To the Editor:

Dr. Matti and his colleagues (Blood 42:999, 1973) are mistaken in suggesting that other investigators have failed to find a correlation between iron content of epithelial cells and iron absorption or that the effect of "messenger" iron has not yet been detected. Our previous work in rats has shown that the iron content of the epithelial cells indeed varies, as Dr. Matti et al. have shown, and that, in iron deficiency, depletion is associated with a reduction of mitochondrial iron and of iron-enzyme activities (Br J Haematol 23:605, 1972). The intravenous administration of transferrin-bound $^{59}$Fe is followed by the appearance of the tracer in the epithelial mitochondria, and this process is more rapid in iron-deficient animals (Br J Haematol 22:265, 1972). Iron uptake from the lumen is related to the iron status of the epithelial cell and in the first 4 hr after an oral dose of iron transfer from the cell to the plasma is related to the appearance and disappearance
of iron in a nonferritin “carrier” fraction of the cell sap (Br J Haematol 20:587, 1971; Nature 299:409, 1971). It is suggested that iron supply (the “message”) from the body to the epithelial cell determines the level of mitochondrial heme synthesis and this, in turn, controls iron uptake from the lumen (Clinics in Haematol 2:323, 1973). It is clear that this is not the whole story, but it appears to be a significant part.

A. JACOBS
M. WORWOOD
Department of Haematology
Welsh National School of Medicine
Heath Park
Cardiff, U.K.

To the Editor:
Jacobs and Worwood’s observations (Br J Haemat 22:265, 1972), even though of great interest, were only related to the subcellular distribution of iron in different states of iron rep- letion, failing to show any substantial difference in the actual amount of iron of the intestinal mucosa of the three groups of animals, expressed as percentage of the given dose of iron; furthermore no significance was given in the absorption rate of normal and iron loaded rats, reportedly having 61% and 74% absorption, respectively. Thus, in that experiment, we could not find the correlation between high absorption and low epithelial iron, on one side, and low absorption and high “macrophage” iron, on the other, observed in our rats. The long segment of intestine used by Jacobs and Worwood could conceivably explain some of the discrepancy, by introducing a “diluting” factor to a phenomenon, otherwise mostly confined to the duodenum. Furthermore no attempt was ever reported to measure the hemoglobin content of their specimens. The technique employed is likely to disrupt the microvasculature of the villi, with possible contamination from hemoglobin iron.

In another experiment (Br J Haematol 23:605, 1972), whereby iron absorption was not tested, the total iron content of a filtered homogenate failed to show a difference between normal and iron-loaded rats. As some contamination from the lamina propria, namely that portion in the tips of the villi (shown by us to contain many iron-laden macrophages in the iron-loaded rats), is inevitable with the technique used by Jacobs et al., higher iron contents should have been found in the “homogenate” of the iron loaded group, as documented by us by chemical and histologic techniques. Our animals had been iron loaded through intravenous injections, not using the unreliable intramuscular route; this could account for possible differences in the amount of iron present in the intestinal mucosa.

WILLIAM H. CROSBY
Scripps Clinical Research Foundation
476 Prospect Street
La Jolla, California 92037

ROBERTO MATTI
Tufts University School of Medicine
Boston City Hospital
Harrison Avenue and Bennett Street
Boston, Massachusetts 02111

To the Editor:
I note with interest in the correspondence columns of your journal, Vol. 43, No. 1, page 155, January 1974, a description of a case of congenital dyserythropoietic anemia Type I with megakaryocytes showing a curious morphology with distinct internuclear bridges. The author observes that this hitherto unobserved abnormality may be an expression of the same nuclear membrane defect involving both erythroid and megakaryocyte series.

In the latter part of 1972 I had occasion to study an 83-yr-old female patient with a refractory anemia of 9 years' duration. Her peripheral blood and marrow findings in 1972 and a review of a marrow taken in 1966 showed the features of C.D.A. Type I. (1) As she had not complained of any symptoms of anemia nor had been examined hematologically prior to 1963, it is uncertain if this is a forme fruste example of C.D.A. with expression in late adult life or whether her dyserythropoietic anemia is of an acquired nature.

Notwithstanding this uncertainty as to the precise time of onset of her disease, the appearance of her megakaryocytes was noted to be abnormal. Her platelet count in the past year has varied between 76,000 and 122,000/μl. She has had no bleeding manifestations.

Both marrow samples taken in 1966 and 1972 show erythroid bridges and other accepted changes of dyserythropoiesis (Fig. 1A). Also a considerable percentage of her megakaryocytes from both specimens show marked abnormalities varying from bilobular chromatin masses connected by a single chromatin bridge through to more complex nuclear arrangements similarly joined by narrow chromatin strands (Figs.
1B–1D). We have made preliminary studies of the ultrastructure of her most recent marrow aspirate and have failed to show any gross abnormality in either the erythroid or megakaryocyte series.

It appears that this minimal clinical lesion, though relatively easily recognized by light microscopy, cannot confidently be recognized by the electron microscope. It remains questionable whether this is the same disease as described by Heimpel et al. and whether the putative membrane defect in these cases presenting in late adult life is not more fundamental in nature and involves a stem cell.

T. A. J. PHAURE
Department of Pathology
The Churchill Hospital
Headington, Oxford, OX3 7 LJ, England

REFERENCES