Bronchiectasis and chronic suppurative lung disease among Indigenous children

Rosalyn Singleton- Alaska
Anne B Chang - Australia
Faculty/Presenter Disclosure

Rosalyn Singleton and Anne Chang have no relevant financial relationships with the manufacturer(s) of commercial services discussed in this CME activity.

And

Rosalyn Singleton and Anne Chang do not intend to discuss an unapproved/investigative use of a commercial product/device in our presentation.
Objectives

In Indigenous children, to:

1. Understand the epidemiology and risk factors for CSLD/bronchiectasis

2. Recognize interventions to prevent pneumonia and development of CSLD/bronchiectasis

3. Recognize evidence-based treatments for CSLD/bronchiectasis
Overview

• Why CSLD and BE is important
• Epidemiology and risk factors
• Interventions to prevent lung injury
• What works in children with BE: evidence based approach
Why CSLD-bronchiectasis is important

- Prevalence; increasingly recognised
- Burden, QoL, lung function, death
- Non-resp impacts including link to cardiac disease
- Secondary prevention possible
Prevalence

- Alaskan Inuit: 2000/100,000 (one in 63)

- Central Australia
  - 1470 per 100,000 Aboriginal children (1 in 68)
  - CF in Aus = 1 in 30 000

- NZ Maori/Pacific: 50/100,000
  - Samoa: 600/100,000
  - UAE: 28/100,000
  - Australia-wide and international implications
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cohort (N=346)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protracted bacterial bronchitis</td>
<td>142 (41.0%)</td>
</tr>
<tr>
<td>Asthma/RAD n (%)</td>
<td>55 (15.9%)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>31 (9.0%)</td>
</tr>
<tr>
<td>Resolved w/out specific diagnosis</td>
<td>48 (13.9%)</td>
</tr>
<tr>
<td>Tracheomalacia</td>
<td>21 (6.1%)</td>
</tr>
<tr>
<td>Habitual-psychogenic</td>
<td>15 (4.3%)</td>
</tr>
<tr>
<td>Pertussis</td>
<td>12 (3.5%)</td>
</tr>
<tr>
<td>Aspiration Lung Disease</td>
<td>8 (2.3%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3 (0.9%)</td>
</tr>
<tr>
<td>Upper airways</td>
<td>5 (1.4%)</td>
</tr>
<tr>
<td>Mycoplasma</td>
<td>5 (1.4%)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1 (0.3%)</td>
</tr>
</tbody>
</table>

Indigenous children with chronic cough increased risk of BE OR=4.4 (95%CI 1.9, 10)
Is Bronchiectasis increasing?

Trends and Burden of Bronchiectasis-Associated Hospitalizations: USA, 1993-2006

Amy E Seitz, Kenneth N Olivier, Claudia A Steiner, Ruben Montes De Oca, Steven M Holland and D. Rebecca Prevots

Chest 2010
Hospitalisation data

- Indigenous
- Non-Indigenous
- Total*

Age standardised rate per 100,000 population

Year

2005 2006 2007 2008 2009
P value for trend increase <0.001
Adult data: Central Australia

- 12 month retrospective study (2004-05)
- 61 adults, 126 admissions (mean 2.8 per person, all but 2 Indigenous)
- 23% aged < 30 years old
- 70% recc LRTI in childhood
- mean FEV₁ 36 (SD 11), FVC 47% (SD 11.7)
- 8 (13%) died within 12-mo (7 from resp illness)
Chronic wet cough/infections & CV disease

- Independent risk factor for CV disease

  - 3-yr follow-up: 19,444 randomly selected Finnish
  - Risk ratio$_{adj}$ 1.5 (95% CI 1.3-1.8) for coronary dis
  - Risk ratio$_{adj}$ 1.7 (95% CI 1.4-2.1) for cor death

- Kiechl et al, *Circulation* 2001;103:1064-70
  - 826, aged 40-79 yr olds, 5-yearly carotid atherosclerosis high-resolution duplex scans
  - Any chronic infection versus none, OR$_{adj}$ 4.1, (95% CI 2.42 to 6.9; p<0.0001)
N = 103; 80 % from childhood (<15 yrs)

Total n = 150
≤ 20 yrs = 88 (~60%)
Cohort data

The importance of early recognition and effective treatment
z-score of FEV₁ (slope 0.17 p=0.039, 95% CI 0.01 to 0.34) with Rx over 2 years, 59 children

- Over 4 years, 31 children; no significant change
- Older children at referral had poorer lung function
FEV$_1$ $\geq$ 80% pred at presentation

Predictors of decline in 52 children

- no. of severe exacerbations: $-1.95\%$ each hosp exacer
- later Dx: decrease by 1.64% points for each year, NS
- no difference for gender, aetiology

Kapur et al, Chest 2011
FEV1 % pred

-0.51 in non smokers
-0.44 in total grp
both p< 0.001

of chronic cough

King et al, COPD 2009;6:130-6
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Child n=107</th>
<th>Adult onset n=75</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of productive cough, years, med</strong></td>
<td>50 (40–60)</td>
<td>5 (1–15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Volume of sputum, mls, median (range)</strong></td>
<td>30 (15–50)</td>
<td>15 (5–40)</td>
<td>0.159</td>
</tr>
<tr>
<td><strong>MRC dyspnoea score, mean (SD)</strong></td>
<td>2.1 (1.0)</td>
<td>2.0 (1.1)</td>
<td>0.526</td>
</tr>
<tr>
<td><strong>Haemoptysis in the past year, n (%)</strong></td>
<td>32 (30)</td>
<td>12 (16)</td>
<td>0.097</td>
</tr>
<tr>
<td><strong>Rhinosinusitis, n (%)</strong></td>
<td>78 (73)</td>
<td>20 (27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hospitalisations in the past year, n (%)</strong></td>
<td>27 (25)</td>
<td>23 (32)</td>
<td>0.419</td>
</tr>
<tr>
<td><strong>Exacerbations, mean (SD)</strong></td>
<td>3.1 (1.8)</td>
<td>2.0 (1.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signs</th>
<th>Child n=107</th>
<th>Adult onset n=75</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crepitations, n (%)</strong></td>
<td>68 (64)</td>
<td>15 (20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Wheeze, n (%)</strong></td>
<td>24 (22)</td>
<td>17 (23)</td>
<td>0.970</td>
</tr>
<tr>
<td><strong>Clubbing, n (%)</strong></td>
<td>1 (0.9)</td>
<td>1 (1)</td>
<td>0.999</td>
</tr>
</tbody>
</table>

| FEV<sub>1</sub>                                |             |                  |       |
| **Litres, mean (SD)**                          | 1.57 (0.73) | 2.20 (0.81)      | <0.001|
| **Percent predicted, mean (SD)**               | 65 (24)     | 83 (26)          | <0.001|

| CT                                            |             |                  |       |
| **Lobes with bronchiectasis, mean (SD)**      | 2.50 (1.06) | 2.15 (1.09)      | 0.017 |
| **HRCT score, mean (SD)**                     | 29 (17)     | 21 (13)          | <0.001|
Bronchoscopic and High-Resolution CT Scan Findings in Children With Chronic Wet Cough

Konstantinos Douros, MD; Efthymia Alexopoulou, MD, PhD; Aggeliki Nicopoulou, MD; Michael B. Anthracopoulou, MD, PhD; Andrew Fetzayas, MD, PhD; Panayiotis Yiallouros, MD, PhD; Polixeni Nicolaidou, MD, PhD; and Kostas N. Priftis, MD, PhD

Chest 2011

$r=0.23$, $p=0.028$
Defining BE and CSLD
Limitations with use of HRCT definition

- When does HRCT signs of bronchiectasis occur?
  - Less sensitive than bronchography in adults
  - False negative results are more likely to occur when the disease is mild
  - MDCT more sensitive than conventional HRCT

- HRCT findings derived from adult studies
  - bronchoarterial ratio infl by age \( (r = 0.77, p<0.0001) \)
  - Lung morphology, tissue changes with age

- Pediatric criteria required

Spectrum?

Progression of disease process (at least in a substantial number)

- Protracted bronchitis
- CSLD
- Radiological BE

Pediatric Pulmonol 2008;43:519-31

State of the Art

Chronic Wet Cough: Protracted Bronchitis, Chronic Suppurative Lung Disease and Bronchiectasis

A.B. Chang, PhD,1,2* G.J. Redding, MD,3,4 and M.L. Everard, MD5
Thus….

- Prevention – most important strategy
- Early detection really important
  - Know risk factors and look out for these
  - Recognize the early symptoms and signs
- Once known: intensive Rx prevents deterioration

Diagnosing and preventing CSLD and bronchiectasis
Paediatric Resp Review 2011; 12:97-103
# Aetiologies of childhood bronchiectasis

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Nikolaizik (41)</th>
<th>Aust-Ind (65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-infectious (sev pneumonia)</td>
<td>29%</td>
<td>90%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0</td>
<td>1.5</td>
</tr>
<tr>
<td>Inherited immune deficiency</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Primary ciliary dyskinesia</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Congenital malformations</td>
<td>15</td>
<td>1.5</td>
</tr>
<tr>
<td>Secondary immune defects</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Aspiration of exogenous toxicants</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>GERD or aspiration</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>CF-like or CF</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

(Arch Dis Child 1994;70:141) (Pediatr Pulmonol 2003;35:477)
Case control study summary

Association between a history of hospital pneumonia and bronchiectasis (OR 15.2, 95% CI 4.4-52.7)

- recurrent hospitalised pneumonia (P-trend < 0.01)
- severe pneumonia episodes with longer hospital stay (P-trend < 0.01)
- requiring oxygen (P-trend < 0.01)
- presence of atelectasis (OR = 11.9. 95% CI 3.1-45.9)
- overall number of pneumonia episodes rather than its site was associated with bronchiectasis

PIDJ 2004; 23: 902-8
Case control study summary

- Other risks: malnutrition, prematurity
- Odds ratio for development of bronchiectasis similar for lobar and bronchopneumonia
- No relationship between lobar pneumonia site and bronchiectasis site, or age of first pneumonia
- Breastfeeding protective OR 0.2 (95%CI 0.1-0.7)
In-patient and Out-patient bronchiectasis visit rates among American Indian/Alaska Native and the general US child population <18 years of age, 2002-2005

**Databases:**
- Indian Health Service (IHS):
  - National Patient Info. Reporting System
  - All hospitalization discharge records and outpatient visit data from IHS/tribal and contract
- General US population:
  - Nationwide Inpatient Sample
  - National Ambulatory Medical Care Survey
  - Ntl Hospital Ambulatory Medical Care Survey

**Data Extraction:**
- Visits in children <18 years with discharge or visit code:ICD-9-CM 494.(Bronchiectasis)
- 2002-2005 for IHS and US population

3rd International Meeting on Indigenous Child Health

Ottawa 2015
Bronchiectasis Outpatient Visit Rate 2002-2005
Non-CF Bronchiectasis

- Alaska Native children from YK Delta and other indigenous children have extremely high rates of non-CF bronchiectasis
- Early/Recurrent pneumonias in childhood is the major risk factor


Groom AV et al. Pneumonia and Influenza Mortality...American Indian and Alaska Native, 1990-2009. AJPH 2014
Pneumonia-associated hospitalizations in AI/ANs <1 year of age, by region, 2009-2011

<table>
<thead>
<tr>
<th>Region</th>
<th>Pneumonia-associated hospitalizations/1000 per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaska</td>
<td>67.6</td>
</tr>
<tr>
<td>East</td>
<td>11.9</td>
</tr>
<tr>
<td>Northern Plains East</td>
<td>9.4</td>
</tr>
<tr>
<td>Northern Plains West</td>
<td>44.3</td>
</tr>
<tr>
<td>Southern Plains</td>
<td>8.0</td>
</tr>
<tr>
<td>Southwest</td>
<td>41.9</td>
</tr>
<tr>
<td>US</td>
<td>11.7</td>
</tr>
</tbody>
</table>

I.H.S. National Patient Information Reporting System, 2014
Pneumonia-associated hospitalizations in Alaska Native infants <1 year of age, by region, 2009-2011

<table>
<thead>
<tr>
<th>Region</th>
<th>Pneumonia-associated Hospitalizations/1000 per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>YK Delta</td>
<td>117.4</td>
</tr>
<tr>
<td>Maniilaq</td>
<td>172.5</td>
</tr>
<tr>
<td>A</td>
<td>110.2</td>
</tr>
<tr>
<td>B</td>
<td>99.1</td>
</tr>
<tr>
<td>C</td>
<td>42.3</td>
</tr>
<tr>
<td>D</td>
<td>13.9</td>
</tr>
<tr>
<td>Anchorage</td>
<td>16.1</td>
</tr>
<tr>
<td>US</td>
<td>11.7</td>
</tr>
</tbody>
</table>

I.H.S. National Patient Information Reporting System, 2014
Global Estimate of severe Respiratory Syncytial Virus (RSV) infection: Alaska Native children
Rate of Severe or Hospitalized RSV/1000 infants/yr

Pneumonia-associated hospitalizations in AI/AN and US infants, 1998-2011

- AI/AN <1 year
- US <1 year

PCV7

PCV13

Ottawa 2015
Rural Alaska Household Characteristics

- Household crowding
- 20% have no piped water
- Many use outhouses or “honeybuckets” for sanitation
- High rates of tobacco smoke exposure
- Many use wood burning stoves
- Poor ventilation

Houses in the village are often...

- Small: often 300-800 ft²
- Crowded: Hooper Bay
  Avg. 5 person/home
- Hot (65°-81°F)
- Old
- Dry (humidity often below 30%)

- Built and maintained in difficult environments
- Used for a workshop
- Reduced access to qualified installation and repair personnel
Household Crowding in the U.S. 2000 Census Data

Figure 9. Crowded Housing: 2000

Risk Factors for RSV hospitalization in Alaska Native children.

RSV Case Control Study

Factors associated with decreased risk of RSV hospitalization
- Breastfeeding
- Parent educational level

Factors associated with increased risk
- Household crowding
- Prematurity/medical conditions

Risk Factors for Respiratory Hospitalization in Alaska

Respiratory Virus Case Control Study
Hospitalized, < 3 y.o., Controls: Age and region matched

- Risk factors for hospitalization:
  - Medically high risk,
  - woodstove,
  - bottle fed,
  - vomiting during feeds

- Protective Factors:
  - 2 or more rooms with sinks in home

Hospitalization rate among infants by percentage of rural Alaska village homes with water service, 1999–2004

Rates of infectious disease in 4 rural Alaska villages 3 years before and after introduction of water service adjusted for age

Clinic encounters and hospitalizations per 1000/yr

- Respiratory infections: Pre-piped water 1520, Post-piped water 1370
- Skin Infections: Pre-piped water 310, Post-piped water 250
- Gastrointestinal Infections: Pre-piped water 50, Post-piped water 30
Prevalence of Chronic Respiratory Symptoms in Alaskan Native School Children*

N=466; 1997 data
* Mean age = 13 ± 1.4 years

Lewis, Toby

Ottawa 2015
Features Associated with Childhood Bronchiectasis

Antecedent pneumonia  70%
Antecedent bronchiolitis  17%
Tuberculosis      2%
Aspiration pneumonia  2%
LRI in first year of life  80%
# LRI < 2 years of age  4

N=76

What is being done to address bronchiectasis in indigenous children?

MULTICENTRE BRONCHIECTASIS STUDY

The high rates of bronchiectasis among indigenous populations in affluent countries led to the first international study of non-CF bronchiectasis in

- Aboriginal and Torres Strait Islanders
- New Zealand Pacific Islanders and Maoris
- Alaska Natives from YK Delta

Study design

OBSERVATIONAL STUDY – follow clinical course on standard treatment
INTERVENTIONAL STUDY – randomised controlled trial of long term Azithromycin
Demographic features in children with bronchiectasis vs. local and national population: YK/Australia

Ros’ talk
Airway damage + obs causing increasing b’iectasis

Endo-bron infection +/- injury

Hyper-secretion +/- AHR

Impaired muco-ciliary app

Muco-active Rx

Nutrition, Toxicant avoidance

Host factors
• Innate imm
• Adap imm
• Prematurity
• Env effects
• Early RTIs
• Prev injury

Pathogen factors
• Viral + bacteria infections
• Co-infections
• Other infections
• Non-culturable org

Anti-microbials

Anti-inflammatory, -oxidants

Muco-active, AW clearance, BD, ICS

Vaccines

Host factors and Pathogen factors are interconnected with arrows indicating causality. The diagram shows the progression from airway damage and obstruction to increased b’iectasis, followed by infection and further complications. The lower part of the diagram outlines potential therapeutic strategies, including anti-inflammatory, anti-oxidant, anti-microbial, and muco-active treatments. The top part of the diagram lists various host and pathogen factors that contribute to these processes, such as innate and adaptive immunity, prematurity, environmental effects, early respiratory tract infections, and previous injuries. The bottom part highlights interventions like nutrition, toxicant avoidance, and vaccination. The central node represents the core process of airway damage and obstruction leading to increasing b’iectasis, which is influenced by both host and pathogen factors.
Treatment principles

- Diagnose early and look for treatable etiologies
- Reduce infection-inflammation
  - Treat early and exacerbations ‘aggressively’
  - Airway hygiene clearance
  - Vaccinations
- Improve other factors contributing
  - Attention to nutrition
  - Detect complications, pollutants
- Systematic care
  - Regular review, multi-disciplinary care
  - Education, enhance self care and management
Clinical: early recognition

- Productive/ moist cough - predominant symptom
- Worse in mornings
- +/- Effort limitation
- +/- Wheeze, haemoptysis, chest pain
- +/- Chest wall hyperinflation
- +/- Digital Clubbing
- +/- Nutrition
- +/- Crepitations
TABLE 3—Investigation Results

<table>
<thead>
<tr>
<th>Investigation</th>
<th>No. preformed (%)</th>
<th>Number abnormal (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mantoux</td>
<td>58 (89.2%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>pH, esophagoscopy or barium meal</td>
<td>31 (47.7%)</td>
<td>6 (19.4%)</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>33 (50.7)</td>
<td>13 (39.7%)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>40 (61.5%)</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>IgG, A, M (total)</td>
<td>62 (95%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>IgG subclass</td>
<td>62 (95%)</td>
<td>5 (8.1%)</td>
</tr>
<tr>
<td>Ig to diphtheria</td>
<td>40 (61.5%)</td>
<td>13 (23.5%)</td>
</tr>
<tr>
<td>Ig to CH50 or CH100</td>
<td>27 (49%)</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Lymphocyte function</td>
<td>27</td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td>Neutrophil function</td>
<td>27</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Routine Ix should be undertaken in all
Treatment principles

- Diagnose early and look for treatable etiologies
- Reduce infection-inflammation
  - Treat early and exacerbations ‘aggressively’
  - Airway hygiene clearance
  - Vaccinations
- Improve other factors contributing
  - Attention to nutrition
  - Detect complications, pollutants
- Systematic care
  - Regular review, multi-disciplinary care
  - Education, enhance self care and management

Ottawa 2015
Reduce infection-inflammation

The principles

- Infection leads to increased inflammation

Clinically:

- Most kids look well
- Generally only wet (productive) cough
- In exacerbations: fever very rare
- When first Dx, possible to get kids cough free
Antibiotics

- Antibiotics breaks infection/inflammation cycle
- Need prolonged courses; likely biofilm related
- Oral followed by IV if insufficient
- When first diagnosed
  - Aim for cough free as baseline
- Post Dx
  - Intermittent
  - Maintenance
  - Types?

Marsh et al, 2014
Evidence that reducing bacteria load reduces inflammation

- Cohort studies – all adult
- Older and more data- consistent message

(White et al. Thorax 2003;58:680)
(Stockley et al, Thorax 1984;39:414)
(Chalmers et al. AJRCCM 2012,186:657)
(Angrill et al. AJRCCM 2001;164:1828)
Chronic bronchitis

**p<0.001

†p<0.05

Day 1

Day 10

Day 1

Day 10

Bacteria eradicated by day 10

Bacteria persisting at day 10

White et al

Thorax 2003
Adult data

- Recent study in 385 patients (Chalmers 2012)
- Median age 67 years
- 81.6% idiopathic/post-infective bronchiectasis
Adult data

- Higher bacterial loads were associated
  - more severe respiratory symptoms (SGRQ)
  - more severe cough (LCQ)

- Over 1 year, high bacterial loads had
  - a higher frequency of exacerbations
  - more likely to require hospitalization with severe exacerbations

- Relationship independent of severity of bronchiectasis (CT or spirometry)

Ottawa 2015
(Chalmers et al. AJRCCM 2012,186:657)
Sig improvement in inflammation markers (airway MPO, NE, IL8, TNFa, IL-1B)(blood ICAM-1)
## Systemic inflammation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Start of exacerbation (Rx IV Abs)</th>
<th>End of exacerbation (Rx IV Abs)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-h sputum volume mL</td>
<td>30.4 ± 21.9</td>
<td>8.5 ± 8.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FEV1 L</td>
<td>1.45 ± 0.57</td>
<td>1.52 ± 0.58</td>
<td>0.07</td>
</tr>
<tr>
<td>FVC L</td>
<td>2.35 ± 0.78</td>
<td>2.5 ± 0.86</td>
<td>0.01</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>61.4 ± 12.3</td>
<td>60.4 ± 11.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Exercise capacity m</td>
<td>217.0 ± 168.0</td>
<td>271 ± 184.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>WCC # x10^9.L^-1</td>
<td>10.8 ± 7.1</td>
<td>7.2 ± 2.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESR mm.h^-1</td>
<td>40.1 ± 27.4</td>
<td>22.3 ± 14.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRP mg.L^-1</td>
<td>66.9 ± 70.7</td>
<td>7.4 ± 11.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Malaysia 2012, Ottawa 2015*
Maintenance Antibiotics

- Double blind RCT
- Azithro $n=45$ vs. placebo $n=44$
- Weekly doses for 24 mo
- Indigenous (Aus) and Maori (NZ)
- Primary outcome: exacerbations

Lancet Resp Med 2013;1:610
<table>
<thead>
<tr>
<th>Medical chart review items§</th>
<th>Azithromycin</th>
<th>Placebo</th>
<th>OR* or IRR† or MD‡ (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pulmonary exacerbations (median [range])</td>
<td>104 (2 [0-9])</td>
<td>195 (4 [0-14])</td>
<td>IRR 0.50 (0.35 to 0.71)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of hospital-managed pulmonary exacerbations (median [range])</td>
<td>8 (0 [0-5])</td>
<td>14 (0 [0-3])</td>
<td>IRR 1.08 (0.19 to 6.26)</td>
<td>0.93</td>
</tr>
<tr>
<td>Children exacerbation-free at 24-months</td>
<td>9 (20%)</td>
<td>4 (9%)</td>
<td>OR 0.39 (0.11 to 1.41)</td>
<td>0.15</td>
</tr>
<tr>
<td>Children exacerbation-free (hospital-managed) at end of intervention period</td>
<td>42 (93%)</td>
<td>35 (80%)</td>
<td>OR 0.25 (0.06 to 1.07)</td>
<td>0.06</td>
</tr>
<tr>
<td>Last study clinic visit items¶</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) weight-for-age Z score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current cough in the past 3 months</td>
<td>13 (30%)</td>
<td>17 (41%)</td>
<td>OR 0.56 (0.22 to 1.39)</td>
<td>0.21</td>
</tr>
<tr>
<td>Normal respiratory examination</td>
<td>24 (55%)</td>
<td>19 (46%)</td>
<td>OR 1.32 (0.51 to 3.47)</td>
<td>0.56</td>
</tr>
<tr>
<td>Wheeze on auscultation</td>
<td>1 (2%)</td>
<td>2 (5%)</td>
<td>OR 0.50 (0.04 to 5.97)</td>
<td>0.58</td>
</tr>
<tr>
<td>Respiratory crackles on auscultation</td>
<td>3 (7%)</td>
<td>8 (20%)</td>
<td>OR 0.31 (0.08 to 1.29)</td>
<td>0.11</td>
</tr>
<tr>
<td>Mean (SD) predicted FEV₁, % **</td>
<td>84.7 (12.9)</td>
<td>81.0 (18.3)</td>
<td>MD 4.08 (-5.23 to 13.40)</td>
<td>0.38</td>
</tr>
<tr>
<td>Sputum present ††</td>
<td>6 (14%)</td>
<td>11 (27%)</td>
<td>OR 0.44 (0.14 to 1.39)</td>
<td>0.16</td>
</tr>
</tbody>
</table>
**Treatment principles**

- Diagnose early and look for treatable etiologies
- Reduce infection-inflammation
  - Treat early and exacerbations ‘aggressively’
  - Airway hygiene clearance
  - Vaccinations
- Improve other factors contributing
  - Attention to nutrition
  - Detect complications
- Systematic care
  - Regular review, multi-disciplinary care
  - Enhance self care and management (?)

Not all things that work in CF is applicable
Multi centre RCT, 24 weeks

In pulmozyme grp:
- Risk of exacerbation RR 1.35
- FEV1 decline significantly higher
Treatment principles

- Diagnose early and look for treatable etiologies
- Reduce infection-inflammation
  - Treat early and exacerbations ‘aggressively’
  - Airway hygiene clearance
  - Vaccinations
- Improve other factors contributing
  - Attention to nutrition
  - Detect complications, pollutants
- Systematic care
  - Regular review, multi-disciplinary care
  - Education, enhance self care and management
Treatment principles

- Diagnose early and look for treatable etiologies
- Reduce infection-inflammation
  - Treat early and exacerbations ‘aggressively’
  - Airway hygiene clearance
  - Vaccinations
- Improve other factors contributing
  - Attention to nutrition
  - Detect complications, pollutants
- Systematic care
  - Regular review, multi-disciplinary care
  - Education, enhance self care and management
Recommendation-31: Providing healthcare for Indigenous people in rural-remote regions requires flexible and adaptive arrangements. However, it should not alter the objective of delivering best practice treatment to this population.

*GRADE-Strong; Evidence-Low*

Recommendation-32: Given the high prevalence of CSLD/bronchiectasis in Indigenous Australians, Māori and Pacific Island children and adults, a high index of suspicion with early diagnostic investigation and institution of best practice treatment should be established. Interpreters and local health-workers should be available for education regarding disease and management.

*GRADE-Strong; Evidence-Moderate*
What are we doing?

ALRIs

Recurrent +/- persistent infection & inflammation

CSLD COPD

B’iectasis COPD (severe)

Predisposing factors
- Low birth weight
- In-utero ETS
- Genetics

Modifiable factors*
- Hygiene practices
- Health education
- Socio-economic
- ETS/pollutants
- Vaccinations
- Nutrition
- Housing

Factors affecting clinical outcomes or consequences
- Quality care, access, service and family factors
- Microbial factors
- Modifiable factors*
  - Host factors

Prim and sec prevention, Rx and Basic science
Translational Research

Improved lung health in children and adults

Research

Clinical service

Education
(health professionals & patients)

Capacity building
(future researchers)
DO YOU COUGH?

Your lungs could be sick. See your health worker.

www.lunginfo.net.org.au

Chronic Suppurative Lung Disease/Bronchiectasis (Chronic Lung Sickness)
Summary

- Importance of bronchiectasis
- Diagnosis of BE by radiologists has limitations – CSLD concept
- Epidemiology and risk factors
- Prognosis dependent on early diagnosis and appropriate Rx
- Principles of Mx and evidence based
- Together, we can make a difference