

Artificial Womb Technology with Dr. Kelly Werner

Jennifer Cohen and Kelly Werner

Jennifer Cohen 0:03

Welcome back to Voices in Bioethics. I'm Jennifer Cohen and it's my great pleasure to welcome Dr. Kelly Werner to the podcast. Kelly, thank you so much for joining us today.

Kelly Werner 0:13

Thank you so much for having me.

Jennifer Cohen 0:15

Dr. Kelly Werner is the chief fellow in the Division of Neonatal Perinatal Medicine at the Yale School of Medicine. She completed medical school through a combined degree program at Siena College and Albany Medical college, graduating with a distinction in bioethics, and she is currently completing a Masters in Health Science through the Yale School of Medicine with a Concentration in Bioethics. She's published in the American Journal of Medical Genetics, and the American Journal of Bioethics. In addition to bioethics, her research interests include the care of children with medical complexity, incorporation of new technologies in clinical medicine, and health equity. Kelly, in 2017, Nature published an article on a research project at the Children's Hospital Philadelphia with University of Pennsylvania, on an artificial womb technology that had successfully gestated a number of lambs. And this got a huge amount of attention and really created a lot of excitement in the medical world, in the bioethics world. I believe another platform is under research in Australia, the Eve Platform I think it's called. I think the one at UPenn is called Extend. I believe there's a lot of research going on in this area in Japan. What is an artificial womb and how does it work?

Kelly Werner 1:35

Yes, so an artificial womb is essentially a way to support an animal in the cases of research or a human being when we eventually get to that stage, outside of its native womb. So instead of a fetal lamb, for instance, growing inside the uterus, inside a mother, it's actually being transferred from its mother's uterus, to a plastic bag, commonly referred to as a Biobag in the cases of the Extend model, which is being developed at the University of Pennsylvania. And the way this actually looks is that a fetal lamb would be inside this plastic bag, known as a Biobag, submerged in a sterile fluid. And then tiny tubes, also called catheters, would be used to connect its umbilical artery and its umbilical vein from the fetus and then outside the bag, to an external device called an oxygenator that's outside the bag. And what the oxygenator does is, essentially, it's a membrane that functions like

a placenta, in that it infuses oxygen and helps remove carbon dioxide from the fetus' blood as it passes through, and then returns oxygenated blood back to the fetal lamb. And then IV nutrition is provided into the blood vessels in this way as well.

Jennifer Cohen 2:59

Okay, so sort of a circuit is put in place.

Kelly Werner 3:02

Yes, so the models at the University of Pennsylvania, and the model developed through combined efforts at Tohoku University in Japan and the University of Western Australia, the Eve model, are both similar in that way.

Jennifer Cohen 3:18

Okay. And is the lambs own heart pumping or is that part of the circuit as well?

Kelly Werner 3:24

Yes. So these two models are actually unique. And I think that they tried various different ways of having the blood being pumped to the circuit. But they found that the best way was using the umbilical vessels as the delivery method, rather than the carotid vessels, for example, for the fetus' native cardiac output to be pumping the blood to the circuit the same way that it would in utero pumping blood to the placenta.

Jennifer Cohen 3:54

Okay, so how long were they able to keep these lambs inside this Biobag gestating?

Kelly Werner 4:01

So what they did was they chose particularly lambs that corresponded to a human gestational age of around 23 to 25 weeks gestation. So for the model at Children's Hospital of Philadelphia, and UPenn, the Extend model, that was lambs that were at about 105 to 117 days gestation. And they kept them in there for a few weeks actually, and then transition them to conventional care. So the same way that they, for example, care for a neonate after it was born, and using a breathing tube and a ventilator, and then they were able to support the lambs until term, and then they did show long term survival for some of these lambs as well.

Jennifer Cohen 4:51

It's just astonishing. And I really encourage listeners to go to the internet and look at the pictures of these lambs in

the Biobag. It's really incredible. So why is this technology needed? What, what is this technology designed to do that present technology cannot do.

Kelly Werner 5:10

Alright, so this is what's actually very exciting to me as a neonatologist is that the research is targeted to help what would be neonates at borderline viability. So the Extend model says that their target is for fetuses who had reached say, 23 to 25 weeks gestation, and they were going to be delivered either way. So this would be a non-elective form of care. But if a mother came in to the hospital, for instance, and she was in preterm labor, she was progressing into labor at 23 weeks, and this baby was going to come out either way, this would be a good candidate for the artificial womb. The other candidate would be a person who came in pregnant at 23- to 25-weeks with extremely high blood pressure, and it was dangerous for her to stay pregnant. So they needed to do a C-section and get the baby out, in order for her to, for her to, to help bring her blood pressure down. This would be another good candidate for the artificial womb. So really, it's to care for, in particular, fetuses that would have been delivered at this border line of viability and care for them in a better way. So currently, the way that we care for these neonates after they're born is with mechanical ventilation. So, if I'm in the delivery room, and I'm waiting for a fetus to come out, and this baby is then born at 24 weeks, I'm prepared and expecting to put a breathing tube in immediately and hook up this baby to a mechanical ventilator. And that baby might be on a mechanical ventilator for weeks or even months. And that's traditional and conventional NICU care, as we see it now. And the problem with using mechanical ventilators is that they in themselves cause damage. So these baby's lungs are already not fully developed yet. And then we're hooking them up to a ventilator that's giving them positive pressure into these lungs, it over time is causing what we call a chronic lung disease. So even by the sheer process of us trying to save the babies and keep them alive, our mechanism of keeping them alive also causes long term damage. And then one thing that we worry about, especially here at Yale, we resuscitate babies as early as 22-weeks, so our 22- and 23-week babies might end up needing a ventilator for such a long period of time that they need a tracheostomy. So one of those openings in the neck, connect them to a ventilator. And that's just due to the long-term damage of mechanical ventilation, being intubated. Some of the other risks that our babies at these early gestational ages face is, you know, things like cerebral palsy and developmental delays. Other things that they might suffer from in the future is when we eventually get that breathing tube out, they've had that in their mouth for so long. They don't want to feed from a bottle, and they might need a permanent or semi-permanent feeding tube put in their stomach. And then if we think about all of these very, you know, trying and invasive things that we need to do to these babies, then it eventually comes time for them to leave the hospital. And their parents are then tasked with taking care of a medically complex child. So some of them actually require some degree of nursing care at home, either 24 hour nursing or different periods of time of nursing. And then some of these babies born at our earliest gestational ages are even too sick to go home and then end up going to a chronic care facility. So this is, you know, an extreme, but these are things that we do see, and we're kind of at a standstill with our current care in that we're having difficulties improving our outcomes with what we're currently doing. We've made some improvements in survival, but it's very difficult for us to improve survival for these earliest babies. And it's extremely difficult for parents to go through this NICU stay, especially with all of the difficulties that these babies face. And it's also caused a lot of moral distress for you know, the doctors and the practitioners and the nurses. So what we would like to do with the artificial womb is take, you know, one of our babies who had come to our NICU because they were going to be born anyway, so non-electively, and we want to bridge them through a few crucial weeks in lung development. So, if a baby's born at 23-weeks, we want to put them on the artificial womb instead of a mechanical ventilator. So we're going to support them in a different way and preserve their lungs for a few crucial weeks. So, if we could keep the baby on the artificial womb for two or three weeks and

allow their lungs to grow and develop, and then, perhaps, when they're 28-weeks gestation or so, they can come off the artificial womb and not need a breathing tube. Maybe they can require some oxygen and pressure support in their nose instead. Then that would be a way for us to drastically improve, not only our survival rates, but also our morbidities for our NICU babies.

Jennifer Cohen 10:21

Okay, that's an incredibly persuasive case. So in essence, this is a delay tactic, this is a way to, because while the, and again, this has only been used for lambs, but the lambs in the Biobag have fluid in their lungs, they are not breathing air. So this is a delay tactic to wait for that development to progress and then to be able to intervene with traditional NICU interventions.

Kelly Werner 10:49

Yes, that's exactly it.

Jennifer Cohen 10:50

Okay, that's really helpful for in terms of the science and why it's needed. Can you give us, before we end with sort of the scientific understanding of how this works, can you give us just a quick overview of the functions of some of the aspects of this you've already mentioned? The placenta, amniotic fluid, the umbilical cord, what do they do and how are they replicated again, in this artificial womb technology?

Kelly Werner 11:15

Yes, so the placenta's main function is providing oxygen and nutrients to the developing fetus. And these are functions which we can attempt to replicate with the artificial womb, this membrane can provide oxygen, and we can use IV nutrition, and give that into the bloodstream to help the fetus grow and develop. But there are also a variety of growth factors and immune factors and hormones, which the placenta provides, which would be much more difficult for us to replicate. And the artificial womb models that are developing now don't even attempt to do so. So those are some functions that the artificial womb would lack. The amniotic fluid also has extremely complex roles in fetal development and another area of research that scientists are continuing to learn about, even today.

Although the amniotic fluid provides cushioning as a basic function, that's something we can replicate by submerging the fetus who then becomes the human being in the artificial womb in a sterile fluid that can also provide the cushioning and protection, but we're far from understanding and replicating the growth factors that amniotic fluid provides. And then even the uterus itself, so there's not really a mechanism in place with the current model of the artificial womb to replicate the uterus. What a uterus does for a developing fetus is providing a protective mechanism, providing a cushion and a barrier to the outside world. But also, the uterus is a muscle and it's helpful for the muscle development of a fetus, the fetus is moving against a uterus in some ways and developing its own muscle tone. And that's something that the artificial womb would also, as it's currently being described to us, doesn't have a mechanism to replicate that.

Jennifer Cohen 13:09

Okay, was there a particular reason why fetal lambs were chosen as subjects?

Kelly Werner 13:13

So there are some important similarities in the development of fetal lambs and human fetuses. So I think one of the important similarities would be the size of the heart and the amount of the blood that the heart is pumping. That is one of the limiting factors of how small and how immature a fetus can be transitioned to the heart of the artificial womb is a heart strong enough to pump blood through the oxygenator. In addition, the blood vessels would be similarly sized as well. A third really important similarity would be the stages in lung development. So they particularly chose stages in lung development of the lamb, that very closely mimicked a 23- to 25-week human fetus. There are some important differences which would include the size, so even though a lamb at 105-days gestation is similar to a 23-week gestation human fetus, the lamb is much larger. So they did have to conduct experiments just to make sure that a smaller lamb would have the blood vessel size necessary to mimic a 23-week fetus. And then another important difference would be the brain development. Our infants at borderline viability which we, you know, consider the 23- to 25-week range, sometimes as young as 22-weeks, they have very fragile blood vessels in their brain which are prone to bleeding. That is one of the ways in which their development can be different from that of their peers who were born full term is that they are prone to these bleeds in their brain which can cause developmental delays. And that's compared to a fetal lamb, their blood vessels actually strengthen and develop a little earlier. So these fetal lambs will be less prone to this brain bleeding.

Jennifer Cohen 15:10

Okay, is the next step going to be Primate Research?

Kelly Werner 15:14

So actually, as Dr. Flake had recently presented to the Yale School of Medicine a couple of years ago, they had described being in conversations with the FDA about human trials, but they have not discussed the stages of Primate Research.

Jennifer Cohen 15:32

Interesting. Okay, what are the risks of this technology, I guess, looking forward to humans, do we know yet?

Kelly Werner 15:41

So some of the risks that I could foresee would be related to the bleeding in the brain. So part of using these very small catheters in the blood vessels connected to an oxygenator requires that they use a little bit of blood thinning medication like heparin to keep the blood from clotting. And then using something like heparin could affect the human being in the artificial womb, who has immature blood vessels, make them more prone to brain bleeding,

also known as intraventricular hemorrhage. So that's something that we're always screening for and looking out for in our babies in the NICU, something we're always worried about. That's something that could also potentially happen for babies supported by the artificial womb. What would be helpful is that babies in the artificial womb would not be on a ventilator, and maybe have more blood pressure stability. If they were more stable than a baby being cared for in the conventional way in the NICU on the ventilator, that stability in itself might make them less prone to these brain bleeds. Other risks that we could foresee would be the risk of infection, for example, requiring antibiotics. And then you know, less technically, but if you think of that the you know, the bonding that would occur from a baby being in utero, a lot of that will be lost by being in in the artificial womb, but similarly to how a baby would develop in the NICU. But I think a lot of NICU parents would tell you that bonding is very difficult when you have these physical barriers between you and your baby. So that's another important consideration.

Jennifer Cohen 17:26

Yeah, I was going to mention that the 2017 Nature article brought that point up directly I'm going to quote from the article, "an additional disadvantage that has been raised is parental perception of having their fetus in a 'bag.' It is important to consider that the comparator is the extreme premature infant on a ventilator and in an incubator, we feel that parents will be relatively reassured that their fetus is being maintained in a relatively protective and physiologic environment. The clinical device will be designed with many features that should allow the parent to be connected with the fetus, including ultrasound, or darkfield camera allowing real-time visualization of the fetus within its darkened environment, and the ability to play maternal heart and abdominal sounds to the fetus. We therefore feel that the advantages far outweigh the disadvantages of exposure of the fetus to the conventional care imposed on the critically preterm infant in the neonatal intensive care unit environment." So just this point, you're discussing and amazing considerations about playing a heartbeat and sounds and so forth while this fetus is gestating.

Kelly Werner 18:28

And these are things that could theoretically be done for our infants in incubators.

Jennifer Cohen 18:35

Right.

Kelly Werner 18:35

But we don't currently do.

Jennifer Cohen 18:37

Interesting. Is there any understanding of the cost of this yet?

Kelly Werner 18:42

So I haven't seen any figures presented about the cost, but we could extrapolate to some extent. You know, neonatal care is expensive. It's 1000s of dollars per day per baby in a NICU in the United States. And many of these babies who would be born at these earliest gestational ages would be there for months. So a NICU hospital stay is very expensive. That being said, it is more cost effective and less costly overall than other forms of intensive care, you know, for children or adults. And then, as I had mentioned about our infants born at maybe 22- and 23-weeks and the morbidities that they can suffer as a result of just being born preterm, hopefully, better outcomes for these infants would result in an eventual cost savings. If you think about that, we wouldn't for a potential infant who was going to be in the hospital for months and then maybe go home with either 24-hour nursing or need to go to a long term care facility, maybe if that infant were able to go home once they reached term age, and they reached 40-weeks and they could go home with breathing room air, that would be a cost savings for the health care system. So it's definitely an important consideration, but I think we don't have a good estimate yet.

Jennifer Cohen 20:03

Okay, that's a very good overview of the science behind this technology. Let's turn now to a discussion of the ethics. So you've already mentioned this, but I want to get a little more deeply into it – a lot of the ethical frameworks in neonatology stem from a decision about viability. Can you explain the significance of viability in neonatology and how an artificial womb might affect the current thinking around viability?

Kelly Werner 20:30

Yes, so viability can have a few different definitions, but the most common one would be something like median viability. So viability we can just generally think of it as the earliest a baby can survive outside the womb. When we talk about the womb, we mean the native womb. So right now, in our current care, viability is limited by the stages of lung development. Because a fetus in utero, so in its mom, is getting oxygen from the placenta, its lungs remain filled with amniotic fluid, it's not using its lungs for gas exchange, gets oxygen from the placenta, and the lungs can remain fluid filled, and grow and develop. But once the fetus is born, that fluid is expelled, a fetus tries to take its first breath, and then that baby is needs to rely on its lungs for gas exchange. So if the lungs are not developed enough, then there is no way for the oxygen to diffuse from the lungs into the bloodstream, and no way for the carbon dioxide to diffuse from the bloodstream back out to the lungs to be exhaled. So I think a good way to think of this is if you think of a tree with many branches, that's somewhat of how the lungs are looking as they're developing. Eventually, you know, around the time of 24-weeks, we need to start seeing those branches actually grow some leaves. And those leaves would be like the alveoli in the lungs. So those actual air pockets that exchange oxygen and carbon dioxide, so the earliest a baby can survive now outside of its native womb is 22- to 24-weeks because it has, essentially, its lungs or trees without many leaves yet. So if a human being in the artificial womb does not need its lungs to get oxygen, we're providing the function of the placenta, it's conceivable that the limit of viability as we currently think of it could inch downward lower than 22-weeks. And we're not exactly sure yet, then what is the next limiting factor? So right now, our limiting factor is lung development. But if we take away lung development from the equation, then we're not exactly sure what's the next limiting factor of viability.

Jennifer Cohen 22:57

Okay, we are recording this on Monday, June 27th. And on Friday, June 24th, the Supreme Court ruled in *Dobbs vs. Jackson* that there is no constitutional right to an abortion. Therefore, states can pass laws to protect fetal life at all stages of a pregnancy, including the pre-viability stage, provided there's a rational basis for the regulation. And the Mississippi law in question had banned elective abortions after 15-weeks, and there's no way a fetus could be considered viable at 15-weeks. So, both sides of the case argued that if the Mississippi law were allowed to stand, it would mean the overturning of *Roe* and *Casey* and that's indeed what happened. And one of the reasons the court came to its conclusion is that I'm quoting, "the viability line makes no sense. It was not adequately justified in *Roe*, and the dissent has not even tried to defend it today," close quotes. So I'm wondering if you could comment on how you see this technology, which potentially, as you're saying, had, normally we would say viability is outside the, quote, native womb. Now you might have a fetus a neonate, outside of its native move much, much earlier, is that more or less viable? How do you see this intersecting with the legal debate going on right now?

Kelly Werner 24:19

Right. So I think that what might be helpful going forward is if we are implementing the artificial womb as a mechanism for neonatal care, then it would be helpful to have two words for viability. So maybe we should be talking about natural viability and separately, we could be talking about artificial viability. So in that way, the artificial womb would not change the limit of natural viability. And it does seem that while the limit of viability does make sense to me as a physician and as a neonatologist, apparently it did not make sense to the court, but regardless, what doesn't change as a result of the artificial womb is anyone's right to bodily autonomy. So I've seen a lot of, you know, popular articles, even prior to the court's decision, worried about, would the artificial womb changing the limit of viability, change our abortion laws. And it does seem like even before the artificial womb there was they decided to change that for us anyway. So if we talk about the right to bodily autonomy for an example, I only bring this up because I've also seen this in a few popular articles related to the artificial womb. So just as a few examples, like if I were to go to the emergency room with abdominal pain and fever, and they told me I had diverticulitis, they need to take my infected colon out, I have the right to say no, even if that means I will die, right. And the same is true is if I go to the hospital at 25 weeks pregnant, or even 35 weeks pregnant with abdominal pain and fever, and the obstetrician says that they want to do a C section because the fetus appears to be in distress. I can also say no, even if that means I will die, or even if that means the fetus may die, I can always decline a C section. So I've seen things come up about could I be forced to transition my fetus to the artificial womb, because now that fetus is technically viable using that form of support, instead of being able to terminate a pregnancy? The answer is no, because there's no logistical way to do so without violating my bodily autonomy. So for example, doing a C section without my consent. So another practical aspect, I would say, would be that the current technology, Extend or Eve, could only lower the limit of viability by a couple of weeks. So saying that we don't necessarily know what is the next lower limiting factor of viability – so is that the size of the umbilical blood vessels, maybe? Is that the size of the heart and how much blood it can pump? So in that sense, we're probably only able to lower the limit of viability with this technology by a couple weeks, I would say. So in a country, such as the United States where 90% of abortions are performed in the first trimester, us lowering the limit of viability by a couple of weeks with the artificial womb does not seem that it could feasibly overlap when abortions, or most and the majority of abortions are actually being performed. And I think what's also important is that prior to clinical trials, it's going to be important for the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and other professional medical bodies to make sure that they instate policies and issue statements, which ensure these protections against improper use. And then if we're going to have state or federal

laws passed related to this, we should make sure that they're done so with the input of physicians and scientists and ethicists rather than driven by politicians and their ideologies. So I think that none of these are reasons to not pursue the artificial womb, because its advantages are so important for both parents and babies. But we want to make sure that these protections for women are in place, and that I think, could be done by codifying a distinction between natural and artificial viability.

Jennifer Cohen 28:30

Those are all critically important points as we move forward, and ones that I'm not seeing mentioned enough. So I'm, I'm thrilled to hear you bring them up. I know you've thought a lot about nomenclature. And this, you bring up this distinction between artificial and natural viability. And you've also thought a lot about how to refer to the unborn. Can you talk a little bit about how the artificial womb technology affects that debate about what to call the developing patient for lack of a better word, one that's in a natural womb, one that's in an incubator, one that might be in a future artificial womb?

Kelly Werner 29:09

Yes. So you can tell that even I struggle with this sometimes to try and not influence anyone's opinion, as I describe it, I try and say human being as best I can. And I think that describing the nomenclature and the moral status of the human being in the artificial womb is super important. And one way that I have tried to do this is by a thought experiment with three rooms. So if we think of room one is a pregnant person at 23 weeks gestation, and she comes in preterm labor, and she receives a prenatal consult from a maternal fetal medicine doctor, as well as a neonatologist. She's actually counseled about the risks and benefits of delivery, and she's counseled as well about the survival rate of this fetus as well as the morbidities that the fetus could suffer as a result of being born at 23-weeks. Due to a low survival rate, in this particular case, she declines the C section, and she opts for comfort measures for her fetus. And then down the hall, say in room three, we have a neonate at 23-weeks gestation in an incubator on a ventilator. So although this neonate is at 23-weeks, the same gestational age as the fetus down the hall, this neonate no longer depends on its mother's body for survival. And in many ways, this neonate's rights are more and this neonate possesses more rights than a fetus does. And then say, in the middle of these two in room two, we have someone at 23-weeks gestation supported by an artificial womb. So in many ways, they're treated similarly to the neonate next door in room three. So the neonate is getting nutrition from the doctors who are giving IV nutrition. It's getting its, you know, its oxygenation from the ventilator. The patient on the artificial womb is also getting its IV nutrition from the doctors rather than the mom. It's getting its care from the nurses, and it's getting its oxygen from the oxygenator. So we have to kind of decide, does this human being in this patient in the artificial womb, are they similar to the fetus at 23-weeks in room one? Or are they similar to the neonate at 23-weeks in an incubator on a ventilator in room three?

Jennifer Cohen 31:38

Wow.

Kelly Werner 31:41

Yeah, so

Jennifer Cohen 31:42

That's a tough one.

Kelly Werner 31:43

It definitely is. And I think that, as a neonatologist, I'm going to be treating the patient on the artificial womb similarly to the neonate. And that's because the patient on the artificial will no longer relies on its mother's body for support. And in many ways, some of the changes that happen after birth, so for example, both parents have equal decision making capabilities, both parents have equal custody, rather than just the mother or the gestational parent, both parents can then bond equally, although less so than if this patient were still in utero. So in many ways, it does seem like we would be treating and caring for a patient on the artificial wombs, similarly to a neonate.

Jennifer Cohen 32:28

Okay so in that analytical framework, the moral status is very much interlaced with the human being's ability to be independent of its mother, its native womb, and then how much it is equally – its goods are equally decided by both parents. That's the way you've laid, that's the way you're thinking about this issue?

Kelly Werner 32:51

Yes. So with respect to the moral status of the human being in the artificial womb, a lot of that is going to be contingent on you know, which which label we use for this human being. So, it's been proposed by some, including Elizabeth Romanis, to use the term "gestateling." If we have a new, unique human being in history, we need a unique word. And there's been a handful of other words proposed. But I think what that is doing is if we're using a different word, we're implying a different moral status. So, if we are using the term fetus, we're implying the moral status of a fetus. If we're using the term neonate, we're implying the moral status of a neonate. And if we use an in between word, we're implying something less. And what's important about the moral status of a neonate is we can debate when a human being achieves full moral status and the degrees of moral status of a fetus. But we have nearly universally agreed upon that a neonate has the same moral status as any of us, right? A neonate has the same moral status as an infant that's almost a year old, as a child, as a teenager as an adult. So if we're using the term neonate, for our patients in the artificial womb, we're implying a full moral status and all the rights that come along with having full moral status in our society.

Jennifer Cohen 34:19

And just to be clear, it's it has those rights, because it's left its mother's native womb.

Kelly Werner 34:24

Yes.

Jennifer Cohen 34:26

Okay. Interesting. So, sometimes in the literature, I see people trying to make a distinction between what is happening in an incubator, and what will be happening in an artificial womb. But if you're assigning the same status to the neonate, in the incubator, and the I know, you don't like this term, gestateling, but what is in the artificial womb, then are you seeing a big scientific difference between what's happening in the incubator and what's happening in the artificial womb?

Kelly Werner 34:53

So, the physiology of the two is different, but there are a lot of similarities, which I can discuss and I think go along with the two being cared for, in a similar way, and receiving the same rights from from society. So, we haven't discussed yet the example of Extracorporeal Membrane Oxygenation–

Jennifer Cohen 35:15

Right

Kelly Werner 35:16

–also called ECMO, E-C-M-O, which is similar to cardiac bypass. And that is something that we do for full term babies in our neonatal intensive care unit who have severe are born with severe lung problems or severe heart problems and we need to bridge them to recovery or bridge them to a surgery, for example. And what this does, is supports a full-term baby in a very similar way to the artificial womb. So essentially, blood is taken out through a catheter, it's put through a pump, it's put through an oxygenator and then it goes back through another catheter back to the body of the baby. So the blood leaves, it gets oxygenated, and then it returns to the patient. And that's essentially the same as what is happening in the artificial womb. The only difference is the patient supported by the artificial womb is much smaller than the full-term baby supported by ECMO. So we have kind of a hybrid between traditional preemie NICU care and full term ECMO care in the form of the artificial womb. So the ways in which it's similar to traditional preemie NICU care, are that the incubator is essentially like the Biobag. It's a clear protective barrier that's preserving heat, and it's preventing insensible law water losses. It's keeping the skin moist. So for us as neonatologists, it seems like a natural step for us to care for a human being in the artificial womb. It's kind of a hybrid way from the hybrid way between the way we care for our preemies and the way we care for our full-term babies with heart and lung issue. So from that standpoint, it does seem like although I've seen, you know, various arguments in the literature about how the physiology is different, and things like that, the physiology is the same as other things that we do for full-term babies. So this would almost be a natural progression of our NICU care. And it wouldn't be something out of the realm of the care that the nurses, the practitioners, and the

physicians already do. It would pretty much be the same personnel using our same knowledge base and applying it in a different way.

Jennifer Cohen 37:38

Right. And you've mentioned a number of times that this is not, you know, envisioned as an elective technology. However, assuming it becomes successful and widely used, can you envision a time when an artificial womb would become preferable to traditional gestation given that you could completely control conditions of gestation: you could avoid exposure to drug and alcohol use, smoking, poor diet, even trauma? Can you imagine that one day being preferable and even optimal?

Kelly Werner 38:12

Yeah, so assuming that technology is successful, it would definitely be preferable to some forms of conventional NICU care, like using a breathing tube and being on a ventilator for weeks or months. If we were looking to make it an elective type of technology, we are probably generations away from this technology being superior to traditional gestation, what you know, when the time comes, I think would be preferable in many ways to ensure that we're improving our survival rates. So if it is safer for a baby to be and it has, the baby has a higher chance of survival in the artificial womb, it does make sense for the sake of both the baby and the parents to try to expand the use of the artificial womb, you know, for these types of patients.

Jennifer Cohen 39:08

Okay, and let me end our fascinating discussion with a couple really philosophical ontological questions for your bioethicist hat to think about is that there seems to be a bit of some feminist backlash in some of the stuff I've read about this technology. Again, going back to the 2017 Nature article, the author's wrote quote, "[f]inally, our system offers an intriguing experimental model for addressing fundamental questions regarding the role of the mother and placenta in fetal development." And there have been some that I read an Australian sociologist Robin Rowland, who thought artificial wombs were an attempt to eliminate a vital power that women have. Their have their's a long line of feminist thought, most notably by the late Canadian feminist Shulamith Firestone, who, oh, who saw pregnancy as a type of tyranny that women needed to be freed from. How do you think about that, that type of question how it affects mothers, females who traditionally gave birth? And then finally, is there something about being born from a human body that makes us fundamentally human assuming that one day this technology is gestating fetuses from the get go from the lab onward? Have you thought about that very, that very, in some ways old question? As you've discussed in your work, this goes back to early 20th century and *Brave New World* and all sorts of ideas about ectogenesis that we saw from J.B.S. Haldane back in the 1920s. How have you been thinking about that issue?

Kelly Werner 40:50

So I guess I'll kind of start with J.B.S. Haldane's original reason for coining the term ectogenesis and what he was talking about, because I think that helps, helps me form my opinion on on this topic and my opinion on eventual

full ectogenesis. Originally, in 1923, when he coined the term, he meant to use that as a word for a human being created outside the womb. And he predicted that by 2073, a third of newborns would come from artificial wombs. And this was just a thought experiment. The reason he brought it up is because he thought this would be a great thing to free women from the necessity of pregnancy. And then I think it was two years later, in 1925, when Dora Russell, a feminist intellectual, she agreed, and what she wrote about was that the future of science is going to help disrupt the gender imbalance in society. And I think I started from that framework when I started to think about the benefits of full exogenesis. And I think that you know, it's different for every feminist and it's, you know, it's different for women who and people who have given birth versus not given birth and had that experience, but I do think the option of decoupling being born female from pregnancy and childbirth could be an important step toward equality and liberation from the societal tyranny of, of motherhood. What I do think would be, you know, devaluing is if this was the only way that women could give birth and people could give birth in the future. And then another important component of this is that when we eventually have full ectogenesis, when, when that's a you know, that's a couple centuries away, who was having access to it, of course. So we want to make sure that if we are decoupling being born female and having a uterus from pregnancy and childbirth, that that is something that is equitable and accessible for anyone who desires it. So I think that one of the ways that that could be important for people who can't have children, for LGBTQIA individuals, for example, to eliminate the necessity of gestational carriers, for instance, which is like inherently a can be an exploitative for some people. I think that justly applied, it can eventually be a very promising way for us to live in not necessarily a post-gender world, but a world with fewer gender differences.

Jennifer Cohen 43:21

Dr. Kelly Warner, thank you so much for such a fascinating discussion and for committing yourself to think about this issue so carefully, thoughtfully, compassionately. I'm very glad you're at the forefront of the way this will unfold. Best of luck in the future.

Kelly Werner 43:37

Thank you so much for having me, Jennifer. I greatly appreciate it.