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Cord Blood: Emerging Clinical Applications

Narrator:

Welcome to CME on ReachMD. This segment: Cord Blood, Emerging Clinical Applications, is sponsored by Omnia Education. Your host is Dr. Karen Taylor who welcomes Dr. Charles Cox, Professor of Pediatric Surgery at UT Health in Houston, Texas.

Dr. Taylor receives consulting fees from Cord Blood Registry.
Dr. Cox receives consulting fees from Cord Blood Registry; contracted research: Cord Blood Registry, Athersys, Inc. and Biostage. He has ownership in Emit and Coagulex.

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Dr. Taylor:
Regenerative medicine is focused on replacing or regenerating of human cells, tissues, or organs, so as to restore or establish normal function. Cord blood stem cells are currently being researched for their regenerative utility for issues such as brain injury, hearing loss, autism, diabetes, and congenital heart disease. Today, we are focusing on what are the current and future applications for cord blood in this field?

This is CME on ReachMD and I am Dr. Karen Taylor. With me today is Dr. Charles Cox who joins our program to discuss the various roles that cord blood stem cells will likely play as medicine advances towards using the body's stem cells for treatment in disease. Dr. Cox, welcome to ReachMD.

Dr. Cox:
Thanks for having me.

Dr. Taylor:
It's nice to have you.

Just for a little background, the first cord blood transplant was successfully done on a young boy with a fatal disease called Fanconi's anemia in 1988. That boy is alive and well today. Dr. Cox, how many diseases can be treated today with cord blood stem cells and what are some examples of these diseases?

Dr. Cox:
There are a number of diseases that can be treated with cord blood stem cells, mainly the liquid tumors that require ablative chemotherapy, bone marrow conditioning, and then bone marrow transplantation. There is a range of different hematologic disorders that cause problems with the production of the body's endogenous blood elements, and then there's a host of inherited metabolic disorders. Fanconi's anemia or the Hurler's syndrome, the mucopolysaccharidoses, some of the other inborn errors that have been treated with transplantation of cord blood.

Dr. Taylor:
So, these are the groups that we would put the label traditional or transplant medicine indications on. As we look forward into the future,

there appear to be thousands of clinical trials looking at regenerative medicine indications. How would you define regenerative medicine in general terms for us, and how do you differentiate this field from the current traditional transplant medicine indications?

Dr. Cox:
The differences between regenerative medicine applications for cell therapy versus transplant medicine applications for cell therapy is the transplant designation is replacing the cells in their homologous function, meaning, the cells are going to do what is thought to be and what the FDA considers to be their normal function, meaning reconstituting the immune system, the blood-borne immune system and/or the production of red cells. So, that's the transplant indication and you categorize it based on that homologous use moniker that's attached to it. Regenerative medicine means to either restore or replace damaged or malformed tissue towards a more normal functional state and that is often then using, in terms of cell-based therapy, for things that are non-homologous. And that's usually done to tackle or address a non-hematologic organ system.

Dr. Taylor:
Dr. Cox, when we talk about the stem cell in regenerative medicine, the general population a lot of times envision that the stem cell is simply replacing the damaged cell, or just engrafting. What are some of the other mechanisms of action in regenerative medicine cellular therapy that you see?

Dr. Cox:
From the 1990s to the early 2000s, the fundamental thought process is that these cells would transdifferentiate, so turn into the type of cell that was missing in a regional environment. So if you'd get the cells to an area where there are missing types of tissue, then they would transdifferentiate into that cell type that was needed and then help restore that function. I think we've learned over the years that that's probably not what's happening. And so, the mechanisms of action are now starting to center around modulating some of the body's endogenous reparative processes through secondary messenger cells. And so, even though that end result may be the same, i.e. repair of that endogenous tissue, it's not about engrafting, but it's about promoting the endogenous repair systems so that the healing is promoted.

Dr. Taylor:
That's fascinating. When we look at a lot of these regenerative medicine clinical trials we're looking at treating conditions that a lot of OB providers are exposed to in their practice of medicine. For example, cerebral palsy or in utero stroke, even rare conditions like hypoplastic left heart syndrome. And Dr. Cox, as a pediatric surgeon whose research specializes in the cellular therapy of traumatic brain injury, but also other neurological conditions like congenital brain injuries and spinal cord injuries, can you share with us your most recent findings and what you're investigating right now?

Dr. Cox:
Our work in cell-based therapies is what you touched on in the last question. We use these different cell therapies to reset the immune response to specific injury, whether that's traumatic brain injury or similar types of lesions. And the brain responds to an initial kinetic injury that causes tissue damage with activation of resident immune cells called microglia and then infiltrating immune cells, macrophages that act like microglia. And these cells have a dual function of being both inflammatory and reparative, and that has to do with their regional microenvironment. And the trick, for us, is to not turn off all inflammation, because a little bit of inflammation is good. It helps remove dead or dying tissue, bacteria. But if that inflammatory process is out of control, then there can be a lot of secondary off-target effects, tissue can be further damaged, and then it can start to amplify and propagate that inflammatory response. These cell-based therapies that we've been pursuing tend to push that inflammatory response from pro-inflammation to pro-reparative and that's the effector cells T-regulatory cells and macrophages. That then allows some of the endogenous repair mechanisms mediated by those cells to allow restoration of damaged, but not dead, tissue. What we're doing is salvaging that injured, but not necrotic and dead tissue, and bringing it back online so that the function is improved. That inflammatory response in multiple organ systems is remarkably conserved across these different organs, such that that's the big opportunity with the cell-based strategy.

Dr. Taylor:
When you are transfusing these cells into the body and they're no longer present in the circulation, does that endogenous repair go on long after those cells are noticed?

Dr. Cox:
Exactly. That's because they're working through these secondary effector cells, it's about reprogramming that secondary effector cell strategy. And that happens in a couple of organs, principally the spleen and the lung. And this has been shown by a number of laboratories in pre-clinical studies and then now is being translated into clinical trials.

Dr. Taylor:
As we speak to our OB colleagues, in an attempt to motivate the OB providers in being patient and collecting quality cord blood units,

has it been important in your research when choosing cord blood stem cells to find a quality sterile unit?

Dr. Cox:
Indeed. The better the unit the more flexibility we have and there's a big dosing component to things. So, the more we have, the better. Units that aren't contaminated, are better. If we're going to use these in some type of any expansion strategy, sterility is critical.

Dr. Taylor:
You wouldn't want to expand the contaminant as well, so sterility is extremely important, especially in a collection in a vaginal delivery scenario which is a non-sterile field for obstetricians.

The next thing I wanted to ask you, Dr. Cox, is there are a lot of clinical trials that our obstetric patients may qualify for in the present day but, in your opinion, how close do you think we are to an FDA-approved indication for any type of cellular therapy?

Dr. Cox:
FDA approval meaning having a biologic license application for that, we're probably still five years away from something like that. There are a number of Phase II clinical trials which then typically means you're going to need another three-four years to get that through Phase III. Some things, however, may leapfrog over that because there aren't enough patients currently to enroll in a Phase III trial, and so, you have to go to the FDA with Phase II data and ask for conditional approval with long-term follow-up.

Dr. Taylor:
And Dr. Cox, how can OB providers use this information that we have discussed to help educate their patients who are even just trying to decide whether or not to bank cord blood?

Dr. Cox:
If you don't have an in utero diagnosis, what you're buying is insurance. If you put insurance into three big types of buckets, there's asteroid insurance that you're probably not ever going to need and if you did need it, it didn't matter. An asteroid probably isn't going to hit the earth. Then there's, if you're like me, you live down on the Gulf coast, hurricane insurance. You may use that in your lifetime and the time to buy it is not when the hurricane is in the Gulf. The time to buy it is beforehand. And then, there's car insurance that, if you're like me, with a number of young drivers, you're going to use that every couple of weeks. And so, it's not asteroid insurance and it's not car insurance. It's probably something along the lines of hurricane insurance; something that you'd really like to have if you're facing a potentially difficult situation. And talking about things in abstract numerical terms becomes really difficult to assimilate when somebody tells you, "one in five thousand births in the region will require this type of intervention." People have no way of calibrating what that means. I think that the other component to this that's not completely knowable is, what does the state of the science look like ten years from now? If you believe that things are going to continue to accelerate like they are, then the probability of needing a cord blood unit only increases. It doesn't decrease. The other factor there is personal finances and that's just something that I tell people that if you have to make a decision between paying the mortgage or getting a cord blood unit, I would say pay the mortgage. But if you have an option to where it really isn't creating financial strain, then I think it's really a legitimate discussion to have about that. And then I just offer examples of some of the things that cord blood can be used for now, what it looks like in the future for use, and leave it at that.

Dr. Taylor:
Yes, I think that's really helpful and I really like that analogy. Before we close, is there anything you would like to discuss that we haven't yet touched upon or anything that you'd like to re-visit?

Dr. Cox:
I think another area that's really growing is in the field of cord tissue. The gelatinous substance that's within the umbilical cord is an area of research in wound healing and bone regeneration and some other applications like a cleft palate. I think that's going to be an area of massively expanded indications for the use of, not just the cord blood cells, but the cord tissue. And I think that that's going to be an exciting area of expansion, and it's going to get rid of that whole discussion of banking for something that may happen in the future. In utero diagnoses of some of these diseases will make cord tissue collection a much greater probability of use in the ultimate surgical repair of the defect.

Dr. Taylor:
You mentioned one of them with the cleft palate which we obviously visualize for on any of our routine anatomy ultrasounds. What are some of the other findings that we can find in utero that cord tissue stem cells might be useful in treating?

Dr. Cox:
Things such as hydronephrosis where there may be vesicoureteral reflux. Obviously hydronephrosis can come from a number of things, but if it turns out to be vesicoureteral reflux there are now pre-clinical, and I want to emphasize pre-clinical, work using this similar to the injectables that are now used to be injected along the submucosal plane between the ureter and bladder to create a valve. So, there's a

chance that we can switch that over to an autologous hydrogel injection for that approach. There's a whole host of things like that and also in other craniofacial reconstructive procedures. That's where the field is going now.

Dr. Taylor:
It's all very exciting. Thank you so much for this information. Thank you for joining us today, Dr. Cox, and sharing your insights on Emerging Clinical Applications for Cord Blood.

Dr. Cox:
You're welcome. Thanks for having me.

Dr. Taylor:
I'm Dr. Karen Taylor, inviting our audience to access this and other CME Expert Interviews on ReachMD, where you can be part of the knowledge. Thank you for listening.

Narrator:
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