ROBERT BARTLETT: Thanks to Ed, and to Rick, and the rest of you for inviting me to share a little bit of this information. So I am going to talk about extracorporeal support, or-- in pediatrics. It applies in many areas, but since you're all in the pediatric area, we can focus on that, and also primarily on hearts.

So this is the typical story. Here's a little girl that's about six years old, happy and healthy one day, dying the next day of H1N1 plus strep pneumonia. She's on all the pressors, and in septic shock, and on maximal ventilator settings, and dying. And this is the kind of patient that we would like to intervene with a mechanical life support system, so-- which we did. So this is her x-ray the next day with a big catheter in her right atrium, another catheter in her inferior vena cava. And her gas exchange is being managed with a mechanical device.

So this approach is called extracorporeal life support or extracorporeal membrane oxygenation, not a very descriptive word for what it actually does, but we tend to stay with it. And it refers to support of heart or lung function with mechanical devices, which is temporary, days to weeks, nowadays to months. It can be partial or total support, most importantly, avoids ongoing iatrogenic injury. So when we use this, we can turn off all those pressor drugs, which are wonderful , but have bad side effects, we can turn off the ventilator, which is wonderful, but has bad side effects, and simply sustains life while bridging to organ recovery, which we hope will happen with this little girl, or in some patients, replacement with a device or a transplant.

So the indications for doing this are acute, severe, cardiac or pulmonary failure, which is unresponsive to other conventional management, in which recovery can be expected-- we used to say within two to four weeks. And that's probably still right, although we're getting to the point where it might be might be longer than that. So those are easy to describe and adjectives, quite hard to describe in nouns.

When is cardiac or pulmonary failure so severe that it's not going to get better doing whatever we do, and it's worth the risk of something that has inherent risks of its own, and is expensive, and for a long time was experimental? So how to get from straightforward indications and adjectives to defining it is part of the challenge of developing this whole technology.

So some of the early history is shown here-- sorry. Back in the middle '60s, cardiac surgery using a heart-lung machine was a relatively new technology. I happened to be a resident at the Boston Children's Hospital where the Chief was Robert E Gross, deity in surgery to any of us.

And we were-- he was doing cardiac surgery in children. And the mortality was 50%. Half of those children died. And I had the temerity to go to Dr. Gross and say, why don't we just keep these kids on a heart-lung machine for a couple of days? Because we knew, if they got through the first day or two, they'd be OK.

Well he said, of course, that's why they're dying. The heart-lung machine is lethal if you use it for more than two hours, which it was. But why don't you work on that? Hence a 50-year career, that's mentoring. Why don't you try to solve that problem?

Now this is a picture of an engineer named Phil Drinker. And Phil, and I, and some others built membrane oxygenators to replace the bubble oxygen that was being used at the time. And what do you know, that solved the problem of the mortality of the heart lung machine itself. So this shows a dog that's been on extracorporeal circulation for four days, pretty exciting in the early '60s.

And then, as Ed said, then we-- when I left residency, went on to UC Irvine. It turned out to be an important move, because it was a brand-new medical school. It opened the day we arrived. And they say we, because another resident buddy, Alex Zuniga, and I went out there and quickly got assigned the job of running a county hospital, and doing whatever you want to do. There was no one around to say we don't do it that way, so we did a lot of wild stuff, including working on this particular technology.

In 1971, the first clinical case was done by a friend of ours, a surgeon named Don Hill from San Francisco. This was a patient who was in Santa Barbara. It was the first successful patient. We worked on this ourselves. We did, as I said, we were doing all the surgery in our little hospital, including the cardiac surgery and the pediatric cardiac surgery.

And we did a Mustard operation. A few of you remember that procedure. And this little boy who was dying post-op of low cardiac output syndrome and so on. And we brought our machine from the lab and cleaned off the sheep saliva and things like that, and hooked it up. And what do you know, he recovered after a couple of days.

That was the first cardiac survivor. And the system we used-- sorry, very sensitive-- is shown here. So you recognize just a stripped down heart-lung machine. We'd gained access to the right atrium through the jugular vein. We drained blood out, heparinized it, run it through a membrane lung, warm it up again, and put it back in the patient into the systemic circulation, in this case, through the carotid artery.

And we're on venoarterial cardiopulmonary bypass, just like we were in the operating room, but with different access and with different devices. So we learned that this would work. And that we could do this for days at a time with complications, but people could survive.

In 1975, we were asked to see this little girl, a newborn infant with severe respiratory failure. You can see a nice, full-term baby whose lungs didn't work at all. And so this was not unusual, because we were the pediatric surgeons to this hospital, as well as the cardiac surgeons, and general surgeons, and everybody else, so it was not unusual for the neonatologist the call us and say, you want to bring your machine over here try it on this baby? Well, we did that.

And what do you know, she recovered over about a week. And she happened to be an orphan, because her mother had delivered her, was in the country illegally, and left having been told her baby would die. So the nurses named her Esperanza. So she's become, kind of, a famous patient in the ECMO world, because she's been to meet several other people. And people know about the story about Esperanza. She's now 43 years old, has children of her own.

But the important thing is that she recovered and did well. And that led to another case, and another case. So we learned that this particular technology would work in that particular group of patients. This describes the number of cases in red and the number of-- in yellow, and the number of cases in red that were experimented with this technology.

And in 1980, I moved back here to the University of Michigan. So this technique has really grown here in Michigan as sort of the fountainhead of this technology. Ever since that time, we've continued lab studies. We did clinical trials, did a variety of things. And this became a more widespread technology by about 1990.

In 2008, an important thing happened in this technology. One was a worldwide epidemic of H1N1 flu. You might remember the swine flu. It was very contagious. It was not particularly virulent except for some patients. But young patients, pregnant women tended to get this, and had severe respiratory failure. And it turned out that ECMO was the only treatment that was successful in those patients with an 80% survival, pretty unusual.

The other thing that happened in 2008 was some companies decided to make actual ECMO machines. Prior to that, we took devices that were intended for cardiac surgery, and used for cardiac surgery, and modified them in various ways to use them for a longer period of time. But it was pretty complex and difficult to do, required someone to sit at the bedside continuously to manage this in case something went wrong, which it often did. And it looks sort of like this.

With the new devices that-- and there are three of them. And they're all made in Germany. They were much improved. They were simpler. They were easier to manage. They had much less complications. And so it became possible for anybody who has a good intensive care doc with a good surgeon could hook this up and get it to work first time out of the box. That made quite a difference, as you'll see.

So the application of this technology extends to any situation in which there is a severe heart and lung failure that's not responding to conventional management. It all depends how you hook it up. So for cardiac support or support of the circulation, you have to use venoarterial access, cardiopulmonary bypass, as I showed you earlier. And we can hook this up through the neck vessels, through the femoral vessels, or, in fact, just through the right atrium and aorta, as you'd use for cardiac surgery.

And in fact, one significant application for all of you is that. It never happens to Ed. It occasionally happens to Rick. But every now and then, you have a patient who can't come off bypass in the OR after-- oh, some of you-- you might have been there. So you know, when you can't off bypass, and you're giving all the drugs, and so on, an alternative is just to convert that to an ECMO machine, because that can go on for a few hours or a few days if you have to do that. So access directly through the chest is one way of hooking it up.

If the primary problem is respiratory failure, like the little girl I'd been telling you about, you can do venoarterial bypass. And it works fine. And we did that for the babies, for example. But you can hook it up in a venovenous mode, draining blood from the inferior and superior vena cava and pumping it back into the right atrium, which allows you to substitute for the lungs.

You can remove the CO2, you can add oxygen. Provides no cardiac support, so it's a little different mode, but for this little girl, like I had been showing you, her heart is fine once we got through the septic shock area. And we're just supporting her lung function with venovenous access.

That kind of gets to be important, because the-- all the blood goes through the heart and lungs, including the damaged lungs, which we think is good. And also any blood that comes out of the ECMO system goes into the venous circulation, so there are little crumbs and emboli that come out of that circuit all the time. And if they go into the systemic circulation, they find their way into the brain, and the kidneys, and the lungs, so venovenous has access advantages for very long-term support.

So once you're doing this, now managing the patient in the ICU, as all of you know who have taken care of ECMO patients, is very different than what you were doing just two hours before when all you had to work with was a lot of drugs and the ventilator. And now we don't need that. You can just turn all that off.

So how to manage the patient? It requires a fair amount of orientation and education among the staff. A patient who used to have an arterial sat at 91 and we were worried about it now has an arterial sat with venovenous bypass of 80%. We say that's fine.

So you have to have some education on old-fashioned physiology. You have to decide when the heart or lungs are better enough to try to get off the machine. You need to have people who are really good at managing this, that is, day-to-day, hour-to-hour, minute-to-minute.

Doctors are not good at that. We get bored pretty quickly. So even perfusionists who do this for a living, they do it for two or three hours in the OR. They hate sitting there at bedside for a day, or two, or three.

So we've developed a category, a professional group called ECMO specialists, who come from nursing, or perfusion, or respiratory therapy backgrounds, and have learned how to manage this technology at the bedside. And that's been a very important part of the development of this technology, so that by 1990-something, certainly by 2000, this became a fairly routine ICU procedure.

Also, with the new technology, that allowed us to take a totally different approach to managing these patients. So in the early decades, what we did was a lot of sedation, often paralysis. Patients were intubated. They were on the ventilator, but on low settings. A specialist had to be at the bedside nonstop.

We tried to recruit the lungs if there was lung failure. And bleeding was a major problem, often the fatal problem in these patients, because the blood has to be anti-coagulated. And that creates problems.

With the new machinery, we've evolved to a new method of managing these patients. They're in fact alert, and awake, and usually extubated, if they're cardiac patients. And we manage them either extubated or perhaps with a tracheostomy. A well-trained ICU nurse can manage these patients. It's no longer necessary to have someone specific at the bedside.

We've learned that trying to recruit the lungs was a mistake. All it did was make pneumothoraces. It's better to just watch, and wait, and wait for the lungs to get better. And bleeding is still the major complication, but it's now an annoyance rather than a fatal problem.

Other centers around the world learned to do this, mostly came here and we trained people how to do it, and ask to them only that they let us know what their results were, so that led to the registry of patients. And we have a fairly complete registry of most of the patients that have been managed with this technique. And that led to the formation of a group called the Extracorporeal Life Support Organization, or ELSO, which began in 1989.

That was the first meeting. We just came from the 28th meeting, where there were 900 people, kind of unlike the early days. And what ELSO does is maintain the registry of patients, but also provide a time when all the centers that are involved in this technology can get together, can meet, can share information, can decide what we're doing poorly, what we can do better, and so on. These are the ELSO member centers, about 600 of them currently.

So I'll show you a little bit of data from the registry. These are the types of patients in the registry, so that in the early days, they were almost all newborn infants here with respiratory failure, but-- and that number of patients stays about the same. But as a percentage, it's gotten much smaller as we use this technique for children and adults with cardiac failure, which is now the major application of this technology, or children and adults with respiratory failure where it's currently growing quite rapidly.

These are the results in the registry as of about a year ago. And we collect this information and report it in three categories-- neonates, which is up to 30 days, pediatric patients, and adult patients, with primary indication being either pulmonary failure, cardiac failure, or there's a category called ECPR, which is CPR for cardiac arrest supplemented with venoarterial ECMO, which in fact this is fairly successful.

So you can see there are, totally, about 85,000 patients in the registry. And the survival for ECMO itself is about 70%. About 10% of those patients still die in the hospital. That's a problem we're still working on. So the overall survival is about 50%, 60%, not bad, considering we only put on patients who we think are going to die otherwise.

On the other hand, lots and lots of room for improvement, so we keep working on this in the laboratory. And I'll tell you a bit more about that in a while. So you can see the results in terms of survival are best for newborn babies because their lungs are basically normal. They just need to live a little longer. And worst of all, as you might imagine for ECPR for adults, the people who were arrested and we used this technique to try to help resuscitate them.

So that's the whole picture. From here on, I'm just going to talk about pediatric cardiac problems, because I know what you're focused about. And we can talk about some of the other categories later on if you wish.

So these are the number of cases in the registry each year. These are neonatal cardiac cases. Now, this starts in 1988 when there weren't any neonatal cardiac cases, and thanks in large part to Ed and some of the rest of you, you can now operate on babies within the first day, week, month of life, and fix those lesions which we used to fix-- we, when I was a resident with Dr. Gross, we would fix a tetralogy after the blalock, after the pots, after they graduated from high school then they'd come in and we could fix it-- I'm not kidding-- so to fix these lesions early on, I don't have to tell you, is a major step ahead.

And what do you know, this technology works for newborn infants, so that you can use this if you have a baby in the very early days who's not doing well from a cardiac, either pre-op or post-op, and provide reasonable success while other things are being fixed. You can see that this increases pretty dramatically starting at about 2008 for the reasons that I showed you. And the results in neonates or infants for cardiac surgery, almost all are operated on for congenital defects with overall about 40% survival.

Pediatric patients in our registry will run from 30 days of age to age 18. And as you can see, there about 600 or 700 a year in the registry. And congenital defects are still the most common indication.

But you start to see cardiomyopathy and myocarditis as indications for doing this. And the results in those patients are considerably better. Most of the congenital defects are, as we said, babies who can't come off the pump in the OR or they get to the ICU but they're failing hours later. So the patients with intrinsically normal hearts to begin with do a little bit better.

You will get involved with adult cases. And as you can, see adult cardiac cases really took off after 2008 when the machine really became available. And much of this is in patients with cardiogenic shock from myocardial infarction, or other causes in the cath lab with a disaster, or something like that, so it's really a very different category of patients.

I see Frank [INAUDIBLE] here. So Frank published the first paper-- remember this, Frank-- bridging to VADs from ECMO. When was that back, in the mid '80s or somewhere when everyone thought we were crazy? Why would you want to do that? But now it's become a fairly routine way to bridge from severe cardiac failure in adults to something else, which might be a VAD, might be transplant. And the indications in adults are cardiogenic shock, most of the cases, and there are more cases with myocarditis and cardiomyopathy.

Here at U of M, this is our experience since we've started in 1980, some 500 cardiac support patients in children with an overall 52% survival. And of course, the most of the cases are congenital heart disease, although cardiomyopathy or myocarditis have a little better results.

So the algorithm for managing these patients, it goes on for pages with respiratory failure, but for cardiac failure, it's become a lot simpler, because if the heart's not recovering after a day, or two, or three, it's very unlikely too. It's probably not going to get better. Myocarditis is different. They may take a week or two for it to recover. But everyone else, if you had a big myocardial infarction or if your repair of a tet or whatever is not working well and the heart is damaged, it's probably not going to get better.

So the algorithm is on day two or three of management, how's the brain? That's first question. Often times, it doesn't work. And often times, we just have to turn it off. The most common reason for failure is there was brain damage associated with the reason for cardiac failure.

But if the brain is working OK, and cardiac function is returning, you're probably going to be all right, so you just keep going. And the average run is about six or seven days. And those patients get better. If not then you have to think, early on, is this patient a transplant candidate?

If the answer to that is no, then you probably ought to have that discussion with the family, and say, you know, we're trying this. It's not working. You know it's not going to work. So let's, three days from now if we're not better, we're going to have to turn this off. If the answer is maybe the patient's a transplant candidate, then you can go to a mechanical support device, a VAD of some type, and sustain that patient long enough to get on the list, and perhaps get a heart transplant, or perhaps go home and wait for a heart transplant these days, as you all know how that works.

So how to do it? We've talked about vascular access, and the machinery itself is pretty simple. This is VA access, again, in a neonate. In a large child or an adult, we would prefer to go from the femoral vein, that is, draining the inferior vena cava to the femoral artery.

And the reason is that it does not have to sacrifice the carotid artery. You might worry about whether that's a bad thing to do, to ligate the carotid, but-- I'm looking for Hannah. She's a pretty good example of the fact that you can get along without your right carotid artery. But the older you get, the more you have to rely on collateral circulation.

So for adults, if you use the carotid, which I've used a lot of times, the stroke rate is about 15%-- unacceptable. So what age would you say, OK, we're going to go to the femoral vessels? Somewhere around age 6 to 12, somewhere like that, is probably the time to do that.

The problem there is that you're perfuming retrograde, so the bright, red blood goes up the aorta, but it mixes with whatever blood is coming out of the left ventricle somewhere in the aortic arch. So if the lungs are not working, that blood is going to be hypoxic. So we have ways of dealing with that phenomenon.

We've talked about ECPR. And ECPR is very successful in children. These are data from 10 years ago, but the current data is still the same. The survival rate for ECPR is about 40% in cases in the registry. And as you saw, there are a couple thousand such cases in children.

This is a little misleading, because the only time we can use ECPR V-A ECMO associated with cardiac arrest in children is when we're all tooled up to do it. So what this means is, here's a patient who is doing poorly and not doing very well. We've got our ECMO machine. And we've got it primed. We're thinking about maybe going on. On Now the a child arrests. OK, quick, hook him up, but-- because we're all ready to do it.

To do it from scratch is nearly impossible, although that's happening now in our emergency room and other emergency rooms around the world. A patient comes in with out-of-hospital cardiac arrest. If the ER team is trained, and that takes a couple of years. The ER docs can put that patient on V-A ECMO. And we're just in the process of studying that phenomenon.

As you all know, now a days, if you have a child who might be a transplant candidate, you can go to the Berlin Heart. What do you know? Isn't that exciting? Well, we have some responsibility for that.

We're very proud of that, because when the Berlin Heart company wanted to qualify their BiVAD, basically, with the FDA, the FDA said, you have to do a controlled, randomized trial. We said, what do you mean? Because the alternative is, here's a child who's dying, about to be dead. And we only use this for that kind of patient.

So the FDA, to their credit, said, why don't you do a matched-pairs trial? So take the patients with your device and compare it to patients from the registry, which there were 700 patients who were being bridged to transplantation. And of course, they did very well. And the device was on the market in 2011.

And we in the ELSO community are very proud of that, because it's the first time that the FDA has ever permitted registry data to be the control group for patients. And it solved the ethical problem. It solved the logistic problem. We got the device approved, so we're particularly proud of that.

So to summarize all of that, the details of managing a patient on ECMO, it's all about physiology. So this is physiology that you all learned in year one of medical school or nursing school, but it's amazing how many intensive care people have forgotten it. So you have to go back and talk about what the oxygen requirements are, what the oxygen delivery system is, how much do you need, how do you measure it. And you measure it by measuring mixed venous saturation, and so on.

It's great to talk to all of you, because you know about maintaining a normal hematocrit. I love it when the neonatologist say, the hematocrit's down to 50. We better do something.

Because in the adult world, there's a fad that's going on that's just crazy. The more anemic you are, the better it is. And if you're really sick, you ought to be really anemic. And hospitals have rules. You can't transfuse patients, because we all know how bad it is. And that's all written by people who forgot all their freshman physiology.

But it is important in any of these patients to maintain a normal hematocrit, because that's the basis of oxygen delivery. You have to learn a lot about gas exchange. If you're on for cardiac support and the heart is not working at all, the left ventricle and left atrium will gradually fill with bronchial venous blood, so you have to vent that. That's rarely a problem in children, because their right ventricular-dependent, usually the left side works all right.

You have to anticoagulate these patients. It still is the major complication. It's a big problem. We're looking at different types of anticoagulants and different non-thrombogenic circuits. We haven't solved it yet.

What is important is that we now manage these patients fully-awake and alert. And if they're old enough, meaning after the age of about four, because if you wake up a two-year-old, he's going to pull the catheters out in the middle of the night. It's a very different approach to management of these patients, of managing them awake, so you can talk to them.

In fact, it has important implications that I'll show you in a minute, keeping it dry while using hemofiltration, so on. Maintaining some flow through the heart is important. Otherwise, if it's just stagnant, that blood will clot, even though the patient's anticoagulant. So this has now become the standard treatment for severe cardiac or pulmonary failure in children. And what that means is, any of your ICUs will have to have this technology or have a system to transfer such patients to a center that does it.

So I'll close by telling you a little bit about some of the new stuff that's happening. And in lung failure, it starts with this little girl. You can see here, whose name is Reese. At the age of seven, about three and a half years ago, she had a 30% total body burn plus severe smoke inhalation.

She was treated at Hopkins. She had a cardiac arrest in the process. She was on V-A ECMO for two weeks. Her heart got better, but her lungs did not, so she was on V-V ECMO for a couple of months. Then the fibrosis got so bad that she one into right-heart failure.

And so what they did was convert to a version that, through, by a thoracotomy, cannulated the right atrium and the pulmonary artery, put an oxygenator in the circuit. And she's on ECMO through that particular connection for 15 months of time. During that time, her lungs recovered. And what recovers first is always oxygenation, so she was-- didn't need oxygen support, but still could not excrete CO2, which is part of the pathophysiology. She was on V-V ECMO for another two months, and then weaned off after 605 days of support.

I just came from the ELSO meeting, which was in Baltimore, which happened to be where this little girl was. So here, you have a picture of Reese, this little girl. She's a year and a half later, and happy, and healthy, and getting along fine here with her mom and her Doctor, Chris Nelson at Hopkins.

And her doctor is important, because can you imagine how many times someone came around saying, what in the hell are you doing here? It's been-- you know, her heart's failed after being on ECMO for two months. Turn her off. Don't you read the literature about it?

Yeah, but she's alert and awake. And she's in school. She's Skyping with her class. Uh, OK-- and then the administrator, you know how much money we've spent to have this little child here? She's taking a bed in the ICU. After a while the cardiac surgeon comes around and says, that's very nice, but don't you know someone's talking about canceling my case for tomorrow, so get rid of-- take this kid out of here.

So this one particular case is so incredibly instructive, because-- and she's not the only one, but she's the most dramatic one. And now we've learned in hundreds of patients that the lung has a remarkable capability to regenerate and recover all the way back to normal in patients that we used to say this is irreversible lung damage. And I'm looking around at some of my friends here. Remember when we turned patients off after a week, or two weeks, or a month of time because the lung wasn't working, so this is going to work?

And we turned it off. Patient died. They'd go to the morgue. And the pathologist would say, I don't even know what tissue this is, just this junk is in the chest. Now we know it can recover back to normal function. Who would have guessed that, so a whole new era in lung biology made possible by supporting these patients for a period of time with mechanical devices.

Now that's not new. You do all that with the heart, so if the heart doesn't work, you can use a mechanical device. Sometimes the heart recovers. Sometimes you have to replace it. And if you're old enough to remember the days when we first used dialysis for acute renal failure in the ICU-- well, I'm looking around. There's no one who's that old.

But one of my first patients as an intern was a patient who was on dialysis because of acute renal failure. And what do you know, those kidneys all recover. So we've been through this before, we're just finding it out now with regard to the lung.

So this offers new practical problems. How are you going to take care of a patient for two or three months, let alone two or three years, in your ICU? So we have to develop systems that get those people out of the ICU, out of the hospital, just like we did with VADs, and just like we did with dialysis in the past.

And it offers new scientific opportunities. How does that happen? It's clearly a stem cell phenomenon. But if you add stem cells to the lung in lung-injured patients, to date at least, nothing happens. But there are endogenous stem cells in the lung, which eventually get turned on and will grow new lung tissue. It's really exciting.

To get the patient out of the hospital is going to involve getting the artificial lung hooked up to the patient and sending them home, just like a VAD. Some of you remember when a VAD patient had to stay in the ICU until they got a donor. Now they walk around and become vice presidents, things like that.

So we're working on this in the lab. And the approach for children is to go from the pulmonary artery to the left atrium, because the problem is pulmonary hypertension, right ventricular failure, or perhaps a gas exchange, or perhaps just a growth problem. This is the problem in diaphragmatic hernia, for example, if the lung is just too small to support.

So this was first done in St. Louis as a bridge to transplantation in 2014. And there have been several hundred patients since then. We're on this in the lab to try to simplify this technique. And Ron Herschel has a nice grant to work on that particular problem.

One other bit of research that's going on is the problem with cardiopulmonary bypass, I said now, even for cardiac surgery, we use membrane oxygenators. We can use it for hours at a time without killing the patient. But if you're on cardiopulmonary bypass for not two, but four, or six, or eight hours, eventually that patient gets an extreme inflammatory response. The kidneys fail. The heart fail. The lungs fail.

But why does that happen? Interestingly, well, we think we're getting a clue to that. And then comes this paper from Australia. So they put nitric oxide in the sweep gas during cardiac surgery for congenital cardiac cases, and what do you know, it could significantly decreased the SIRS response, renal failure, cardiac failure, lung failure, and so on.

How does that work? Well, we're working on that in the lab. We've developed a nitric oxide generator, because otherwise it would be very expensive. And with that, we've learned that nitric oxide in the sweep gas prevents white cell activation, which we think will become standard treatment for cardiopulmonary bypass in children and adults, probably, in the future, eliminating the 5% or 10% that get post-op complications.

Gabe Owens was sitting over here. And Martin [INAUDIBLE] came to us a few years ago saying, you know, the biggest problem in pediatric transplantation is you can't get a donor. You have to have the right size and the right blood type. Why can't we maintain hearts on an ECMO machine for a few weeks until we can match it up to a patient? Well, we thought that was crazy. But we thought it was worth looking at, so we've been focused on the question of why it is that you can't perfuse an organ for more than about six hours. And that remains the limitation in transplantation of any organ. But we got working on this. And we like to think we might--

[AUDIO PLAYBACK]

- Again, AVHP 522 2017 without pericardium. This is hour 72.

So this is a three-day heart perfusion.

- It actually picked up speed.

Unprecedented-- isn't that amazing?

[END PLAYBACK]

So we're really excited about that possibility. We're just getting onto it, but it's pretty exciting stuff. And finally, we've looked at this technology for extreme prematurity. I think George is going to talk about this in a few minutes, so I won't go on, but it's stuff we're doing in the lab which is, we're working on to push this technology on to the next stage.

So in summary, in the future, the ECMO machine will have a variety of modules. So you can already plug-in the renal failure module, soon you'll be able to plug in the liver failure module and the sepsis module. We'll be using materials that do not require systemic anti-coagulation.

Hooking the patient up is a big problem. It takes two experienced people, usually surgeons, to do this. And we're aiming to get that down to any one intensivist that can put in an IV can put a patient on ECMO. We're building new membrane lungs. We're automating the system. We're working on the placenta and the organ culture aspects of it.

So remember Serena, the little girl I was telling you about. here. She is day 32. We used to turn these kids off at day 14, but she's alert, and awake, and still getting along, so no one could quite bring themselves to turning her off. But you could see there's zero lung function.

But a few days later, what do you know? The lung gets better. And what we've learned is this is what happens. There's no way you can speed it up, but when that regeneration reaches a point where it suddenly works, then the patient recovers. So here she is about to go home.

So I thank you for your attention. And I'll be glad to answer any questions. Rick, I don't know what the format is. You want to just proceed or take some time?

If anybody has any questions for Dr. Bartlett, that would be great.

Yes, sir?

John Mayer from Boston.

Sure, hi John.

One of the ideas that's sort of been floating around in my head for a long time is a way to regionally release anticoagulant. And although I know we've all been focused on the so-called soluble coagulation system, obviously platelets have got a big piece of this. And for some years, I tried to talk the Berlin Heart people into putting an extra little side cannula that would go right down to the inflow end of the cannula and maybe drip any platelet agents in there, adenosine being the one that I'm particularly fond because it's such a potent platelet aggregator inhibitor, and also goes away pretty fast, because--

So John-- Hi, John, good to see you again-- asked about a regional anti-coagulation, just anti-coagulating the blood that's outside the patient and then reestablishing normal coagulation when it goes back in. And in fact, that's done routinely in dialysis and hemofiltration, where we put a calcium chelator going into the dialysis circuit and put calcium back going out. And it works very well.

We have tried to do that with ECMO patients, but you're too close to the margin. We either got bleeding or clotting. And it's because ECMO involves the entire cardiac output, not just 300 or 400 CCs a minute. But it's a great possibility, using another drug like adenosine, as you say, that is very short acting would be a good approach. But it has to be so safe that it doesn't fail on the downstream side.

What we've worked on in the lab is something sort of similar. And that is we've developed plastic that secretes nitric oxide. So as you say, the real secret is the platelets, not the fibrin formation. So the way the normal endothelium works, it secretes nitric oxide. And you all know it affects the smooth muscle on one side. But on the other side, it prevents platelets from sticking to the endothelium.

So we've been at this for several years. We can make plastic. It secretes nitric oxide at the same rate the endothelium does. And it really does prevent platelets from sticking to the surface. So we're still in the process of developing it.

There are heparin-bonded circuits and other type of circuits that prevent the fibrin formation, but it doesn't solve the problem because the platelets. So you're quite right, that if we could solve the coagulation, as you heard me say earlier-- I think we're close to it. We'll be able to do this without systemic anti-coagulation pretty soon. All right, thank you very much.

[APPLAUSE]