# Paediatric Chronic Suppurative Lung Disease

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## Introduction

The true prevalence of chronic suppurative lung disease (CSLD) and other respiratory illness in Indigenous children is unknown. There is however little doubt that the burden of CSLD is disproportionately high in remote and rural Indigenous communities. In Central Australia the prevalence of high resolution computed tomography (HRCT) proven bronchiectasis in children (<15 years) is at least 4.2 per 1000 children (denominator based on ABS statistics for 2000 and includes population of the Anangu Pitjantjatjara Lands). This far exceeds the prevalence of children with cystic fibrosis in non-Indigenous Australian centres, yet there is no concerted program or resources to manage these children who succumb to premature death from their lung disease and have significant morbidity in childhood and adulthood. Many children remain undiagnosed and there is wide variation in the management of those identified with CSLD, varying from a minimalist approach (no treatment) to intensive physiotherapy and antibiotics. Reasons for the minimal approach include the perception that 'nothing can be done', and the lack of resources, both in the community and hospital levels, not dissimilar to community attitudes for cystic fibrosis several decades ago. The value of early recognition and intervention/management of these disease processes for the regression (where possible), and prevention and/or slowing down, of the advancement of the disease process is increasingly recognised in asthma, chronic lung infections and chronic obstructive airway disease (COAD).[1,2,3,4,5] Based on this principle, national and international programs currently exist for other respiratory diseases such as asthma, chronic airflow limitation, cystic fibrosis and non-respiratory diseases such as diabetes and chronic heart disease.

In late August 2001, a workshop to discuss the issues around CSLD in remote Indigenous children was attended by adult and paediatric respiratory physicians, general physicians and paediatricians, researchers, and public health physicians from around Australia and New Zealand. The management approach outlined in this article was reached by consensus of the group.

## Literature review and discussion

### Why children with CSLD are different from adults

The respiratory system, like any other system, undergoes a process of maturation in infancy and childhood. While external features, such as walking and talking, are obviously developing, the developmental process of

internal features, such as control of the respiratory system, respiratory muscles, thoracic cage and glandular development of the respiratory tree are often forgotten by adult-focused practitioners. Insults to the respiratory system at a young age may impair lung growth and lung potential.[6] Interventions at an early age before permanent irreversible changes take place are increasingly recognised in disease processes such as asthma.[1]

Another aspect of paediatric respiratory disease is the influence of prenatal factors and, when insults to the system occur, growth potential can be lost.[6] In the respiratory system, it has been well documented that lower respiratory infections (LRTI) in children can lead to later respiratory morbidity, chronic lung disease and lung function abnormalities.[7–12] In adenovirus and many viral acute lower respiratory infections (ALRI), the young child has increased risk of developing lung function abnormality.[8,13] Management should arguably be intensive in children as it is now increasingly appreciated that inflammatory disease processes may impair lung growth in addition to accelerated respiratory function decline in later years.[3,14,15]

### Principles/goals of management

CLSD has been termed an 'orphan disease'[16] because of its perceived low frequency, neglected in research and treatment because of a lack of commercial interest. In the absence of adequate data, the cystic fibrosis (CF) approach (the commonest cause of chronic suppurative lung disease in non-Indigenous children) is utilised. With intensive and improved management in CF, the median life expectancy for an Australian child with CF is now in the mid forties, a far cry from the situation three or four decades ago when children succumbed in their first decade of life. The outcomes of this approach have been documented by the Danish group.[17] CF and CSLD share common respiratory manifestations as CF is a variety of CSLD. In contrast, the presumed initial insult in children with CSLD usually occurs in infancy or early childhood.

The main general management points for children with CSLD are similar to that of the respiratory management of a child with CF; directed against infections, secretions, airway obstruction, and complications (e.g., hemoptysis, hypoxemia, growth failure, cor pulmonale). In addition, specific management is aetiology specific e.g., the use of pooled immunoglobulin for immunodeficiency. Treatment is aimed at reducing morbidity from exacerbations and complications of CSLD, and reducing lung inflammation by reducing the bacterial load. Management should arguably be intensive in children as it is now increasingly appreciated that inflammatory disease processes may impair lung growth in addition to accelerated respiratory function decline in later years.[3,14,15] In adults, accelerated lung function decline have been found in patients with asthma[18], COAD with mucous hypersecretion[19], smoking[20], and coronary heart disease.[18] In CSLD, the presence of features of asthma is a known bad prognostic factor.[21]

## Management of CSLD in children

### Diagnosis

CSLD should be considered where children have one or more of the following symptoms and signs: chronic moist or productive cough, exertional dyspnoea, symptoms of reactive airways disease (RAD), growth failure, recurrent chest infections, pulmonary hypertension, chronic hypoxaemia, clubbing, and

hyperinflation. CSLD should be differentiated from radiologically defined bronchiectasis. Pathologically, bronchiectasis is defined as an abnormal and permanent dilatation of the subsegmental airways.[16] Radiologically, the characteristic finding in bronchiectasis is the presence of 'signet ring' where a dilated bronchi is greater than the diameter of the accompanying blood vessel in cross-section.[22,23] However, the absence of this characteristic finding does not exclude the presence of bronchiectasis. Children with suspicious features of CSLD should be referred for evaluation and a management plan.

**Assessment**

The primary aim is to search for familial and treatable causes and, second, to define disease severity which impacts on treatment intensity. Pastuer and colleagues recently reported the aetiological causes of bronchiectasis in 150 newly diagnosed adults with bronchiectasis and identified one or more causes in 47%.[24] They concluded that patients with bronchiectasis deserve thorough investigations.[24] In the Alice Springs series,' other major contributing factor' was identified in 12.2% children (IgG subclass deficiency, congenital lesion, severe aspiration, TB). In addition, bronchoscopy in 16 of those who had localised changes revealed localised bronchomalacia in the corresponding lobe in six children. Reactive airway disease manifested clinically by recurrent wheeze is sometimes present with underlying CSLD and bronchiolitis obliterans.[25] This should be treated on its own merits. Children referred for assessment usually undergo (a) high resolution CT scan of the chest (b) a series of blood tests (c) pulmonary function test if over six years (d) bronchoscopy if localised changes are present and (e) sputum evaluation.

**Antibiotics and other medications**

Based on Cole's model for the pathophysiology of bronchiectasis[26] and using the childhood CF approach, intensive management of children with CSLD is advocated. Exacerbations may require intermittent hospitalisation with intravenous antibiotics and intensive physiotherapy and other airway clearance methods (exercise and nebulised therapy). The Danish model of CF utilises a three-monthly 'chest tune-up' regimen[17] where children are hospitalised for the above treatment regimen, irrespective of whether an exacerbation is concurrently present. However, all exacerbations are intensively managed either as an outpatient, 'hospital-in the home', or as an in-patient. The hospital-in-the-home model is impractical in remote Indigenous communities. Outpatient management may also be impractical in some situations. Thus, children with moderate or severe CSLD are likely to require hospitalisation. Brief antibiotic intervention has been shown to significantly improve inflammatory profile in the airways[27,28] and systematically[27,28], as well as improve quality of life measures.[28,29] A 12 month trial in adults with non-CF pseudomonas colonised bronchiectasis showed a reduced number of hospitalisations for those on the continuous treatment when compared to those in the symptomatic treatment arm.[30] Another 12 month trial using a randomised controlled design showed that the symptoms of cough expectoration, haemoptysis and general disability were significantly less in the those treated with tetracycline than to those treated with oral penicillin or placebo.[31] Long-term intervention trials are unavailable. The use of sputum colour has recently been shown to be a good reflection of neutrophilic airway inflammation.[32] Using a nine-point (0–8) colour chart ranging from clear (water colour) to yellow to dark green,

Stockley and colleagues showed that ‘sputum colour graded visually relates to the activity of the underlying markers of bronchial inflammation and concluded that simple visual analysis of sputum provides guidance concerning underlying inflammation and its damaging potential’.[32] Sputum bacteriology is associated with quality of life in adults with non-CF bronchiectasis.[29] Using quality of life instruments, Wilson and colleagues showed that patients infected with pseudomonas had significantly worse scores than those infected with Haemophilus and the non-chronic infected groups.[29]

The use of maintenance antibiotics may be suitable in selected situations where frequent exacerbations occur.[33] However, its use may be limited by practical factors. In adults regular use of macrolides and trimethoprim have shown to be beneficial in reducing pulmonary inflammation, infective exacerbations and improving lung function.[33,34] This has not been evaluated in children.[35] The recommendation for the choice of antibiotics should be guided by sputum bacteriology, severity of disease and patient factors such as allergy, tolerability and medication compliance. For example, an older child would best tolerate roxithromycin on a daily basis but a young child with moderate bronchiectasis would be best on amoxycillin-clavulanic acid on a twice-daily regime rather than amoxicillin on a tds regimen. The high dose regimen is recommended. Current data from sputum in Central Australian children with bronchiectasis indicate that the first choice (if feasible) should be amoxil, as most have microbes that are sensitive to amoxil. For practical reasons amoxycillin-clavulanic acid may be preferable. Roxithromycin may be considered in those with less severe bronchiectasis. Discussion of patient factors with local community health staff is encouraged.

The use of inhaled corticosteroids for children with bronchiectasis has not been evaluated. In adults, such studies were only of 4–6 weeks duration, with a trend to improve lung function.[36] Kolbe and colleagues concluded in their recent Cochrane review that there is insufficient evidence to provide clear guidelines to guide practice.[36] When inhaled steroids are used consideration to once daily, rather twice daily, dosing may be appropriate in settings where adherence to treatment regimens may be a concern.

**Physiotherapy**

Chest physiotherapy in children is a specialised area as physiotherapy techniques differ for infants and children in comparison to adults.[37] Techniques such as ‘bubble PEP’ commonly used in children are not used in adults. Chest physiotherapy to improve mucociliary clearance is a standard treatment regimen in children with CF and has been shown in a meta-analysis to significantly improve sputum clearance.[37] Cochrane and colleagues showed that physiotherapy can reduce airways obstruction and sputum has a detrimental effect on pulmonary function.[38] In line with adults with bronchiectasis and sputum producing COAD[39], we advocate the use of daily physiotherapy in children with CSLD, using the CF model. There are many forms of physiotherapy and these different methods have not been evaluated in children with CSLD. Reviews on physiotherapy are available elsewhere.[40,41,42]

Postural drainage was standard therapy for CSLD in the past. Recent data has shown the use of this may indeed increase lung dysfunction related to increased gastro-oesophageal reflux and possible aspiration.[43,44] In CF, this manoeuvre is no longer used in many paediatric centres.

**Nutrition**

Good nutrition (both macro and micro) is highly important, not only for reduction of acute respiratory infections in children[45,46,47] but is also related to improved lung function in children with CSLD.[48] The effect of nutrition in the developing lung (children) is more significant than that on the developed (adult) lung. Aggressive nutritional support is one of the mainstays of the current management of CF.[48] Some children will be on caloric supplements.

**Minimisation of further lung injury**

The impact of both active and passive environmental tobacco smoke (ETS) is highly significant in all situations throughout life and in utero. Rates of smoking amongst Aboriginal males in NT is higher than the Australian average (59% vs 54% respectively).[18] Whilst the prevalence of smoking in the mainstream Australian community is declining, that of Indigenous communities is increasing (personal communication), reflecting the same pattern as in developing countries.[49] Reviews on ETS and its effects on the developing lung and accelerated lung decline are available elsewhere.[50–53] Ezzati and Kammen have recently demonstrated an exposure response effect of increased exposure to indoor biomass combustion on ALRI, and called for public health initiatives to reduce average exposure to below 2000µg/m$^3$.[54]

In addition to public health factors, there is little doubt that immunisation is fundamental in preventing the development of respiratory infections, one of the presumed leading cause of CSLD in Indigenous children. Currently the 23 valent polysaccharide pneumococcal (Pneumovax 23) vaccine is recommended for children >18months and the 7-valent conjugate pneumococcal vaccine (Prevaner) is expected to reduce the incidence of pneumonia by at least 30%.[55] There is some evidence that the response of Indigenous children to vaccination can be sub-optimal[56] and repeated immunisation may be required in selected individuals. There is recent evidence that polysaccharide pneumococcal (Pneumovax) immunisation of targeted groups only is suboptimal.[57] Booster pertussis and annual influenza vaccination should also be considered.

**Follow-up**

The aim of regular review is to optimise potential lung growth in children, prevent premature respiratory decline (where possible) and optimise quality of life. Indigenous children in remote communities should not be denied the recommended follow up for children with any form of CSLD. In the CF model, a three-monthly review is recommended: lung function (for children aged over six years), assessment and management of pulmonary decline and infective exacerbations (sputum and cough changes, exertional dyspnoea), complications of CSLD (pulmonary hypertension, chronic hypoxaemia, poor growth, sleep disturbance, RAD, haemoptysis) and a review of contributory factors (e.g. gastro-oesophageal reflux, asthma, environmental smoke exposure). In our experience of remote Indigenous children, cough is often under-reported and it is often necessary to exhibit the cough to gain an appreciation of the nature of the child’s cough. Practitioners need to be cognisant of these factors and, in addition to a three monthly medical review, we advocate a minimum half-yearly review by a respiratory physician. Ideally an intensive team approach with incorporation of allied health expertise (nursing, physiotherapy, dietitian), as this model has been shown to improve health outcomes for different diseases.[17,58] The

recommended frequency of medical and specialist review for children with CSLD is based on the experience in Central Australia where significant co-morbidities and underlying cilia disease were frequently found. Specialist programs have shown the greatest impact in the care of children with bronchiectasis from cystic fibrosis and cilia dyskinesia patients in other centres.[59,60]

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