

### Antimicrobial resistance in *Helicobacter pylori* – a 10-year perspective from Gastrointestinal Bacteria Reference Unit (GBRU), Public Health England

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**Objectives:** Antimicrobial resistance in *Helicobacter pylori* is an emerging problem. National guidelines[1] for England and Wales recommend performing gastric biopsies for *H. pylori* culture and antimicrobial susceptibility testing for patients with dyspepsia who have failed first- and second-line treatments, have limited options due to drug hypersensitivity or live in an area with a high local resistance rate. Gastrointestinal Bacteria Reference Unit (GBRU) is the national reference laboratory for *H. pylori* in England and Wales. We sought to determine antimicrobial resistance rates of *H. pylori* from gastric biopsies and culture isolates referred to GBRU over the last 10 years.

**Methods:** All gastric biopsies and *H. pylori* isolates referred to GBRU from January 2004 to December 2013, excluding duplicate specimens, were analysed. Culture for *H. pylori* was undertaken for all specimens and those which were culture-negative were tested for *H. pylori* using an in-house PCR assay. *H. pylori* cultures were tested for phenotypic susceptibility to clarithromycin, metronidazole, amoxicillin, tetracycline, levofloxacin, rifabutin and rifampicin using disc diffusion and E-tests. Culture-negative specimens which were *H. pylori* PCR-positive were tested for mutations conferring clarithromycin and tetracycline resistance using an in-house multiplex PCR assay. Data were analysed using Excel 2010 and Epi Info v7. Time trends were analysed by linear regression and Pearson's correlation.

**Results:** 3792 specimens were tested by GBRU over the ten-year period, of which 2282(60.2%) were gastric biopsies and 1510(39.8%) were culture isolates. *H. pylori* was detected in 2303(60.7%) specimens, 2084(90.5%) by culture and 219(9.5%) by PCR. Phenotypic resistance to antimicrobial drugs were as follows: clarithromycin 45.0% (937/2084 tested), metronidazole 63.7% (1328/2084 tested), amoxicillin 0.5% (10/2084 tested), tetracycline 0.6% (12/2084 tested), levofloxacin 15.8% (89/564 tested), rifabutin 2.1% (5/233 tested) and rifampicin 6.0% (20/331 tested). Multidrug resistance (defined as resistance to  $\geq 2$  antimicrobial drugs) was found in 41.0%(854) and monodrug resistance in 28.2%(588). There was a significant increase during this time period in clarithromycin resistance from 18.2% to 78.8% ( $r=0.92$ ,  $p=0.0002$ ), metronidazole resistance from 37.8% to 92.9% ( $r=0.96$ ,  $p<0.0001$ ) and multidrug resistance from 12.8% to 80.7% ( $r=0.95$ ,  $p<0.0001$ ). Of the culture-negative *H. pylori* PCR-positive specimens, clarithromycin resistance mutations were found in 75.3%(165), tetracycline resistance mutations in 9.1%(20) and both in 6.8%(15).

**Conclusions:** Our data suggest that antimicrobial resistance rates of *H. pylori* in difficult-to-treat dyspepsia may be high and increasing in England and Wales. More research is needed to determine the incidence of and risk factors for developing antimicrobial resistance in such patients to guide treatment and prevention strategies.

[1] British Infection Association and Health Protection Agency. *Test and treat for Helicobacter pylori in dyspepsia*. London: Health Protection Agency; 2004, updated 2012.

Antimicrobial resistance in *Helicobacter pylori* from specimens referred to GBRU from 2004 to 2013

