

Tissue Engineering
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Lecture - 28
Bioethics of Tissue Engineering Part 1

Hello everybody. Today we are going to talk about the Bioethics of Tissue Engineering. We have discussed tissue engineering; we have now seen the different aspects of tissue engineering, what promises it holds. However, with any advance developments, especially in the areas related to human life, ethics becomes a major question. So, it is important for us to look at the ethical questions which need to be addressed well while we are performing research when it comes to tissue engineering.

Today we will be talking about the different ethical questions which are posed for the researchers and also the society when it comes to the area of tissue engineering.

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Ethics vs. Regulations

- Do you know the difference?
- Ethics
 - Moral guidelines based on individual values
- Regulation
 - Rules imposed by an external agency
 - Examples of such agency relevant to biotechnology?



When you first talk about bioethics, the first aspect which I would like for you to know about is the difference between ethics and regulations. So, please think for a minute, what is ethics, and what are the regulations? Do you understand that they are different, or do you think they are the same? So, think about this; ethics are moral guidelines that are based on individual values. What are regulations then? Regulations are rules, which are imposed by an external agency.

The fundamental differences are ethics is based on our own morals. It could either be what an individual person believes or the society believes, or his religion believes versus regulations being what governmental agencies actually enforce. So, regulations are usually from external forces; however, in an ideal society, the ethics should be of higher standards than regulations. It is important that we understand this difference. Today, we will be focused on the ethics of these issues. Regulations of tissue engineering is a whole another debate which involves a lot more legal issues which will not be discussed as part of this course.

So, when we are talking about regulations, we said that it is enforced by external agencies. Can you name a few such agencies? Think about it, what would be the external agencies which act as regulatory bodies when it comes to biotechnology. Most of you would have thought of the FDA, which is the Food and Drug Administration in the US. This organization is the one that approves what is used for food products and what is used as drugs. This is also the agency that approves medical instruments and also any of the tissue-engineered products which might reach the market.

However, this is an agency that is set up by the United States government, and it is implemented only for the US. So, you could get an FDA approval, but that is only required if it needs to be marketed in the US. However, if you are looking for something to be marketed in India, where do you go? Where do you get the approvals? So, in India, you have two regulatory bodies: one is the FSSAI, which approves the food-related products. And, then you have the CDSCO, which is the Central Drugs Standard Control Organization. These two regulatory bodies approve food and drug-related products when it comes to India.

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What Will Not Talk About

- Agencies involved in policy making
- Regulations governing ethical debates
- These vary with countries and states



As I mentioned, we will not be talking about regulations, which means we will not be talking about the agencies which are involved in the policy-making, the regulations which are governing the ethical debates. One of the reasons we would not be talking about these is, this can vary from country to country or even state to state depending on the values of the particular environment. So, we will focus primarily on the larger debate, which are ethical dilemmas. We will focus on major questions which are post in front of us, when we talk about tissue engineering.

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What is Bioethics?

- Study of ethical issues related to advances in biology and medicine



This area is called bioethics. Bioethics is the study of ethical issues related to advances in biology and medicine. Tissue engineering ultimately wants to be developing a product that can help in improving the quality of life of people and develop into a biomedical product. Bioethics governs how tissue engineering research should be carried out.

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Factors in Ethics/Bioethics

- Legal factors
 - Rules can guide what is right and wrong
- Organizational factors
 - Ethics of the leader
 - Values imbibed through policies, publications, and speeches
- Individual factors
 - Moral development
 - Personal values and personality
 - Religious influences
 - Family and peer influences
 - Life experience
 - Situational factors



When we are talking about bioethics, what are the factors? What influences bioethics or even ethics in general? You can have legal factors, the rules that can guide what is right and wrong. These are basic rules, which are enforced, and if somebody does not have their own guidelines, the legal guidelines which are set forth by the external agencies will act as the ethical guidelines as well. So, that is not the highest standard that needs to be met.

You could also have organizational factors. So, organizational factors depend on the ethics of the leader or the values imbibed through policies and publications and speeches by the organization. For example, you could be working in a company where there would be certain rules about what to wear or the timings in which you need to work, and these are policies that are implemented by the company. You have these organizational factors which decide how you behave. So, the ethical guidelines here are not just dependent on the legal bodies, but on the organizational bodies.

Technically, these are not binding because you can leave the company and go to a different place. There is no law forcing you to work in that company. By choosing to

work there, you have agreed to abide by the organizational values of the place where you are working. This could also apply to colleges or in general, any society. In a family get together, you would have a certain organizational value, which may be unsaid, but you still have to follow them because that is how your family would function. So, that is the organizational factor.

Then comes the more important factor, which is the individual factor. As an individual, all of us have our own moral standing. So, when we have these moral standings, this is what will drive us towards doing something or not doing something? We need to realize what can be done and what should not be done, and that comes from our own belief system. It could be either moral development or personal values and personality. It could also be religious influences or family and peer influences; it could be life experience or situational factors. So, these are the governing factors when you are talking about how an individual behaves.

Moral development is based on so many things, right. So, you need to have a certain set of values on different issues, and this comes from who you are; this defines who you are. Personal values are based on personality. So, there may be certain things I would feel uncomfortable doing; however, someone else might be more comfortable doing, and that comes simply because of the personality. There can also be religious influences; all of us follow our own religion. Individual religions have different guidelines that people follow. Some religions would restrict certain activities whereas, other religions might not be so strict. Depending on religious beliefs, somebody might follow or do certain things, while others might not, and this plays a huge role in how a person behaves. Family and peer influences; looking at your peers and your family, you learn values. Looking at your parents, you know what they do and what they do not do. If a parent does not stop at the red signal while crossing the road, then the kid assumes that it is ok to do that although the legal guidelines say otherwise. So, the values are imbibed by looking at the peers and your family.

Life experiences would also change your values. As you grow either more experiences you have, you see more things. Based on that, your value system will evolve; some of the values you held dear when you are younger would not be seen as such strict things and thinks might change over some time. The last and crucial factor is a situational factor. There are certain things which we would find repugnant today when we have all the

facilities and amenities; however, when we are pushed to a corner, then the situation might demand us to cross a line which we would not cross today.

So, how do we take all these factors when we are looking at ethics? So, when we are talking about bioethics, all these factors can play a role. We will talk about some of the major questions which actually haunt the field of biology and even tissue engineering, specifically, which need to be addressed and discussed.

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Embryonic stem cells

Ethical issues in tissue engineering



We will first talk about one of the major ethical debates when it comes to tissue engineering; it is the embryonic stem cells. So, what are embryonic stem cells?

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Embryonic Stem Cells (ESCs)

- What are stem cells?
- What are embryonic stem cells?
- What are the other types of stem cells?
- Why embryonic stem cells?



First, we need to know what are stem cells. In this course, we have already discussed what stem cells are; so, I am assuming you would already know what stem cells are. So, if you do not, basically stem cells are cells that actually can differentiate to different types of cells. These do not have the functionalities already determined. They can differentiate to form different cells; they are also self-renewing cells. So, this is what a stem cell is. So, what is an embryonic stem cell, and why is it so special?

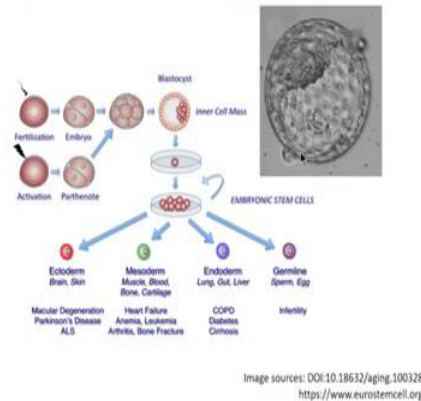
An embryonic stem cell is a cell which is obtained from the embryo. These stem cells have much higher potency; these are pluripotent, and that makes them a useful tool for research. So, what are the other types of stem cells? There are many other types of stem cells; you can find stem cells in all parts of your body. So, you have the mesenchymal stem cells, you have the hematopoietic stem cells, you can have adipose-derived stem cells and many other there, the dental pulp has stem cells. Stem cells can be found in many parts of your body.

So, why is the fuss about embryonic stem cells? As I mentioned, these are pluripotent stem cells, which means they have a lot more potency when it comes to differentiating and growing. Recent research has also shown that the somatic cells can be converted to induced pluripotent stem cells. So, these are called the iPSCs or Induced Pluripotent Stem Cells. By incorporating certain transcription factors, the somatic cells can be converted to pluripotent stem cells, which are called the iPSCs. So, these are the different

types of stem cells. As I already mentioned, embryonic stem cells show pluripotency, and that is why that has been a lot of interest in working on embryonic stem cells.

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How are ESCs obtained?



Before we look at the ethical question about embryonic stem cells, we need to understand how embryonic stem cells are obtained. In this, the first step is fertilization of an egg, and you create an embryo, and this embryo is allowed to grow till it reaches a stage called the blastocyst. In the blastocyst, you have an inner cell mass, which is the mixture of cells that contains the embryonic stem cells. From this inner cell mass, you obtain the embryonic stem cells.

The fertilized egg which grows to a blastocyst is disrupted to get your embryonic stem cells. These embryonic stem cells can then be differentiated to form different types of cells. It could form endoderm, mesoderm, and ectoderm cells. For this reason, there has been a lot of interest in looking at embryonic stem cells.

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What is the Ethical Dilemma?

- Choose between two moral principles:
 - The duty to prevent or alleviate suffering
 - The duty to respect the value of human life
- Impossible to respect both
 - To obtain ESCs, early embryo has to be destroyed → Destroy potential human life
 - ESC research could lead to treatments that can alleviate suffering
- How do we decide which is more important?
 - Based on how we view an embryo

Source: <https://www.eurostemcell.org>



Now, what is the ethical dilemma? So, the major question which plagues the discussion on bioethics of embryonic stem cells is you need to choose between two moral principles. The first principle is the duty to prevent and alleviate suffering. As human beings, we have to prevent or minimize suffering. When you see somebody who is suffering, you should try to do what you can to help them and alleviate the suffering. So, this is one of the moral guidelines that humans are driven by.

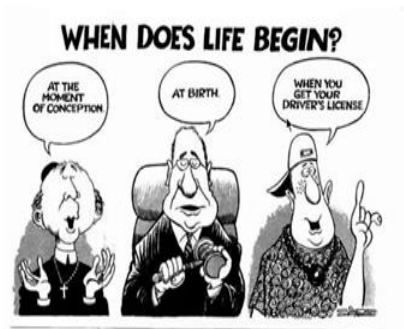
The other guideline is the duty to respect the value of human life. Human life is one of the most precious things; we need to value it, and we cannot sabotage it. So, these are two principles which end up being conflicting when you talk about embryonic stem cell research. There is no way to respect both when you are working on embryonic stem cells. What happens here is to obtain embryonic stem cells, an early embryo has to be destroyed, which means you are destroying potential human life. But embryonic stem cell research can lead to treatments that can alleviate suffering.

So now, these are two guidelines which we said are moral principles that we are driven by. But these end up being conflicting when you talk about embryonic stem cell research. So, that is what makes it a hard question to answer. How do we decide which is more important? Do we say that alleviating suffering and preventing suffering is way more important, or do we say that respecting the value of human life is way more

important? So, this is dependent on how we view the embryo. The embryo can be seen in different ways, and what do we see it as, is the question.

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Ethical Question: When does life start?



Cartoon from The Hartford Courant



The ethical question we are faced with is, when does life start? So, life starting at the time of conception is one of the beliefs. Legally, life starts only at birth, but you have to decide when exactly life starts to address this question. Can we come to a consensus on that? That is the million-dollar question.

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Status of the Embryo

- This is a complex question
- Some of the common view points
 - Embryo has full moral status from fertilization onwards
 - Embryo has full moral status after 14 days of fertilization
 - Embryo has an increasing status as it develops
 - Embryo has no moral status
- No scientific consensus on when life starts

Source: <https://www.eurostemcell.org>



The status of the embryo is a complex question; there are many, many viewpoints when it comes to how an embryo should be viewed. Whether the embryo should have rights, whether it should be treated as equally as a human or whether it should not be, whether it should be treated only as a mass of tissue or mass of cells. So, how do you view an embryo? We will talk about some of the common viewpoints here.

The embryo has full moral status from fertilization onwards. So, this belief is where you believe that life starts at conception. What you are saying here is an embryo as soon as it is formed, the time after fertilization, it needs to be treated equally as a human. So, this is one of the arguments; however, if you were to believe in this, then embryonic stem cell research cannot be done. This would also mean abortions which are done to save the lives of the mother or even for other reasons; if there is a non-viable embryo and you still think that it needs to be protected. So, then that would be the guideline-driven by the moral status of thinking embryo has full moral status at that the time of fertilization itself.

There is also a group of people who believe that an embryo should have a full moral status after 14 days of fertilization. Why 14 days? What is the specialty there? After 14 days, the embryo is implanted, and it does not have a chance to divide to become twins. In the first 14 days is when it can form twins. This means that the belief is after 14 days, the embryo has reached a stage where it now has the potential to form human life. Within 14 days, the embryo could also be lost without implantation. So, we people believe the 14-day cutoff would be a good point to start. If this is going to be the guideline, then how does this control embryonic stem cell research, how do we then proceed? So, that is another question.

The third option, which people believe is, the embryo has an increasing status as it develops. An embryo at the time of fertilization has no moral status; however, as it develops into more of a human form, you would have more of a right as a human. This is one of the generally accepted views.

The last one is an embryo has no moral status at all. So, until the time of birth, life does not start. So, these are the four different views, and people see it differently. Based on how one sees it, the ethical guidelines which are driving the embryonic stem cell research would also evolve. However, there is no scientific consensus on when life starts.

This needs to be stated because there is no scientific consensus; there is no real way of saying this is the point at which life starts. You can only decide on that based on your belief system; it is not based on any scientific proof.

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Using Spare Embryos from Fertility Treatment

Arguments for using spare embryos	Arguments against using spare embryos
<ul style="list-style-type: none">Embryos have been created for IVF and destroyed when not implanted for many years. This has not changed on how we value life	<ul style="list-style-type: none">Human embryos could be exploited as therapeutic agents, which might decrease the respect for human life
<ul style="list-style-type: none">Many embryos created in IVF are not implanted and are left to perish. So, the moral dilemma of ending human life is not applicable	<ul style="list-style-type: none">This is a slippery slope, which can lead to embryos being created with the sole aim of destroying them
<ul style="list-style-type: none">It is better to use these spare embryos for research than to let it go to waste	<ul style="list-style-type: none">This could encourage society to tolerate the loss of life to save a life

Source: <https://www.eurostemcell.org>



One of the compromises which people have looked at is to use spare embryos from fertility treatment. People have been doing IVFs or the In-Vitro Fertilization to have kids. In that case, what happens is eggs are fertilized to form multiple embryos, and not all of them are used for being placed in a womb for further growing the human being. However, embryos that are not used are discarded. So, people have said that these embryos are anyways going to be discarded; so, why not use them for embryonic stem cell research.

Now, the question is, are there arguments for and against this as well? As one would expect there are. We will talk about some of the arguments which support using spare embryos and the arguments which oppose using spare embryos. Embryos have been created for IVF treatment and will be destroyed when it is not implanted, and this has been done for many years, and this has not changed how we value life. So, it is not a problem; however, if you argue against this point is human embryos could be exploited as therapeutic agents, which can decrease the respect for human life. So, when you are only doing it for IVF, you are not intentionally creating it as therapeutic agents; you are creating it with the hope of creating human life. Whereas, when you start doing it as a

creating it for therapeutic agents or therapy, then what you are doing is you intend to create them for a different use, which might lead to abuse. So, these are the two arguments which have put forth.

And the next thing is many embryos are created in an IVF, which are not implanted and are actually left to perish. So, the moral dilemma of ending human life is not applicable here. You are anyway going to destroy them. So, it is not like you are destroying human life because it is being done already, but the argument against it is this is a slippery slope. What can happen is potentially, people can start creating embryos with the sole goal of destroying them for therapeutic purposes, which is not an acceptable thing for many people. So, this is where the issue comes in when it comes to this argument.

There is also the argument that is put forth saying that it is better to use these spare embryos for research rather than to let it go to waste. However, the argument against this is this could encourage a society that tolerates the loss of life to save a life. So, these are the different viewpoints that are put forth. It is up to you to think of what is acceptable. So, when it comes to framing guidelines or regulations, the ethical guidelines will be the driving principle. And, the rules which would be put forth or the regulations will be put forth should be driven by our ethical guidelines as a society. Overall societal ethics would dictate what would be seen as acceptable for the society we live in.

Here, I am only presenting the arguments for and against some of these points. I want to be very clear that I am not supporting or opposing any of the arguments, and I am not interested in selling one of the ideas to you. What I am interested in is for you to look at this and see that there is an argument, then there is a debate that is going on, and both sides have valid arguments. It is important to see both sides of the argument; it is important to reach across the table and find a compromise that will work for both parties.

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Animal testing

Ethical issues in tissue engineering



Moving onto the next topic of animal testing. Animal testing has long been an ethical question in bio-research. When it comes to tissue engineering, it will again be a problem. Anytime you were working on creating tissues, you would have to test it before you can use it for humans. So, do we test it in animals? So, when we test it in animals, it creates an unethical dilemma. In the next lecture, we will talk about animal testing as one of the ethical questions.

Thank you.