There are significant differences in the risk of respiratory disease epidemics among U.S. Army, Navy, Marine Corps, and Air Force personnel, and service-specific prevention programs [9–11] have been developed with these differences in mind. Service-specific epidemiological study and efficacy calculations, based upon the duration of vaccine protection, will be necessary to effectively consider potential future U.S. military acellular pertussis vaccine use.

Third, let us assume that acellular pertussis vaccines used in military populations would need to decrease the susceptibility rate substantially within the first week of training in order to be valuable. It is plausible that a single dose of acellular pertussis vaccine, administered upon entry into training, could impact susceptibility within the first 7 days. Although not directly correlated to protection, specific humoral and cell-mediated immune responses have been demonstrated for adults within 7 days of receiving acellular pertussis vaccines [12, 13].

We agree with Drs. Christopher, Pavlin, and Bustamante that the dynamics of pertussis infection among military populations are complex and that they are dependent upon a number of variables. Our study [1] was intended to evaluate the burden of pertussis illness among symptomatic military trainees and the potential for the reduction of respiratory disease-associated morbidity with future vaccine use.

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References

Fluconazole and the Changing Epidemiology of Candidemia

Sir—We read with great interest the article by Abi-Said et al. [1] concerning the epidemiology of candidemias at The University of Texas M.D. Anderson Cancer Center. The authors documented a decrease in the incidence of infections due to Candida albicans and Candida tropicalis, an increase in the incidence of infection due to Candida krusei, and a trend toward an increase in the incidence of Candida glabrata fungemia during the 5-year period between 1988 and 1992. This change in the local epidemiology appeared to correlate with the administration of fluconazole prophylaxis, which was introduced in 1989 and had become standard practice since 1990 for treatment of patients with leukemia. However, in an editorial response, White [2] objected, stating that establishment of a causal relationship remains controversial for the following reasons: (1) this correlation was seen in only retrospective and uncontrolled analyses [1, 3, 4], whereas other prospective and placebo-controlled studies did not demonstrate an impact of fluconazole prophylaxis on the etiology of candida infections [5–6]; (2) in some retrospective studies of patients with cancer, it has been determined that C. krusei infection is not associated with fluconazole use [7]; (3) the proportion of cancer patients with candidemia due to C. krusei has not varied over the past 2 decades [8]; and (4) finally, the influence of undetected nosocomial factors other than fluconazole use could contribute to occasional increases in non—C. albicans candidal infections [9].

At our center between 1990 and 1993, most of the patients who underwent intensive chemotherapy for a hematologic malignancy received fluconazole prophylaxis. During that period, we participated in a multicenter comparative trial that demonstrated that fluconazole, at a dose of 150 mg/d, is as effective as oral amphotericin B in the prevention of fungal infections in patients with leukemia [6]. Since then, the administration of oral amphotericin B
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Candida parapsilosis; ■ ■ ■ = Candida krusei; X X X = Candida tropicalis.

Figure 1. Episodes of candidemia per year of onset and cause of different Candida species (Dipartimento di Biotecnologie Cellulari ed Ematologia, Rome, 1986 through 1997). — C. parapsilosis; ○ = C. albicans; ▲ = C. krusei; X = C. tropicalis.

prophylaxis has become standard practice for patients who undergo intensive chemotherapy or autologous bone marrow transplantation, and fluconazole has been administered only to those receiving allogeneic bone marrow transplants. From January 1986 to September 1997, 145 episodes of candidemia in patients with hematologic malignancies were documented at our institution. The overall incidence of candidemia was 15.5 episodes per 1,000 hospital admissions. C. albicans was isolated in 24% of the patients, Candida parapsilosis in 34%, Candida guilliermondii in 14%, C. tropicalis in 11%, C. krusei in 8%, C. glabrata in 2%, and other Candida species in 7%.

As shown in figure 1, the incidence (per 1,000 hospital admissions) of C. albicans and C. tropicalis infections did not change significantly over the years. There was an increasing incidence of C. parapsilosis infection, as we reported recently [10], probably associated with the progressively increasing numbers of central venous catheters inserted in our patients. Of 11 episodes of C. krusei fungemia that occurred over an 11-year period, 9 episodes (82%) occurred during a 4-year period, 1990–1993, which corresponded exactly to the period during which we used primarily fluconazole for prophylaxis. In fact, the use of fluconazole prophylaxis and its replacement with oral amphotericin B corresponded to an increase and to a decrease, respectively, in the incidence of C. krusei fungemias.

With the limitations due to the retrospective analysis and to the relatively low incidence of C. krusei fungemias, a temporal correlation of fluconazole use and of the increasing incidence of C. krusei infections appears to be suggested strongly by both Abi-Said et al. [1] and our own experience.

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