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### Metronidazole resistance among clinical isolates belonging to the *Bacteroides fragilis* group: time to be concerned?

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Sir,

Despite metronidazole (5-nitroimidazole) now being in its fortieth year, this remarkable drug remains extensively and effectively used for the prevention and treatment of anaerobic infections, as well as for the treatment of patients with infections caused by *Trichomonas vaginalis* and *Helicobacter pylori*. There is, however, a paucity of data on the incidence of resistance to metronidazole among clinical isolates of anaerobes, although there has been a recent report of metronidazole treatment failure in a patient with an appendectomy wound infection caused by isolates of *Bacteroides fragilis* and *Bacteroides ovatus* that were resistant to metronidazole (MICs > 32 mg/L).<sup>1</sup>

The Anaerobe Reference Unit (ARU) provides a service for the identification of anaerobic bacteria isolated from clinical material and routinely determines the susceptibilities of these isolates to a range of antibiotics, including metronidazole. This surveillance has demonstrated a possible increase in the incidence of metronidazole resistance among *Bacteroides* spp. During 1998, 93 isolates referred to the ARU were identified as belonging to the *B. fragilis* group; 7.5% of these were resistant to metronidazole (MICs > 16 mg/L),<sup>2</sup> compared with 1.9% of the isolates evaluated in 1995 and 3.8% in 1997. This trend may be the result of a selection bias, as some isolates were referred solely to confirm putative resistance to a 5 µg metronidazole disc, or it may reflect a true increase in the incidence of resistance, an observation that would have major implica-

tions for clinical microbiology laboratories, as well as for the prophylactic and treatment regimens administered to surgical patients.

The precise incidence of resistance to metronidazole is difficult to estimate. Standard practice in busy diagnostic laboratories is currently to screen specimens for the presence of obligate anaerobes by placing a 5 µg metronidazole disc in the streaked inoculum of the primary anaerobic culture plate. After incubation, any zone of inhibition is regarded as indicative of the presence of obligate anaerobes. Colonies growing within the zone are normally presumed to be facultative anaerobes (as opposed to obligate anaerobes with reduced susceptibilities to metronidazole) and not investigated further. It is possible, therefore, that the true incidence of resistance to metronidazole is being underestimated, a situation that emphasizes the need for a study to assess more accurately the susceptibilities of clinical isolates of *Bacteroides* spp.

The ARU is currently investigating isolates belonging to the *B. fragilis* group exhibiting resistance to metronidazole for the presence of chromosomal and plasmid-borne *nim*<sup>R</sup> genes, which encode resistance to nitroimidazoles.<sup>3</sup> A point prevalence study designed to determine the true level of metronidazole resistance is also planned but, in the mean time, any apparently resistant isolates should be referred to the Unit for further assessment. Diagnostic microbiology laboratories and surgeons alike should be aware that the incidence of metronidazole resistance among clinically significant anaerobes may be increasing.

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