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USE OF BETA-LACTAM/BETA-LACTAMASE INHIBITORS IN FEBRILE NEUTROPENIC PATIENTS

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Over the past 2 decades there has been a shift in the etiologic agents responsible for bacteremia in febrile neutropenic patients; currently approximately 70% of these infections are caused by Gram-positive organisms. Among these organisms, viridans streptococci comprise a significant majority. Also, over these years a large number of new antibiotics have been studied as empirical therapy for fever in granulocytopenic patients. Piperacillin-tazobactam (P/T) is a combination of a beta-lactam antibiotic with good activity against Gram-positive and Gram-negative bacteria plus a beta-lactamase inhibitor, which inhibits bacterial enzymes that would inactivate penicillins. P/T was studied in an in vitro dynamic model using an isogenic pair of *E. coli* with and without the Blac gene. Piperacillin alone inhibited the Blac negative organism but not the Blac+ bacteria. P/T readily eradicated both organisms as well as beta-lactamase producing *S. aureus*. The IATCG of the EORTC has completed a study of ~700 febrile neutropenic patients treated with P/T (4.5 G q6 hr) plus amikacin or ceftazidime plus amikacin. Clinical response occurred in 61% of P/T + amikacin treated patients and in 55% of patients treated with ceftazidime + amikacin (P = 0.05). Similar results were reported from a French trial using a lower dose. A current IATCG study is examining the role of P/T alone or with vancomycin in febrile neutropenic patients. Antipseudomonal penicillins with beta-lactamase inhibitors are useful in the empiric treatment of neutropenic patients with fever.