What is chILD
The Spectrum of Children’s Interstitial Lung Diseases

Martha Fishman MD
Boston Children’s Hospital

Courtesy of chILD Foundation
The Human Lung: A Remarkable Organ
The Alveolus:
The functional unit at the end of the airway

Modified from slide courtesy of Alicia Casey MD
The Alveolus: Nature’s beautiful design for gas exchange

P1: type I pneumocyte
P2: type 2 pneumocyte
C: capillary
M: mesenchymal cell
E: endothelial cell

Thin layer between airspace and blood vessel
Contrast: Abnormal alveolus in ILD

Wider Interstitium: space between alveolar lining cells and vessels

Thick wall-increase barrier to gas exchange
Abnormal structure affects breathing

Thick alveolar walls (interstitial disease):
• barrier to O2 diffusion
• stiffer lungs = more work to expand

Abnormal airways (airway disease):
• obstruction to airflow
• difficulty moving air in and out
How abnormal lung structures can affect patients

- Low oxygen (need oxygen therapy)
- Rapid breathing
- Retractions/ ‘belly breathing’
- Low weight (need more calories)
- Feel ‘short of breath’
- Difficulty with exercise

A Boston Children’s Hospital patient
Our understanding of chILD has changed

_As more lung biopsies were done in children, we learned that_

kids with _similar symptoms and x-rays_

can have very _different diseases_

involving _different parts of the lung_

and _different cellular processes_

Courtesy of chILD Foundation
‘Classic’ ILD
(alveolar walls too thick)

Pulmonary Interstitial Glycogenosis

Sara Vargas MD
10X
Alveolar walls and alveolar spaces abnormal

Surfactant dysfunction disorders
Alveolar spaces filled

Protein material

Alveolar macrophages

Surfactant dysfunction disorders

Sara Vargas MD
40X
Airways with abnormal cells

NEHI
Too many neuroendocrine cells (stained brown)
Airways obstructed

Bronchiolitis obliterans

Barker et al NEJM
Broader definition has evolved for ‘chILD’

An ‘umbrella’ term for a diverse group of diffuse chronic lung diseases
chILD Syndrome

3 of the following 4 criteria in the absence of another etiology

- Respiratory signs (e.g. tachypnea, retractions, clubbing, crackles, wheezes, poor weight gain)
- Respiratory symptoms (e.g. cough, shortness of breath, exercise intolerance)
- Hypoxemia
- Diffuse abnormalities on imaging

ATS Clinical Practice Guidelines, AJRCCM, Kurland et al, 2013
Similar symptoms ≠ Different Diseases

The faces of...

CHILD

Children's Interstitial Lung Disease

Courtesy of chILD Foundation
# chILD Diseases

<table>
<thead>
<tr>
<th>Classification Category</th>
<th>Specific Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disorders more Common In Infancy</strong></td>
<td></td>
</tr>
<tr>
<td>Developmental Disorders</td>
<td>Alveolar Capillary Dysplasia with Misalignment of Pulmonary Veins; Congenital Alveolar Dysplasia</td>
</tr>
<tr>
<td>Growth Abnormality Disorders (Alveolar simplification)</td>
<td>Pulmonary hypoplasia; associated with chromosomal disorders; associated with congenital heart disease</td>
</tr>
<tr>
<td>Specific Conditions Unknown Etiology</td>
<td>Neuroendocrine Cell Hyperplasia of Infancy (NEHI); Pulmonary Interstitial Glycogenosis (PIG)</td>
</tr>
<tr>
<td>Surfactant Dysfunction Mutations</td>
<td>Surfactant protein B (<em>SFTPB</em>), Surfactant protein C (<em>SFTPC</em>), ATP-binding cassette A3 (<em>ABCA3</em>); thyroid transcription factor-1 (<em>NKX2.1</em>) <em>(Some of these presenting in later childhood)</em></td>
</tr>
<tr>
<td><strong>Disorders Related to Systemic Disease</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Disorders of the Normal Host / Environment Exposure</strong></td>
<td>Autoimmune and rheumatologic diseases; storage diseases; sarcoidosis; Langerhans cell histiocytosis</td>
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<tr>
<td><strong>Disorders of the Immunocompromised Host</strong></td>
<td>Post infectious process (e.g. bronchiolitis obliterans); hypersensitivity pneumonitis; eosinophilic pneumonia; idiopathic pulmonary hemorrhage</td>
</tr>
<tr>
<td><strong>Disorders Masquerading as Interstitial Lung Disease</strong></td>
<td>Related to transplantation and rejection; related to stem cell transplant; opportunistic infections; LIP</td>
</tr>
<tr>
<td><strong>Unknown</strong></td>
<td>Pulmonary biopsy tissue that cannot be classified</td>
</tr>
</tbody>
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(Adapted from Deutsch et al AJRCCM 2007 and Kendig Chapter 54)
Pathology distribution in children under 2

Deutsch, Young et al, AJRCCM, 2007 - **187 biopsies in children under age 2**

- **Alveolar growth abnormalities**: 24%
- **Disorders of normal host**: 12%
- **Disorders related to systemic disease**: 3%
- **Disorders of immunocompromised host**: 15%
- **Disorders of immunocompromised host**: 10%
- **Surfactant dysfunction disorders**: 10%
- **Unclassified**: 12%
- **PIG**: 3%
- **Disorders masquerading as ILD**: 5%
- **Diffuse developmental disorders**: 6%
Pathology distribution in older children

Fan et al, 2105 - 191 biopsies in 2-18 year olds

- Disorders of immunocompromised host: 41%
- Disorders related to systemic disease: 22%
- Disorders of normal host: 16%
- Masquerading as ILD: 7%
- Unclassified: 9%
- Surfactant disorders: 1%
- NEHI: 2%
- Alveolar growth abnormalities: 5%
- Other: 9%

191 biopsies in 2-18 year olds
YOU ARE NOT ALONE

Individual diseases are rare, but together they are not

For example, in just the past 2 years at Boston Children’s Hospital, about 100 new patients have been referred to our ILD program, half of which are from out of state.
chILD Foundation:
Advocacy, education, research and support

Welcome
The chILD Foundation is helping provide guidance, education, and support to all families with children diagnosed with Interstitial or Diffuse Lung Disease.
Learn More

Child Diagnosed with ILD?
You are not alone. Click the link above to register your child for our support and research programs.
Family Support

Living with ILD?
Through our education and support programs, get information on how to give your child the best care.

Are You a Professional?
If you are a doctor health care professional, we can help you with information and connections to other professionals.
Physician Support

www.child-foundation.com
We Are All A Team
Clinician/Patient/Scientist

A patient with ABCA3 disease, with her clinician and the scientist who discovered her gene mutation
chILD Foundation Family Conference 2015
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WITH GRATITUDE

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