Round Table Discussion: Children's Interstitial Lung Disease

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Robin R. Deterding: We have the opportunity today to talk about children's interstitial lung disease (chILD) with experts in that field. My hope is that we can have a lively discussion about what we know is important in chILD and what we see coming on the horizon.

I would like to begin our discussion with a question: Why is it important to recognize that chILD differs from interstitial lung disease (ILD) in adults? Lisa, would you like to give your thoughts about this?

Lisa R. Young: I think this is an extremely important question, about which we have learned a lot in the past several years. A major reason for the importance of distinguishing chILD from adult ILD has to do with what patients read and think about with respect to these 2 diagnoses. A family that turns to the Internet in the belief that it has a member affected by ILD can become very quickly frightened, for example, in reading about the prognosis in idiopathic pulmonary fibrosis (IPF), a common form of ILD in adults but one that does not occur in children.

Robin R. Deterding: Alan, what are your thoughts as a radiologist?

Alan S. Brody: I agree with Lisa, and I think that some things that look like but are not the same as adult IPF may be a problem for the radiologist as well as for the clinician who does not deal with chILD, as well as for the families of patients. The 2 conditions should not be treated in the same way; they do not have the same prognosis. We did not know that years ago, but today it is very clear, as Lisa observed, that IPF, the most common adult form of ILD, does not occur in children, and if someone gives a child that diagnosis, we can tell the family right away that it is not correct, that there is more work to do to understand their child's ILD. The prognosis of chILD is very variable and often much better than adult IPF.

Lisa R. Young: We're also learning that the etiology of chILD is often very different from the types of ILD

seen in adults, and we think that understanding the etiology of the childhood disorder is a key step toward its treatment.

James S. Hagood: I agree. For adults and physicians caring for adults with ILD, by far the largest category of disease is IPF, which does not appear to occur in children. And while many secondary forms of ILD and pulmonary fibrosis may be similar to what we see in older children and adolescents with rheumatic disease or hypersensitivity pneumonitis in terms of specific causes, the prognosis and management may differ in children.

Robin R. Deterding: All of these are excellent observations. The only thing I would add is that ILD in infants and children may improve or transform into a different type of lung disease, that may be similar to or different than adult ILD, as they grow older. It is very difficult to know what may happen until we can correctly classify these various conditions and follow them over time.

I would like to discuss the presentations of ILD in children. What are your experiences with this, and when might you think you are dealing with a child with ILD?

Lisa R. Young: The children I see generally have 2 different categories of ILD. One of them has a very dramatic presentation, such as respiratory failure, and this generally presents in neonates at birth. I find it can be more difficult to identify ILD in older children, which may be insidious in onset. Children may present with progressive exercise intolerance marked only by a gradual slowing and falling behind their friends or siblings in their physical activities. In babies, the symptoms of this may include trouble with feeding, and may look like reflux or other feeding problems, but may instead be related to their difficulty with breathing.

Alan S. Brody: As a radiologist, most of the children sent to me are referred, and for a number of reasons, but there is almost always some concern about the presence of lung

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disease. If we confirm the presence of lung disease, we seek further information on the lung diseases that would be most likely with the patient's specific presentation.

James S. Hagood: I've found that these patients often present as a clinical enigma with persistent respiratory symptoms that have been treated for another diagnosis, such as asthma or presumed immunodeficiency, sometimes for months and sometimes for years, either without responding to treatment or following a more severe course than is usual for these conditions.

Lisa R. Young: That's a critical point, because the symptoms of chILD overlap those of many more common pulmonary disorders. Often, it is only the failure to respond to other treatments, or the chronicity of the patient's symptoms, which gives the clues to chILD as opposed to some more common cause of respiratory symptoms.

Robin R. Deterding: Age also plays a role in the presentation and diagnosis. In the young child or neonate the symptoms of a respiratory disorder may appear acutely, and you have to consider the diagnosis right away, whereas a teenager may have had symptoms for months or years before people start thinking about the possibility of ILD.

James S. Hagood: That's right. And another scenario I've seen involves children who may have had some problems in the neonatal period and may have what is labeled as chronic lung disease, perhaps even with ventilator dependency, but who may in fact have an unrecognized form of ILD, such as pulmonary interstitial glycogenosis (PIG).

Robin R. Deterding: What specific signs and symptoms do we need to consider when we see a child who presents in this way?

Lisa R. Young: A couple of the key elements are historical. A family history of unexplained or other chronic lung disease should direct the workup. Beyond that, I pay attention to chronicity of symptoms. Most of these children will have tachypnea, exercise intolerance, or a chronic cough even when they otherwise seem well, and not only when they have a superimposed illness such as a viral infection. Therefore, hearing from the parents that the child always breathes in a particular way, even without whatever condition may have prompted the current medical visit, is a key indicator for going forward with a further workup for chILD.

Robin R. Deterding: The chILD Research Network began discussing this and came up with clinical features they felt would be hallmarks to consider when deciding if a child should get a workup for chILD. The Network coined the term "chILD syndrome," linking it to the 4 abnormalities of: (1) respiratory symptoms, coughing, rapid breathing, or exercise intolerance; (2) signs such as crackles or adventitious breathing sounds, digital clubbing, or intercostal retractions; (3) a low blood oxygen tension or hypoxemia; and (4) abnormalities in chest X-ray films. If a child has 3 of these 4 abnormalities without a known underlying etiology such as cystic fibrosis or immune deficiency, they fall into the category of having chILD syndrome and should at least be considered for an evaluation for chILD. Do you all think this is a reasonable approach?

James S. Hagood: Very much so. That is a very useful set of criteria that will help guide clinicians about when to suspect chILD. Another group of children for clinicians to

consider are those who may have been labeled as having a particular disease, such as asthma, but are not responding to treatment or are experiencing a more severe course of disease than would be expected. An example of this would be a child who is admitted to the hospital several times a year for what appears to be viral respiratory illnesses, but who has prolonged hypoxemia requiring supplemental oxygen, or who fails to respond to the usual therapeutic interventions for such illnesses.

Equally important is the child in the neonatal intensive care unit who may be labeled as having chronic lung disease but for whom there is really no clear explanation for the severity of the lung disease.

Lisa R. Young: I agree with Jim about the importance of thinking about children whose symptoms are out of proportion to what would be anticipated for an underlying respiratory disorder, such as prematurity or congenital heart disease, since some forms of chILD may exist with these co-morbidities.

Alan S. Brody: I think that use of the term "childhood ILD syndrome" is immensely important because it moves chILD from being a pathologic diagnosis to a clinical diagnosis, on the basis of which we can establish whether or not a further diagnosis is appropriate. In the review by the chILD Research Network published in the *American Journal of Respiratory and Critical Care Medicine* in 2007, etiologies such as congenital heart disease and heart failure were not uncommonly seen as chILD syndrome.¹

Robin R. Deterding: We have seen a few patients at the Children's Hospital in Denver who have come in with persistent crackles diagnosed as symptomatic asthma, but in reviewing the clinical notes asthma therapy was not effective and they did not really cough, making a diagnosis of asthma unlikely. Instead, these patients had the specific form of ILD called neuroendocrine cell hyperplasia of infancy. As a result, we tell our students as a teaching point that persistent crackles are abnormal and not indicative of asthma.

Lisa R. Young: We have also had that experience with persistent crackles and NEHI, but regarding chILD syndrome, we still don't fully know the specificity of the 4 criteria set forth by the chILD Research Network. The criteria are not intended to imply specificity, but I do think they are very helpful as a framework for approaching unexplained respiratory symptoms and findings in children in whom we need to proceed with further evaluation.

Robin R. Deterding: I agree. The 4 criteria for chILD were focused more specifically on children from birth to 2 years of age, and may not be quite as effective at identifying ILD either in adolescents or in children who have rheumatologic disorders.

James S. Hagood: Yes, those criteria were developed with younger children in mind.

Lisa R. Young: Children who have known systemic disorders associated with ILD pose a different challenge in screening and diagnosis than do children without accompanying systemic disorders. As a result, the starting point for the ascertainment and evaluation of chILD is different in the case of older children with rheumatologic disease or known immunodeficiency. The cases that probably pose the greatest challenge for me are those without any clues to coexisting systemic disorders. Those are the cases in which I find the criteria for chILD syndrome much more helpful.

Robin R. Deterding: I'd like us to now turn to the more difficult issues of the treatment and management of children with ILD. Do you have any thoughts about this?

James S. Hagood: In terms of specific treatments for specific entities, we have no guidance from evidence-based medicine because we simply do not have controlled trials. However, I do think that on the other hand, most of these children benefit from nonspecific interventions to reduce their work of breathing and improve their quality of life. Providing supplemental oxygen, for example, is a fairly straightforward measure if needed, and monitoring for adequate nutritional intake and growth is very important in the management of children with ILD. So, conversely, they are avoiding factors that might cause respiratory irritation or injury, such as environmental smoke, respiratory infection, and other risk factors.

Lisa R. Young: Jim has summarized the situation perfectly. While the diagnosis of ILD is quite challenging, we have very little in the way of specific therapies for most types of chILD, and the management of children with these diseases is very similar to that of children with other chronic pulmonary conditions. When children have underlying disorders such as connective tissue disease or immune dysfunction, managing the lung disease is closely tied to therapies for the systemic disorder.

Robin R. Deterding: One area in which I think we have made progress in terms of diseases related to chILD is in understanding and classifying the pathology and pathophysiology of neuroendocrine cell hyperplasia. Studies of its pathology and the clinical histories of affected children, as well as discussions with their families, have shown that high-dose, long-term steroid therapy does not change the long-term symptoms of chronic hypoxemia and tachypnea in this condition. Moreover, its pathology shows no significant inflammation, and a limited evaluation of biomarkers in the bronchoalveolar lavage fluid (BAL) of patients with chILD has not found any significant inflammatory mediators. Therefore, I do not think of neuroendocrine cell hyperplasia of infancy as a traditional inflammatory process and do not treat it with long-term oral steroid administration, which carries significant morbidity.

Lisa R. Young: I completely agree with that, and it represents an area in which we can have a major impact on morbidity by recognizing those patients who will not benefit from corticosteroids, and then not using them. The example of neuroendocrine cell hyperplasia provides an excellent illustration of why it is insufficient to simply make a diagnosis of ILD in a child, and why it is essential to establish a specific etiology of lung disease in a child whenever possible because of the treatment and prognostic considerations.

Alan S. Brody: One of our contributions in many cases is being able to rule out ILD as a likely source of a respiratory problem in a child. There are certainly children who will benefit from a consideration of other possible sources of respiratory symptoms, including many of those who have unexplained tachypnea or who may have a viral infection and a history of rapid breathing, and who may very well have an abnormal chest X-ray as a result of their viral infection. The last thing we would want is to start treating these children with steroids and other drugs that have potentially damaging side effects simply because we think they may have chILD.

Robin R. Deterding: Another important matter is the recognition that some of these conditions are genetic. Surfactant protein mutations fall into that category. In some instances disease stemming from mutant surfactant protein B or some cases of ABCA3 is not felt to be survivable, and making the diagnosis in such cases may guide management to a pediatric lung transplant center sooner than might otherwise have occurred. Identifying these genetic conditions also has significant implications for the patient's family. We have diagnosed surfactant protein mutations on more than one occasion in a child, where there have been adults with severe lung disease who have been able to be referred to an adult ILD center or transplant center on the basis of a diagnosis made in a child within the family. In some of these genetic disorders, it is very important to think about the entire family.

James S. Hagood: That is an excellent point that takes us back to Lisa's point about the importance of a thorough family history in all patients with ILD. It also raises the important point of the need for psychosocial support of these families. Often, the parents have suspected that something was wrong with a child over a long period, while having been reassured by care providers that the child has asthma or another reasonably manageable condition. When they are then suddenly told that the diagnosis is a rare disorder or something difficult to classify, and find themselves needing a lot of support for dealing with a child who has a chronic illness.

Lisa R. Young: I agree. For a family that has been searching for years for answers to their child's problem, undergoing extensive medical testing, and trying therapies that generally fail to work, a diagnosis can be both overwhelming and a relief at the same time. Many children with chronic tachypnea and crackles from neuroendocrine cell hyperplasia of infancy may be repeatedly treated for pneumonia. I recall one patient in particular who was given intramuscular ceftriaxone or was hospitalized whenever the child was brought for well-child visits. So, sometimes establishing a diagnosis can prevent or stop all this and allow the safe and gradual withdrawal of treatments that are not helping.

Robin R. Deterding: As has been said by our participants today, the emotional stress on the patient's family who has received an erroneous or uncertain diagnosis can be daunting, and I think that the chILD Foundation [www.childfoundation.us] has filled a significant role in easing that for many families. It was established in 2004 as a tax exempt, nonprofit corporation under Section 501(c) of the United States Internal Revenue Code, and is focused on these families' education and support, and on research in finding better ways of caring for children with ILD, as well as on finding cures for children with these diseases. The chILD Foundation has done a tremendous job in filling roles that physicians and other care providers may not be able to fill. Putting the family of a child with ILD in touch with other families of children with such disease can help a family tremendously to understand possible treatment and management from families who have gone through similar experiences.

Robin R. Deterding: What disorders should be referred to a lung transplant center for treatment and management?

James S. Hagood: I think that as you mentioned earlier, mutations in surfactant protein B presenting in the neonatal period, and possibly mutations in ABCA3 that present in

the neonatal period, are conditions with a very poor prognosis short of lung transplantation. In the case of children with other diagnoses or those who present later in life, a lot has to do with the clinical scenario, the morbidity and progression of the patient's disease, and the presence or absence of pulmonary hypertension. Those are decisions best made in consultation with a specialist in caring for children with ILD, and by clinicians who specialize in lung transplantation, and should never be undertaken lightly or made rapidly.

Robin R. Deterding: Another indication for lung transplantation is alveolar capillary dysplasia with misalignment of pulmonary veins (ACDMPV), which can be a severe and rapidly fatal form of chILD. Because of the intensive care needed to maintain a child for 2 to 3 months before lung transplantation, it is sometimes very difficult for these children to get to a pediatric lung transplant center and then survive long enough to receive donor lungs.

I also wanted to mention that in the neonatal period, mutations in surfactant protein C may not manifest the same disease course as those of surfactant protein B or ABCA3, and may not be universally fatal. Patients with mutations in surfactant protein C may present very sick in the newborn period but they may also present later in childhood, although the phenotype of this disorder is so variable that those it affects can even present in adulthood. Our center has had experience with a few patients with this disorder who have required significant intensive care and chronic ventilation through a tracheostomy for a few years after birth, yet have improved with time, even to the point of having been decannulated and off oxygen.

Lisa R. Young: That is another excellent point about the need to determine the specific etiology of a patient's ILD, and to consider the age at presentation in the diagnostic and therapeutic context. As Jim said, these are not easy decisions, and early consultation with a lung transplant center is recommended.

Robin R. Deterding: We all seem to be avoiding the idea of using corticosteroids, but I do think our discussion would be incomplete without their consideration. I am sometimes uncomfortable with the discussion because we don't always know exactly how a patient will respond and we don't have good evidence for their use. What are your approaches to using glucocorticoids in patients with chILD?

James S. Hagood: Historically, the use of glucocorticoids in chILD comes from the experience with their use in adult ILD. IPF, the most common and severe form of adult ILD, is nonresponsive to corticosteroids, and they actually contribute to the morbidity and mortality of this disorder and so are not routinely used in its treatment.

However, there are forms of adult ILD, particularly those that are secondary to inflammatory and immune disorders, that are steroid-responsive, and it is this that has led to the tendency to use corticosteroids in chILD.

What I have seen is that some patients with chILD show a clinical response to systemic corticosteroids, with stabilization of their lung function, a reduction in their need for supplemental oxygen, and a decreased frequency of hospitalization. But these patients need to be identified individually, and treated with corticosteroids in a very controlled manner and at a center that has significant experience in managing such children.

Lisa R. Young: I agree that the issue with corticosteroids goes back to the point about what type of ILD that we're dealing with, and that by itself, a diagnosis of chILD is not enough to justify their use. As Jim mentioned, I think they have a role in some types of ILD, including connective tissue disorders, as well as in some of the pulmonary hemorrhage syndromes that include capillaritis or other vasculitides, postinfectious forms of ILD, and lymphoproliferative disorders, which can be exquisitely steroid-responsive and in which aggressive immunomodulatory therapy with steroid-sparing agents are also needed.

In these diseases, one should not be shy about using corticosteroids, but should think about how to approach their use with the safest possible protocol, including monitoring for adverse side effects such as immunosuppression, osteopenia, cataracts, diabetes, and hypertension. In pediatric patients, steroid-sparing agents often have to be used together with corticosteroids to minimize the risk of these effects.

I think that some of our hesitancy about when to consider using corticosteroids relates to patients in whom we don't know the cause of a respiratory disease or, as has been mentioned, those with a noninflammatory condition such as neuroendocrine cell hyperplasia of infancy. Those are situations in which we would really like to spare the patient from the toxicities of what is likely to be an unhelpful trial of corticosteroids.

Robin R. Deterding: What about PIG? Lisa, you and Dr. Gail Deutsch of the Seattle Children's Hospital published an interesting report last year in *Pediatric and Developmental Pathology* of a single case of neonatal PIG being successfully treated with corticosteroids, although many clinicians working with chILD have used them for treating PIG in children.²

Lisa R. Young: The group at Toronto Sick Kids originally reported a cohort of children with PIG who were found to be steroid-responsive. And yes, the child we reported was exquisitely responsive to intravenous corticosteroids, and this has been our overall clinical experience here in Cincinnati with similar cases. However, we are learning that this is not the situation for all cases of PIG, and that it is a much more complicated disorder. Specifically, PIG can also occur in the context of other disorders, such as abnormalities in lung development, deficient alveolarization, and congenital heart disease. This finding came from a retrospective review of data from the chILD Network which was published in the *American Journal of Respiratory and Critical Care Medicine* in 2007.¹ As a severe abnormality in lung growth may contribute to the clinical picture in chILD, treatment with corticosteroids may not fully address the respiratory issues in such cases. I am also always a bit hesitant in thinking about steroids for PIG in neonates because we know that it affects postnatal alveolarization and has long-term effects on neurodevelopment.

I think that the use of glucocorticoids in chILD is an area in which much more research is needed to understand their role and their relative risks and benefits in this patient population. Hopefully we can develop more targeted molecular therapies.

Robin R. Deterding: When we are dealing with children who have an ILD that we can't diagnose, I'm frequently guided by the histopathology findings and by how helpful

sitting down with the pathologist and examining the state of inflammation of the patient's pulmonary tissue can be. If there is a lot of inflammation and it looks very active, I will often prescribe a set course of corticosteroids because doing so and assessing the response makes pathophysiologic sense for that patient's condition.

Does anyone have any other observations about the treatment and management of chILD?

Alan S. Brody: As a radiologist and not a pulmonologist I think that one of the most important things for children with ILD is to put them under the care of someone who is familiar with these diseases and with the management of chronic pediatric lung diseases. The management of these children is very difficult in terms of decision making, as we have discussed, and it is very easy to put them under the care of someone who has not had much experience with chILD. Take the case of a child who gets a winter cold, perhaps a bad one, and is given steroids, and in 10 days is dramatically better. We know that that child would have been dramatically better in 10 days without the steroids, but to the inexperienced, the child's recovery becomes evidence that it responds to steroids, and they are then used all the time to treat that child. But in fact this represents a situation in which a child should be referred to and carefully evaluated by an expert in pediatric pulmonary disease who has a lot of familiarity with ILD.

Robin R. Deterding: I'd like us to now turn our attention to the prognosis in chILD and to spend a few minutes on this. What are your thoughts on the long-term prognosis for children with ILD?

James S. Hagood: It depends absolutely on the underlying diagnosis within the category of chILD. There are so many different specific diagnoses, with such very different prognostic significance, that you first have to establish what you're dealing with. Given that, however, it is possible to make some generalizations, such as that children who present with hypoxemia at rest and evidence of pulmonary hypertension usually tend to have a poorer overall prognosis than children who do not exhibit these effects.

Lisa R. Young: The data support the concept that pulmonary hypertension is a poor prognostic factor in ILD, as in most other forms of chronic lung disease in which it has been studied. We have also found that infants in particular are at risk for a poorer long-term prognosis in chILD, and several studies have borne this out.

Robin R. Deterding: Something we do not know is the long-term adult lung health of children who present with ILD as newborns or as older children. The natural history of disease takes a long time to follow and understand, but is very important as we progress in the study of chILD.

James S. Hagood: That is very important, and I think that chILD may have a lot to teach us about adult lung disease. To take a hypothetical example, there may be a diagnosis within the realm of chILD that represents the extreme end of a clinical phenotype associated with a genetic abnormality that underlies more common adult lung diseases, so that if we follow these children over a long period and observe the evolution of their lung disease, we may learn something new about adult lung disease.

Lisa R. Young: We're cautiously optimistic about the prognosis in most forms of chILD, much more so than in many forms of adult ILD. But I tell families that we really

cannot know the long-term prognosis until these disorders have been studied in a more systematic way nationally and internationally.

Robin R. Deterding: What is on the horizon for chILD? What opportunities are there, and what discoveries may be around the bend?

James S. Hagood: Robin and Lisa can probably speak to this better than I can, but one tremendous thing on the horizon is the imminent ability to track these children through a patient registry in which we can collect information across centers and in some cases worldwide, and so track the natural history of chILD and work toward a better understanding of its prognosis and response to treatment.

I also think that the tremendous speed at which the technology for genome-wide analysis is improving, with the high-throughput molecular analysis of many genotypes, increases the possibility of our learning about possible genetic or other molecular causes even of rare disorders. So I think there is a lot to be hopeful about as we look forward in addressing chILD.

Lisa R. Young: I think we're also seeing examples of how the genetic mechanisms so far identified for chILD not only have a bearing on adult lung diseases, but may also play a role as gene modifiers in other, more common pulmonary disorders, such as neonatal respiratory distress syndrome (RDS).

Robin R. Deterding: As Jim mentioned, I think the ability to collect data on children with ILD in one place that can serve as one worldwide "clinical database" will help us begin to really understand some of the things that we've been struggling with, such as the impact of corticosteroids on different types of chILD, natural history, and new medications that might merit open-label trials. Reports in the literature on medication response for these disorders are currently entirely anecdotal. Furthermore, being able to collect data on natural history, of which we have only limited understanding, may be a tremendously powerful tool for caring for children with chILD.

Something that I think will come forward through the growth of molecular and proteomic techniques will be better biomarkers for chILD. Many of the children it affects have to undergo multiple diagnostic evaluations, including lung biopsies, and a reliable biomarker would go a long way in helping to identify some of these children. Many of these children also have very significant disease that will not change rapidly over the short term, and having a biomarker that would more quickly identify a response to treatment could be very helpful in directing effective treatment for chILD and as a therapeutic end point in open-label clinical trials.

So I think there is much that we need to learn about chILD, but this will only happen in the foreseeable future if we have a universal international clinical database through which to study these children. We are all very committed to that, and I am very hopeful about it.

Lisa R. Young: I echo that, and would add that an area in which we're already seeing great change in our clinical practice is in the use of noninvasive diagnostic techniques for some forms of chILD. We've mentioned genetic sequencing for several types of chILD, but I wonder whether Alan would like to comment on what he sees as the future role of imaging in the noninvasive diagnosis of chILD.

Alan S. Brody: It is difficult to see into the future to answer this question. However, I think that an important point is that there has been a great deal of intense concern about the risks of radiation from computed tomography (CT) scanning, which is the primary modality for the diagnosis and evaluation of chILD. A major effort now underway and which will continue is to reduce the radiation dose and thus the radiation risk to patients undergoing CT and other types of radiography.

That said, it is also very important to recognize that the risks of radiation in the diagnosis and evaluation of chILD are theoretical rather than proven, and even on a theoretical basis are far smaller than the benefit of an accurate diagnosis of chILD.

The exciting issue in radiology probably relates to Robin's point that as we learn more about chILD, and share our experiences with it, we're going to be able to reach conclusions about the impact on a patient of a specific manifestation of chILD. This has to do with determining whether there are CT scan characteristics of the various forms of chILD that may help with the prognosis or treatment for different patients. I think that the answer to this will definitely be yes.

That has already been a turning point for imaging in chILD, for where we used to have only a collection of related diseases that we did not understand and recognized simply through rote memorization, we now have a framework for organizing such information and a large group of investigators working toward a deep understanding of the diseases that fall within the realm of chILD.

Lisa R. Young: As a pulmonary scientist, one of the things that I find most interesting about looking at the various forms of chILD is that they occur in a lung that is still developing, which challenges us to understand how they relate to lung development and how various mechanisms of lung injury and repair differ in the developing and the adult lung. I think that we can also exploit some of these discoveries for benefit in treating various forms of lung disease in adults.

James S. Hagood: I'd like to mention a couple of other issues relating to the future of chILD. One relates to some very exciting studies of impaired lung development in animal models, in which lung development has been greatly accelerated through the use of stem cells or bone marrow stromal cells, which may help the future clinical management of various forms of chILD marked by impaired development.

Another issue has to do with support for the families of children with ILD. The chILD Foundation has developed a number of educational materials and is in the process of developing additional materials that will help these families to learn more about their children's disorders and also to educate their primary care providers and other physicians about them.

Robin R. Deterding: There has been an explosion in our understanding of agents targeting different disease mechanisms related to pulmonary fibrosis, inflammation, and even neuroendocrine cells. As we gain more understanding of chILD disorders, the children we treat will be able to benefit from some of these agents.

I am hopeful because of the energy that the chILD Foundation, the Children's Interstitial Lung Research Network, and many centers treating children with pulmonary disease are exerting individually and cooperatively in studying respiratory disease in children that the future is bright. So I think that as we look ahead, the opportunities for recognizing, understanding, and treating chILD are great, and are limited only by our current state of knowledge about these relatively rare diseases of children.

I thank all of the participants in today's roundtable for their contributions to this enlightening discussion.

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