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# Antimicrobial treatment of ENT infections

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# ABSTRACT

Ear, nose and throat (ENT) or upper respiratory tract infections (URTI) are the most common infections in children and the leading causes of antibiotic prescriptions. In most cases, these infections are due to (or are triggered by) viruses and even when bacterial species are implicated, recovery is usually spontaneous. The first imperative is to refrain from prescribing antibiotics in a large number of URTIs: common cold, most cases of sore throat, laryngitis, congestive otitis, and otitis media with effusion. On the contrary, a decision to treat sore throats with antibiotics is based primarily on the positivity of the Group A Streptococcus (GAS) rapid antigen diagnostic tests. For ear infections, only (a) purulent acute otitis media in children under 2 years of age and (b) complicated or symptomatic forms of purulent acute otitis media (PAOM) in older children should be treated with antibiotics. Severe ENT infections (mastoditis, epiglottitis, retroand parapharyngeal abscesses, ethmoiditis) are therapeutic emergencies necessitating hospitalization and initial intravenous antibiotic therapy.

ENT infections are the most frequent infections in children and in many countries the leading reasons for antibiotic prescriptions [1,2]. The vast majority are viral in origin or triggered by viruses. Furthermore, even if bacterial species are implicated, most are self-limited diseases [3–5]. This explains why antibiotics are most often unnecessary, except in the most severe forms, for which diagnosis and treatment must begin at an early stage. The first message in the recommendations of the Groupe de Pathologie Infectieuse Pédiatrique de la Société Française de Pédiatrie (GPIP-SFP) and the Société de Pathologie Infectieuse de Langue Française (SPILF), which were included in the 2021 Haute Autorité de Santé (HAS) guidelines, is that antibiotics should not be prescribed in cases of common cold, non-streptococcal tonsillopharyngitis, laryngitis, congestive acute otitis media or otitis media with effusion [6,7]. The second message is that in most cases, prescription of "critical antibiotics" ("watch" and "reserve" antibiotics in the WHO classification) should be avoided. They include:

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- 2nd and 3rd generation cephalosporins, which favor the emergence of extended-spectrum ß-lactamase-producing enterobacterales,
- amoxicillin-clavulanate (amox/clav), of which the spectrum is unnecessarily broad,
- azithromycin, with half-life inducing prolonged selective pressure [8,9].

A decision to treat sore throat with antibiotics is based mainly on the results of rapid diagnostic antigen tests (RADT) for group A streptococcus (CAS). While positive GAS-RADT justifies antibiotic prescription, negative GAS-RADT most often does not [6,7]. With regard to otitis, only purulent acute otitis media (PAOM) in children under 2 years of age and symptomatic or complicated forms of PAOM in older children should be treated with antibiotics [6,7].

Decreased antibiotic resistance largely ascribable to pneumococcal conjugate vaccines and reduced antibiotic prescriptions for the two most frequently involved bacterial species (*S. pneumoniae* and *H. influenzae*) explain why antibiotic choices have been restricted in recent years and, more specifically why, in most cases, amoxicillin is now the first-line treatment [6–8]. However,



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## Table 1

Antibiotic therapy for outpatient ENT and stomatological infections.

Clinical situations and <i>Bacteriological</i> target	Recommended regimens	Alternatives (contra-indicated preferred treatment)	Comments
Common cold	No antibiotics		Viral infection.No
			demonstrated efficacy of antibiotic treatment
Congestive acute otitis media	No antibiotics		Viral infection.No
			demonstrated efficacy of antibiotic treatment
Otitis media with effusion	No antibiotics		No proven medium or long-term effectiveness of antibiotics
<u>Purulent acute otitis media</u>	Amoxicillin (oral)	Cefpodoxime (oral)	Properly diagnosed purulent AOM should be treated with antibiotics until the
	80–100 mg/kg/day	8 mg/kg/day	age of 2 years. From the age of 2, only the most severe forms (high fever, intense
Main targets of antibiotic treatment	in 2 divided doses	in 2 divided doses	otalgia) or complicated forms
S. pneumoniae	(maximum 3 g/day)	(maximum 400 mg/day)	(otorrhea, recurrent otitis) should be treated with antibiotics.
H. influenzae	The star at dometic a	The star and denotion	The set of a distance of the set of the set of the second set of the set of the set
Other bacteria – M. catarrhalis	Treatment duration	Treatment duration	For other conditions, a wait-and-see attitude is recommended. Antibiotics are indicated in case of persistent symptoms (over 48 hours).
– M. catarrhans – S. pyogenes	- 5 days for children	– 5 days for children	In 2022, in France, fewer than 7% of pneumococcal strains and fewer than 20% c
- 5. pyogenes	older than 2 years	older than 2 years	<i>H. influenzae</i> strains isolated from the nasopharynx of children with ear
	older than 2 years	older than 2 years	infections were resistant to amoxicillin (ACTIV data).
	– 10 days for children under 2 years and after	– 10 days for children under 2 years and after	incetions were resistant to unioxicinin (nerry data).
	this age, only for	this age, only for	Reserve ceftriaxone for exceptional situations of digestive intolerance or strong
	<ul> <li>otitis-prone children (recurrent AOM)</li> </ul>	• otitis-prone children (recurrent AOM)	suspicion of resistant pneumococcus.
	<ul> <li>otitis media with otorrhea</li> </ul>	<ul> <li>otitis media with otorrhea</li> </ul>	
<u> Otitis + conjunctivitis syndrome</u>	Amoxicillin (oral)	Cefpodoxime (oral)	Decreased resistance to amoxicillin due to the production of <i>H. influenzae</i> ß-
	80–100 mg/kg/day	8 mg/kg/day	lactamases in recent years support the use of amoxicillin, even for otitis-
Main target of antibiotic treatment	in 2 divided doses	in 2 divided doses	conjunctivitis syndrome.
	(maximum 3 g/day)	(maximum 400 mg/day)	Ceftriaxone is reseved for exceptional situations of digestive intolerance or
H. influenzae	or Americales (anal)		strong suspicion of resistant pneumococcus.
	<b>Amox/clav</b> (oral) 80 mg/kg/day		
	in 2 divided doses		
	(maximum 3 g/day)		
	Treatment duration	Treatment duration	
	– 5 days for children	– 5 days for children	
	older than 2 years	older than 2 years	
	– 10 days for children under 2 years and after	- 10 days for children under 2 years and after	
	this age only for	<ul><li>this age only for</li><li>otitis-prone children (recurrent AOM)</li></ul>	
	<ul> <li>otitis-prone children (recurrent AOM)</li> <li>otitis media with otorrhea</li> </ul>	<ul> <li>otitis-prone children (recurrent AOM)</li> <li>otitis media with otorrhea</li> </ul>	
Otitis with stambas		Cefpodoxime (oral)	Before the age of 3 years, the most frequent bacterial species is <i>H. influenzae</i> . It i
<u>Otitis with otorrhea</u>	<u>RADT +</u> Amoxicillin (oral)	8 mg/kg/day	often involved in recurrent otorrhea [13].
Main target of antibiotic treatment	50 mg/kg/day	in 2 divided doses	After 3 years of age, GAS is the first species found [13].
H. influenzae	in 2 divided doses	(maximum 400 mg/day)	······································
S. pyogenes	(maximum 3 g/day)		
S. pneumoniae	(mannan s grady)		
	RADT -	Cefpodoxime (oral)	After relaxation of NPIs imposed by COVID-19 pandemic, GAS has increased,
	Amoxicillin (oral)	8 mg/kg/day	including in children under 3 years old [17].
	80–100 mg/kg/day	in 2 divided doses	Because GAS remains susceptible to all ß-lactams, GAS-RADT could help to guid
	in 2 divided doses	(maximum 400 mg/day)	antibiotic treatment. Furthermore, the low MICs of amoxicillin for GAS allow
	(maximum 3 g/day)		lower doses than H. influenzae
	or		
	Amox/clav (oral)		
	80 mg/kg/day		
	in 2 divided doses		
	(maximum 3 g/day)		
	Duration of treatment 10 days regardless of age	Duration of treatment 10 days regardless of age	The sensitivity and specificity of these tests in this situation is close to 100%. In addition, GAS is rarely associated with other bacteria in ear infections.

Table 1 (continued)

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Clinical situations and Bacteriological target	Recommended regimens	Alternatives (contra-indicated preferred treatment)	Comments
Acute otitis media after failure of first antibiotic treatment	Failed after 1 <sup>er</sup> treatment:	Second line	<b>Definition of failure</b> Persistence or recurrence of clinical signs during treatment or within 72 hours o
antibiotic treatment			discontinuation.
Main target of antibiotic treatment	Amoxicillin (oral) →	Amox/clav (oral)	Treatment failures with amoxicillin treatment are mainly due to H. influenzae
H. influenzae		80 mg/kg/day	
S. pneumoniae		in 2 divided doses	
		(maximum 3 g/day)	
		Duration of treatment 10 days	
		<b>Cefpodoxime</b> (oral)	
		8 mg/kg/day	
		in 2 divided doses	
		(maximum 400 mg/day)	
		Duration of treatment 10 days	
	<b>Cefpodoxime</b> (oral) $\rightarrow$	Amoxicillin (oral)	Treatment failures with cefpodoxime treatment are due to penicillin-resistan
		150 mg/kg	pneumococcus.
		in 3 divided doses	pheambeoceasi
		(maximum 3 g/day)	
		Duration of treatment 10 days	
	Amor/alay (anal)	<b>Ceftriaxon</b> e	Path hastonia and ha involved in (vom news) failung of smary plausiants
	Amox/clav (oral) →		Both bacteria can be involved in (very rare) failure of amox-clavulanate.
		50 mg/kg/in 1 dose	Tympanocentesis for bacterial examination should be considered.
		(IV or IM)	
		(3 days)	
<u>Maxillary or frontal sinusitis</u>	Amoxicillin (oral)	Cefpodoxime (oral)	Treatment is indicated:
	80–100 mg/kg/day	8 mg/kg/day	<ul> <li>in frontal sinusitis or in the following situations of maxillary sinusitis:</li> </ul>
	in 2 divided doses	in 2 divided doses	<ul> <li>In the "severe-acute" form, the rarest with fever &gt; 39 °C, headaches, purule</li> </ul>
	(maximum 3 g/day)	(maximum 400 mg/day)	rhinorrhea, evolving > 3-4 days
Main target of antibiotic treatment	Duration of treatment 10 days	Duration of treatment 10 days	<ul> <li>In any clinical form with risk factors: asthma, heart disease, sickle ce anemia.</li> </ul>
S. pneumoniae			<ul> <li>Without these risk factors, in both forms of the most common maxillar</li> </ul>
H. influenzae			sinusitis (rhinopharyngeal symptoms lasting more than 10 days with r
M. catarrhalis			sign of improvement or secondarily aggravating), treatment should l
W. cuturmuns			discussed or delayed according to intensity of symptoms, their duration
			and failure of symptomatic treatment.
Toncillo nhammaitic			The vast majority of sore throats are viral in origin. The only important bacter
<u> Tonsillo -pharyngitis</u>			species for ambulatory patients in childhood is GAS. It is no longer acceptable
Main target of antibiotic treatment			treat patients with antibiotics without first obtaining positive RDT.
S. pyogenes (GAS)			
	No antibiotics	No antibiotics	
GAS-RADT -	Amoxicillin (oral)	Cefpodoxime (oral)	All GAS strains remain susceptible to ß-lactams. Resistance to macrolides vari
	50 mg/kg/day in 2 doses	8 mg/kg/day in 2 doses	depending on the area and the times. Over the last 5 years, the rate of resistant
	(maximum 2 g/day)	(maximum 400 mg/day)	has been very low (less than 5%) in the strains isolated in children with GAS
		Duration of treatment 5 days	pharyngitis.
		or	
GAS-RADT+	Duration of treatment 6 days	Clarithomycin (oral)	
	-	30 mg/kg/day in 2 divided doses	
		(maximum 500 mg/day)	
S. pyogenes (GAS)		(maximum 500 mg/day) Duration of treatment 5 days	

Infectious Diseases Now 53 (2023) 104785

# Table 1 (continued)

Clinical situations and Bacteriological target	Recommended regimens	Alternatives (contra-indicated preferred treatment)	Comments
Recurrent GAS Tonsillo-pharyngitis GAS carrier state GAS eradication in invasive GAS infections	<b>Cefalexin</b> (oral) 50 mg/kg/day in 2 divided doses (maximum 2 g/day) For 10 days		For GAS carriage state and GAS eradication in invasive GAS infections, antibiotics are only exceptionally indicated [19].Penicillin V, Penicillin G or amoxicillin are not the optimal treatments. Alternative treatments give better results in terms of GAS eradication. Several hypotheses have been raised to explain these differences (biofilms, internalization, bacterial interferences)
	<b>Amox/clav</b> (oral) 50 mg/kg/day in 2 divided doses (maximum 2 g/day) For 10 days		
	<b>Azithromycin</b> (oral) In one daily dose 20 mg/kg/day for 3 days		
	Amoxicillin (oral) 50 mg/kg/day in 2 doses (maximum 2 g/day) For 10 days		
Cervical lymphadenitis	+ <b>Rifampicin</b> (oral) 20 mg/kg/day in 2 doses The last 4 days of amoxicillin treatment If GAS-RADT +:	If GAS-RADT + or -	Rapid diagnostic tests for GAS are recommended in cervical adenitis if antibiotic
Main target of antibiotic treatment	Amoxicillin (oral) 50 mg/kg/day in 2 doses (maximum 2 g/day)	<b>Clarithromycin</b> (oral) 15 mg/kg/day in 2 divided doses (maximum 500 mg/day) or	therapy is considered: if positive, an antibiotic targeting this bacterial species may be prescribed [19]. If the infection is severe and hospitalization is indicated prescribe the same antibiotics as for peri-pharyngeal abscesses, if possible after puncture.
	If GAS-RADT -:		
S. pyogenes S. aureus (SAMS)	Amox/clav (oral) 80 mg/kg/day in 2 doses (maximum 2–3 g/day)	<b>Clindamycin</b> (oral) 30 mg/kg/day in 3 divided doses (after 6 years) (maximum 1.8 g/day)	
	Duration of treatment 10 days	(maximum 1.8 g/uay)	
		Duration of treatment 10 days	
Uncomplicated dental abscess	Amoxicillin (oral)		
Main target of antibiotic treatment	50 mg/kg/day in 2 divided doses (maximum 3 g/day)	<b>Clarithromycin</b> (oral) 15 mg/kg/day	
Streptococcus viridans and anginosus	Duration of treatment days	in 2 divided doses (maximum 500 mg/day) Duration of treatment 6 days	
and other anaerobes Dental abscess complicated by cellulitis	Amox/clav (oral)	Clarithromycin	
Main target of antibiotic treatment	80 mg/kg/day In 2 divided doses	(oral) 15 mg/kg/day	
Cover in addition Bacteroides species	(maximum 3 g/day)	in 2 divided doses (maximum 500 mg/day)	
	Duration of treatment 10 days	+ Metronidazole (oral) 30 mg/kg/day in 2 divided doses, (maximum 1500 mg/day) Duration of treatment 10 days	

Table 1 (continued)

Clinical situations and Bacteriological target	Recommended regimens	Alternatives (contra-indicated preferred treatment)	Comments
Laryngitis	No antibiotics		Viral infection.No proven effectiveness of antibiotics.
Acute parotitis of bacterial origin	Amox/clav (oral)	<b>Cotrimoxazole</b> (oral)	Outside of the neonatal period, most parotitis is viral in origin, particularly
(except in neonates)	80 mg/kg (oral) or 100–150 mg/kg IV in 3 doses (maximum 4 g/day) Duration of treatment 10 days	30 mg/kg/day of Sulfamethoxazole in 2 divided doses (maximum 1600 mg/day)	mumps virus (at over 10 years of age, effectiveness of the vaccine, even after 2 doses, does not exceed 85%), and enterovirus. In a parotitis of bacterial origin, pus is retained at the orifice of Stensen canal, ar inflammatory aspect of the parotid gland (suggesting abscessation and high inflammatory biological parameters (CRP and/or PCT).
Main target of antibiotic treatment		<b>Clindamycin</b> (oral) 30–40 mg/kg/day	Recurrences are frequent [20].
S. aureus meti S (SAMS)		in 3 divided doses	
Anaerobes		(maximum 2,4 g/day)	
		Duration of treatment 10 days	

#### IV: Intravenous. IM: Intramuscular. RADT: Rapid Antigen diagnostic test. Amox-clavulanate: Amoxicillin-clavulanate combination.

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Table 2

Antibiotic therapy for serious ENT and stomatological infections.

Clinical situations and Bacteriological target	Recommended regimens	Alternatives (contraindicated preferred treatment)	Comments
Peri-pharyngeal or retropharyngeal abscess Severe acute suppurative adenitis	Amox/clav (IV) 150 mg/kg/d IV in 3 divided doses (maximum 6 g/day)	Cefotaxime (IV) 200 mg/kg In 3 divided doses (maximum 12 g/day) +	Oral relay after the clinical improvement
Essential target of the treatment	Duration 10–14 days	<b>Metronidazol</b> e 30 mg/kg/d in 2–3 IVL	
S. pyogenes		(maximum 1.5 g/day)	
SASM		or	
S. pneumoniae		Clindamycin	
Fusobacterium spp.		40 mg/kg/d in 4 IVL	
Bacteroides spp.		(maximum 2.4 g/day)	
		Duration 10–14 days	
Ethmoiditis			Even if the bacterial etiologies are identical, antibiotic treatment depends on the severity of the clinical picture and CT imaging. The Chandler-Hubert classification defines 5 stages of
Essential target of the treatment			increasing severity:
S. pneumoniae			Stage 1: Inflammatory eyelid edema, with or without orbital edema.Stage 2: Subperiosteal
H. influenzae			abscess, (a) with edema of the eyelids and orbit, (b)
Peptostreptococcus			spread of pus to the eyelids.
S. aureus			Stage 3: orbital abscess.Stage 4: orbital cellulitis, (a) severe, (b)
Fusobacterium Necrophorum			mild.

Infectious Diseases Now 53 (2023) 104785

Clinical situations and Bacteriological target	Recommended regimens	Alternatives (contraindicated preferred treatment)	Comments
Minor pre-septal forms (Chandler-Hubert Stage 1)	Amox/clav (oral) 80 mg/kg/d in 3 divided doses	<b>Ceftriaxone</b> (IV or IM) 50 mg/kg/d in 1 daily dose (maximum 2 g/day)	Stage 5: Thrombosis of the cavernous sinus. Even if the bacterial etiologies are the same, the use of amoxicillin-amoxicillin in the pre- septal or usual forms is justified by its good microbiological activity and the need to avoid
<b>Ethmoiditis usual forms</b> (Chandler-Hubert Stages 2 and 3)	(maximum 3 g/day) Duration of treatment 10 days	(maximum 2 g/uay) Duration of treatment 5 days	cephalosporins more inductive of extended-spectrum enterobacterales &-lactamases. However, for stage 4 and 5 forms, the risk of lessened diffusion of clavulanic acid renders preferable the cefotaxime-metronidazole association.
Ethmoiditis (Chandler-Hubert stage 4 and 5) (Chandler Stage 4 and 5)	Amox/clav (IV) 150 mg/kg/d in 3 divided doses (maximum 4 g/day) or	Cefotaxime (IV) 200 mg/kg/d 3 or 4 divided doses (maximum 12 g/day) +	
	Cefotaxime (IV) 200 mg/kg/d 3 or 4 divided doses +	Metronidazole (IV) 40 mg/kg/d in 3 divided doses	
	<b>Metronidazole</b> (IV) 40 mg/kg/d in 3 divided doses	Duration of treatment 10 days	
	Duration of treatment 10 days		
Acute mastoiditis Simple form	<b>Amoxicillin</b> (IV) 150–200 mg/kg/day in 3 or 4 divided doses	<b>Cefotaxime</b> (IV) 200 mg/kg/day in 3 or 4 divided doses <sup>6</sup> (maximum 12 g)	The choice of amoxicillin as a first-line treatment is justified by the low proportion of amoxicillin-resistant pneumococci, which was less than 7% in 2022 (ACTIV Data) Duration of treatment must be adapted to clinical and biological evolution.
<b>Essential target of the treatment</b> S. pneumoniae	(maximum 8 g/day) Duration 10–14 days	or <b>Ceftriaxone</b> (IV) (75 mg/kg/day) in 1 daily dose (maximum 2 g/day)	
S. pyogenes		Duration 10–14 days	
Acute mastoiditis Dragging form (>5 days)	<b>Amox/clav</b> (IV) 150 mg/kg in 3 or 4 in divided doses	<b>Cefotaxime</b> (IV) 200 mg/kg/day in 3 or 4 divided doses (maximum 12 g/day)	
<b>Essential targets of treatment</b> S. pneumoniae S. pyogenes Fusobacterium sp	(max 4 g/day) Duration 10–14 days	+ <b>Metronidazole</b> (IV) 40 mg/kg/d in 3 divided doses (maximum 1.5 g/day)	
		or <b>Ceftriaxone</b> (IV) (75 mg/kg/day) in 1 daily dose (maximum 2 g/day)	
Anuto mostoiditie	Colotavino (IV)	<b>Metronidazole</b> (IV) 40 mg/kg/d in 3 divided doses Advice on Pediatric Infectious Diseases is	
Acute mastoiditis Complicated form (neurological damage, thrombosis)	Cefotaxime (IV) 200 mg/kg/d 3 or 4 divided doses (max 12 g/day)	required	
	+ <b>Metronidazole</b> 40 mg/kg/day in 2–3 IVL (max 1,5 g/day)		

Table 2 (continued)

Clinical situations and Bacteriological target	Recommended regimens	Alternatives (contraindicated preferred treatment)	Comments
Epiglottitis	Cefotaxime (IV)	Advice on Pediatric Infectious Diseases is	
Essential targets of treatment	200 mg/kg/d	required	
	3 or 4 divided		
S. pneumoniae	doses		
H. influenzae serotype b			
	Duration 5–7 days		
	(maximum 12 g/day)		
	or <b>Ceftriaxone</b> (IV)		
	50 mg/kg in 1 injection		
	(maximum 2 g/day)		
	Duration 5–7 days		
Bacterial laryngotracheobronchitis	Amox/clav (IV)	Cefazolin (IV)	A rare disease, it is an infection of the trachea causing dyspnea and stridor. Most children have
, , , , , , , , , , , , , , , , , , ,	100–150 mg/kg	100 mg/kg	symptoms of viral respiratory infection for 1–3 days before severe symptoms appear.
Essential targets of treatment	in 3 divided doses	in 3 divided doses	Diagnosis is based on clinical, laryngoscopy and/or imaging. In addition to antibiotics,
S. aureus S. pneumoniae	followed by oral relay	followed by oral relay	treatment is based on airway control.
S. pyogenes			
Acute bacterial parotitis of the newborn (no	Amox-clav (IV)		
meningitis)	100–150 mg/kg		
	in 3 divided doses		
Streptococcus agalactiae (Group B	+		
Streptococcus)	Gentamicin		
SASM	5 mg/kg/day in one IV (30		
	minutes)		
	for 48 hours if <b>septicemic</b>		
	form		
	Duration of treatment		
	10 days		

#### Table 3

Oral relay according to the molecule initially administered in IV.

Initial antibiotic	Oral relay
– – Amoxicillin: 150–200 mg/kg/day in 3–4 IVL	<ul> <li>- Amoxicillin: 100 mg/kg/day in 3 doses</li> </ul>
<ul> <li>Amox/clav: 150 mg/kg/day IV in 3–4 divided doses</li> </ul>	<ul> <li>Amox/clav: 80 mg/kg/day in 3 divided doses.</li> </ul>
<ul> <li>Cefotaxime: 200 mg/kg/day IV in 3–4 divided doses.</li> </ul>	<ul> <li>Amox/clav: 80 mg/kg/day in 3 divided doses</li> </ul>
<ul> <li>or Ceftriaxone: 75 mg/kg/day in 1 IVL</li> </ul>	<ul> <li>Penicillin allergy:</li> </ul>
	Cefalexin*: 100 mg/kg/day in 3 divided doses
	Cefpodoxime-proxetil : 8 mg/kg/day in 2 divided doses
<ul> <li>Clindamycin: 40 mg/kg/day in 3–4 IVL</li> </ul>	<ul> <li>Clindamycin: 30–40 mg/kg/day in 3 divided doses</li> </ul>
<ul> <li>Metronidazole: 40 mg/kg/day in 2–3 IVL</li> </ul>	<ul> <li>Metronidazole: 40 mg/kg/day in 3 doses.</li> </ul>

IV: Intravenous.

\* Target spectrum restricted to Gram-positive cocci (SGA, SAMS) possible cross-allergy with penicillin (to be avoided in case of severe allergy and in the absence of allergological exploration).

\*\* No activity on S. aureus even meti-S.

it cannot be ruled out that these favorable trends be reversed in the coming years [10,11]. The therapeutic choices proposed in this manuscript are in line with the latest GPIP-SFP-SPILF recommendations, which were adopted in the 2021 HAS guidelines [6,7].

As for PAOM complicated by otorrhea or cervical lymphadenitis, GAS-RADT is recommended. In extra-pharyngeal infections as well, studies have shown excellent sensitivity and specificity and justify GAS-RADT. When antibiotic therapy seems called for, it is possible prescribe a narrow-spectrum compound targeting GAS only [12–14].

The COVID-19 pandemic and the non-pharmaceutical interventions (NPIs) imposed so as to control SARS-CoV-2 spread have had dramatic impacts on epidemiology in many ambulatory pediatric infectious diseases, including URTI (Upper respiratory tract infections). When NPIs were massively applied, sharply decreased URTI frequency was observed, but after the relaxation of COVID-related restrictions, extensive "COVID rebound" was reported [15,16]. The changes concerned not only incidence or frequency, but also the distribution of pathogens in different clinical situations [13,17].

Severe ENT infections (mastoiditis, epiglottitis, retro- and parapharyngeal abscesses, ethmoiditis) represent therapeutic emergencies that most often justify hospitalization and intravenous (IV) antibiotics [14,18]. No data are available on the recommended duration of treatment for these severe forms. That said, total duration of 10–14 days, depending on the initial severity and the rapidity of therapeutic response, seems reasonable by extrapolation from other clinical situations. An oral relay may reduce hospitalization duration when certain conditions are met: clear clinical improvement in fever, pain and local signs; markedly reduced biological inflammatory syndrome. These clinical and biological objectives are generally achieved after 2–5 days of initial IV treatment. If this is not the case, a medical-surgical re-evaluation of the situation must be considered in view of identifying a complication (an abscessed focus...).

As regards ambulatory ENT infections, Table 1 presents, in different clinical situations: the pathogens most often involved (targets of antibiotic treatment), the preferred choice of treatment and the alternatives in case of contra-indication (allergy...).

As regards serious ENT infections requiring hospitalization, Table 2 likewise presents, in different clinical situations: the pathogens most often involved (targets of antibiotic treatment), the preferred choice of treatment and the alternatives in case of contraindication (allergy, etc.).

Table 3 presents the proposed oral relays according to the compounds initially administered by intravenous (IV) route.

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### **Contribution of authors**

RC and VC wrote the first draft and all of the authors revised and approved the manuscript.

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# References

- Trinh NTH, Cohen R, Lemaitre M, et al. Community antibiotic prescribing for children in France from 2015 to 2017: a cross-sectional national study. J Antimicrob Chemother 2020;75(8):2344–52. <u>https://doi.org/10.1093/jac/ dkaa162</u>.
- [2] Trinh NTH, Bruckner TA, Lemaitre M, et al. Association between national treatment guidelines for upper respiratory tract infections and outpatient pediatric antibiotic use in France: An interrupted time-series analysis. J Pediatr 2020;216:88–94.e4. <u>https://doi.org/10.1016/j.jpeds.2019.09.017</u>.
- [3] Spinks A, Glasziou AP, Del Mar CB. Cochrane Database System Rev 2021;12 (12):CD000023. <u>https://doi.org/10.1002/14651858.CD000023.pub5</u>.
- [4] Venekamp RP, Sanders SL, Glasziou PP, Del Mar CB, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database System Rev 2015;2015(6): CD000219. <u>https://doi.org/10.1002/14651858.CD000219.pub4</u>.
- [5] Falagas M, Giannopoulou K, Vardakas K, Dimopoulos G, Karageorgopoulos D. Comparison of antibiotics with placebo for treatment of acute sinusitis: a meta-analysis of randomised controlled trials. Lancet Infect Dis 2008;8:543–52. <u>https://doi.org/10.1016/S1473-3099(08)70202-0</u>.
- [6] ANTIBIOTHERAPIE DANS LES INFECTIONS RESPIRATOIRES HAUTES; 2011infections-respir-hautes-princ-messages.pdf (infectiologie.com) [cited 09/11/ 23].
- [7] Choix et durées d'antibiothérapie préconisées dans les infections bactériennes courantes; 2021. https://www.has-sante.fr/jcms/p\_3278764/fr/choix-etdurees-d-antibiotherapie-preconisees-dans-les-infections-bacteriennescourantes [cited 08/31/23].
- [8] Actualisation de la liste des antibiotiques critiques disponibles en France pour l'exercice libéral et en établissements de santé. Comité des référentiels de la SPLIF; 2022. https://www.infectiologie.com/fr/actualites/antibiotiquescritiques-disponibles-en-france\_-n.html. [cited 08/31/23].
- [9] The WHO AWaRe (Access, Watch and Reserve) antibiotic Book; 2022. https:// www.who.int/publications/i/item/2021-aware-classification [cited 08/31/23].
- [10] Rybak A, Levy C, Bonacorsi S, et al. Antibiotic resistance of potential otopathogens isolated from nasopharyngeal flora of children with acute otitis media before, during and after pneumococcal conjugate vaccines implementation. Pediatr Infect Dis J 2018;37(3):e72-8. <u>https://doi.org/ 10.1097/INF.000000000001862</u>.
- [11] Rybak A, Levy C, Ouldali N, Bonacorsi S, et al. Dynamics of antibiotic resistance of streptococcus pneumoniae in France: A pediatric prospective nasopharyngeal carriage study from 2001 to 2022. Antibiotics 2023;12:1020. https://doi.org/10.3390/antibiotics12061020. PMID: 37370339.
- [12] Cohen R, Varon E, Bidet P, et al. Diagnostic accuracy of group A streptococcus rapid antigen detection test on middle ear fluid in children with acute otitis media with spontaneous perforation: A prospective multicenter evaluation. Pediatr Infect Dis J 2023. <u>https://doi.org/10.1097/INF.0000000000004009</u>.
- [13] Levy C, Varon E, Bidet P, et al. Otorrhea bacterial profile, epidemiology before widespread use of the third-generation pneumococcal conjugate vaccine in French children, a prospective study from 2015 to 2023. Infect Dis Now 2023;16:104738. <u>https://doi.org/10.1016/j.idnow.2023.104738</u>.

- [14] Couloigner V, Sauvage J-P, Bensimon J-L, Bingen E, Chaudré F, Gehanno P. Recommendation for clinical practice: locoregional complications of pharyngitis. ANAES; 2008. https://www.orlfrance.org/wp-content/uploads/ 2017/06/RPC10\_pharyngites.pdf [cited 08/31/23].
- [15] Cohen PR, Rybak A, Werner A, et al. Trends in pediatric ambulatory community acquired infections before and during COVID-19 pandemic: A prospective multicentric surveillance study in France. Lancet Reg Health Eur 2022;22:100497. <u>https://doi.org/10.1016/j.lanepe.2022</u>.
- [16] Cohen R, Levy C, Rybak A, et al. Immune debt: Recrudescence of disease and confirmation of a contested concept. Infect Dis Now 2023;53(2):104638. <u>https://doi.org/10.1016/j.idnow.2022.12.003</u>.
- [17] Cohen JF, Rybak A, Werner A, et al. Surveillance of noninvasive group A Streptococcus infections in French ambulatory pediatrics before and during

the COVID-19 pandemic: a prospective multicenter study from 2018–2022. Int J Infect Dis 2023;134:135–41. <u>https://doi.org/10.1016/j.ijid.2023.06.003</u>.

- [18] Grimprel E, Hentgen V, Lorrot M, et al. Antibiotic therapy of severe ENT infections in infants and children. Therapeutic proposals of the Groupe de Pathologie Infectieuse Pédiatrique (GPIP) of the Société Française de Pédiatrie. Archives de Pédiatrie 2017;24(125):S9–S16. <u>https://doi.org/10.1016/S0929-693X(17)30512-2</u>.
- [19] Conduite à tenir autour d'un cas d'infection invasive à Streptocoque du Groupe A. https://www.infovac.fr/docman-marc/public/divers/1863-conduite-a-tenircas-contact-infections-invasives-a-sga/file [cited 31/08/23].
- [20] Chandler's Classification or Chandler-Hubert Classification. https://journals. lww.com/op-rs/Citation/2022/05000/Chandler\_s\_Classification\_or\_Chandler\_ Hubert.22.aspx [cited 31/08/23].