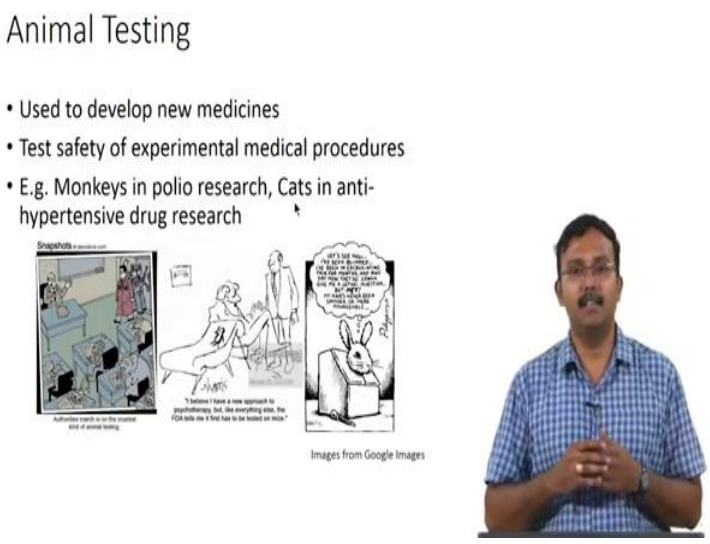
Tissue Engineering
Prof. Vignesh Muthuvijayan
Department of Biotechnology
Indian Institute of Technology, Madras

Lecture – 29
Bioethics of Tissue Engineering Part 2

Welcome back. Today, we will continue with the ethical discussion on Tissue Engineering problems. In today's topic, first we will talk about animal testing. As I mentioned in the previous lecture, when you test any tissue which you have developed in vitro, it has to be studied for in vivo using animals before it can be taken to humans.

These in vivo studies are performed on different animals; it could either be a small animal or a large animal. However, these animal tests are crucial before you can take it forward to human tests so that you can prove the viability. However, is this the best way? Are animal models truly representative? So, these are some of the ethical questions which we need to look at.

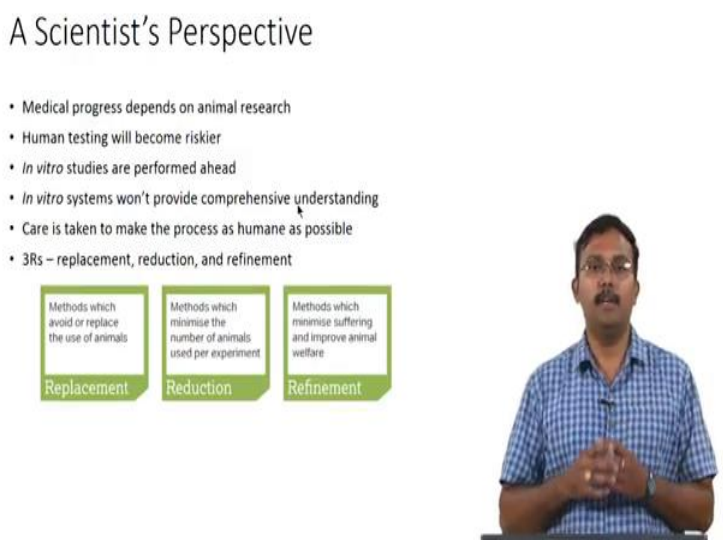
(Refer Slide Time: 01:12)



What is the dilemma which comes here? When you are talking about animal testing, people have done this in the past; it is used to develop new medicines or therapies, testing the safety of experimental medical procedures is important to be done in animals before it can be tested in humans. Some of the examples would be monkeys that were used for polio research or cats for hypertensive drug research.

These are some of the common things which people have done. However, is this acceptable? Is this truly a representative model? Those are some of the questions which cause an ethical debate.

(Refer Slide Time: 01:52)



When you are talking about a scientist's perspective, you would be looking at it from the medical progress. Medical progress depends on animal research; human testing will be much riskier if we do not do it on animals. So, it is not that animals will give us 100 percent accurate results; there is no guarantee that any results you obtain from animals will be absolutely applicable in humans.

However, if we do not do animal testing at all, then you are increasing the risk for humans multiple folds. Is that a risk which we are willing to assume? In vitro studies are also performed ahead of performing in vivo studies, what this means is there are extensive studies which are done at lab scale to make sure that the product which we are testing on animals is reasonably safe. So, we do make sure that there is a lot of guidelines on how we do it. It is not that every material which is developed or every product that is developed is randomly and indiscriminately tested on animals, which means we do have a certain standard. Only when the standards are met, we are able to perform it in animals.

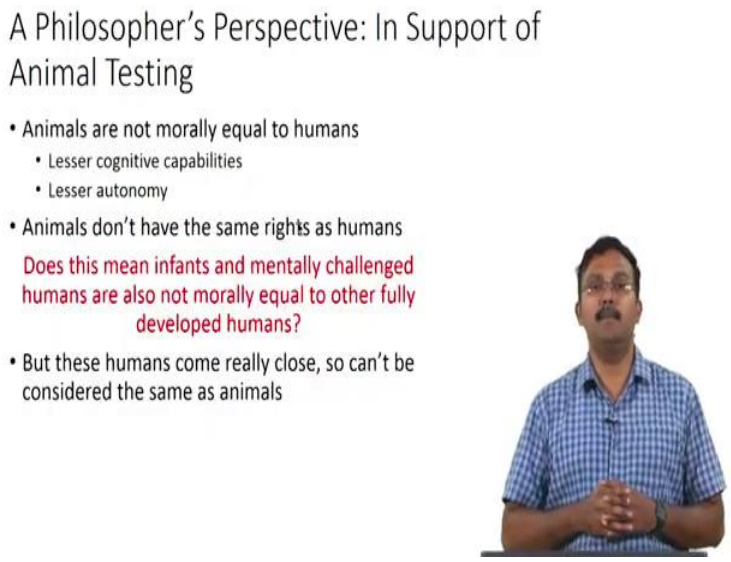
At the same time, in vitro studies can only take you so far. They cannot give you a complete understanding; in vitro studies at lab scale are probably done using cell lines or primary cells, or even if you create tissues; you are only looking at one single thing.

Whereas, in an in vivo system or animal model, what you have is the interplay between different tissues and organs and also the organ systems. So, this can all play a role in how the toxicity or effectiveness of the product which is developed is. So, it is important to test it for animals before you take it to humans.

As scientists, care is taken to make sure that the process is as humane as possible; it is not the intention of a scientist to harm or cause pain to an animal. The intention of a scientist is to make medical breakthroughs that can help in improving the quality of life of individuals. This means they would also take immense care in making sure that the process is as humane as possible, causing very minimal pain and discomfort to the animals.

Also, the three Rs, the principles of replacement, reduction, and refinement is always looked at; which means if you have a way to test it without using animals, then that is what is first looked at. So, that is a replacement. The reduction is where you minimize the number of animals. So, you do not test it on a large number of animals. You test it on the required number of animals to get a significant and scientifically valid result. Refinement is using the methods which are more refined, which will cause lesser pain to the animals and minimize the suffering and improve animal welfare as well. So, these 3Rs are always followed by any scientist. These are the arguments that are put forth by a scientist. Now let us see what would be the argument of someone who is not a scientist.

(Refer Slide Time: 05:25)



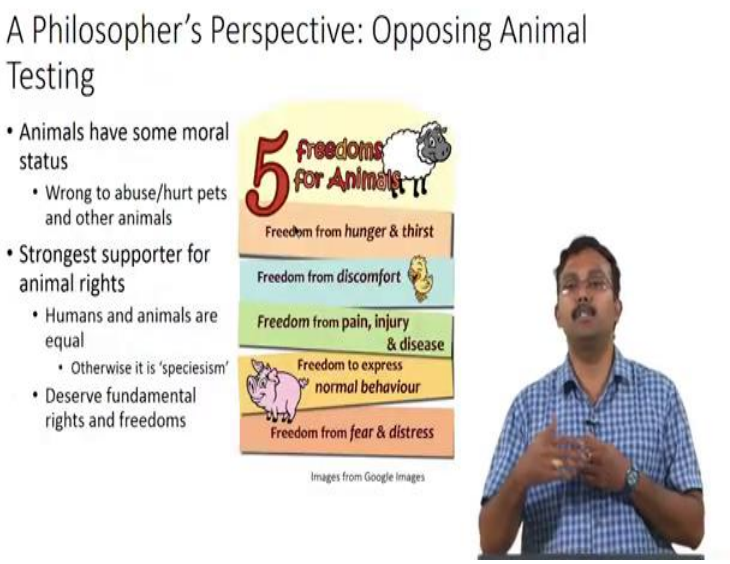
Let us look at it from a philosopher's perspective, if you have a philosopher who supports animal testing in general. How can a philosopher make arguments to support it? These are the arguments which are philosophical arguments to support animal research. One of the things which is said is animals are not morally equal to humans; they have lesser cognitive abilities and lesser autonomy.

So, you cannot fully treat them as equals; we do kill animals for food; we do treat animals as second-class species in this world. We may want to deny that, but that is the reality. Nobody is going to be hanged to death for running over a dog. So, that is a problem, so we as a society do understand that animals are not morally equal to humans. However, is this the only thing that can be looked at. That becomes the question.

From a philosopher's perspective, you can say that animals because they are not morally equal to humans, they do not have the same rights as humans. The reason for saying animals have lesser moral value than humans is they have lesser cognitive abilities, which means they do not actually understand or they are not independently thinking beings. They also have lesser autonomy compared to humans.

All these reasons give us reason to say that animals do not have the same rights as humans. However, by applying these rules, you can also say that infants and mentally challenged humans are also not morally equal to other fully developed humans; would this be an acceptable thing? So, then you have to find a compromise and say that these are humans who come really close to a fully developed human. So, they cannot be considered the same as animals, or they either have the potential to be fully developed humans, or they are very close to fully developed humans. Either way, we cannot fully say that they are equivalent to an animal. So, these are the arguments philosophical arguments that can be placed in support of animal research.

(Refer Slide Time: 07:54)



What would be the philosophical arguments you place if you are opposing animal research? A philosopher who opposes animal research would put forth these things. Animals have some moral status. Nobody is saying that they have the exact moral status as a human being; they already have some moral status. We do understand that running over a dog might not be seen as a crime. But if somebody tortures and abuses a pet or other animal, it is a crime. So, we do understand that. The strongest supporter of animal rights would agree with the philosopher's perspective, can even say that humans and animals are equal. Otherwise, it can be called speciesism, which like racism, is a way of discriminating because of the species.

We should say that they deserve the fundamental rights and freedoms as a human. Some of the rights that animals should have from a philosopher who opposes animal testing, his perspective would be they need to have freedom from hunger and thirst, which means they should get food and water. They should have freedom from discomfort. So, we should not be causing pain and suffering for the animals. They should be free from pain, injury and disease, freedom from pain injury and disease. They should have the freedom to express normal behavior. So, whatever an animal would do regularly as a normal animal should be allowed, we should not interfere with it. There should be freedom from fear and distress, they should not be forced into something, fearful environment, and distressful environment should not be created.

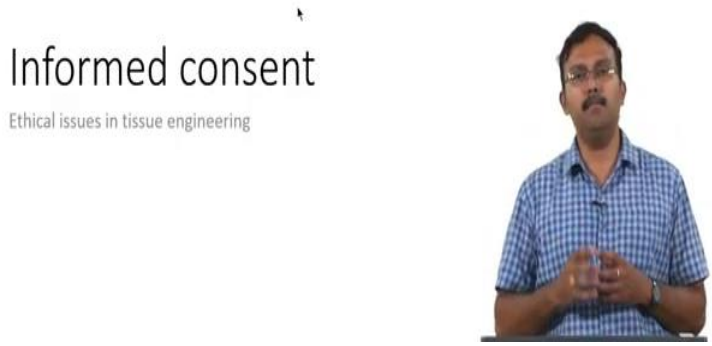
When we are performing animal testing, some of these basic freedoms are violated, which means animal testing should not be done. So, this is a philosopher's perspective opposing animal testing.

(Refer Slide Time: 09:52)

Finally, you also have the animal rights activists. The animal rights activists believe that animals are exposed to too much suffering, and there are arguments about better alternatives then animal research. There have been many studies that have shown that the data cannot be directly extrapolated from animals to humans. For that reason people think that it is you are better off are not doing animal studies at all.

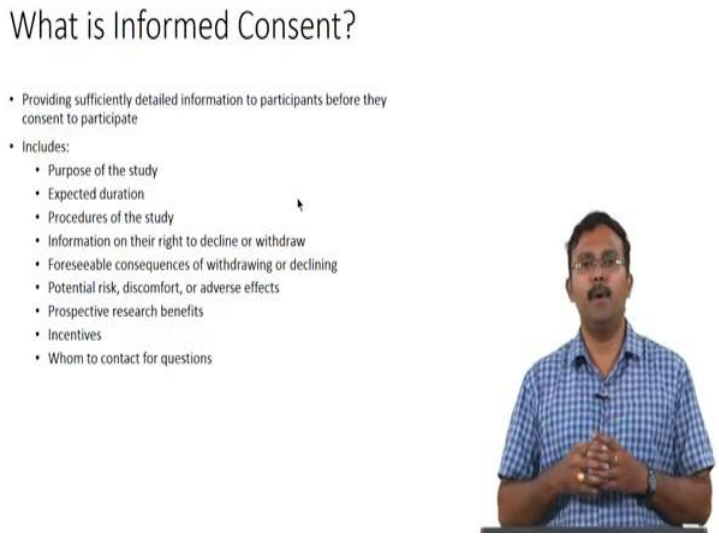
The last point which is usually presented is we do not have the right to exploit nature's beings. Although we are humans and we believe that we have to save each other's lives, that does not give us the right to take the life of another living being. These are the arguments that are usually put forth when it comes to an animal rights activist.

(Refer Slide Time: 10:48)



Another important ethical debate when it comes to any biomedical research, including tissue engineering is informed consent.

(Refer Slide Time: 11:04)



What is informed consent? Informed consent is providing a sufficiently detailed information to participants before they consent to participate. If you are going to recruit patients or volunteers to test your product, then you need to inform them of all the potential risks, give them the benefits and tell them all the information that can actually

be useful for them to understand and then they will decide whether they want to be a part of the study or not.

This informed consent should include the purpose of the study, expected duration, procedures of the study, information on their right to decline or withdraw. So, the volunteers or the patients have the right to decline or withdraw. Foreseeable consequences of withdrawing and declining. In the sense that if the middle of the trial if they withdraw or what could be the consequences and potential risk, discomfort or adverse effects by taking part in the study, prospective research benefits which the society gets to gain. Incentives, if any, and if they have any queries who they should contact?

All this information needs to be presented to the participant or the volunteer in a language that is understandable; it cannot just be some random legal document that you force them to sign; it needs to be explained to them so that they fully understand what they are doing and be involved in the decision-making process.

(Refer Slide Time: 12:41)

Why is this important, and why has this become an issue? When you do not have this, it can lead to exploitation. We will talk about a couple of examples where informed consent was never obtained and what kind of ramifications this has had. One major case which is studied when it comes to informed consent is the case of Henrietta lacks. Henrietta lacks was a woman who died in 1951, she was 31 years old, and she died of

cervical cancer at Johns Hopkins. Dr. George Gey, who was at that point, working on culturing human cells received Henrietta lacks cells. Henrietta lacks cells were obtained without informed consent. These cells survived and reproduced an entire generation every 24 hours.

(Refer Slide Time: 13:40)

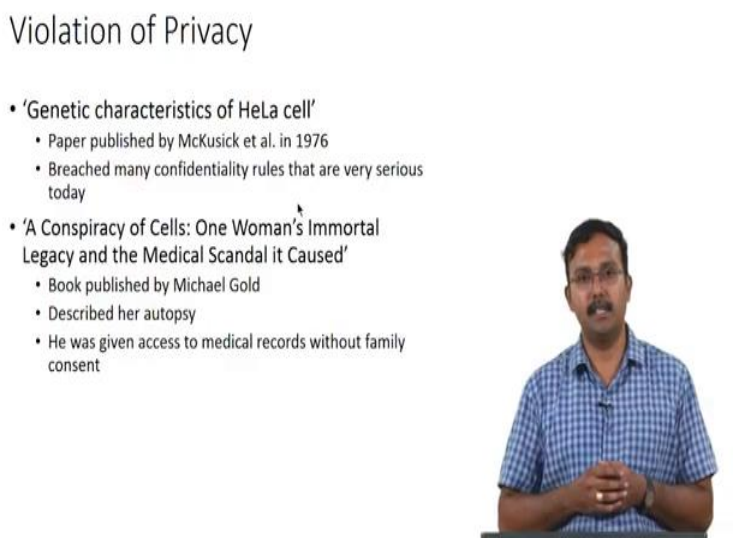
This was the first time human cells grew and reproduced outside the human body. The first immortal cell line, which is the HeLa cell lines which you might have heard of, was created. Over the last 60 plus years, close to 70 years, more than 50 million tons of HeLa cells have been grown, and over 60000 papers have used her cells. Publications that have been published in research journals are more than 60000, and they have all used HeLa cells.

Millions and millions of dollars have been spent and generated because of the HeLa cells. Thousands of scientific carriers have been made, and hundreds of millions of patients have been benefitted because of the use of HeLa cells. However, these cells were obtained without consent.

Had she been asked for informed consent or her loved one been asked for informed consent and had they declined, none of these things would have happened. So, all these scientific advancements and medical advancements would not have happened. Had they given the informed consent form to the family and they had declined it, we would have

been set back decades when it comes to medical research. However, what is the other side of it?

(Refer Slide Time: 15:10)



There has been a significant violation of privacy. In 1976, there was a paper that was published titled as Genetic characteristics of HeLa cells. This breached many confidentiality rules that are very serious today. However, 43 years back, it was not that big a deal, and people published it, and this was privacy information that should not have been revealed had there been informed consent. Then Henrietta lacks, and her family would have had control over what was actually being revealed.

There was also a book which was published by Michael gold called "A conspiracy of cells: one woman's immortal legacy and the medicals scandal it caused." This actually described her autopsy. He was given access to medical records without family consent. So, these are serious violations, and one would not want this to happen. Having informed consent, we can prevent something like this.

(Refer Slide Time: 16:19)

In 2013, her genome was published without permission. This was done as recently as 2013. Now, after all this NIH and Lacks family have come to an agreement, where the family gets some control over access to cell's DNA code, acknowledgments in scientific papers. Two family members have joined a 6-member committee, which will regulate the access to the genetic code of these cells. So, not having the informed consent helped the medical field; however, by not having this kind of form or this procedure, a severe violation of privacy has also happened.

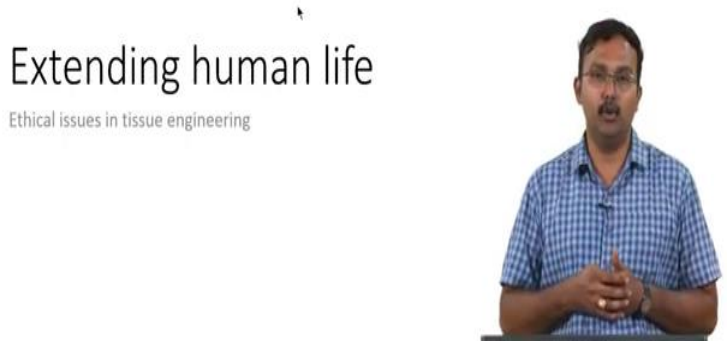
(Refer Slide Time: 17:11)

Another case where informed consent was never obtained is the Tuskegee Syphilis Experiment. Here, people actually suffered significantly. This happened from 1932 to 1972, and this was done by the US public health service. The study was to understand the natural progression of untreated syphilis in rural African American men in Alabama.

The participants were not informed about their disease; the participants were not treated, although, at that time, penicillin was identified as an effective antibiotic against syphilis. People with this disease were only seen as a volunteer for the study, and they were not informed that they are not being treated for a disease which they have. By not treating them, you were doing significant harm to the patient. However, had there been an informed consent, the people would have understood what they are signing up for, and if somebody signed up for this and wanted to withdraw, they would have still been able to do that. Because information was hidden from the patients, they underwent severe trauma, although they did not have.

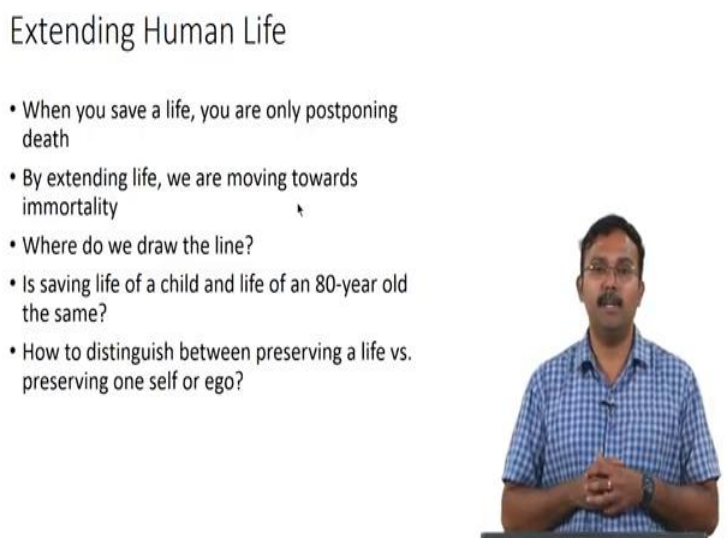
So, the next ethical dilemma when it comes to tissue engineering or any biomedical research is Extending human life.

(Refer Slide Time: 18:35)



Anytime we are looking at biomedical advances; you are looking to extend human life. Is this a good thing? So, that is a question which people ask.

(Refer Slide Time: 18:47)

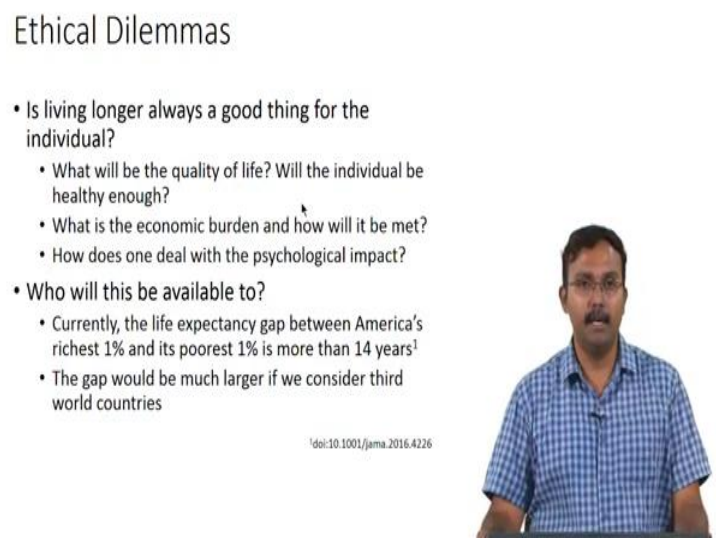


What you do is you are saving a life; when you save a life, you are not making them directly immortal. However, you are postponing death, but by postponing death indefinitely, you are moving towards immortality.

Is this a good thing for society, where do we draw the line? Not all things can be seen as equal, right? Saving the life of a child versus saving the life of an 80-year-old cannot be seen as the same thing; the child has the entire life ahead, whereas an 80-year-old might have had a fulfilling life already. So, do we still treat these two things equally or extending the lives of these two individuals seen as the same thing? We do not see it that way.

Then how and where do we draw the line? How to distinguish between preserving a life versus preserving oneself or ego? See in most religions, people believe that life is valuable, people always value life, and they say that no life should be destroyed. At the same time, most of the religions will also believe that life ends at some point, and trying to beat death is seen as preserving one's own ego, it is seen as a sin, or it is seen as a wrong thing to do. So, where do we draw the line? where do we find the difference?

(Refer Slide Time: 20:18)



The ethical dilemma when it comes to this extending life is living longer always a good thing for the individual? When we first think about extending life, we always say that the individual should be happy, because they get to live for a very long period of time. Let us say if somebody lives on to be 120. 120 years on this earth, people might see it as wow they were blessed; they lived a long life.

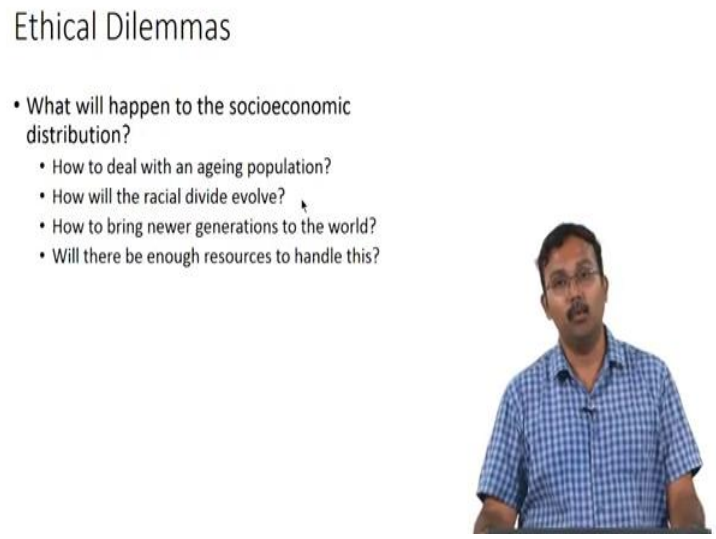
However, what would be the quality of life? It is not enough if somebody lives a long life, will they be able to live a healthy life? Will they be able to live a productive life? Or will they be able to do their own things? Or will they be dependent on people? So how is that going to affect them? What is the economic burden on such a person?

See, in today's world, a person retires when he is 60, and if you have to live on to be 120, you basically are retiring at around half the time you have. So, how do you then meet the economic burden for the rest of their life? You cannot earn for 30 or 40 years and live for another 60 years. How does it work, will the economic burden be met by society or the government, or how do we work on that?

Above all, what would be the psychological impact? Living on forever doing the exact same thing can take a toll on somebody's mind. I will be boring; It will be routine; It can drive one mad. What would be the effect of that? The next important question is, who will these facilities be available to, will it be available to everybody, or is it going to be available only to the elites. Currently, the life expectancy gap between America's richest

one percent and the poorest one percent is 14 years; it is actually slightly more than 14 years. If you are going to compare the expected life expectancy of the top one percent of the US with a third world country, the gap will be way way larger; Is this something we want? Do we really want a society where only the elites get to live on while the others perish? Is that the kind of society where you would want to or want one to live, where do we draw the line, how do we develop this.

(Refer Slide Time: 22:49)



Then what happens to the socio-economic distribution. How do you deal with the aging population as people live longer, the average population age is going to go much higher. How do you then deal with that? What are the ramifications of that, what are the medical expenses associated with that? What is going to be the societal impact of that?

Will there be a racial divide when this happens because if it is only available to certain society, say part of the society, how does it affect the racial distribution. Will we be able to bring newer generations to the world, if the world is already going to be filled with all these old people how do we bring newer generations and the younger generation. Will there be enough resources to handle all this as the population keeps increasing endlessly, will the resources available on this earth be sufficient for us to survive.

These are some of the ethical questions which have to be answered before we fully understand whether advances in tissue engineering or any biomedical sciences can actually solve problems or will it raise more problems. Guidelines need to be evolved

based on what is acceptable for society, and things need to be done in a way that it helps society on a large scale.

As I had mentioned earlier as well, I am not trying to present any one particular viewpoint here; I only want to actually present the ethical debates which are happening. And, it is important for you to think through them, argue about them and develop guidelines which would be acceptable for all.

Thank you.