Science for Communities

Antimicrobial susceptibility of invasive *Haemophilus influenzae*, 2017

The antimicrobial susceptibility of 83 invasive isolates of *H. influenzae* referred to ESR in 2017 was tested. Ampicillin, amoxicillin-clavulanic acid, cefaclor and cefuroxime minimum inhibitory concentrations (MICs) were determined by gradient strip on Mueller-Hinton Fastidious (MH-F) agar. Cefotaxime, ciprofloxacin, co-trimoxazole, erythromycin, rifampicin and tetracycline susceptibilities were determined by disc diffusion on MH-F agar. Except for cefaclor, MICs and disc diffusion zone diameters were interpreted using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints.[1] Cefaclor MICs were interpreted using the Clinical and Laboratory Standards Institute (CLSI) breakpoints.[2] Four (4.8%) of the 83 isolates were serotype b.

Seventeen (20.5%) isolates produced β-lactamase. In addition to the 17 β-lactamase-positive isolates, a further 6 isolates were ampicillin resistant, giving a total rate of 27.7% ampicillin resistance (see table).

Notably resistance to 3rd-generation cephalosporins was detected for the first time among invasive *H. influenzae* isolates in 2017. Four (4.8%) isolates were cefotaxime resistant by routine disc testing, and further testing with gradient strips confirmed these isolates were resistant to cefotaxime (MICs 1-2 mg/L) and ceftriaxone (MICs 0.25 mg/L). All four isolates were resistant to cefuroxime (MICs ≥128 mg/L), three were also amoxicillin-clavulanic acid resistant (MICs 8 mg/L), and none produced β-lactamase.

Antimicrobial resistance among *Haemophilus influenzae* isolates from invasive disease, 2017

Antibiotic[1]	Number tested	Number resistant	Percent resistant
Ampicillin	83	23[2]	27.7
Amoxicillin-clavulanic acid	83	4	4.8
Cefaclor	83	11	13.3
Cefuroxime (IV)[3]	83	14	16.9
Cefuroxime (oral)[3]	83	17	20.5
Cefotaxime	83	4	4.8
Ciprofloxacin	83	2	2.4
Co-trimoxazole	83	5	6.0
Erythromycin	83	0	-
Rifampicin	83	0	-
Tetracycline	83	1	1.2

1 Results for the full range of antibiotics tested are presented. Many are not appropriate for the treatment of invasive *H. influenzae* disease or the chemoprophylaxis of contacts.
2 17 of the 23 ampicillin-resistant isolates produced β-lactamase.
3 The EUCAST breakpoints for cefuroxime are variable depending on whether the drug is administered parenterally or orally.

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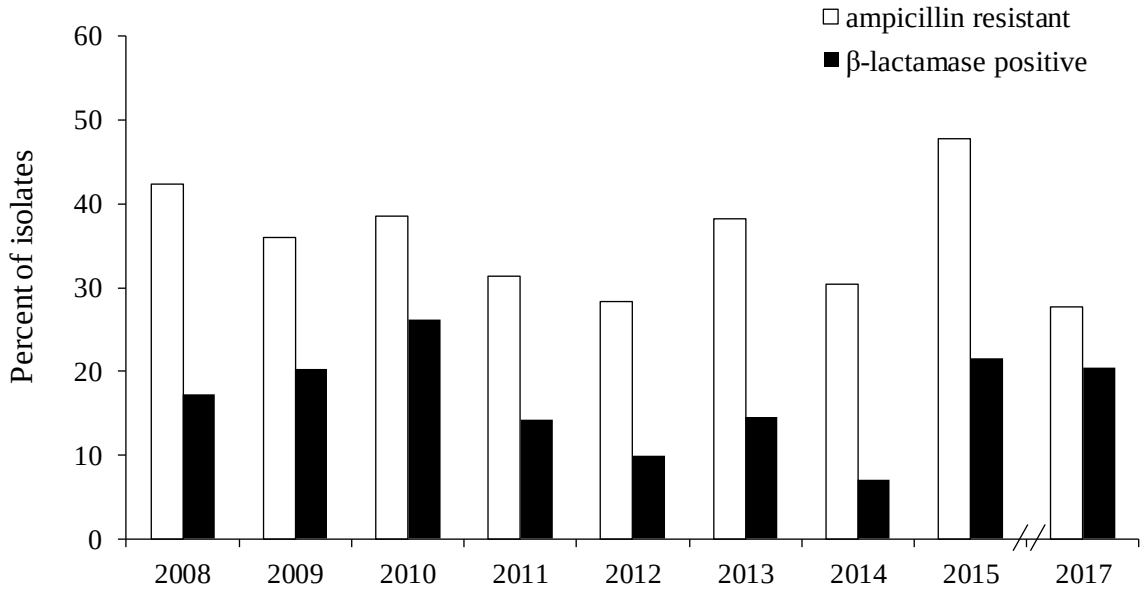
Also for the first time in 2017, ciprofloxacin resistance was identified among invasive *H. influenzae* isolates. Two (2.4%) isolates were ciprofloxacin resistant by routine disc testing, and further testing with gradient strips confirmed these isolates were resistant to ciprofloxacin with MICs of 8 and 32 mg/L. Neither ciprofloxacin-resistant isolate was one of the isolates resistant to 3rd-generation cephalosporins. Also none of the isolates resistant to 3rd-generation cephalosporins or ciprofloxacin were serotype b.

Trends in ampicillin resistance and β-lactamase production among invasive *H. influenzae* over the last 10 years are shown in the figure below. The proportion of isolates over this period that were β-lactamase positive is comparable. However, due to changes in antimicrobial susceptibility testing methods, the rate of ampicillin resistance in 2017 is not directly comparable with the rates for earlier years (see footnote 2 to the figure).

Ampicillin resistance and β-lactamase production among invasive *Haemophilus influenzae*, 2008-2017



Footnotes for the figure:

1 There is no data for 2016 as the antimicrobial susceptibility of invasive *H. influenzae* isolates referred to ESR that year was not tested.

2 **The rates of ampicillin resistance estimated for the years 2008 to 2015 are not directly comparable with the rate for 2017, due to changes in test methods used.** Before 2017, CLSI susceptibility testing standards were used, and isolates determined to have a mechanism of β-lactam resistance other than β-lactamase production were categorised as ampicillin resistant irrespective of the results of the actual ampicillin susceptibility test. In 2017, EUCAST susceptibility testing standards were used, and the ampicillin susceptibility of isolates, determined to have a mechanism of β-lactam resistance other than β-lactamase production (eg, in the 1 unit penicillin disc screening test for β-lactam resistance), is reported according to the actual results obtained in the ampicillin susceptibility test. However conversely, the EUCAST breakpoint for ampicillin resistance is lower (MIC ≥2 mg/L) than the CLSI breakpoint (MIC ≥4 mg/L).

References:

1 European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 7.1; 2017 Mar. Available from http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_7.1_Breakpoint_Tables.pdf.

2 Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 27th ed. Wayne, USA: CLSI; 2017. CLSI supplement M100.