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Editorial Comment

Bloodstream infections in cancer patients

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The significance of bloodstream infections, or bacteremia, in the immunocompromised host with malignancy becomes increasingly confusing. The article by Castagnola and colleagues [1] brings good news about this once feared life-threatening complication of intensive anti-cancer therapy. In addition to showing a correlation between the intensity of chemotherapy and rates of infection, a more remarkable observation has been made. In the 153 bloodstream infections and 22 invasive mycoses in children with leukaemia, the fatality rate due to infection was 1.3%. Similarly favorable survival rates have been reported recently in a Canadian study [2]. Of 121 episodes of bacteremia in 76 paediatric oncology patients 100% survived the infection.

Surprisingly, the fatality rates in immunosuppressed children with cancer are impressively lower than those found in otherwise healthy children with community-acquired bloodstream infections. Gray [3] reviewed data on 2364 consecutive episodes of bloodstream infections over a seven-year period at Birmingham Children's Hospital in UK and reported an overall fatality rate of 2.4% and a fatality rate in previously healthy children of 5.3% (four times that of the paediatric oncology patients).

What accounts for the paradox of higher survival rates in life-threatening infections in immunocompromised patients with leukemia than in otherwise healthy immunocompetent children? One can speculate on many factors, with the development of new and more effective antibiotics being only one. Over the past three decades oncology centers have developed intensive, aggressive, comprehensive, and protocol-driven approaches to empirically initiate antibiotic therapy at the earliest appearance of fever or other signs of infection. Much of the reduction of fatality rates from approximately 25–30% in the early 1970s to the 1.3% of the current study can be attributed to this effort. Such an approach is often not taken with the otherwise healthy child who comes to the emergency room with only a symptom of fever.

A point of confusion comes in deciding the significance of a bacterium cultured from the blood. Is it a contaminant from the skin or mucous membrane flora? Does it represent a transient bacteremia that might clear without treatment; or, is it the cause of severe life-threatening disease? For example, within the 26 cases of coagulase negative staphylococcal bacteremia in Castagnola's study the spectrum of disease could range from none with a contaminated culture, to a localised catheter-site infection, or a serious life-threatening endocarditis. Unfortunately, in many instances we have no dependable method to definitively prove the relationship of isolates to disease processes, except perhaps clinical–pathological correlation with autopsy findings. Much research is now directed toward the development of new techniques to detect bacterial and fungal organisms, viable or not. These include DNA-based techniques, PCR-based detection, hybridisation probes; or protein-based methods by mass spectroscopy. Unfortunately, these molecular techniques give little, if any, insight into the disease process needing treatment.

Although the infection-related mortality has been greatly decreased with current antimicrobial therapy, infectious episodes continue to carry high morbidity and interrupt anti-cancer therapy. Thus, prevention of infection is desirable. Several regimens of antibacterial prophylaxis have been successfully utilised during high risk periods of neutropenia. This success is countered by potential adverse-effects of antimicrobial drugs,

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effects on bacterial resistance and the report in some studies that antibacterial prophylaxis has no impact on overall mortality rates.

van de Wetering and colleagues [4] applied meta-analysis and trial-specific odds ratios to compare studies published from 1966 to 2002. With the power of a rather large sample population accrued to randomised controlled trials they assessed the use of oral antibiotic prophylaxis for effectiveness in decreasing bacteremia and infection-related mortality in oncology patients during high risk periods of neutropenia. Prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMZ, cotrimoxazole) or quinolone-based regimens were compared to no prophylaxis. They found oral prophylaxis with either antibiotic regimen decreased the rate of Gram-negative bacteremia and infection-related mortality. The impact on mortality rates is especially encouraging for the use of antibiotics prophylactically in such patients.

Another important argument against the use of prophylactic antibiotics is the promotion of drug-resistant bacteria. The recent study of Kern and colleagues [5] is of interest in this regard. They showed the development of *in vitro* resistance of *Escherichia coli* (>50% of isolates) to fluoroquinolones during a five-year period of fluoroquinolone prophylaxis. When prophylaxis was stopped the incidence of Gram-negative bacteremia increased from 8% to 20% ($P < 0.01$). When fluoroquinolone prophylaxis was resumed the incidence of bacteremia decreased to pre-intervention levels of approximately 9%. This suggested the rates of *in vitro* resistance to *E. coli* is a poor indicator of the potential benefits associated with fluoroquinilone prophylaxis and adds another dimension to prophylactic antibiotics to be investigated further.

TMP-SMZ was originally introduced in the 1970s as prophylaxis for *Pneumocystis carinii* (also referred to as *P. jiroveci*) pneumonitis (PCP) in children with leukemia and other malignancies [6]. This regimen reduced the rate of the life-threatening pneumonitis from 20% to 0% and showed reduction in the incidence of other infections as well. Quinolones have no anti-PCP effect.

What is one to do? Plan your practice to fit local circumstances, which vary from institution to institution and country to country. National and global guidelines by expert panels are available for management of infections in febrile neutropenic patients and the use of antimicrobial prophylaxis for bacterial, fungal and *Pneumocystis* infections. We prefer to use TMP-SMZ for PCP prophylaxis in all patients at risk for this infection and add additional antibiotic prophylaxis only during neutropenic periods for special problem cases.

Conflict of interest statement

None declared.

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