COMMENCING September 2014

Australian Paediatric Surveillance Unit
STUDY PROTOCOL
Childhood Interstitial Lung Disease (ChILD)

BACKGROUND

Childhood interstitial lung disease (ChILD) refers to a heterogeneous group of rare chronic respiratory disorders of childhood that are associated with significant morbidity and mortality.[1-3] The disorders defined by ChILD feature remodelling of the lung interstitium and distal air spaces, which results in abnormal gas exchange between blood and air. The cause of ChILD is often unknown but the disease may be a consequence of genetic mutation, environmental exposure or a sequela of a systemic disease. The definition and classification of ChILD has changed over the past ten years as novel disorders have been identified and diagnostic techniques advanced. It is now recognised that ChILD may exist when diffuse infiltrates on computed tomography and hypoxemia accompany respiratory symptoms or signs and, common causes of diffuse lung disease have been excluded.[3]

From an audit of medical records of the Sydney Children's Hospitals Network (SHCN) (The Children's Hospital at Westmead and the Sydney Children's Hospital) over a ten year period, it is estimated that the SCHN saw 1.5 new ChILD cases per year (estimated incidence of 1.1 cases/1 million children/year). Each specific ChILD disorder is extremely rare. The rarity of ChILD disorders, their complexity and absence of randomised clinical trials, means that current clinical guidelines for diagnosis and management are based primarily on clinical experience and informed judgement, rather than systematic study.[3] Diagnosis of a specific ChILD disorder usually requires a CT scan, lung biopsy and/or genetic test. The most common treatments are corticosteroids, hydroxychloroquine and oxygen therapy. Rarely do children recover spontaneously without the need for treatment and disease management is usually required for many years.

Currently there are no Australian national data describing the frequency of ChILD, demographics, presentation and diagnoses or short-term outcomes.

STUDY OBJECTIVES

1. Estimate the incidence of ChILD (and specific ChILD disorders) in Australia.
2. Describe the following for cases of ChILD:
    a. Demographic features of affected children (area of residence, ethnicity, age, sex)
    b. Clinical features at presentation
    c. Means of diagnosis and time from presentation to diagnosis
    d. Initial treatment
3. Facilitate enrolment of reported cases into the Australasian Registry Network for Orphan Lung Diseases (ARNOLD www.arnold.org.au) at the Lung Foundation Australia (www.lungfoundation.com.au)

CASE DEFINITION [1,3,4]

Child < 15 years of age, with diffuse infiltrates on computed tomography scan and diagnosed with one or more of the ChILD conditions listed in the table below. Common causes of diffuse lung disease are to be excluded.

REPORTING INSTRUCTIONS

Please report any child newly diagnosed with Childhood Interstitial Lung Disease that meets the case definition whom you have seen in the last month and not previously reported to the APSU.

Diagnoses for inclusion:

Diffuse developmental lung disorders
- Acinar dysplasia
- Congenital alveolar dysplasia
- Alveolar capillary dysplasia with misalignment of pulmonary veins

Surfactant dysfunction mutations & histology consistent with surfactant dysfunction
- Surfactant protein B mutation
- Surfactant protein C mutation
- ABCA3 mutation
- TTF-1/Nkx2.1 mutation
- Pulmonary alveolar proteinosis
- Chronic pneumonitis of infancy
- Desquamative interstitial pneumonitis
- Early interstitial pneumonitis
- Non-specific interstitial pneumonitis

ChILD of undefined cause
- Neuroendocrine cell hyperplasia of infancy
- Pulmonary interstitial glycogenosis
- Infantile cellular interstitial pneumonitis

ChILD associated with systemic disease
- Immune-mediated/collagen vascular disorders
- Storage disease
- Sarcoidosis
- Langerhans cell histiocytosis

ChILD of the normal host
- Usual interstitial pneumonia
- Eosinophilic pneumonia
- Related to environmental agents:
  - Hypersensitivity pneumonitis
  - Toxic inhalation

Disorders masquerading as interstitial lung disease
- Arterial hypertensive vasculopathy
- Veno-occlusive disease
- Lymphatic disorders

Common causes of diffuse lung disease to be excluded:

- bronchopulmonary dysplasia (chronic neonatal lung disease)
- bronchiolitis obliterans
- primary ciliary dyskinesia presenting with newborn respiratory distress
- cystic fibrosis
- immunodeficiency
- drug-induced diffuse lung disease
- congenital heart disease
- recurrent aspiration

FOLLOW-UP OF REPORTED CASES

Clinicians who notify a case of ChILD will be asked to complete a 2 page questionnaire requesting de-identified details about patient demographics, birth history, family history, clinical presentation, diagnosis and treatment. The questionnaire will be sent to clinicians via email or post, or may be downloaded from the APSU website (www.apsu.org.au).

Please return the completed questionnaire to the APSU by post or fax as instructed on the questionnaire.

Any questions should be directed to:

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REFERENCES

1. Deutsch GH, Young LR, Deterding RR et al on behalf of the ChILD Research Co-operative. Diffuse lung disease in young children: Application of a novel classification scheme. *Am J Respir Crit Care Med*. 2007;176:1120-1128.
2. Clement A, Nathan N, Epaud R et al. Intersititat lung diseases in children. *Orphanet J Rare Dis*. 2010;5:22.
3. Kurland G, Deterding RR, Hagood JS et al on behalf of the American Thoracic Society Committee on Childhood Interstitial Lung Disease (chILD) and the chILD Research Network. An official American Thoracic Society clinical practice guideline: Classification, evaluation, and management of childhood interstitial lung disease in infancy. *Am J Respir Crit Care Med*. 2013;188:376-394.
4. Clement A and ERS Task Force committee members. Task force on chronic interstitial lung disease in immunocompetent children. *Eur Respir J*. 2004;24:686-697.
5. Griese M, Haug M, Brasch F et al. Incidence and classification of pediatric diffuse parenchymal lung diseases in Germany. *Orphanet J Rare Dis*. 2009;4:26.

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