Yield of Bone Marrow Culture in the Diagnosis of Infectious Diseases in Patients with Acquired Immunodeficiency Syndrome

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Patients with acquired immunodeficiency syndrome (AIDS) are more susceptible to opportunistic pathogens, which include Pneumocystis carinii (4), Salmonella spp. (7, 15), Toxoplasma gondii (L. R. Sharer and R. Kapila, Acta Neuropathol., in press), Mycobacterium tuberculosis (10), Mycobacterium avium-Mycobacterium intracellulare complex (MAI) (10), Mycobacterium xenopi (5), and Cryptococcus neoformans (R. H. K. Eng, E. Bishburg, S. M. Smith, and R. Kapila, Am. J. Med., in press). These infections can present with an insidious onset, and the diagnosis can often be difficult. Therefore, it is important to know the diagnostic yields of the procedures used to recover these pathogens. Hence, the medical records of AIDS patients were retrospectively reviewed to determine the yield of bone marrow aspirations and cultures for the diagnosis of these infectious diseases.

The medical records of patients diagnosed as having AIDS from June 1981 to June 1985 at the Veterans Administration Medical Center, East Orange, N.J., and University Hospital, Newark, N.J., were reviewed. These two institutions have a total of 1,200 acute-care beds and serve the Newark and Northern New Jersey area. Only patients who met the criteria for AIDS as determined by the Centers for Disease Control were included in the study (3).

Specimens of bone marrow and other deep body sites were cultured on blood, chocolate, and Sabouraud dextrose agars and into brain heart infusion and chopped meat glucose broths. The specimens were inoculated into Dubos broths with subcultures onto Lowenstein-Jensen agar. All cultures were incubated in 5 to 8% CO2 at 35°C. When requested, specimens from other sites (spuva, urine, and stools) were also cultured on Lowenstein-Jensen agar for mycobacteria (16).

Blood was cultured for bacteria and fungi in BACTEC 6B and 7D bottles and monitored radiometrically. A limited number of blood specimens were processed for mycobacteria in the Du Pont Isolator (Du Pont Co., Wilmington, Del.) with inoculation onto blood, chocolate, Lowenstein-Jensen, and Sabouraud dextrose agars (11). Only data obtained from specimens submitted in Du Pont Isolators were included in the analysis of mycobacterium yields.

Acid-fast bacilli were referred to the New Jersey State Department of Health, Trenton, N.J., or to the Veterans Administration Reference Laboratory for Tuberculosis and Other Mycobacterial Diseases, West Haven, Conn., for identification. Yeasts were identified by microscopic morphology and the Uni-Yeast-Tek (Flow Laboratories, Inc., McLean, Va.) or Minitek Yeast Assimilation system (BBL Microbiology Systems, Cockeysville, Md.) and by pigment production on birdseed agar. Filamentous fungi were identified by microscopic morphology.

During the 4-year period, 200 patients with AIDS were diagnosed, with 50 (25%) having had bone marrow aspirations or bone marrow biopsies performed. This group consisted primarily of patients with a history of parenteral drug abuse (90%). Of these 50 patients, 37 had the marrow examined for evaluation of unexplained fever, 10 had it examined for suspected granulomatous infections, and 3 had it examined for evaluation of a deficiency in peripheral blood elements. These 50 patients had been diagnosed for less than 12 months or were pre-AIDS at the time of examination and subsequently met the criteria for AIDS. Twenty-five patients (50%) had one prior hospital admission for AIDS-related diseases, 16 (32%) had two prior admissions, and 9 (18%) had three or more prior admissions. Half the 50 patients had prior opportunistic infections, of which 64% were caused by P. carinii.

A comparison of AIDS patients in whom marrow cultures were positive (42%) with those whose cultures were negative (58%) indicated that all patients had normal to mildly elevated serum alkaline phosphatase levels, the same incidence of granulocytopenia and thrombocytopenia, and the same degree of pyrexia. All patients had additional suspected sites of infection, including the lungs and meninges. Neither group had evidence of bone pain, and there were no predictive clinical parameters to distinguish patients with positive bone marrow cultures.

For 14 patients in whom the bone marrow was aspirated as well as biopsied, organisms were seen microscopically on histologic examination on all specimens. Mycobacteria were seen in abundance without accompanying formation of granuloma, or cryptococci were seen without accompanying evidence of marrow necrosis. Of the three bone marrow aspirations performed because of abnormal peripheral blood

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counts, only one was culture positive. For the 47 bone
marrows obtained because of unexplained fever or sus-
ppected granulomas, the pathogen yield was 42.5% (20 of 47).
The concurrent culture results from the different body sites
are shown in Table 1. Four of 13 patients with C. neofo-
rmans infections had positive bone marrow cultures. All four
patients also had the organism recovered from blood cul-
tures. The remaining nine patients with cryptococcal infec-
tions had the organism isolated from only the cerebrospinal
fluid. In cryptococcal infections, the most sensitive test was
a serum cryptococcal antigen determination (Eng et al., in
press). For the 17 patients with MAI infections, the bone
marrow aspirate was a sensitive test, with 16 of 17 patients
being positive. Additional specimens which gave significant
yields included liver (4 of 6) and sputum (5 of 12) specimens.
Of the six patients who had blood processed by the Du Pont
Isolator, only one was positive for MAI. Also, 3 of 10
patients had MAI isolated from the stool. For M. tubercu-
losis infections, sputum had the highest yield (10 of 20). The
overall pathogen yield of bone marrow cultures in all AIDS
patients was 21 of 50 or 42%.

For comparison, results for 161 bone marrow aspirations
or biopsies from non-AIDS patients from 1976 to 1985 were
reviewed. Some of these specimens could have been from
undiagnosed AIDS patients. Four of the 161 specimens were
culture positive, one each for MAI, M. tuberculosis, Esch-
erichia coli, and Basidiobolus spp. The latter was considered
a laboratory contaminant, and the patient improved with
out therapy. The patient with MAI was a drug addict lost to
follow-up and could have had AIDS. The diagnostic yield
in this group was 2.1% (3 of 161), a value much lower than that
of confirmed AIDS patients.

Bone marrow culture was previously reported to be a
valuable diagnostic procedure (8, 13, 14). In this study, the
yield was 42%, similar to that reported by Horsburgh et al.
(8), 41%. In the present study, marrow examination had a
yield of 94.1% for MAI, 30.8% for C. neoformans, and 5%
for M. tuberculosis.

Bone marrow examination has been shown to be useful for
the diagnosis of infections by intracellular organisms in
non-AIDS patients (1, 2, 6, 9, 12, 17), and its usefulness
was also affirmed in this study of AIDS patients. Our patients
had a conglomeration of indications for marrow examination,
and the many factors which contributed to the arguments
for the procedure cannot be retrieved, but the overall results
were rewarding because the pathogens isolated were treat-
able. The number of Du Pont Isolator blood cultures ob-
tained from patients with MAI was small, and a comparison
of this method of culture and bone marrow culture was not
possible. Enthusiasm for bone marrow culture should how-
ever be tempered, because it is still considered an invasive
procedure. In view of the wide availability of the DuPont
Isolator, blood cultures by this noninvasive procedure
should always be performed first. Our data with the Du Pont
Isolator did not indicate a high yield, but the data are limited
and the blood samples were split among four types of culture
media, of which only one can support mycobacterial growth.
When no organisms are isolated from the blood, perhaps
bone marrow cultures may be considered as a low-morbidity
adjunctive procedure for diagnosis in the febrile AIDS
patient.

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### TABLE 1. Relative diagnostic yield from culture of specimens from various body sites

<table>
<thead>
<tr>
<th>Organism isolated</th>
<th>Bone marrow</th>
<th>Liver</th>
<th>Sputum</th>
<th>Urine</th>
<th>Blood</th>
<th>Stool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptococcus neoformans</td>
<td>4/13</td>
<td>2/3</td>
<td>0/5</td>
<td>0/13</td>
<td>5/13&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Mycobacterium avium-Mycobacterium intracellulare</td>
<td>16/17</td>
<td>4/6</td>
<td>5/12</td>
<td>0/16</td>
<td>1/6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3/10</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>1/20</td>
<td></td>
<td></td>
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</table>

<sup>a</sup> The denominator is the number of AIDS patients with the infection who had samples submitted for culture from the site.

<sup>b</sup> Data from BACTEC 6B and 7D system bottles.

<sup>c</sup> Data from Du Pont Isolator.

