prompt investigation and empirical treatment of presumptive acute bacterial infection. Analogously, the association between the eosinophil count and parasitic infection is well known [1]. However, the possible usefulness of the eosinophil count as an indicator of bacteremia has not been well studied.

A marked diminution in the number of circulating eosinophils is generally regarded as a physiologic consequence of acute bacterial infection. Peripheral blood eosinopenia was documented by Bass [2] in experimentally induced bacterial infection in mice. Xanthou [3] and Weinberg et al. [4] studied blood counts in newborn infants and found that eosinophil counts decreased to as low as 0 in subjects who developed acute bacterial infection. Peripheral blood eosinopenia is well described in adult and pediatric patients with typhoid fever [5] and has been observed in association with other agents of sepsis [6].

The potential utility of eosinophil counts as predictors of bacteremia was investigated by Lipkin [7] in a study of 75 adult inpatients with positive results of blood cultures that showed that, as the number of positive blood culture results per patient increased, the percentage of eosinophils in the peripheral blood smear decreased [7]. No patient with >2 positive blood culture results had a peripheral blood smear with >1% eosinophils, demonstrating a possible correlation between eosinopenia and bacteremia. We sought to confirm this relationship between decreased eosinophil count and bacteremia.

We reviewed the inpatient medical records of 171 patients with blood cultures positive for gram-negative bacilli, *Staphylococcus aureus*, and *Streptococcus* species during a 6-month period at the University of North Dakota School of Medicine and Health Sciences (Fargo). Immunosuppressed patients with bacteremia were excluded from analysis, as were patients with neutropenia (i.e., those with <1000 WBCs per high-power field). Case patients were age- and sex-matched with control patients with negative results of blood cultures during the same study period. Total leukocyte count and relative and absolute eosinophil counts were determined for both case and control patients, and χ² analysis was used to compare results (table 1). Sensitivity, specificity, and positive and negative predictive values were calculated in the usual manner. We found no utility associated with eosinopenia (defined as a relative eosinophil level of 0%) for predicting bacteremia and conclude that the absence of peripheral blood eosinophils cannot be used as a clinically reliable marker of bacteremic infection.

<table>
<thead>
<tr>
<th>Eosinophil level, % of WBCs</th>
<th>Results of blood cultures for bacteremia, no.</th>
<th>Statistical data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>➔1</td>
<td>75</td>
<td>91</td>
</tr>
<tr>
<td>0</td>
<td>96</td>
<td>83</td>
</tr>
</tbody>
</table>

Table 1. Relative eosinophil counts in and results of statistical analysis for 171 patients with or without bacteremia.

**Pyomyositis and Cutaneous Abscesses Due to Mycobacterium avium: An Immune Reconstitution Manifestation in a Patient with AIDS**

Sir—The immune reconstitution syndrome (IRS) comprises inflammatory responses to preexisting infections triggered by restoration of immune function in HIV-infected individuals receiving HAART [1, 2]. Although IRS associated with *Mycobacterium avium* complex (MAC) is reported to cause focal lymphadenitis in the early weeks of HAART [3, 4], herein we describe an unusual case in a patient who presented with pyomyositis and skin abscesses.

A 45-year-old Ugandan female residing in the United Kingdom presented with cryptococcal meningitis and HIV-1 infection with a CD4 lymphocyte count of 84 × 10⁶ cells/L and a plasma virus load of >5 × 10⁶ RNA copies/mL. She received amphotericin and flucytosine for 2 weeks,
followed by oral fluconazole, and she made a good recovery. Trimethoprim-sulphamethoxazole was also given as PCP prophylaxis. At follow-up 1 month later, she mentioned incidentally that she had experienced mild discomfort in her left calf for $\sim 1$ year. A focal, noninflammatory swelling 3 cm in diameter was evident within the left gastrocnemius muscle, and outpatient radiological imaging was arranged.

The patient commenced HAART consisting of zidovudine, lamivudine, and efavirenz. Two weeks later, she was readmitted to the hospital ill with fever (temperature, 39°C), a tender, inflammatory swelling measuring 9 cm in diameter in the left gastrocnemius muscle, and bilateral inguinal lymphadenopathy. During the following week, 8 fluctuant skin abscesses, each $\sim 3$ cm in diameter, also developed over her limbs. A chest radiograph showed a new, small area of cavitating consolidation in the left upper lobe although the patient had no respiratory symptoms. Her serum C-reactive protein concentration was 113 mg/L (normal range, $< 10$ mg/L). Both routine and mycobacterial blood cultures were sterile. A soft-tissue mass within the gastrocnemius muscle was visualized by MRI (figure 1).

Aspirations of this mass, the inguinal lymph nodes, and skin lesions all yielded pus that contained numerous acid-fast bacilli. Conventional quadruple-drug antituberculosis treatment was started, and the muscle abscess was surgically incised and drained. Histological examination of specimens revealed granulomatous inflammation. *M. avium* was subsequently cultured from pus samples, and so antituberculous treatment was changed to rifabutin, clarithromycin, and ethambutol.

The rapid development of pyomyositis, lymphadenitis, and skin abscesses coincided with a marked fall in plasma HIV load to $10^3$ copies/mL and a rise in CD4 count to $110 \times 10^3$ cells/L after only 2 weeks of HAART. Although the patient’s mild discomfort in the left calf suggests that low-grade MAC pyomyositis may have been present for $\sim 1$ year, the development of a severe local and systemic inflammatory reaction to *M. avium* infection 2–3 weeks after starting HAART suggests that these clinical manifestations were attributable to IRS. With good adherence to treatment, the skin abscesses and the discharge from the calf incision site resolved within 5 months.
This is the first report of MAC pyomyositis and skin abscesses presenting as IRS in a patient receiving HAART. There were previous single reports of MAC pyomyositis [5] and MAC skin abscesses [6] in patients with AIDS during the era before HAART. Of interest, however, in both of these earlier reports, the unusual clinical presentations developed shortly after the patients had started zidovudine monotherapy. We speculate that these may have been due to IRS that was not recognized in the pre-HAART era.

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References

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Therapy for Severe Histoplasmosis: What’s Best?

Str—The interesting case of disseminated histoplasmosis presented by Ayi and Smith [1] raises several topics for consideration. Demonstration of splenic nodules too numerous to count is somewhat unique but not unexpected, since calcified splenic lesions are common in patients with cured histoplasmosis. Other important issues raised by this case include selection of antifungal therapy for severe histoplasmosis and the role of adjunctive measures.

Despite excellent care and therapy with high-dose amphotericin B lipid complex, the patient died of septic shock and acute respiratory distress syndrome (ARDS), which poses the question: What is the best antifungal agent for severe histoplasmosis? Earlier studies showed that mortality rates approach 50% among patients with AIDS and severe histoplasmosis, usually because of renal impairment that interfered with aggressive administration of amphotericin B (AmB) [2].

 Accordingly, a double-blind trial was conducted comparing liposomal AmB with AmB deoxycholate [3]. The liposomal formulation was selected because it was the least nephrotoxic, permitting aggressive therapy; because it achieved the highest blood levels, in case that was important to the outcome; and because it penetrated the CNS best, since CNS involvement is prominent in fatal cases. Mortality was significantly lower with liposomal AmB treatment (1 of 53 patients died, but not of histoplasmosis) than with AmB deoxycholate treatment (3 of 24 patients died of histoplasmosis).

Unfortunately, because of cost, use of the liposomal formulation of AmB is often restricted, and it is not available unless therapy with the other lipid formulations fails or patients are intolerant of these cheaper formulations. Whether the other lipid formulations would work as well as liposomal AmB is unknown, but their efficacy should not be assumed.

What about combination therapy? Although there are no data for humans, my colleagues and I have studied combination therapy in a murine model, which showed antagonism between AmB and fluconazole [4, 5]. Although itraconazole was not antagonistic to AmB, outcomes with this combination were no better than with AmB alone. The activities of caspofungin [6, 7] and nikkomycin Z [8, 9] against histoplasmosis are uncertain, and use in combination with AmB cannot be recommended.

A second issue is the role of adjunctive therapy. Corticosteroids have been used in conjunction with AmB in patients with severe pulmonary histoplasmosis [10] and appear to hasten recovery (author’s unpublished observation). Whether they would be effective in patients with ARDS and septic shock is unknown, but experience in patients with AIDS coinfected with Pneumocystis carinii and Histoplasma capsulatum suggests that the combination can be administered safely (author’s unpublished observation). Granulocyte-macrophage colony-stimulating factor and IFN-γ have demonstrated marginal benefit in murine models [11, 12] but have not been studied in human patients, and use of these agents is not recommended.

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References
5. Haynes RR, Connolly PA, Durkin MM, et al. Antifungal therapy for central nervous system...