Emergence of Metronidazole-Resistant Bacteroides fragilis, India

To the Editor: Members of the Bacteroides fragilis group are the most commonly isolated anaerobic pathogens in humans. Metronidazole has been the drug of choice for preventing and treating such infections for 40 years. Although B. fragilis exhibits the broadest spectrum of recognized resistance to antimicrobial agents among anaerobes, the worldwide rate of metronidazole resistance remains low, <5% (1,2). We report here the first metronidazole-resistant strain of B. fragilis from India.

A 34-year-old man with myelodysplastic syndrome was admitted to our hospital with a short history of myalgia, general malaise, and bleeding gums. Bone marrow examination showed evidence of severe aplastic anaemia, for which he was treated with cyclophosphamide and blood transfusions. Ceftazidime and amikacin were also administered empirically for febrile neutropenia. The patient remained in the intensive care unit of our medical oncology ward and was given repeated courses of chemotherapy and blood transfusions. He also had repeated episodes of febrile neutropenia, which resolved with a combination of vancomycin, aminoglycosides, and third-generation cephalosporin. After 4 months in the hospital, during an episode of febrile neutropenia, the patient’s condition started to deteriorate, and high-grade fever developed. Physical examination showed temperature of 38°C, heart rate 80/min, blood pressure 100/70 mmHg, and marked pallor. Laboratory investigations showed a hemoglobin level of 4g/dL and marked neutropenia (absolute neutrophil count 320/mm³). Liver and renal function test results were within normal limits. Peripheral blood smears were negative for malarial parasites. Culture of urine revealed no growth, and the Widal test was negative. Two blood samples were collected in Wampole isolator tubes (Wampole Laboratories, Cranbury, NJ), for isolation of aerobic and anaerobic bacteria. Subsequently, intravenous antimicrobial therapy with vancomycin, metronidazole, and ceftazidime was started. The patient died a day after collection of blood for culture.

Antemortem blood cultures grew Pseudomonas aeruginosa and B. fragilis. The isolate of B. fragilis was identified by conventional tests and Rap ID ANA II system (Innovative Diagnostic System, Norcross, GA). P. aeruginosa was sensitive to piperacillin but resistant to amikacin, ceftazi-
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Single Nucleotide Polymorphisms in Mycobacterium tuberculosis Structural Genes

To the Editor: A recent article by Fraser et al. (1) discussed the frequency of single nucleotide polymorphisms (SNPs) in two genomes of Mycobacterium tuberculosis, strains H37Rv (2) and CDC1551 (unpublished). The article contains an inaccurate representation of our published M. tuberculosis data on SNP frequency. The authors state that “detailed comparison of strains H37Rv and CDC1551 indicates a higher frequency of polymorphism, approximately 1 in 3,000 bp, with approximately half the polymorphism [sic] occurring in the intergenic regions. In other words, 50% of the polymorphisms are in 10% of the genome. While this rate is higher than that suggested (3), it still represents a lower nucleotide diversity than found in limited comparisons from other pathogens.”

On the basis of comparative sequence analysis of eight M. tuberculosis structural gene loci (open reading frames [orf]), we initially published an estimated average number of synonymous substitutions per synonymous site (Ks value) that indicated that this pathogen had, on average, approximately 1 synonymous difference per 10,000 synonymous sites (4). This finding was unexpected given the relatively large population size of M. tuberculosis and paleopathologic...