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A previously unsuspected national clone of *Proteus mirabilis* with acquired CIT-type AmpC in the UK and Ireland

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BACKGROUND

The BSAC Bacteraemia Resistance Surveillance Programme (www.bsacsurv.org) monitors resistance in the pathogens of bacteraemia in the UK and Ireland.

METHODS

From Jan 2010 to Dec 2013 a total of 57 clinical laboratories (37-39/year) contributed 825 isolates of *Proteus mirabilis* from blood.

MICs were measured centrally by BSAC agar dilution and interpreted by BSAC (EUCAST) breakpoints.

Isolates with ceftazidime or cefotaxime MIC ≥1mg/L were tested for ESBLs by cephalosporin-clavulanate Etest and, if negative, by cefotetan-cloxacillin Etest for AmpC and multiplex PCR[1] for *ampC* genes.

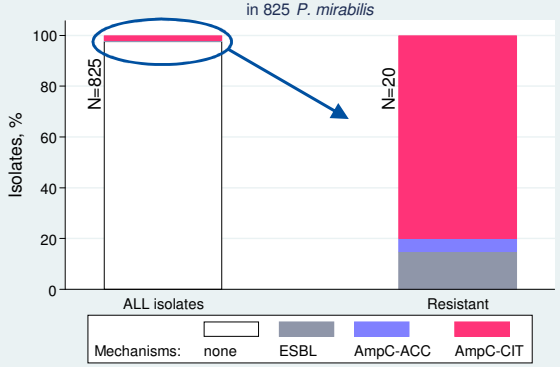
ampC-positive isolates were typed by PFGE of ApaI-digested genomic DNA.

RESULTS

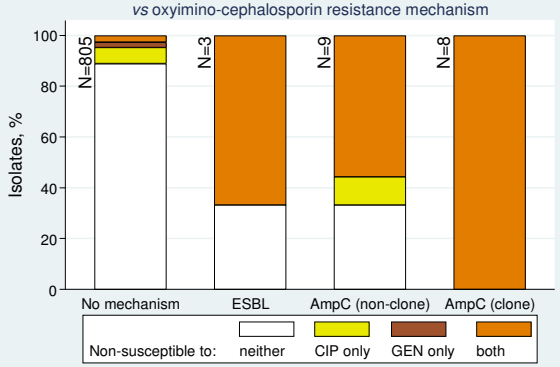
Twenty of 825 isolates (2.4%) were resistant to ceftazidime or cefotaxime - three with ESBLs, one with an ACC-type *ampC* and 16 with CIT-type *ampC* genes.

Phenotypic confirmation of AmpC activity was often not possible because the MIC of cefotetan-cloxacillin was typically off-scale at ≤0.5 mg/L and that of cefotetan alone seldom high enough (≥2mg/L) to confirm 4-fold synergy.

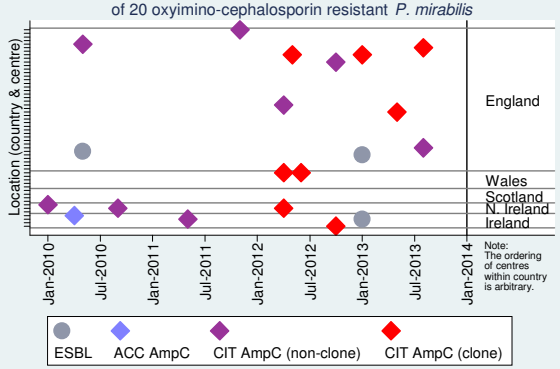
Oxyimino-cephalosporin resistance prevalence
in 825 *P. mirabilis*



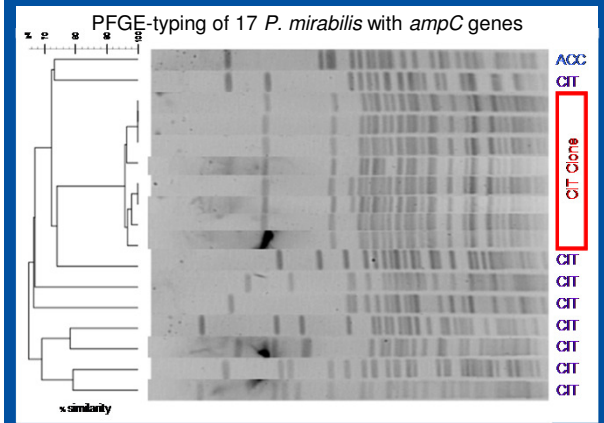
CIP and GEN resistance in *P. mirabilis*
vs oxyimino-cephalosporin resistance mechanism



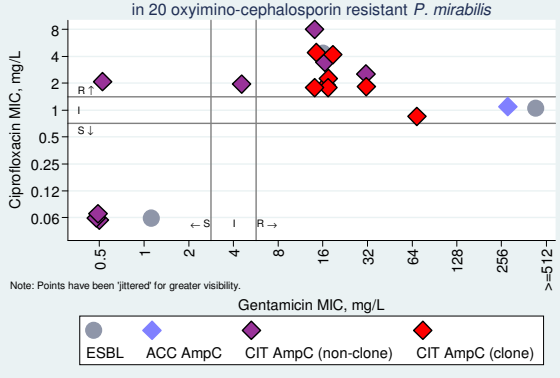
Location, date & mechanism of resistance
of 20 oxyimino-cephalosporin resistant *P. mirabilis*



PFGE-typing of 17 *P. mirabilis* with *ampC* genes



Resistance to ciprofloxacin and gentamicin
in 20 oxyimino-cephalosporin resistant *P. mirabilis*



TYPING

Of 16 isolates with CIT-type *ampC* genes, eight showed >95% similarity in their PFGE profiles, indicating clonality.

The remaining nine *ampC*-positive isolates (eight CIT- and one ACC-type) were much more varied (<80% similarity).

RESISTANCE

The 805 isolates lacking ESBLs or *ampC* genes were generally susceptible to ciprofloxacin (91%) and gentamicin (95%).

All eight clonal CIT-positive isolates were non-susceptible to both ciprofloxacin (MICs 1-16 mg/L) and gentamicin (MICs 16-64 mg/L).

DISTRIBUTION

The eight clonal CIT-positive isolates were found in six separate centres and in four of the five countries of the UK and Ireland, but only in 2012-2013.

The nine non-clonal *ampC*-positive isolates were spread across nine separate centres and all four years of the study.

Overall, *ampC*-positive *P. mirabilis* numbered 6/418 (1.4%) in 2010-11, and 11/407 (2.7%) in 2012-13.

CONCLUSIONS

- Resistance to oxyimino ("3rd-generation") cephalosporins is rare as yet in *Proteus mirabilis* in the UK and Ireland. (It has not become widespread as in e.g. Poland[2] and Italy[3].)

BUT

- A previously unsuspected clone with acquired CIT-type *ampC* and additional resistance to ciprofloxacin and gentamicin has gained a wide distribution recently.

References: [1]Pérez-Pérez & Hanson; J Clin Micro, 2002, **40** (6) 2153-2162. [2]Empel *et al*; AAC, 2008, **52** (7) 2449-2454. [3]D'Andrea *et al*; AAC, 2006, **50** (2) 618-624

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Collecting Laboratories: *See* www.bsacsurv.org *or* White 2008, JAC 62 (Suppl 2) ii3–ii14.

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