Haemophilus influenzae (LTR79351)

Edit Approved By: Dragan, Tatiana (07/31/2023) **Revision: 4.00**

Organism	**Haemophilus influenzae**
Clinical	*H. influenzae* may colonize the nasopharynx, conjunctiva, and occasionally the genital tract of humans. This organism may also colonize the lower respiratory tract of individuals with chronic obstructive pulmonary disease (COPD). *H. influenzae* may cause meningitis, epiglottitis, cellulitis (including periorbital cellulitis), septic arthritis, osteomyelitis, otitis media, sinusitis, acute exacerbations of chronic bronchitis, pneumonia, empyema, conjunctivitis, bacteremia, neonatal and maternal sepsis, and rarely urinary tract infections.
Usual susceptibility pattern	These organisms have variable susceptibility to ampicillin, and TMP-SMX. Ampicillin resistance is most often mediated by β-lactamase production and less frequently by mutation in the penicillin binding protein (PBP3). Alteration of PBP3 usually affects only ampicillin, cefaclor and minimally cefuroxime. One specific mutation may also affect third generation cephalosporins. Combination of both β-lactamase and altered PBP results in very high level resistance to ampicillin. Although resistance has been described, most strains remain susceptible to third generation cephalosporins, rifampin, quinolones, aminoglycosides, tetracycline and chloramphenicol. These organisms are resistant to first generation cephalosporins. Of the oral cephalosporins, cefuroxime and cefixime have the best activity, while the activity of cefprozil and cefaclor is less reliable. Although azithromycin has the best activity, the activity of macrolides is not reliable. Resistance to macrolides is mediated mostly by efflux mechanisms. Rare imipenem or meropenem resistant isolates have been observed mainly among β-lactamase negative ampicillin resistant isolates.
Susceptibility method	Modified Kirby-Bauer or Etest method using Haemophilus Test Medium (HTM) incubated in 5% CO_2 at 35°C for 16-18 hours (20-24 hours for Etest). **Note:** For Etest use 0.5 McFarland suspension in broth. For mucoid strains use 1.0 McFarland

Haemophilus influenzae, Continued

* 1. Eye samples: Follow ASTM

* 2. Resp/Ear samples:
- do BL
- if BL negative, add drug comment #BLN
- if BL positive, add drug comment #BLP

Susceptibility reporting

	CSF/ Brain	Blood	Sterile Body Site	Eye* (See Note)	Other*	Comments
β-lactamase	*	*	*	*	*	Test but do not report
Amox-Clav					2	2nd line if β-lactamase positive **or** anaerobes/Moraxella/ Staph aureus present on smear or culture **If amox-clav I/R see Special Considerations**
Ampicillin	✓*	✓*	✓*	✓	✓	*Etest method If β-lactamase positive – report amp R **If ampicillin I/R and β-lactamase negative see Special Considerations**
Cefotaxime	*	*	*	*	3*	*Report if patient <1 month instead of ceftriaxone Etest method 3rd line if cefuroxime I/R **See Special Considerations**
Ceftriaxone	✓	✓	✓	✓	3	Do not report if patient <1 month Etest method 3rd line if cefuroxime I/R **See Special Considerations**
Cefuroxime		2	2	2	2	2nd line if beta lactamase positive **If cefuroxime I/R see Special Considerations**
Ciprofloxacin		✓	✓	✓		Do not report in patients < 18 y Etest method **See Special Considerations**
Meropenem	2	2	2		4	Etest method 2nd or 4th line if cefotaxime/ceftriaxone not susceptible **See Special Considerations**
Rifampin	*	*	*			*Report if rifampin I/R **If rifampin S see Special Considerations**
Tetracycline					✓	Do not report in patients < 8 y
TMP-SMX			✓	✓	✓	

Note

Deep eye specimens:	Perform susceptibility test if: • vitreous fluid • canaliculitis • corneal ulcer / scrapings • chamber aspirate • endophthalmitis • contact lens related infections • intraocular fluid • donor sclera • ophthalmology clinic/ward • keratitis • chorioretinitis • history of failure of therapy • injury/surgery • cornea • preseptal/orbital cellulitis
Superficial eye specimens:	Susceptibility testing of superficial eye specimens not routinely performed. Add comment: "Susceptibility testing of topical antibiotics is not standardized and is not routinely performed on superficial eye specimens".&A89

Special considerations

<table>
<tr>
<td>Amoxicillin-clavulanate / Ampicillin / Cefuroxime:</td>
<td>Ampicillin resistance is usually due β-lactamase production.
In some strains that are ampicillin resistance and β-lactamase negative (BLNAR) resistance is due to alteration of penicillin binding proteins.
<table>
<tr><th>IF…</th><th>THEN…</th></tr>
<tr><td>Ampicillin I/R
and
β-lactamase negative</td><td>• Do not report amoxicillin/clavulanate or cefuroxime
• Repeat β-lactamase testing
• Confirm ampicillin by Etest
• If confirmed as ampicillin I/R and β-lactamase negative, this indicates an altered penicillin binding protein mechanism of resistance (BLNAR).
• Consult microbiologist
• Ampicillin, cefuroxime and amoxicillin/clavulanate should be reported as R.</td></tr>
<tr><td>Amoxicillin-clavulanate I/R
and
β-lactamase positive (ampicillin R)</td><td>• Do not report amoxicillin/clavulanate or cefuroxime
• Repeat β-lactamase testing
• Confirm amoxicillin/clavulanate by Etest
• Consult microbiologist
• If confirmed as β-lactamase positive and amoxicillin/clavulanate I/R, this indicates multiple mechanisms of resistance including both β–lactamase production and altered penicillin-binding proteins (BLPACR).
• Ampicillin, cefuroxime and amoxicillin/clavulanate should be reported as R.</td></tr>
<tr><td>Amoxicillin-clavulanate I/R
and
Ampicillin S</td><td>• Unusual susceptibility pattern
• Do not report ampicillin or amoxicillin/clavulanate
• Confirm ampicillin and amoxicillin/clavulanate by Etest
• Consult microbiologist</td></tr>
<tr><td>Cefuroxime I/R</td><td>• Confirm cefuroxime by Etest
• Consult microbiologist</td></tr>
</table>
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<tr>
<td>Cefotaxime/ Ceftriaxone/ Meropenem:</td>
<td>Haemophilus sp. should be susceptible to these antibiotics. Consult Supervisor if not susceptible. If I/R, the identification of the organism and its susceptibility should be confirmed by repeat testing. Consider sending confirmed isolates to reference laboratory.</td>
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</table>

Special considerations (continued)

<table>
<tr><td><u>Ciprofloxacin:</u></td><td>Current CLSI breakpoints may underestimate resistance. Use EUCAST breakpoints for interpretation:
<table><tr><th>MIC</th><th>Interpretation</th></tr><tr><td>≤ 0.06 µg/mL</td><td>S</td></tr><tr><td>≥ 0.12 µg/mL</td><td>R</td></tr></table>Add comment:
“Interpretation is based upon EUCAST breakpoints.” #2117</td></tr>
<tr><td></td><td>Consult microbiologist if cipro R</td></tr>
<tr><td><u>Rifampin:</u></td><td>If rifampin susceptible report only upon microbiologist’s request.
Add comment:
"Rifampin is appropriate ONLY for prophylaxis of case contacts. These interpretations do NOT apply to therapy of patients with invasive disease." (23751)</td></tr>
</table>

Interpretation

For Etest, report actual MIC result. For interpretation (S, I, or R) report according to the nearest higher doubling dilution **(Appendix 1)**.

Use **CLSI** interpretive document for ***Haemophilus influenzae*** **and** ***Haemophilus parainfluenzae*****.**

For ciprofloxacin - Refer to **Special Considerations**