Interstitial Lung Disease – Paediatric

Interstitial Lung Diseases in Children
Interstitial Lung Diseases (ILD) are a group of rare lung conditions that cause chronic chest problems or breathlessness. Whilst there is some overlap with adult disease, ILD in children often has a very different clinical picture. The problem may occur straight after birth, or may present at any age in childhood. Generally, the causes of these diseases are unknown but they may be inherited. They are not contagious.

The lungs are responsible for the delivery of oxygen into the blood stream and the removal of carbon dioxide. The major problem in ILD is inflammation of the lung tissue which leads to scarring (fibrosis) of the air sacs (alveoli) that interferes with the ability of the lungs to deliver oxygen. If the problem gets worse, the lungs become stiff and shrink, resulting in increased breathlessness.

What are the symptoms?
The term, "chILD Syndrome" has been coined to describe the way children can present with ILD. The majority of children present with fast breathing, low oxygen concentrations, failure to thrive, chronic cough, and on listening with a stethoscope, persistent noises in the chest called crackles or wheezes. One of the most striking features is marked breathlessness with exercise.

It is uncommon for children to develop chest pains or to cough up phlegm. If these other symptoms develop then another problem needs to be considered. The breathlessness in ILD, unlike in asthma, is generally constant from one day to the next and if it deteriorates, does so over a period of months to years.

What causes these diseases?
In 50% of cases, the cause of ILD is unknown. Sometimes it is caused by a rare gene abnormality which affects surfactant fluid production - surfactant fluid is fluid which lines the alveoli and helps keep the airways open. We are just beginning to understand more about ILD as it is quite complicated. A classification has been proposed for widespread involvement of lung disease in children which includes many types of ILD.

Lung disorders more prevalent in infancy

- Diffuse developmental disorders (abnormal lung formation) affecting the alveoli (air sacs in the lungs).
• Acinar dysplasia (poorly developed air sacs).
• Congenital alveolar dysplasia (poorly developed air sacs).
• Alveolar capillary dysplasia (air sacs, which are poorly aligned with lung blood vessels).

Lung growth abnormalities reflecting decreased numbers of air sacs
• Pulmonary hypoplasia (underdeveloped lungs).
• Chronic neonatal lung disease.
• Related to chromosomal disorders.
• Related to congenital heart disease.

Specific conditions of undefined cause
• Neuroendocrine cell hyperplasia of infancy.
• Pulmonary interstitial glycogenosis.

(Both of these conditions have specific characteristics when seen on a lung biopsy).

Inherited surfactant disorders
• Surfactant protein B mutation.
• Surfactant protein C mutation.
• ABCA3 mutations.

(These affect the production of surfactant).

Histology consistent with surfactant dysfunction without a yet recognised genetic cause
• Pulmonary alveolar proteinosis.
• Chronic pneumonitis of infancy.
• Desquamative interstitial pneumonitis.
• Non-specific interstitial pneumonia.

Disorders less prevalent in infancy
• Disorders related to disease processes in the body's systems.
• Immune mediated/collagen vascular disorders (inflammation of the body's blood vessels).
• Storage disease (rare inherited diseases).
• Sarcoidosis.
• Langerhans cell histiocytosis.
• Malignant infiltrates.

Disorders of the normal immune system
• Related to infections.
• Related to environmental agents.
• Hypersensitivity pneumonitis.
• Toxic inhalation.
• Aspiration syndromes.
• Eosinophilic pneumonia.

Disorders of the weakened immune system
• Opportunistic infections.
• Related to therapeutic intervention e.g. drug or radiation therapy.
• Related to transplantation and rejection.
• Widespread alveolar damage of unknown cause.

Disorders that resemble ILD
• Arterial hypertensive vasculopathy (disease of the blood vessels).
• Congestive changes related to cardiac dysfunction.
• Veno-occlusive disease (a disease affecting the blood vessels).
• Lymphatic disorders (a disease affecting the lymph vessels which carry fat).

How is ILD investigated?
After a careful patient history is taken and an examination is carried out, a doctor will undertake a number of investigations to confirm a suspected diagnosis of ILD.

*Chest x-ray*: This simple investigation provides very important information to a treating doctor, particularly if there are previous x-rays available for comparison. A patient should be encouraged to locate any previous chest x-rays, no matter how old.

*Lung function testing*: These tests performed in a respiratory laboratory provide the doctor with a functional assessment of the lungs. The tests allow doctors to assess the severity of the scarring in the lungs and monitor the progress of the disease. They are usually done in children from five years of age, as they rely on cooperation from the child.

*Blood tests*: Occasionally ILD can be the first complication of a more widespread illness, or an inherited disorder. Blood tests are required to help with the diagnosis.

*Computed Tomography (CT scan)*: Inevitably, this investigation is required to confirm the presence of ILD. Based on this investigation, a doctor would probably recommend a surgical biopsy.

*Bronchoscopy*: Examination of the bronchial tubes with a fibre-optic instrument that allows samples of fluid to be taken from the lung is useful in diagnosing some forms of ILD. This is usually done under general anaesthetic.

*Lung biopsy*: The removal of some lung tissue at surgery is recommended in most patients to help the diagnosis of ILD. This investigation requires a hospital stay and is generally performed in a specialist centre. It may be performed by keyhole surgery.
*Other investigations:* The doctor may perform other investigations such as the use of a pH probe looking for gastro-oesophageal acid reflux which can mimic ILD.

**Disease treatment**
Unlike in adults, the pattern on the chest x-ray or CT scan does not correlate with the degree of changes on a lung biopsy and the outcome. As this disease is so rare, there are no controlled trials available to guide the best treatment for your child. Treatment depends on the cause of the ILD.

It is important to exclude and treat gastro-oesophageal acid reflux. In most cases, treatment normally consists of using medications which decrease the inflammation, such as high-dose steroids, or alternatives such as methotrexate, azathioprine or cyclosporin.

Hydroxychloroquine and an antibiotic called azithromycin has also been used. Some children may need oxygen therapy. In all cases, it is important to optimise nutrition to allow for adequate lung growth.

It is important that children have all their vaccinations including annual flu vaccine. Some children may need long-term support with oxygen. Lung transplant may be an option in some children.

The prognosis is extremely variable. There may be complete recovery, partial response with long term problems, or no response at all. The overall death rate is 15% and the recurrence rate within families is 1 in 8.

It is recommended that patients diagnosed with ILD should be managed in a specialist centre, with access to clinical trials and the availability of lung transplantation for suitable candidates.

**Research initiatives**
Current therapies for ILD suppress the immune system and are aimed at reducing lung inflammation. Unfortunately, this approach only addresses part of the process that causes lung injury in ILD and does not prevent scarring. New treatments are focused on preventing the scarring process and are currently focused on the following areas:

*Genetics:* It is likely that the presence of certain genes makes individuals more susceptible to scarring of the lungs. It is hoped that identifying these genes and the products that they are responsible for producing (proteins) will lead to the development of new therapies. Furthermore, the genetic causation of many ILDs in children is being increasingly understood.

*Anti-fibrotic medication:* Drugs that stop scarring in the body are currently the subject of clinical trials involving a large number of diseases. It is likely that lessons learnt in these more common conditions will be applied to ILD and offer hope for more effective therapies.
Collaborative networks: The formation of collaborative networks such as the Children's Interstitial Lung Disease (ChILD) Network in the USA the British Paediatric Orphan Lung Disease Registry (BPOLD) and the Australian Registry Network for Orphan Lung Disease (ARNOLD) will lead to an increased understanding of what causes ILD and will hopefully lead to new treatments.

Patient support
To date, there have been no local support groups set up specifically for children with ILD and their families. The Lung Foundation Australia provides information and support to patients with all forms of lung disease including ILD and advocates on their behalf. We encourage you to call the Lung Foundation's Information and Support Centre toll-free on 1800 654 301.

A number of internet sites exist that provide useful information relating to ILD:
- Childrens Interstitial Lung Disease Foundation: http://www.childfoundation.us
- Australian Registry Network for Orphan Lung Disease: www.arnold.org.au
- British Paediatric Orphan Lung Disease Registry: http://www.bpold.co.uk/
- http://breathtakers.co.uk
- http://rarediseases.org/
- http://www.orpha.net/
- www.lungfoundation.com.au
- http://www.pulmonaryfibrosis.org/

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