Antibiotic resistance in *Haemophilus influenzae* isolates obtained from patients at outpatient departments in Germany, 2019/2020

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Laboratory-based surveillance study

- Study design
  - Collection of up to 10 non-duplicated *Haemophilus influenzae* isolates known or suspected to have caused an ENT infection
  - 23 laboratories across Germany
  - 6 months (from Oct 2019 until Mar 2020)
- Objectives
  - to provide data on the antimicrobial susceptibility of *Haemophilus influenzae* to oral antibiotics
  - to study the genetic background of resistances to β-lactam antibiotics and ciprofloxacin

Antimicrobial susceptibility (n=213 isolates)

- **132 (62.0%) fully susceptible isolates to all antibiotics tested**
- **34 (16.0%) trimethoprim-sulfamethoxazole-resistant isolates**
- **30 (14.1%) amoxicillin-resistant isolates**
  - 1 **β-L**actamase-**N**egative and **A**moxicillin-**R**esistant isolate (BLNAR)
  - 1 **β-L**actamase-**P**ositive and **A**moxicillin-**C**lavulanic acid **R**esistant isolate (BLPACR)
  - 28 **β-L**actamase **P**ositive and **A**moxicillin **R**esistant isolates but amoxicillin-clavulanic acid susceptible (BLPAR; TEM-type)
- 9 (4.2%) imipenem-resistant isolates
- 7 (3.3%) cefixime- and cefpodoxime-resistant isolates
- 4 (1.9%) ciprofloxacin-resistant isolates
- No resistance to doxycycline

Resistance mechanisms

- Resistance to β-lactam antibiotics (n=67)
  - 29 isolates with β-lactamase (all bla_{TEM})
  - Sequencing of *ftsI* encoding the penicillin-binding protein 3 (PBP3)
    - 33 isolates with PBP3 substitutions

Resistance profile (n)	No. of isolates with PBP3 substitutions	PBP3 group (n)
AMX, AMC, CXM, CPP, CFI (1)	1	III+
AMX, CXM, CPP, CFI, T/S (1)	1	III-like
AMX, CXM, CPP, CFI (2)	2	IIa, III-like+
CXM, CPP, CFI, T/S (3)	3	III, III-like (2)
CXM (17)	14	IIa (5), IIb (2), IIc, IId (2), III (3)
CXM, CIP (1)	1	IIa
CXM, CIP, T/S (2)	2	IIa (2)
CXM, IMP (3)	3	IIb (2), III
CXM, IMP, T/S (5)	4	IIa, IIc, IId, III
CXM, T/S (4)	2	IId, III

AMX, amoxicillin; AMC, amoxicillin-clavulanic acid; CXM, cefuroxime; CPP, cefpodoxime; CFI, cefixime; IMP, imipenem

PBP3 group	PBP substitution
I	Arg**517**His
II	Asn**526**Lys
III	Ser**385**Thr

- Resistance to ciprofloxacin (n=4)
  - Characteristic mutations in *gyrA* and *parC* (n=3)

Summary

- Majority of isolates was fully susceptible (62.0%)
- Highest relative resistance rate was found to trimethoprim/sulfamethoxazol (16.0%)
- Resistance rates and mechanisms are comparable to those in invasive isolates (data not shown)