test cross so what will be the Geno type of the other fruit fly you want to cross off this particular fruit fly and you want to do test cross. So, what we did for the test cross in Mendel pea experiment. Anybody recall Homozygous recessive.

(Refer Slide Time: 05:29)



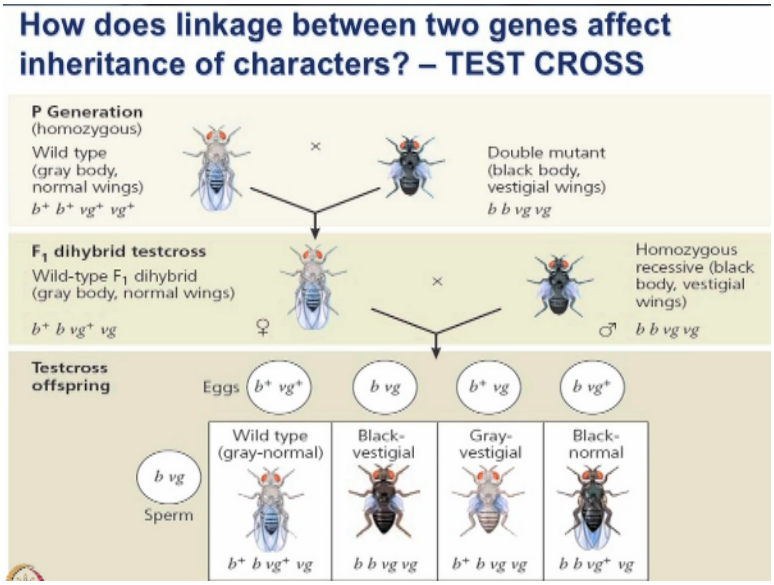
Is this a homozygous recessive? This is right alright well so now can we see this thing? This wild type of f1 and we do a test cross with Homozygous recessive with double mutant. We will do that.

(Refer Slide Time: 06:12)



Write down this gamets and make the square now you can write these gamuts. So, now how will this look okay now you try other. **"Professor - student conversation starts"** there are four different types of eggs actually produce it will cross with We will discuss after doing the cross first alright "**Professor - student conversation ends"** and now if you can read from here there is a gray body and normal wing.

(Refer Slide Time: 07:04)



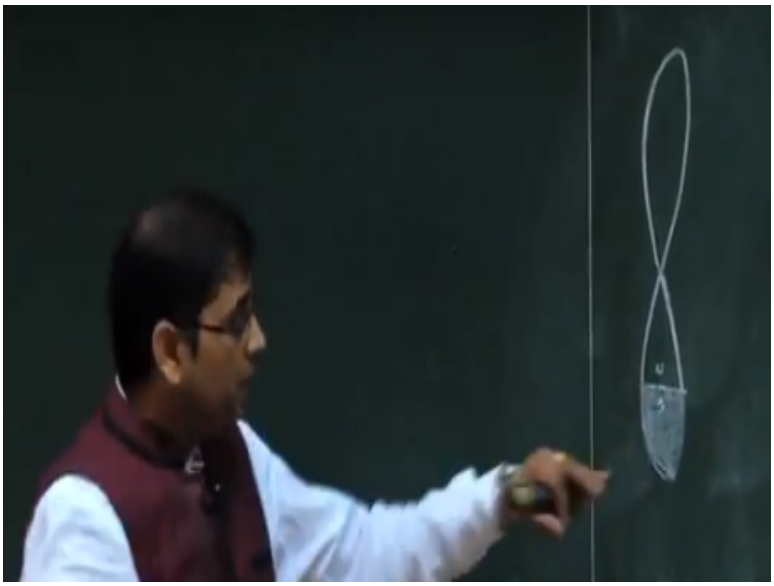
And this is black body vestigial wings. Could also write down what will be the phenotype of these flies. Write down what are the phenotype of these files trust means wild type. **"Professor - student conversation starts"** yes so that I was telling in all of these problems good idea to write

b+vg+ and b and vg because they are like this because these are not different chromosomes so ideally same thing.

But when it + here it means it is wild type and if it is not + it is mutant. "**Professor - student conversation ends."** So we have now these four different types of phenotypes. And what we are observing here that one is gray normal one is black normal one is black vestigial, and one is gray vestigial. So, in addition to the two which were original phenotype what we had we have two different new phenotypes as well.

So, what Morgan was trying to understand from the experiment whether these genes are very closely linked to each other or they are very much far apart.

(Refer Slide Time: 08:53)



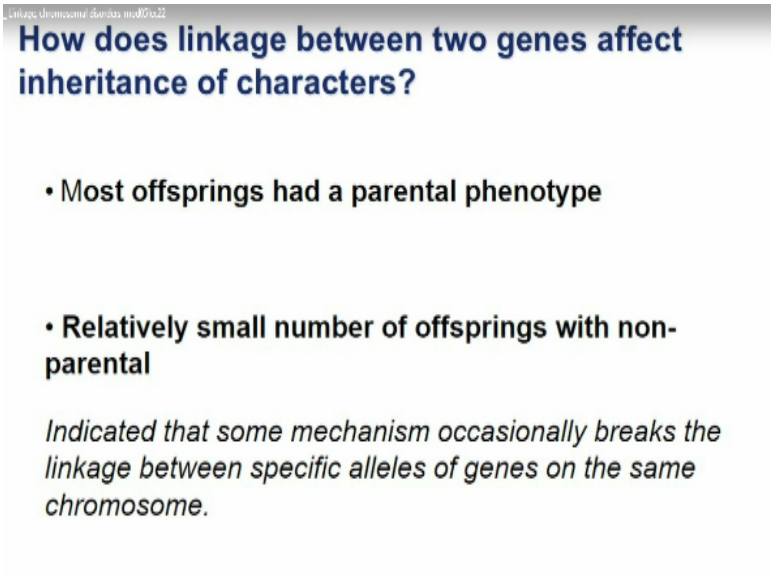
So, if you think about you know just imagine that on this chromosome if this part is getting recombined and these two genes which we are studying one is this part and one is you know going to get separated it will be not linked. But if that these two genes are here, or these two genes are here these are going to be a linked right here very close to each other. So, then if they are close to each other.

So, even if they are getting recombined is still, they are transporting together. So, therefore these two genes you know a higher proportion of this looks like they are linked to each other. But there

are some progenies you know some flies which are also found off other phenotype which may be that you know some recombination event might have happened. So, he was the first time we were looking at not only that how genes are being transmitted.

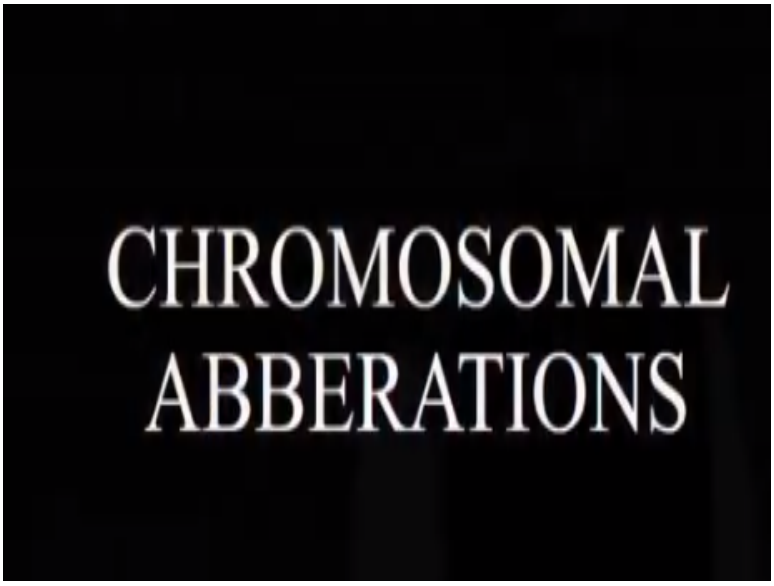
But where they are located on the chromosomes and are, they linked to each other or not. So, this is where he was looking at the linkage phenomenon.

(Refer Slide Time: 09:59)



And what he concluded that most off springs had parental phenotype. Whereas very small number relatively very small number of the flies were also having the non-parental phenotype which means that you know there might be some mechanism which break this particular type of linkage. And some recombination events might happen which is being transmitted from one to next generation which happens usually during the meiosis process.

(Refer Slide Time: 10:25)



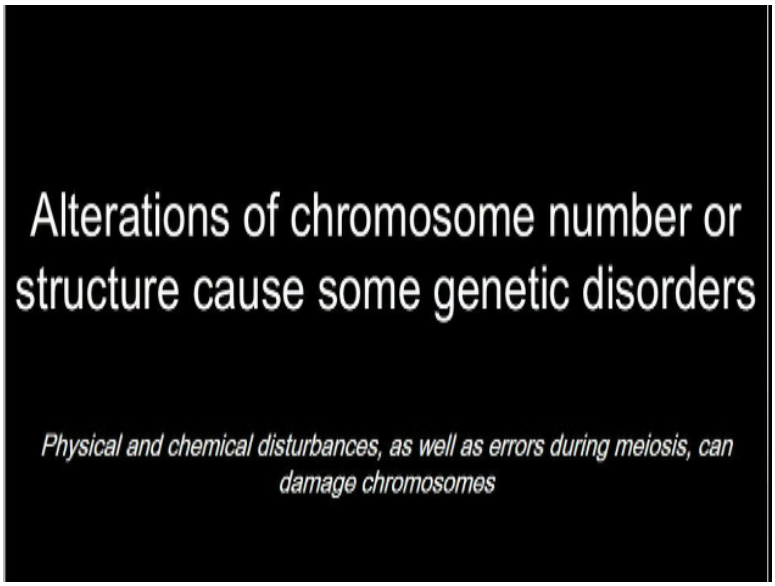
(Refer Slide Time: 10:26)

Alright let us take a short break and let me show you a clip. Hi, is this is your son yeah (Video starts 10:30 – Video Ends 11:35) (FL) Okay alright it will not be quick question but what is this movie? Paa very good and what is the character? What is this character? Character name. Auro. And what is this disease come from which syndrome? That will be the question. Alright so you know I am sure you know you have appreciated.

When you would have at least watched the trailer of this movie that you know there are some child who might be suffering from these kinds of chromosomal glitch to say. And those sometime could just be because of one gene defect and in this case, it was based on a Lamin A

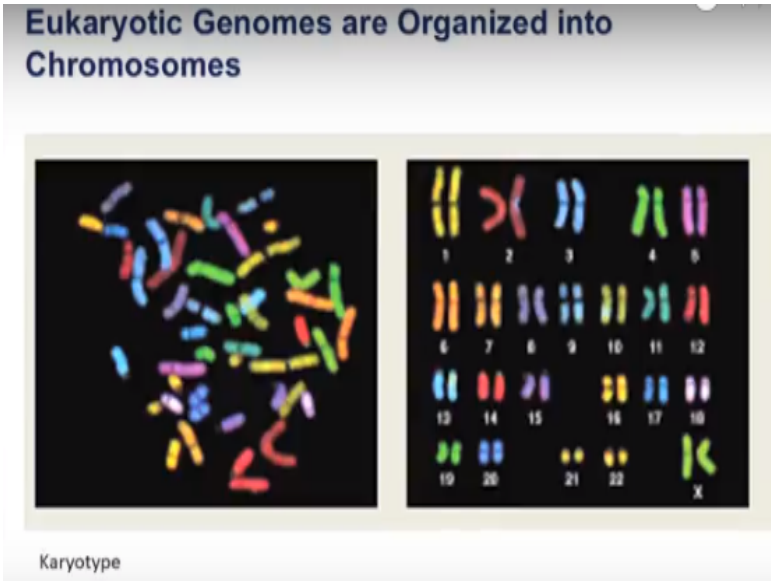
gene which is defective. So, there are many diseases which happened because of certain alterations happening at the chromosome level.

(Refer Slide Time: 12:29)



And lets kind of not a discuss some of these kinds of genetic disorders which are happening because of abnormality in the chromosome number or the structure.

(Refer Slide Time: 12:41)

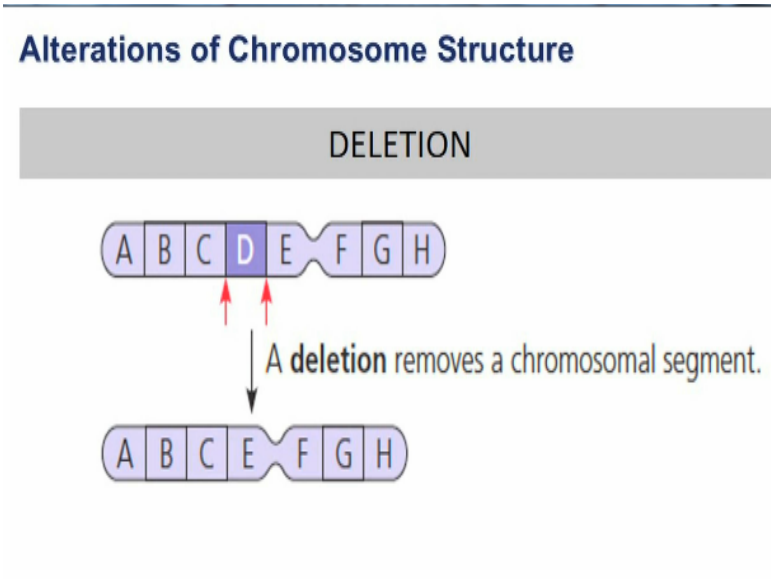


Certainly want to study about all the chromosomes. If you think about at the some part developmental study, we talk that you want to map the karyotypes you want to look at their all the chromosome patterns and it is just color coded differently for each pair of chromosomes. So,

it is possible that. You know while various recombination events are happening in various genetic events that are happening some part of chromosomes get structurally changed.

And it does not happen in always do not happen very often. But once in a while it happens and those may happen.

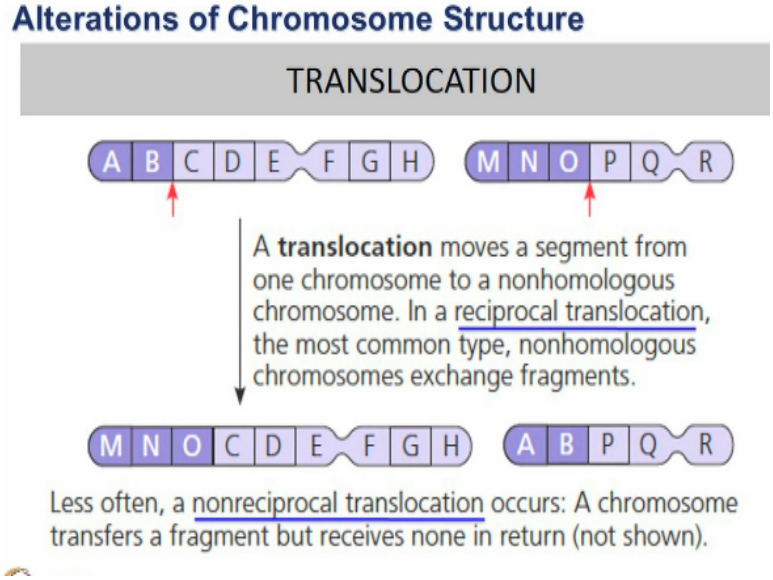
(Refer Slide Time: 13:23)



And those may happen in a small part of the chromosome get deleted and in this case this D part is deleted. So, this is known as deletion of chromosome so all the genes which are a part of that part of the chromosome is going to be absent or it can be inverted. For example, if the gene sequence is ABCDE. Now BCD became inverted so now you have ADCB so many of the actually the cascade of the gene signaling will get changed.

Because of this inversion part or a segment of it like B C in this case here gets duplicated. So, you know you have two copies of B and two copies of C.

(Refer Slide Time: 13:57)



For most situation is translocation a part of these chromosomes move from one to other chromosome like AB in this case moved to MNO and MNO moved to A B and so now they became very different characteristics or sometime it can be nonreciprocal it means it is just going to get attached to other chromosome not the vice versa. So, there are many things which can happen at the chromosomal structural level.

And these are all different types of operations which result in to different type of diseases different disorders.

(Refer Slide Time: 14:29)

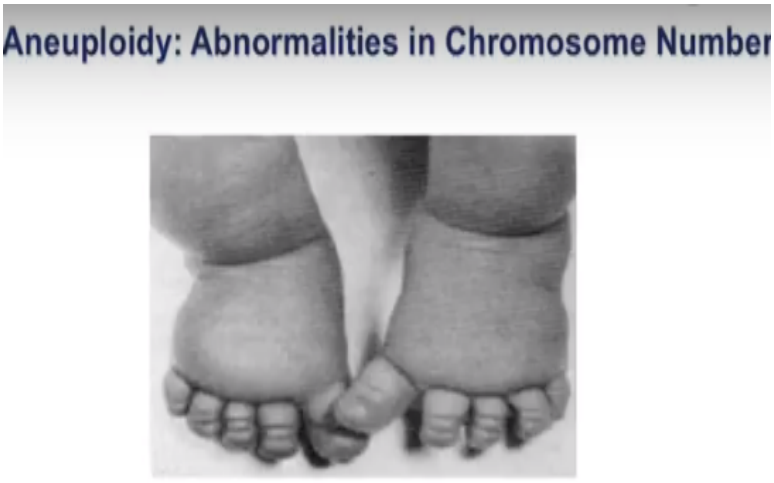
For example, you see this child here suffering from Down syndrome. One of the very commonly found syndrome which is having three copies of the 21st chromosome which is known as trisomy. Trisomy which means 3 copies of the chromosome for Down's syndrome is usually the result off an extra 21st chromosome. So now they are total chromosome number 47 so there is a disbalance and these trisomy of 21 will not people do test for this.

You know at the prenatal level for testing whether the features might be getting this syndrome or not.

(Refer Slide Time: 15:09)

So, another syndrome which is something very similar which is trisomy of 18 chromosome that is known as adverse syndrome.

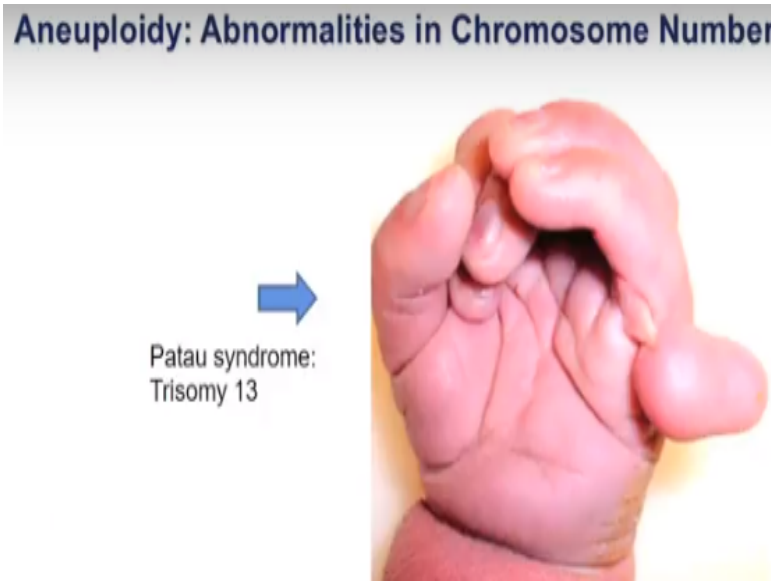
(Refer Slide Time: 15:20)



Turners Syndrome: Absence of one or both copies of X chromosome

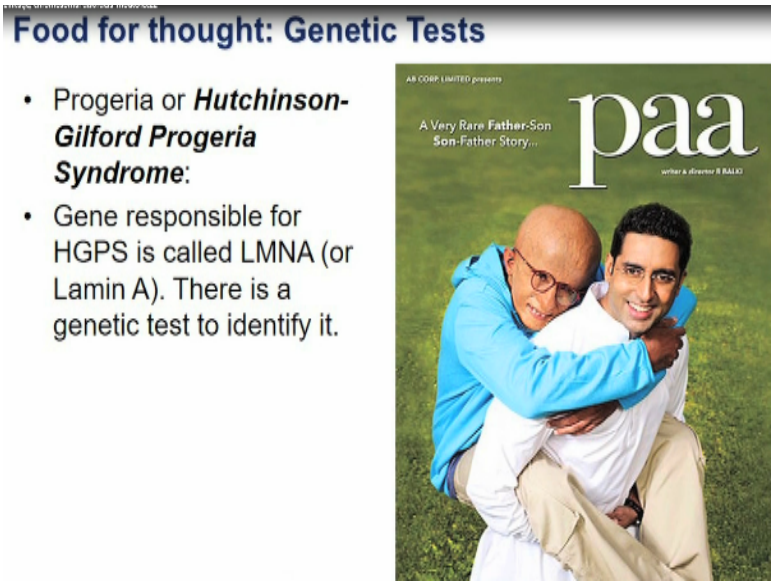
You can see this particular phenotype here Turner Syndrome which is based on the absence of the certain genes from the x chromosomes.

(Refer Slide Time: 15:24)



And now here you can see a phenotype for Patau syndrome which is a trisomy of chromosome 13 so three copies of chromosome 13 is present in this case. So, many of these things are in know some abnormality which happen because of the way chromosome would have shown some changes at the structural level.

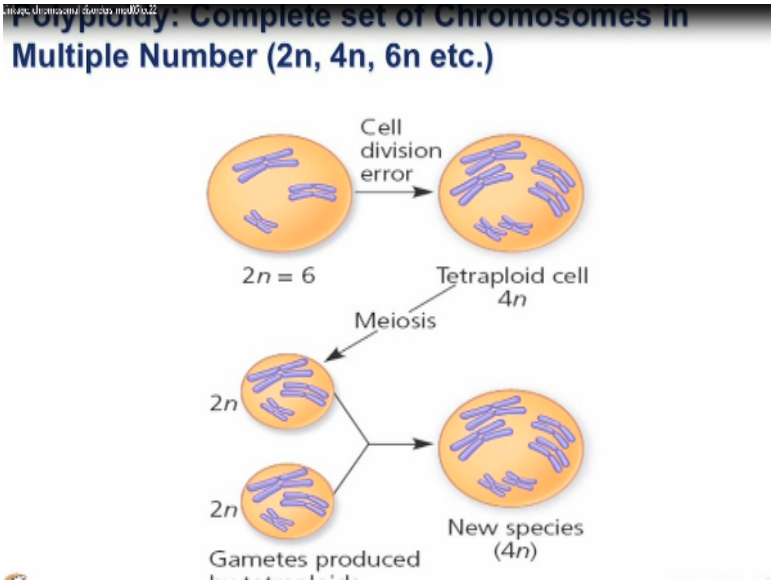
(Refer Slide Time: 15:45)



And we have seen this example that even sometime as specific gene like Lamin A gene in this case having some mutation and as a result resulted into this Hutchinson Gilford Progeria Syndrome and then this kind of child is being born which now people can do genetic testing and try to find out these kinds of genetic abnormalities beforehand. And that is where our understanding of molecular biology.

And lots of genetic tools are becoming really important in medical field.

(Refer Slide Time: 16:17)

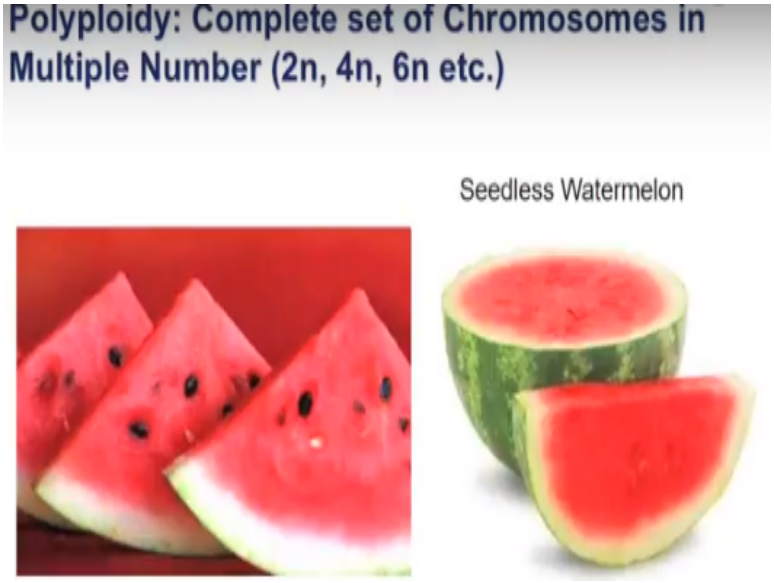


But what happened at the plant level so many times plants also show this kind of changes but not always this changes are detrimental for plants. So, in plants what is more common occurrence is

that certain chromosomes just totally get duplicated or they make 4 copies or 6 copies or 8 copies and this phenomenon is known as polyploidy. You have multiple ploidy level of those chromosomes.

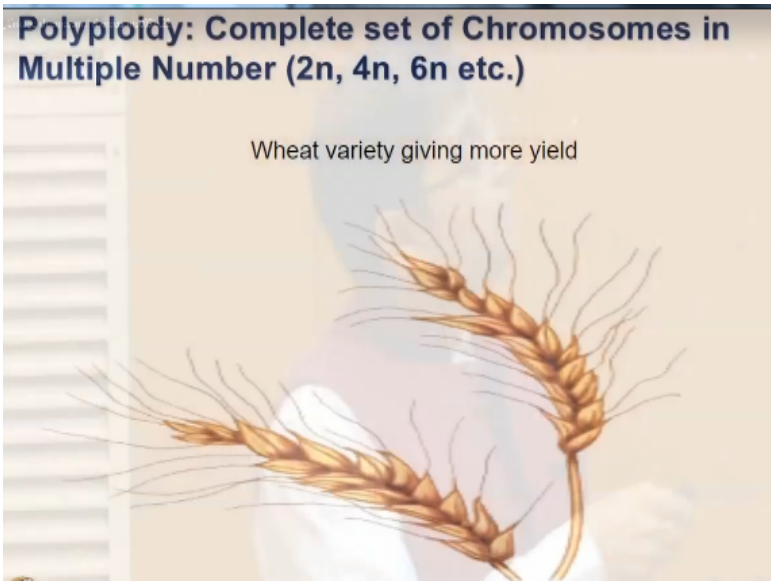
So, rather than only 1 chromosome making you know a third copy or 4 th copy the entire chromosome set has become duplicated. And this is what is shown you here that 2n 4n or 6n of the whole chromosome sets.

(Refer Slide Time: 16:59)



Look at this particular watermelon I am sure you would love to eat watermelon without seeds right that is seedless watermelon and those are actually polyploids those are having extra set of chromosomes. And sometimes those results in to beneficial properties in plants.

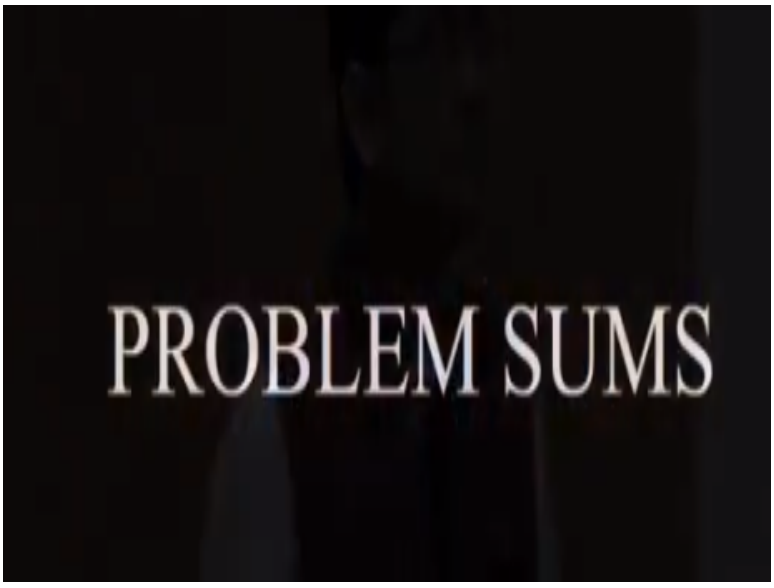
(Refer Slide Time: 17:15)



For example, many of the high yielding wheat variety those are head haploid wheats, so it is not always that you know if you have some extra chromosomes that are going to have some problems in this case it is much more advantageous. But what is important here to note in plants we have a full set of chromosomes getting duplicated and that is usually is much more easy to retain for the cell as compared to only one chromosome getting extra.

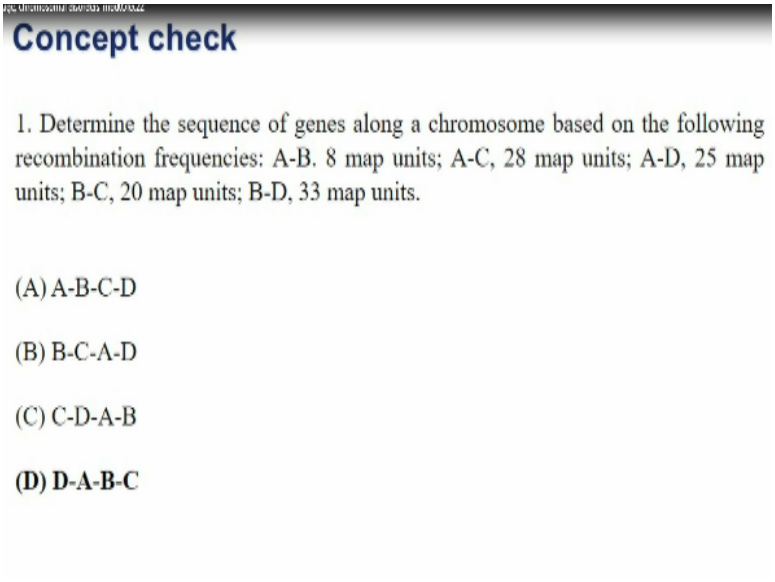
So, that is where I think you can see these are still giving us some positive results in the plants.

(Refer Slide Time: 17:49)



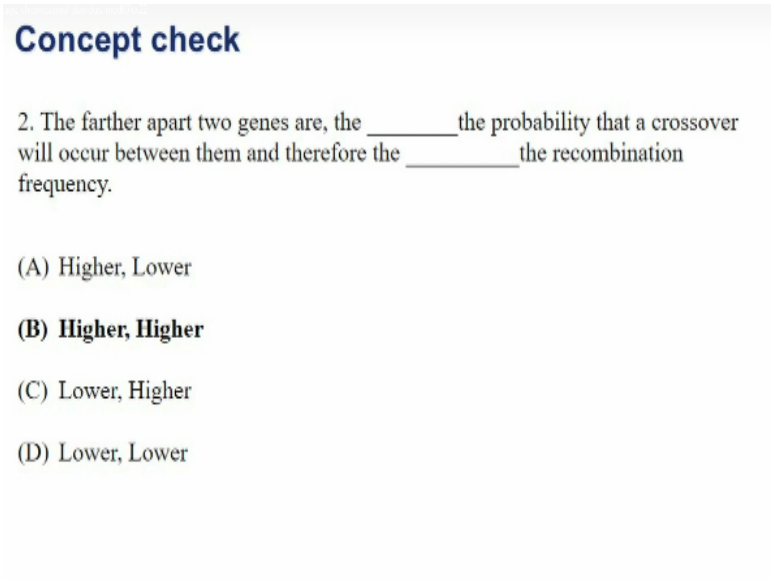
Let us now solve few sums for genetic problems based on this concept but before that these questions will help you revise your concepts. If you do not get this right, please refer back to the slides before you begin the problem sums.

(Refer Slide Time: 18:06)



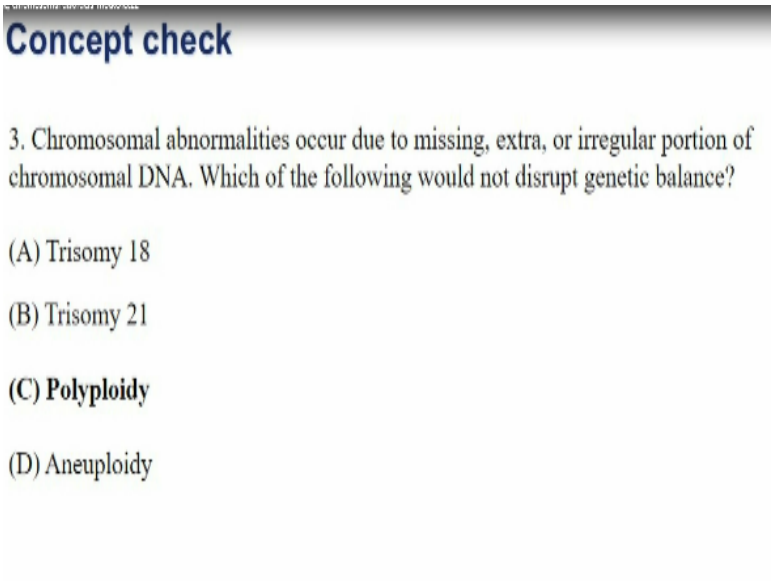
Determine the sequence of genes along a chromosome based on the following recombination frequencies. A-B 8 map units; A-C 28 map units A-D 25 map units and B-C 20 map units B-D, 33 map units.

(Refer Slide Time: 18:47)



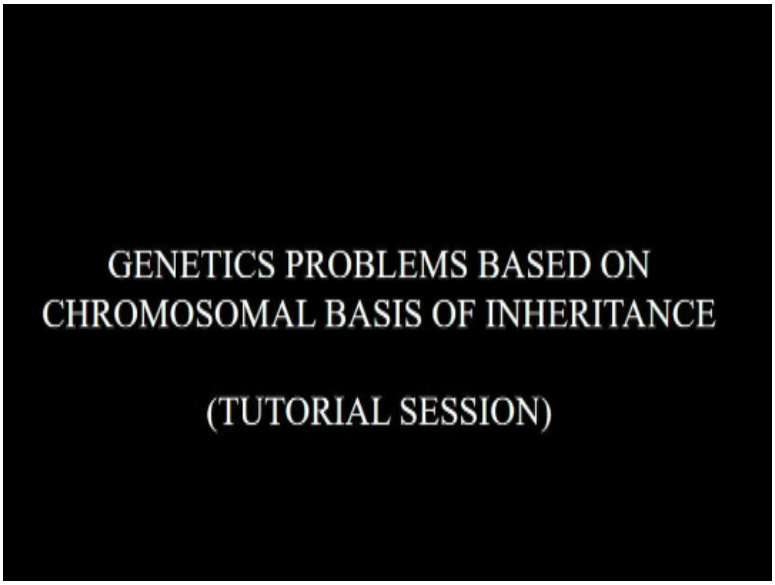
The farther apart two genes are what could be the probability that a cross over will occur between them and therefore what will be the recombination frequency?

(Refer Slide Time: 19:16)



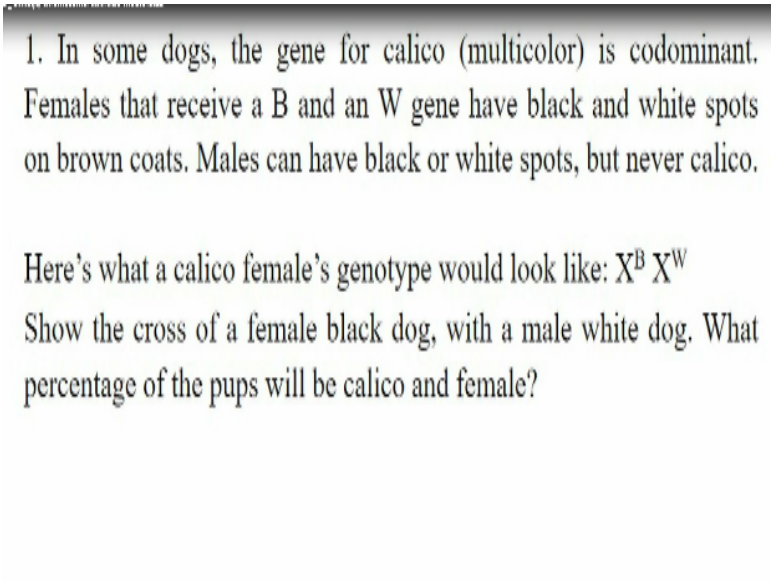
Chromosomal abnormalities occur due to missing, extra or irregular portion of Chromosomal DNA. Which of the following would not disrupt genetic balance?

(Refer Slide Time: 19:42)



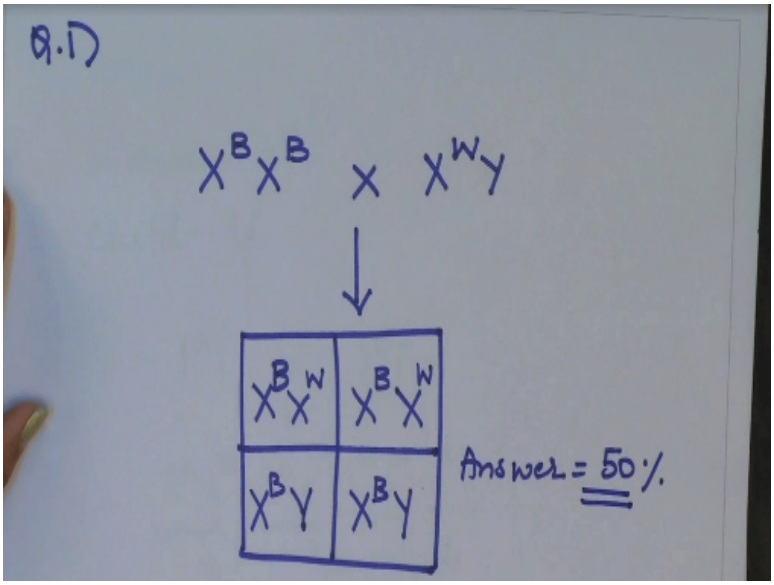
Let us now begin with some problems based on chromosomal basis of inheritance. My TA will assist you in this process.

(Refer Slide Time: 19:54)

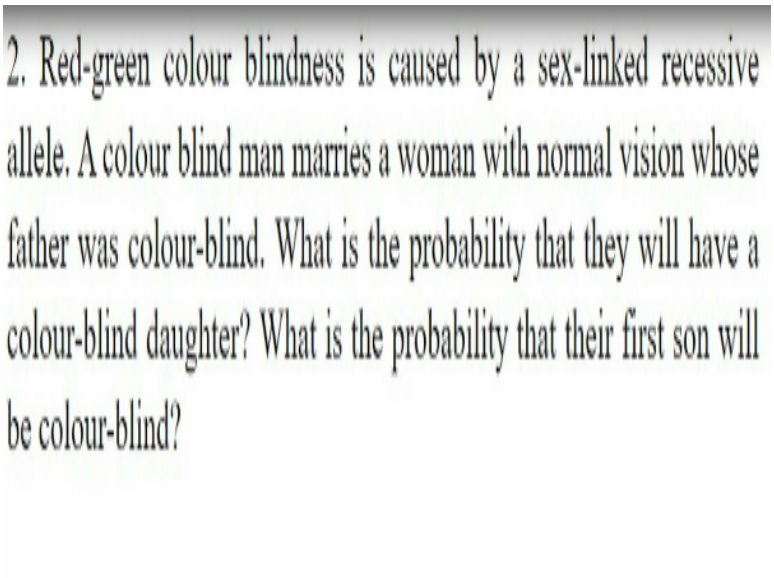


In some dogs, the gene for calico (multicolor) is codominant Females that receive a B and an W gene have black and white spots on brown coats. Males can have black or white spots, but never calico. Here is what a calico females genotype would look like: X B XW. Show the cross of a female black dog, with a male white dog. What percentage of the pups will be calico and female?

(Refer Slide Time: 20:45)

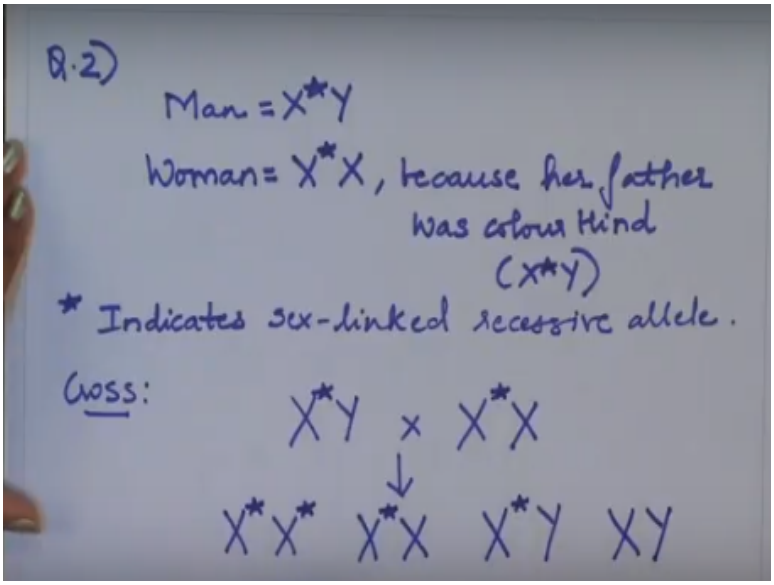


(Refer Slide Time: 21:36)

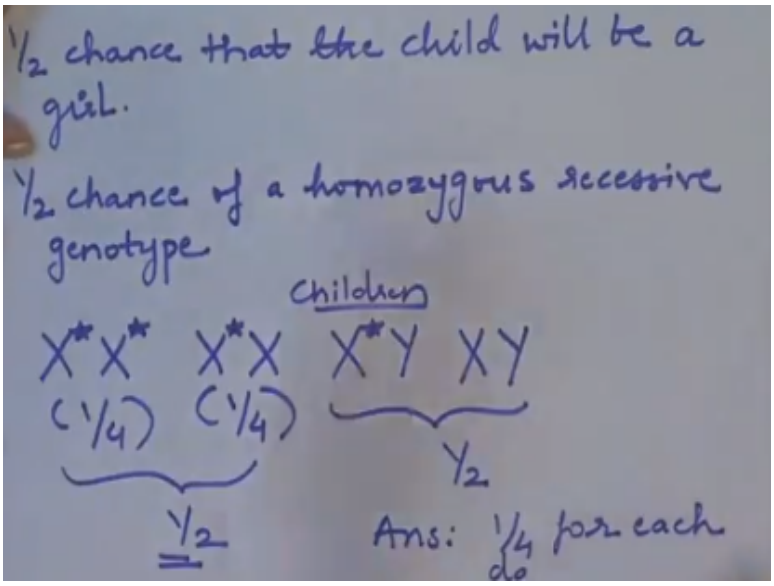


Red- green color blindness is caused by a sex - linked recessive allele. A color blind man marries a woman with normal vision whose father was color- blind. What is the probability that they will have a color–blind daughter? What is the probability that their first son will be color blind?

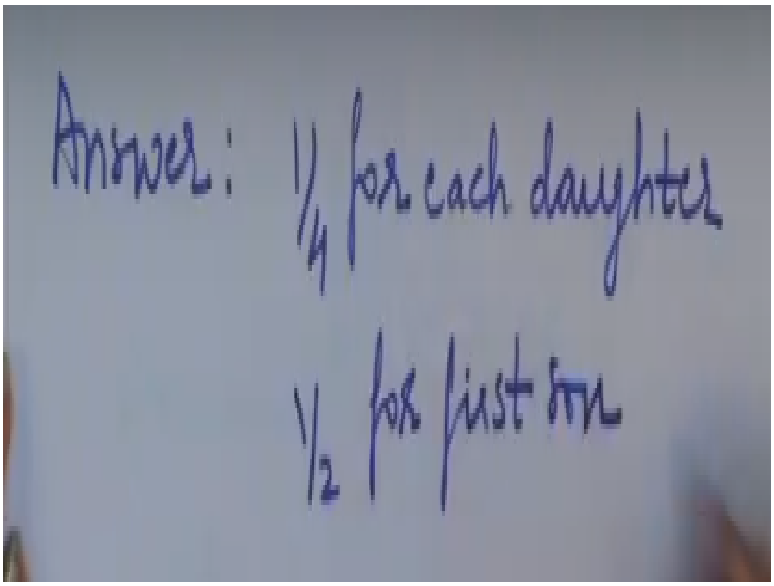
(Refer Slide Time: 22:02)



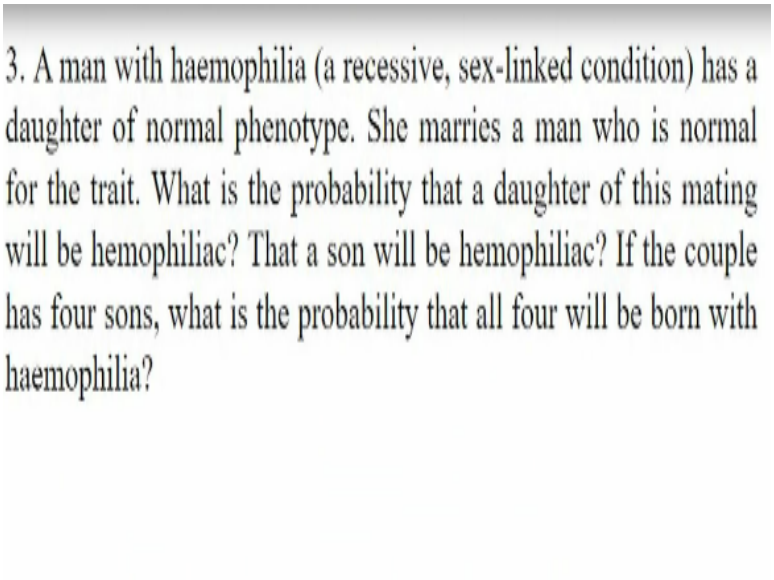
(Refer Slide Time: 24:02)



(Refer Slide Time: 25:42)

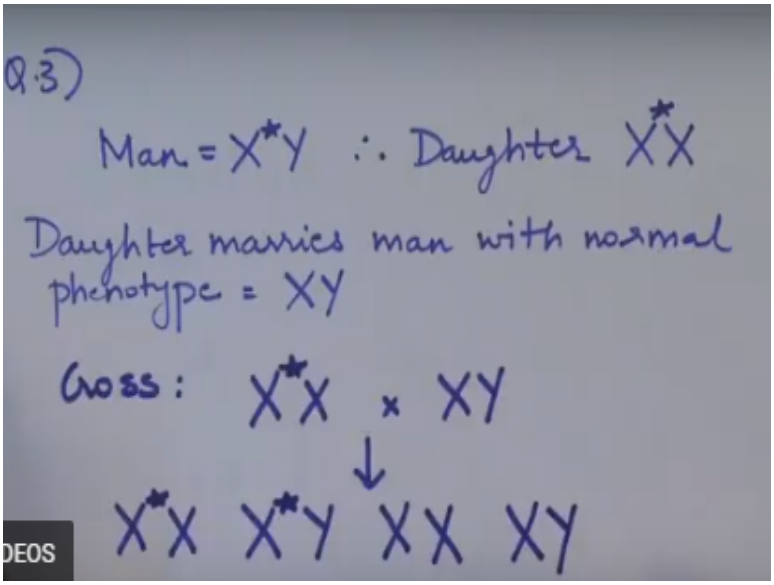


(Refer Slide Time: 26:04)

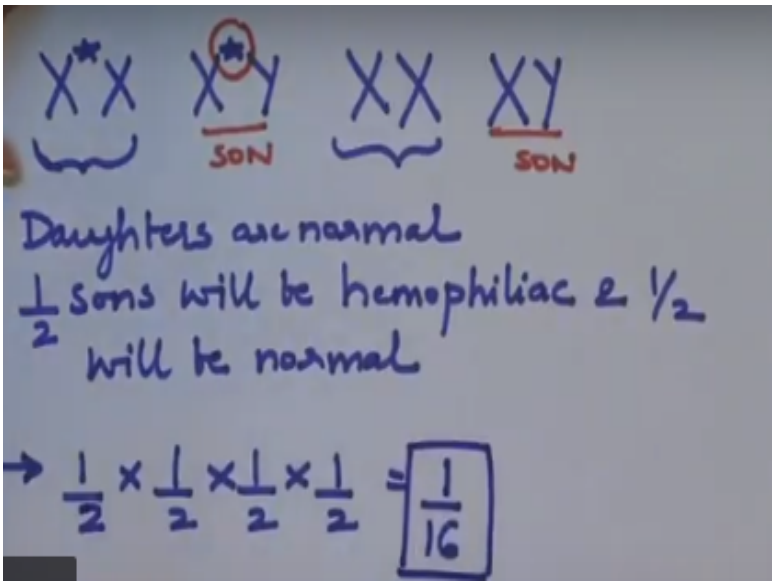


A man with hemophilia which is a recessive, sex linked condition has a daughter of normal phenotype. She marries a man who is normal for the trait. What is the probability that a daughter of this mating will be hemophiliac? That a son will be hemophiliac? If the couple has four sons, what is the probability that all four will be born with hemophilia?

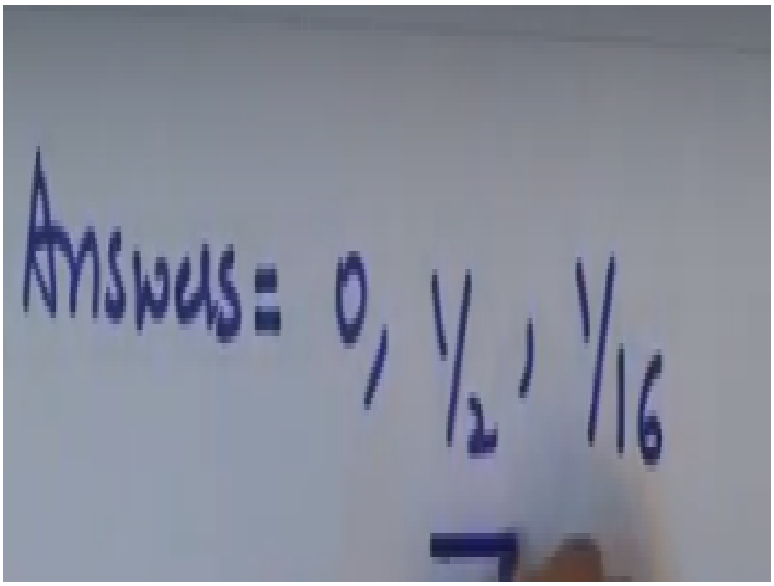
(Refer Slide Time: 26:36)



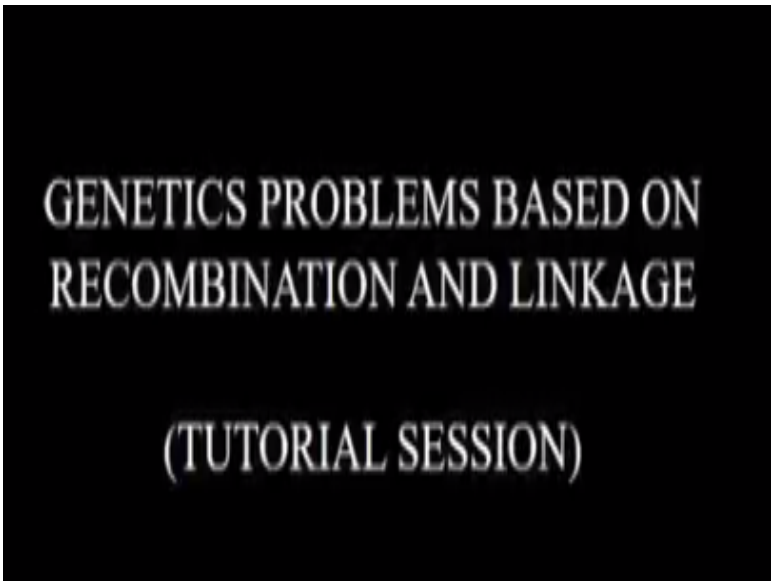
(Refer Slide Time: 27:50)



(Refer Slide Time: 29:21)

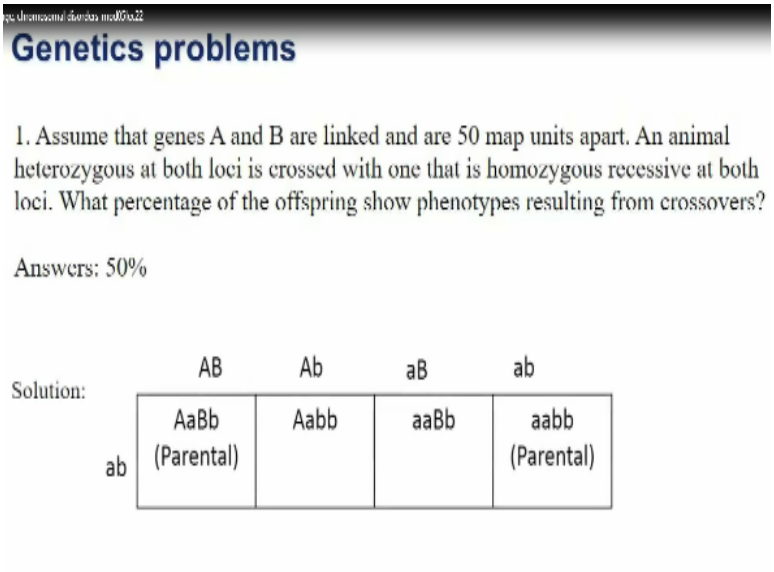


(Refer Slide Time: 29:32)



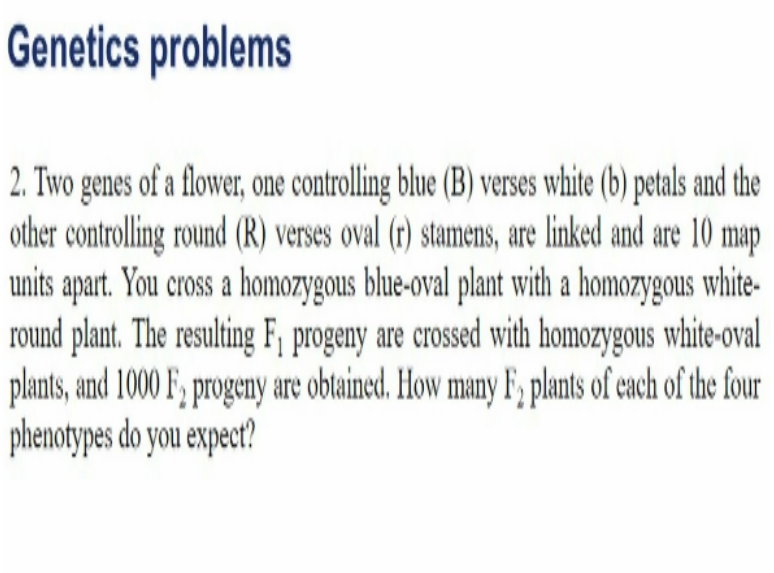
Now let us solve two sums based on genetics linkage.

(Refer Slide Time: 29:37)



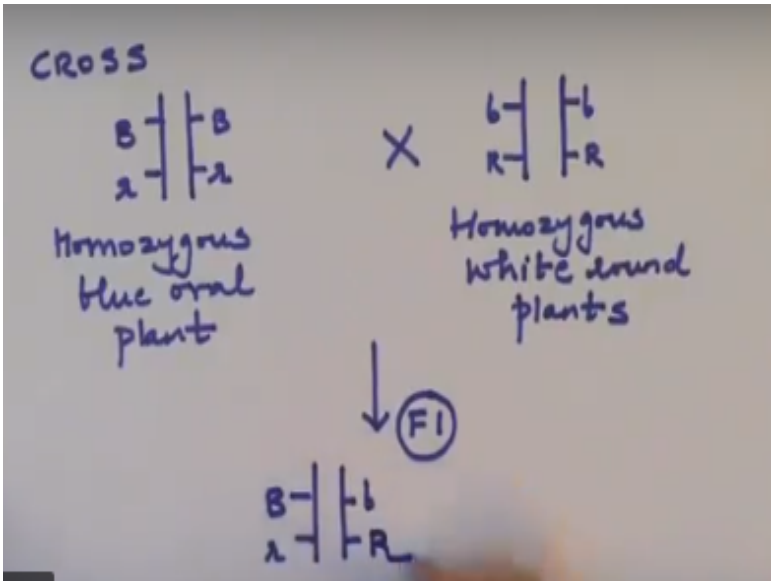
Assume that genes A and B are linked and are 50 map units apart. An animal heterozygous at both loci is crossed with one that is homozygous recessive at both loci. What percentage of the offspring show phenotypes resulting from this crossovers?

(Refer Slide Time: 30:05)

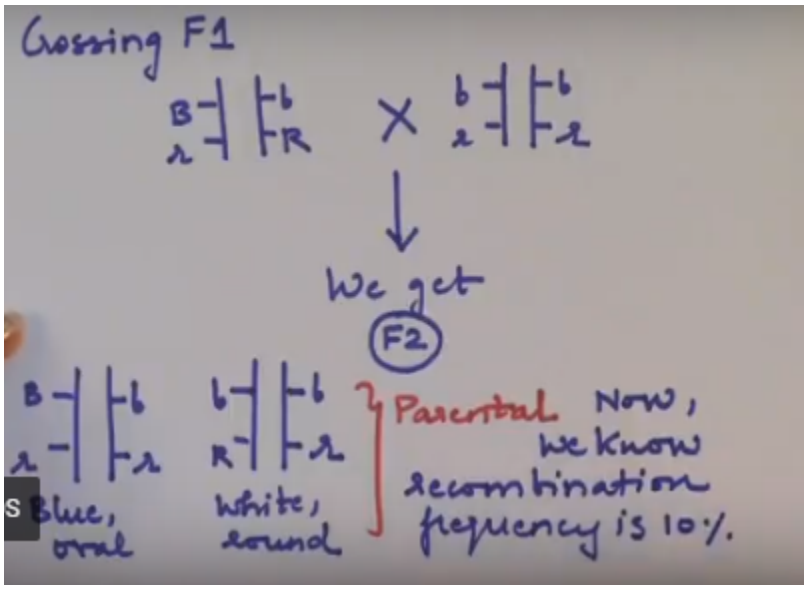


Two genes of a flower, one controlling blue B verses white b petals and the other controlling round R verses oval r stamens are linked and are 10 map units apart. You cross a homozygous blue oval plant with a homozygous white round plant. The resulting F1 progeny are crossed with homozygous white oval plants and 1000 F2 progeny are obtained. How many F2 plants of each of the 4 phenotype do you expect?

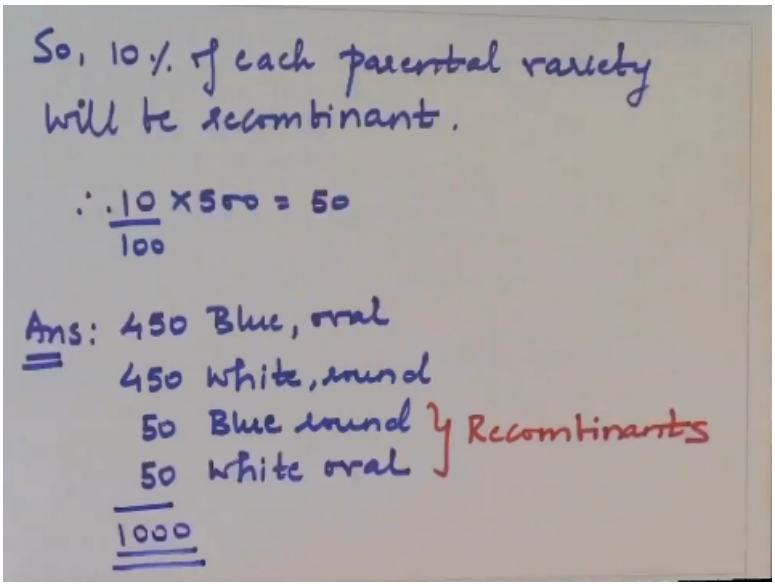
(Refer Slide Time: 30:50)



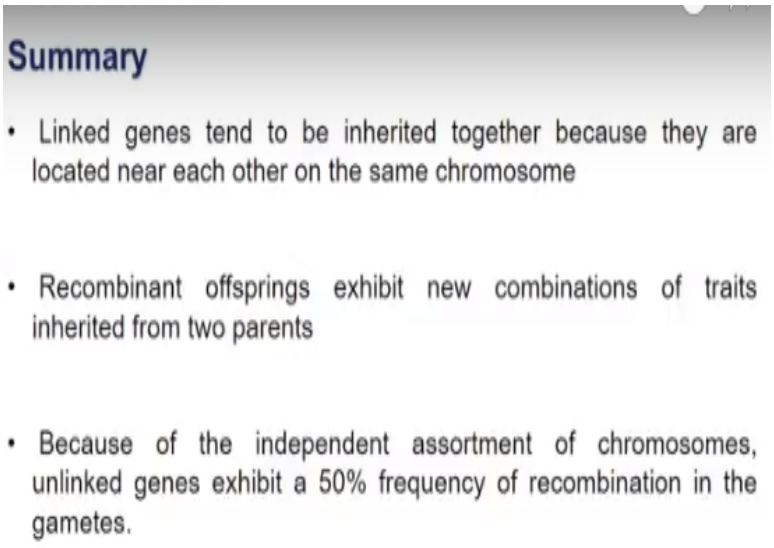
(Refer Slide Time: 32:00)



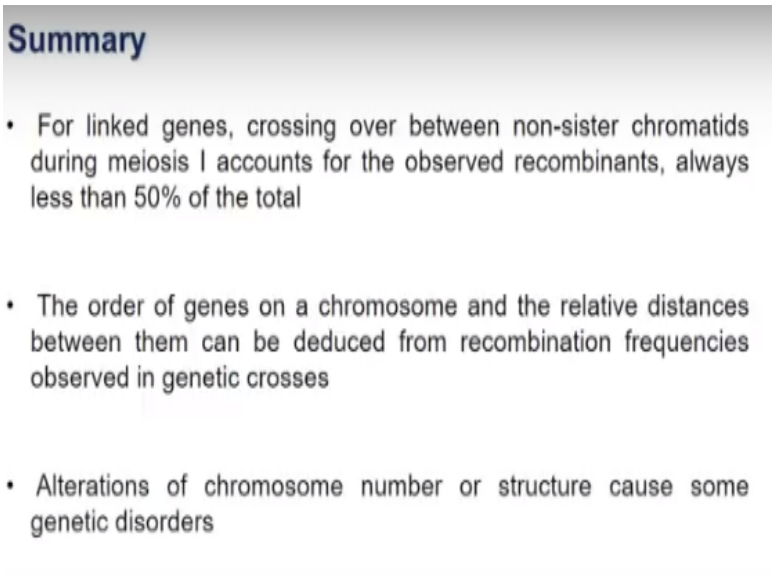
(Refer Slide Time: 33:44)



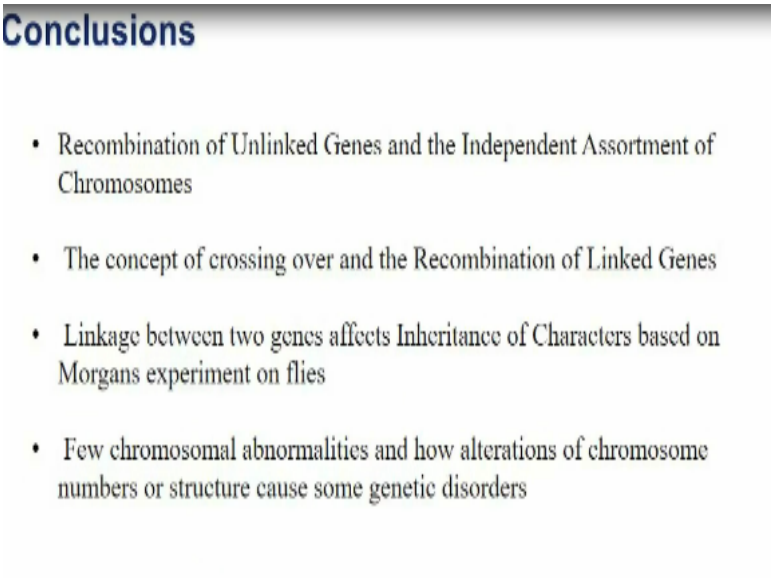
(Refer Slide Time: 35:06)



(Refer Slide Time: 35:22)



(Refer Slide Time: 35:39)



So, in the conclusion in today class we studied recombination of unlinked genes and the independent assortment of chromosomes the concept of crossing over and recombination of linked genes. We also looked at how linkage between the two genes affect inheritance of characters based on Morgan experiments on fruit flies. We then discussed a few chromosomal abnormalities. And how alteration of chromosome numbers or structure can cause some genetic disorders.

In the next class, we will understand the molecular basis of inheritance with the help of some classical genetic experiments. Thank you and see you next week.