Bronchiectasis

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Disclosures

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• Advisory Boards for Glaxo Smith Kline and AstraZeneca
Outline

– Basic Anatomy and Physiology
– What is bronchiectasis
– Aetiology
– Assessment
– Treatment
Outline

– Basic Anatomy and Physiology
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The Respiratory Tract

Upper

Lower

Anatomy of the Lower Respiratory Tract
Host defenses along the airways

- Ambient air
- Dust
- Noxious gases
- Microorganisms

**Particle size (diameter):**

- > 10 μm
  - Anatomic barriers
  - Angulation of airways
  - Mucociliary clearance
  - Cough
  - Secretory IgA

- 3–10 μm

- Air-exchange surface
  - 0.5–3 μm
    - Surfactant
    - Opsonins — IgG, fibronectin
    - Complement
      - (alternate pathway)
  - < 0.5 μm
  - (stays in gaseous phase)
    - Alveolar macrophages
    - PMNs
    - Plasma components
    - Vasoactive mediators

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Interactions of respiratory epithelium and microbes

- **Viruses** (cytotoxic)
- **Mycoplasma** (shear off cilia)
- **Bordetella pertussis** (proximal part of cillum)
- **Streptococcus pneumoniae** (do not attach to cilia; produce IgA protease and substances that slow or paralyze cilia)
- **Pseudomonas aeruginosa**
- **Neisseria meningitidis** (attach to microvilli, then phagocytized by cell; also have pili and IgA protease)
Mechanisms of microbial attachment and host resistance
Immunoglobulins; targeting proteins, critical for immune function

- **Monomer**
  - IgD, IgE, IgG

- **Dimer**
  - IgA

- **Pentamer**
  - IgM
Outline

– Basic Anatomy and Physiology
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Definition of Bronchiectasis

- “bronckos” (airway) and “ektasis” (widening)

- Bronchiectasis is characterised by abnormal, irreversible bronchial dilatation or a fixed increase in airway diameter

- Bronchiectasis is a common lung disease characterised by chronic infection in small airways

- Results in some parts of the lung becoming damaged, scarred and dilated, allowing infected mucus to build up in pockets

ALF Fact Sheet, Sept 2014
CT Scan of Chest

Direction of patient transport

Path of continuously rotating X-ray tube and detector

Start of spiral scan

\[ z, \text{ mm} \]

\[ t, \text{ s} \]
Bronchiectasis

- The diagnosis of bronchiectasis requires a CT scan of the lungs which demonstrates abnormal widening of the airways or bronchi.

- Despite its low profile, bronchiectasis is a common condition and patients will often have symptoms for many years before a diagnosis is made.
Other Respiratory Infections

• Pneumonia
  – Infection of the lung parenchyma, (alveoli)

• Acute Bronchitis
  – Inflammatory Change in large airways and bronchi, may be bacterial or viral

• Bronchiolitis
  – Inflammatory change in peripheral bronchioles, usually viral

• Lower Respiratory Tract Infection
  – Any of the above, or combination thereof
Other Chronic Respiratory Conditions

• Chronic Obstructive Pulmonary Disease
  – Chronic lung injury, usually due to smoking, with narrowing of the airways due to chronic bronchitis or emphysema, or a combination thereof

• Chronic Bronchitis
  – Chronic cough and sputum production due to chronic inflammation of the airways

• Emphysema
  – Destruction of the airspaces within the lung, with loss of radial traction on the airways
Outline

– Basic Anatomy and Physiology
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### Aetiologies and factors associated with bronchiectasis

- **Cystic fibrosis**
- **Post-infection** (e.g. tuberculosis, adenovirus, recurrent pneumonia)
- **Primary or secondary immune deficiency** (e.g. hypogammaglobulinaemia, lung and bone marrow transplantation, malignancy, HIV/AIDS, HTLV1)
- **Mucociliary dysfunction** (e.g. primary ciliary dyskinesia)
- **Chronic obstructive pulmonary disease and smoking**
- **Congenital causes** (e.g. Mounier-Kuhn syndrome, Young syndrome)
- **Postobstruction** (e.g. with a foreign body)
- **Pulmonary fibrosis and pneumoconiosis** (e.g. silicosis)
- **Recurrent small volume aspiration** (e.g. from upper airway secretions or gastric contents)
- **Allergic bronchopulmonary aspergillosis**
- **Systemic inflammatory diseases** (e.g. rheumatoid arthritis, sarcoidosis)

## Aetiology of bronchiectasis

<table>
<thead>
<tr>
<th>Cause</th>
<th>n (% of study)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post infection</td>
<td>51 (32)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>42 (26)</td>
</tr>
<tr>
<td>PCD</td>
<td>17 (11)</td>
</tr>
<tr>
<td>ABPA</td>
<td>13 (8)</td>
</tr>
<tr>
<td>Immune deficiency</td>
<td>9 (6)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Young’s syndrome</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Pan bronchiolitis</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Yellow nail syndrome</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Mycobacterium infection</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>2 (1)</td>
</tr>
<tr>
<td>CF variant</td>
<td>2 (1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>161</strong></td>
</tr>
</tbody>
</table>

ABPA = Allergic bronchopulmonary aspergillosis, PCD = Primary ciliary dyskinesia, CF = Cystic fibrosis
A VICIOUS CYCLE OF INFECTION AND INFLAMMATION

- Inflammation
- Microbial Infection
- Tissue Damage
- Impaired Lung Defences
- Inflammation
Foreign Body

Peanut in Left main stem bronchus which had increased in size as it absorbs the secretions within the bronchus. Courtesy Dr Trent Quinlan, ENT surgeon, Omaha Childrens Hospital (CHS).
https://www.mypacs.net/cases/FOREIGN-BODY-ASPIRATION-AT-LEAST-TWO-PEANUTS-5220614.html
Sputum retention

Sputum retention and occlusion of right lower lobe bronchi in an elderly women with depressed cough.
Cystic Fibrosis

• Autosomal recessive condition
• 1 in 2000 to 1 in **2500**
• 1 in 25 people carry a mutation of the cystic fibrosis gene
• ethnic variation
  – African American 1 in 15,300
  – Hispanics 1 in 8000
  – occurs in Asian populations
# CFTR Mutation Frequency

<table>
<thead>
<tr>
<th>Mutation</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ F508</td>
<td>66</td>
</tr>
<tr>
<td>G542X</td>
<td>2.4</td>
</tr>
<tr>
<td>G551D</td>
<td>1.8</td>
</tr>
<tr>
<td>W1282X</td>
<td>1.5</td>
</tr>
<tr>
<td>N1303K</td>
<td>1.2</td>
</tr>
<tr>
<td>R553X</td>
<td>0.9</td>
</tr>
</tbody>
</table>
Cystic Fibrosis Transmembrane Conductance Receptor (CFTR)

Calculated net charge on the CFTR is indicated by color intensity. The darkest red is +12 and the darkest blue is -6.

Copyright 2005 by Elsevier Science
Normal Airways
Cystic Fibrosis Airways

NaCl + water hyperabsorption

Cystic fibrosis

Copyright 2005 by Elsevier Science
<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No synthesis</td>
<td>Block in processing</td>
<td>Block in regulation</td>
<td>Altered conductance</td>
<td>Reduced synthesis</td>
<td></td>
</tr>
<tr>
<td>Nonsense</td>
<td>G542X</td>
<td>Missense</td>
<td>Missense G551D</td>
<td>Missense R117H</td>
<td>Missense A455E</td>
<td></td>
</tr>
<tr>
<td>Frameshift</td>
<td>394delITT</td>
<td>AA deletion</td>
<td>ΔF508</td>
<td></td>
<td>Alternative Splicing</td>
<td></td>
</tr>
<tr>
<td>Splice junction</td>
<td>1717-1G→A</td>
<td></td>
<td></td>
<td></td>
<td>3849+10kbC→T</td>
<td></td>
</tr>
</tbody>
</table>
CFTR Mutation and Clinical Consequence

Normal

CBAVD, COPD, pancreatitis, etc.

PS  CF  PI

Severity scale

Typical mutations

Atypical mutations
Organs Affected by Cystic Fibrosis

The genetic defect underlying cystic fibrosis disrupts the functioning of several organs by causing ducts or other tubes to become clogged, usually by thick, sticky mucus or other secretions.

AIRWAYS
Clogging and infection of bronchial passages impede breathing. The infections progressively destroy the lungs. Lung disease accounts for most deaths from cystic fibrosis.

LIVER
Plugging of small bile ducts impedes digestion and disrupts liver function in perhaps 5% of patients.

PANCREAS
Occlusion of ducts prevents the pancreas from delivering critical digestive enzymes to the bowel in 65% of patients. Diabetes can result as well.

SMALL INTESTINE
Obstruction of the gut by thick stool necessitates surgery in about 10% of newborns.

REPRODUCTIVE TRACT
Absence of fine ducts, such as the vas deferens, renders 95% of males infertile. Occasionally, women are made infertile by a dense plug of mucus that blocks sperm from entering the uterus.

SKIN
Malfunctioning of sweat glands causes perspiration to contain excessive salt (NaCl). Measurement of chloride in sweat is a mainstay of diagnosis.
Outline

– Basic Anatomy and Physiology
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### Features that may suggest bronchiectasis in a patient presenting with chronic respiratory symptoms

<table>
<thead>
<tr>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chronic cough and sputum production</td>
</tr>
<tr>
<td>• Digital clubbing (this is rare in COPD and asthma)</td>
</tr>
<tr>
<td>• Lack of a significant smoking history (less than an average of 20 cigarettes per day for 10 years) in a person with suspected COPD</td>
</tr>
<tr>
<td>• History of recurrent and/or severe pneumonia including tuberculosis</td>
</tr>
<tr>
<td>• Presence of 'unusual organisms' in sputum (eg. Aspergillus, atypical/nontuberculous mycobacteria, <em>Pseudomonas aeruginosa</em>, <em>Escherichia coli</em>, <em>Klebsiella pneumoniae</em>)</td>
</tr>
<tr>
<td>• Childhood associated with significant environmental and social disadvantage*</td>
</tr>
</tbody>
</table>

* This includes Aboriginal and Torres Strait Islander people, as well as people who have immigrated from low income countries. In this group of people, tuberculosis as the cause of chronic respiratory symptoms should also be considered.

Maguire, C. Bronchiectasis A guide for primary care Australian Family Physician Volume 41, No.11, November 2012 Pages 842-85
### Recommended investigations for secondary causes of bronchiectasis

<table>
<thead>
<tr>
<th>Investigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Full blood count</td>
</tr>
<tr>
<td>• Immunoglobulin classes IgG, IgA, IgM, and IgG subclasses</td>
</tr>
<tr>
<td>• Sputum culture including mycobacterial culture</td>
</tr>
<tr>
<td>• Serological tests for Aspergillus and total IgE level in adults, especially if there is a history of wheeze/asthma</td>
</tr>
<tr>
<td>• Test for primary ciliary dyskinesia in children</td>
</tr>
<tr>
<td>In addition, consider the following:</td>
</tr>
<tr>
<td>• A sweat test</td>
</tr>
<tr>
<td>• Test for cystic fibrosis transmembrane conductance regulator gene mutations</td>
</tr>
<tr>
<td>• Bronchoscopy for foreign body or airway abnormality and to obtain specimens for culture of respiratory pathogens, including mycobacteria</td>
</tr>
<tr>
<td>• Barium swallow</td>
</tr>
<tr>
<td>• Additional immunological tests – total IgE level in children, neutrophil function tests and lymphocyte subsets, and antibody responses to protein and polysaccharide antigens</td>
</tr>
<tr>
<td>• Test for primary ciliary dyskinesia in adults</td>
</tr>
<tr>
<td>• HIV and HTLV153 serology</td>
</tr>
</tbody>
</table>

Note: suggested investigations before specialist referral are highlighted in bold

Maguire, AFP 2012
Investigations of New Patient

- Aetiology – blood work up
- CT extent/pattern of bronchiectasis
- Lung function/exercise capacity
- Bacteriology: routine, fungus, AFB
- Selected cases: cilia, sweat test, nasal potentials, genotyping
What routine investigations to do at follow up appointment

- Sputum: routine culture every visit, AFB annual
- Spirometry every visit
- Oxygen saturations + exercise every visit
- CXR, if any new development or 3 years
- Lung function, perform when stable 3-5 years
- CT?
- Bloods usually monitoring only eg ABPA, CVID, safety azithromycin
Host Defence Workups  
March 2001 - March 2006  
165 patients with confirmed bronchiectasis

<table>
<thead>
<tr>
<th>Bacteriology result</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not productive at the time of assessment</td>
<td>16</td>
<td>10%</td>
</tr>
<tr>
<td>No bacterial growth</td>
<td>53</td>
<td>32%</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>42</td>
<td>25%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>37</td>
<td>22%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>12</td>
<td>21%</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>11</td>
<td>7%</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>7</td>
<td>4%</td>
</tr>
<tr>
<td>Coliform sp</td>
<td>1</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Pasturella sp</td>
<td>1</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Proteus sp</td>
<td>1</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Betahaemolytic streptococcus</td>
<td>1</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

17 patients cultured more than one species
Effect of Bacteriology on Quality of Life

SGRQ Activity score

Mean scores

Pa  Hi  O  NG  Non-Pa

*P<0.01 of Hi, NG & Non-Pa
Post-infectious bronchiectasis
Panbronchiolitis
Allergic Bronchopulmonary Aspergillosis (ABPA)
ABPA

Before bronchoscopy

After bronchoscopy
Mucus plugging with ABPA

Bronchoscopy of left upper lobe

Macroscopic view of sliced left upper lobe of lung showing obstruction of lower segmental bronchi
### Predisposing conditions (one must be present):
- Asthma
- Cystic fibrosis

### Obligatory criteria (both must be present):
- *Aspergillus* skin test positivity or elevated IgE levels against *Aspergillus fumigatus*
- Elevated total IgE concentration (typically >1000 IU/mL, but if the patient meets all other criteria, an IgE value <1000 IU/mL may be acceptable)

### Other criteria (at least two must be present):
- Precipitating serum antibodies to *A. fumigatus* or elevated serum *Aspergillus* IgG by immunoassay
- Radiographic pulmonary opacities consistent with ABPA
- Total eosinophil count >500 cells/μL in glucocorticoid-naïve patients (may be historical)

---

IgE: immunoglobulin E; ABPA: Allergic bronchopulmonary aspergillosis.

Reference:
CF-Bronchiectasis
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Outline

– Basic Anatomy and Physiology
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– Treatment
  • Specific Treatment
  • General measures
  • CF Therapy
# Specific Treatment of bronchiectasis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune Deficiency</td>
<td>Immunoglobulin infusions</td>
</tr>
<tr>
<td>Allergic Broncho-Pulmonary Aspergillosis</td>
<td>Antifungal Therapy</td>
</tr>
<tr>
<td>Mycobacterial Infection</td>
<td>Anti-mycobacterial therapy</td>
</tr>
<tr>
<td>Airway Obstruction</td>
<td>Removal of foreign body</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>Immuno-suppressive therapy</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Anti-inflammatory</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Anti-reflux measures</td>
</tr>
</tbody>
</table>
Outline

– Basic Anatomy and Physiology
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  • General measures
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Rationale for Treatment of Bronchiectasis
A VICIOUS CYCLE OF INFECTION AND INFLAMMATION

- Inflammation
- Microbial Infection
- Impaired Lung Defences
- Tissue Damage
Physiotherapy and Bronchiectasis

- Cochrane review 2000: not enough evidence to support practice
- Mutalithas 2008: n=53 open study, 4 weeks physio; improved cough and QoL
- Murray 2009: n=20 randomised crossover trial, 3 months plus one month washout; improved cough (Leicester Cough Questionnaire) and QoL (SGRQ), increased sputum volume
Physiotherapy Options

- Postural drainage
- Huffing Techniques
- Flutter valve devices
  - Flutter
  - Acapella
  - Aerobika

https://youtu.be/n7X3QP8HJKA
Thorax 2002;57:446–448
Antibiotics (consider dosage and length of course)

- Non pseudomonas: first line co-amoxiclav; second line doxycycline, ciprofloxacin; azithromycin
- Pseudomonas: first line ciprofloxacin; second line azithromycin (co-amoxiclav)
- Stenotrophomonas: co-trimoxazole, minocycline.
- Inhaled: colomycin, gentamicin, tobramycin, amikacin
Antibiotic prophylaxis in bronchiectasis

Key messages
- Reduce exacerbation days
- Reduce sputum volume/purulence
- May ↑ lung function
- Side effects
- Emergence of resistance (oral)
Antibiotic Prophylaxis

Options

- Oral antibiotic eg doxycycline
- Inhaled antibiotic eg colomycin
- Macrolide eg azithromycin
- Summer break
Risks of Antibiotic Resistance

Analysis: Antibiotic apocalypse

By James Gallagher
Health and science reporter, BBC News

Some bacteria are becoming resistant to our best drugs

A terrible future could be on the horizon, a future which rips one of the greatest tools of medicine out of the hands of doctors.

A simple cut to your finger could leave you fighting for your life. Luck will play a bigger role in your future than any doctor could.

The most basic operations - getting an appendix removed or a hip replacement - could become deadly.

Cancer treatments and organ transplants could kill you. Childbirth could once again become a deadly moment in a woman's life.

It's a future without antibiotics.

This might read like the plot of a science fiction novel, but there is genuine fear that the world is heading into a post-antibiotic era.

The World Health Organisation has warned that "many common infections will no longer have a cure and, once again, could kill unilaterally."

The US Centers of Disease Control has pointed to the emergence of "nightmare bacteria."

And the chief medical officer for England Prof Dame Sally Davies has echoed parallels with the "apocalypse."

Antibiotics kill bacteria, but the bugs are incredibly wily foes. Once you start treating them with a new drug, they find ways of surviving. New drugs are needed, which they then find hard to survive.

Deadly
Inhaled Antibiotics

- Reduce sputum bacterial load
- Increase likelihood of eradication of pseudomonas
- Reduce the risk of acute exacerbations,
- Do not reduce risk of hospitalisation
- Do not improve lung function
- Do not improve quality of life
Evidence for Antibiotics; reduced bacterial load

<table>
<thead>
<tr>
<th>Study</th>
<th>Antibiotics</th>
<th>Duration</th>
<th>Bacteria</th>
<th>WMD (95% CI)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barker [9] and Couch [20]</td>
<td>Tobramycin</td>
<td>4 weeks</td>
<td>PA</td>
<td>-4.56 (-5.44 -- 3.68)</td>
<td>21.05</td>
</tr>
<tr>
<td>Haworth [30]</td>
<td>Colistin</td>
<td>4 weeks</td>
<td>PA</td>
<td>-1.40 (-2.07 -- 0.73)</td>
<td>21.55</td>
</tr>
<tr>
<td>Serisier [33]</td>
<td>Ciprofloxacin</td>
<td>4 weeks</td>
<td>PA</td>
<td>-4.12 (-6.54 -- 1.70)</td>
<td>15.53</td>
</tr>
<tr>
<td>TR02-107 [26, 27]</td>
<td>Amikacin</td>
<td>4 weeks</td>
<td>PA</td>
<td>-0.38 (-0.82 -- 0.06)</td>
<td>21.96</td>
</tr>
</tbody>
</table>

Overall ($I^2=95.2\%, p<0.001$)
Test for overall effect $Z=3.0$ ($p=0.003$)

Note: weights are from random effects analysis
Mucolytic Therapy

• Tablets
  – Bromhexine (also Syrup), Bisolvon
  – N-acetyl cysteine

• Inhaled therapy
  – Hypertonic Saline
  – Mannitol
  – DNAase
Other Supporting Services

Essential
- Immunology (common variable immunodeficiency)
- ENT (most NCFBE have chronic rhinosinusitis)
- Thoracic surgery (isolated disease or “sump”)

Helpful
- Cystic fibrosis (milder genotypes)
- Gastroenterology (reflux, inflammatory bowel disease)
- Rheumatology (rheumatoid arthritis, Sjogren’s)
- Fertility Clinic (PCD, cystic fibrosis, Young’s syndrome)
- Antibiotic allergy service
Eosinophilic fungal rhinosinusitis or allergic fungal sinusitis

Patient with chronic symptoms of nasal obstruction, loss of smell and nasal polyps
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– Treatment
  • Specific Treatment
  • General measures
  • CF Therapy
Cystic Fibrosis: Possible Therapies

• Gene Therapy
• Anti-inflammatory/Anti-infective
• Hypertonic Saline
• Ivacaftor
• Transplantation
Gene Therapy

• Still looking for the right vector
• Most give short term expression
• Use of stem cells?
• Still waiting for breakthrough
Proposed actions of Macrolides

• Modulation of inflammatory pathway
  – reduced neutrophil chemotactic activity
  – reduced cytokines: IL-8, TNF-a, GM-CSF

• Neutrophils
  – chemotaxis, oxidation, apoptosis

• Pseudomonas
  – suppression of quorum sensing factors
  – virulence factors: adherence, alginate, mobility

• Alteration of biofilm properties
Inate lactoferrin

Planktonic growth

Biofilm formation

Antibiotic susceptibility

Pili Flagella

QS (homoserine lactones)

Proteases Hemolysins Exotoxin A Pyocyanin Superoxide dismutase Catalase

LasR RhIR

Antibiotic resistance

Effect of long term treatment with azithromycin on disease parameters in cystic fibrosis: a randomised trial
J Wolter, S Seeney, S Bell, S Bowler, P Masel, J McCormack
Thorax 2002;57:212–216

Table 3  Acute exacerbations of respiratory disease: antibiotics and admissions in placebo and AZM groups

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>AZM</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of courses of IV treatment</td>
<td>1.1 (0.5, 0–7)</td>
<td>0.4 (0, 0–2)</td>
<td>0.016</td>
</tr>
<tr>
<td>Total days IV treatment</td>
<td>7.1 (1, 0–44)</td>
<td>2.0 (0, 0–17)</td>
<td>0.009</td>
</tr>
<tr>
<td>Total days home IV treatment</td>
<td>2.1 (0, 0–14)</td>
<td>0.2 (0, 0–5)</td>
<td>0.037</td>
</tr>
<tr>
<td>Total hospital days</td>
<td>5.2 (0, 0–36)</td>
<td>2.1 (0, 0–15)</td>
<td>0.056</td>
</tr>
</tbody>
</table>

Values are mean (median, range).

Table 4  Mean (SD) QOL scores over time: baseline and final assessment (month 3)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Azithromycin</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>QOL score</td>
<td>n</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(range 5–35)**</td>
<td>28</td>
<td>22.75 (4.86)</td>
<td>28</td>
</tr>
<tr>
<td>(range 5–35)**</td>
<td>19</td>
<td>25.82 (5.27)</td>
<td>22</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
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<tr>
<td>(range 4–28)</td>
<td>30</td>
<td>18.87 (5.37)</td>
<td>30</td>
</tr>
<tr>
<td>(range 4–28)</td>
<td>20</td>
<td>18.85 (4.70)</td>
<td>24</td>
</tr>
<tr>
<td>Emotion</td>
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<tr>
<td>(range 7–49)</td>
<td>30</td>
<td>37.97 (6.84)</td>
<td>30</td>
</tr>
<tr>
<td>(range 7–49)</td>
<td>20</td>
<td>39.70 (5.66)</td>
<td>24</td>
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<td>Master</td>
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<tr>
<td>(range 4–28)</td>
<td>30</td>
<td>24.37 (3.69)</td>
<td>30</td>
</tr>
<tr>
<td>(range 4–28)</td>
<td>20</td>
<td>25.25 (3.64)</td>
<td>24</td>
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<tr>
<td>Total</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(range 20–140)</td>
<td>28</td>
<td>103.14 (14.00)</td>
<td>29</td>
</tr>
<tr>
<td>(range 20–140)</td>
<td>19</td>
<td>109.30 (14.78)</td>
<td>23</td>
</tr>
</tbody>
</table>

*Interaction of treatment effect and time. **Minimum and maximum score possible for each domain.
A Controlled Trial of Long-Term Inhaled Hypertonic Saline in Patients with Cystic Fibrosis

Mark R. Elkins, M.H.Sc., et al for the National Hypertonic Saline in Cystic Fibrosis (NHSCF) Study Group

Volume 354(3):229-240 2006
Ivacaftor

- Selective CFTR potentiator
- Improves function of the CFTR protein
- Only benefits those with G551D mutation
- Improves lung function by 10%
Bilateral Lung Transplant
Aust & NZ 1992 -2005

- Cystic Fibrosis 40%
- Emphysema 19%
- CFA 5%
- Bronchiectasis 11%
- Miscellaneous 9%
- PPH 4%
- Other PH 1%
- AAT 9%
- Eisenmengers 1%

ANZCOTR 2005
ADULT LUNG TRANSPLANTATION

Survival comparisons
COPD vs. IPF: p < 0.0001
Alpha-1 vs. CF: p = 0.0248
Alpha-1 vs. IPF: p < 0.0001
Alpha-1 vs. PPH: p = 0.0021
CF vs. COPD: p = 0.0006
CF vs. IPF: p < 0.0001
CF vs. PPH: p < 0.0001
CF vs. Sarcoidosis: p = 0.0007

HALF-LIFE  
Alpha-1: 5.1 Years; CF: 5.8 Years; COPD: 4.8 Years; IPF: 3.7 Years; PPH: 4.3 Years; Sarcoidosis: 4.0 Years

ISHLT 2005
J Heart Lung Transplant 2005;24: 945-982
Life Expectancy with CF

CF described

Sweat test

Antibiotics anti pseudomonas

Abnormal Nasal PD

CF gene

Inflammation targeted

Tests of basic defect

Centres, Comprehensive care, CF Foundation

rhDNase

Median survival age

Calendar year

Optimal medical therapy?

Summary

- Investigate to exclude treatable causes
- Mucus clearance/exercise
- Effective treatment of exacerbations
- Antibiotic prophylaxis
- Anti-inflammatory/macrolides