CORRESPONDENCE

Erythropoiesis

To the Editor:

In their paper entitled “Erythropoiesis after Exchange Transfusion in Hemolytic Anemia,” which purports to disprove our thesis of a dual control of erythropoiesis, Erslev and McKenna have overlooked basic features in the consideration of the steady state, leading to misinterpretation of data which we have presented on the effect of exchange transfusion on red cell production in hereditary spherocytosis.

In our patient who was described in detail and subsequently referred to in a review article which Erslev and McKenna cite, the study was described as follows:

"The patient had a hemoglobin that varied from 13 to 13.8 Gm. per cent; reticulocytes, 150 to 225,000/cu. mm.; indirect bilirubin, 4 mg. per cent; fecal urobilinogen 380 mg./day; and 51Cr T ½, 14 days. This patient had a partial exchange transfusion in which 1500 cc. of her blood was removed and replaced with 1500 cc. of normal blood. In the 100 days following the transfusion, the hemoglobin remained in the range of 13 to 13.8 and the mean values were slightly lower than those observed prior to transfusion. The reticulocytes decreased immediately after transfusion and in the first 30 days ranged from 85 to 120,000/cu. mm. Thereafter, there was a gradual rise to the pretransfusion level."

There are two points to be considered: (1) the reticulocyte count remained suppressed for a period of 30 days, and (2) there was no rise in hemoglobin. A decrease in reticulocyte values for a period of 30 days cannot be "easily explained" by "mechanical removal" of reticulocytes during the course of exchange, as stated by Erslev and McKenna. It has been reasonably well established that the reticulocyte lifespan is 1 or 2 days. Accordingly, a reticulocytopenia of 30 days cannot be attributed to "mechanical removal" of such a short lifespan cell.

The other argument we advanced was that the hemoglobin remained constant for a period of 100 days after exchange. It is noteworthy that in Erslev's 3 cases of exchange of hereditary spherocytosis, the hemoglobin either remained constant or decreased slightly during the rather brief period of observation. In their case of autoimmune disease, there was no change in hemoglobin in the 5 days after exchange and prior to the hemolytic transfusion reaction; the reticulocyte count fell from an average of about 5 per cent prior to exchange to 2–3 per cent after exchange.

The relationship of peripheral hemoglobin (or hematocrit) to the rate of production and destruction is a simple one:

a. In a steady state the hemoglobin is constant and production = destruction.

b. When the hemoglobin is increasing production > destruction.

c. When the hemoglobin is falling production < destruction.

It can be seen that if the hemoglobin remains constant after an exchange transfusion, production must equal destruction.

If, as Erslev and McKenna contend, the rate of destruction decreased substantially and the production rate remained constant, there must be a rise in hemoglobin concentration.

In contrast to our case, the authors have followed their patients only 3 to 5 days after completion of the exchange transfusion. This may not have been sufficient time to evaluate either the peripheral reticulocyte count or the hemoglobin.

The authors have chosen to use the iron turnover/100 ml./24 hours as a measure of cell production. The difficulties of equating iron turnover with red cell production are, we believe, pointed up in some of the authors' data—for example, J. D. This patient had an increase in iron turnover from 1.6 before, to 2.4 after, exchange. It seems clear that if in addition to a decrease in the rate of destruction there was a further increase of 50 per cent in the rate of production, there should have been a rapid rise in circulating hemoglobin. This was not evident.
One can only conclude that the serum iron measurements do not adequately portray the events which are occurring in respect to cell production. The conclusion is supported by much recent work (e.g., Sharney et al., whose work raised serious questions of the validity of a single pool model, particularly without concomitant measurement of red cell uptake). The argument that the failure to observe an increase in hemoglobin may reflect changes in plasma volume, is inadmissible, because it would also negate the measurement of iron turnover per 100 ml which assumes a constant plasma volume throughout the period of study.

We feel that the simple, but unassailable observation that the hemoglobin did not change in our patient during several months provides cogent testimony that following the exchange production decreased. Erslev and McKenna's observations fail to provide contrary evidence. In fact, the lack of rise in hemoglobin would tend to support our observation.

FREDERICK STOHLMAN, JR., M.D.
St. Elizabeth's Hospital
Tufts Medical School
Boston, Massachusetts 02135

REFERENCES

(Rebuttal)

To the Editor:

A number of important observations on anephric man and on patients with compensated hemolytic anemia have seriously challenged the hypothesis that red cell production is controlled exclusively by hypoxia via the production of renal erythropoietin. These observations have suggested the existence of dual or even multiple control mechanisms. The study reported by Erslev and McKenna was designed to confirm an interesting observation in support of the thesis of a dual control of red cell production made by Dr. Stohlman and reported by him in the New England Journal of Medicine. Dr. Stohlman reported that exchange transfusion in a patient with hereditary spherocytosis led to a "prompt decrease in red cell output."

Our data on the effect of exchange transfusion in four patients completely failed to confirm Dr. Stohlman's observation. The erythroid activity in our patients was assessed by three different methods: daily reticulocyte counts, bone marrow examination, and serum iron turnover. We hold no brief for the absolute accuracy of any of these methods in measuring the rate of red cell formation. However, they are recognized to be of value in assessing changes in the rate of red cell production in the same patient and it seems difficult to disregard the fact that all three parameters in four patients failed to reveal a significant decrease in red cell production after exchange transfusion.

The patients were followed only 3 to 5 days before they underwent splenectomy, and we do not know what would have happened to the hemoglobin concentration if they had been followed long enough. However, we find it hard to accept the significance of the "simple but unassailable observation" of Dr. Stohlman in regard to hemoglobin concentration, when we were unable to confirm the more important aspect of his observation dealing with red cell output.

Unfortunately, our study did not shed light on the question of how a patient can maintain an accelerated rate of red cell production despite a normal hemoglobin concentration (compensated hemolytic anemia), and we certainly did not "purport to disprove the thesis of a dual control of erythropoiesis." We merely attempted to confirm one important observation—and we failed.
CORRESPONDENCE

ALLAN J. ERSLEV, M.D.
Cardeza Foundation
Jefferson Medical College
Philadelphia, Pennsylvania 19107

P. J. McKENNA, M.D.
Cardeza Foundation
Jefferson Medical College
Philadelphia, Pennsylvania 19107

Auer Bodies

To the Editor:

I was glad to read that Dr. James A. Freeman in his recent article "Origin of Auer Bodies," in your April issue of Blood agrees with my original proposal that Auer bodies are abnormal lysosomes (Blood 24:305, 1964).

In order to prevent any possible further misquotation in the literature, I would like to correct the misstatement in his article that I demonstrated alkaline phosphatase activity in Auer bodies. This is not so. In fact, I made a special point of suggesting "that while acid phosphatase is present in Auer bodies, the absence of alkaline phosphatase may be indirect evidence that this enzyme resides in a different organelle from the granule containing acid phosphatase in mature leukocytes."

ARTHUR F. GOLDBERG, M.D.
Department of Hematology
Hospital for Joint Diseases
New York, N. Y. 10035

Myeloblastic Leukemia

To the Editor:

We should like to report briefly on an unusual association of a bee sting and myeloblastic leukemia.

M. H., a 22-year-old Polytechnic Institute student, was stung by a bee on the right thigh while riding a motorcycle in his shorts (August 7, 1965). He removed the sting at once. Twenty minutes later the site of the sting became red and swollen and on the following day he developed fever up to 38 C., experienced joint and muscle pain, and his supraclavicular lymph nodes became greatly enlarged. Five days later, the temperature returned to normal and the lymph nodes decreased in size. The white blood count was 15,000 with a normal differential count.

Several days later cervical lymphadenopathy recurred and was most marked in the right supraclavicular region. Biopsy was taken and the histologic examination (Prof. Kowalszykowa) was strongly suggestive of neoplastic proliferation (? lymphosarcoma).

A month after the original episode the patient was admitted to the clinic (October 6, 1965). Examination revealed generalized lymphadenopathy, which was most pronounced in the right cervical area. Examination of the blood showed: hematocrit 15 per cent; red blood count 2,000,000; white blood count 48,000, of which 87 per cent were blast forms (myeloblasts ?); platelet count. 4000; clotting time 9 minutes, prothrombin consumption time 9 seconds; EST '52/165; serum iron levels, iron binding capacity, copper levels and other chemical tests were all normal. Blood and urinary RNase were within normal limits. Blood proteins were 6.1 Gm. per cent with increase in a1 and a2. Immunologic. immunolectrophoresis, cytochemical and cytoenzymatic studies were all normal.

Bone marrow examination showed myeloblastic and paramyeloblastic proliferation, typical of myeloblastic leukemia.

The patient died on December 10, 1965, with signs of profound hemorrhagic diathesis. Autopsy performed in the Department of Pathologic Anatomy revealed changes of typical myeloblastic leukemia.

Our observation is not a unique one. In 1924, Parrisius and Heimberger reported a similar case (Deutsche Archiv. Klin. Med. 145:555). We hope that this letter will call attention to the rare but not isolated coexistence of insect bite and leukemia, and will prompt further reports.

J. Aleksandrowicz, M.D., Professor
IIIrd Medical Clinic
School of Medicine
Krakow, Poland

L. Pawlik, M.D.
IIIrd Medical Clinic
School of Medicine
Krakow, Poland