Prevention of Cerebral Palsy

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Dr. Robert Clancy: "I'm Dr. Robert Clancy, I'm a Child Neurologist from the Children's Hospital in Philadelphia, Pennsylvania and I deal with newborns with acute brain disease. My interest is in pharmacological protection, and I think what I'm interested in looking into the future are the role of the caspases as a class of drugs that inhibit apoptosis. Unfortunately, the only caspases I know of right now are those that are given inside the ventricle so that's not a very convenient route."

Dr. McGregor: "So could you tell us what caspases are because some people think those are the enzymes that have to carry forward to the apoptosis."

Dr. Robert Clancy: "The caspase inhibitors are what we're looking for. I guess the notion is that we're not even sure what exactly is the cause of brain damage in newborns - to what extent is it frank necrosis, to what extent is it apoptosis, or some combination of that. So that's one of our research areas with congenital heart disease is now to look at the pathology and try to determine when we see lesions on the MRI - are they actually necrotic or are they apoptotic because that may take us in one direction or the other. What's on our immediate horizon are the use of drugs like Desflurane which are very broad spectrum with respect to neuro protection so they turn out to inhibit the apoptosis, necrosis, and glutamate. It really is a shotgun approach."

Dr. McGregor: "Isn't desflurane an anesthetic agent?"

Dr. Robert Clancy: "It is, it's an anesthetic agent that pharmacologically can mimic KTP-ases which are part of the biology of what you were looking for."

Dr. McGregor: "Cell activation."

Dr. Robert Clancy: "Now cell activation and also like preconditioning, so in preconditioning we might induce a sub lethal injury to the heart or the brain so that when it's repeated a day or so later, even a larger insult does not produce damage. The question is can we mimic preconditioning because preconditioning does protect an organ from ischemia, and the answer is, in fact, that Desflurane will mimic some of those changes from preconditioning. So if it's an operating room situation, you can add Desflurane over or on top of the ordinary anesthesia like for congenital heart disease surgery and continue that drug until they're in the post-op period. Then do it as an experimental trial, a blind and randomized trial and hopefully show that you can protect the heart and the head. Because one of the things that's sort of obvious but no one talks about is that even after birth asphyxia if you don't protect the heart, you have a harder time protecting the head because if the heart is asphyxiated too, and then even after the baby is born, they're not profusing their brain so that the two have to be protected together. The heart and brain should be protected together and things like Desflurane can do that."

Dr. McGregor: "So to sum up, you're looking at neuro-protective interventions which you could actually give ahead of or at the time of that intervention which might even include a birth where there is asphyxia associated."

Dr. Robert Clancy: "Exactly, we don't know what the window of opportunity is to treat after an event. Honestly, if you could do it before the event that would be fine, and that day may come but there must be some period, some grace period after the fact of asphyxia that you can still make things better. You may not have a chance to protect 100% but if you could protect it somewhat that would be worth the effort."

Dr. McGregor: "And these can even be translated into adult medicine because, say, patients who are going on the pump for heart surgery or patients who suffer an acute stroke, they may benefit from your kind of research as well."

Dr. Robert Clancy: "Exactly, and again, the advantage of this is simply that you know ahead of time when you're going to have surgery. If you can't show it in a controlled situation like this, it's..."
going to be very hard to do it in an open field situation where the person can be found down and different diseases, different times, different temperatures, and things like that."

**Dr. McGregor:** "So from your view as a Child Neurologist who works in the nursery at the Children’s Hospital in Philadelphia, Pennsylvania - the most important intervention we could do in terms of cerebral palsy or birth asphyxia would actually be to prevent the situation such as infection and inflammation which actually may be occurring during pregnancy."

**Dr. Robert Clancy:** "Right, and obviously for anything neurological once it’s a done deal you’re in deep already at that point. I would like to think that there will be controlled trials of recognizing a chorioamnionitis early, treating, immune modulators, or something to interfere with that process before it’s simply recognized at birth that the baby’s depressed."

**Dr. McGregor:** "In essence, perhaps in a football metaphor, how would you sum up everything?"

**Dr. Robert Clancy:** "Protect your quarterback."

**Dr. McGregor:** "Thank you. That was Dr. Robert Clancy, he’s Professor of Pediatrics & Neurology at the Children’s Hospital of Philadelphia. Thank you."

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