Medical Biomaterials
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Lecture - 40
Sterilization/Device failure

Hello everyone, welcome to the course on Medical Biomaterials. We are going to talk about sterilization and device failure. Sterilizing a material is very, very important whether it is for a short duration like your catheter or medium duration like cardiovascular, stents or even total knee replacement joints and so on actually. So, if devices do not get sterilized properly, infection is being carried inside which may lead to biofilm formation and finally, rejection of the material and the material has to be explanted out. So, sterilization is extremely important. Then we are talking about a biomaterial which is made up of metal or a polymer or a ceramics, so we cannot follow the same sterilization procedure because the polymer might not be able to withstand a very high temperatures, whereas metal will be able to withstand high temperatures. So, we need to have different strategies. So, we are going to look at some of those in this particular class.

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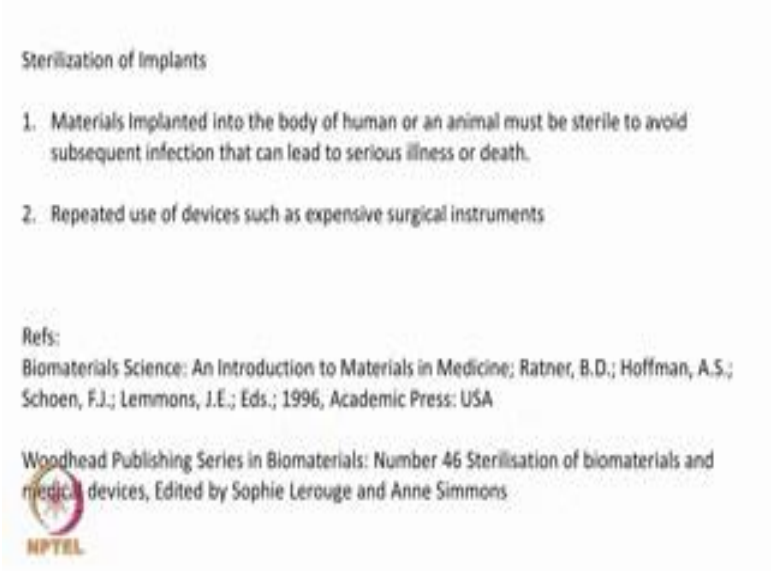

So, sterilization of implants, so materials implanted in the body or human or an animal must be sterile to prevent infection which can lead to serious illness or death to the host

number 1. Number 2, if you are using expensive instruments we do not want to throw them out. So, we would like to use them recycle them. So, we need to sterilize. So, whereas, if it is very cheap instruments like your catheters or even your syringes or needles, it can be disposed, but very expensive instruments of course, you need to sterilize.

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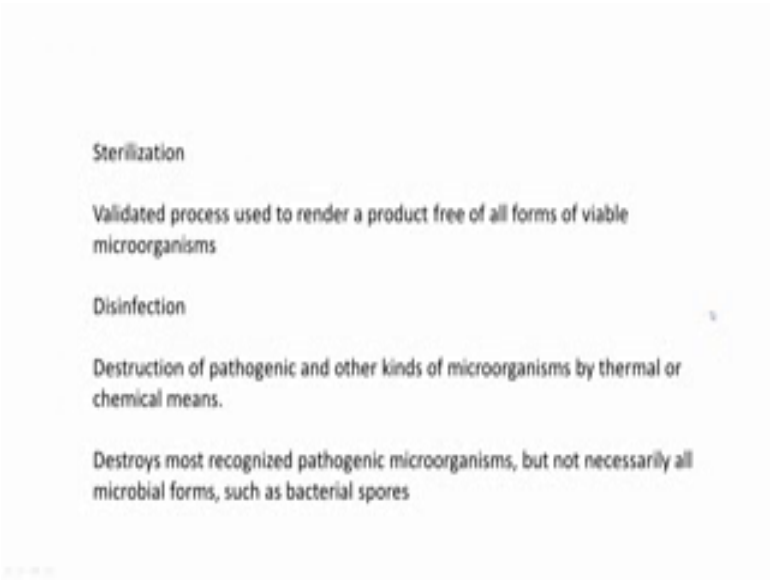

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These two are good references to have a look at. If you are looking at materials in medicine and is issues related to sterilization have a look at these two all. So, we need to have a validated process because every time we cannot use an ad hoc sterilization procedure. So, it has to be repeater, it should be rendered a product free of all forms of viable microorganism. So, sterilization is has to be a validated process. Disinfection on the other hand is destruction of pathogenic another kinds of microorganisms by thermal or chemical means. So, it destroys most recognized pathogenic microorganism, but not necessary all microbial forms, like spores because spores may be able to last longer and they may be able to withstand high temperatures. So, it might kill many, but not completely. So, it depends upon the threshold the lower limit.

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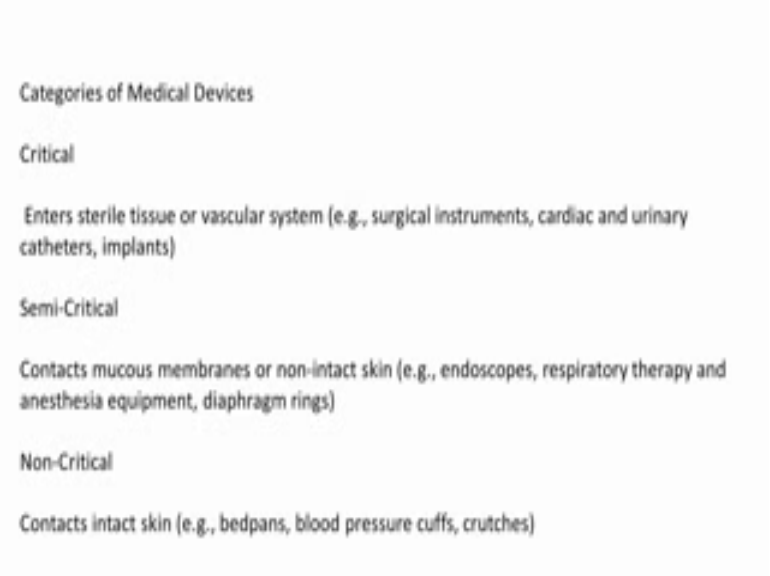

So, if you look at categories of medical devices, one is called the critical, semi-critical, non-critical. What is this critical, like sterile tissue or vascular system, surgical instruments, cardiac, urinary catheters, implants, they are supposed to be critical systems. Whereas, semi-critical materials which are in contact with the mucous membranes, or non-intact skin like endoscope, respiratory therapy, unaesthetic equipments, diaphragm rings and then non-critical will be mostly bedpans, blood pressure, cuffs, crutches. So, they just come temporarily in contact and generally it will not be in contact with the body fluids much so they can be called non-critical. So, the critical is that which is going to be in contact with the body fluids may be kept inside the human system that is the critical one.

So, there is something called sterility assurance level this is a generally accepted minimum sterility for implants, generally it is called a probability of 10 power minus 6 that means, 1 in a million that the implant will remain non-sterile 1 in a million. So, there is still possibility of 1 in a million. So, if a hospital conducts 1 million surgeries, if you are following this SAL sterility assurance level then chances are there could be one in a million which will not have a sterile biomaterial.

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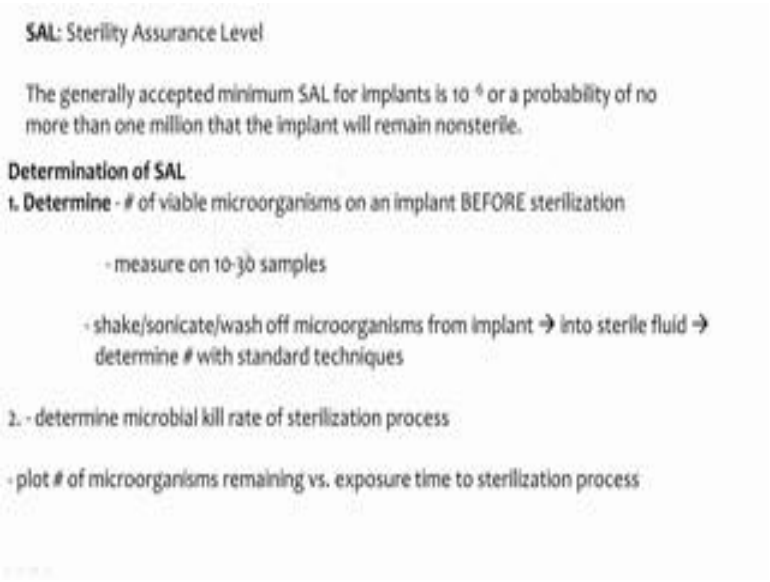

So, how do you determine this sterility assurance? So, we determine the number of viable microorganisms on an implant before sterilization that means you take 10 or 30 samples then we shake it sonicate wash off the microorganisms from the implant in to the fluid then determine the colony count it is called number of colony by growing them in agar incubating it over 24 hours. These are the standard procedures. Then after that you follow your sterilization procedure, and again repeat the whole thing and see; what is the effect of sterilization on the microbial kill rate.

Suppose, I am looking at time should I do for 10 minutes or 20 minutes or 30 minutes or 40 minutes sterilization? So, I can do at different times and see; what is the percentage of organisms that got killed. So, I plot a graph and then from there I decide what should be the time necessary for me to do the sterilization process, so that is optimizing with respect to time. Same thing we can do with temperature also, suppose I want to think about should I use 80 degrees, 90 degrees, 100 degrees. So, I can do the sterilization at various temperatures and then see what is the killing rate and then and decide on what should be my optimum temperature.

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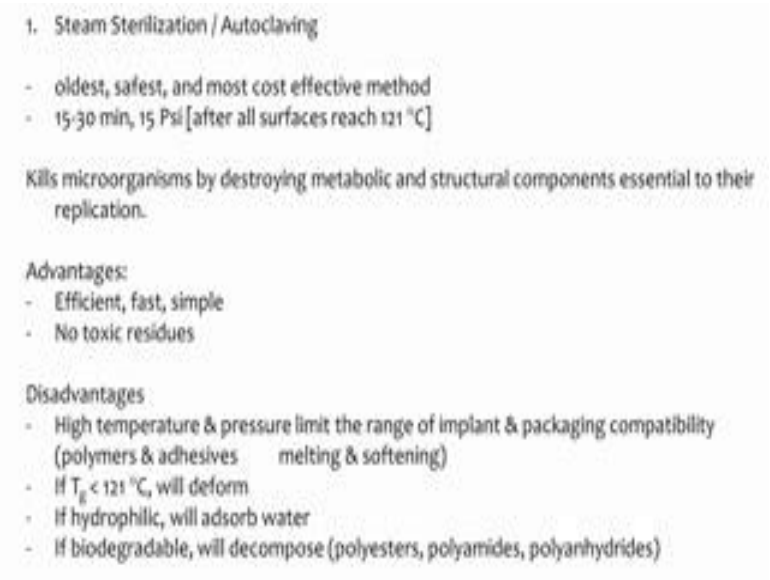

The easiest steam sterilization, this is the oldest method safest method. It is very, very cheap that means, we do it for about 15 to 30 minutes 15 psi. So, we can reach about 120 degrees it kills microorganisms by destroying metabolic and structural components essential for the replication. So, advantages they are very efficient fast, simple, no, it does not leave any toxic residues. Disadvantages of course, we cannot use it for packaging material, we cannot use it for polymers, adhesives, materials which may melt or soften; that means, if TG is less than 121 then material will get deformed, if I raise the temperature to 121 c. If it is a hydrophilic material, it may absorb moisture; if it is a biodegradable or decomposing material like polyesters then steam sterilization is not a good method.

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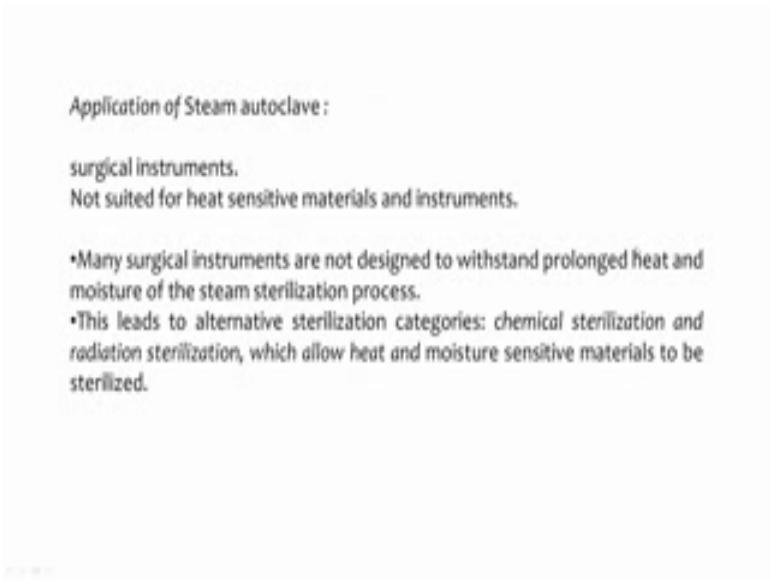

But it is the cheapest and it is been of course, we cannot do very prolonged heating because the moisture of the steam sterilization process may damage the material. So, we may have to go to chemical sterilization, radiation sterilization which can be done on heat sensitive or moisture sensitive materials. They are slightly more expensive.

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Radiation what do you do we use cobalt 60 gamma rays. So, it produces ionizing radiation of cobalt 60 isotope source. And then the dose sufficient dose is focused on the material then the material becomes sterile that is call the radiation.

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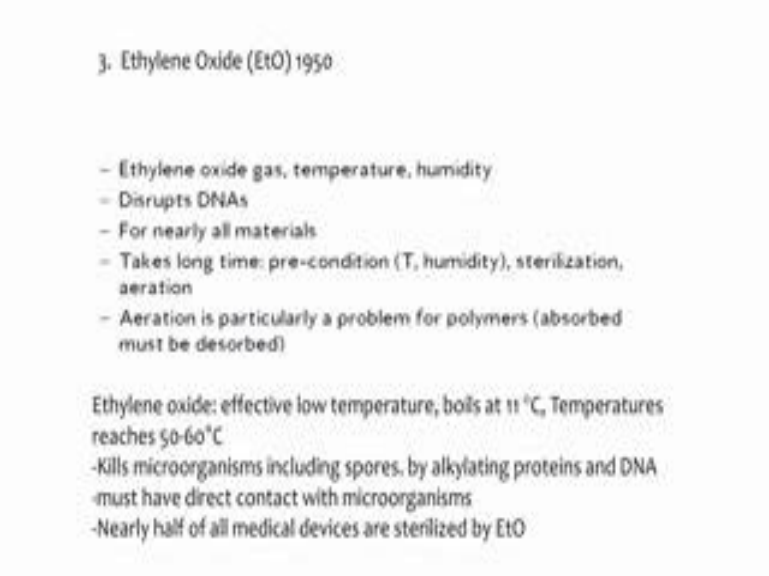

Approach another approach is ethylene oxide this also has been there for a long time. Ethylene oxide is a gas, it disrupts the DNA, and it can be used for all materials. Of course, it takes long time precondition, temperature humidity, aeration is a problem, but then if you are going to aerate it, then polymers if they are present, they may start absorbing air that is a big problem actually. So, ethylene oxide generally 50 to 60 degree centigrade, it kills microorganism including spores by alkylating proteins and DNA. So, they should have direct contact with the microorganism, because ethylene oxide will directly get in contact on with the microorganism and then do the job unlike the normal autoclaving approach. So, this is very, very widely used as it says half the medical devices or sterilized using ethylene oxide.

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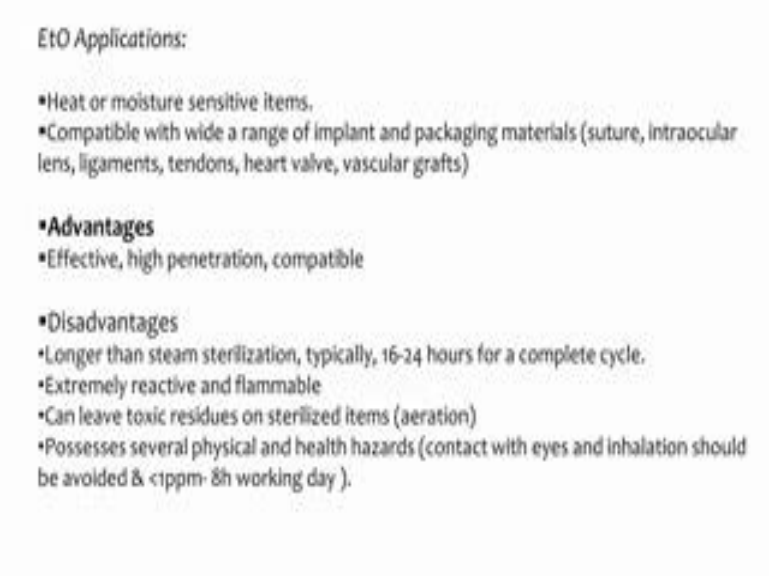

Heat or moisture sensitive material can be done with this. Compatible with a wide range of implant material packaging materials suture, intraocular, lenses, ligaments, tendons, heart valves, vascular grafts. So, it is very effective high penetration because it is a gas, it penetrates through the interstices and kills compatible. Disadvantage, it takes much longer time 16 to 24 hours, whereas steam sterilization we are talking in terms of 30 minutesm it is extremely reactive and flammable. So, we need to handle with care can leave toxic residues. So, we need to aerate it completely to remove them. It has lot of physical and health hazards contact with eyes inhalation should be avoided by the person who is doing this type of sterilization.

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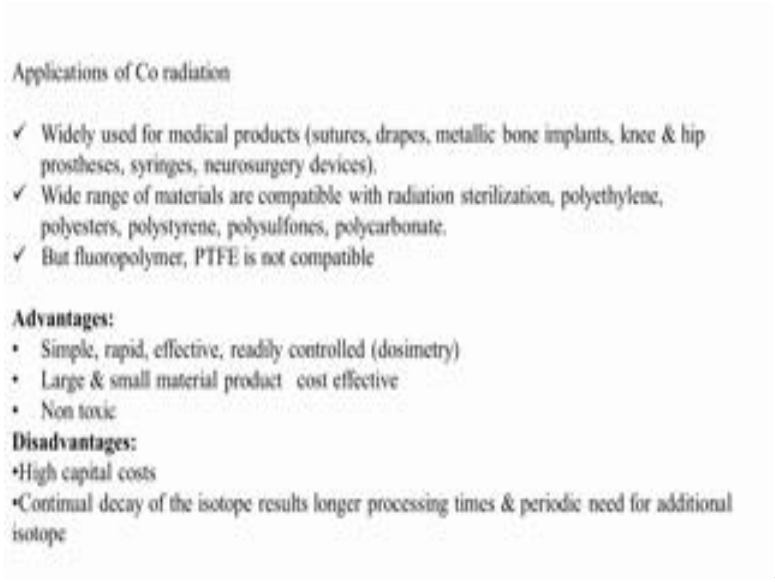

If you look at the gamma radiation, cobalt widely used for medical products against sutures, drapes, metallic bone implants, knee hip, prostheses, syringes, wide range of materials are compatible with the radiation. Polymers like polyesters, polyethylene, polystyrene, polysulfones, and polycarbonate of course fluoropolymers like PTFE is not compatible. It is a simple rapid effective can be compared controlled by proper dosing. Large and small materials can be done cost effective not toxic, but it is very expensive because we need to have a cobalt 60 source and we need to get lot of approval from the atomic energy for handling a cobalt 60. There will be continual decay of the isotope. So, we need to do a very long processing time, so that all the cobalt 60 is completely decayed out.

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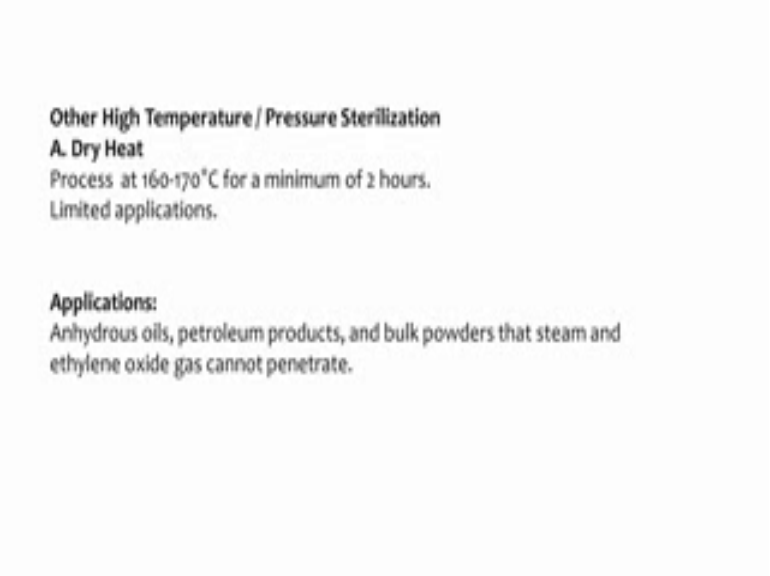

So, other high temperature techniques, dry heat; we can go up to 160, it is not a steam sterilization it means you do not use steam, it is just dry heat, 2 hours limited applications. Oils, petroleum products, bulk powders that steam and ethylene oxide can penetrate because if I am having these steam that is water can penetrate in to these or even ethylene oxide can penetrate into this, so that is called the dry sterilization. Temperatures are high and it is a limited application.

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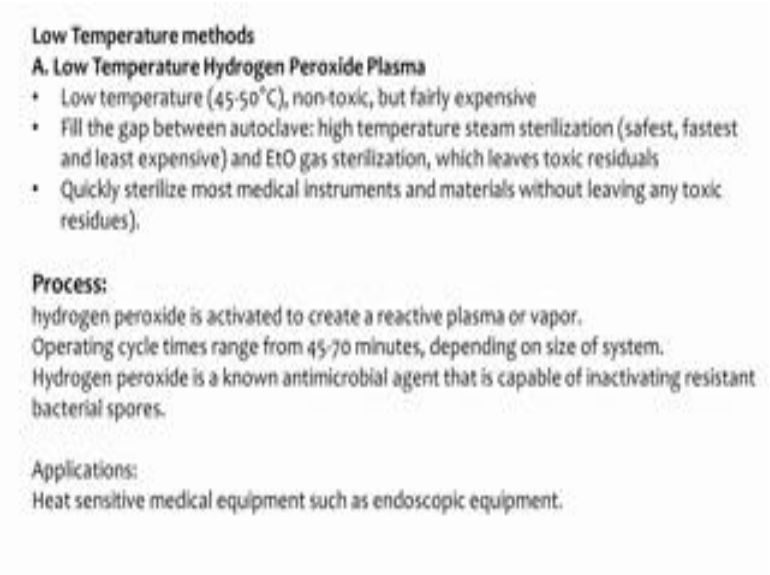

Then of course, we have lower temperature methods like hydrogen peroxide plasma around 45 to 50, of course, it is expensive because we are using plasma. So, this is a method good between autoclave and high temperatures sterilization, because ethylene oxide may leave toxic residuals, so high temperature is better. Quickly sterilize most and medical instruments material without leaving any toxic material because hydrogen peroxide is a gas, it is activated to create a reactive plasma or vapor. The time is also less 45 to 70 minutes. Hydrogen peroxide of course, it is a very good antioxidant and then it is very good antimicrobial agent, so it can kill many spores also. So, you can use this for heat sensitive material equipment such as endoscopic equipment that is called hydrogen peroxide plasma method.

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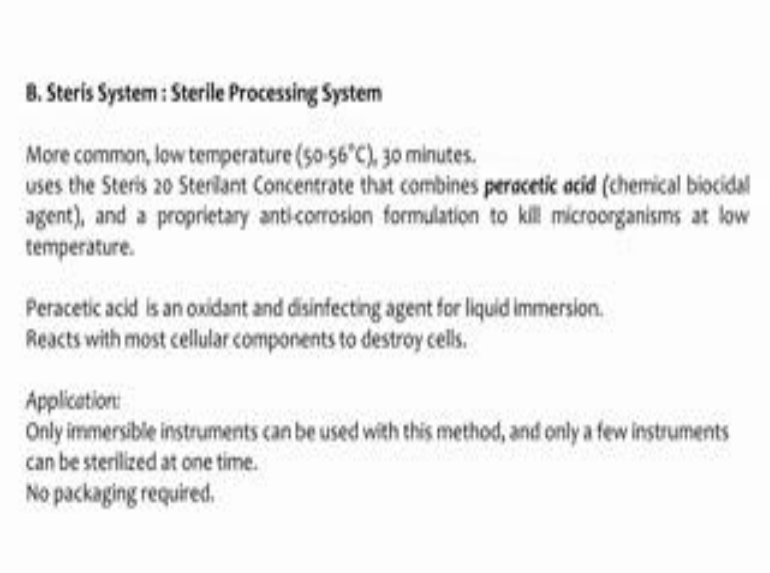

Then we have sterile processing systems, where we are using 50 to 56 degrees 30 minutes. We use peracetic acid, where peracetic acid as is an oxidant and a disinfectant, so we can use this. So, it can kill microorganisms at low temperatures. So, we do not have to go 100 in autoclave or 150 or something. So, it reacts with most cellular components to destroy. So, it is a sterile processing system using peracetic acid. So, what we do is we have to immerse the material or the instrument. And if the material cannot be immersed then we cannot use this method and we do not need to have a packaging for the material also. So, it is got some disadvantages.

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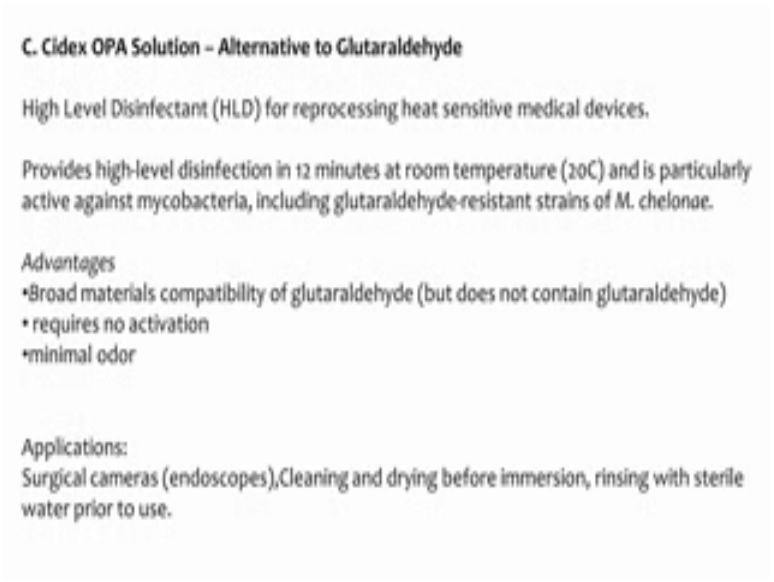

Then there is another method where you are using high level disinfectant HLD, this alternative to glutaraldehyde, because glutaraldehyde also can be used as a sterilizing agent. In 12 minutes at room temperature and it is very good even for mycobacteria including glutaraldehyde resistance chelonae. So, here you are using high-level disinfectant. Broad materials compatibility of glutaraldehyde requires no activation minimum odor, so surgical cameras, cleaning and drying before immersion, rinsing with sterile water prior to use and so on actually. This called as cidex OPA solution this contains high level of disinfectant.

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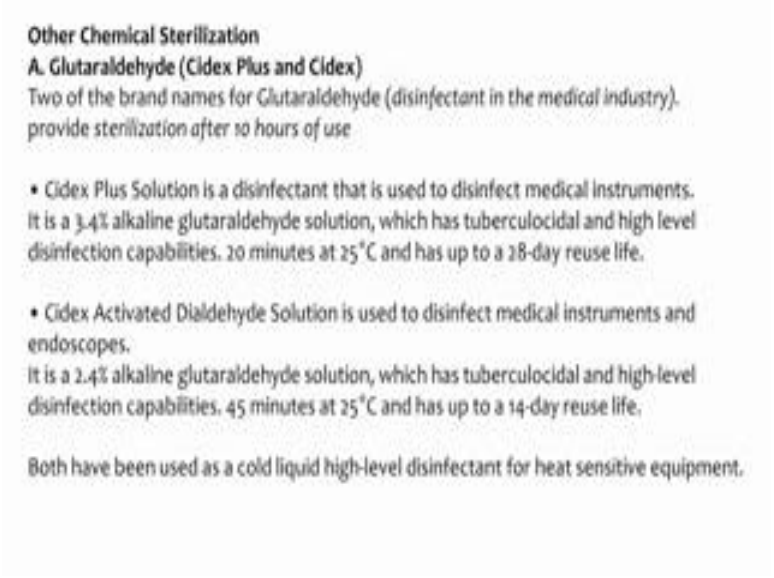

You can use glutaraldehyde also of course glutaraldehyde after sterilization will give smell. So, you need to have it left out, so that all glutaraldehyde vapor evaporates. Now, there are some band products I mean there are some brand products there brand names for glutaraldehyde cidex plus and cidex. So, the side cidex plus is contains 3.4 percent alkaline glutaraldehyde. So, 20 minutes, 25 degrees, so we can take in lot of bacteria even tuberculocidal and high-level disinfection.

The other one is cidex activated dialdehyde solution this contains 2.4 percent alkaline glutaraldehyde solution. So, you need to put it for 45 minutes, 25 degree centigrade. So, we can use it at a very room temperature that is 20-25 degree centigrade and it is got very high-level disinfectant only. So, these are solution based we have high concentration of a sterilizing instrument disinfecting liquid or we can use glutaraldehyde, alkaline glutaraldehyde of two different compositions these are a liquid based method. So, we can dip the material in that.

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Then hydrogen peroxide in vaporized form for sterilization and then plasma is called a VHP MD series. Cycle time is 2 hours, operating temperature 30 to 40 degrees centigrade. So, we use hydrogen peroxide and as you know hydrogen peroxide is very good antioxidant, so it can kill. And then we use plasma radiofrequency energy. It is very expensive it of course, takes care between steam sterilization and ethylene oxide gas sterilization.

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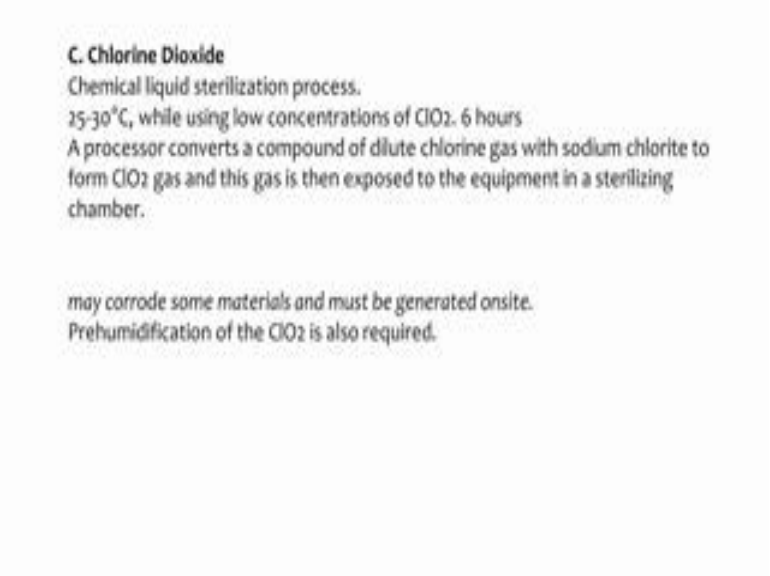

Chlorine dioxide this is the liquid and so this is a liquid base sterilization 25 to 30 degree, 6 hours. So, how do you produce this liquid dilute chlorine gas with sodium chloride to form chlorine dioxide gas, and this gas is then exposed to the equipment in a sterilizing chamber. So, we have sodium chloride, we have chlorine gas, so they produce this chlorine dioxide and even equipment is exposed to this. Of course, material may get corroded, because this chlorine dioxide extremely corrosive, we have oxygen and chlorine both can corrode metals. Prehumidification of chlorine dioxide is also required so that means we need to add little bit of moisture in to them. So, lot of different methods.

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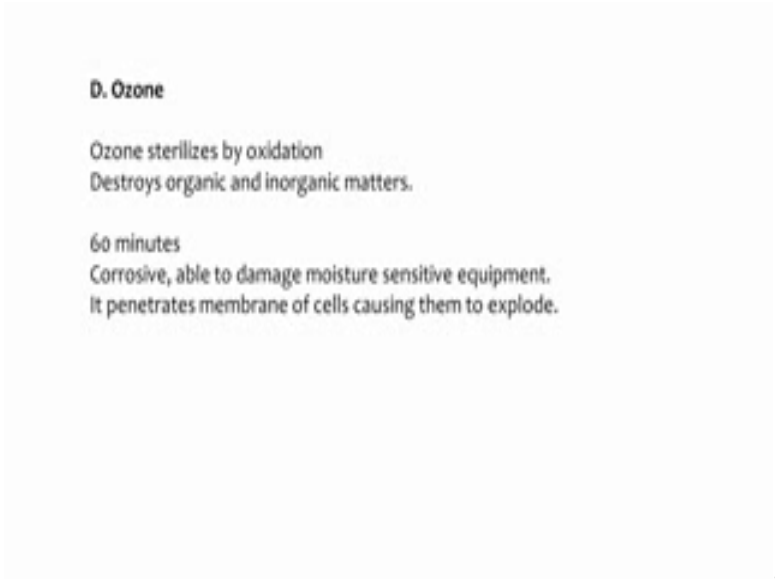

Of course ozone, ozone as you know it is a very good an oxidant. So, it can also sterilize, it destroys organic and inorganic matters, generally 60 minutes, it is also very corrosive, it may damage moisture sensitive equipment. It penetrates membrane cells causing them to explode.

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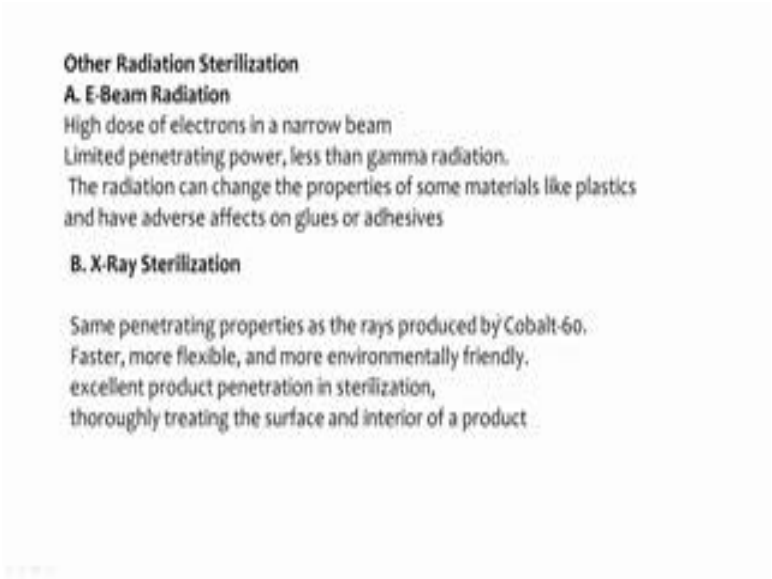

Of course, other radiation sterilization X-ray, E-beam like that is electron beam radiation, high dose of electrons in a narrow beam; it is got very limited penetrating power less than gamma radiation. Of course, the radiation can change the properties of the material,

especially plastic they may lose some of the mechanical properties even optical properties. X-rays again same penetrating properties as cobalt 60, faster, more flexible, more environmentally friendly, it is good for penetration, it also helps in thoroughly treating the surface or inferior of a product. So, large number of methods we saw. We have the steam, we have the dry heat, then we have the ethylene oxide, which is widely used and then we have different types of a liquids glutaraldehyde, chlorine dioxide, hydrogen peroxide then disinfect and high concentration of disinfectant where the material is a dipped in and so on.

But of course, the ethylene oxide takes care of 50 percent of the biomaterials that needs to be in sterilized. The steam sterilization is cheap method that takes care of many of these products. Of course, that is not very suitable if the material is heat sensitive or it starts absorbing moisture and then we may have to go for a glutaraldehyde other type of make methods. Of course, the smell of glutaraldehyde has to go, so it has to be left open for a long time and so on. So, different methods are being practiced in the area for biomaterial, because material before implanted into human or animals needs to be completely sterilized, it should be free from bacterial infection.

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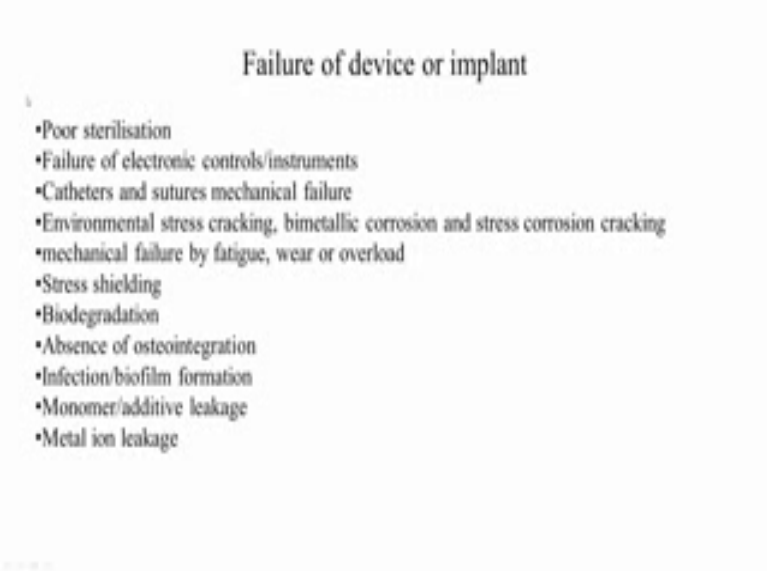

So, device failures, devices fail many, many reasons are there for the failure of devices. We saw some of them during the course of our lectures, and they could lead to either debilitating effect or very serious even death. There have been many examples of a

device related death as well as a permanent damage to the human. Poor sterilization of course, we saw that if the sterilization is poor and you have bacteria entering the human system, it could lead in to biofilm formation infection, inflammation, finally rejection of the material. Failure of electronic control instruments nowadays lot of electronics is being used your pacemakers as well as assisted ventricular devices, artificial heart so many devices and nowadays defibrillator they all have some electronics in to it there will be some controls; failure of these electronics that could be one problem.

Mechanical failures like we use catheters, we use sutures, they just break and the internal fluid may pop out or infection bacterial may go inside. If you are using a urinary catheter, it breaks because of mechanical, you are going to have a lot of body fluids getting mixed up that is the mechanical failure. And of course, diaphragm valves can have a mechanical failure and so on actually, but your vascular grafts can have mechanical failure, your dental implants can have mechanical failure, they were orthodontic materials can have mechanical failures, mechanical failure could include the stress related or it could be compression related or and so on actually.

Environmental stress cracking bimetallic corrosion stress corrosion. Metals have one big problem they corrosion different types of corrosion - bimetallic corrosion, stress corrosion, heterogeneous distribution of elements corrosion and so on actually, because the body fluids contain lot of inorganic salts pH conditions are very acidic. So, they are all very easy to be get corroded. So, the corrosion is a big problem especially in orthopedic area and as well as in dental area. So, wear, fatigue, like I said diaphragm valves, joints knee joints they may undergo fatigue where the ball and socket overload. So, you are putting too much load.

So, the materials could break or crumble or crack because of overlord. Stress shielding. So, we have stainless steel or titanium implants going parallel to the bone. So, most of the load is taken by these metals. So, there is a lot of the bone loses, the load carrying capacity, so stress shielding can happen biodegradation. So, if you have a polymers they may start to degrading because we have a enzymes like lipases, (Refer Time: 23:09) inside the body which may slowly degrade of course, we have oxygen also. So, there could be oxidation taking place. So, polymeric material may start degrading, so that is a issue.

Once it starts slowly degrading, you may lose its mechanical strength it may lose other properties. Absence of osteointegration, so if you have material, which do not integrate, so they will remain separately from rest of the surrounding of course, they may lose an out. This can happen in teeth, this can happen in the orthopedic area, so loosening of joints, because they do not integrate with the surrounding tissues. Infection biofilm formation, this is a very serious problem because of a poor sterilization or because of practices bacteria may enter which may get multiplied it may get attached on the surface of the polymers and lead to biofilm formation infection rejection we studied a lot. And in the early rejection of a biomaterial the first few days the week is predominantly because of this biofilm an infection that is why generally large amount of antibiotics are given to the patient to prevent bacterial infection and biofilm formation.

Monomer additive leakage this is also very common. Dental acrylic acid leakage is a problem, rest of the body you can have the polymeric plasticizers and other material other material which may be leaking out, so that could be toxic to the person actually, like additives. Of course, when metal on metal interaction or where could lead to a release of a metal debris which could be toxic, sometimes patients have a nickel toxicity or cobalt toxicity and so on actually. So, that is the metal ion leakage especially that is a problem and artificial knee joints. So, a lot of issues are there because of which your biomaterial can fail, so one need to consider all these aspects when you are designing a biomaterial, be it a metal, be it a polymer, be it a blend or be it a ceramic.

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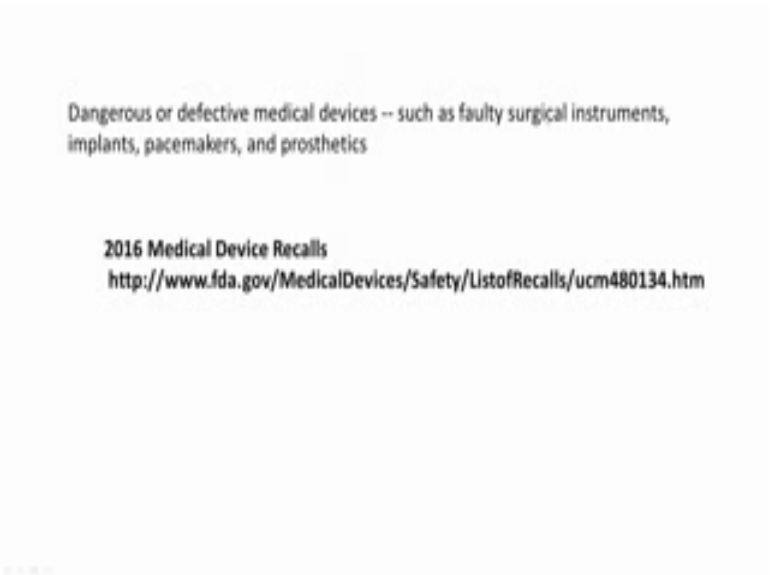

And of course, a dangerous defective medical devices faulty surgical instrument, implants, pacemakers, processes and so on. You can have a look at this website it shows you some real examples of a list of recalls of medical devices by various companies because of the faulty designs, it is very interesting to read some of these problems

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So, FDA also had observed many device failures, recent medical device failures. And they have listed them like inadequate sterilization. As you can see sterilization bacterial infection is the most important; inadequate sterilization for an orthopedic surgery tool, rust in an injection, ventilators with defective components, infant resuscitators with assembly error. So, if you have multiple parts which need to be assembled, there could be assembly error. Guidewire with flaking coating, so we have guide metal guidewires we may we may coat it with oxides to prevent corrosion, then as those could be flaking out.

Tracheal tube that kinks tracheal tube should not kink because if it starts kinking the area for the liquid to flow decreases, so the liquid might not flow at all. Unclear labeling that is another problem if the label is not clear which can lead to surgeon making a mistake either putting it in the wrong direction or the wrong product. So, these are some device failures that FDA had observed in their recent and this you can see it from this particular website. Again it is very, very interesting to have a look at them.

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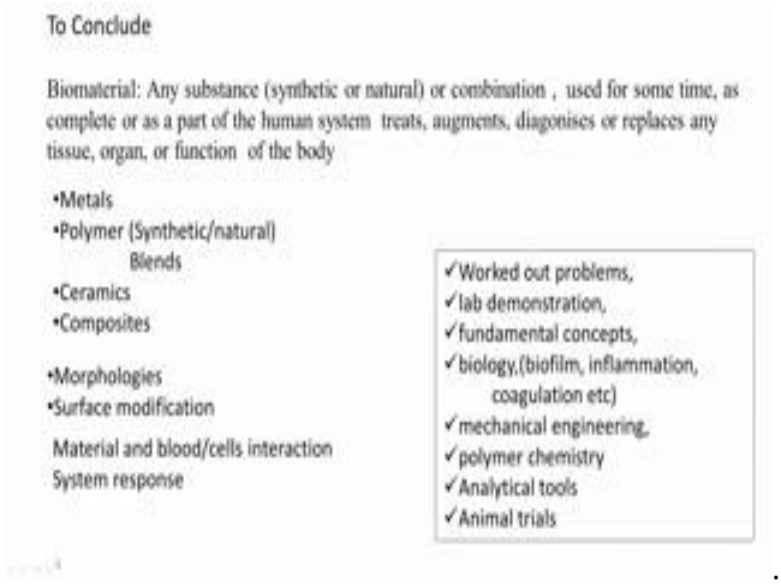

So, let us conclude on this course, the 20 hours course on Medical Biomaterials. We have had about 40 lectures; we have covered a lot in the past 40 lectures. So, biomaterial is any substance synthetic or natural or combination of this used for some time or for a very long time inside the human body. It could be a part of the human body, it treats, augments, diagnosis or replace. Diagnosis means it could be a biosensor something or. Replace any of the tissue or organ or function of the body that is called a biomaterial that is how it is been defined

Of course, drug is not a biomaterial, whereas if you have a drug delivery system, the polymeric system, which is carrying the drug that is a biomaterial. So, we have been spending a lot on this particular topic in past 40 lectures. So, we looked at metals, polymers, synthetic polymers; different types of synthetic polymers, natural polymers, polysaccharides, and proteins. Then we looked at blends that are polymer-polymer combination. Then we looked at inorganic material, ceramics, calcium phosphate, calcium sulfate, alumina, then silicates glass that is silica glass then we looked at composites combination of a carbon reinforce polymers, metal limping and then glass impregnated polymers and so on. So, we looked at large number of this.

Then we looked at morphologies. Different types of morphologies we also had some demonstrations of a experiments how to prepare beads, how to prepare nanoparticles, how to prepare films, how to prepare electro spin fabrics, how to prepare polymer gels.

So, different morphologies we saw experimentally. Then a surface modification using a dip coating method, using a spinning method, how to modify a polymer surface or a metal surface, so we can have antibiotic or antibacterial material coated on surfaces. So, again we looked at it experimentally as a demonstration. So, we studied the material and blood interaction, material cell interaction, system responds like inflammation a large number of a biological functions that take place, when a material is implanted into the body. So, we looked at all those as well.

So, this course you can see it is very interdisciplinary, we had problems related to mechanical engineering, problems related to biology and some problems related to polymer chemistry. So, here we worked out a lot of problems we had lab demonstration we looked at fundamental concepts in mechanical engineering and polymer in biology we looked at what is this biofilm, inflammation, blood coagulation etcetera. Then we also study in polymer chemistry, I spent a few lectures on analytical tools because biomaterials has lot of analytical tools used for looking at the surfaces looking at the bulk looking at changes in their chemical properties and so on actually. So, lots of analytical tools are used, so we looked at them. And then we spent short time on animal trials. How these animal trials are conducted, what are the issues in animal trials one needs to consider, what animals are used for what type of study and so on.

So, the whole course has been a combination of a engineering, biological science, analytical chemistry, and polymer chemistry. And I hope you enjoyed this entire course, we also had lot of assignments at the end of a each week, which was which was supposed to help you to recap what you studied in that particular week, so that should have been very beneficial for you. And you can always use this video as your future resources as well. So, whenever you have any doubts or you want to refresh certain areas, you can go back to that particular video, and have a look at them. And of course, we also will be having a final exam where you can test your knowledge and your capability based on what you have learned in the past 40 lectures. So, I hope you enjoyed the course and you benefited from the course.

Thank you very much.