Biochemistry
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Lecture - 16
Nucleic Acids - I

We start our discussion on Nucleic Acids and their components. Before we understand what nucleic acids are, so far we have studied all the other molecules basically for life. Molecules for life meaning the carbohydrates, the lipids that form the cell membranes and other component basically amino acids and proteins. Now when we go on to nucleic acids, we will see how important they are in their manifestation; in the formation of the proteins that we have studied so long. Okay.

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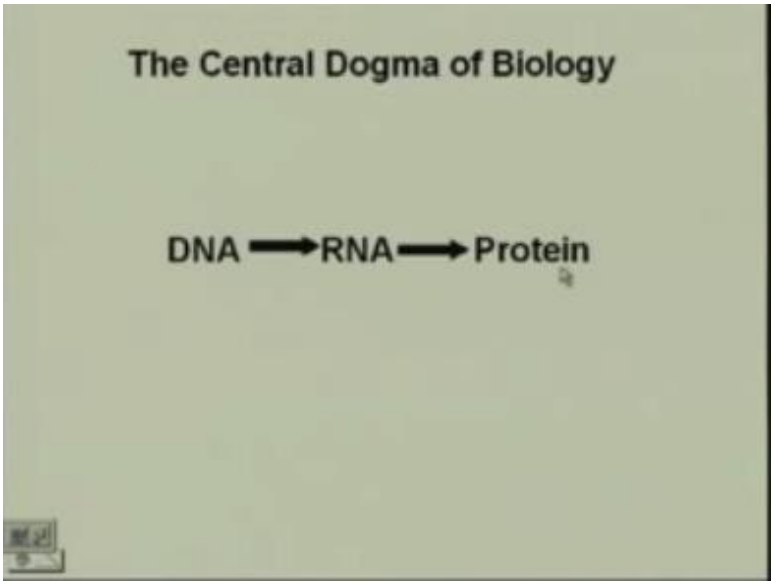

Now, when we look at the Central Dogma of Biology which goes as follows. It is DNA to RNA to Protein, this known as the central dogma of biology going from DNA to RNA the process known as transcription. RNA to Protein is a process known as translation. And, we know that all the information is stored in DNA that is our storage medium. It is then formed a rather transcripted to RNA forming the transmission medium that then forms the protein expressing a protein is what we mean by this protein formation.

That ultimately is required in all the activities that go on in the body in term of enzymes and so on and so forth. What we are going to do in nucleic acids is we have looked at some of the components, but we will see how the structures are related and how actually some of this processes are going through.

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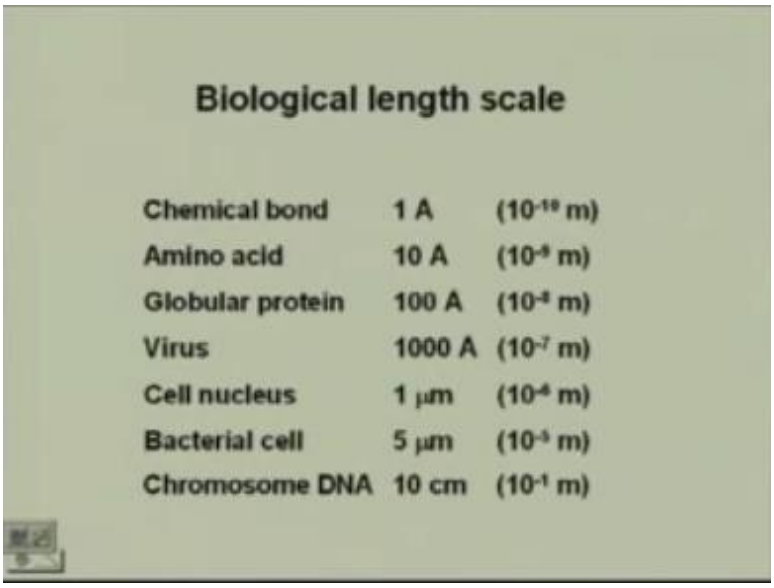

So if we look at just some idea of the biological length scale, we have looked at chemical bonds something that you looked at for a long time now. They are in the order of Angstroms. If we look at the Amino acids, they are in the order of 10s of Angstroms. When we look at proteins they are in the order of 100s of Angstroms, okay. And as we go higher and higher, you see how this length scale actually goes on and ends at DNA which is actually 10 centimeters, which is pretty long.

If you look at it from a protein point of view considering that you have a globular protein that is instilling the Angstrom (())(03:06) where you have it in the order of a 100 Angstroms. We have a chromosome DNA that is around 10 centimeters. Now, the fact that you have DNA replication, DNA processing going on extremely fast in the body, it is extremely important to understand how structurally it is placed in the body, how it is located and what holds the two as we will study later on the two strums of the double helix together. Okay.

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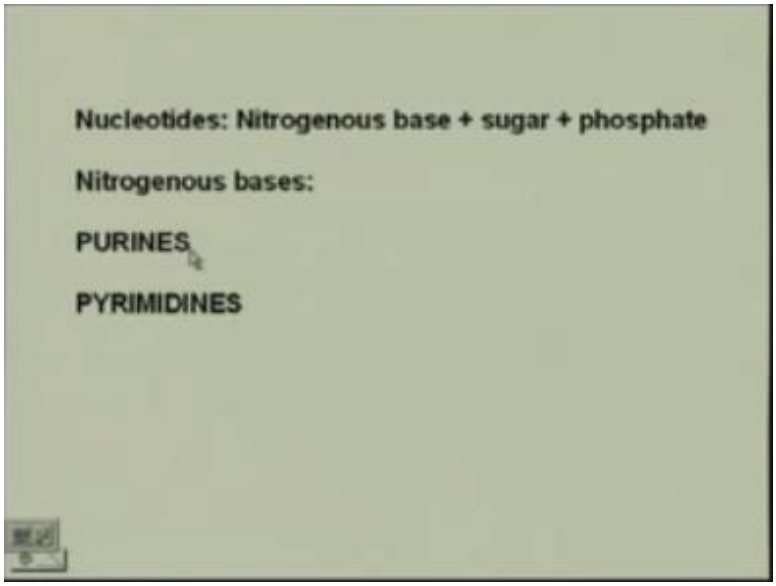

Now, this is something we have looked at before when we were doing vitamins and coenzymes. We consider what are called Nucleotides, DNA is deoxyribose nucleic acid and RNA is ribose nucleic acid. Now, the formation of these RNA, these nucleic acids DNA and RNA there are certain terminologies that we have to go through once more to understand their structure they are bonding.

In Nucleotides, we have what is called a Nitrogenous base, a sugar and a phosphate. You now know what a sugar is. You all know what a phosphate is, and we will just brief to what a nitrogenous base is. Now when we consider this nitrogenous base is there are two types of bases what we consider PURINES and PYRIMIDINES. This is something that we consider when we did vitamins and coenzymes, but just to revise what we had studied there.

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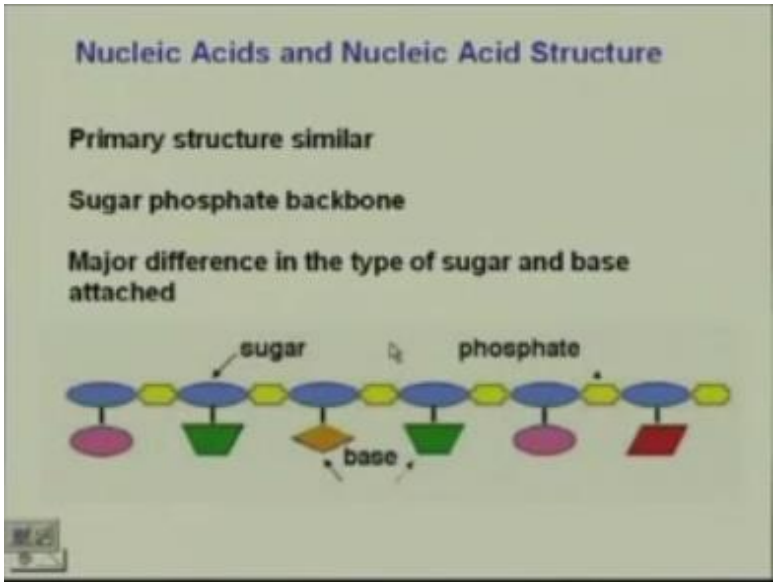

When we consider this these acids i.e. we have the sugar and phosphate which is actually called a Sugar phosphate backbone. Okay. Now, the primary structures of both DNA and RNA are similar. They have a Sugar phosphate backbone, the difference is in the type of sugar because one is a ribose and one is a deoxyribose sugar. Now the difference again also lies in the type of base that is attached to the Ribose or the deoxyribose ring, okay.

So what we have, is we have a phosphate that shown in yellow here, the sugar that is shown in blue and we have different kinds of bases depending on the nucleic acid that is attached to the sugar, okay. So what we have basically is a sugar phosphate backbone and we have the bases attached to the sugars in the backbone.

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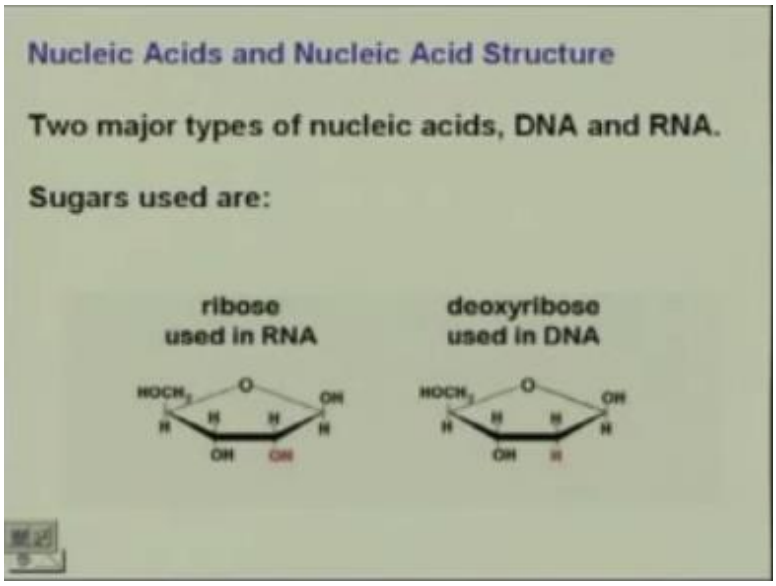

The sugars that are used in these two types of nucleic acids are ribose, ribose is used in RNA and the essential difference between ribose and deoxyribose is the missing OH at the two prime position of the sugar ring in DNA. Okay, so when we have this linkage, this five and will attach to a phosphate, this end will attach to a base and the bases will be different, the sugar is essentially different.

When we link these together as we will see, we will have RNA; if we link these together we will have DNA. Okay, there is a basic difference between the structure and this is also going to be reflected in the stability of RNA and DNA.

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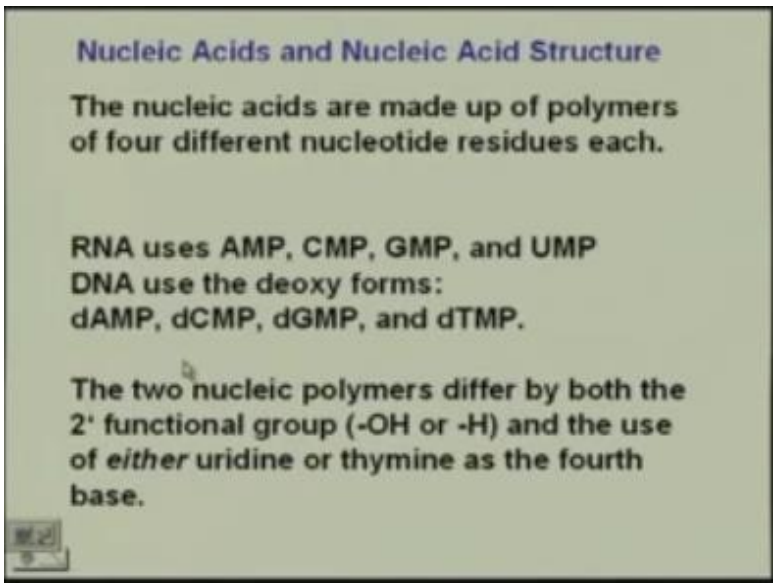

So we have the nucleic acids that are made up of polymers of four different nucleotide residues. We will see what these are in the moment. We have A, C, G, U that makes up the alphabet of RNA. And A, C, G, T that makes up the alphabet of DNA. And because the ribose sugar is in its deoxy form we have this small d, prefixed to the AMP, CMP, GMP and TMP. Okay. By default, if you write AMP it is a ribose sugar.

You have to specify, the deoxy type of the sugar by writing the small d which means that at the two prime functional group, you do not have the OH attached to it.

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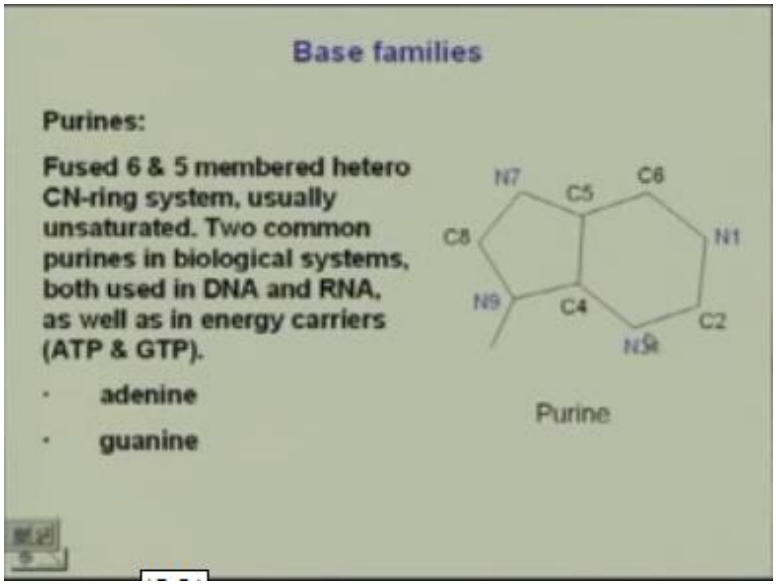

So what are these Base families? We have the nitrogenous bases, Purines. What are these purines? They are fused 6 and 5 membered rings, a hetero carbon-nitrogen ring system and the two commonly used ones in DNA and RNA are adenine and guanine. These are the purines.

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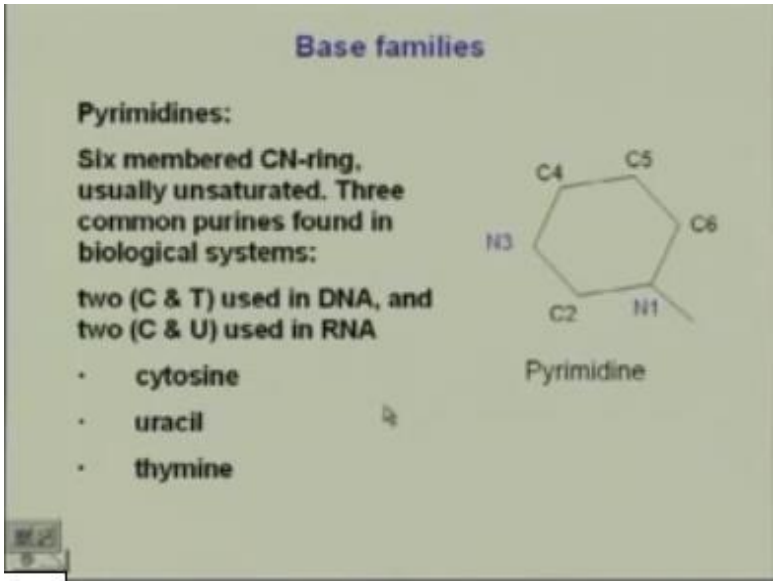

The Pyrimidines are six membered carbon-nitrogen rings that are usually unsaturated and there are three common purines that are found in biological systems, C & T are used in DNA that's cytosine and thymine, cytosine and uracil are used in RNA. Okay. So we have the purines and the pyrimidines that are going to form the nitrogenous bases of the nucleotide that are going to be attached to the sugars in the nucleotide structure to form our nucleic acids.

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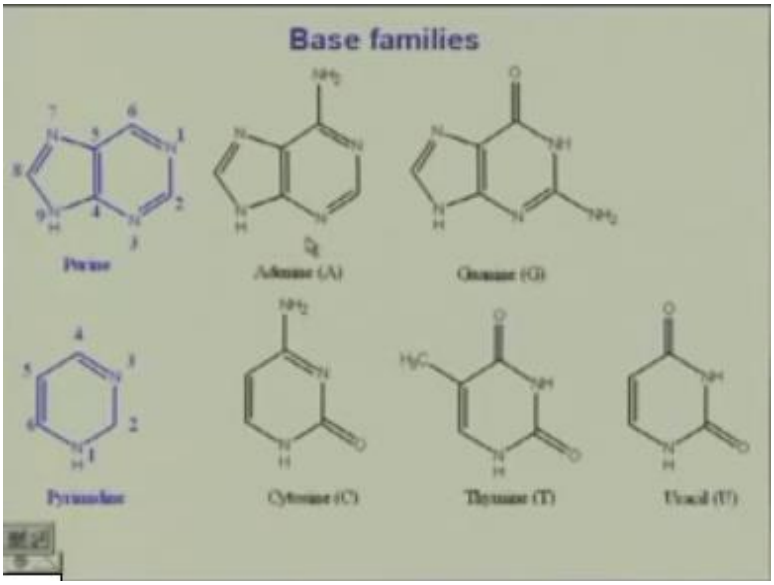

So these are our purines and pyrimidines. These are the definite structures, this is the numbering system that you have for purines, the numbering system that you have for pyrimidines. Okay and as we mentioned before that when we are looking at DNA, we have A, G, C and T. When we have RNA we have A, G, C and U instead of T. So these are our different base families.

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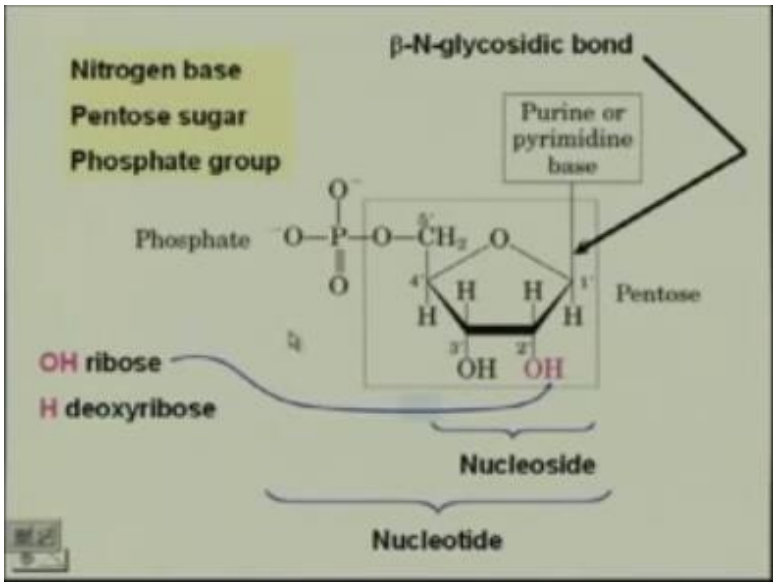

Now this is something that we looked at before, when we are forming the nucleotide, we have our sugar. The sugar in this case is a ribose sugar because the OH at the two prime positions is present. We have a Beta-N-glycosidic bond, we know why it is beta, we know why it is glycosidic and we know why it is N. Right. Why is it beta? Because, it is (()) (09:44) to the CH2OH. Why is it N? Because, it is linking with the N of the purine or the pyrimidine base.

Why is it glycosidic? Because you are linking a sugar, anytime you link a sugar it becomes a glycosidic linkage. Okay, so this is Beta-N-glycosidic linkage that is linking the sugar ring to the purine or the pyramidine base at the one prime position. At the two prime positions you have either OH or you have H being either a ribose sugar or a deoxyribose sugar. Then you have the phosphate attached to the five prime where you have either just one phosphate or you can have three phosphates as we looked at the structure of ATP.

So we have, when we the OH we have the ribose, when we have just the H we have the deoxyribose and we know how to designate these by writing either a small d or without the d where we want to specify a ribose sugar. So when we have just the base and attached to the sugar we have a nucleoside. As soon as the phosphate is attached to the five prime position we have a nucleotide, okay.

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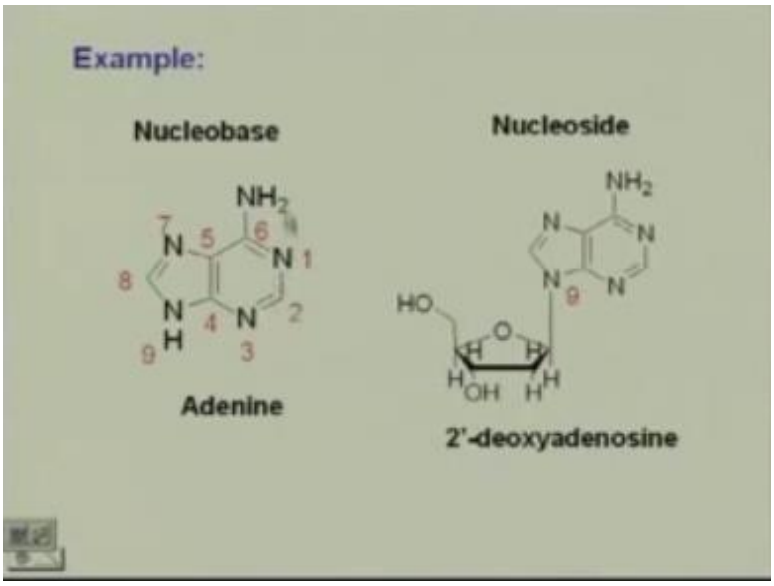

So we have our Nucleobase and Adenine. We have a Nucleoside which is the base attached to the sugar, the sugar in this case is 2'-deoxy which means there is just the H here, there is no O.

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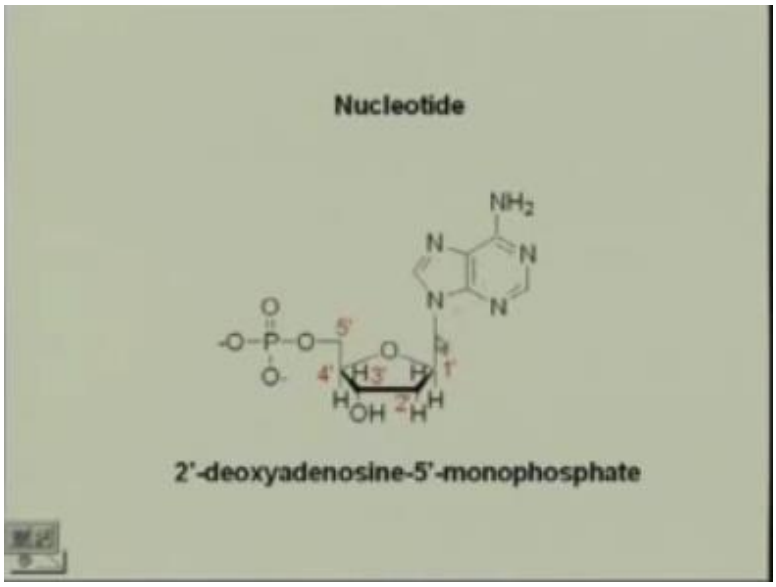

Then, we have our Nucleotide which is 2'-deoxyadenosin-5'-monophosphate. But I could have just written this as dAMP, okay. Just writing it is dAMP you know, that this is structure. Okay. The d signifying no OH here, the A is signifying this and the NP signifying the monophosphate. Okay, so each of this. So the dAMP you know, exactly how you have to write it. Even for the dCMP or the dAMP, ATP whatever, you know how to write it. Okay.

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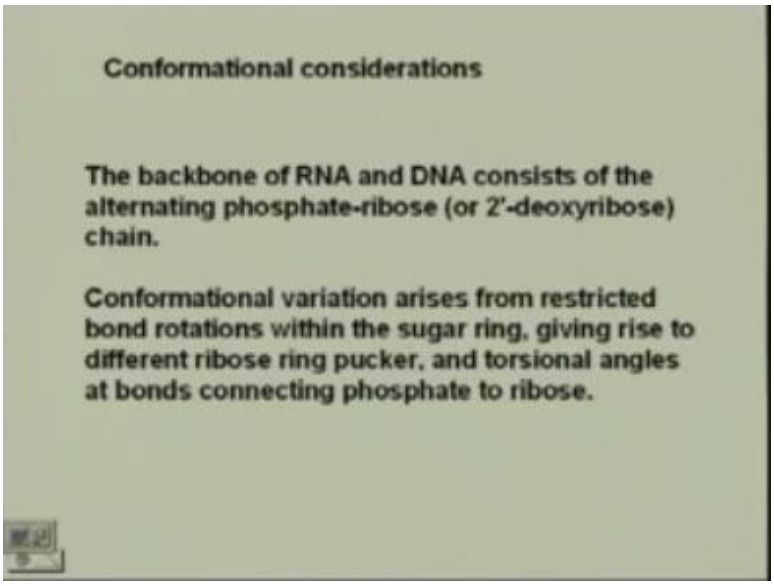

Now, considering that we have the sugar and the phosphate attached to one another and we have these bases basically sticking out. Okay, that is what I showed you in the first picture. So it means that we have to look at some conformational consideration? Conformation consideration, in term of the backbone, just like we had in the protein. What did you had in the protein? You had certain five Psi angles that mentioned how the backbone would be oriented and we had, what did we have sticking out from the backbone, the side chains.

The different R groups was sticking out from the amino acid C alpha groups of the backbone and we had different orientations possible. We can have that same here. Okay. What is that? So this backbone of RNA and DNA consists of the alternating phosphate-ribose or deoxyribose – 2'-deoxyribose chain. You understand that now. Okay, so we have alternating phosphate, and ribose.

You will see how that is formed once we understand the torsional angles. Now we have conformational variation this arises from you understand restricted bond rotations. Okay. Now where are we going to restricted bond rotations? We have a sugar ring. Okay. We have single ring, what do we have? We have something like this.

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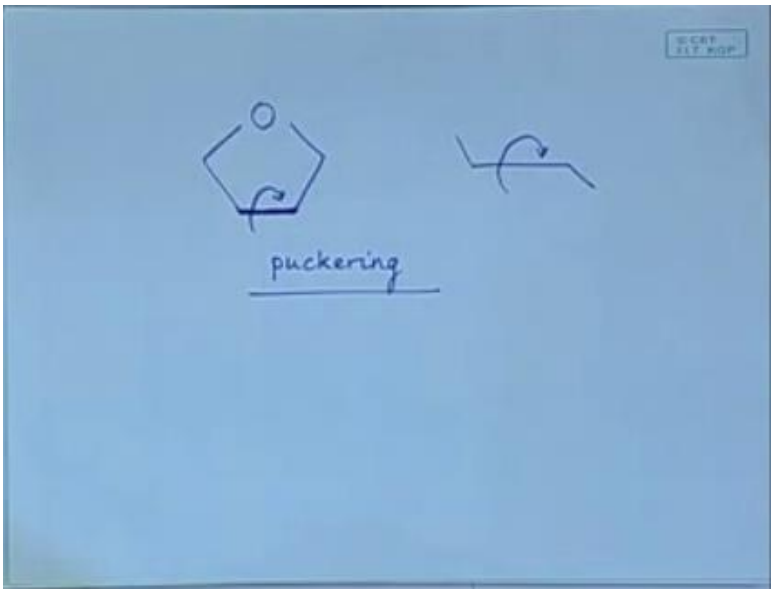

This is our sugar ring. Now you have to remember all of these are single bonds. So what is possible? Puckering is possible. We do not call this rotation because it is restricted in it rotation. If you have just a single bond, we know that we can rotate all the way through. But when we have something like this you cannot have this go all the way through because it is going to twist the molecule. This twisting is what is known as puckering.

So what kind of observations can we have? We can have the oxygen go up, go down with respect to this bond here, right. So what we can have is we can have restricted bond rotations within the sugar ring because we have a ring system, where they are not free to rotate all through. This gives rise to different ribose ring pucker, okay. And, torsional angles at bonds that connect the phosphate to the ribose. Now, let's see what we mean by that.

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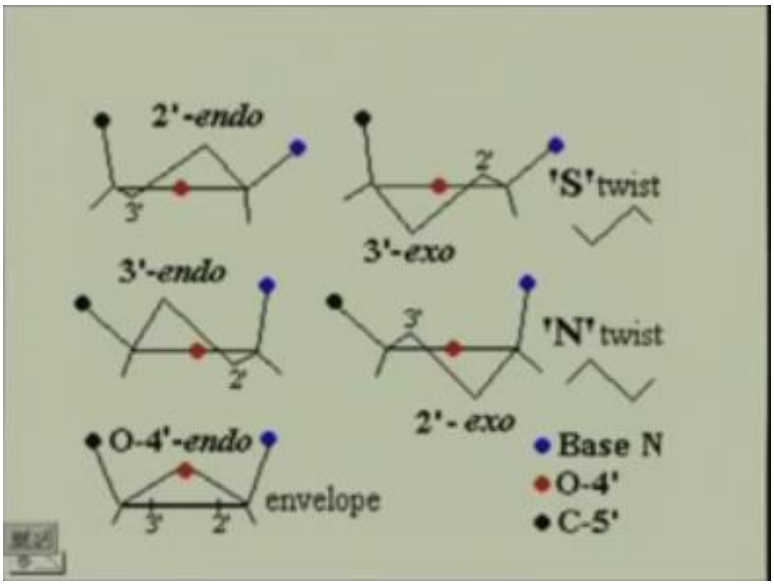

This is what we mean. We have here; just look at one of these figures first. This red sphere is the oxygen of the sugar ring, okay. We have a 5 membered sugar ring. So if you just look at the different, so this is 1, 2, 3, 4 and 5 these are the five atoms that we have connected to form the 5 membered rings. This is the 5 prime carbon-atom that is usually attached to the phosphate. Okay. See, this is what we looking at.

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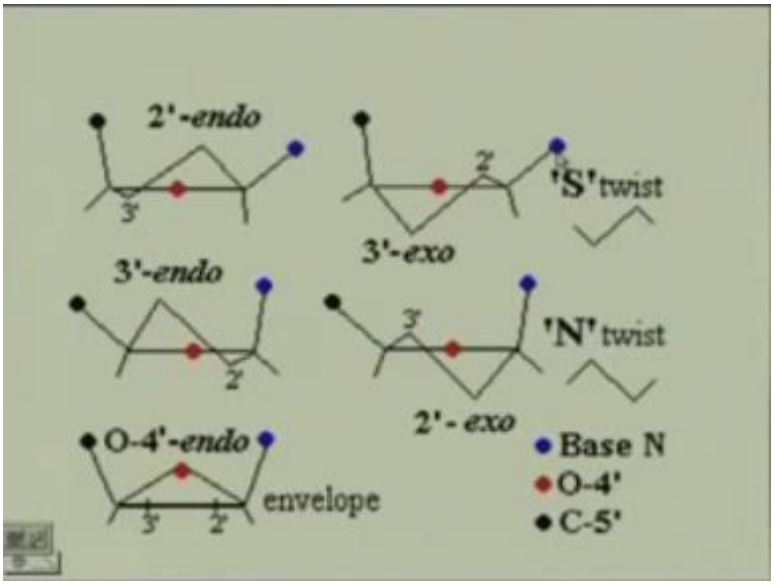

You have something like this, this is attached to the phosphate and where is this attached? This is attached to the base, right? So-- and this is our two prime, this is our three prime. This is our two prime and this is our three prime position, fine. This is our one prime, this is our four prime and

this is our five prime. So now when we go back to this, we recognize; what is happening here? We have 1what is this attached to? The base.

So the blue circle represents the base nitrogen that is attached to. We remember that this is a N-glycosidin bond, so the sugar is attached to the base by the nitrogen, it is beta because these are cis to one another, fine. So we have the phosphate or rather let's look at the five prime carbon for now. So we have basically the five prime carbon here which is essentially attached to the phosphate and we have the base.

Now we are looking at what can happen to the sugar ring. The sugar ring can bend in such a way that we can have something that is called 2* -endo, 3*-endo, and O-4*-endo. Now if you look at each of these structures you will see that the bond or rather the atom that is forming the endo conformation is getting close or rather in the same direction as the phosphate and the base. When you have the 2*- end pucker up to be cis to the phosphate and the nitrogen you have a 2*-endo.

If the 3* sticks up to a -- in the same direction as the base and the phosphate you have a 3*-endo. If the oxygen sticks up in the same direction you have an O-4*-endo. Is that clear? Okay, so the endo configuration is when you have some carbon atom or the oxygen atom, push to a position or pucker to a position that is in the same direction as the base attachment and the phosphate attachment.

Okay, only if these are in the same position would you have what is called, an endo conformation. So you would have the opposite you have an exo. You can have a 3*-exo which would mean that the 3* carbon is away from the phosphate and the nitrogen. The 2*-exo means that you would have the 2* carbon away from the phosphate and the base, okay. So now if you look at just the way, if you trace the numbers here or we just trace the carbon here.

If we go down this way, then up this way and down this way, you are basically tracing a letter S, this way. Okay, so you are going down this way because you are say 3*-endo then you are going up at 3* and coming down again, okay. So what you are looking at is you are looking at what is called an 'S' twist. The twist is such that you can just imagine twisting the wire. If you just

connect wires where you have one as an oxygen then you connect these wire you just twisting in such a way that you have at ‘S’ twist.

You can twist it in the opposite direction that is going to give you what is called an ‘N’ twist, okay. So if you just trace the atoms here, we will have, in this case when we have 3*-endo and we follow the direction from this carbon up we have this, this and this. What is it tracing? Something like, the letter ‘N’. If you go in this way, the 2*-exo, we would have this up, down again, up again.

Tracing something that looks like a letter ‘N’, so this is way there is two names given to this called the ‘S’ twist and the ‘N’ twist, okay. So this is how we represent the sugars in the -- now this is important because not if you look at the orientation of the phosphate and the nitrogen there is a slight change in how the bases are connected, okay. Now, how is we – we are going to see, how this is going to help later on in the overall structure, okay.

Because, basically we are going to have a polymerization, a polymer formation. Now based on the orientations of the sugar rings and their conformational considerations you can position the base. Now the reason why we need to position the base is to form favorable interactions. Okay.

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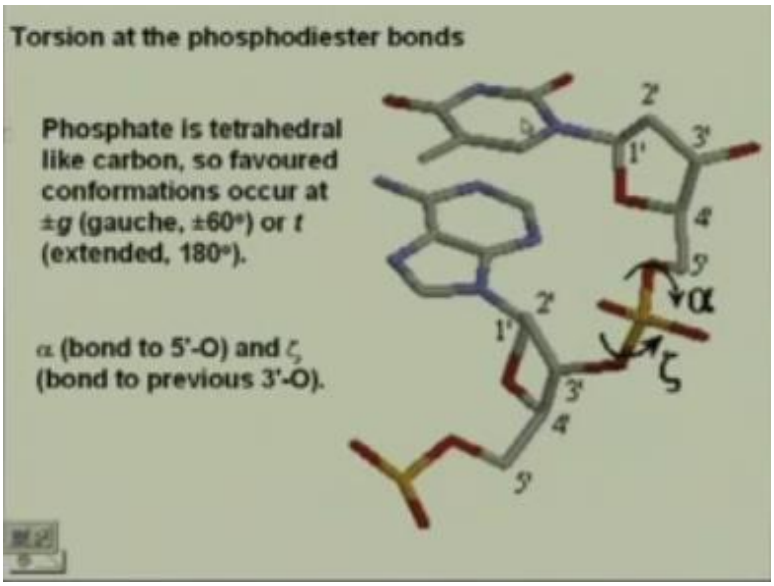

So this is what we have. We have now here, a dinucleotide. Why do I call this a dinucleotide? Because, I have two nucleotides. You recognize here, that you have this red we know is the oxygen of the sugar. This is the nitrogen of the base. This is the other sugar. And what do we have here, we have this again this is the 5* that is linked to the phosphate, this is the phosphate. Okay, try and recognize this.

So we have a 2*. Does the 2* have the oxygen? Does it have the oxygen? It does not have the oxygen. So what is this? It is a deoxyribose, okay. Now we are just going to look at this (()) (22:16) configuration because now we know that when we have the single unit, okay. Let's consider a single unit. When we have – so this is one unit here, okay the top is one unit and this is another unit, right.

We have linked these two units together; we will see how they link together later on. But, we have to first understand how actually the conformational considerations are going to play an important role. Now what we have learned from the previous slide is we can have puckering in this sugar ring, right and also in this sugar ring. Now due to the puckering what is going to happen?

The positions of these phosphates and the positions of the base are going to change, right. The positions of – because see this is the overall backbone, if this is the overall backbone we can have positional changes due to the ring puckering. We can also have positional changes due rotations about this bond and this bond. Remembered the five Psi angles of proteins? Okay.

Now if we just consider that we have the sugar, the phosphate, the sugar, the phosphate. We have here single bonds. What do single bonds allow? They allow free rotation, okay. And because of this rotation we can have again changes in the position of the bases and the position of the phosphate. What happens if I rotate above this Psi angle? The base is going to come up all the way on the other side, right.

So, what is going to happen if I rotate above this? This based on shift, right. So we have an alpha rotation and we have a Psi rotation (()) (24:38) rotation rather, okay. So we have to -- now the reason why we are looking at this is if you look at the previous slide what happen here?

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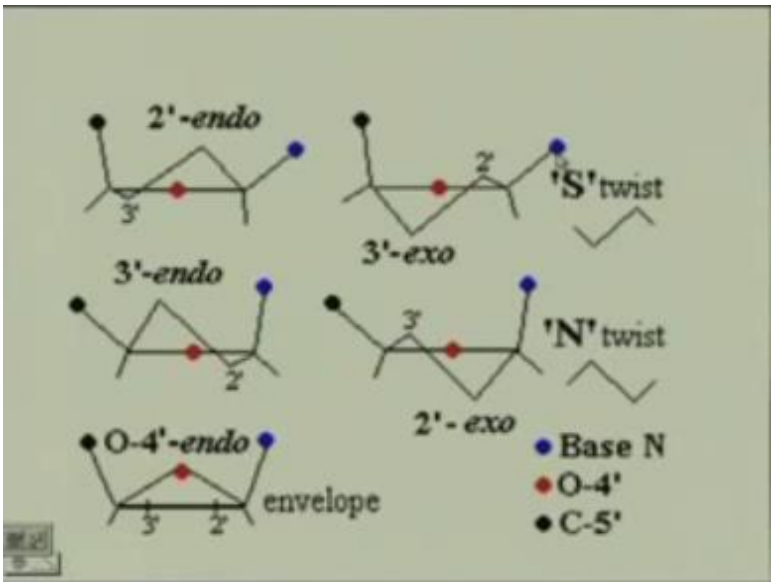

Is you had changes in the orientation of the bases why because of the puckering due to the sugar. What is that doing? That is changing the position or the orientation of the base and also the phosphate.

But, you can also have rotations above these two angles. What is that going to lead to? That is also going to lead to change in the position of the bases. The changing in the positioning of the bases is going to help in the bond formation that we are going to see later on.

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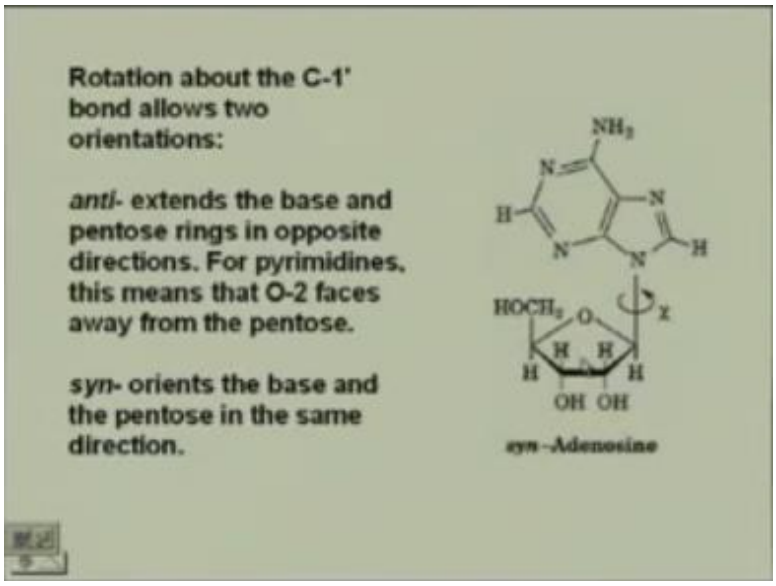

Okay, now we have to look at in another Psi angle, this is the Psi angle. Now what we are looking at here is, what is this? Is this a nucleoside or a nucleotide? It is a nucleoside, why because it does not have the phosphate attached to it. It has the base attached to the sugar. Now you have to remember again we have a single bond here, so what is possible? Rotation above the bond is possible, okay.

This is a syn orientation, okay. Because, we have – in the purine case we have 6 membered and the 5 membered rings fused to one another, right. And when you have a syn orientation you have the base and the pentose that's the part of the sugar on a same side.

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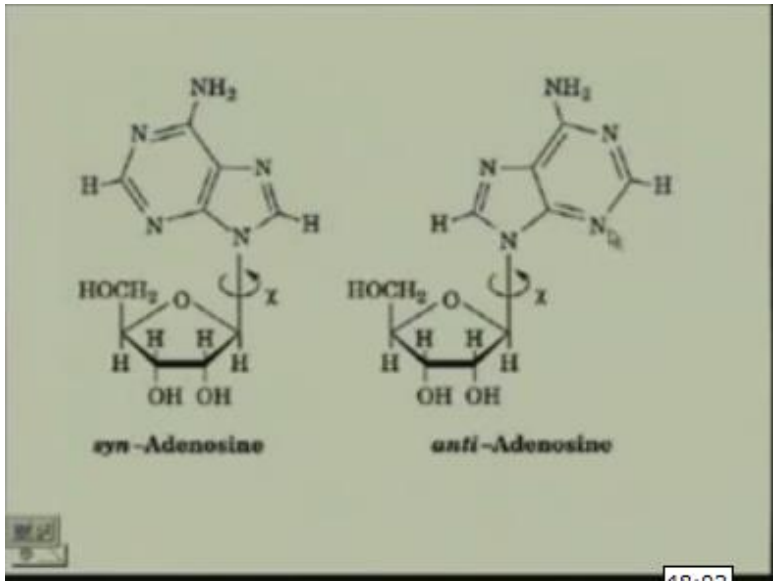

It is anti when it goes on the other side. Okay. Now this rotation is also possible. So you, what we getting at; is we getting, since we have to study nucleic acids structure and it is components we are looking at all the different structural aspect possible. And these structural aspects are possible because you have the single bonds. These singles bonds are now rotation. And the sugar ring allows puckering, okay. So, all these put together you are going to get this into a very, very flexible structure.

But the structure in a sense is not that flexible as we will see later on, okay. So what we have is we can have syn-Adenosine or we can have anti-Adenosine, where we have the sugar ring and the base away from the pentose sugar.

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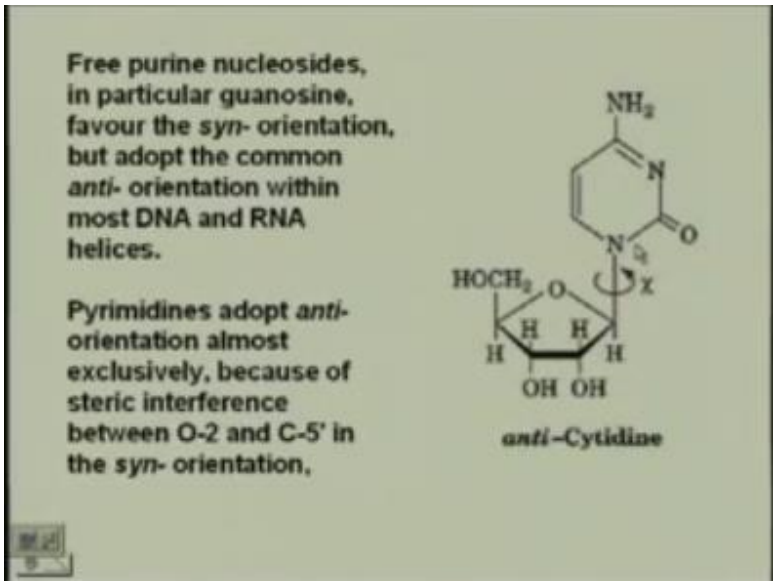

When we the purine nucleosides, we have an anti-configuration when this oxygen is away from this part we can have the syn orientation when there is rotation above this and this oxygen comes above this part, okay. So usually the pyrimidines adopt this anti configuration because we obviously going to result in some steric clash if this oxygen comes here and then again we have the phosphate attached to this in so on and so forth.

Okay. So we rather have an anti-orientation. But this -- since this allows rotation it may be possible that in some cases you might have a syn orientation also.

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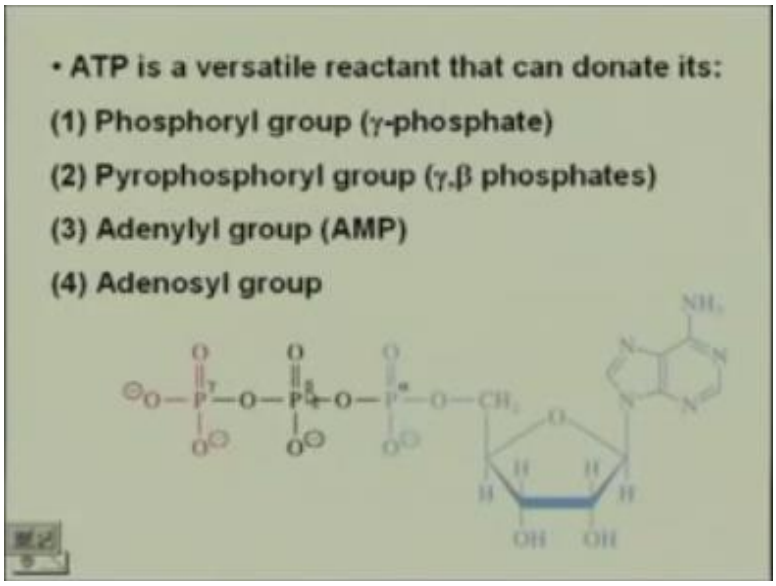

Okay. Now, before we get into how these are formed we need to look at the structure of ATP ones more. Okay, what we, we looked at -- what is this now? As soon as we attach this phosphate is becomes a nucleotide, okay. So now that we have the nucleotide, we have an alpha position, a beta position and a gamma position, okay. This is the alpha phosphate that forms AMP. When we have the phosphorylation here also it is ADP, right.

Then when we have at the gamma position as well it is ATP. So we have AMP, ADP and ATP. Okay now we are going to see how we can actually form these.

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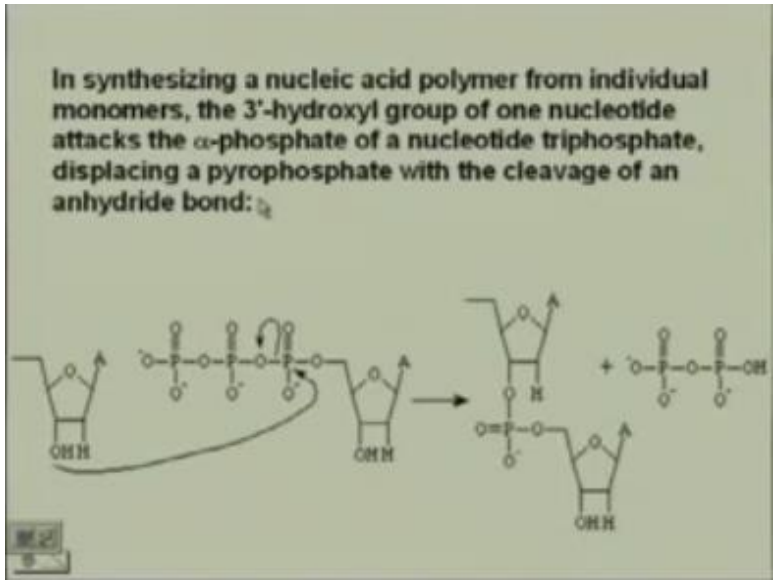

Now, we are synthesizing a nucleic acid polymer, okay. Essentially, what we have is we have something like this.

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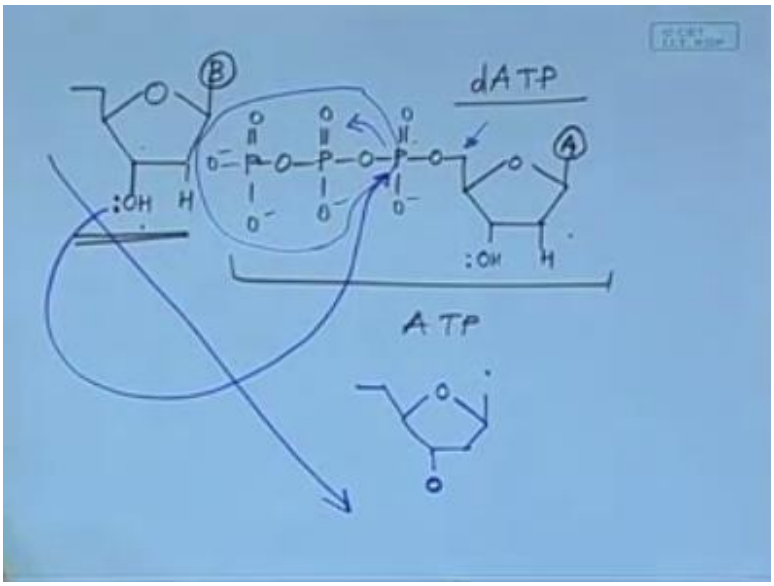

We have -- this is our sugar. What do we have attached to this position? A base. What do we have? We have something else attached here. If we have the phosphate, then we have the nucleotide. We have the OH here, and we have this here. So what was this, deoxy. Now we have ATP. ATP means I have O here, I have what – what do I have here, I have A basically here, OH here, this is then what? dATP, right? Then I have O-P-O-P, so what do I have? I have dATP.

O, O-, O-. So I have one part here and ATP here. What is happening now is this one pair, attack this phosphate, okay. So what we have is this lone pair attacking this phosphate. What are I am going to form them? What is going to happen? I am going to have – what are I am going to have here? If we had this A here, this oxygen is now link to this phosphate, right. This oxygen is now linked here and we have this part released.

So what that I essentially we done? I have linked this with this, right. Where have I linked it? At this position. What is this position? The 5* position, the 3 is going to the 5. Now what can this now do? This has now it is 3* position open. So what can it do? It can now attack another one with another base here within our GTP. So what am I going to have here then? My base is going to be different, right.

So I am actually linking or polymerizing into forming a linear chain of the sugar phosphate backbone. You recognize why this is now a sugar phosphate backbone? Let's get back to slides here.

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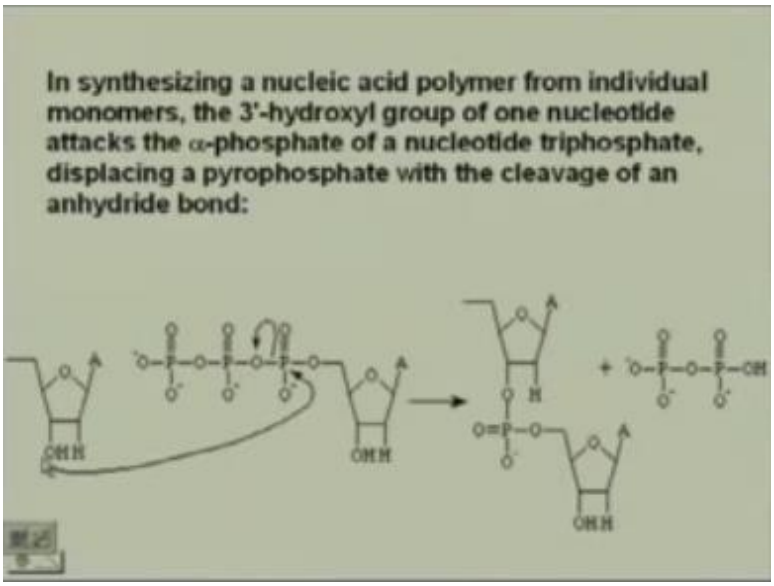

And what we looking at is we have the three prime hydroxyl group here, what is it do? Attacks this phosphate of the tri-phosphate released in the pyrophosphate with the cleavage of an anhydride bond and what do you have? What is this? It is a dinucleotide now. Now this three prime OH can do what? It can go and attack another triphosphate that has another base attached to it, and it is going to then form a linear chain of the nucleic acid polymer, okay.

So what do we have? We have a sugar, a phosphate. A sugar if we have another linkage another phosphate and so on and so forth.

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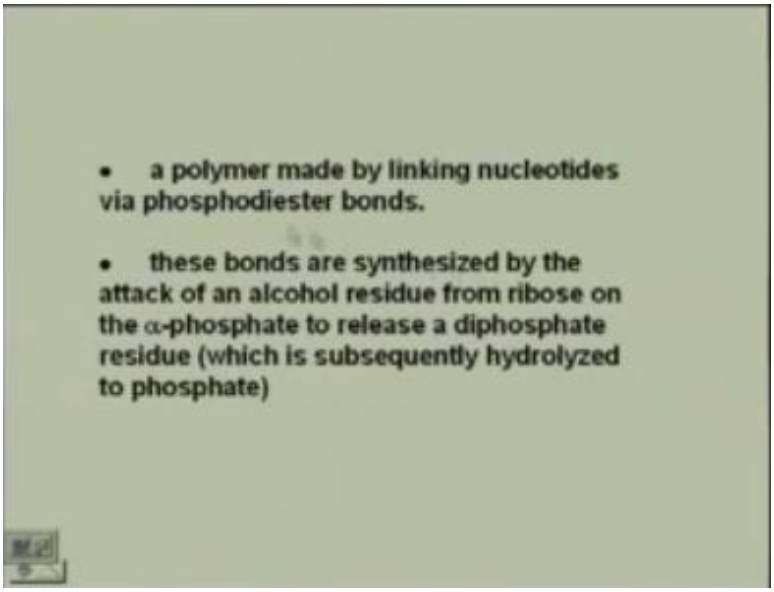

So we have the polymer made that by linking nucleotides via phosphodiester bonds. And how these formed, they are synthesized by the attack of the alcohol residue from the ribose on the alpha phosphate to release a diphosphate residue, what is the diphosphate we are talking about?

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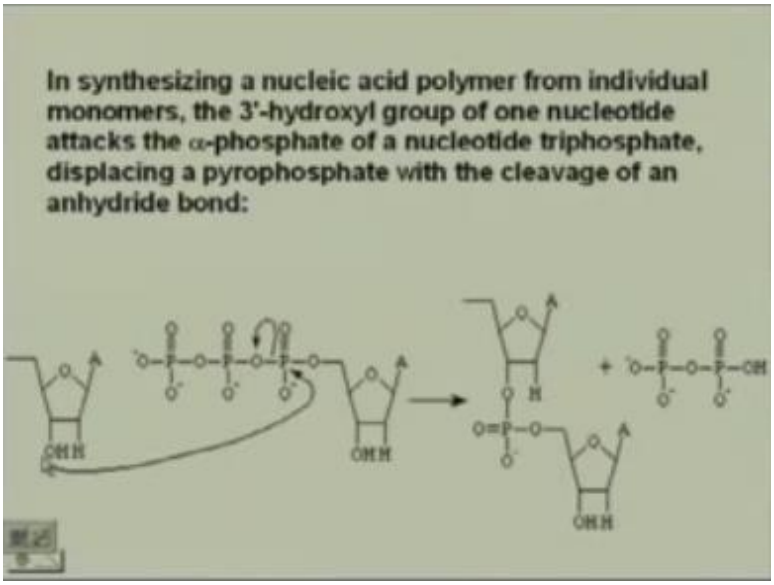

The pyrophosphate that comes off after this attack takes place, right. Then what do we have.

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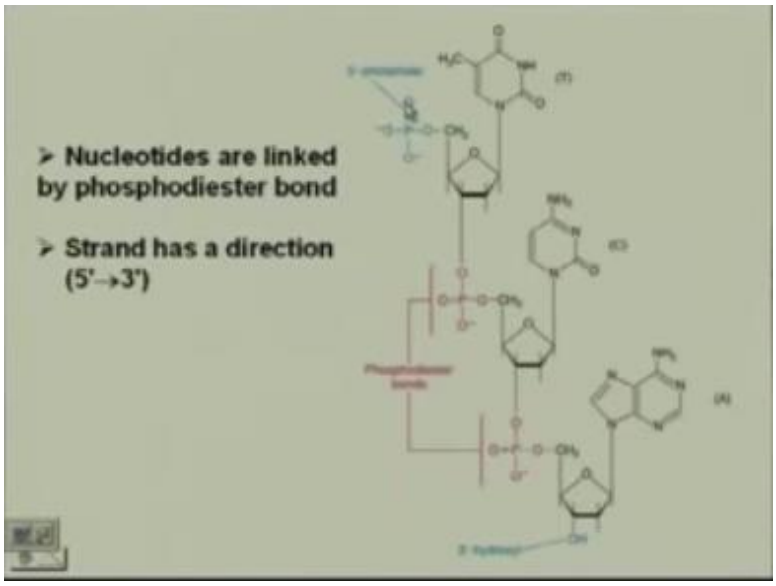

So we have this linkage. So what are we looking at? We are looking at a five prime phosphate. It was this OH that attack to what? CTP, right. It attack CTP and you linked T and C together. Is that clear? What you are essentially doing is you have a 5* phosphate here. You have the base attached by this glycosidin linkage to the sugar. Now what is happening, this OH is free to attack the triphosphate.

What happens? You then have the formation of a dinucleotide. But this OH is again free. What can that do? It can go and attack another phosphate. In this case, it now has attack ATP. This is Adenine. So it has attacked ATP so we have now a trinucleotide which has the sequence T-C-A. So just like we did in proteins, what do we need to know? We just need to know the bases what are attached.

Because – and we just need to know the type of sugar, that's all the information you need. So if just right now if you looked -- I am sure you have seen books or just the DNA sequence. When you look at the DNA sequence, what do you see? Just A-C-T-G, and so on and so forth. But what is that means? It means that the structure is like this. Because you have that specific sugar, you have it linked by phosphodiester bonds in the sugar phosphate backbone; the difference lies in the types of bases that are attached to the sugar. Just like in a protein.

Do we write the peptide bonds? We do not. We just write V-A-G-T whatever, what does that mean? We have valine, alanine, glycine and threonine**.** But we know that they all linked by peptide bonds, the same things here. We have the sugar phosphate all the information I need to know is just what are the bases. That's all the information I need, because I know that and I need to know whether it is deoxyribose or ribose.

And the strand has the direction hat is referring to as 5* to 3*. This 3* then attach to another one and so on and so forth. And you can have the increasing length of the nucleic acid, okay based on this.

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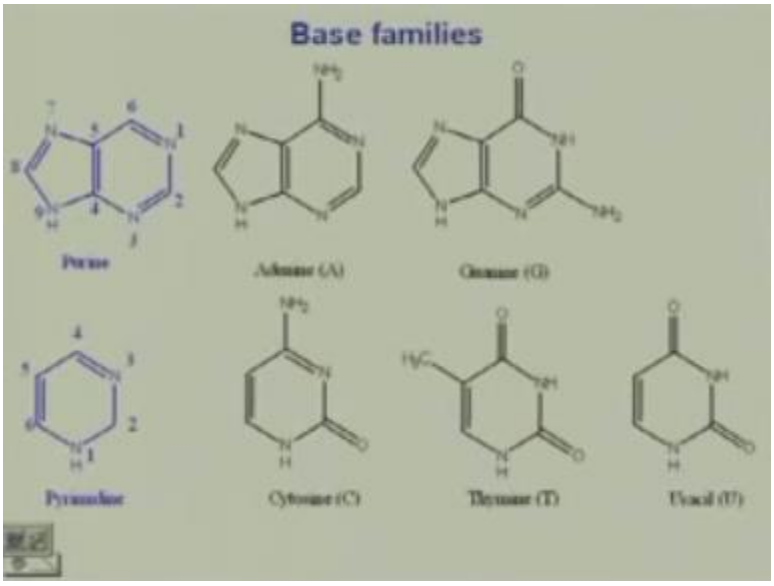

So if we look at these Base families all the information you need to know is what is attached to what. So if I say A-G-C-T, you know what it means. I say I have a linear polymer that is A-T-G-C. What do we know by that? First of all, you know it is DNA. Why do you know it is DNA? Because I have included T instead of U. So you know what sugar you have to draw, you know what bases you have to draw and you know that they are linked by the phosphate backbone.

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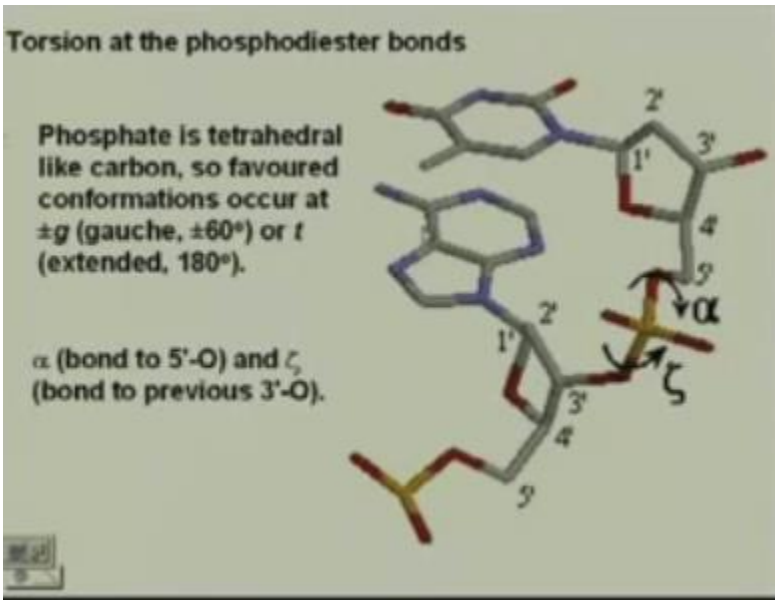

Okay so now when -- let me just go back to one structural aspect. So now know what this looks like, right? So now you understand that you have the phosphodiester linkage. So with the phosphodiester linkage what can happen apart from the sugar puckering which is going to change the orientation of the base, we can also have rotation above this because that is also going to change the directionality of the bases. Okay. Now how does that help?

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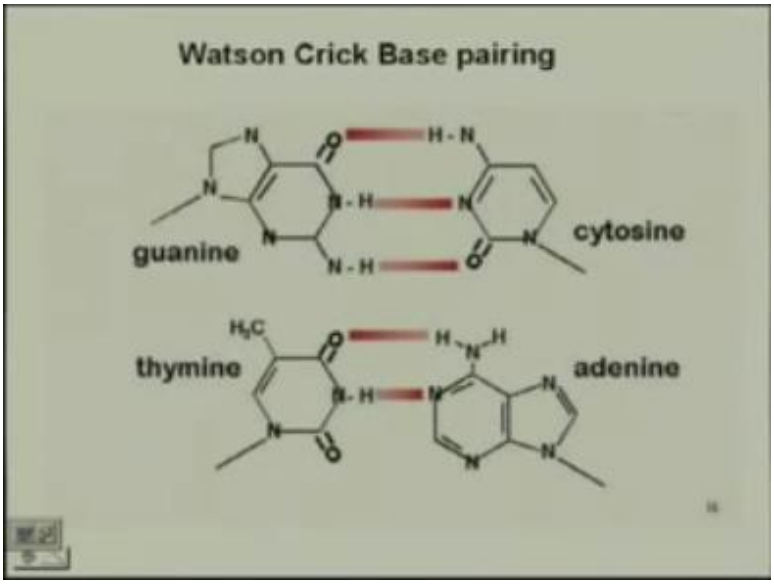

Or what can that do? So once we have these bases we can have base pairing. What is base pairing? Base pairing is when we have say -- now know that we have the sugar phosphate backbone.

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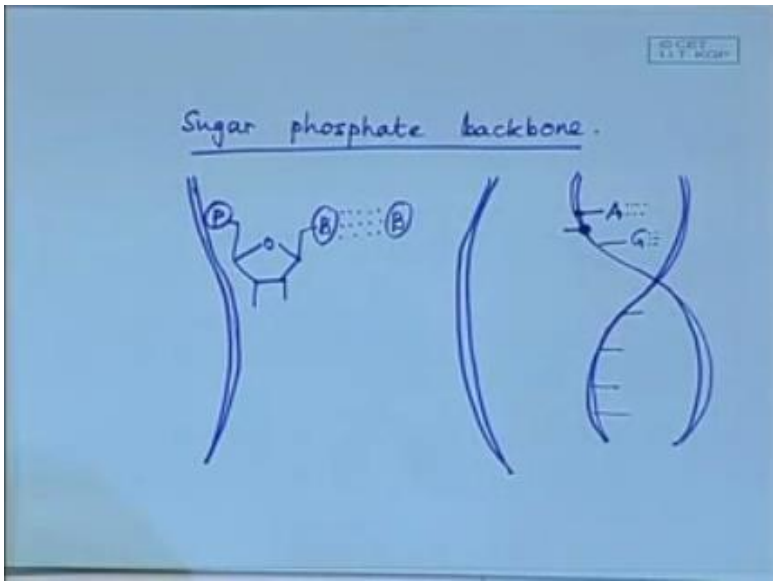

Sugar Phosphate backbone. What is that sugar phosphate backbone mean? It means you have this and you have your P, right. And you have your base attached here. Again what you are going to have is you are going to have one strand here and another strand here. Okay we are going to look at how this happens later on. In this pairing what you have, is you have specific hydrogen bond interactions between bases.

Between the two strands, so what is this is strand made of, this is just the sugar phosphate backbone, right. This is the sugar phosphate backbone and we have basically the bases sticking on, so when, you see when DNA is actually drawn is just drawn with A, G and so on and so forth. Where is this coming from? This is linked to the sugar that forms part of the sugar phosphate backbone.

So what do we have here? In between we have the phosphodiester linkages. Here we have the sugar the base attached to the sugar. So this is a strand of DNA. This is another strand of DNA. And what do we have? We have linkages between the bases. These linkages and this pairing is extremely important in the structure of DNA.

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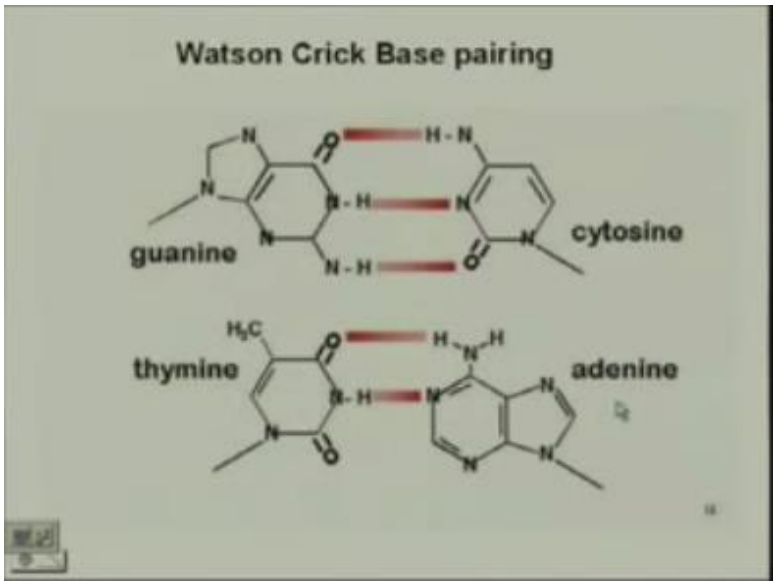

We have here what is called 'Watson Crick Base Pairing'. Now if you notice, you have here guanine and cytosine. What is guanine? Guanine is a purine. Cytosine is a pyrimidine, right. So you have a link between a purine and a pyrimidine. If we look at the other base pairing, we have adenine. What is adenine? It is a purine. What is thymine? It is a pyrimidine. So we have purine, pyrimidine pairing.

Now in the pairing you will notice which is extremely important for the structure of DNA, we have hydrogen bond formation. These red- thick red lines are actually representations of hydrogen bonds. Now what are we talking about here? We are talking about an oxygen, hydrogen, nitrogen. Here is one hydrogen bond, here we have another hydrogen, here we have another hydrogen bond. So we have three hydrogen bonds in the pairing of G and C. We have two hydrogen bonds in the pairing of T and A, okay.

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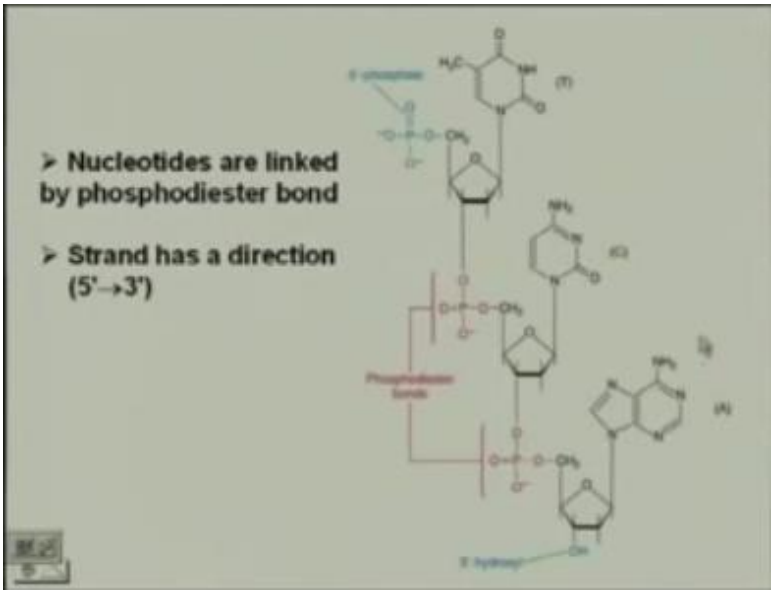

So now if we look at the structure, what is going to happen? When we have T at this position, we are going to have a linking of the T with an A of the other strand, right. If you are looking at this C here, we are going to have this link with a G of the other strand. If we have A on this strand it is going to link with the T on the other strand.

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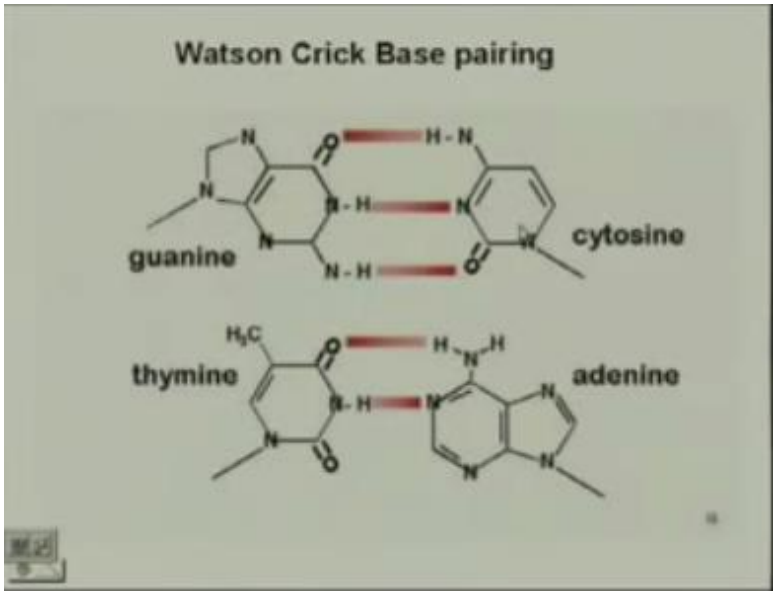

Now, if you look very carefully the pairing as I mentioned is between a purine and a pyrimidine, a purine and a pyrimidine. So there is one member of the pair that has a fused 6 & 5 membered ring part of a purine family and we have just this 6 CN ring that is part of the pyrimidine family.

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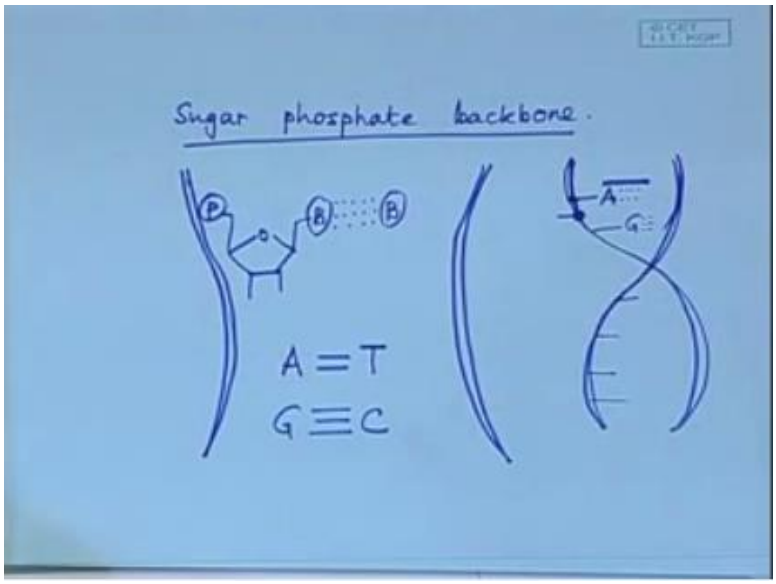

Now this is extremely important that if you look at the, the distance between these two, okay. So we have a – so what kind of pairing are we going to have? We can A = T, that is represented like that. Or we can G, C. What is that mean? It means you have two hydrogen bonds here and here you have three hydrogen bonds, okay. And we have purine and pyrimidine base pairing.

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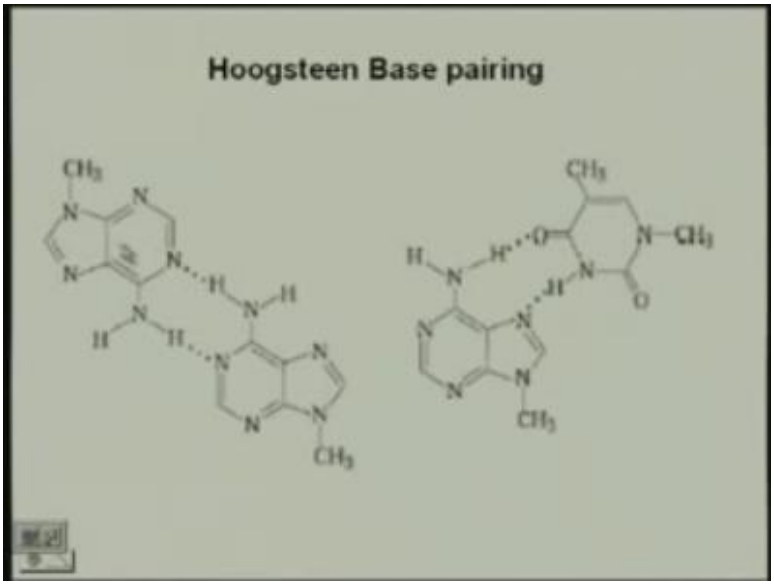

We have another type of base pairing. The one that I mentioned before is 'Watson Crick Base' pairing. There is another type of base pairing that is called 'Hoogsteen Base' pairing. Now what do you notice here? What is this?

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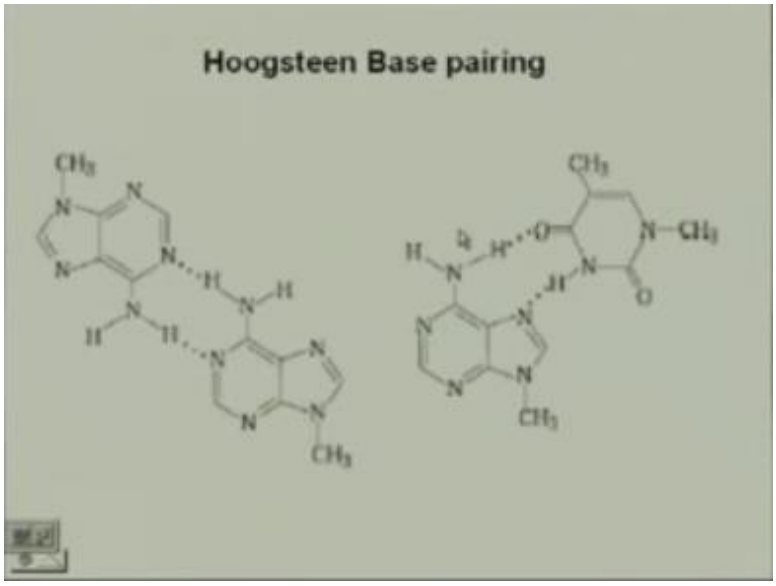

What is that? This is a purine or a pyrimidine? Purine. What is this? It is also a purine, okay. So in this case, you not only have purine-pyrimidine base pairing, you can have purine-purine base pairing also. But we will see how this is not seen in double stranded DNA. Okay, because double stranded DNA you recognize if it has to form a uniform distance between the helices you have to have a purine-pyramindine fit in every case. Okay.

So when we have the two strands of the DNA coming together, so we have one strand this way and one strand this way and the length between has to be the same. So we have one purine that's a 6 & 5 membered ring fuse together. You have one pyrimidine that's 6 membered, okay. So both of them coming together gives the exact distance that is the distance between the strands. But in the 'Hoogsteen Base' pairing what you can have, you can have the base pairing between the purines.

You also have purine-pyrimidine base pairing. But since this is also possible you do not see this in double stranded DNA, but there are some cases where this is observed, okay.

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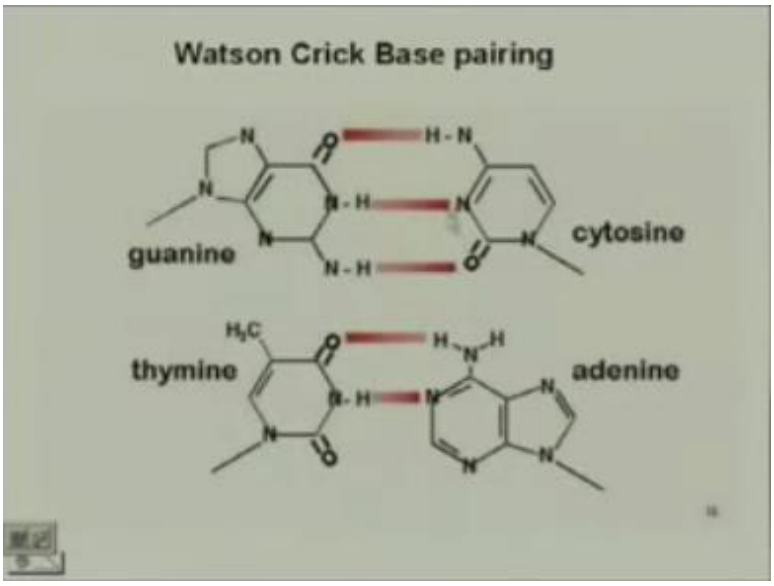

But, so far what we need to know, is the basic pairing between the purines and the pyrimidines that form the bases of double stranded DNA where we have three hydrogen bonds between G and C and two hydrogen bonds between A and T.

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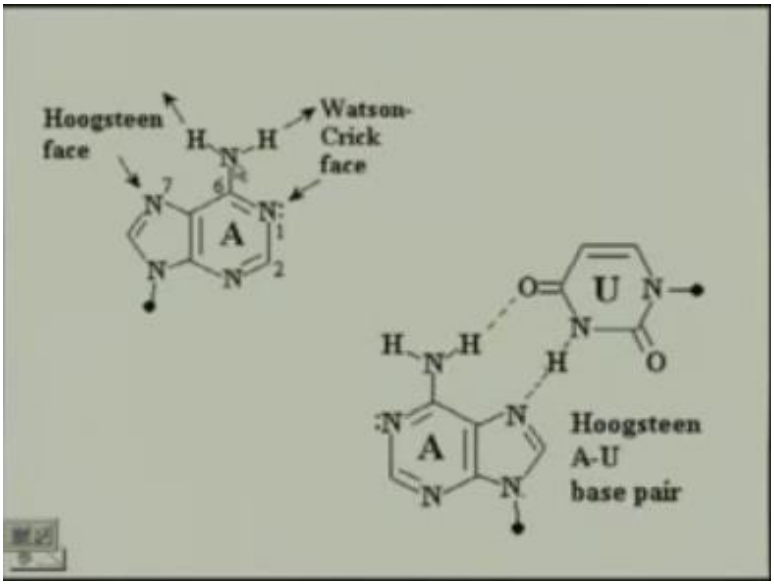

Okay so we look at basically adenine here, we have this face which forms – how many hydrogen bonds do we have in adenine? 2, A-T in the Watson Crick face. Here also in the Hoogsteen face, that is part of the 5 membered ring, and the NH of the NH2,

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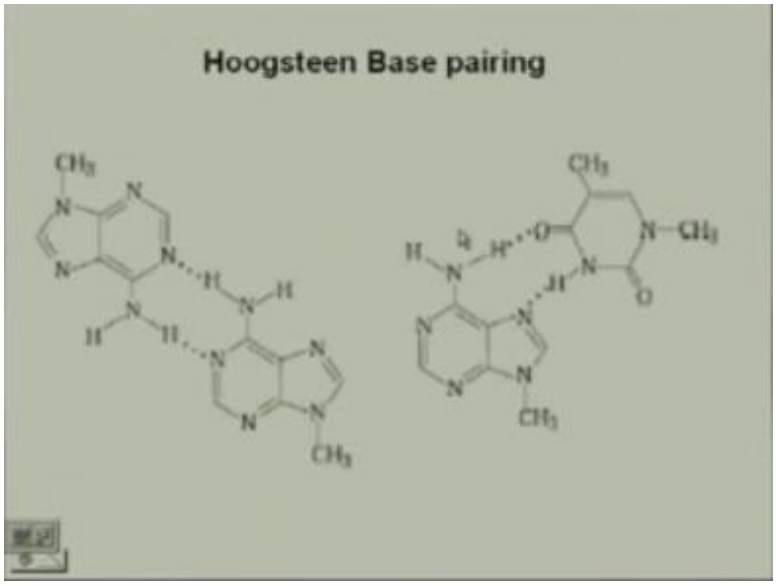

Okay. So if we go back, if you look at where this is formed, you see this is a Hoogsteen pairing, this is between what? This is between the 6 membered ring here and the 6 membered ring here. And in this case when we look at the A – this is between what 2 A's or 2 purines. When we look at a normal Hoogsteen base pairing, the difference between the Watson Crick pairing is.

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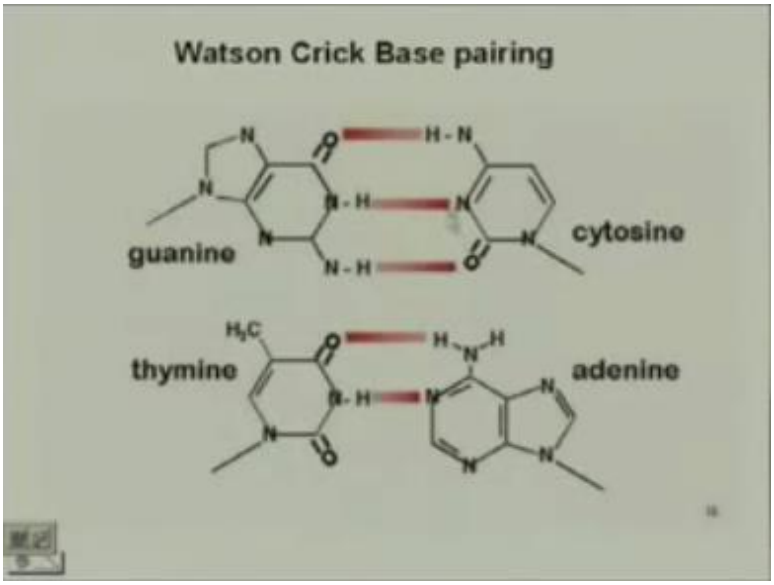

Let's look at the Watson Crick pairing, we have, where is the hydrogen bonding? It is all from the 6-membered ring, right. In the Watson Crick base pairing the base pairing that adenine forms with thymine is from the 6-membered ring. But you have a fused 5-membered ring.

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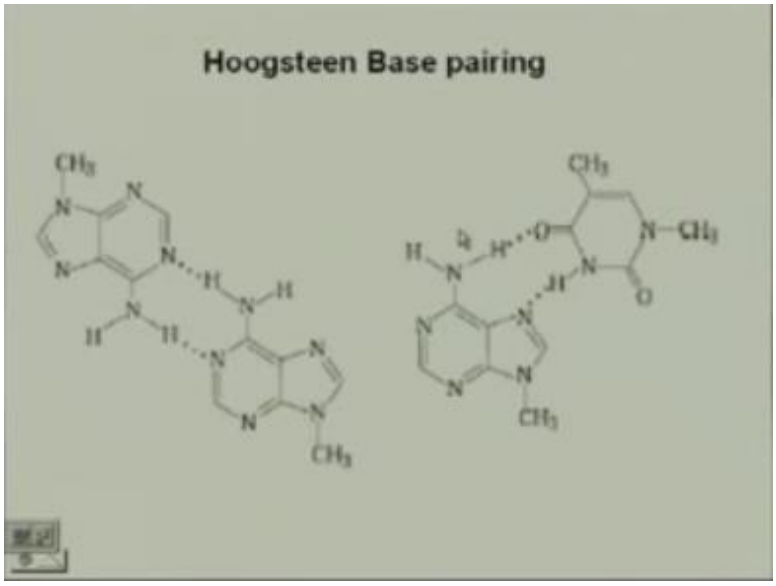

In the Hoogsteen base pairing, -- so what did we had, we had this face that was forming the hydrogen bonds in the Watson Crick base pairing. In the Hoogsteen base pairing, we have one hydrogen from the 6-membered ring, and the nitrogen taking part in the hydrogen bonding from the 5-membered ring.

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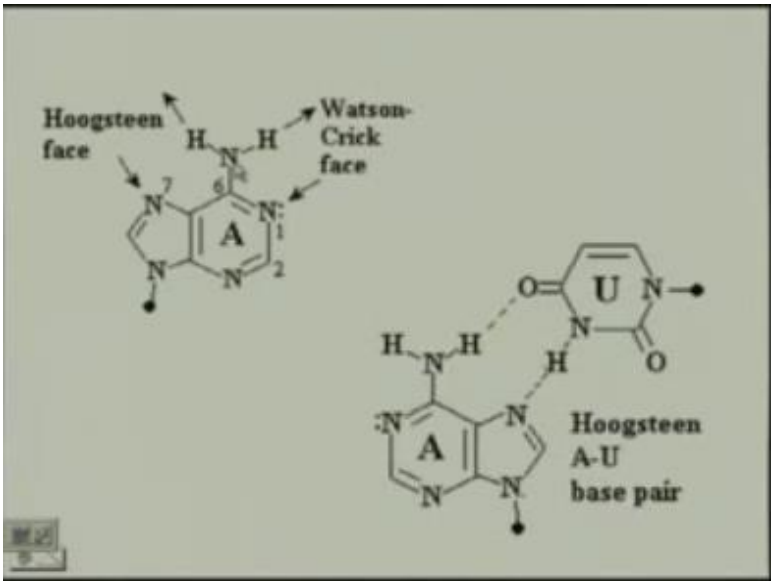

So what we essentially have is, we have what is called Hoogsteen face where it is a 5-membered ring nitrogen and the NH of a 6-membered ring taking part in the – what is it taking part in, in the hydrogen bonding. And for the Watson Crick face it is only the 6-membered ring that is taking part. Okay this is the essential difference in the pairing that occurs, so when we have a Hoogsteen, so what is this, this is a normal purine-pyrimidine linkage A and U.

U is found where in RNA. So when we have an A and U linkage and you see that the linkage is between, obviously you are going to have it between two electro negative atoms. But you see it between what, or what is taking part, that is what you have to look at. What do we see taking part? Here we see the 6-membered ring taking part and we see the 5-membered ring taking part. So what kind of base pairing is this? Hoogsteen base pairing.

Okay that is essentially what we have to recognize. And when we see Watson base pairing in this case, what would happen? The linkage would beyond this side. Because, it would the 6-membered ring that would be involved in the base pairing. So we have a Watson Crick face, we have a Hoogsteen face, okay. But by far, it is a Watson Crick base pairing that is the most important, okay. So now essentially what we have done is we have looked at how we have the linkages of the base pairs.

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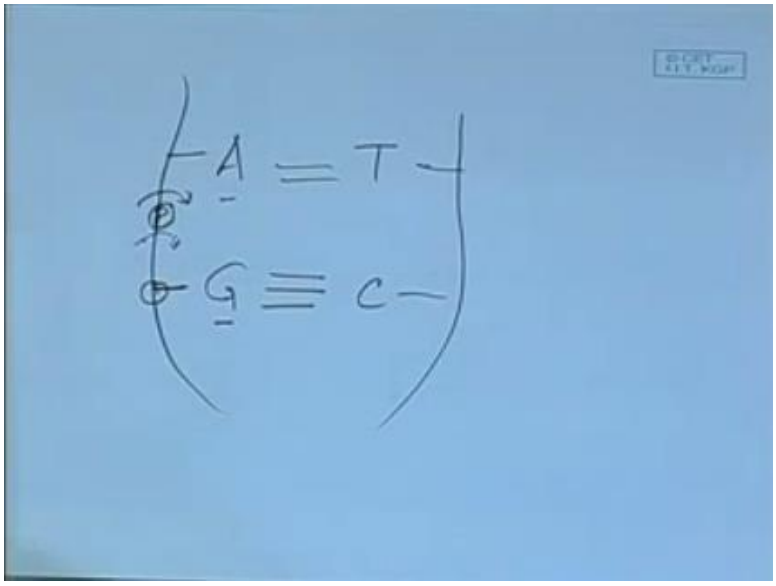

So we have A, T. We have G C. Two hydrogen bonds, three hydrogen bonds. These are coming from where, they are coming our sugar phosphate backbone, that's essentially what is happening, okay. And we have essential rotations about the backbone, where are these rotations possible? We have the phosphodiester, okay. So if we have the phosphate atom here, we have rotations above this, we have the sugar ring somewhere here, we have puckering above the sugar ring.

So now what is going to happen? This rotation is going to – this puckering is going to orient the G in the specific position. This rotation is going to orient the overall backbone in the specific position. What is that going to assist in? That is going to assist in orienting the bases in such a manner that you can have the specific hydrogen bonding possible. Without this slight flexibility it would not be possible to have the hydrogen bonding.

You understand that, because you have to have the nitrogen and the oxygen specific orientation, specific distance requirements for this to occur, okay.

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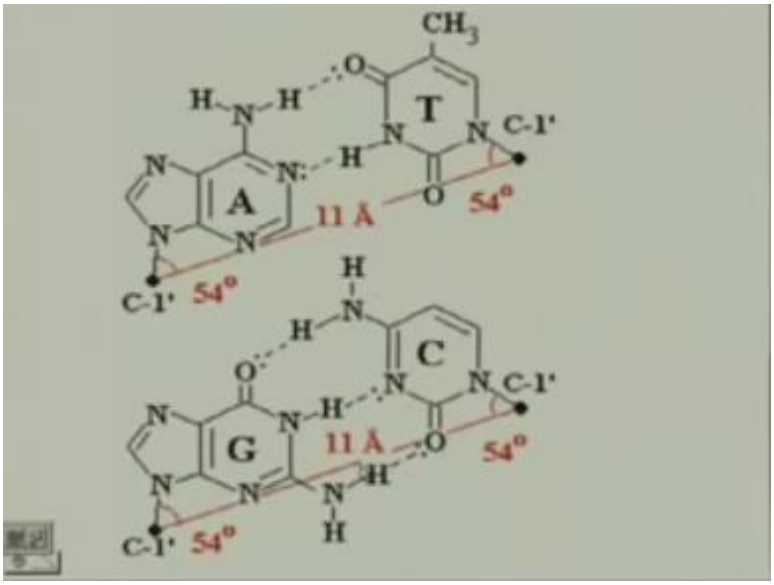

And if you look at this result here, we have A and T, what is this base pairing? What base pairing are we looking at here? Only the six membered ring involved, so it is Watson Crick. If you look at the A and T pairing and the G and C pairing you see the distance form C-1* here and the C-1* here, what is a C-1*? It is where it is attached to the sugar. The beta and glycosidin linkage that is where the C-1* is.

What is a distance? 11 Angstroms. When you have A and T. When you have G and C, it is also 11 Angstroms. So you see how nature has sort of designed in such a manner that you would have a purine and pyrimidine link together.

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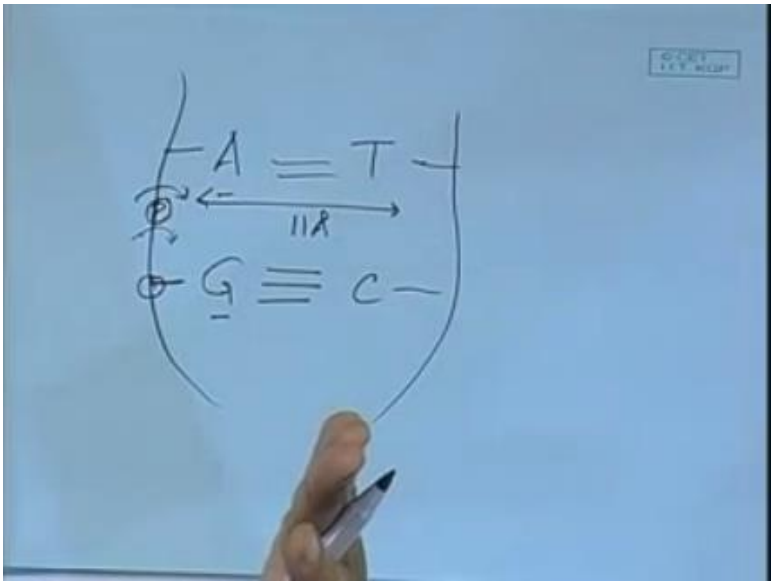

You would have a constant distance here that would give you that is actually 11 Angstroms that holds the bases together, you have base pairing in such a way that -- not only the distances but also the hydrogen bonding is complimentary and you also have the flexibility possible that also makes it feasible for the hydrogen bonding to (()) (52:56), okay. Thank you.

We continue our discussion on nucleic acids. Now what we learnt last time was how we have these specific bases the purines and the pyrimidines interact to form with double bonded – a hydrogen bonded structures, how they form complementary bases basically.

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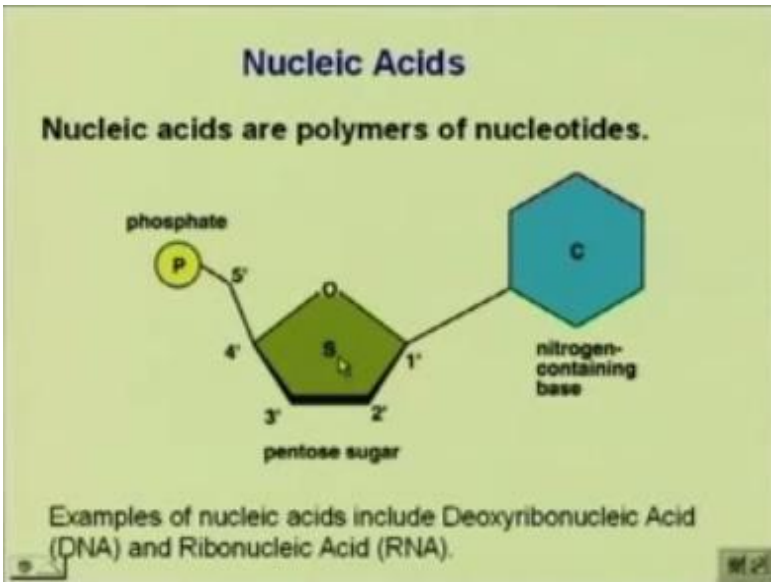

Okay so what we have here if we look at the nucleic acids, we know that they are now comprised with this pentose sugar, a phosphate and a nitrogen-containing base, right. And we know that this pentose sugar can be of two kinds either a deoxy kind or a ribose. A deoxyribose or a ribose depending on the type of nucleic acid that are you are considering. Now, obviously we have these two types, deoxyribose nucleic acid where what is missing at the two prime position, the OH is missing at the two prime position. And we have the sugar and the phosphate.

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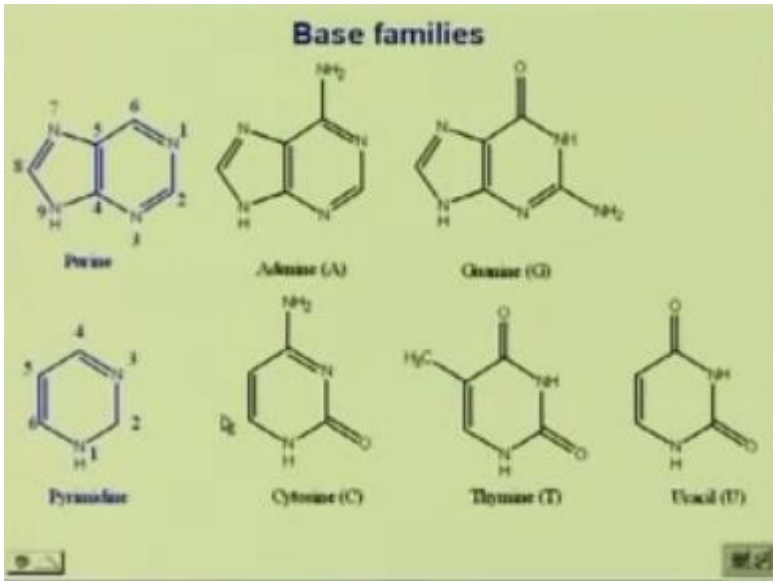

And the base families are the purines and the pyrimidines and what do they do, they interact with hydrogen bonding, a purine and a pyrimidine to form a two bases coming together in a hydrogen bonded network.

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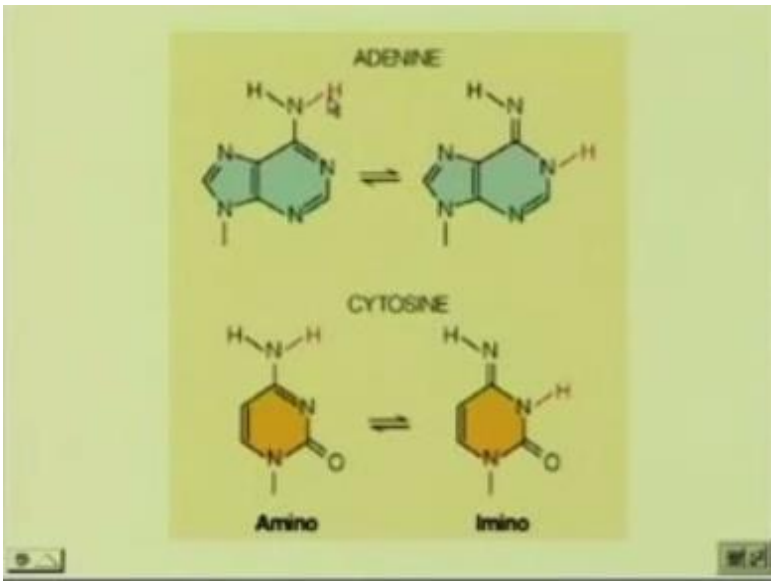

Now there is an additional factor that has to be considered here, that is a tautomerization possibility of the bases, okay. Now if you look at the Adenine consideration here, what do you have, here you have an NH2 group, okay. Now what can happen to that NH2 group is this H can – you all know about keto-enol tautomerization. What happens in keto-enol tautomerization? What happens there? You have a C double bond O and that is converted to an OH from a adjacent HCH_2, right.

So you have keto-enol tautomerization. Here we are having an Amino type and Imino type, okay. But the basic ideas are the same is that you are shifting this hydrogen in the case of Adenine to the adjacent nitrogen. In the keto-enol tautomerization, what do you do? You have the H shifted from the carbon to the oxygen, right where you have a keto-enol tautomerization. But what we talking about here, is an amino and imino case which is possible in adenine and cytosine. And there are 10.5 bases per turn. Just like we had a picture of alpha helix it is similar to something like that.

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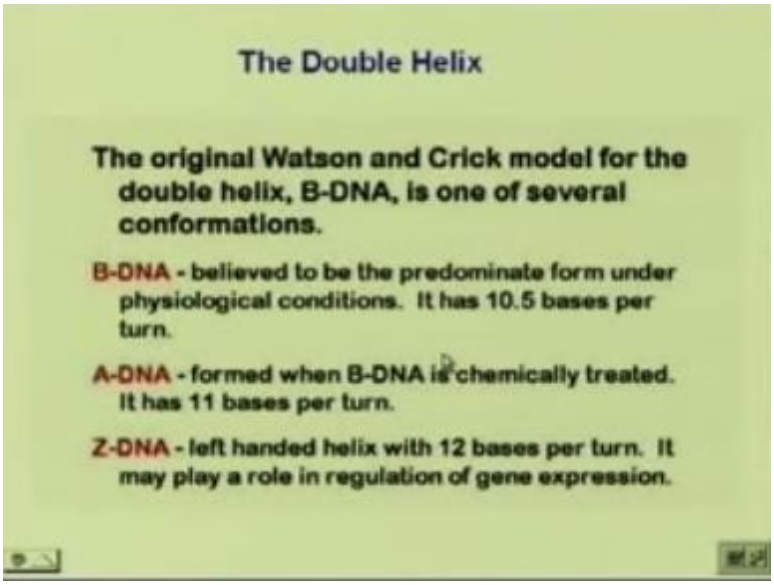

When you have the A-DNA this is formed when B-DNA is chemically treated. But basically, it does not have those water molecules in the water spine, that's what A-DNA is. And it has 11 bases per turn. The Z-DNA as it is called is a left-handed helix with 12 bases per turn and it usually plays a role in gene expression. So, these are the three forms of DNA, and the most common by far is the B-DNA, okay.

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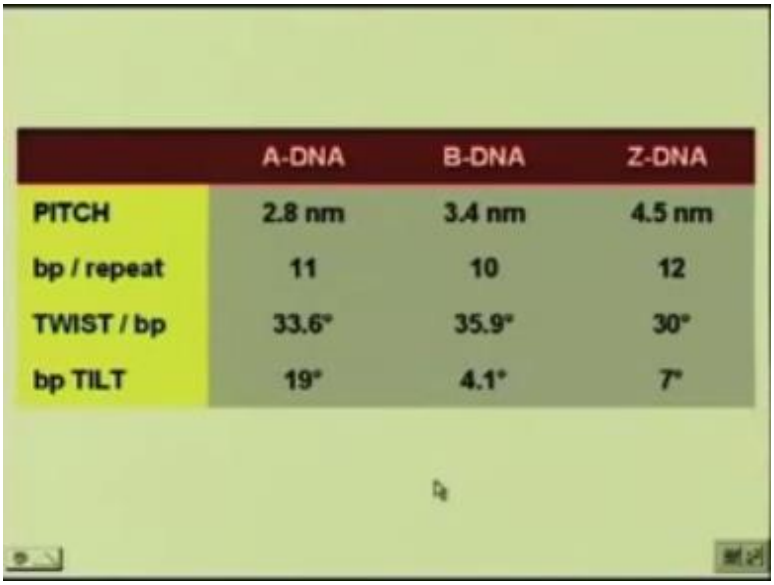

These are some of the futures of the A-DNA, B-DNA and Z-DNA. We have a PITCH. What is this PITCH? What is a PITCH? The distance covered by one rotation. So the A-DNA pitch is 2.8nm, the B-DNA is 3.4nm and the 4.5nm for Z-DNA. The base pair repeats are 11 bases per

turn, 10 bases per turn and 12 bases per turn. The TWIST per base pair. You realize that there is a slight twist at the base pair. Like you would also have angle disposition for the alpha helix. These are the twist per base and we have a slight base pair TILT which is not very much in the B-DNA just four degrees, okay that's a slight base pair TILT.

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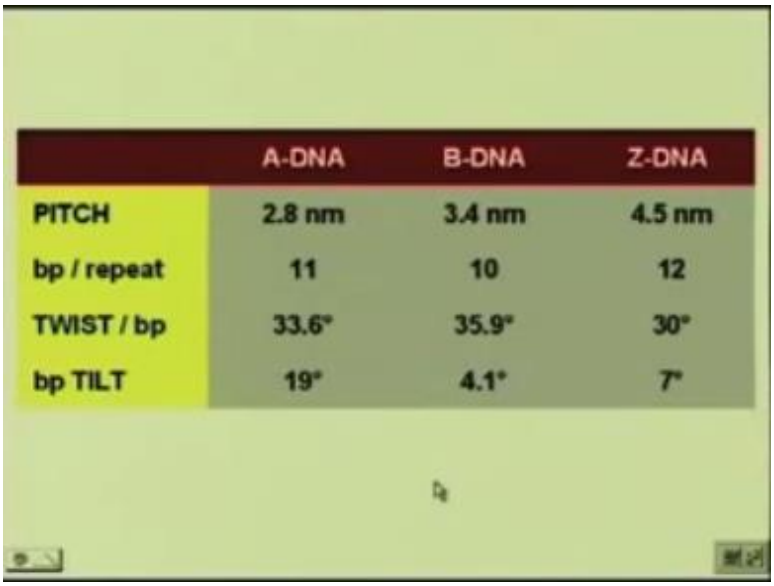

So the three DNA is we have the B-DNA, the A-DNA and the Z-DNA and the most common structure that we will be considering is just the B-DNA, okay. That has the 10 base pairs per turn, 3.4nm and a base pair TILT of four degrees.

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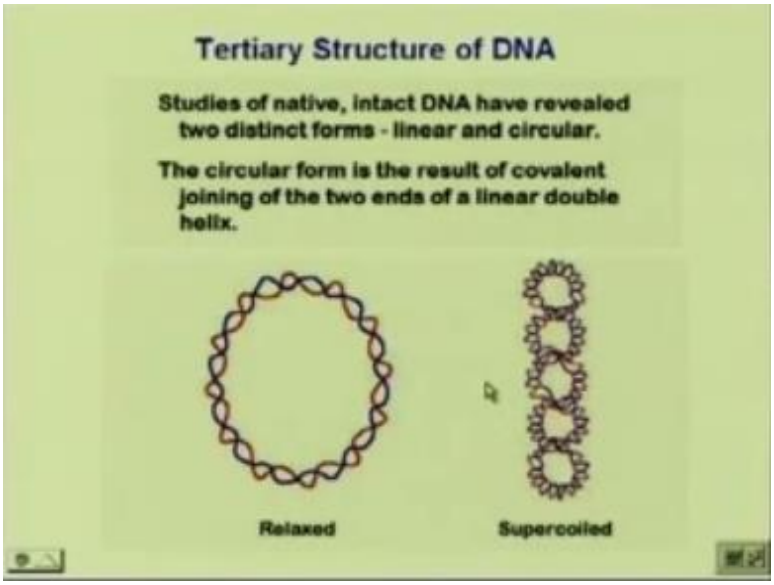

So that, the double helix of DNA actually -- well it would not be a secondary, so that is a structure of DNA. But there are other forms of DNA also. Our studies have shown that the native intact form of DNA can be linear and circular.

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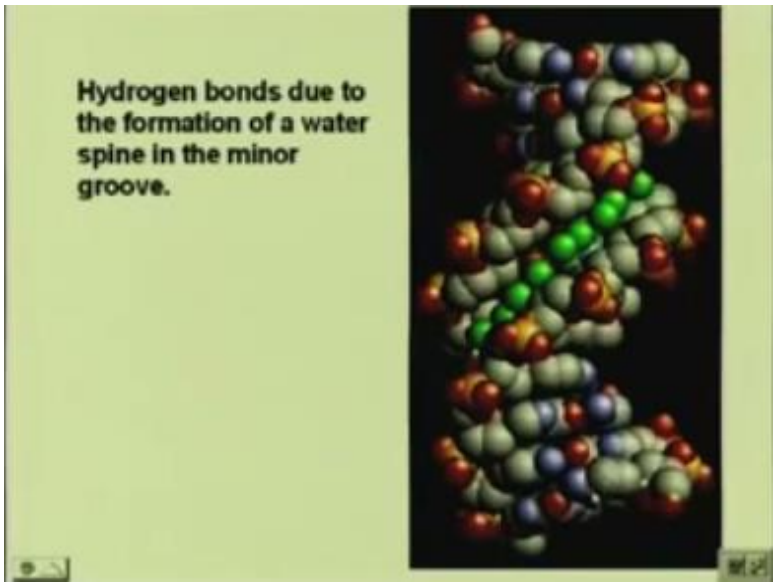

If you look at the double helix here, it goes straight up and straight down we will have a linear structure.

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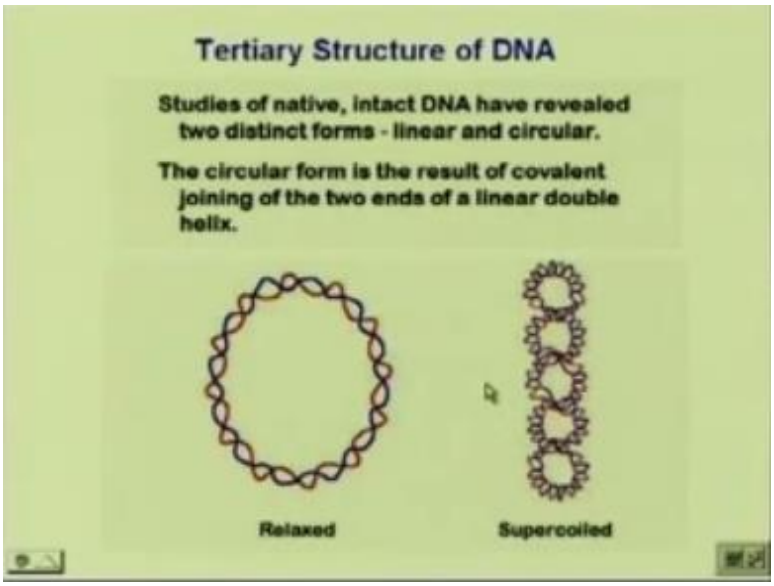

Now what happens is if the two ends are covalently join together, okay. If we chop this out we are going to get a linear from (()) (58:30).