Comparative yield of Salmonella typhi from blood and bone marrow cultures in patients with fever of unknown origin

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Abstract
Over three years, a comparative study on 100 selected patients with fever of unknown origin was undertaken to determine the yield of Salmonella typhi from their blood and bone marrow cultures. The results indicate that in patients who had an infection with S. typhi the organism was isolated from the bone marrow in all of them and from the blood in only 66%. This suggests that bone marrow cultures may be attempted when blood cultures are negative for bacterial growth after three to four days of incubation.

Infection with Salmonella typhi is one of the commonest causes of typhoid fever in Karachi, Pakistan. Over three years, we processed 21,356 blood samples from patients suspected of typhoid fever. The average isolation rate for Salmonella from these blood cultures was 5.15%. Further subtyping of these Salmonella species showed an incidence of S. typhi 83%, S. paratyphi A 11.8%, S. paratyphi B 4.1% and S. paratyphi C 0.9%. Definitive diagnosis is made on the basis of isolation of the organism from blood. Without antibiotics blood cultures are positive in over 80% of the patients seen in the first week of illness. Twenty to 30% of untreated patients have positive blood cultures as late as the third week of illness.

Antimicrobial treatment diminishes the possibility of recovery of the organism in blood. In patients who have been treated cultures of supplementary sites such as bone marrow may be a better source of organisms than blood. We conducted a study on 100 selected patients whose blood and bone marrow were cultured for S. typhi to determine the yield of S. typhi from these two sites.

Methods
Blood and bone marrow samples were collected from 100 patients who had fever of unknown origin. Each sample was collected in two blood culture bottles containing brain heart infusion and thioglycollate broth, respectively. About 5 ml of venous blood was inoculated in each bottle containing 45 ml of broth; similarly, 0.5 ml-1.0 ml of bone marrow was collected in each bottle containing 45 ml of broth. Bottles were sent immediately to the laboratory and incubated at 37°C for seven days. Each bottle was examined daily and subcultured on to blood agar and MacConkey's media after 24, 48, and 72 hours, and on the seventh day of incubation.

Non-lactosing fermenting colonies from MacConkey's medium were tested for S. typhi by slide agglutination test with specific antisera. Biochemical tests were performed by using API 20E strips.

Results
The samples of blood and bone marrow were processed at The Aga Khan University Hospital's diagnostic laboratory. S. typhi was isolated from the blood (n = 58) or bone marrow (n = 88). The blood and bone marrow cultures of 12 patients showed no growth for any bacteria. Thirty blood samples from 88 patients (whose bone marrow were positive) showed no bacterial growth.
Discussion
Of the 100 patients, 88 had S typhi in their blood or bone marrow, or both. This confirms our observation that S typhi is a common cause of fever of unknown origin in Karachi. The remaining 12 patients whose blood or bone marrow cultures did not grow any organism recovered without any antibiotic treatment. This suggests that these patients probably had some viral infection(s).

In the patients with S typhi infection (typhoid fever) the organism was isolated from the bone marrow of all of them. The organism was also isolated from the blood of 58 (66%) patients. This means that bone marrow culture could confirm a diagnosis of typhoid fever in patients whose blood cultures are negative.

One of the reasons for blood cultures being negative and bone marrow being positive in typhoid fever may be antibiotic treatment before collection of blood for culture. An inappropriate or suboptimal antibiotic regimen may diminish or eliminate the organism from blood, but S typhi, being an intracellular organism, persists in the reticuloendothelial system including bone marrow. The intracellular location of bacteria protects them from conventional chemotherapeutic measures.14

We recommend that when typhoid fever is suspected blood for culture must be taken before antibiotics are given. In the case of patients who have already received antibiotics and whose blood cultures do not show any bacterial growth after three to four days of incubation, bone marrow should be cultured.

Abstract
Although most circulating T cells in normal subjects express both CD3 and CD5 antigens on the cell surface, a small number lack the CD5 antigen. Recipients of allogeneic bone marrow transplants develop increased numbers of CD3+ CD5− cells, particularly those who develop graft versus host disease (GVHD). This CD3+ CD5− population may rise transiently in patients who have received an autologous bone marrow transplant (BMT) and in patients following completion of intensive chemotherapy for acute myeloid leukaemia (AML). These findings suggest that these CD3+ CD5− cells are a normal component of the regenerating lymphoid system after BMT or chemotherapy.

The CD5 molecule is a 67 000 molecular weight glycoprotein present on the surface of most human thymocytes and peripheral T cells and on a subpopulation of B cells.14 A small proportion of CD3+ T cells in normal subjects do not express CD5.5 These cells are CD2+, CD8+, CD4− and CD16− and express low levels of CD7.5 They seem to be functional in that they have been shown to express normal cytolytic activity.5

In this study we measured CD3+ CD5− cells after autologous bone marrow transplantation and after drug treatment.

Methods
Samples of whole blood were collected in