NON-CYSTIC FIBROSIS BRONCHIECTASIS - ANTIBIOTIC TREATMENT - CHW

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- These guidelines have been formulated to assist in the management of patients with non-cystic fibrosis bronchiectasis.
- Sputum samples should be obtained from patients with non-CF bronchiectasis to determine the presence of bacterial pathogens and to direct therapy.
- Airway clearance using chest physiotherapy is a standard part of care for children with non-Cystic Fibrosis Bronchiectasis.
- Non-typeable *Haemophilus influenzae* is the most common bacteria isolated, followed by *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Staphylococcus aureus*, in order of decreasing prevalence. In patients with more advanced non-CF bronchiectasis isolation of *Pseudomonas species* may occur.
- During a flare of respiratory disease the use of a broad spectrum antibiotic such as amoxycillin or Augmentin (amoxycillin + clavulanic acid) will provide appropriate cover for the most common bacteria isolated in non-CF bronchiectasis. It is recommended that a minimum of 14 days treatment is given. If there is a slow clinical response physiotherapy should be instituted or increased.
- Options for treatment for *Pseudomonas species* are 4 weeks of nebulised gentamicin plus 2-3 weeks of oral ciprofloxacin or intravenous anti-pseudomonal antibiotics as highlighted in more detail in the guidelines.

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st July 2017	**Review Period**: 3 years
Team Leader:	Head of Department	**Area/Dept**: Respiratory CHW

CHANGE SUMMARY

- Due for mandatory review – no changes made.

READ ACKNOWLEDGEMENT

- Senior and Junior Medical Staff (especially Respiratory & General Medicine) and Pharmacy staff caring for Respiratory patients are to read this document.
- Relevant nursing and Allied Health staff are to be aware of this document.

Note:

*The following comment is listed in the **manufacturer's information regarding ciprofloxacin use in paediatrics**. Parents/carers should be made aware of these issues and informed to seek medical advice if the patient develops pain in muscle, weight-bearing joints, or tendons.*

"Ciprofloxacin is not recommended for use in prepubertal children, except for use in inhalational anthrax (post-exposure). Toxicological studies have shown that ciprofloxacin…, can produce erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species. Long-term safety data, including effects on cartilage, following the administration of ciprofloxacin to paediatric patients are limited."

US FDA Black Box warning for fluoroquinolones:

"Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture. This risk is further increased in… those on concomitant steroid therapy, as well as in kidney, heart, and lung transplant recipients. The fluoroquinolone should be discontinued if the patient experiences pain or inflammation in a tendon (symptoms that may precede rupture of the tendon), or tendon rupture. Advise patients, at the first sign of tendon pain, swelling, or inflammation, to stop taking the fluoroquinolone…"

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

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Preamble

These guidelines have been formulated to assist in the management of patients with non-cystic fibrosis bronchiectasis. They have been adapted from protocols used in cystic fibrosis (CF) patients supplemented by a review of the limited available literature on antibiotic treatment in non-CF bronchiectasis. They have been adopted as a consensus guideline developed by the Departments of Respiratory Medicine & General Medicine and the Antibiotic Stewardship Service.

Unlike CF patients, routine sputum surveillance has not been the standard practice for patients with non-CF bronchiectasis. **In order to determine the presence of bacterial pathogens and to direct therapy, sputum samples should be obtained for patients with non-CF bronchiectasis during admissions** to hospital, **at follow up visits** if feasible and **at the time of a respiratory exacerbation**.

Case series of children with non-CF bronchiectasis have demonstrated that non-typeable *Haemophilus influenzae* is the most common bacteria isolated, followed by *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Staphylococcus aureus*, in order of decreasing prevalence. In patients with more advanced non-CF bronchiectasis isolation of *Pseudomonas species* may occur and this progression of disease appears to occur more often in patients with neuro-developmental abnormalities.

Note: Many tracheostomised patients may become colonised with Pseudomonas without having underlying bronchiectasis. In this situation caution should be exercised in interpreting sputum cultures from the tracheostomy. Pseudomonas may be difficult to eradicate and the main indication for considering treatment would be during an acute respiratory illness.

Administration of Nebulised Antibiotics

Directions for staff on how to administer nebulised antibiotics is covered in the Administering Nebulised Antibiotics – CHW Practice Guideline. This outlines equipment and set-up required.

Education must be provided to families who are to administer nebulised antibiotics in the home environment. The Giving Nebulised Antibiotics at Home – Homecare Guideline is a resource that may assist.

Many families will be required to purchase or hire a nebuliser if they do not already have one.

This Guideline may be varied, withdrawn or replaced at any time.

Antibiotic Treatment of Organisms (other than *P. aeruginosa*)

(see also Table 1)

- During a flare of respiratory disease (tracheitis, bronchitis, pneumonia) the use of a broad spectrum antibiotic such as amoxycillin or Augmentin (amoxycillin + clavulanic acid) will provide appropriate cover for the most common bacteria isolated in non-CF bronchiectasis.
- Bactrim (sulfamethoxazole + trimethoprim) can be used in penicillin allergic patients.
- Augmentin (amoxycillin + clavulanic acid) has the advantage of covering beta-lactamase positive *Haemophilus influenzae* and *Moraxella catarrhalis* and providing anti-staphylococcal activity in methicillin SENSITIVE *S. aureus* (MSSA).
- If *Staphylococcus aureus* is the only pathogen isolated during an episode of respiratory illness, then flucloxacillin is recommended if sensitive.
- Cephalexin is an alternative anti-staphylococcal antibiotic and is more palatable in syrup formulation than flucloxacillin.
- It is recommended that a minimum of 14 days treatment is given and this can be extended to 21 days if there is a slow clinical response.
- Occasionally intravenous antibiotics may be required, with the choice being directed by sputum culture results.

Table 1

Organism	Oral Therapy	Intravenous Therapy	Duration
H. influenzae, *M. catarrhalis*	**Amoxycillin + clavulanic acid** 22.5 mg/kg (amoxycillin)/dose (max 875 mg - amoxycillin) BD **Sulfamethoxazole + trimethoprim** 4 mg/kg(trimethoprim)/dose (max 160 mg – trimethoprim) BD	**Cefotaxime** 25-50 mg/kg/dose q8hourly	14 days
S. pneumoniae	**Amoxycillin** 12.5-25 mg/kg/dose (max 500 mg-1000 mg) TDS (use higher dose if reduced penicillin sensitivity demonstrated)	**Benzylpenicillin** 30 mg/kg/dose (max 1200 mg) q6hourly	14 days
S. aureus	**Flucloxacillin** 25 mg/kg/dose (max 500 mg) QID **or** **Cephalexin** 12.5 mg/kg/dose (max 500 mg) QID	**Flucloxacillin** 25 mg/kg/dose q6hourly (max 1000 mg) **or** **Cefazolin** 25 mg/kg/dose (max 1000 mg) q8hourly	14 days

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Antibiotic Treatment of *Pseudomonas aeruginosa*

Outpatient treatment with nebulised and oral antibiotics

(see also Table 2)

1. Check sputum culture and sensitivity prior to commencement
2. **Treatment for Pseudomonas eradication on first isolation**:
   - 4 weeks of nebulised gentamicin & 3 weeks of oral ciprofloxacin. Ciprofloxacin is only available in tablet form so may be difficult to administer to some children. There are also limited safety data on ciprofloxacin use in children under the age of 5 years (See note on page 2).
   - Patients who fail this regimen may be retreated with a second identical course, provided the pseudomonal isolate remains ciprofloxacin-sensitive. Alternatively, treatment with parenteral anti-pseudomonals may be considered.
   - On re-isolation of *P. aeruginosa* after a period of successful "eradication", the same ambulatory regimen may be used again, provided the isolate remains ciprofloxacin-sensitive.
3. **Treatment for clinical exacerbations in patients chronically colonised with ciprofloxacin-sensitive pseudomonas**:
   - 4 weeks of nebulised gentamicin plus 2 weeks of oral ciprofloxacin. This may be extended to 3 weeks ciprofloxacin after clinical review if there is a slow response.
4. **Continuous treatment of patients chronically colonised with pseudomonas**:
   - Regular nebulised gentamicin 80 mg BD can be considered for patients with significant respiratory morbidity based on the results of a recent RCT of nebulised gentamicin in non-CF bronchiectasis[8]. Gentamicin is the preferred initial choice but tobramycin could be considered if the organism is resistant to gentamicin and sensitive to tobramycin.

Table 2

Indication	**Therapy**	**Duration**
First isolation	Ciprofloxacin 15 mg/kg/dose (max 750 mg) BD ***plus*** Gentamicin nebulised 160 mg BD (80 mg BD in children <1yr) **Failure to respond: re-treat with same protocol or use intravenous anti-pseudomonal agents**	21 days 28 days
Subsequent (chronic) exacerbations *(check sensitivities)*	Ciprofloxacin 15 mg/kg/dose (max 750 mg) BD ***plus*** Gentamicin nebulised 160 mg BD (80 mg BD in children <1yr)	14 days 28 days
Regular Treatment	Gentamicin (or tobramycin) nebulised 80 mg BD (if chronically colonised; with significant morbidity)	Continuous

Inpatient Treatment for Clinical Exacerbation in patients with previous *Pseudomonas* isolation

1. Check sputum culture and sensitivity prior to commencement of antibiotics.
2. The options for inpatient treatment include:
    i. Nebulised gentamicin and oral ciprofloxacin (as outlined above),
    ii. Intravenous anti-pseudomonal treatment (see below).

    The decision of which option to use will depend on the individual clinical situation including (but not limited to):

    - the primary reason for admission,
    - the severity of any respiratory exacerbation,
    - the presence of a cannula or other venous access device, and
    - the degree to which pseudomonas is felt to be contributing to the respiratory exacerbation.
3. In penicillin allergic patients consider ceftazidime or cefepime.

Intravenous Anti-Pseudomonal Treatment

(see also Table 3)

Standard Therapy

- IV gentamicin plus Tazocin (piperacillin + tazobactam) (if sensitive)

Duration

- Usually 14 days (up to 3 weeks may be used if a change in antibiotics is instituted during treatment due to *in vitro* antibiotic resistance).
- Duration of treatment may be less if *Pseudomonas* is not felt to be the primary contributor to respiratory exacerbation. The treatment can then be changed to nebulised gentamicin and oral ciprofloxacin to complete the course, either as an inpatient or outpatient.
- In selected difficult patients, an ambulatory course of “consolidation” nebulised gentamicin and oral ciprofloxacin therapy following intravenous therapy may be considered for ciprofloxacin-sensitive isolates, in consultation with the Antimicrobial Stewardship Service.

Table 3

Intravenous Therapy	Duration
Tazocin (piperacillin + tazobatam) 100 mg/kg (based on piperacillin content) (max 4000 mg) q8hourly ***plus*** **Gentamicin** 7.5 mg/kg/dose daily (monitor renal function and serum levels)	14 days
Alternative beta-lactam agent: (check sensitivities) **Ceftazidime** 50 mg/kg/dose (max 2000 mg) q8hourly **Cefepime** 50 mg/kg/dose (max 2000 mg) q8hourly	14 days

Therapy if Gentamicin and/or Tazocin (piperacillin + tazobactam) Resistant

If not responding after first week of treatment, review most recent susceptibility results and discuss best ongoing treatment option with the clinical Microbiologist or Antibiotic Stewardship Consultant.

Therapeutic Drug Monitoring

Treatment with nebulised aminoglycosides does not require therapeutic drug monitoring for efficacy or toxicity. The use of intravenous aminoglycosides does require therapeutic drug monitoring. Please refer to the Aminoglycoside Dosing and Monitoring – CHW Practice Guideline for information on therapeutic drug monitoring and for further discussion on the risks of aminoglycoside toxicity.

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