Biology for Engineers and other Non-Biologists
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Lecture Number 16
Mendelian Genetics: Genetic Disorders

Welcome to the set of lectures on 'Mendelian Genetics'. Mendelian refers to Mendel, Gregor Mendel. We will refer to him during the course of this lecture and it will also become clear to you why we are looking at something that is so old. What is the relevance nowadays.

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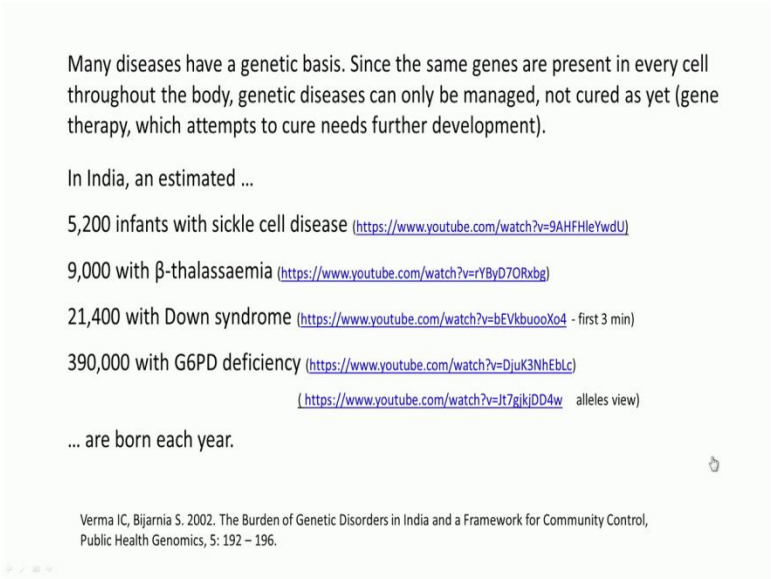

Many diseases have a genetic basis. You know that each cell in the body has the same set of genes; each somatic cell in the body has the same set of genes, and it does not matter whether it is the brain cell or the liver cell or a skin cell and so on so forth, they all have the same set of genes that we inherited from our parents.

They could be expressed differently depending on where they reside and so on and so forth, we will not get into that. But, the basic material is the same. And since the same genes are present in every single cell throughout the body, genetic diseases will manifest across and there is nothing much can be done, it can only be managed. It is rather difficult to cure them as yet. Genetic, or gene therapy has some promise, it is , it has been studied for quite a long time; it has had a few

successes, but I think it needs quite a bit of development before it gets to a good acceptance stage.

Let us start with some data. In India, an estimated five thousand two hundred infants with sickle cell disease, nine thousand with something called (beda) beta thalassaemia, twenty-one thousand four hundred with Down syndrome and (thirty-nine), three hundred and ninety-thousand with G6PD deficiency are born each year, okay? These terms, some of which we have seen earlier; sickle cell disease you know, sickle cell anaemia, the same thing, it is called sickle cell disease. If you want, you could look at this video, which is also given in the pdf file, which can be clicked from the pdf itself. This is an optional video to know about sickle cell disease, nice video, but it is an optional video.

Similarly, you could look at this video for knowing what thalassaemia is, specially beta thalassaemia; there is alpha thalassaemia and beta thalassaemia, you could click on this, again an optional video. Down syndrome, I would suggest that you watch the first three minutes of this video. It has a very nice overview of the genetic basis itself, and it gives an introduction to the Down syndrome, and then it gets into a lot of research aspects, that might be a little beyond this course, the research aspects, the first three minutes are very nice, I would recommend that you watch this, the first three minutes of this video.

And then there is something called G6PD deficiency which seems to affect a large number of infants born every year, right? This is a social aspect that is given an optional video, and this is an allele view that is given of G6PD deficiency, which you may want to look at, okay? These are optional. Except the first three minutes, I would say is highly recommended. This is actually from the source because these are numbers and these are estimates; this is actually from a source, a paper published in two thousand two by Verma and Bijarnia; 'The Burden of Genetic Disorders in India and a Framework for Community Control'. It was published in 'Public Health Genomics'. This was in two thousand two, the numbers, of course would be different now, but atleast we have something that we can hold on to, in terms of numbers. That is why this is chosen. Gives you an idea of the prevalence of such diseases in India.

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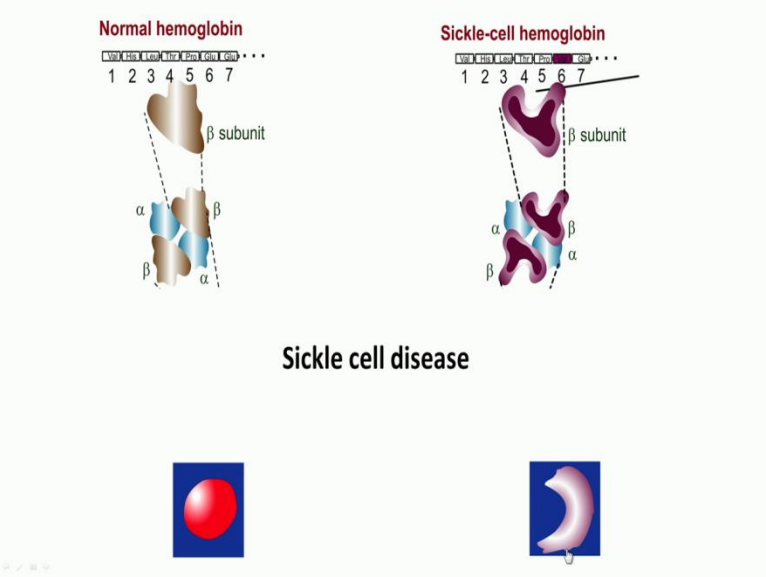

We have already seen the sickle cell disease; let us review this. We know that normal haemoglobin is made from the haemoglobin, haemoglobin is a protein, therefore it is made from the genes that correspond to the various sub-units that code for the various sub-units. In a normal haemoglobin gene, there is a glutamic acid in the sixth position. If that glutamic acid becomes a valine, right? If, if that is changed, then just that one change can bring about a different conformation, different three dimensional folding in the case of the various protein sub-units, and we get a haemoglobin molecule that can easily crystallize out, it will not have an ability to carry oxygen as a normal haemoglobin molecule does.

And therefore, we get sickle cell anaemia, right? This is, it is as simple as that. The, if the haemoglobin is normal, the red blood cell would look nicely disk shaped, and if it happens to have, if it happens to be diseased with sickle cell anaemia, then the red blood cell takes on a sickle shaped, sickle shape. And this causes major difficulties as you have already seen in an earlier video, in an earlier recommended video in this course.

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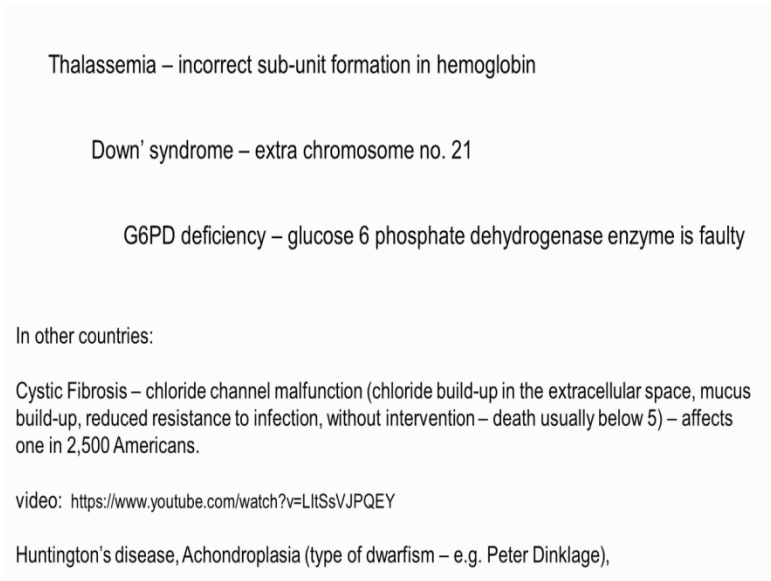

Similarly, thalassaemia is incorrect sub-unit formation in (haela)(hein) haemoglobin; either the alpha sub-unit or the beta sub-unit are incorrectly formed, it is different from sickle cell anaemia. Down syndrome is caused by an extra chromosome number twenty one. Typically people have two chromosomes, right? The chromosome twenty one has three; there are three twenty number twenty one chromosomes. If that happens, this happens in each cell, if that happens, it results in Down syndrome, and it manifests in different ways that you can pick up from the video that was recommended, that was suggested, it is an optional video.

And then, this G6PD deficiency, which stands for 'Glucose 6 Phosphate Dehydrogenase' deficiency, this enzyme is called faulty; and because this enzyme is faulty, it leads to a lot of difficulties, major difficulties, right? Again recall that 'Glucose 6 Phosphate Dehydrogenase'; It is an enzyme, which means it is a protein, it is coded by a gene, right? And therefore, it is a genetic disorder. This is in India. In other countries, cystic fibrosis; it is a very very common genetic disorder in the US; it arises because the channel for chloride in the membranes malfunctions, okay, because the protein which is actually the the channel the chloride channel protein, that is not properly formed and therefore, that malfunctions, the chloride cannot move in and out of the cell.

If that happens, there is a chloride build up in the extra cellular space, and that results in mucus build up, reduced resistance to infection, and without proper intervention, death usually occurs

below five years of age, okay? With intervention, people live much longer, and it affects one in two thousand five hundred Americans, it's a very prevalent. You can look at this video which gives you some idea of cystic fibrosis, it is a let us say an optional video. And similarly, Huntington's disease, which actually manifests above fourty five, is a genetic disorder. Achondroplasia, which is a kind of dwarfism, okay. You might recall Peter Dinklage, from 'Game of Thrones', right? Tyrion Lannister, is it? , that person, has Achondroplasia; it is a type of dwarfism. That is an inherited disorder; a special type of inherited disorder as we will see later.

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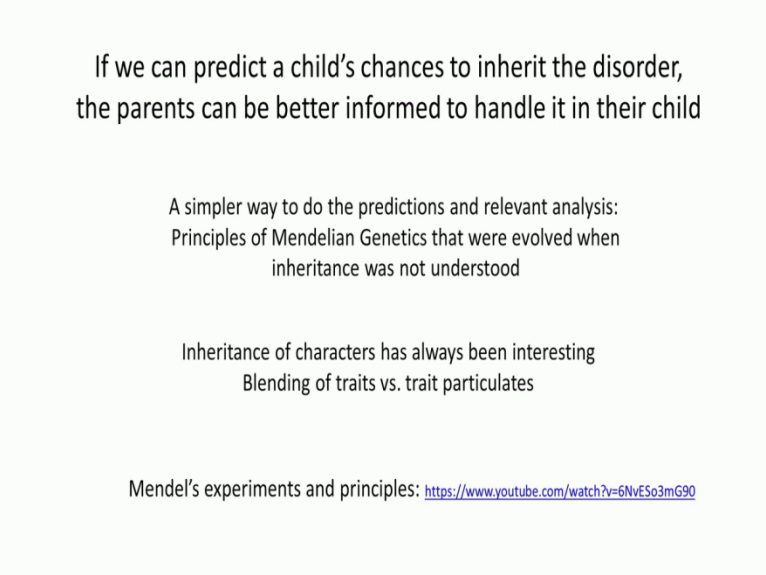

Now, we said all this for this reason: if we can predict a child's chances to inherit a disorder, okay, something as major as cystic fibrosis, the parents can be informed to handle it in their child, okay? They will be atleast expecting this difficulty in their child, they would be mentally prepared to handle it and so on and so forth in (the), in their own ways, and that would be, that is a big thing, that is already being done, and that is a very big thing and the basis for that is what we are going to see in this particular lecture.

A simpler way to do the predictions and the element analysis, we know a lot today and there are various ways to do this analysis; but a very simple way in which this analysis can be effectively done is by using the principles of 'Mendelian Genetics', and the principles of Mendelian Genetics evolved, may be a century and a few decades ago, when inheritance was not even

understood, when people did not understand how, what is the basis of the the (fath) the son or the daughter looking like their father or the mother, and sometimes looking like their grandmother or the grandfather and so on and so forth. People just did not understand.

Right? It was during that time, late eighteen hundreds, that these principles were developed; we will very briefly look at it by Gregor Mendel, seminal piece of work, and those principles are very effective today, although they are, you know Basel principles and there are huge variations known to them, those principles are still very useful to do this to be able to predict a childs chances to inherit a disorder; and that is the reason we are studying or we are looking at Mendelian Genetics even today.

In any case, historically it is nice to know what Mendel did and the development of that if you are interested in genetics; but there is a very useful angle to it. When inheritance was not understood, may be a (couple) century and a half ago, century ago, the inheritance of characters, of course has , has always had a good appeal with people. People were always curious to know why people inherit characters, why a son behaves like the father or the mother, or the daughter behaves like the father or the mother and so on, or sometimes even like the grandfather or grandmother.

Many felt that there was always a blending of traits; there was some trait from the mother, some trait of the father, the son or the daughter has, or the offspring has the traits that are a blend of these two traits, that was what was believed for a very long time. Although, there were many different situations where this clearly was not valid, okay. That has always puzzled people but they were skeptic about it and so on and so forth, till Mendel came and told us that the traits are actually passed on by trait particulates. There are there are aspects that determine traits in an appropriate fashion and if you understand this, it it, you can predict to a certain extent what will happen.

So that is, that was a big contribution by Mendel, Gregor Mendel, and I would like you to watch this very nice video. I would I would say it is a required video; it is a very nice video, slightly long, about twenty, twenty five minutes; so long, old, but it is a very nice video, okay, I would like you to watch this video to know some parts of Mendel's life, which is very interesting and Mendel's experiments and some of the principles that he brought forward, okay? In this lecture,

or these set of lectures, we will see what is relevant for us, okay, not everything, but we will see, just see what is relevant for us.

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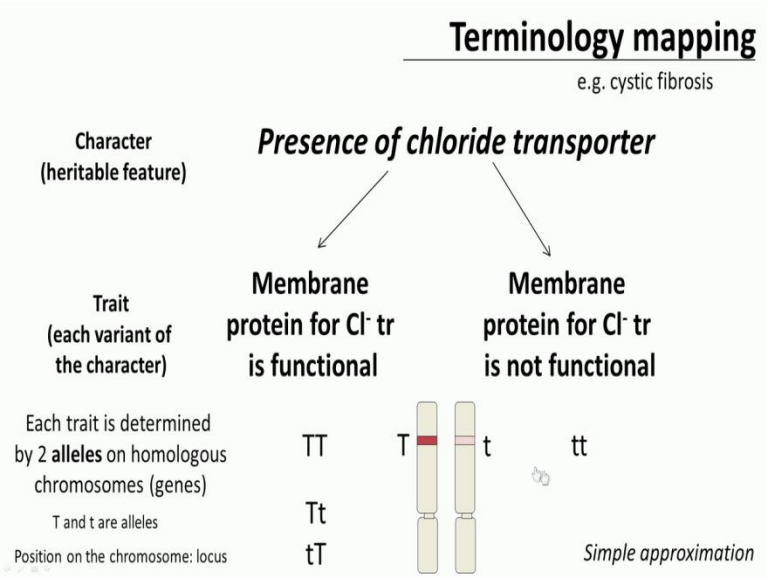

To do that, let us, we will have to map our current terminology to the terminology that existed during the development by Mendel, okay, or, soon after that for many years. To do that, let us consider cystic fibrosis. The presence of the chloride transporter is important, because if that is absent, cystic fibrosis arises. There are two possibilities; the membrane protein for the chloride transporter, is either functional or the membrane protein for the chloride transporter is not functional, right? These are the two possibilities, and if this is the case, the person is normal, if this is the case, then cystic fibrosis itself.

The presence of the chloride transporter is a character or a heritable feature, okay? Heritable feature is called the character. Sometimes it is not as, not in molecular terms as this, it could be the height of a person, or it could be the colour of the eye, and so on and so forth. Those are, those are typical those are typical observable traits, or in other words, the characters usually an observable thing, I am just using a terminology mapping here, so this aspect, if it can be observed, it is called a character, and it is a heritable feature.

The variants of each character, each one of them is called a trait. Okay? For example, the presence is a trait, the sorry, the functionality is a trait, the non functionality or the absence is a trait. Tall, tall is a trait or short is a trait, okay? Blue colored eyes is a trait, brown colored eyes is

another trait, and so on. So, if the character happens to be eye colour, blue eye colour and brown eye colour are the two traits, or many, two of the many traits of that particular character. If height of something is a character, then tall is a trait and short is another trait, and so on. You get the idea.

So we are going to deal in terms of characters, traits and so on. Each trait is (determined), is determined by two alleles on homologous chromosomes, okay, and this is what is equivalent to the genes that we know of, right? On homologous chromosomes means, you know that they exist in pairs and therefore, we just talked of pair number twenty one, if there is an extra one, then Down syndrome (())(15:35), but those two twenty ones or those two twenties or those two, let us say one two three, they are all homologous chromosomes; and two alleles on homologous chromosomes determine each trait is what Mendel is is the equivalence here.

So if these two are homologous chromosomes, capital T is a an allele, and small t is another allele. So you could have various combinations, both could be capital; they could be alternate, one could be, this one could be T, this one could be small t, this one could be small t, this one could be T, or both could be small ts. And these different combinations result in different traits of that character; different yeah different traits of that character. The position on the chromosome of that allele is actually called a locus, this is just for the terminology, okay?

Remember that this is a simple approximation, there are variations possible, we will point them out when we come to them. I think at this point in time, we will take a break for the next (lec), and cover the other things in the next lecture. It will be very nice if you can see the recommended video or the required video on Mendel and his work, we will see that, okay. And then, let us meet in the next lecture to take things forward. See you then.