

Bioethical Dilemmas: Dr. Robert Klitzman on the Changing Landscape of Genetics and Reproductive Technology and on COVID-19

Jennifer Cohen 0:04

Welcome to the Voices in Bioethics podcast. I'm Jennifer Cohen, and it's my great pleasure to welcome Dr. Robert Klitzman to the podcast today. Dr. Klitzman You are a professor of clinical psychiatry in the College of Physicians and Surgeons and the Joseph Mailman School of Public Health. You are the founder and director of the Masters of Bioethics program at Columbia University. You co-founded and for five years co-directed the Center for Bioethics and for 10 years directed the Ethics and Policy Core of the HIV Center. You've written nine books and authored or co-authored over 150 articles. Your work has appeared in the Journal of the American Medical Association, Science, as well as the New York Times, Newsweek, The Nation, and other publications. You've received numerous awards and fellowships for your work. You sit on the New York State stem cell Commission, the ethics working group of the HIV prevention trials network, the Council on Foreign Relations, and you've been a member of the research ethics advisory panel of the US Department of Defense, your reputation as one of the leading public intellectuals in bioethics and public health has made you a sought-after expert for many news outlets, including the New York Times, The Wall Street Journal, The Washington Post, NPR, PBS, CNN, and others. And we are very grateful that you've agreed to speak with us on the podcast today about your work.

Robert Klitzman:

Thank you. I'm delighted to be here.

Jennifer Cohen:

Let's jump right into your latest book 'Designing Babies: How technology is changing the way we create children' published in 2020 by Oxford University Press. Your fascinating book is an overview of the technological breakthroughs in the field of medicine known as assisted reproduction technology (ART) and the staggering array of choices those breakthroughs now offered to patients and clinicians when it comes to creating children. And one of the many ethical issues that you address is around preimplantation genetic diagnosis or PGD, the process of screening embryos for genetic mutations or markers of one kind or another, and then selecting or discarding embryos based on their genetics. There are two basic reasons it seems to me to focus on the genetics of an embryo. One is to avoid creating a child who will develop a debilitating genetic disease. And the other is to create a child who will have enhanced or desirable, however that is defined, genetic abilities. First, can you discuss whether embryo selection to achieve genetic enhancement is possible today, assuming it is or that it's coming, which factors should go into the process of distinguishing between preimplantation genetic diagnosis to avoid a genetic disease and PGD to achieve enhancement?

Robert Klitzman 2:41

Well, great questions. So, the story is that there is PGD that is now being used for what I'll call socially desirable characteristics. So, at the moment, this is largely sex selection. So, people come in and say, I want a boy, and we give them a boy. And particularly individuals and families from certain countries, often in East Asia, South Asia, sometimes the Middle East. In those cultures, often, men feel that it's very important to have a son, a male heir to carry on the name, etc. And so, they come to clinics and say, I want a boy, and we just transfer into the womb, the male embryos. So, this raises a number of questions. There are two different scenarios, of course. One is if someone just having one child: 'Do, they have one girl, and they want one boy, and they think it would be nice to have a boy?' versus in the case, let's say someone has six girls, and they want to boy. So there is some difference in that. And the problem is the American Society for Reproductive Medicine, which is the professional organization of doctors involved in IVF and assisted reproductive technology, that group has said that social selection or sex selection for social reasons is okay if it's for "family balancing," but they don't define family balancing. So that could mean I have one girl and now want a boy. So presumably, there's less concern, though, they're still concerned for many people, if it's six girls, and you want a boy versus one in one or just one, and you want to be a boy. And of course, there are countries in which there are increasingly more males and females born every year. And this obviously raises concern.

From the standpoint of what one might call eugenics, or movements towards eugenics, which is trying to select or alter the genes of a population-based not on medical reasons, but on social reasons, this is a concern. As it turns out, I think a reason that there's not been more enhancement of traits, like IQ, for instance, is because we increasingly realize that for most "socially desirable traits," there are multiple genes involved, not just one gene. So, for IQ, for instance, there are scores and scores of genes, each of which contributes a teeny bit to your IQ. The gene that has the strongest impact on one's IQ gives you an extra one point on your IQ test. So, it's undoubtedly a bunch of different genes. And of course, it's harder to screen embryos on multiple genes as opposed to one gene.

That being said, though, increasingly, we are and will be finding genes that will give you more height, let's say in a child, or more likely give the child blond hair blue eyes. And so, as we develop these genes, even if they're two or three genes, if we alter, or select based on one or two of those, we're having an effect. Another concern I would argue is that even with using PGD for diseases, there are other concerns ethically that come up. So, for instance, right now, breast cancer, unfortunately, harms both wealthy people and poor people, yet increasingly, wealthy people are able to perform PGD on their embryos, so that if they have the breast cancer gene, the so-called BRCA gene, they are able to ensure that that mutation does not get transmitted to the next generation or future generation. So basically, wealthy people are now able to screen out genes for diseases like breast cancer, whereas poor people can't. And so, diseases like breast cancer particular, is increasingly becoming the disease of poor people. And I think that raises a lot of social concerns. Because if there is a disease that affects poor people more than wealthy people, I would be concerned, and many people would be concerned that there may be less resources given to Treatment and Research for that condition. It's a long-winded answer to your very good question but suggests that we do now select for socially desirable traits. We'll do that more. And, of course, there is the possibility of gene editing which raises these questions even more acutely.

Jennifer Cohen 6:56

Yes, I want to get to all of that incredibly informative answer. One of the two quotes you selected in the epigraph to the book is from Genesis, the famous verse that God created children in God's image, people are tasked with multiplying, but God is the Creator, the ultimate designer, in control of a process that we humans should really not be tampering with. And that sentiment seems to be the foundation for religious and ethical arguments against PGD. How does a rebuttal to that kind of argument work?

Robert Klitzman 7:27

So, it's a great question. I would say that, as you suggested, in your first question to me, a few minutes ago, if there is a way of reducing the risk of a child having a terrible disease, the child's going to die of the disease at early age, or even later in life, something like Huntington's disease or cystic fibrosis, these are diseases that we can now screen out through PGD. Also Down syndrome, for instance. Now, of course, all these raise ethical questions. And so, we believe in autonomy in the US that parents have a right to choose to make these decisions. One could argue that we are tampering with nature. However, I would argue that it means that parents can have a child who does not have a debilitating disease and dies at a young age and causes great stress in the parents lives and the lives of other siblings, etc. If instead that parents can have a healthy child, I don't see a priori, many risks with that.

Now, some may say, well, that's tampering with what God wanted. On the other hand, we do a lot of things that alter quote, "what God may have wanted." So even treating someone for cancer or for any disease, someone could say, well, if someone has cancer, this is God's way, we are only all live to a certain point, God's decided this person only has so many years to live. Well, we've decided that at times, even though nature may take its course and give someone cancer that if we can treat the cancer and the person can live longer, even though it goes against what quote "God may have planned," we do it. So, for many of us, even though God is important in human societies in current day, human society, many of us think in many ways. In this particular instance, I would argue that if there's a way that we can avoid risk and harm and disease and extend someone's life, but those are good things to do.

On the other hand, I think and part of the reason I chose the quote, for the beginning of the book is to show that these issues do involve religious concerns at certain points. And so, when we get into, for instance, eugenics and altering genes, we need to be careful. And I think that there are issues of hubris that there have been, and we could talk about this, for instance, Dr. He Jiankui, who went ahead and created children using embryos that he edited, he jumped the gun, many of us feel and that the technique you use for gene editing was not as precise as it should have been. So, what he thought he was doing is different than what he did. So may be long term medical consequences for the children born, we should be reminded that we're mere mortals and we make mistakes. And we need to reduce the risks of those as much as we can.

Jennifer Cohen 10:11

In a previous podcast I interviewed author Lydia Den Werth and we discussed her book about her son's deafness. And her burgeoning understanding of deafness as two things little d, deafness, a medical condition, and big D, Deafness, a cultural social model with its own language, its own traditions, does that bifurcated paradigm apply to other medical conditions? In other words, if we, as a culture saw disease as something more as a social construct, would that inform this decision about editing out embryos or genes that carried disease mutations?

Robert Klitzman 10:52

Yes, and again, it's a great question. I see these issues as falling under what I call sort of a disability critique of some of what happens in bioethics and in medicine and health care. So certainly, attitudes have been changing. And we now know thanks to the disability community, which has been active in many ways that certain conditions that people without that disability might think of as being enormous obstacles to life, or some people see those conditions as being stigmatized and often historically, unfortunately, have impinged on the rights of people with disabilities to have equal access, the disability community has shown us that many people with disabilities live very fulfilled lives. And they remind us that we need to ensure that people with disabilities have fully equal rights, that there should not be societal discrimination against people on the basis of disabilities. Now, of course, we have a DA the Americans with Disabilities Act, and yet they're still unfortunately discrimination that goes on, of course, with race and ethnicity,

gender, disability, and other areas as well. Just having a law against discrimination is a crucial step but does not guarantee that all discriminations subtle and not so subtle, will immediately disappear.

So, I'm actually now involved in a study with Wendy Chung and Paul Applebaum and others, where we're doing genetic testing on individuals who have autism, in which we're finding the genetic cause of severe autism. And we're finding out whether parents want this information, what they do with it, what it changes, what doesn't change. I've also been interviewing, in this part of the study, individuals are a part of autism advocacy organizations who tend to have relatively higher functioning autism, I should say that people for whom, where finding the genes tend to be people with very severe autism, some can't speak or communicate, some can't control their bowels, for instance, they have seizures, etc. But when I asked autism advocates, as I've been doing recently, what they think of genetic testing, they say, "Well, if it can help have early interventions for people born with a gene, that's great, but if it's going to be used to, quote, 'do a eugenics thing on us,' and to eliminate people with autism, either as embryos, or we'll make the embryos before they become people or lead to termination of pregnancies," that raises many questions and problems for them, obviously, and for many of us. And so, I think that distinction between the genetic cause and what might be seen as a symptom, and then how society views, the condition, these are very different things. And we need to be very aware of these and be aware that people look in our diverse society, these issues very differently. Suddenly, with Down syndrome today, many parents say, getting back to your earlier question of God gives him a child with Down syndrome, that is their child, and they are happy to raise him, or her. Other people say I couldn't do that, I would find that too stressful, and I want to know if I am going to have a child with Down syndrome, and I will screen out the embryo or I will terminate the pregnancy because that's something I just can't do. In our country we let people make these choices at the moment.

Jennifer Cohen 14:11

That's yeah, really a difficult problem. You've mentioned Huntington's and cystic fibrosis as diseases where there seems to be a consensus in the medical community in the bioethical community that these would be cases where PGD selection would be justified. I think one of the people you interviewed in the book had the Huntington's mutation and said that if she aborted a fetus that had that same mutation, would that mean that her life had not been worth living? And that that question had haunted you? Do you see that same sort of understanding in the disability community spilling over to diseases like Huntington's or cystic fibrosis? Or do you think that there is a consensus that those are instances where PGD to bring an embryo up to a "normal health status" would be justified.

Robert Klitzman 15:05

So again, great question. And as you say, the reason I wrote the book *Designing Babies* is I actually wrote a previous book called *Am I, my genes? Confronting Fate and Family Secrets In The Age Of Genetic Testing*, and it was in doing the research for that book in which I interviewed people at risk of who had Huntington's. And one of the people I interviewed for that book is the person who said, the biggest issue I face is should I not have kids? Should I not get married? Therefore, should I adopt? Should I have a screen embryos or undergo abortion? What should I do? And if I decide to abort such a fetus or screen on embryo, what am I saying about the value of my own life? as you just said, does that mean my life was not worth living? And that led me to wonder about this issue more broadly, and interview other people and how are people making these decisions.

So, we let individuals prospective parents make these decisions for themselves. So, we say for Huntington's I think there's consensus that if someone says, Look, I don't want to have a child with Huntington's is a uniformly fatal disease, it usually kills people in their 40s or 50s. Woody Guthrie famously had the disease and unfortunately died of it. It causes psychosis causes dementia to really a terrible disease once symptoms start. So ethically, if the parent wants to abort the fetus, at the moment, or screen embryos to eliminate the mutation from being passed on, we say that's

fine. Some parents may say, no, I'm, because of the argument that we just mentioned, that is that I will be speaking negatively, or I would therefore have not been born. I don't want to do that. So, we let parents make the choice. In the case of sex selection, or in the case of sex selection, that we've allowed. But in the case of other kinds of "enhancements" or choosing for socially desirable traits, let's just say another example, is there are single genes that are responsible for different kinds of athletic ability being a sprinter and that we find that certain genes are at a certain proportion in the general population, but much, much higher among Olympic athletes, for instance, and so people can easily screen embryos for that today, for instance, if they want. So, on some of those traits, we say that the consensus among a lot of bioethicists is that becomes problematic because it's not a medical condition. So, I think that parents may want that. And we say, many of us feel that that is going too far. Whereas for disease like Huntington's, again, we think that's okay if parents want, and some parents indeed decide to do it.

Jennifer Cohen 17:40

Ever since the advent of contraception, and the pill, particularly a lot of the unease with ART is the separation of the biological processes of reproduction from physical sex. You quote Hank Greely, a Stanford law professor who argues that soon sex will just be for recreational pleasure, and IVF will be used in all cases for reproduction so that specific genes can be chosen a scenario straight out of *Brave New World*. Do you agree with that prediction?

Robert Klitzman 18:08

I don't and part is, well, let me put it this way. I think that for most people that will not occur. And the reason is, it's expensive. So, IVF, would you need to do in order to do PGD is in vitro fertilization, where you take sperm and egg and have them become fertilized in a petri dish, and then transfer to the woman that cost \$25,000. Most cycles of IVF don't work. And so, you need to do it, say it works 40% of the time, if you're otherwise healthy and fairly young, goes down to less than that as a woman gets older, for instance, or if the man has infertility problems, low sperm count, etc. So, if you need to undergo two cycles of IVF, to do PGD, that's \$50,000, plus the costs of PG days, you're talking at least \$50,000 in the US to do this. So wealthy people can readily afford that, but a lot of people can't afford that extra \$50,000 when the alternative is you can become pregnant "for free." So with no money exchanging hands if you have sex with the person you want to have a child with, if you're straight couples, so I think that is the rate limiting step is that where some people may say, Well, let's have a child or design a child and make sure that we don't have these certain genes that get passed on that has a price tag \$50,000 Plus, and there are people now able to afford to do that. And certainly, if someone has a serious disease in their family for which there's a clear gene like Huntington's, they may say, Look, that's worth it to us, because rather than have the person die in their 40s, have terrible disease that can live and have a normal lifespan without the mutation. I think those are some of the issues involved.

Jennifer Cohen 19:52

Your book talks about the balancing of parents' rights to the kind of trial they want, and you've discussed so eloquently about the stresses of bringing up a child that's going to have medical challenges against possible risks of harm to a future child and the right of a child to have, quote, an open future. Can you flesh out that notion of a child's right to avoid pain and suffering, presumably, and some sort of write to an open future one that might include disease?

Robert Klitzman 20:23

Yes. So, I feel like in a number of instances in the book, and I should say in the kinds of decisions that come up in IVF clinics, and that parents and providers involved with assisted reproductive technology phase are questions in which the rights of the future child are not considered. There are some cases which are somewhat apocryphal, but apparently have happened where, for instance, two Deaf parents have said that we want to have a deaf child, genetically, and we want to screen embryos to make sure the child has the genes for deafness or to dwarf parents

have said that we want to make sure that we have a child who's also a dwarf. I think one problem with that, and apparently some doctors have said yes, in these instances, I think a problem is that the child obviously has no saying this, I think that obviously I agree with the disability community to be born deaf is not a life sentence to a terrible life and people who are deaf have fulfilling lives, dwarfs have fulfilling lives. But if we don't know how the child him or herself will look at that. A child may say, I didn't want to be born deaf, or I didn't want to be born dwarf.

One case I heard about recently, apparently, it was done with a case of a deaf child. And I asked her, why can't the child just learn sign language, and therefore communicate, the parents apparently said, well, we only sign and we don't want a child who's not going to sign. Well, rather than create a deaf child, you could teach the child to sign for instance. So similarly, let's say we select children to have certain kinds of athletic ability, and to be an Olympic sprinter as I mentioned, with the case of the gene that's found in a huge number of Olympic sprinters, even though it's a fairly low rate of being found within the population. The child may not want to be an Olympic sprinter, or the child may not want to even be an athlete. Parents may say, look, we spent \$50,000 to create you, so you'll be an Olympic sprinter because that's what I want to do as a parent, and I didn't get to do it. I think that's unfair to the child. Maybe the child's interested in being an Olympic sprinter, maybe the child's interested in being a poet or a musician or a gardener, who knows what. And so probably, especially if parents have paid a lot of money 50 to \$75,000 to, quote, "create a child to do a certain thing and the child doesn't want to do that," I think that creates a lot of stress. And so, an undue stress. So, I think children have a right to an open future meaning where their future has not been predetermined in that way, or in these kinds of restrictive ways, or these kinds of expensive ways that have lots of parental expectations attached to them. That could lead to tensions. I think, rather than that, children do have a right to have an open future and make these choices for themselves about what kind of life they want.

Jennifer Cohen 23:09

Fascinating. I want to return to something you raised earlier, when people hear about preimplantation genetic diagnosis, gene selection, gene editing, even the phrase designer babies, I think the immediate historical reference will be to Nazi eugenics, the US Supreme Court case of Buck vs. Bell, which affirmed practices of involuntary sterilization for people in the United States who were perceived to have low intelligence or antisocial behavior. How does that past history of eugenics inform today's debate?

Robert Klitzman 23:43

Well, it's a great question again, and I think should inform the debate, it doesn't always on some sides as much as I think it should. But I think what it shows is that, in the past, our efforts to control the genes of individuals or future population have in retrospect, been horrific. So, for instance, in Buck v. Bell, there was a woman who was in some kind of, quote, "mental institution," and one of the Supreme Court justices said famously, three generations of imbecility is enough. Well, it's not clear what the genetics were whether there were genetics involved. So, we need to be careful about saying that some people shouldn't reproduce and again, this a lot here and elsewhere, there's sort of a slippery slope, if we start to say, well, these people shouldn't reproduce. What about those people?

Of course, the Nazis took this to horrific ends where they said we want to improve the genes of Germany, so we're going to kill all the Jews, all the gypsies, homosexuals, people with disabilities, Asperger's, etc. Let's kill them all. So again, some of these things are not genetic, obviously, but we need to be careful because there's enormous hubris involved in that it violates the rights of certain individuals, obviously, the fact that they killed people with disabilities, we now believe many of us and certainly in America that people with disabilities have rights can be fully functional and contribute to society into their families in all kinds of ways. So, it's a very narrow, limited misinformed approach to think we are going to improve genetics of people. And it turns out that genetics is much more complicated than anyone thought.

So, when the human genome was first sequenced about 20 years ago, or so, it was found that most of our DNA does not form proteins and was there for called junk DNA. Well, invariably, it's not junk DNA, it's doing something we just don't know what it is. So, some people call it junk DNA. But so, we know very little about genes, we share 90% of our genes with mice. So, when mice were found to have whatever, let's just say, for argument's sake, 20,000 genes, there are geneticists who said, well, humans must have 100,000 genes. Well, it turns out we have not that much more than mice. And so, what becomes apparent is that it's the instructions that are embedded in DNA of when different genes should be turned on and off, and how and how much and when, that create the human body and the human brain and all the advances that have taken place, evolutionarily in the past few million years that have led to us evolving from mice or from other mammals that are non-primates, etc. So, there's a lot we don't understand.

Similarly, even with Dr. He Jiankui in China, incapacitated the CCR5 gene, which is what he did in creating these two children, or at least two children that we know of that have been written about the CCR5 gene lets HIV the virus get into cells. So, he worked with fathers who have HIV to give them a child who wouldn't get HIV. But if you disable that gene, the CCR5 gene, HIV doesn't get into cells as well. But other viruses get into cells more easily. So, there's a higher risk of influenza or West Nile virus getting into cells. Plus, he clipped out too much DNA, we don't know what the long term effects of that will be. Plus, genes perform multiple functions. So, a gene may be involved in HIV, getting in your cell but it may also be involved with brain development, let's say. So, if you disable that gene, it may have other kinds of effects that are unforeseen. So, we just don't know enough to be, quote, "playing with Mother Nature here," so to speak. And I think that's another way in which we should be humble and avoid hubris. So, I think these are considerations and the fact that there have been gross errors made in the goal of "eugenics." These should make us hesitate and proceed with great caution. How much caution varies. I mean, some people say one, or that's the past, and now we can control things more, I still think we need to be proceeding with great caution.

Jennifer Cohen 27:51

So, in most cases, as you said, creating a baby requires not only no money, but no medical knowledge, no medical intervention. Your book really highlights how complex some of these technologies are. And your previous answer did so as well, how much we still need to learn about the way genetics work. But there seems to be, and you talk about this in the book, a need for education, about reproduction, and fertility and these technologies, both in the referring clinical doctor realm and in the public. People think they know about fertility, but it turns out, they don't know very much. Why do you think there is still such a lack of knowledge about human fertility? And some of these technologies like IVF, as you discuss, they've been around since the late 70s. What is the reason for that do you think?

Robert Klitzman 28:38

Again. Great question. I think there's a few reasons one is, "sex is a taboo." So, a lot of people don't want to talk about their infertility problems. And I should say that about 10% of men and 10% of women have infertility problems, which means that 20% of all heterosexual couples have infertility problems. That is if they want to have a child, they're going to have difficulty doing so. And assisted reproductive technology can help them. A lot of men, though, feel that if it's their fault, biologically, so to speak, that is if they have a low sperm count, are impotent, that they're not macho, and there's a stigma to that. It violates their sense of machismo, so to speak. So, a lot of men are very much ashamed of their infertility. A lot of women also don't want it discussed. So, for instance, women, when they reach 40, have a much-decreased viability of their eggs. And so many women over 40 ends up using another woman's eggs to create a child. And they tend to feel quite strongly that they don't want the child to ever know that they are not the genetic mother of the child because they're afraid the child won't love them as much for instance. And so, we know that here in the US, most mothers and fathers who use someone else eggs or sperm never tell the child and never intend to tell the child. So, this has though created problems recently because with 23andMe people are now finding out on their own when they send their sample in as adults to 23andMe or other direct consumer genetic testing companies that

in fact, the person they thought was their mother or father genetically is not an that they instead have a mother fathers genetically somewhere else. And often, sometimes scores of half siblings. So, I think that suggests the kind of taboos it exists about talking about this. So people don't want it known that they are infertile and people don't want to feel shame, some most poignant episodes that I described in the book to me, and when I did the interviews, these were among the most poignant moments are when people said how hard it was to not be part of the parent club, where everyone else they know when their age group is having kids, and people would say to them: "Well, I guess you're too concerned about your career to want to have kids, huh?" And they feel hesitant to say, actually, we're impotent. Something's wrong with me medically in terms of my ovaries, or the womb, or my husband has a low sperm count. People don't want to talk about this. There are taboos about this. So, I think those are some of the reasons in the technology is new, as well. So, it's not something that is part of people's consciousness growing up, etc. So, I think those are factors that all contribute to much less public discussion or awareness of assisted reproductive technologies compared to what should be happening.

Jennifer Cohen 31:31

I think you've stated but let me ask you directly, whether you consider how Jiankui's achievement of creating HIV resistant children to be a type of physical enhancement? Or do you consider that to be more in the realm of disease prevention, bringing a child to the status quo of what is generally perceived as normal?

Robert Klitzman 31:51

It's a great question. So, in some ways, the answer is neither. And that obviously wasn't preventing a disease that kids may never be exposed to HIV, in which case they don't need to have the gene disabled. Moreover, I should say there are other much simpler ways for an HIV positive father to avoid passing on HIV to a child there is something known as sperm washing, where you take this sperm, and you remove the fluid around it. And so therefore, you remove the HIV around it. So, it wasn't creating, it was this sort of in between area so to speak, in that it wasn't to prevent a medical condition from being passed on, HIV is not passed on that way necessarily. So, it doesn't have to be, yet it not exactly social enhancement. Practicing safer sex is an easy way to avoid HIV and plus there is pre-exposure prophylaxis at this point to prevent HIV transmission, even with sexual partners, etc. So, I think he would argue that it was medically indicated but I think the medical indication is minimal at best given that there are much easier, simpler, safer, more effective ways of preventing HIV from getting into a child.

Jennifer Cohen 33:02

And one of the consequences of this announcement was the establishment of an international commission on the clinical use of human germline genome editing, a collaboration between the US National Academies of Science and the UK Royal Society. You've recently written about the commission's report issued in September 2020. Can you assess the report's findings and what you see as some of its shortcomings?

Robert Klitzman 33:25

Yes. So, I should just back up a second and say that after Dr. Dr. He Jiankui announced that he created these twin girls, there was a huge outcry. And so, there were two entities formed. The as you say, the National Academy of Science in the United States with the Royal Society in Great Britain formed one commission, and the WHO the World Health Organization created a committee and it was decided that the committee would look at, quote, "governance issues," and the National Academy of Science would look at scientific and medical questions, as well as the ethical and social ones. What ended up happening is that the National Academy of Science and Royal Society commission included almost all scientists only a handful a very small number of bioethicists where's the WHO one included many more bioethicists than scientists. And I think this was a mistake. In retrospect, some could have predicted earlier perhaps.

So, this scientific commission came out that report and focused in its discussion basically just on the scientific issues and sort of ignored the ethical and social ones saying, well, the WHO will look at that. The WHO report, and they have been very transparent, what they've been doing is looking at very broad governance issues such as the need for transparency, the need for stakeholder involvement. What becomes clear is that neither has looked at exactly how individual risks and benefits should be looked at. So, what the National Academy of Science with the Royal Society report said is that, basically I'm paraphrasing, but once CRISPR on human embryos to create human beings is found to be safe, then here are three sets of conditions, then it could be used for when parents don't have another option for having a healthy child. And when the condition causes premature death, for instance, well, a problem is many conditions cause premature death, heart attacks cause premature death. So, they then gave three examples. Obviously, other conditions would fit under the rubric of causing premature death. So, the examples I gave her a Huntington's mutation from both parents, both parents having cystic fibrosis, for instance. In other words, where it looks like the children will all have the condition. But in some of these instances, first of all, extremely rare so the only cases where parent has Huntington's from both parents at both parents at Huntington's are in rural areas, isolated rural areas in Venezuela, and the Dominican Republic, the report itself said that on some of these instances about more than, you know, five or 10 parents in all of the United States and Britain put together. Also, for some of these conditions, it's unlikely if one parent had Huntington's mutations of both parents, they probably wouldn't reach reproductive age. And the odds of both parents having Huntington's disease are exceedingly low. So, my concern is that, because on paper, these conditions might warrant it, but you're creating a huge loophole or Trojan horse for other conditions, potentially. So, I think without consideration of those, and I think instead of saying premature death, they could have said infantile death, for instance, or childhood death. So, I think there are those kinds of problems that come up with the report.

And again, I think that a problem also is you want to be careful about creating such loopholes, because we now have global reproductive travel where parents can go to another country and have a procedure done. It's another procedure called mitochondrial replacement therapy, in which you take the nucleus of one woman's egg, the surrounding cellular material from another woman's egg, and then a man's sperm, you have three parents involved. This is illegal to use in the United States, that is to transfer such an embryo into the womb. And so, the embryo was made in Massachusetts, it was implanted in Mexico, and the child was born in New York and the charge parents were from another country. So, with that kind of global travel, this becomes very difficult to monitor. And also, to know at what point then does it become safe enough? Well, you need to do it first to know how safe it is. And so, there's going to be a lot of nitty gritty questions about is it now safe enough? Or should we allow it for this particular instance, that are going to fall into individual institutions and individual doctors and as I tried to show in the book, designing babies, the IVF industry and assisted reproductive technology industry now in the US, is very lightly and poorly regulated.

So, this the kinds of problems that occur with assisted reproductive technology already bodes poorly for our ability to oversee and regulate use of CRISPR technology on human embryos for creating humans in the future. So, I think we need to be very, very careful all over the world, knowing that doctors are going to easily get involved in gray areas, especially when there's money to be made. Parents are going to want various things done doctors we see with even sex selection, as I've mentioned earlier, people have just for basically any reason means that we can't look to doctors as being the ethical gatekeepers. And I think one of the points I was trying to make in the book is that we therefore all need to be aware of these issues and discuss these issues and make decisions societally as well.

Jennifer Cohen 38:43

So interesting. Okay, let's shift gears, I'd like to ask you about one of my favorite books of yours *When Doctors Become Patients*. You start your *Designing Babies* book, another wonderful book of yours that I hope we can get to in another podcast. The ethics police, about IRBs, you start both those books with personal anecdotes. And you share with the

reader that this personal involvement with an ethical issue altered your perspective in a way that might not have otherwise happened. The book when doctors become patients, explores that theme extensively and opens with a very personal story. Would you feel comfortable discussing the experience of being a physician that lives through personally lives through what some of their patients are going through and how that affects patient care?

Robert Klitzman 39:33

Yes. So, what you're talking about is unfortunately, my sister died on 9/11. She worked at the World Trade Center for Cantor Fitzgerald. And, I got a call one morning from my mother, I'm sitting in my office saying, you know, did you hear an airplane hit the building where Karen works, I thought, Oh, I'm sure she's fine. You know, you hear about an earthquake somewhere and everyone thinks, everyone they know, the whole area must be affected. Of course, that rarely is the case or usually luckily is not the case. But in this case, unfortunately, my sister died and took us a few days to realize that and give up hope on the possibility she might be alive. It was a very, very difficult period for all of us who were in New York City and throughout the world, unfortunately, after that terrible day, and for the next few weeks, we had to plan a memorial service and then eventually pack up her belongings and empty her apartment and sell her apartment and go to the FBI, and list her as a missing person, officially, etc., etc. And we did all those things. And then my body just gave out, as I described in the book. And so, for a few weeks, I felt I had the flu, I just wanted to lay in bed, I didn't want to do anything. I didn't feel like watching TV or leaving listen to music, the only place I felt comfortable is lying in bed with the cool sheets. And, as I said, I thought I had the flu. And Fred said, "well, no, this is grief. It's depression, it's part of grief." I said, "no, no, no, I have the flu." And I was a psychiatrist. But I was surprised how bodily the symptoms were. In other words, it wasn't like, I mean, obviously, I was grief stricken, I felt grief stricken. But what my body was feeling were very bodily symptoms. It just hurt to move, my eyes hurt, my eyelids hurt to move. I just lost pleasure in things. I wasn't always thinking about Karen, my sister, it was like, as if I felt like I had the flu. And it then occurred to me, my God, well, if this is here, I'm a psychiatrist, and I didn't realize how patients with depression and symptoms of grief are experiencing it. Wow. What else? Are we as doctors not understanding about our patients?

And so, I got funding from the NIH and elsewhere to do a study of when doctors become patients to see what is it that we as doctors then learn that we didn't know beforehand about the experience of becoming a patient. And I found many, many things, as I described in the book, from seeing the suddenly for many doctors, spiritual issues became important. For instance, that meant number of these doctors said things like, you know, patients used to say to me, Doc, would you pray for me? And I go, yeah, yeah, whatever. And I poopoo it, they tell me, and these doctors would say, then I became a patient and thought I was going to die, you know, serious cancer, etc. And I suddenly realized how important those issues were. Or another doctor told me who was a surgeon told me that the night before he underwent surgery, his surgeon said to him, you know, there's a 5% chance you may die tomorrow in the operating room. And the surgeon told me that night I couldn't sleep. And it's only later that I realized that my surgeon could have said to me instead, gee, there's a 95% chance that things should go okay, tomorrow. And the surgeon turned to me and said, you know, I've been a surgeon for 40 years, and I never before realize that those two bits of information 5% chance die, 95% chance do okay, those two bits of information, which are statistically the same, have such completely different meanings personally, to a patient, I never realized that. Then another doctor said, you know, I went to see my doctor. And you know, he kept me in the waiting room. 40 minutes, I was driven up the wall. So, I said, well, have you ever kept the patient waiting, he said, I don't know. I never thought about it. But he now says to every patient, I'm sorry to have kept you waiting, even if he doesn't know if the patient's been waiting. He says he now sees it sort of melt some of the tension in the room that he didn't even know existed. So again, on many levels, these doctors learned a great deal that I tried to synthesize in the book to help both doctors but also patients and families understand what some of the tensions and divisions across this gap and divide are.

Jennifer Cohen 43:42

it's such a wonderful book, and I cannot recommend it highly enough. It's helped me so much in my interactions with physicians as patients and advocating for other people. Thank you for writing it. So finally, Dr. Klitzman as both an academic and a public intellectual, how did you approach your role during the pandemic? And what ways were you able to provide and share your expertise with policymakers, pharma researchers, the public patients, how did you see a role?

Robert Klitzman 44:14

Well, thank you also great question. So early on, in February when there were not more than 20 cases, the United States, I realize that there were enormous bioethical issues involved with COVID with our response to COVID with prevention with treatment, etc. From How should we address it? Should you prevent anyone from China coming to the country? Who should get the ventilators? Should hospitals say no to all patients with all other conditions? Who shouldn't get masks? Should you require masks in hospitals? These are fundamentally ethical decisions, that is, your questions of how do we assess individuals right to let's say not want to wear a mask if they don't want or individuals rights to get a ventilator against what the benefits were of getting or the treatment risks versus the risks of if you did one course of action or another, if you mandated mass or if you let people decide to wear them or not, and leave it up to them. And then there were justice issues of, you didn't want to unduly burden or disadvantage people who were worse off to start, who may have been from disadvantaged minorities, etc. And so, I was struck by the fact that there was a surprisingly little recognition of these ethical issues, and there wasn't much guidance, people were sort of flying by the seat of their pants is both at a federal level of state level institutional level, there was a lot of uncertainty on what to do. And so, I thought that it was our responsibility as bioethicists to try to provide shed some light on these issues, ways of approaching them, frameworks. So, I started to write about them.

I wrote a few pieces for the New York Times for CNN for elsewhere and also for academic journals, on how we should allocate ventilators, whether we should require masks what some of the issues were about why people did not want to wear masks and how we should best educate them. There were huge misunderstandings about a lot of these issues. There were questions in hospitals in New York State, for instance, in which families have the right to say I want everything done for my loved one who's dying, doctors realized that if we did cardiopulmonary resuscitation is on a patient who had COVID, especially in the beginning of a pandemic, using a bag to sort of pumping a bag by hand over the patient's mouth, would lead to virus being spread all over the room lead to risks of COVID, to the healthcare workers who'd be there. And yet there was essentially no chance of the patient surviving or leaving the hospital alive. And yet if doctors didn't do it, they could be sued. And so, there was a need for guidance from states to say that doctors that we could have crisis standards of care.

Similarly, for instance, because of the overload, the surge, whereas normally might have one nurse for every four patients in an ICU, there was such a huge shortage of nurses in the ICUs, you might have made other wards into ICU, but you might have one nurse for 10 patients. Well, let's say a patient died, the patient's family could potentially sue saying My father died because there was only one nurse for 10 patients as opposed to there should have been one nurse for four patients, that's the standard of care, normally, and so there needs to be recognition that at times, unfortunately to alter the standards of care when you're in a real emergency. And yet, this did not happen in many states. In New York, Governor Cuomo said he would give doctors legal protection if long as they weren't being negligent if they followed this crisis standards of care that he released, and then he never released any. So, there's a lot of confusion. I thought that they were important roles for bioethicists to provide to educate policymakers at different levels to educate an institution, statewide, etc. And so, I felt that through writing and talking about this, and I spoke to people in the media, was interviewed in the New York Times and elsewhere, that these were important roles that we as bioethicists could and should have.

Jennifer Cohen 48:14

Dr. Klitzman, thank you for all your tireless work in the field of bioethics on behalf of protecting vulnerable patients and research subjects and for your work as an academic preparing the next generation of bioethicists. It's been a pleasure speaking with you today.

Robert Klitzman 48:29

Well, thank you very much. It's been great having this conversation. So, thank you.

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