Estimation of Bone Marrow Cellularity: Reply

To the Editor:

We appreciate Dr. Drewinko's clarification of the term "aspirate" as used in our report. Although the technique of the aspirate smear preparations was described in Materials and Methods, the more precise term "aspirate smear preparation" would be more appropriate.

The experience by others as described by Dr. Drewinko has in general demonstrated the superiority of cellularity determination using the marrow aspirate clot section technique as opposed to the smear or spread preparation. We have not routinely employed the former technique, however, preferring the routine use of the biopsy for nearly all marrow examinations at our institution. Furthermore, our report concerned the results of marrow cellularity primarily in children with leukemia (241 of 244 biopsies); 39% were hypercellular by biopsy. In 36% of these hypercellular marrows, it was difficult to find adequate marrow "flecks" or spicules for selection of smear preparations, thus leading to the false impression of a hypocellular marrow. It is in this circumstance that the biopsy proves most helpful. Whether concentration of the marrow by the "clot section technique" would have provided an adequate number of "bone marrow units" for inspection is questionable.

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Endotoxin Contamination of Some Erythropoietin Preparations: An Emerging Question

To the Editor:

In recent correspondence,1,2 a question has emerged about the possible contamination of erythropoietin preparations and the possible interference with its activity on hematopoiesis. Dr. Boggs has written:1 "I have assumed no proof for that assumption." Dr. Chamberlain has replied:2 "Without endotoxin assay, however, one cannot assume this to be true, and other contaminants or even erythropoietin may be responsible."

We suggest a possible solution for this problem by the use of the Limulus assay for the qualitative and quantitative detection of gram-negative bacterial products.3 Since this test can be completed in a little over 1 hr, it may be possible to monitor erythropoietin samples shortly before an experiment. On the other hand, in 1974, Siegel et al.4 demonstrated a pyrogenic effect and a positive Limulus assay in erythropoietin preparations from human urine. These authors proposed a method for removing contaminating endotoxin by incubating Limulus amebocyte lysates and the samples.

In our laboratory we have examined some erythropoietin preparations from sheep's plasma (step I and step III) with the Limulus assay and have demonstrated consistent positivity with considerable amounts of endotoxin (ranging between 10 and 1 μg/ml). This level is able to modify the cellularity of the bone marrow and peripheral blood5,6 and can interfere with erythropoietin activity.7 Most recently Spivak et al.8 have proposed a simple method of purification by affinity chromatography for removing contaminating agents. Subjecting this purified material to detoxification by the Limulus amebocyte lysate method should permit a clearer understanding of what effects can be attributed to the hormone.

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REFERENCES

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Endotoxin contamination of some erythropoietin preparations: an emerging question [letter]

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