Chronic Protracted Bronchitis

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Conflict of Interest

• AB has no financial or other COI

• There will be discussion of off-label and unlicensed use of medications
Aims of the Presentation

• Define PBB and how it presents

• Discuss the clinical approach to a child with suspected PBB, including the differential diagnosis

• Suggest criteria for determining which children need detailed further investigation, including bronchoscopy

• Review the literature on pathophysiology
Chronic Protracted Bronchitis

• What is it and how does it present?
BTS Cough Guidelines

• Acute cough (< 3 weeks duration)
  – ‘Prolonged acute’ (3-8 weeks)
  – Recurrent acute
  – (all definitions of time periods arbitrary)

• Chronic cough (> 8 weeks duration)

• Definition limitations
  – MUST assess overall health of the child!

• PBB: Chronic WET cough in an otherwise WELL child
  – Wet cough correlates with secretions seen at FOB
Patients and Methods

- 108 children, median age 2.6 years with >3 weeks history of cough

- Protocol driven investigations, including bronchoscopy (n=102)
  - CXR +/- spirometry
  - Blood tests
  - FOB + BAL or induced sputum
  - Either or both HRCT, pH study
  - Treatment trial
Half were initially give a diagnosis of asthma
What did we learn?

- C. 25% got better spontaneously, so 3 weeks in a WELL child is probably too short a time
- Asthma is ludicrously over-diagnosed and over-treated in the coughing child
- PBB accounts for 40% cases
- Other specific causes are very rare
Multicentre study: Cough >4 weeks

Chest 2012; 142: 943-50
Persistent Bacterial Bronchitis

- Chronic wet or productive cough > 4 weeks
- Resolution with antibiotics
- No features of any other underlying condition

*Pediatr Pulmonol 2008; 43: 519-21*

**ALSO**
- Neutrophilic bronchoalveolar lavage
- Infection with *Haemophilus influenza*, *Moraxella catarrhalis*, *Staphylococcus aureus*
PBB

- Sheffield experience

- A problem of young children (uncommon after age 2 years)

- Prolonged symptoms common

- (Wrong asthma diagnosis common)

*Thorax 2007; 62: 80-4*
Relationship between PBB, & pre-bronchiectasis not yet clear

Thorax 2004; 59: 324-7
Chronic Protracted Bronchitis

• What is it and how does it present?

• What is the differential diagnosis?
PBB: Diagnosis of EXCLUSION!

- **Specific causes of chronic bronchial sepsis**
  - CF, PCD, Immunodeficiency

- **Anatomical defects**
  - Endobronchial mass/foreign body
  - Intramural – complete cartilage rings, malacia
  - Compression – vascular ring/sling. LN, CTM

- **Aspiration syndromes**
  - GERD
  - Inco-ordinate swallow
  - H-type fistula
Could it be CF?

• **General**: Clubbing, weight loss, failure to thrive

• **Respiratory**: Unusually severe chest deformity, unusual organisms (*Ps aer*), nasal polyps

• **Extra-pulmonary**: Hepatosplenomegaly, rectal prolapse, diarrhoea

• *Consider even if you have NBS!*
When to Consider PCD

• Neonatal onset of respiratory distress, rhinorrhea
• Chronic, persistent rhinitis with wet cough
• Bronchiectasis
• Severe CSOM, prolonged otorrhea after tympanostomy tube insertion
• Mirror image arrangement
• Associated ciliopathy spectrum disorders in patient or family
Systemic immunodeficiency (1)

- **Respiratory infections PLUS**
  - Significant extra-pulmonary infections
  - Physical signs outside the chest
  - The chronically ill child
  - Autoimmune disease
  - Malignancy

- **SPUR**
  - Severe
  - Persistent
  - Unusual organisms
  - Recurrent Infection
Systemic immunodeficiency

1. Eight or more new ear infections within 1 year.
2. Two or more serious sinus infections within 1 year.
3. Two or more months on antibiotics with little effect.
4. Two or more pneumonias within 1 year.
5. Failure of an infant to gain weight or grow normally.
6. Recurrent, deep skin or organ abscesses.
7. Persistent thrush in mouth or elsewhere on skin, after age 1.
8. Need for intravenous antibiotics to clear infections.
9. Two or more deep-seated infections.
10. A family history of Primary Immunodeficiency.
Is there a systemic immunodeficiency?

• Rare - true incidences not known

• >100 single gene defects defined

• Estimates:
  – Primary antibody deficiency 1:25000
  – SCID: 1:50000

• Diagnostic delay – average 4y for CVID

• Complications present at diagnosis – esp bronchiectasis
Is there a cause of aspiration?

From above

- Consider neurological causes
  - Peripheral neuromuscular
  - Central

- Local anatomical causes
  - Laryngeal cleft
Aspiration from above
Is there a cause of aspiration?

From the side

- May present even in adult life
- Early onset of symptoms, usually when feeding
- May be missed by a tube oesophagram, mostly missed by barium swallow
Is there a cause of aspiration?

From below

- GERD: complex relationship with respiratory disease
  - Causal of recurrent infections
  - Caused by respiratory disease
  - Fellow traveller of no significance
Think anatomy also!

Post-TOF repair

Achalasia
Airway Disease
Chronic Protracted Bronchitis

- What is it and how does it present?
- What is the differential diagnosis?
- How to manage the condition
Management

• Detailed history and physical examination – any concerning features?
  – Refer if suspicion of another diagnosis

• A SINGLE empirical course of oral antibiotics
  – If resolves and child remains well, no further action; but follow up unless confident Mum will bring child back

• No response to 2 weeks co-amoxyclyclav, or rapid relapse after treatment, REFER: is there bronchiectasis?

• NOT bronchoscopy for all
Antibiotics in PBB

- 50 PBB children, median 1.9 yr, IQR 0-9-5.1, >3 weeks wet cough
- Randomised to 2 weeks co-amoxycilav or placebo
- End-point: ‘cough resolution’ = 75% reduction in cough score
- Antibiotics (48%) vs. placebo (16%), p=0.016; proportion 0.32 (0.08-0.56)

Thorax 2012; 67: 689-93
Chronic Protracted Bronchitis

• What is it and how does it present?

• What is the differential diagnosis?

• How to manage the condition

• What is the pathophysiology?
Role of Viruses?

- N=104 PBB patients (72 male; age 19/12, 12-30), N=49 controls, FOB (PBB BAL neutrophilia)
- ‘parent reported wheeze’ and TBM common
- PBB: more likely in child care, more AV (OR 6.69, 1.59-29.8)
- NK cells increased in PBB (Igs, subclasses & subsets normal)
- **Viruses implicated in PBB?**

*Controls: indication for FOB*

<table>
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<tr>
<th>Condition</th>
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<tr>
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<tr>
<td>cough</td>
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<td>apnoea</td>
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More on Viruses

- FOB evaluation 232 children with all cause cough

- Wet cough (n=143) more likely than dry cough to have bacterial (OR2.6, p<0.001) viral (2.04, p=0.0045) and both (2.65, p=0.0042)

- Co-infection – more BAL neutrophils, p<0.0001 (33.5%; bacteria 20%, viruses 18%, none 6%)

Pediatr Pulmonol 2014; 49: 561-8
Immuneology: Chicken or Egg?

• More IL-8, MMP-9 protein, and TLR-2 & -4 mRNA

• Increased MBL and hβD2 protein; hβD2 higher with airway infection
  – *J Peds* 2012; 161: 621-5

• Increased IL-1β pathway, hαD1-3 protein, lower in resolved PBB
  – *Chest* 2014; 146: 1013-20

• Physiological response to chronic infection, or a pathological cause?
  – Most likely a response to infection
Pathophysiology: Conclusions

- Clearly a transient local immune deficiency of some sort
- Maturational?
- Related to respiratory viral infection?
- Related to the microbiome?
- Related to environmental pollution/tobacco?
- TBM – cause or effect?
- Did God do it or did the Doctor do it: ICS over-use??
Chronic Protracted Bronchitis

- What is it and how does it present?
- What is the differential diagnosis?
- How to manage the condition
- What is the pathophysiology?
- Summary and conclusions
Take-home messages

• Chronic wet cough should be taken seriously, and not treated with escalating doses of ICS for ‘asthma’

• PBB is a diagnosis of exclusion, and serious conditions need to be considered

• A single course of oral antibiotics as a therapeutic trial is legitimate

• If no response, or rapid relapse, then detailed investigation mandated
Thank you for Listening!