Introduction to Biomaterials

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Module No. # 01

Lecture No. # 37

Understanding Design Concepts of Bio-Implants

In this lecture, we learn about the understanding the design concepts of bio-implants. In the, in the field of bio-implants if any student or research is entering, they basically worried about the applicability part of the bio-implants, so, that is the reason it becomes very essential to learn a few design concepts, or to learn what are the parameters or what are the conditions which will decide the applications of bio-implants once it is inserted into the body.

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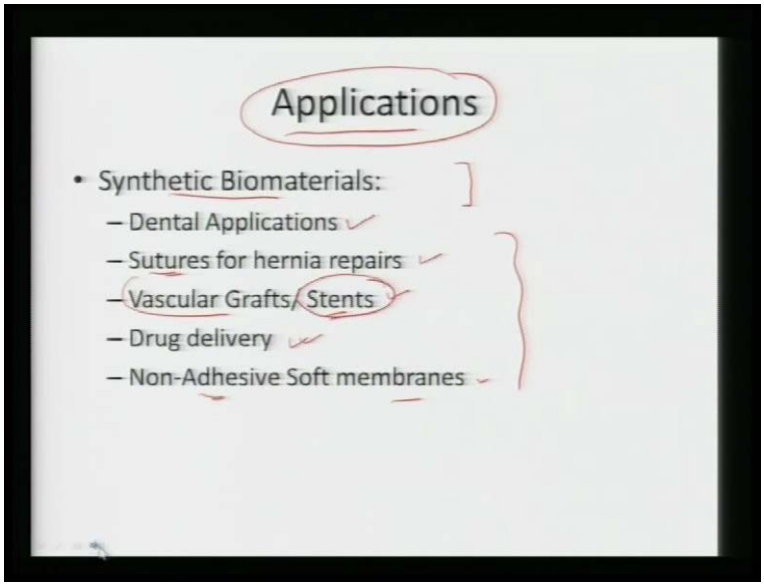

So, the applications are the very, very essential part of it because that decides the overall usability of a particular device material. So, there are certain, so, synthetic biomaterials is basically go in to a applicants such as dental applications, sutures for hernia repairs, they can also be utilized in vascular grafts, or stents, drug delivery and non-adhesive soft

membranes. So, you can see myriad of applicability of synthetic biomaterials, those are not natural biomaterials, but synthetic, so, that is the reason they have to basically undergo certain selection criteria such as for dental applications, those are again more load bearing, they need to also fracture toughness, and again for the sutures, they need to dissolve with time, or they have to be removed if there is a non-dissolvable or non-degradable polymers.

So, again, they can be vascular grafts, there can be stents for basically doing the repair of broken veins or arteries in a heart, and it can again, be for drug delivery, for releasing certain drugs at certain required area, and it could be again be non-adhesive soft membranes to avoid the sticking of to nearby tissues. So, these are certain applications which are very, very essential for utilizing synthetic biomaterials.

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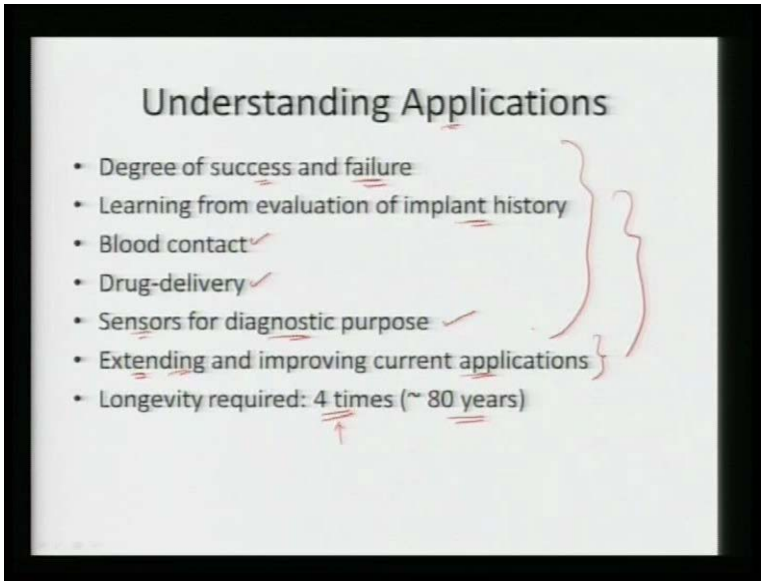

So, it becomes very essential to understand these applications, to understand what are the parameters which will decide the applicability. So, these applications have been there for since last 40-50 years, so, with their usage there have been certain failures as well as certain successes, so, the degree of success and failure also decides the longevity of a particular device which is implanted into the body. So, the degree of success and failure will tell us what we can learn from the evaluation of implant history, if the implant has survive, then what was the reason for it, even if the implant is failed, what was the reason for it, so, we can always improvise on what the devices have been utilized for.

Again, there are certain criteria, which become very, very critical such as blood contact. So, if a devices coming in terms, in contact with blood, there might be thrombosis, or certain information, which can release into the nearby adjacent tissues, it can also be drug delivery for the controlled release of certain drugs into certain areas, it can also be utilized as a sensor for a diagnostic purposes. In certain situations it becomes essential that we can extract some data, or get some diagnostic for a particular blood sample, so, we can also have certain sense and which can exactly sense, it can be the glucose level, it can be the drug released, or it can be any chemical composition of a particular area- so, that is again required for the sensor application.

And again, extending and improving the current application, that again comes from the understanding of the failure or the success of the implant from its implant history, so, that becomes very, very essential. So, again, we need to also extend, extend and improve the current applications. So, only once we have learnt enough then, we can apply further, at the same time we should be able to improvise on what we have learnt and then, develop, or extend the applicability of a certain device. So, that is, there is an, we have we have concentrated much on the extending and improving the current application. So, certain application, which we are not possible earlier, can again be thought of. And again, those applicability again, it has not really, it has not gone up to the expectations, the general implant life is approximately 15-20 years, but in order to sustain that particular implant for a much longer time we need longevity, which is four times as that of a current implant materials. So, the longevity, or the time period of an implant in the body we are looking is around 80 years, that is approximately four times improvement, that is what we require from the current used implants.

So, just reiterating, the understanding the applications is basically based on the degree of success and failure, and that we can learn from the history of that particular implant, and that particular implant can have certain, some sort of a blood contact, or tissue contact, it can again be utilized for drug delivery. So, for control, controlling the particular aspect of the degradation part we again require certain engineering. Again, for sensing, so, sensing also has to be very, very peculiar for a particular place and for what purpose we are utilizing it, it can be for diagnostic purpose, so, we should be able to evaluate the chemical composition, or apply certain drugs to a certain area and so on. So, again, we should not limit our applications to what we have been utilizing, not only for improving

the material, but also to improving the applicability, so, we have to extend the limits of current device materials and be able to extend it for certain other applications as well. And also, we require longevity of those implants because certain implant is inserted, it requires surgery, so, for it to remove the surgical complications, or to remove that costly surgery which is done again and again, may be couple of times for a particular patient which has to undergo a surgery, it becomes necessary that the surgery time can be reduced, or the number of surgeries can also be reduced by extending the lifetime of those implants.

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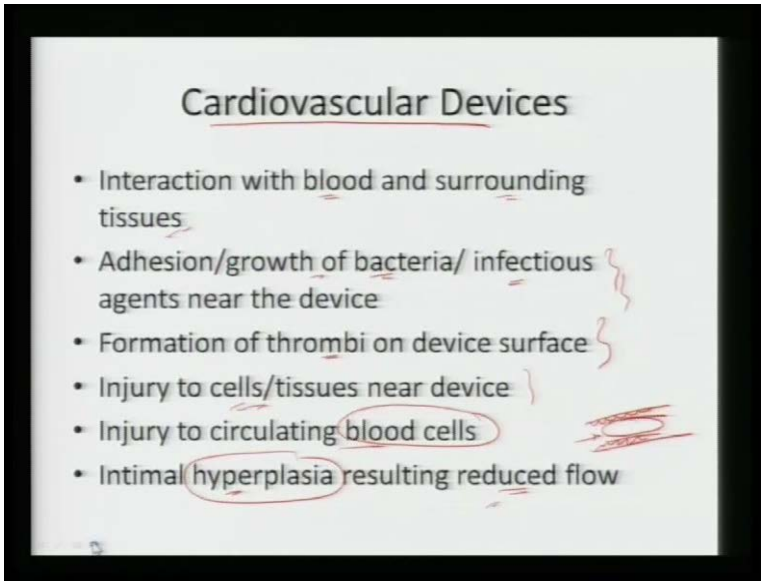

So, in this we can concentrate on the basically, on the cardiovascular devices. So, in the cardiovascular devices we can see that the device is implanted it has to interact with the blood, as well as with the surrounding tissues. So, it can happen that there can be adhesion and growth of certain bacteria or infectious agents near the device- so, that basically will hamper the overall applicability of this particular device. Later on there can be formation of thrombi on the device surface, that will again limit because, now, the surface of the device is now covered with certain fibrous thrombi- so, that can basically limit the overall applicability. And further, this device can also lead to injury of the cells by its basic functionality of the tissues- and, so, that can also hamper the overall applicability of the device.

Also it can cause injury to circulating blood cells- so, again, that may also need to be considered while a particular device is being implanted. And again, there can be intimal hyperplasia, so, there is excessive growth of cells, which can again reduce, can result in the reduced flow because of a particular (( )) are there, it can have certain hyperplasic, an excessive growth of cell, and that can again reduce the overall flow because of the reduce area which is available for the blood to pass through. So, these are the critical issues with the cardiovascular devices because it retains and contact with the blood and with the surrounding tissues. So, the addition of it can lead to infection by the growth of bacteria, or some infectious agent in the device. And it can again form the thrombi on the device surface, that will again limit the overall exposure of this device with the surrounding. Again, it can cause certain injury to cells or tissues near the device. And it can also injure the flowing blood cells. Or it may also lead to hyperplasia which can reduce the, which can result in the reduced flow of a blood stream.

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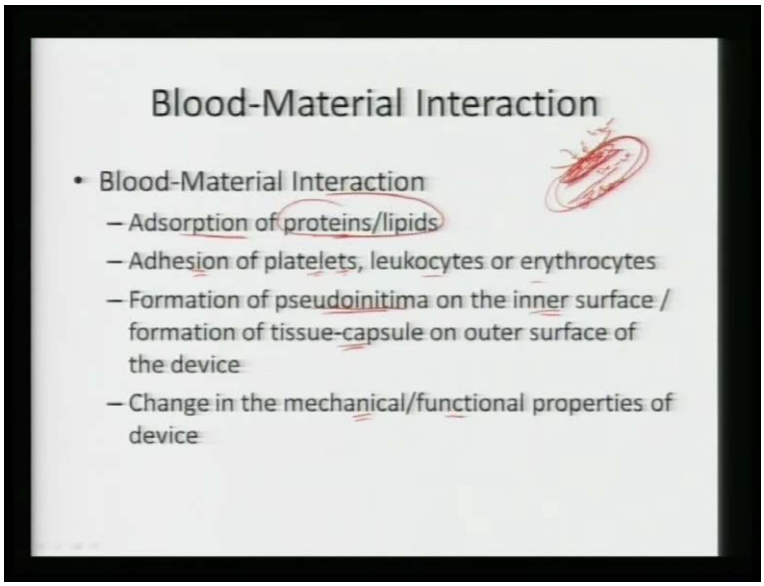

So, it becomes very essential to evaluate the blood material interaction because as soon as the particular material, or a foreign material is implanted into the body there will be, there is an immediate adsorption of proteins or lipid layer on the surface, so, as soon as we have device, it basically gets adsorbed on, it gets adsorbed by proteins or lipids. And it is followed by the adhesion of the platelets, leukocytes or erythrocytes. And later on, there can be formation of pseudoinitima on the inner surface and that basically leads to the formation of tissue capsule on the outside surface of the device. And once that, once

this process has taken place, it can again change the mechanical, or functional properties of device, it can be both beneficial or it may might be deleterious, but this is what is happening in the blood stream after the material has been implanted which is in contact with the blood.

So, we have a device, as soon as we insert the device we see adsorption of proteins or lipids on the surface of the device material, it is followed by the adhesion of platelets, leucocytes or erythrocytes, so, basically the blood protein they get basically adsorbed on the surface, and the formation of pseudoinitima which results in on the inner surface and that results the formation of tissue capsules of a particular device, it will have, it will have first the adsorption of the, so, it will have the first adsorption of proteins or lipid on its surface, it is followed by the adhesion of platelets, So, the platelet adhesion on the surface and then, this formation of pseudoinitima over this, that forms a, that forms a inner layer of the cell or the tissue and then- or it is on the outer surface, this is the device this is nothing, but the tissue- so, the in between layer basically gets pseudoinitima formed on the outer surface of the device, or on the inner surface of the tissue or the capsule- that encapsulates the device and that once the device has been encapsulated it might be beneficial in terms when we require some sort of a cell adhesion on the surface, or it may not be really required, it might be (( )) interaction and that basically affects the mechanical, or the functional properties of the device.

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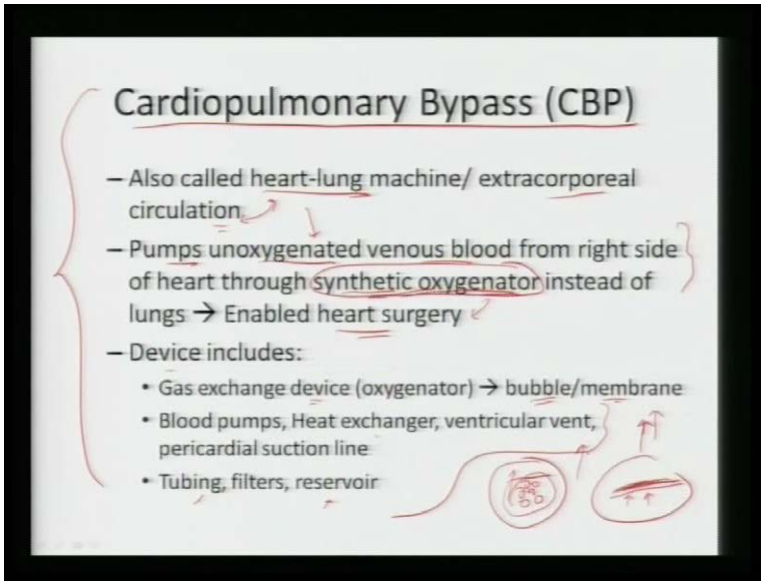

Again, there is second application, which is cardiopulmonary bypass, it is also called as the heart lung machine or extracorporeal circulations. Let us, that is basically required because we want to exchange the oxygen when the heart has been disabled. So, that basically results from replacing, or improving the functionality of the heart. So, in this particular case, the cardiopulmonary bypass, it helps in pumping the unoxygenated venous blood, so, we have the venous blood, which is full of carbon, which does not have enough oxygen, so, this oxygen has to be reactivated. So, the oxygenation of this particular venous blood has to be carried out using certain oxygenator, and that can be done via certain oxygenator which can be either bubble or membrane type device.

So, basically what is happening here is, the cardiopulmonary bypass, it pumps the unoxygenated venous blood from the right side of the heart through certain oxygenators instead of the lungs because this particular blood has to get oxygenated via a lungs, but now this synthetic oxygenator can take care of the oxygen exchange in the venous blood. And this particular development has lead to easiness in terms of doing heart surgery because heart has, the blood which is flowing through the heart has to be oxygenated, it has to have sufficient oxygen to supply to the all the regions of the body. So, instead of getting the oxygen from the lungs it can allow oxygen exchange using this particular synthetic oxygenator. So, this particular device which is cardiopulmonary bypass, this synthetic oxygenator basically includes gas exchange device which can be bubble type or it can be membrane type; in bubble type the oxygen bubbles are basically being released and then, later on it require, it requires defoamers, so, because when bubbles are created it starts forming certain foams. And this membrane type, it again, it basically filters out and then it releases the oxygen, so, this is much more nicer way for the blood to trap the oxygen, but the process is very, very complex and it requires, it is very costly as well.

So, these both practices are being adopted, either it can be membrane type or the bubble type to exchange the oxygen flow. And it also certain blood pumps, heat exchangers, ventricular vent, or pericardial suction like, for certain operations, it also have tubings filters and reservoirs for carrying out this particular bypass. So, in this particular case, we can see cardiopulmonary bypass, it basically is also called heart lung machine because it supplies oxygen instead of letting it, letting the oxygen come from the lung, it supplies the oxygen, it is also called as extracorporeal circulation. So, in this particular case it will

pump out the unoxygenated venous blood from the right side of the heart through certain synthetic oxygenator. So, basically it has enabled the heart surgery.

And the synthetic oxygenator includes gas exchange device which can be either bubble type or membrane type; in bubble type the release of oxygen bubbles, which basically go and react with the it is the venous blood to exchange oxygen or it can be again membrane type, but bubble type starts creating certain (( )), so it needs a deformer whereas, membrane type is much more softer in operation, but it is very, very complicated as well, it requires much complicated devices to take care of this particular exchange of oxygen and passing of this particular blood. And it requires certain other devices such as blood pumps, heat exchanger, ventricular vent, filters and reservoirs and so on, so, in order to carry out this cardiopulmonary bypass. So, we can see the how complicated this particular process is in terms of utilizing a bypass.

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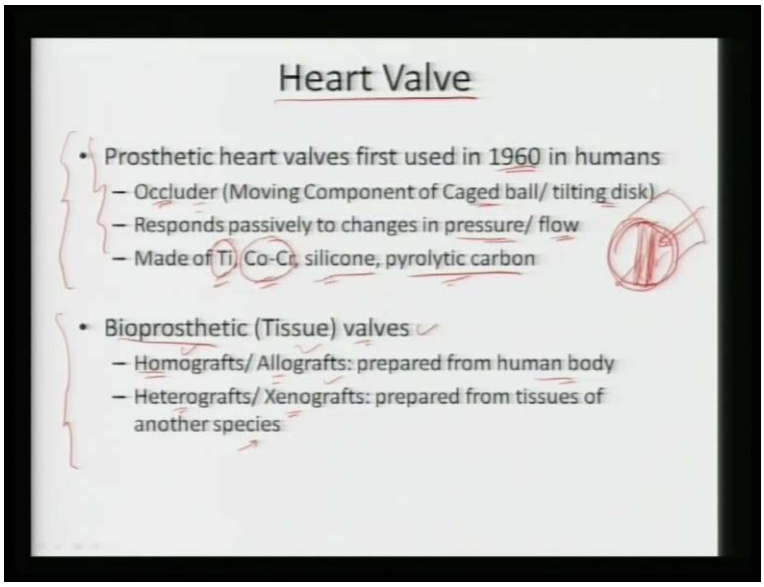

Further, there are certain other devices such as heart valve. So, first of all this prosthetic heart valve was first utilized in 1960 in humans, but again, it basically had certain problems, it basically had certain moving component which are called occlude, they can be made up of either caged ball or tilting disk- so, in this particular case we have sort of a cavity and in that we have certain fins, or tilting disc, so, this is a sort of disc which will basically alter depending on the flow of the blood through the, so, that is what is basically there. And they respond passively to the changes in the pressure of flow.

And they are made up either of titanium, cobalt chromium, silicon or pyrolytic carbon. So, these particular heart valves are utilized, these are nothing but the valves which will have to turn or tilt, they can be either ball type or tilting disk type to alter the, or to direct the direct the flow of the blood, and they can respond very passively to the changes in the pressure or flow, because once the pressure is high or low they need to alter the overall flow of the blood through the valve, So, valve is nothing but controlling the flow of the blood when the pressure is high or low. So, again, they have to respond accordingly to that, so, they have certain either fins or balls which can, in this particular case they have some sort of a disc which can, leaflets which can alter the directionality of the flow.

Again, there can be, these are again synthetic valves or prosthetic heart valves, they can be either bioprosthetic, or tissue valves, and this can again be prepared either from homograft or allograft which are prepared from the human body. Or they can heterografts or Xenografts which are from the foreign body, or prepared from the tissues of another species. So, again there are two sides of the heart valve, they can be the synthetic, and it requires some sort of occluder which is nothing but a moving component. So, we have certain disc available and then, it has a caged ball or some sort of a disc which can allow the directionality, or changing the pressure or flow.

And they are made up of titanium, cobalt chromium, silicon, or pyrolytic carbon. The same time that they did not get, they need to control the flow, so, they need not really get damaged by the flow of blood itself. And this can be again bioprosthetic or the tissue valves and these are more natural, so, they can again come out either from as a, they can be prepared from the human body which are called allograft, or they can be prepared from the foreign tissue of another species, those are called xenografts.

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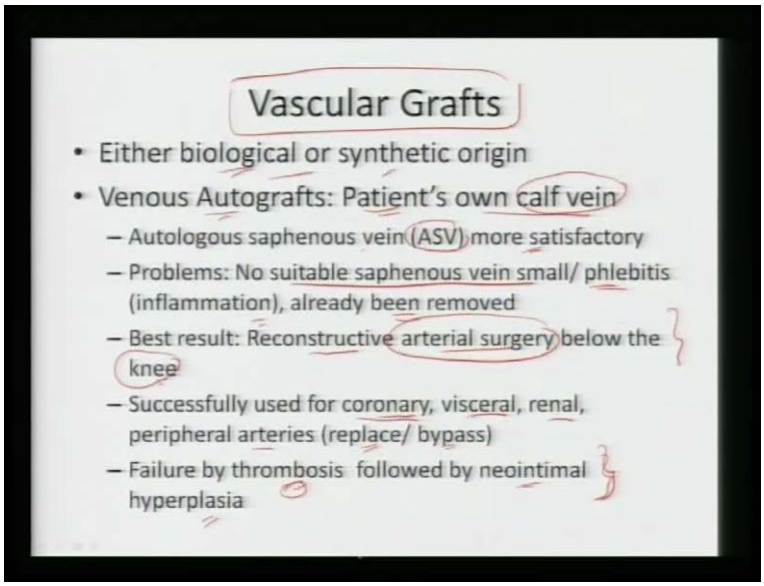

Again, these vascular grafts, they can be either biological or synthetic. So, first, coming to the venous auto grafts, auto means it is from the self part of the veins, so, it comes from the patient's own calf vein and again, the autologous saphenous vein which comes out from the calf of the, calf vein of the patient, it basically performs much more satisfactorily. But again, it can it can induce certain problems like 30 to 40 percent people can have, face problem in case when there is no suitable saphenous vein, or they can be small, or phlebitis inflammation has been occurring, or there is that particular vein has already been removed. So, there can be certain problems which are associated with the venous auto grafts that there is no saphenous vein available inside the body, or that particular venous already been infected, or it is already been removed by some previous surgery.

But they show best result in the reconstructive arterial surgery which is below the knee. So, they are well suited for the arterial surgery which is below the knee. So, they have shown very promising results. They have also been successfully used for other coronary, visceral, renal, or peripheral arteries, both for replacement as well as the bypass surgery. But the basic problem comes from the vascular grafts is it can fail by thrombosis, which is followed by neointimal hyperplasia, it means there is some blood clotting which can be follow by the newly, which can form after a new surgery has been done and there is a formation of new cells which is basically excessive in a normal growing tissue. So, that

problem can occur in the vascular graft that there can be excessive formation of cells in an abnormal way in a normally growing tissue.

So, again, we can see the vascular grafts, they can be biological or synthetic, venous autografts they come out from the patient's own calf veins. So, that is the overall, autografts, they, the body will start reacting to it in a more friendlier manner because that particular vein has come from the body itself and they perform very satisfactorily, but the problem comes when that particular vein is not available, or it has inflamated, or it has already been removed by the surgery. And they show very good results when in the arterial surgery of the knee, And they also been utilized for coronary, visceral, renal peripheral arteries, but the problem comes when there is occurring of thrombosis which is followed by neointimal hyperplasia, or the excessive formation of cells in a normally growing place after surgery has been taken place.

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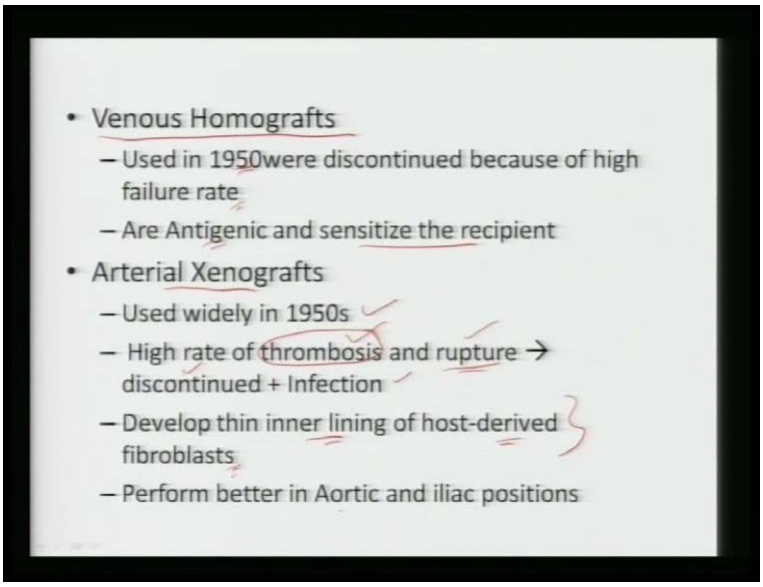

There can be other, venous homograft, so, again, the homograft which are taken from the venous parts and they were discontinued in 1950 because of their high failure rate, and it happens because they are antigenic and they sensitize the recipient, so, that is the reason they were discontinued in 1970s. Further, there can be arterial xenografts, so, these are taken from the arterial regions, from the foreign body, and they were widely used in 1950s, but again the higher rate of thrombosis was observed and higher rate of rupture

was also observed in this particular case and they were discontinued later on, again, in 1970s.

It also was seen that they can also create infection, what happens in the arterial xenografts is they develop inner lining of host derived fibroblasts, so, that is the problem that occurs that either it can lead to a higher rate of thrombosis, and it has also was seen that the rupture rate was very high and also it let to the infection later on, the problem with them is that they develop inner lining of host derived fibroblasts, but they have seen to perform better in the aortic and iliac positions, so, this arterial xenografts are well suited for aortic and the iliac positions of the artery.

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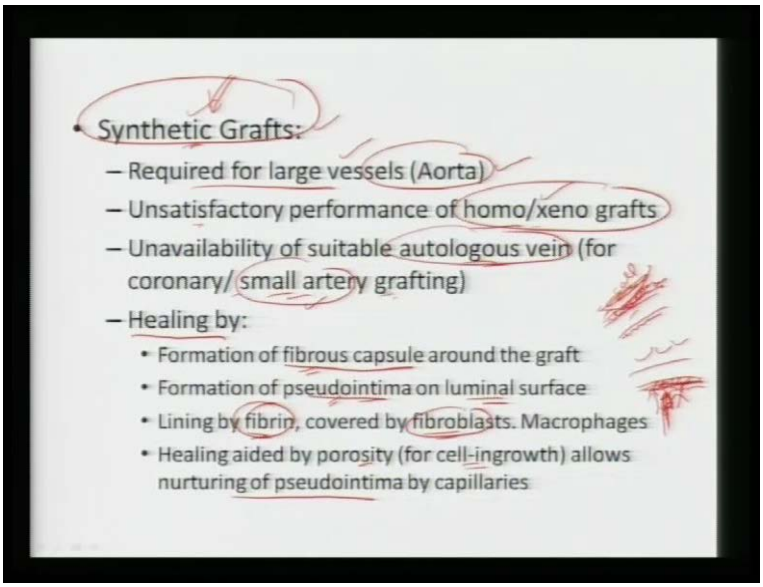

They can as well be, apart from the autograft there can be synthetic grafts as well. So, we for the synthetic grafts, they are basically, they become a requirement because some times in autografts it may not be possible that we have a particular vein available like, an aorta, which is a very large vessel, so, in that particular case it may not be possible to extract a different aorta sized vein from the body, aorta sized vessel from the body, so, it becomes a requirement that we produce synthetic grafts; in certain cases even thinner vein vessels may not be also available, so, in that case also we need to extract, or we need to make, or synthesize a artificial graft for the body.

Again, they are required for very large vessels such as aorta, even for very smaller ones, there this performance becomes unsatisfactory, when the performance of the homograft

or the xenografts become unsatisfactory then also we need to make the synthetic grafts, or if there is unavailability of the suitable autologous vein for either coronary or small artery grafting. So, either when we require large vessels or we require very small arteries, or when the performance of the homo or xenografts itself is unsatisfactory then need to go for the synthetic grafts.

In the synthetic grafts the healing occurs by the formation of fibrous capsule around the graft and then, there is formation of pseudoinitima on the luminal or the inner surface of the cell and then, there is a lining of fibrin which gets covered by the fibroblasts or macrophages and then, healing is aided by porosity, which allows cell in growth and also allows the nurturing of the pseudoinitima by the capillary which are present in the pores. So, we can see in the synthetic grafts it becomes a requirement for large vessels such as aorta or even for the small artery, grafting, that actually occurs when there is unavailability of suitable autologous vein, or when the performance of the homograft or the xenografts is not up to the mark, so, in that particular cases the synthetic grafts becomes a requirement.

In the synthetic grafts the healing occurs by the formation of certain fibrous capsule around the grafts, so, if we have a graft, we have some sort of fibrous capsule around it, so, it encapsulates in it. Then, formation of pseudoinitima, so, we have cells surface in the interfacial region of the graft and that of a cell and the luminal surface of that particular tissue, so, we have tissue and then, the pseudoinitima forms on the luminal interface. And then, you get a lining of fibrin, so, we get a lining of fibrin over it, which is now covered with the fibroblasts or macrophages, and in that particular case if you have a certain porosity, so, we have certain porosity which is available then, what can happen then, it can also lead to the nurturing of the pseudoinitima, so, the pseudoinitima which is formed on the surface of this particular device or this synthetic grafts, it allows nurturing of the pseudoinitima and it cannot form natural intima, so, it needs to have a pseudoinitima over there, so, it can allow the nurturing of the pseudoinitima by the capillaries which are present as in between the pores of certain porous region, we can allow the porosities, or the porosities can allow capillarity which can allow formation of this capillarity and then, that can nurture the pseudoinitima.

So, we can see the healing is occurring by formation of fibrous capsule around the grafts then, formation of pseudoinitima on the luminal surface then, there is some lining of

fibrin, which gets covered by a fibroblasts and macrophages and then, healing is basically being aided by the porosity which allows cell ingrowth by nurturing to the capillaries.

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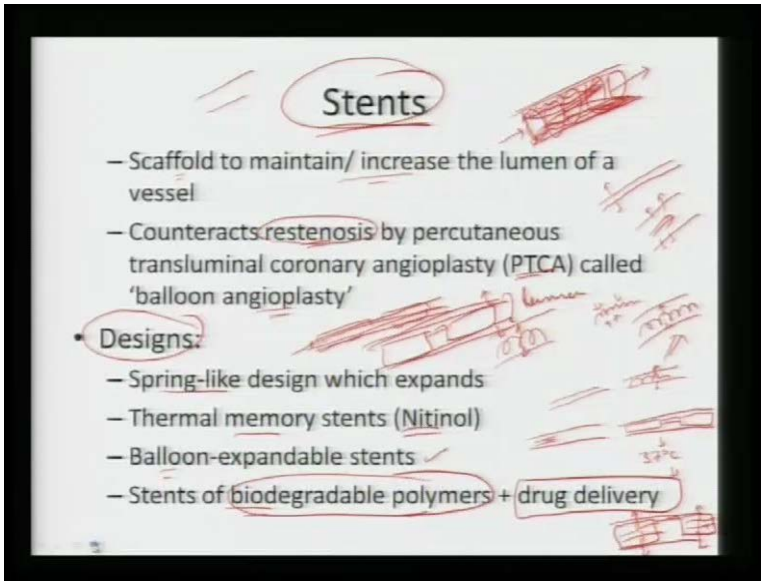

There is another device which is called stent, and this stent is allowed, is basically nothing but a scaffold to maintain or increase the lumen of a lumen of a vessel. So, if you have a vessel, so, if you have particular vessel, then we need to the lumen of it- so, this is nothing but the internal lumen of the of a vessel, inner lining of the vessel, that is what is the overall diameter of the particular vessel, so, it can it has to maintain or increase that particular lumen.

So, in many cases there is some deposition of certain, deposition of certain proteins, or some sort of a decrease in the overall lumen of a particular vessel then it becomes very hard for the blood to flow through it, so, in that particular case we require stents to allow the flow of blood which is basically unperturbed. So, in this particular case if the vessel itself has basically constricted, so, we need to send some artificial material which can again lead to the expansion of this particular vessel and allow easy blood to flow through it. So, it counteracts restenosis by the percutaneous transluminal coronary angioplasty, which is called nothing but balloon angioplasty. So, in certain cases once we have done a surgery and then, basically we see the retinal or the lumen of a particular vessel starts decreasing, so, that again reduces the blood flow. So, need to counteract that by again increasing or ballooning this particular vessel for the smooth blood flow.

So, there are certain designs which are based on this, which are available for this stents. First thing is spring like design which expands. So, we have some sort of a spring like design which can expand itself once it is going through it, initially we can have a compressed spring which upon going inside the overall restrain to it can be released and then, basically they grow and again increase the diameter of this particular vessel. So, initially when we have smaller vessel and then, spring goes and start expanding to further increase the overall lumen of a vessel. There can be also thermal memory stents. So, in this case this metal nickel titanium, this is called nitinol, this is the shape memory stent- so, it regains its shape once it is exposed to the temperature of the blood. So, nitinol is a material which is in inserted into the vessel and then, its starts to increase its shape thus, it will, it can allow the pipe or the tubing to enhance a diameter.

So, that is what is what is happening, once we have this particular stent that will take a particular vessel, we insert the stent part into it, so, we have certain of a tubing and then, basically it is inserted into the body, and as soon as it experiences the body temperature, which is nothing but 37 degree centigrade, this ballooning expands. So, this particular ballooning, this ballooning particular expands and then, it is increases the diameter of the blood vessel. Again, this, so, these are certain designs which are spring like design, thermal memory stent, or it can be balloon expandable. So, in balloon expandable we have a particular tubing, we insert certain balloons and we have stent over it and once we start ballooning, once we start filling in the air in the particular balloon we have also a stent which is lying over the balloon. So, that particular stent also grows in size along with the balloon, this is nothing but the balloon cavity, which basically starts filling in with air, so, the overall lining around it, that is nothing but the tubing or the lumen of the vessel, it also starts increasing. So, we can see that balloon expandable stent can also increase the overall diameter or the lumen of a particular vessel.

There can be fourth type which is stent of a biodegradable polymer.So, we can again have certain polymer biodegradable, polymer which can be inserted as a stent and then it can also start releasing certain drugs which are required for the along that particular regime. So, we can have certain cardio drugs which are available for reducing the thrombosis out there. So, we can see there are certain designs, overall there is certain stents which are required for maintaining or increasing the lumen of a particular vessel and it counteracts the restenosis or the reduced blood flow by a percutaneous

transluminal coronary angioplasty, or which is also called balloon angioplasty. It has certain designs which can be either sprig like, which can expand; it can be thermal memory stent, which can again retain its original shape- so, basically we take it, we take a stent we compress it and then we insert it into the tubing and up on experiencing the temperature of the blood it again starts regaining its original shape which was much bigger diameter and in process that increases the lumen of a vessel.

And it can also be balloon expandable stent in that particular case we have a particular balloon, which has a stent over it, and as soon as we pass the gas or air into that particular balloon it increases in diameter and in process it also increase the diameter of the stent, which remains there for a longer time, and in the process it has a increased the lumen of the vessel. And it can also have, the stent can also be a type of a biodegradable polymer in which case which we have a biodegradable polymer which goes in and starts dissolving so that the original lumen can be restored and with time that polymers starts dissoving and provides the space for the blood flow. And again, this bio degradable polymer can also carry certain drugs if required for the cardiovascular surgery.

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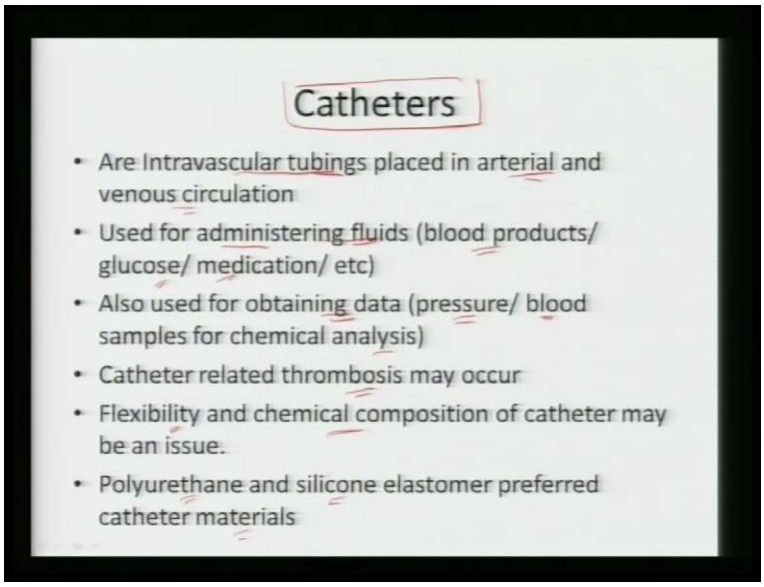

And there is another class which is called catheters, these are nothing but intravascular tubings which are placed either in the arterial or the venous circulation. So, this catheters are the tubings which are basically required for either administering fluids, so, in certain cases when a surgery is done we need to introduce either blood products, glucose or

medication then these catheters come to our rescue. They are also used for obtaining certain data such as what is the pressure or the blood samples for certain chemical analysis. So, that is the overall applicability that catheters or intravascular tubing, which are either placed either as in the arterial or the venous circulation used for administration fluids, which can be blood products glucose or even the medication.

They can also be utilized for the obtaining the data which can be the pressure or blood samples, and, but the problem with catheters is that it can lead to thrombosis. Again, one more requirement of a catheter is that it requires much more flexibility and also its chemical composition should be suitable so that it should not become an issue later on. And there are certain materials such as polyurethane and silicon which are utilized successfully as catheter materials. So, again the catheters, these are nothing but tubings which require either to administer fluid or gather some data, which can be pressure or blood, but there are certain issues which can come as flexibility or the chemical composition of the catheters, and that might lead to thrombosis for long term usage. So, again, certain metals as a polyethylene or silicon have been utilized as catheters.

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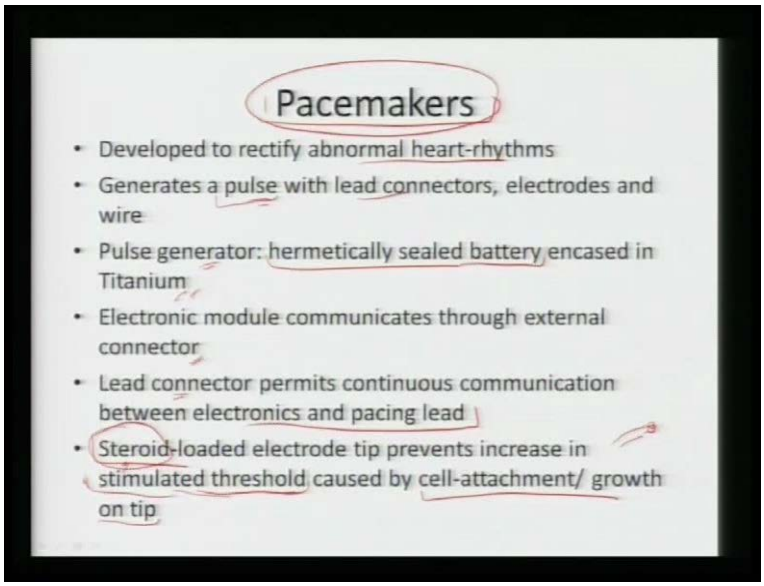

There is another class of device which is called pacemaker and this is utilized for rectifying the abnormal heart rhythms. So, what a pacemaker does is it generates a pulse with certain lead connecters, electrodes and certain lead wires. So, basically, we have pulse generator which is hermetically sealed, which is hermetically sealed battery which

is enclosed again in a titanium and then, electronic module will communicate through external connectors, and this external lead connectors permit continues communication between the electronics and the pacing lead. So, what is happen there is it can also, the lead connectors or the electrode tip should also have certain steroids which will increase the stimulated threshold, which are there to restrict the simulated threshold because in certain cases that can occur by the cell attachment or the growth on the tip. So, if you have a particular electrode it can have a certain cell attachment or the growth on the tip, so, we need certain steroids to prevent that increase in the threshold, so, that particular part is restricted by inducing certain steroids on the tip of the electrodes.

So, we can see the pacemakers are utilized for rectifying the abnormal heart rhythms- it needs to have particular heart rhythm to keep the heart beating. So, it generates a pulse on a particular frequency which are connected with lead connectors, electrodes and wire, and that particular pulse generator is sealed, it is sealed which is encased in the titanium alloy. Again, the electronic module will communicate through external connector, which basically permits continuous communication between the electronics and the pacing lead while providing certain fluidic sealing to it- so, that is what is there. And then, again, there are certain steroids which can be induced on the tip of the electrode to prevent increase in the simulated threshold, if it goes beyond that basically, there can be excessive beating of this particular heart and it will lead to hyper increased pressure in the system.

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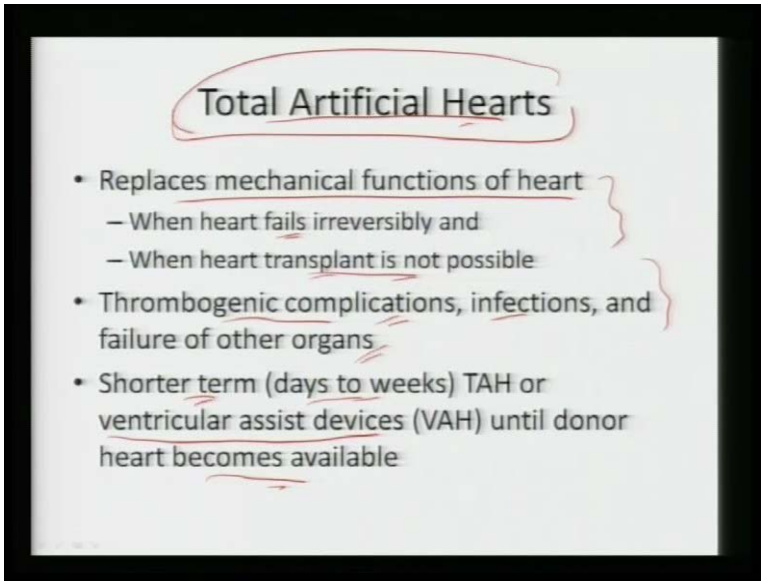

Again, then, one more problem can be eliminated by utilizing total artificial hearts. In this particular case what happens is this total artificial heart replaces the mechanical functions of the heart, and this is required when heart fails irreversibly and again when heart transplant is not possible. So, but this total artificial heart can induce some thrombogenic complications, lead to infections and failure of other organs such as kidneys, or liver- so, in that particular case we require total artificial heart and heart surgery. But again this total artificial heart surgery is very much essential when we do not have a donor which is available right now for a heart transplant. So, ideally, since they cause much more complications and fractions and failures of other organs, they are basically utilized for some shorter terms, from days to weeks.

Also there is some other device called ventricular assist devices, those are utilized until the donor becomes available. So, now, we are utilizing either T A H or V A H for shorter duration until we have a next donor available to donate a heart, and this becomes a requirement when heart is completely failed and when the heart transplant is not immediately possible- so, instead of their longevity these are being utilized for short duration, from days to months, or to weeks.

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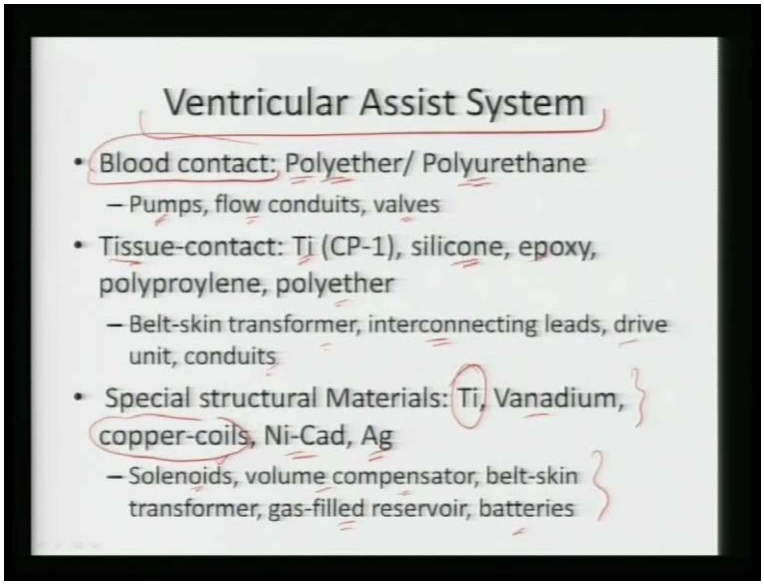

Again, then, ventricular assist systems, they come in blood contact, so, we have certain, in the metal assist systems we have many materials which becomes of importance such as for the blood contact, for the blood contact we have polyether or polyurethane, and the

blood contacts regularly happens either in pumps or flow conduits or valves. So, in that particular case when the blood contacts is occurring we need to utilize certain materials which can be poly ether, polyurethane to assist that total heart replacement.

It can again be tissue contact. So, again, tissue contact will require certain materials such as titanium, which is commercially pure, silicon, epoxy, polypropylene, or polyether; again, these are basically come when we have a belt-skin transformer, which have certain inter connecting leads, certain drive unit, or even conduits. So, this tissue contact will become of prime importance when the device itself is coming in contact with the tissue. So, in that particular case we require material such as titanium, silicon, epoxy, polyether, or polypropylene.

Again, there can be certain special structural materials which need to bear the load, or need to perform certain functionality, those can be solenoids for generating the pulse, it can be volume compensator again, belt-skin transformer, can be gas filled reservoir or even batteries. And these materials require materials which can be titanium, vanadium, copper coils for the solenoids, nickel cadmium, even silver or copper for connectors. So, we can see that overall, in overall either for total heart replacement or the ventricular assist system, we require the device to be in contact with the, so, we can see that in either in total heart replacement or the ventricular assist systems, blood contact and tissue contributes becomes of prime importance. So, in certain (( )) such as which are flow conduits, or even valves, so, there we need to see, we need to particular, design a particular device that can take care of itself, and we need to have certain specification for certain materials which can come out to be polyether, polyethylene, silicon, epoxy, or titanium.

Again, there are certain structural materials which can be also required for performing the structural or the weight bearing part of it, or any other functionality which can come out from the solenoids, volume compensator, belt-skins, gas filled reservoirs, batteries. So, we require certain materials which can be copper coils, nickel cadmiums, silver, vanadium, titanium. So, we can see the overall functionality of this particular device depends on the overall functionality of a particular material which can be utilized in certain regime.

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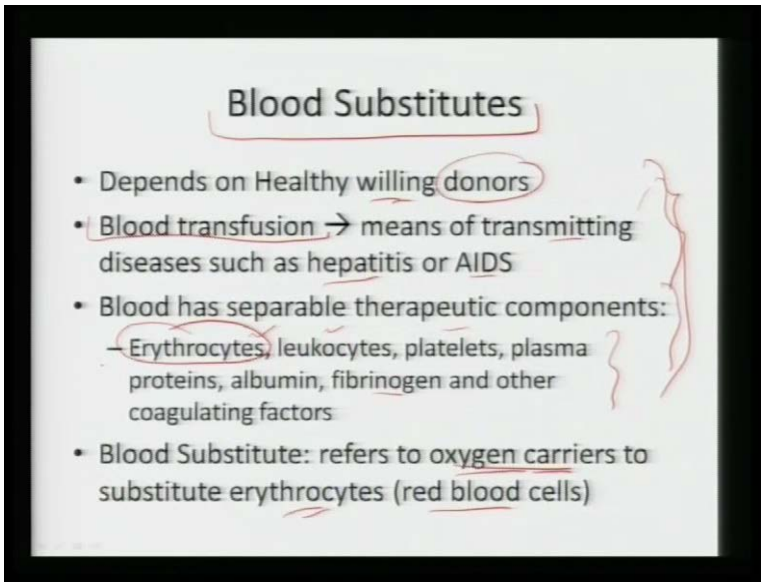

There can again be blood substitutes. Again, blood substitution depends on the healthy and a willing donor, so, that is very much essential that the donor is to be willing and as well as healthy. But again the blood transfusion can create certain problems which become a means of transmitting diseases, which can be even hepatitis, even aids. Blood basically contains certain separable therapeutic components which can be either erythrocytes, leukocytes, platelets, plasma proteins, albumins, fibrinogen and even other coagulating factors- so, we can see that the blood transfer, blood basically has so many constituents, therapeutic components, which can be separated.

But blood substitute refers to the oxygen carriers, which basically (( )) for substituting erythrocytes or red blood cells. So, the blood substitute is nothing but, it refers to oxygen carriers which can contain the oxygen and then, it can substitute red blood cells. Again, it has to, the blood substitution has to depend on a particular or willing or a healthy donor. But blood transmission can creates certain problems- it can transmit diseases such as hepatitis or aids. So, apart from so many constituents, we are mainly concerned about the erythrocytes or the red blood cells to take the functionality of the erythrocytes in terms of oxygen scavenger.

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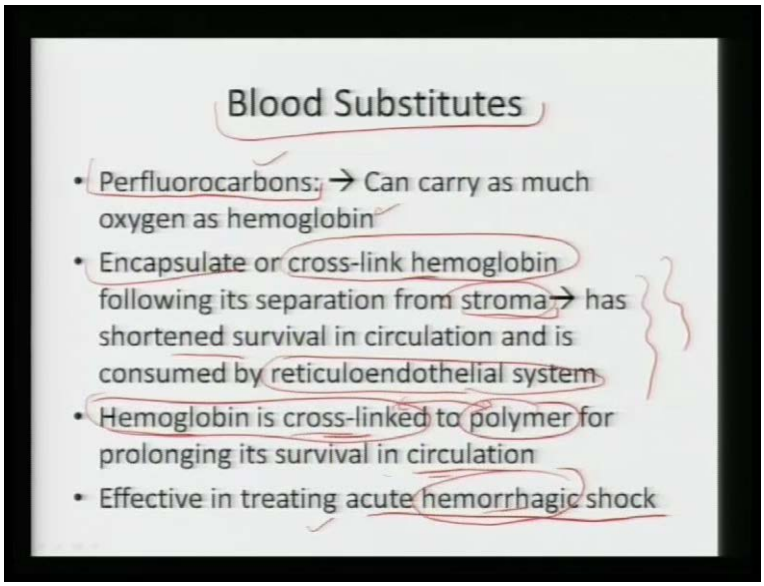

Again, there are certain materials which have something called perfluorocarbon which can carry as much oxygen as hemoglobin. Again, they can be alternatively applied by encapsulating erythrocytes, by cross-linking hemoglobin and basically separating it from the stroma. But the problem with encapsulation is that it has a very short survival time when it comes to the circulation, and it is immediately consumed by the reticuloendothelial system- so, once we cross, once we have the cross link or encapsulated hemoglobin, that once, after that is separation from the stroma its life time in the circulation its very, very short because it get consumed by the reticuloendothelial system. So, the overall over all, basically, aim in cross linking this particular hemoglobin is that it can prolong its survival in the circulation- so, once we have hemoglobin and we cross link it with certain polymer then it can prolong its survival in circulation, and that becomes very, very effective once we are treating some acute hemorrhagic shock.

So, once there is much more problem in treating a particular hemorrhagic shock then, we can supply hemoglobin which is again cross-linked and then, it can reduce the damage by cross-linking into the polymer and then releasing it into the circulation stream. So, in certain hemorrhagic cases it can be effectively applied once it is cross-linked to a certain polymer because that will prolong its survival or the overall survival time in the circulation, so, that can basically assessed in recovery.

So, we can see again blood substitutes, perfluorocarbons can carry as much oxygen as hemoglobin, so, they can be effectively utilized. Alternatively, we can encapsulate this hemoglobin, or cross-link the hemoglobin and then once we have cross-linked then, it can, the survival in the circulation becomes much more prolonged, but encapsulation will make it get consumed very quickly by the reticuloendothelial system and this becomes very, very essential, the cross link becomes very essential once we have certain acute hemorrhagic shock.

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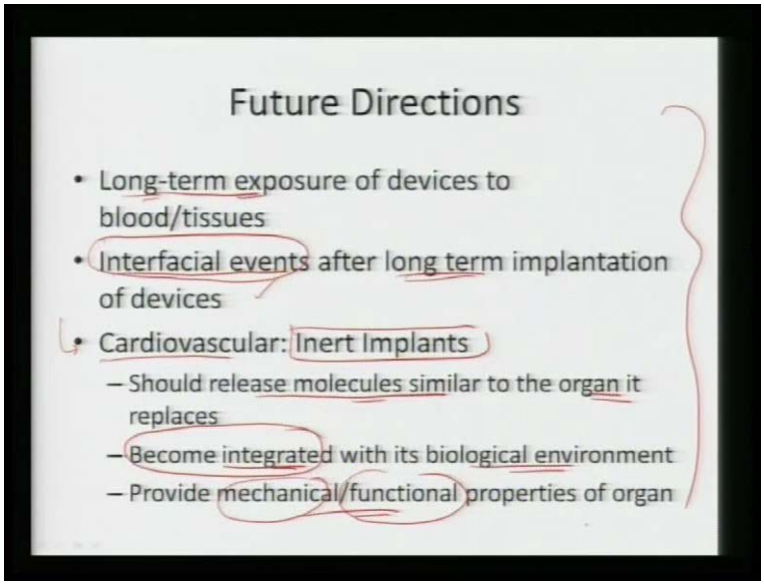

Again, the future directions basically go on to evaluating the long term exposure. So, in this particular case we can, we have to see the long term exposure of devices to bloods or tissue, so, because the short term is very, very easy and it can, it can basically suppress the overall infections, or it takes certain time for the cells to respond to a particular material, so, short term exposures of devices they are now very much limited and the future direction is face towards long term exposure of devices to bloods and tissues. So, the device has to perform satisfactorily under the contact of blood or tissue for a prolonged time- so, that is where the future is basically going. And again, interfacial events they become of prime importance because as soon as this particular device is inserted into the body it will, it will absorb certain protein adsorption then, release of certain harmful bacteria or even infection.

And again, there is some formation of fibril or fibroses or macrophages over the surface, formation of pseudointimal tissues, or such features. So, that basically can degrade the overall functionality or the mechanical properties of the device. So, it becomes essential to study the interfacial events which occur after the long term implantation. So, again long term exposure of devices to bloods and tissues and seeing what is happening at the interface between the device and the surrounding tissues after long term implantation such as something has been proposed for the cardiovascular devices, that it need to have inert implants because we do not want any tissues to grow on it otherwise, it will start reducing the lumen of a particular vessel, or it will remove the, it reduce the functionality in terms of either pacemakers, which need to be free from any cells,, or even drug delivery which needs to supply the drug, or even sensors because sensors need to be exposed to the blood stream continuously. So, overall inert implants can be, inert implant has to be utilized for the cardiovascular devices.

And again, the overall functionality which is required by the cardiovascular devices is it should release molecules which are similar to the organ which it is replacing. So, the overall implant has to release molecules which are basically similar so that the overall functionality of the organ can be mimicked by the device. And again, they should become integrated with its biological environment. So, if a particular device is being now inserted into the body, it should perform as it is natural to the body, so, it should become integrated with the surrounding tissues or the biological environment. And also, it should provide mechanical or functional properties of the organ, it should sustain the mechanical loads which a particular organ has to sustain also, perform the functionality of a particular organ which it is replacing.

So, that is where the overall natural future direction is leading us to, it can, it is long term exposure of devices to bloods and tissues, considering the interfacial elements even after long term implantation, and the usage of inert implants so that there is no toxic or any adverse effect which arises from the surrounding cells or tissues, and they should release molecules which are similar to that of a organ which it is replacing, it should get integrated with the biological environment and it should also provide mechanical as well as functional replacement for the organ which it basically is going to serve.

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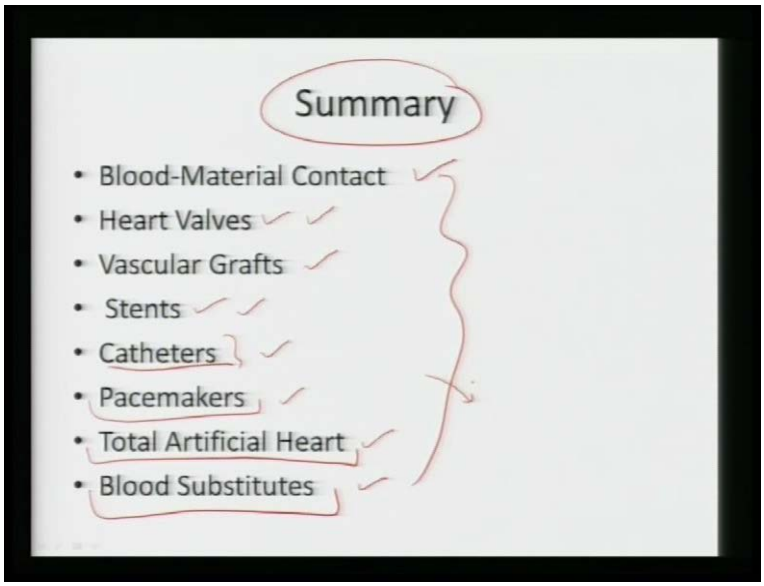

So, in summary we did see that the overall blood material contact is becomes of prime importance, that as soon as blood is basically becomes in contact with the material it starts depositing, adsorbing proteins on the surface then, releases certain acting agents which starts covering, forming the fibrins, or the fibrin which are (( )) the microphages, and then, forms a pseudointimal lining over the implant, so, that can be either helpful in certain cases, may be deleterious in certain cases.

And we also saw that heart valves they can be either of the ball type or the tilt type, so, that can be utilized for assisting the blood flow or catering to the (( )) in the valves. So, these valves have to tailor accordingly. Again, there can be vascular grafts, this can be either autografts or the xenografts, so, depending on where the grafts have been taken from. Sents, these are again utilized for improving the lumen of a particular vessel, they can arise again by ballooning or by spring like, those can again be from the shape memory, nitinol type, or those can again be rising from the biodegradable polymer.

So, again, stents can, they are utilized in terms of restoring the lumen of a particular damaged artery. They can be again catheters for excavating certain data or information, or even supplying nutrients to a particular regime. And they can they can pacemakers for restoring the rhythm of the heart, so, that, in that particular case we require pacemakers for actuating the rhythm at certain frequency. There can be again total artificial heart for in certain cases when we do not have donor rightly available, or when the total

functionality of the heart is being hampered. So, for certain duration, for short durations from weeks to months or even from days, we have to wait until the donor is ready to donate a heart, so, for that particular time, we need that heart has, the functionality of the heart has to be totally given up to certain machine. And there can again be blood substitutes basically, for the erythrocytes or red blood cells when the oxygen scavenging has to be being taken care by certain materials, so, we did see that we can either encapsulate it or we can apply material, supply with a material which can store the hemoglobin for certain duration.

But by storing the hemoglobin or encapsulating it, it gets consumed very quickly in the circulation, so, we need to supply certain cross linking to polymers which will prolong its survival in the blood stream. So, we can see the overall applicability of this particular device is becomes of major importance because of, it undergoes blood material contact, utilized in heart valves, vascular grafts, even stents, catheters, pacemakers, even for total artificial hearts and blood substitutes. But the overall functionality here is very, very different, in some cases we require certain cells to form, certain pseudo lining to form, pseudointimal lining to form over it, in certain cases we do not require any cells to form on it, or the form devices to really become a part of that particular functional organ, or it has to basically refrain from attaching it to the blood. So, there are certain requirements which basically are very, very different for this applications and that gives, that is basically leading us to understand more in detail that how a device can be supplied, how device can be applied for restoring a certain functionality, and what should of materials are required for engineering it. I will close my lecture here. Thank you