RESISTANCE TRENDS AMONG THE COMMON BACTERIAL CAUSES OF COMMUNITY-ONSET LOWER RESPIRATORY TRACT INFECTION IN THE UK AND IRELAND, 2008-2018

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INTRODUCTION

- Comunity-acquired pneumonia (CAP) is a significant cause of morbidity, particularly in those aged >65 years.
- Common bacterial CAP pathogens are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.[1]
- First-line empirical treatment is amoxicillin; doxycycline or clarithromycin are recommended for patients with a penicillin allergy.[2]
- The 13-valent pneumococcal conjugate vaccine (PCV13) was introduced in the UK in 2010.
- The BSAC Respiratory Resistance Surveillance Programme has monitored antimicrobial susceptibility of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* from community-onset lower respiratory tract infections (CO-LRTI) in the UK and Ireland since 1999/2000.
- We review data for 10 surveillance seasons (Oct 2008 – Sept 2018).

METHODS

- Participating laboratories (n=22-39) collected 14-20 consecutive isolates of *S. pneumoniae* and *H. influenzae*, and 7-10 isolates of *M. catarrhalis* causing CO-LRTI per season.
- MICs were determined centrally by BSAC agar dilution[4] and EUCAST breakpoints were used.[5]
- Ceftaroline breakpoints were available for *S. pneumoniae* and *H. influenzae*; ceftobiprole breakpoints were available for *S. pneumoniae*.
- Isolates of *S. pneumoniae* were serotyped from Oct 2013.

RESULTS

S. pneumoniae (n=3921) (Figure 1)

- 12% (n=477) isolates had a raised penicillin MIC (0.12-2 mg/L); 5 isolates had a MIC 4-8mg/L.
- Rates of resistance to amoxicillin, and raised MICs to cefotaxime were low (*c.* 2%, no trend).
- Increasing rates of resistance were seen for clindamycin and tetracycline but not erythromycin.
- Serotyping was completed for isolates ≥3 years into the PCV13 era (n=1832) (Figure 2):
  - 78 serotypes were represented, most commonly 15A (9%), 11A (8%), and 3 (7%).
  - 17% (n=312) had a PCV13 serotype, most commonly 3 (42%), 19F (22%) and 19A (19%).
  - 11% (n=410; 35 serotypes) were resistant to β-lactams, erythromycin and tetracycline.
  - Common multi-resistant serotypes were 15A (18%), 19F (9%) and 19A (5%).

H. influenzae (n=4738) (Figure 3)

- 20% (n=959) were β-lactamase-positive.
- Rates of resistance to aminopenicillins and amoxicillin-clavulanate increased from 2014.
- Rates of resistance to cefotaxime, ciprofloxacin, erythromycin and tetracycline were ≤2% without trend.

M. catarrhalis (n=2266)

- 97% (n=2188) were β-lactamase-positive.
- All isolates tested were susceptible to amoxicillin-clavulanate, cefotaxime and erythromycin.
- Resistances to ciprofloxacin (n=8), cefuroxime (n=4), and tetracycline (n=2) were rare.

- Susceptibilities of ceftaroline and ceftobiprole among three common CAP pathogens (Table 1).

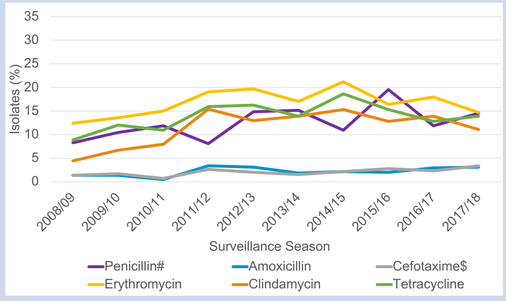

FIGURE 1. Rates of resistance among *S. pneumoniae*.
Key: #MIC values >0.06mg/L; $MIC values >0.5mg/L.

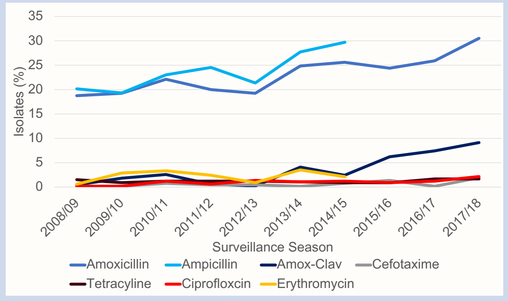

FIGURE 3. Rates of resistance among *H. influenzae*.
Note: Ampicillin and erythromycin not tested from Sept 2014.

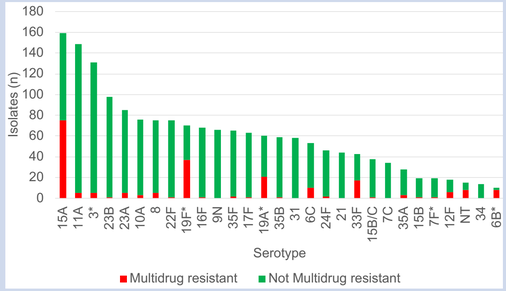

FIGURE 2. *S. pneumoniae* serotypes with ≥10 isolates.
Key: *Serotypes within PCV13; NT, non-typeable.

Agent	Species	Tested (n)	MIC Range (mg/L)	MIC Median (mg/L)	Resistant (n)
Ceftaroline	*S. pneumoniae*	670	0.002 - 0.5	0.008	1 (MIC >0.25)
	H. influenzae	845	≤0.002 - 1	0.008	27 (MIC >0.03)
	M. catarrhalis	395	≤0.002 - >4	4	38* (MIC >4)
Ceftobiprole	*S. pneumoniae*	2570	0.004 - 2	0.015	18 (MIC >0.5)
	H. influenzae	3193	0.004 - >4	0.06	0* (MIC >4)
	M. catarrhalis	1507	0.008 - >4	0.5	18* (MIC >4)

TABLE 1. Susceptibilities of ceftaroline and ceftobiprole among common CAP pathogens.
Key: *No EUCAST breakpoints.

CONCLUSIONS

- Among *S. pneumoniae*, rates of resistance to amoxicillin was low (*c.* 2%); rates of resistance to erythromycin and tetracycline were >10%.
- 11% *S. peumoniae* were multi-resistant and associated with particular serotypes.
- Serotypes within PCV13 accounted for 17% isolates, 24% had a multi-resistant phenotype.
- An increase in the rate of resistance to first line β-lactams was identified in *H. influenzae*.
- *M. catarrhalis* remain largely susceptible to existing antimicrobials.
- Resistance to ceftaroline and ceftobiprole was rare in all three pathogens.
- Continued surveillance is crucial for our understanding of antimicrobial resistance trends in the UK and Ireland, particularly those associated with multi-resistant *S. pneumoniae* and serotypes within PCV13.

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REFERENCES

1) Brown. 2012. Clin Med (12(6): 538-543.
2) Woodhead et al. 2011. CMI, 17(Suppl. 6):E1-59.
3) www.bsacsurv.org.uk, incl. sponsor list.
4) Reynolds *et al*. 2008. JAC, 62, suppl 2: ii15-28.
5) http://www.eucast.org/clinical_breakpoints.

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