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Breathing Beyond Birth: The Symptoms and Treatment of Bronchopulmonary Dysplasia

Dr. Shu:
Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Jennifer Shu, and joining me today to discuss bronchopulmonary dysplasia, or BPD for short, is Dr. Steven Abman. Dr. Abman is a Professor in the Department of Pediatrics at the University of Colorado School of Medicine and the Director of the Pediatric Heart Lung Center at Children's Hospital Colorado.

Dr. Abman, thanks so much for joining us today.

Dr. Abman:
Oh, it's my pleasure.

Dr. Shu:
So why don't we start with some background, Dr. Abman, and just tell us what is BPD, and how does it develop?

Dr. Abman:
So bronchopulmonary dysplasia, BPD, is the chronic lung disease that persists in premature newborns, and it's really an historic name. The term was first described over 55 years ago, and it really characterizes the progression of lung disease from premature babies who have acute respiratory failure at birth related to infant or respiratory distress syndrome and then progresses because of the need for mechanical ventilation, supplemental oxygen, and other kinds of measures to develop chronic problems. And these chronic respiratory problems are associated with significant issues with poor survival and comorbidities, such as worsening brain injury, necrotizing enterocolitis, retinopathy of prematurity, and many other features. And many of these babies still end up being on invasive ventilator support for weeks to months after the acute respiratory disease is managed, and so it's sort of a spectrum of disease in which we have very severe acute problems where survival can be poor early to simply being something that when they get near term corrected age after being born prematurely, meaning weeks to months later, the discharge is just a little bit of oxygen but otherwise have what appears to be a relatively benign ambulatory course as an outpatient.

Dr. Shu:
So given that there's a spectrum of symptoms that might be seen and different severity levels, what would you say would be the most common symptoms that we might expect in premature infants with BPD, and how can we differentiate those symptoms from other respiratory conditions?

Dr. Abman:
So, first of all, what we often see in the babies who get BPD, they're the most immature babies. They're the 22– to 26-week infants where term is about 38 to 40 weeks. So although we've had improved survival, or perhaps because of the improved survival, the very fragile lungs at early stages of development are exposed to high oxygen concentrations to maintain their oxygenation. They need to be on invasive mechanical ventilators or even noninvasive support to sustain them because of how weak they are, how fragile their lungs are, and how they really require significant monitoring and care. And so some of these babies will go on to have an early course where they could come off the ventilator, seem to just need a little bit of oxygen, and as they get closer and closer to term, meaning 36 weeks gestation which is the time we really make the diagnosis officially of having BPD, they could have just very modest respiratory signs and symptoms of tachypnea distress. They might have feeding difficulties. They may need asthma-type inhalational therapies. Significant numbers have pulmonary hypertension or problems with left ventricular function, so the things we monitor closely, but the mildest forms are those who really don't have much in the way of those comorbidities. They may head home with a little bit of supplemental oxygen, which they gradually wean from. And then during the follow-up period during infancy and early childhood, we look for recurrent

exacerbations, sometimes just like asthma with some wheezing, sometimes more profound where a viral illness, especially respiratory syncytial virus or others, can cause setbacks and they need to come back into the hospital, sometimes back on a ventilator in the pediatric ICU. And so there's a range of complications we watch for because about half of these kids will require rehospitalization or frequent emergency room visits or primary care for acute exacerbations on their chronic problems.

So we grade BPD according to mild, moderate, or severe, and it's the severe form where they still need invasive ventilation late in their course in the NICU and sometimes have to go home on ventilators as well. And so it's a whole range of disease early on, but all of them during infancy we do worry about how they're growing, how they're feeding, and if they're really having sufficient lung function where they don't have recurrent breathing difficulties or exacerbations; and so during childhood, we monitor them closely as well even though they've been long discharged from the NICU.

Dr. Shu:
Thank you for all those details and examples. Would you be able to just summarize how BPD would affect a baby's overall respiratory health?

Dr. Abman:
Yeah. So, first of all, the lungs, as they're developing, these babies are often born in what we call the late canalicular phase, and that's where a lot of your central airways have developed but you're just beginning to have more branching, and it's certainly before we start to grow air saccules or alveoli. And so if you're born at that stage and have injury to the lung at that stage, we think that it inhibits or leads to an arrest of lung airspace growth and development and slows it down; and if it's severe enough, it may lead to long-term issues with lungs that just don't function very well with both airways disease as well as parenchymal disease where there's an element of reduced surface area and reduced DLCO that can be apparent early on. Likewise, the blood vessels in the lung. Canalicular phase is a period where there's a burst of proliferation of angiogenesis, and so injury or premature birth and exposure to postnatal stimuli can inhibit angiogenesis, which further impairs alveolar development and also increases the risk for pulmonary hypertension early in the NICU or later in the course, and then it's again something that we see longer term. If one watches some of these infants become adolescents and adults, they could have sustained abnormalities. So it's airways, it's parenchyma of the airspace, and it's the blood vessels and heart that we really focus on in terms of how they're progressing. There is variability in the outcome, but we always need to worry about these kiddos and follow them closely as they become older in life.

Dr. Shu:
For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Jennifer Shu, and I'm speaking with Dr. Steven Abman about bronchopulmonary dysplasia, also known as BPD.

So if we switch gears and focus on treatment, Dr. Abman, what options are available for BPD?

Dr. Abman:
Well, way back when, some of the earliest interventions for prematurity—and they continue to this day—is the use of antenatal steroids for close monitoring of pregnancies and premature birth. The use of maternal steroids is still in vogue and very important because that will hasten maturation of the lungs and other organs as well and help attenuate the severity of acute RDS in the days after birth, and so antenatal steroids are used for prevention.

The big deal in the neonatology, of course, over the decades has been the discovery of surfactant, and certainly giving surfactant to premature babies helps the lungs, when they open up, stay open. They sustain lung volume, and that helps protect the lungs from severe injury acutely. And so that combination of antenatal steroids and surfactant have played a huge role in improving survival now down to 22 to 24 weeks as well as other issues with perinatal care, including nutrition and other kinds of things that we do to the airway and how we use the ventilators and use noninvasive support and things like that, so all of that's been really good.

We use asthma medications. A number of our kids, not all of them, but some of them have asthma-like symptoms from medium-sized or smaller airways, and they show bronchial hyperreactivity early. But again, it could be tough to gauge that at the bedside in the NICU of premature babies, so we look for other features that show respiratory improvement, such as lowering their oxygen requirement or having less distress chronically. We give diuretics because they're at risk for getting more pulmonary edema. And it's a little tricky because not all babies require diuretics. Some babies seem to respond; some don't. And the feeling is that perhaps there's some injury to the lung that makes the vessels leaky early on, and the diuretic might help. It may be that the lymphatics in the lung don't drain fluid, so again, diuretics might be helpful. But we're also recognizing that some babies have an element of left ventricular dysfunction, which may contribute to pulmonary edema, and in those babies, we think the diuretics might help as well.

And then, finally, pulmonary hypertension can be a big part of the picture associated with more severe BPD. For pulmonary hypertension itself, we're beginning to use pulmonary hypertension-targeted medications, like PDE_5 inhibitors, endothelin receptor

antagonists, and a lot of inhaled nitric oxide especially early in the course, to target the pulmonary circulation to help with both gas exchange but mostly with cardiac performance.

Dr. Shu:
Before we close, do you have any other thoughts that you would like to add for our listeners today?

Dr. Abman:
Yeah. So really, I think for the neonatal ICU, or the NICU, which is the haven for all neonatologists and wonderful advanced practice providers and others, we need to get more early subspecialty engagement to work as a team to provide interdisciplinary care early. That's why getting the pulmonologist, the cardiologist, the gastroenterologist, and a therapist to intervene to enhance neurocognitive abilities, so many things we could do as an interdisciplinary team to improve the quality of outcomes, and that's one thing.

The second thing, at the time of discharge, having good continuity of care where we still follow these babies and worry about them, make sure they're vaccinated, and avoid exposures as much as one can to pollutants and secondhand smoke and all these other things. But the other thing too I really want to emphasize is for any adult pulmonologist listening: Get a history. Take a history about perinatal events. Take a history of this prematurity with or without the need for BPD. Worry about their lung function perhaps being under the radar. If you actually measure them, look at their flows, DLCOs, and body box measurements. You'll find that a lot of them are surprisingly impaired, even though they may not show it in terms of their day-to-day symptoms from a respiratory standpoint. The reason why we're worried, again, is this is the next generation of COPD already being recognized, and we need to build bridges between pediatric and adult pulmonology for sure to see that we really don't let these kids slip under the radar as we care for them.

Dr. Shu:
Well, this was a very important discussion, and I want to thank my guest, Dr. Steven Abman, for sharing his valuable insights with me today on bronchopulmonary dysplasia. Dr. Abman, it was a pleasure speaking with you.

Dr. Abman:
Likewise. Thanks so much, Jennifer.

Dr. Shu:
For ReachMD, I'm Dr. Jennifer Shu. To access this and other episodes in the series, visit *Clinician's Roundtable* on ReachMD.com where you can Be Part of the Knowledge. Thanks for listening.