PAEDIATRIC HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 15: RESPIRATORY SYSTEM
NEMLC 25 FEBRUARY 2021

For Final Ratification

MEDICINE AMENDMENTS

SECTION	MEDICINE	CHANGE
15.4.1 Asthma attack, acute	Prednisone	Maximum dose added
15.4.2.2 Laryngotracheobronchitis, acute viral (Croup)	Prednisone	Maximum dose added

General

COVID-19

An external comment was received outlining that there would be a need to add in a section on COVID pneumonia to the Respiratory Chapter. The Paediatric Expert Review Committee (ERC) has recommended the inclusion of a section of management of COVID-19 in paediatrics. This section will be managed independently and added to the relevant chapters once finalised.

15.1.1 Pneumonia

Diagnostic Criteria

External comment was received indicating that for tachypnea, age dependent respiratory rate was not included for over 5 years of age.

This was updated as follows:

Age	Respiratory rate
< 60 days	> 60/minute
2–12 months	> 50/minute
1–5 years	> 40/minute
5-12 years	> 25/minute

(This change was also made for the bronchiolitis section)

General and Supportive Measure

An external comment was received indicating that blood gas measurements are usually use. The text was amended as follows to capture the need for a blood gas:

> Hypoxia (SATS monitor) and/or hypercapnia (blood gas) are indications for ventilatory support.
> ~~Hypercapnia and/or hypoxia are indicatsions for venilatory support.~~

15.1.1.2 Pneumonia due to an anaerobic infection

An external comment was received indicating the need for diagnostic criteria and investigations for this section. The following text was added:

Diagnostic criteria

» Putrid odour from mouth and foul spelling sputum.

Investigations

» Sputum and blood culture using anaerobic media.

15.4.1 Asthma attack, acute

Prednisone: Maximum doses added

The maximum doses for prednisone were added to all prednisone inclusions for asthma.

The following text was added:

Prednisone, oral, 2 mg/kg as a single daily dose for 5 days.

- To a maximum of:

20 mg:	Children < 2 years for 5 days.
30 mg:	Children 2–5 years for 5 days.
40 mg:	Children 6–12 years for 5 days.

15.4.2.2 Laryngotracheobronchitis, acute viral (croup)

Prednisone: Maximum doses added

(as done for Asthma)

15.6 Obstructive Sleep Apnoea

Fluticasone intranasal: retained

An external comment was received indicating that the use of intranasal steroids should be a temporary measure while awaiting referral or further management as the supportive evidence is weak. The Paediatric ERC indicated that this was established care in rhinitis (not so strong in under 6 years of age), and should be retained as status quo therapy.[1]

[1] Maspero JF, Rosenblut A, Finn A, et. al. Safety and efficacy of fluticasone furoate in pediatric patients with perennial allergic rhinitis. Otolaryngology – head and neck surgery. 2008, 138(1).

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NEMLC 19 MARCH 2020

MEDICINE AMENDMENTS

SECTION	MEDICINE	CHANGE
15.1.1 Pneumonia *Empiric antibiotic therapy*	Ampicillin	Removed
	Gentamicin	Removed
	Amoxicillin/clavulanic acid	Added
15.1.1 Pneumonia *Modification of antimicrobial therapy*	Ceftriaxone	Removed
	Cloxacillin	Removed
	Piperacillin/tazobactam	Added
	Amikacin	Added
15.1.1.2 Pneumonia due to anaerobic infection	Ampicillin	Removed
	Gentamicin	Removed
	Metronidazole	Removed
	Amoxicillin/clavulanic acid	Added
15.2.1 Effusion and Empyema	Amoxicillin/clavulanic acid, IV	Added
	Cefazolin	Added
	Cloxacillin	Removed
	Ampicillin	Removed
	Amoxicillin/clavulanic acid, oral	Added
	Flucloxacillin	Removed
15.3.1 Bronchiectasis *Chemoprophylaxis*	Ampicillin	Removed
	Gentamicin	Removed
	Amoxicillin/clavulanic acid	Added
	Azithromycin	Added
15.3.2 Lung Abscess	Ampicillin	Removed
	Gentamicin	Removed
	Metronidazole	Removed
	Amoxicillin/clavulanic acid	Added
	Cloxacillin	Removed
15.4.1 Asthma attack, acute	Salbutamol	Dosing recommendations amended
	Hydrocortisone, IV	Removed
15.4.2.2 Persistent Asthma	Rapid and long acting Beta2 agonists and inhaled corticosteroids	Not Added
15.4.2.2 Laryngotracheobronchitis, acute viral (Croup) *For suspected bacterial infection*	Ampicillin	Removed
	Amoxicillin/clavulanate	Added
15.6 Obstructive Sleep Apnoea	Intranasal corticosteroid - Fluticasone	Added

SECTIONS ADDED:

- **Recurrent Pneumonia**

A section on recurrent pneumonia was provided as this was identified as a common issue clinician deal with. The medicine treatment remained amoxicillin-clavulanic acid, however clear diagnostic, general and supportive measures and referral guidance was added.

- **Obstructive Sleep Apnoea**

The Paediatric Committee acknowledged that obesity rates were on the raise, and that obstructive sleep apnoea in children was becoming an increasing concern. It was noted that while there was not drug therapy, it would be important to outline the general measures like weight reduction, as well as other measures like tonsillectomy and CPAP.

15.1.1 Pneumonia

The classification of pneumonia was updated in line with the updated World Health Organisation (WHO) pneumonia categories:

- Severe or very severe disease
- Pneumonia
- No pneumonia

Empiric antibiotic therapy – severe or very severe disease

Ampicillin: *Removed*
Gentamicin: *Removed*
Amoxicillin/clavulanic acid: *Added*

Amoxicillin/clavulanate IV was added in place of ampicillin plus gentamicin. This change was based on practicalities and changing epidemiology. It will make the IV/oral switch simpler (IV amoxicillin/clavulanate to oral), and will simplify the IV regimen (one product over two). There is non-inferiority data comparing ampicillin plus gentamicin to amoxicillin/clavulanate. The PERCH study[2] demonstrated that that there is a relatively low number of pathogens that are common causes of pneumonia requiring hospital admission in children younger than 5 years.

Modification of antimicrobial therapy

Ceftriaxone: *Removed*
Cloxacillin: *Removed*
Piperacillin/tazobactam: *Added*
Amikacin: *Added*

In the absence of cultures, the Paediatric ERC recommended that the modification of antimicrobial therapy should be changed to piperacillin/tazobactam PLUS amikacin; over ceftriaxone plus cloxacillin, in line with expected epidemiology.[2]

[2] Pneumonia Etiology Research for Child Health Study Group. Cause of severe pneumonia requiring hospital admission in children without HIV infection from African and Asia: the PERCH multi-country case control study. Lancet. 2019, 394: 757 – 779.

15.1.1.2 Pneumonia due to an anaerobic infection

Ampicillin: *Removed*
Gentamicin: *Removed*
Metronidazole: *Removed*
Amoxicillin/clavulanic acid: *Added*

The treatment was changed from ampicillin plus gentamicin plus metronidazole, to amoxicillin/clavulanic acid. This change was based on practicalities and changing epidemiology.

15.2.1 Effusion and Empyema

Amoxicillin/clavulanic acid, IV: *Added*
Cefazolin: *Added*
Cloxacillin: *Removed*
Ampicillin: *Removed*
Amoxicillin/clavulanic acid, oral: *Added*
Flucloxacillin: *Removed*

Amoxicillin/clavulanate IV and cefazolin were added in place of cloxacillin plus ampicillin. The alternative was added due to the issues of availability of cloxacillin, as well as its appropriate cover for suspected pathogens. Likewise, amoxicillin/clavulanate oral was added as an alternative to flucloxacillin or cephalexin.

15.3.1 Bronchiectasis

Ampicillin: *Removed*
Gentamicin: *Removed*
Amoxicillin/clavulanic acid IV: *Added*
Azithromycin: *Added*
As discussed in section 15.1.1 Pneumonia, ampicillin plus gentamicin was replaced with amoxicillin/clavulanic acid.

Azithromycin prophylaxis:

Amoxicillin-clavulanic acid had been previously recommended by a number of guidelines as prophylaxis in bronchiectasis. [3,4,5] Oral amoxicillin-clavulanic acid however required multiple dosing per day and can cause gastrointestinal symptoms, thus azithromyicin was proposed as a favourable alternative.

The BEST 2 study[6] compared the efficacy of oral amoxicillin-clavulanate and azithromycin for the treatment of non-severe respiratory exacerbations in children with bronchiectasis, in a non-inferiority parallel-group, double blind randomised controlled trial. Of the 236 enrolled children, 179 had an exacerbation and were assigned to treatment with either azithromycin or amoxicillin-clavulanic acid. After 3 weeks, 84% (61 out of 73) of exacerbations had resolved in the azithromycin group verses 84% (73 out of 87) in the amoxicillin-clavulanic acid group; risk difference showed non-inferiority (-0.3%, 95% CI -11.8 to 11.1). The exacerbations were significantly shorter in the amoxicillin-clavulanic acid group versus the azithromycin group (median 10 days versus 14 days, p = 0.014). The adverse effects were reported in 21 % of children in the azithromycin group versus 24% in the amoxicillin-clavulanic acid group (RR 0.9, 95% CI 0.5 to 1.5).

15.3.2 Lung Abscess

Ampicillin: *Removed*
Gentamicin: *Removed*
Metronidazole: *Removed*
Amoxicillin/clavulanic acid: *Added*
Cloxacillin: *Removed*

Amoxicillin/clavulanic acid was added in place of ampicillin, gentamicin and metronidazole to enable same coverage and for practical reasons and a simple IV to oral switch.

Cloxacillin was previously recommended if there was a poor response to therapy and no cultures. This however was removed due to the lack of availability of cloxacillin. Instead the following text was added: "Consider local surveillance of pathogens and change accordingly".

15.4.1 Asthma attack, acute

Salbutamol: *Dosing recommendations amended*
Hydrocortisone, IV: *Removed*
Hydrocortisone IV removed, and prednisone oral therapy retained as step 3 in moderate to severe asthma. GINA guidelines do not include IV corticosteroids.[7]

[3] Chang AB, Bell SC, Torzillo PJ, et al. Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand Thoracic Society of Australia and New Zealand guidelines. Med J Aust 2015; 202: 21‑23.
[4] Woodhead M, Blasi F, Ewig S, et al. Guidelines for the management of adult lower respiratory tract infections—full version. Clin Microbiol Infect 2011; 17 (suppl 6): E1‑59.
[5] Polverino E, Goeminne PC, McDonnell MJ, et al. European respiratory society guidelines for the management of adult bronchiectasis. Eur Respir J 2017; 50: 1700629.
[6] Goyal V, Grimwood K, Byrnes CA, et.al. Amoxicillin-clavulanate versus azithromycin for respiratory exacerbations in children with bronchiectasis (BEST-2): Multicentre, double-blind, non-inferiority, randomized controlled trial. Lancet. 2018, 392: 1197 – 1206.

15.4.2.2 Persistent Asthma

Rapid and long acting Beta2 agonists and inhaled corticosteroids: Not *Added*

There is a move away from short acting beta-2 agonists (SABA) in adolescents and adults, being replace by formoterol/corticosteroid (ICS) combination. This combination has been demonstrated in these groups to have better outcomes (symptom outcomes, exacerbation outcomes), which have been evaluated in studies, however there are other end points that have not been evaluated, e.g. pathological outcomes, quality of life outcomes, bronchial hyper-responsiveness.

The Global Initiative for Asthma (GINA) guidelines[7] as well as other guidelines have moved to recommended in children over 12 years, a SABA should not be used, and rather a formoterol/ICS combination should be used. It was noted that there is no data in children under 12 years.

The Committee recommended that the current recommendations should be retained until paediatric data is available.

15.4.2.2 Laryngotracheobronchitis, acute viral (croup)

Ampicillin: *Removed*
Amoxicillin/clavulanate: *Added*

15.6 Obstructive Sleep Apnoea

Obstructive Sleep Apnoea is becoming a bigger problem as obesity rates rise. Although there is no specific drug therapy, there are general measures like weight reduction, tonsillectomy and CPAP that can be considered.

Intranasal corticosteroid – Fluticasone: *Added*
In a randomised placebo controlled trial[8] nasal fluticasone was shown to decrease the frequency of mixed and obstructive apnoeas, index decreased in 12 of 13 subjects treated with fluticasone versus 6 out of 12 patient on placebo, p = 0.03.

[7] Reddel HK, et.al. GINA 2019: a fundamental change in asthma management. Eur Respir J. 2019, 53: 1901046.
[8] Brouillette RT, Manokian JJ, Ducharme FM, et. al. Efficacy of fluticasone nasal for pediatric obstructive sleep apnea. J Pediatri, 2001, 138 (6): 838 – 844.