

## Antimicrobial resistance in medically important anaerobes

Dr. József Sóki

*Institute of Clinical Microbiology, Faculty of Medicine, Albert Szent-Györgyi Medical and Pharmaceutical Centre, University of Szeged, Szeged, Hungary*

Anaerobic pathogens are often undervalued in infectious diagnostics, mainly because of the complicated culturing and special knowledge requirements. However, they can cause severe infections that are difficult to treat. It is a rough general rule that the susceptibility of anaerobic pathogens is inversely related to their clinical significance. After an overview of resistance prevalences, different antibiotic resistance mechanisms will be discussed, according to effector genes, expression mechanisms and the propensity to spread horizontally.

The main resistance mechanism for their  $\beta$ -lactam resistance is the production of 2e  $\beta$ -lactamases, especially among *Bacteroides* and *Prevotella*, spp. In *Bacteroidaceae* isolates a  $\beta$ -lactamase conferring cephamycin resistance can be found. The resistance gene (*cfxA*) is coded on a mobilisable transposon, MTn4555, responsible for the horizontal spread. This gene can also be found on plasmids of aerobic relatives of *Bacteroides*. The most important  $\beta$ -lactamase of *Bacteroides* is the metallo- $\beta$ -lactamase, CfiA, of *B. fragilis*. It is chromosomally coded, and for its expression, insertion sequence elements are needed, as in many antibiotic resistance mechanisms of *Bacteroides*. It destroys all  $\beta$ -lactams except monobactams, belongs in Class B and requires  $Zn^{2+}$  for its activity. *cfiA*-positive *B. fragilis* strains form a subgroup of the species. Another carbapenemase has been reported to occur among *B. (Parabacteroides) distasonis*. In the ceftioxin resistance of *Bacteroides* spp., the role of penicillin-binding proteins has been demonstrated. *C. difficile* is inherently resistant to cephalosporins and imipenem, but not to meropenem and amoxicillin.

Metronidazole resistance is mediated by 5-nitroimidazole reductases produced by mobile *nim* genes, and again IS elements are needed for their expression. Tetracycline resistance among *Bacteroidaceae* is caused by *tetQ* genes residing on conjugative transposons responsible for its spread and mobilizing other genetic elements as mobilisable transposons. For tetracycline resistance among clostridia, another conjugative transposon, Tn5397, is needed, which harbours a *tetM* gene. In macrolid-lincosamine-streptogramin-ketolide (MLSK) resistance, it is mainly *ermF* and *ermB* determinants on regular transposons or mobilisable transposons that act.

1<sup>st</sup> and 2<sup>nd</sup> generation fluoroquinolones are not active against most anaerobic pathogens, but newer agents such as moxifloxacin, gatifloxacin and trovafloxacin are effective. Resistance mechanisms against these drugs involve mutations in the QRDR regions of the gyrase genes or efflux.

### **Selected References for Further Reading**

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