**Medical Biomaterials**
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**Lecture - 01**
**Introduction**

Welcome to the course on Medical Biomaterials. Hello everyone, I am going to talk about a new subject that is called biomaterials. I will be giving 40 lectures each lecture of about 30 minutes of duration. Biomaterials are of an origin I would say compare to other areas of biotechnology, it is encompassing several areas like medical biotechnology as well as materials and instrumentation analytical tools. So, it is a highly interdisciplinary subject and it is going to be very exciting, and I believe that next decade is going to be lot of research activities in the area of biomaterials and lot of industries that will be sprouting out related to biomaterials.

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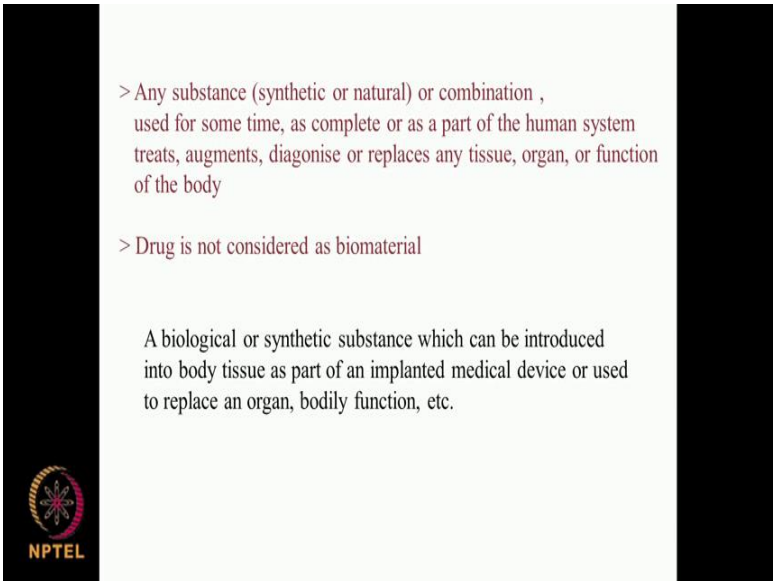


So, what is this biomaterial? Any substance, it could be synthetic or it could be natural substance or combination of these 2, synthetic and natural used for some time as complete or as a part in the human system. The idea could be for treating as some problem in human system or it is enhancing the function of something. It could be a diagnostic or it could be replacing any of the tissue organ or function that is called a biomaterial. See for example, I am keeping as stainless steel implant inside the body. So,

it is trying to replace the broken bone or it is trying to help the bone to heal faster, then that is called a biomaterial. I am keeping a bio sensor inside the body to monitor your glucose level as a function of time.

So, then that could be a biomaterial. I could be keeping a calcium sulfate or a hydroxyl appetite to fill up some parts in the bone than that is a biomaterial. Sometimes they keep pacemaker inside the body, so that it controls the heartbeats that is called a biomaterial. Sometimes they keep devices, so that the blood is pumped properly because sometimes the heart does not work to the full extent. So, it is sort of augments the current heart than that is called a biomaterial.

So, anything it could be a natural material or could be a synthetic polymer or metal or ceramic kept inside the body for a short period of time, it could be for few hours like your catheter urinary catheter, or it could forever if there is a hip replacement that may last for many years. Or it could be a stent inside the cardiovascular system and that is expected to last forever. So, it could be very short duration, it could be a medium duration, it could be a very long duration that is called a biomaterial.

So, biomaterial encompasses several aspects of material and it encompasses the entire body system. So, it can be as simple as the urinary catheter. It could be slightly complicated as your glucose sensor inside the body. Or it could be a permanent fixture like your cardiovascular stent or stainless steel implant to replace a bone and so on. Actually all these are biomaterials. And nowadays, with lots of cosmetics surgery that is coming into picture rehabilitation after an accident or problems associated with congenital again biomaterials are used biomaterials are used for replacing different parts of the facial. So, that sort of it is helps in the cosmetics the implants in the oral cavity they are again called a biomaterial.

So, biomaterials encompass a large number of a material, and various parts of the body which are being replaced or augmented. Sometimes these biomaterials are removed after a short period of time or medium period of time or sometimes the biomaterials are kept inside the body. And it is expected to degrade on it is own. Or sometimes they are removed with a second surgery. For example, they implant some drug allotting biomaterial; once the drug has been allotted the biomaterial may be removed with a small insurgery. So, all these are called biomaterials, but please remember drug is not

considered as biomaterial. Whereas, all other things are considered as biomaterial like the example I mentioned about.

Another definition for biomaterial: a biological or a syntactic substance which is introduced inside the body, as part of an implanted medical device or used to replace an organ. Nowadays, people are talking about artificial heart artificial kidney and dufferin valves cardiovascular stents. So, all these are artificial devices which are kept to replace either a damaged body part or a deceased body part or body part which has been damaged because of accident. So, all these have to do the bodily function. So; that means, it has to do the bodily function. So, if a joint is replaced with metal joint the metal joint has to do the function of the original human joint and it has to last forever until the person is alive.

So, biomaterials encompass several areas of a research know it could be medicine it could be biology it is chemistry tissue engineering material science physics. So, many different areas of a science and engineering disciplines or encompassed as the part of these area of biomaterial. So, anybody can work in the area of biomaterials; that means, it is not possible for one person to become an real expert. And introduce a product to the market you need the help of a several different disciplines to bring out a product from the bench right up to the bed of the patient. So, it is highly interdisciplinary and that is why I said it is biomaterials research is going to be the most important research field in the next coming decades. And there are going to be lot of companies who will be marketing who will be researching or bringing out products in the area of biomaterials. And I believe that India also will be forefront in the area of biomaterial research.

So, there are many issues one need to consider when you are having a biomaterial, because the material is kept inside the body, whether it is for a short period of time or very long period of time. So, the material has to be biocompatible what does this biocompatible means.

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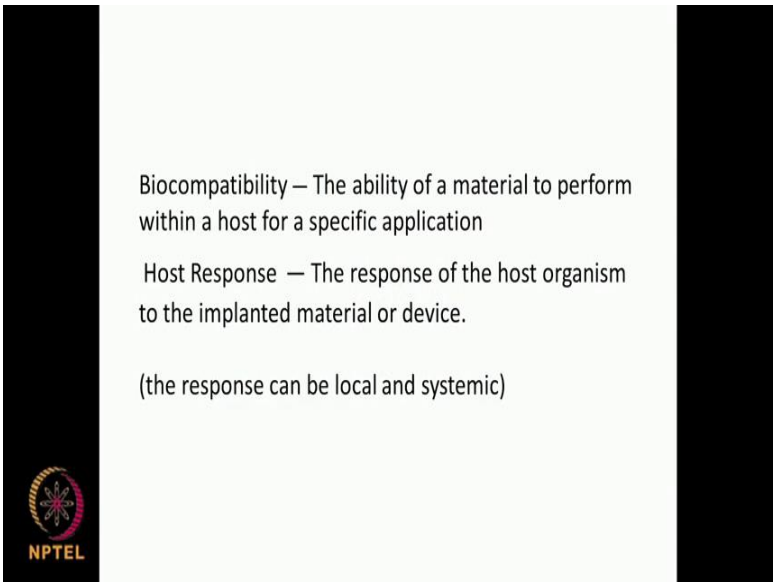


So, when a foreign material is placed inside the body. It should perform it is duty within that host for that particular application. And it should be compatible, it should not be a causing any toxicity or any harm to the host. So, if I keep a cardiovascular stent, it should not cause inflammation it should not cause any other adverse reaction and which may lead into a rejection of the material. So, biocompatibility is very important when you design, material that has to be placed inside the body. Even you must have heard that if urinary catheters are placed inside the body for passing of urine. After a few days the patient feels pain sometimes infection develops and so on because there is non-compatibility between that material and the host.

The next one is host response. What is the response of the host to the implanted material? That needs to be thought of. Sometime the host response can change. The way I respond to a bio material placed inside the body as against you responding to the same biomaterial placed inside the body could be very different. For example, if you take hip joints. These hip joints are made up of nickel chromium type of material and there is always possibility of leaching out or bearing out of these materials and entering the host.

So, some patients may have adverse reactions to these materials a very low concentration. We are talking terms of ppm, but still some patients may have adverse reaction to these materials that is getting leached out whereas, some patients may not have any inverse reactions. So, the worst response can change from person to person for

the same material. The response could be local; that means, wherever it is placed inside the body it could be local or it could be entire system. For example, if you take a poly lactic acid. Poly lactic acid is a polymer; it is made up of lactic acid. And it is a well approved biomaterial. It is approved by the FDA that is food and drug administration authority of USA and it finds many applications inside the human body as a biomaterial.

When this poly lactic acid degrades little bit of lactic acid is produced which is slightly acidic. So, there could be a very local acidity which may harm the cells nearby, but if you take the entire human system the acidity will not change, but in the very local environment there could be acidity which may have certain adverse reaction on the cells or the tissues near where the material is placed. So, local responses can be systemic. Sometimes you place a cardiovascular stent there could be inflammation in the region where it is placed whereas, rest of the body will not have any adverse reaction at all. So, there is always difference between local and systemic.

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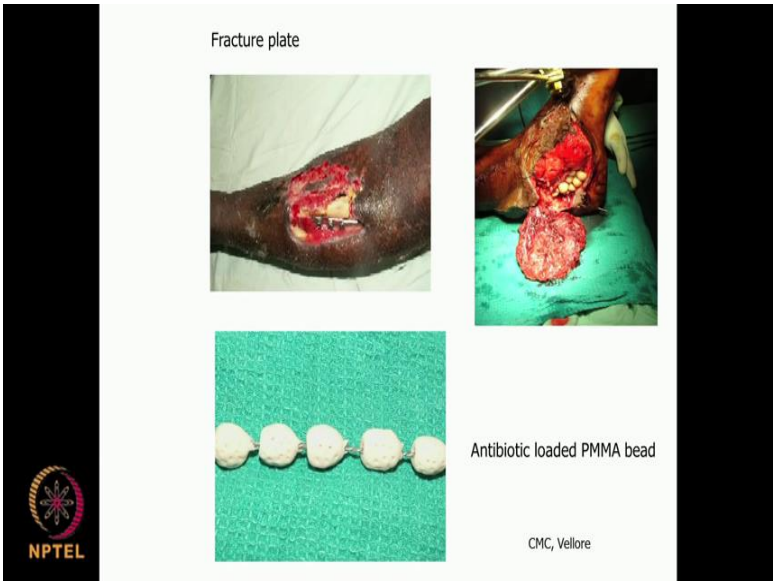


So, I want to show couple of pictures of biomaterials. For example, this is a fracture plate. These pictures are got courtesy from CMC Vellore in Tamil Nadu. So, as you can see there is a stainless steel rod placed. Here as a fracture may augmenting material. After a bone fracture; now they place a poly methyl methacrylate with antibiotic. The antibiotic slowly gets released. So, it prevents infection from and bio film formation on the stainless steel material. In fact, this is what this is the drug loaded poly methyl

methacrylate bead. So, they are placed inside. So, so after fracture they keep these stainless steel rod and they also keep a drug loaded poly methyl methacrylate beads. So, the drug gets slowly released as a function of time. And it prevents the infection; that means the bacterial infection. It will also prevent the attachment of the bacteria or the bio film formation. So, the stainless steel rod here is a biomaterial and the poly methyl methacrylate beads is also a biomaterial.

So, we need to consider all the aspects like biocompatibility whose responds local responds system responds all these when we are designing these biomaterials. We will talk about all these much more in detail later.

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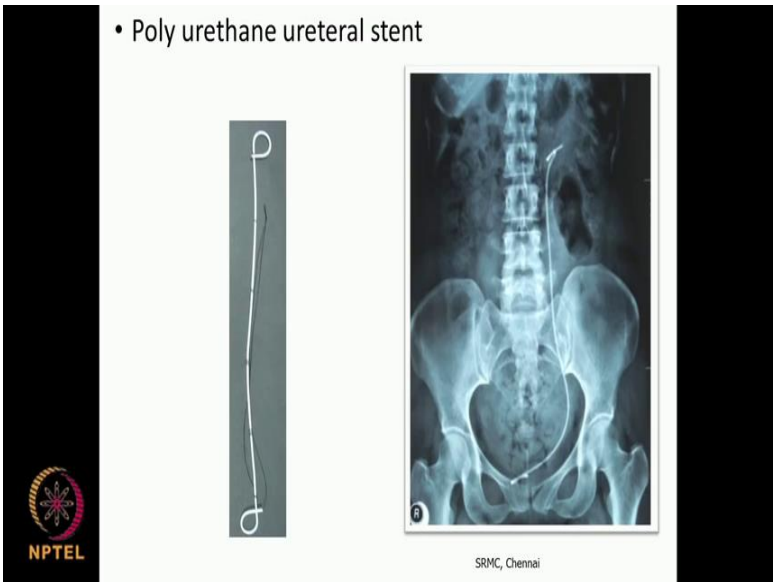


Now, I want to show you another biomaterial. This is a polyurethane ureteral stent. This is a ureteral stent made up of polyurethane. Polyurethane is almost like rubber. So, it is very flexible. This is a x ray of that. So, this ureteral stent is placed between the urethra and the bladder. So, it allows the urine to flow nicely down the bladder. Sometimes there could be stones which may be blocking the ureter. Or sometimes there could be infection which may be preventing the urine to flow. So, they place these ureteral stent as you can see here. So, that the urine flows nicely come down to the bladder.

So, this is a biomaterial this is made up of polyurethane. So, it is very flexible and generally after a stone surgery, generally nowadays stones are not removed through operations, they may use some ultrasound to break the stones. The stones broken stones

will come out through the urine. So, it may take a couple of weeks or 3 weeks. So, they would like to have these ureteral stent placed inside the ureter for about 4 to 6 weeks. So, this this ureteral stent has to perform it is duty; that means, it should be biocompatible should not cause any infection to the patient. It should not break. So, after 4 to 6 weeks the ureteral stent is removed, whereas in the previous case we are talking about a stainless steel implant which is done after the fracture of the bone. So, this stainless steel is going to be there inside the body forever as long as the patient lives or alive.

So, you see 2 different situations where the stainless steel implant stays inside forever, whereas, the ureteral stent has to stay only for 4 to 6 weeks. And look at the environments, environments are very different. Here the polyurethane is facing the urine environment; that means; we have several salts like calcium oxalate and it will be also or going to face bacteria like equalite, protease, and mirabilis. So, this is a very harsh environment whereas, if we go to this environment, there are generally no bacterial infection, there are no salts. You are talking only exposure to blood, plasma, protein and so on actually.

So, this environment is very different, whereas this environment is very different. So, the biomaterial I showed you in the previous case is a stainless steel implant has to stay for several years, but the environment is mild. It should be accepted by the whole system without causing any problems to the human. In this second case we are talking about a polyurethane biomaterial, which as to remain inside for 4 to 6 weeks, but the environment is very harsh it should not cause any salt precipitation which is found in the urine. It should not allow any bacterial infection to get enhanced especially bacteria like equalite protease mirabilis.

So, there is no single answer in while designing a biomaterial. We need to understand in which location it is going to be placed, how long it is going to be placed, whether it is days, weeks, years, months. What is it being functions it has to carry out. Because for example, in these areas the 2 examples I showed you, the biomaterials are inert; that means, it does not have to carry out any function, but whereas, if you are talking about diaphragm valves. They have to move up and down. So, it is carrying out some function or if you are talking about joints the joints rotate move in a 3 dimension. So, it has to carry out some function.

So, when you design a biomaterial, we have to consider the time duration, the location, what is the function it is augmenting and the type of materials we are going to use and so on actually. So, we need to consider quite a lot when you are designing biomaterial. So, there is no single design for biomaterial. So, when you consider all these aspects your design changes. That is why there is lot of scope for doing research and that is why we need expertise from polymer chemist or material scientist or medical practitioners or physical chemist and so on actually.

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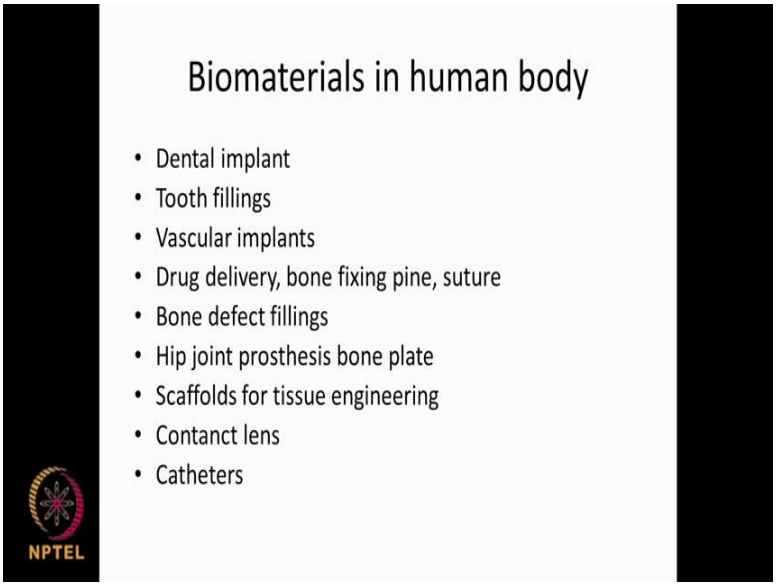


So, as I said biomaterials are being nowadays used in large numbers and trying to replace all parts of the body. Dental implants these have been very old going back to even thousands of years, when many thousands of years back humans had their teeth's replaced with artificial materials. So, dental implants; tooth filling different types of fillings like mercury, like poly methyl methacrylate, acrylic acid and so on. Vascular implants near the heart region, vascular grafts, you have graft from valves, you are replacing different parts of the heart.

So, those are vascular implants. Drug delivery systems, we have different types of drug delivery systems made up of biodegradable material, the drug could be antibiotics, and the drug could be growth enhancers and so on. Bone fixing materials; so of a bone is broken into 2 parts, we are trying to fix it using bone nails or pines or wires. So, all these are biomaterials. Stitches, stitches after an operations external stitches are there, nylon

was used originally which is not biodegradable, but nowadays they use a lot of biodegradable stitches internal stitches. So, again they have biodegradable or bio absorbable polymeric material.

Bone defect filling; defects in the bone which has come due to birth defect or happened due to accident. They use different types of fillings, materials like poly methyl methacrylate, meth acrylic acids, and calcium sulfide hydroxyapatite. Hip joint prosthesis bone plate. So, we have joints, where joints get replaced by using metals, different types of metals, single metals even combinations of 2 3 metals with combinations of polymer. Bone plate, especially after orthopedic or a bone graft, then scaffolds for tissue engineering. This is one area which is growing quite a lot in the past 5 to 10 years. You are trying to grow different cells on surfaces. So, they are called scaffolds. And these scaffolds are generally made up of polymeric materials. So, these tissues once they are grown can replace defective tissues or tissues which are infected inside the human body.

Even your contact lens is a biomaterial, because it is remaining inside eyes for a long period of time. So, it is in contact with the whole system. It should not be causing any adverse reaction. It should not cause inflammation and so on. So, contact lens is a biomaterial. Catheters: different types of catheters urinary catheter cardiovascular catheter, so different types of catheters. They stay inside the patients performing certain function, for a short period of time; that means, that means it could be hours or slightly for a longer period of time that could be weeks. So, all these are biomaterials and much more actually.

And as you can see each biomaterial has to perform certain function each biomaterial has a different location. Each biomaterial stays inside the body maybe spanning hours going right up to years.

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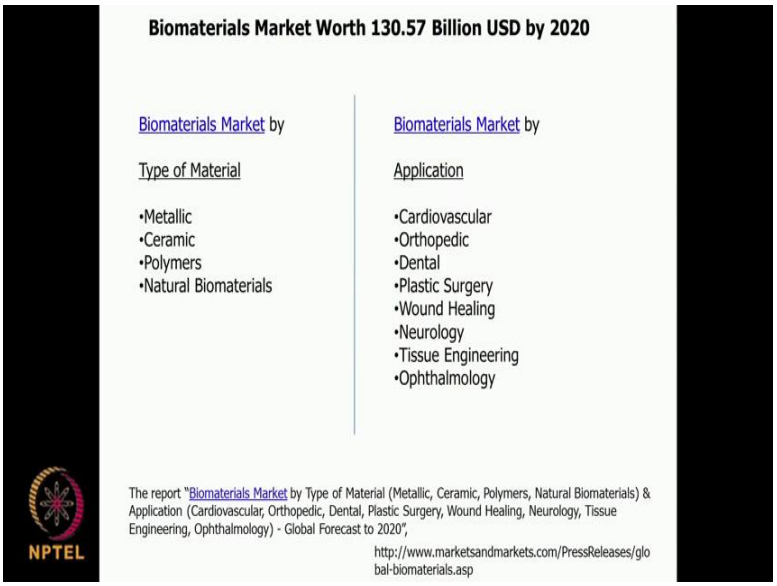


So if you look at the biomaterial market it is a huge business. They estimate that by the year 2020 it could be 130. It could be billion US dollars. So, this market is divided into based on type of material. It could be metallic material like metallic means you are talking about titanium stainless steel chromium nickel. It could be ceramic material hydroxyapatite calcium sulfite oxides. It could be a polymeric material; that means, poly methyl meta methacrylate, poly ethyl ketone, poly lactic acid, poly lactic acid dichotic acid. It could be natural biomaterial, like gluon cyclodextrins hyaluronic acid. So, these are (Refer Time: 23:34). So, all these are called natural biomaterials.

So, it is broken down in terms of type of material or it is broken down in types of application, applications for cardiovascular, it could be a cardiovascular stent, it could be cardiovascular graft, it could be a patch, it could be a diaphragm, orthopedic it could be orthopedic plates, screws, joints. It could be dental, dental means orthodontic application teeth, jaw replacement. It could be a plastic surgery. Plastic surgery is one area which is growing a lot. It could be plastic surgery related to facial parts; it means ear, nose, eyes, and skins. Wound healing, especially after a burn injury or could be chemical injury, harm what type of biomaterials is used patches, which will cure without causing adverse reaction or without creating infection.

Neurological: anything that is related to the neuron brain and so on. Tissue engineering is one area as I said is growing a lot nowadays. Can I grow tissues outside in the lab and

then plant it inside the body? So, can I grow heart muscle tissues? And then patch up my heart can I grow bone tissues and then replace bone defects. Can I grow neuronal tissues and then replace some defects in neuronal region? Can I grow tissues related to orthopedic or ophthalmology and so on actually? So, that is tissue engineering then comes ophthalmology like your contact lenses, ocular lenses all these come under ophthalmology.

So, the biomaterial market is broken down in terms of application and they are broken down in case of material. So, in the application you may have different type of sub material. For example, if you look at the orthopedic you can have stainless steel implants, titanium screws or poly lactic acid, reabsorb able screws or you can have drug delivery system with PLGA. So, you can have combinations of materials also in each of these applications. So, both are possible.

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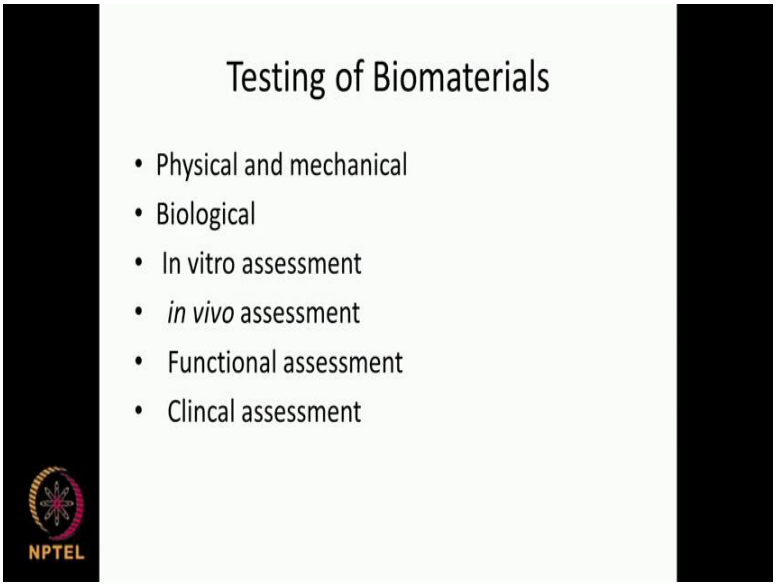


So, testing of biomaterials is also very important. Just like in drug discovery once a drug has been discovered, they go through lot of testing. It goes through animal testing human testing, human testing stage 1 stage 2 stage 3. So, biomaterials also have to undergo lot of testing processes. So, you may have a physical and mechanical testing. So, if it is diaphragm valve it has to open close. So, it has to have certain tensile strength flexural strength. Then biological testing, is it biocompatible, is it causing any toxicity any ginotoxicity.

Then in vitro assessment; that means, using laboratory instruments or using laboratory cell lines, in vivo assessment; that means, using animals maybe rabbit is maybe Ginny pigs, even larger animals like dog or sheep that is in vivo, then functional assessment. If you are talking about artificial valve it has to open and close every few seconds, hundred thousand times. So, can I do that and see whether it really works. Then comes clinical assessment. So, here the clinician comes into picture and they have a look at it maybe test it out or on a voluntary patience and then see whether it performs it is duty.

So, lot of assessments lot of testing has to be done on biomaterials before they are really introduced to the market. It is almost like testing of drugs you need to go through a rigorous testing physical mechanical biological in vitro in vivo, then clinical testing before it is actually introduced to the market. So, the time duration could be several years, just like drug testing. So, you have to keep that in mind. So, one cannot directly bring a product from the lab right into the patients bed. It has to go undergo lot of testing before it is approved.

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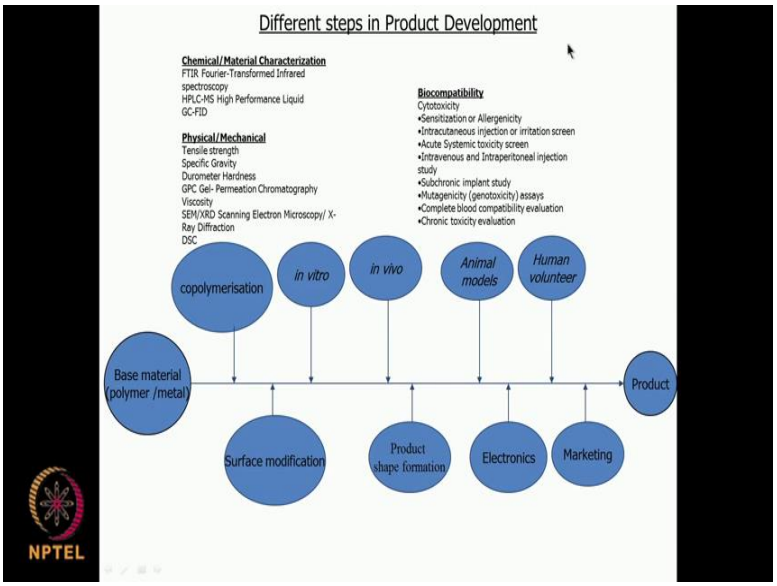


So, there are a large number of steps involved in the product development of biomaterial exactly like drug discovery. So, as soon as you try to decide on a base material it could be a polymer, it could be a ceramic, it could be a metal or, it could be a combination of that. So, we mix them and prepare the material. Then the material needs to be modified into this on the surface. So, that it becomes biocompatible. That is called surface

modification. Once that is done it goes into in in vitro testing. And in vitro testing it may like I said it may involve cell line work, it may involve looking at a physicochemical testing. It may look at mechanical properties like tensile strength specific gravity hardness viscosity depending upon the type of material. Then it goes into in vivo testing when we talk about in vivo it could be animal's different types of animal's small animal's large animals.

Then we need to make the product into the designed shape. For example, if you are talking about a hip joint, then it should have a ball like shape and a socket like, socket may be made up of sub material the ball may be made up of material. So, the product shape formation is there. And then again you need to test it out in the animals to see if it performs well in the animals, and in some cases we may have to include electronics also. For example, if you are talking about devices which help the performance of the heart. For example, there is something called ventricular assist device, which will help in pumping of the blood, because patients whose heart cannot pump blood of enough quantity or rate. These devices are incorporated or embedded inside the body. So, those devices require power. So, we need to have an electronics embedded into them. If you are going to have a biosensor implanted inside the body, it needs to send out signals to the external device. So, there has to be some electronics.

And then once the entire material is prepared comprising of the both the material and the electronics. It may have to be tested on human volunteers. And then finally, the material goes into marketing and product launching. So, lots of steps are involved when one is talking about bringing a biomaterial right from the lab into the bed. Lot of testing physical mechanical, chemical, biological, testing are carried out. That is why it is extremely interdisciplinary area where we talk about experts from different areas, biological sciences, mechanical sciences, chemical sciences. Then when you bring it to in vivo testing then we need the help of clinicians. So, again different discipline is coming into picture. When and the biomaterial involved is some electronics, then we need help from the electronics engineers. And then finally, it goes into clinical trials and into marketing.

So, the whole area of biomaterial is extremely interdisciplinary and we need to have supports from various disciplines if you want to launch a product successfully actually. So, we will continue in the next class.

Thank you very much.