Serum ferritin concentration and bone marrow iron stores: a prospective study

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Ferritin is the intracellular storage form of iron, found chiefly in the cytoplasm of the cells of the reticuloendothelial system.[1] By means of immunoradiometric assays it can be quantitated in human serum.[2] Serum ferritin concentrations have been documented to give an accurate indication of the amount of storage iron in healthy individuals[3] and in persons with iron deficiency or iron overload.[4,5] However, there has been no published report of a study in which the concentration of serum ferritin has been prospectively correlated with the status of bone marrow iron stores in a mixed hospital population. The purpose of the work described in this paper was to assess the usefulness of measuring the serum ferritin concentration to predict the status of body iron stores in an unselected patient population.

Methods

All adequate bone marrow specimens sent to St. Joseph's Hospital's hematology laboratory for evaluation over an 18-month period, a total of 248, were included in the study. Air-dried films of bone marrow aspirates were fixed in methanol for 10 to 20 minutes, then stained by May–Grünwald–Giemsa's stain for morphologic study and by the Prussian blue reaction for evaluation of iron stores.[6] Iron stores were graded as absent, present or increased by one observer who was not aware of the serum ferritin value. Iron was considered to be absent when no iron could be demonstrated in any of the bone marrow fragments and increased when every fragment contained iron deposits covering more than 50% of the area of the fragment. Grading of the iron content between these two extremes was not attempted.

Blood samples were collected at the time of bone marrow aspiration and the serum ferritin concentration was measured by a radioimmunoassay using ferritin labelled with iodine-125 and rabbit antiferritin antibody. Goat antirabbit γ-globulin antibody and polyethylene glycol were used as separating agents. The assay method, described in detail previously,[7] has a working range (range in which no dilution is required) of up to 500 μg of ferritin per litre and requires a sample of 75 μL of serum or plasma for assay at two dilutions. The assay's sensitivity is 1.5 μg/L and its long-term precision 13% (one coefficient of variation).

Results

Of the 248 patients 69 were found to have no iron in the bone marrow, 116 had normal iron stores and 63 had increased iron stores.

Of the 69 patients with no iron demonstrable histologically in the bone marrow 20 had a serum ferritin value of more than 12 μg/L. Of these 20 patients 2 were receiving iron therapy and 2 had received a blood transfusion 4 and 7 days before the serum ferritin concentration was estimated. In the other 16 patients no obvious explanation could be found for the elevated ferritin value; 6 had alcoholic liver disease, 2 had chronic active hepatitis, 5 had renal failure due to chronic glomerulonephritis, 2 had active Hodgkin's disease and 1 had multiple myeloma.

All the patients with normal or increased iron stores had a serum ferritin value of more than 12 μg/L.

The clinical and hematologic diagnoses, summarized in Table I, were representative of the clinical and hematologic problems likely to be encountered in a general hospital. In

Table I—Clinical and hematologic diagnoses in 248 hospital patients

Diagnosis	No. of patients
Clinical	
Thrombocytopenia	50
Liver disease	42
Hypochromic anemia	39
Renal disease	26
Myeloma	20
Macrocytic anemia	19
Collagen disease	19
Pyrexia of unknown origin	11
Myeloproliferative disorder	9
Acute leukemia	7
Lymphoproliferative disorder	6
Hematologic (from bone marrow specimen)	
Nondiagnostic	81
Iron depletion or deficiency	69
Secondary anemia	41
Megaloblastic anemia	12
Hypoplastic anemia	10
Myeloma	9
Myeloproliferative disorder	8
Acute leukemia	7
Sideroblastic anemia	6
Chronic lymphocytic leukemia	5

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39 of the 69 instances of iron depletion the diagnosis was suspected from the specimen of peripheral blood, and in one third of the group (81 of 248) examination of the bone marrow aspirate was not helpful in diagnosing the patient's problem.

The relation between the serum ferritin value and the status of the bone marrow iron stores is shown in Fig. 1. The median ferritin values for the three groups of patients, those whose iron stores were absent, present or increased, were 7, 120 and 312 μg/L respectively.

Discussion

The data reported in this study confirm the usefulness of measuring the serum ferritin concentration to assess body iron stores. A low serum ferritin value is highly suggestive of deficient iron stores: none of the 179 patients whose bone marrow specimens contained iron had a ferritin value of less than 12 μg/L. The converse, however, is not true: 20 patients (29%) had a ferritin value of more than 12 μg/L in spite of a lack of demonstrable iron in the marrow specimen. Therefore, a low serum ferritin value probably indicates iron depletion, while an elevated value does not exclude that possibility. We can only speculate as to the reason for the increased ferritin values in the 20 patients with absent iron stores. Two patients had received 180 mg/d of ferrous sulfate for 10 days before the ferritin concentration was assayed; this treatment might have stimulated the synthesis of intracellular ferritin to a degree that was detectable by radioimmunoassay but not by histologic examination. Another two patients had received a blood transfusion several days before the assay was done; this might have produced a similar effect. No satisfactory explanation can be offered for the elevated ferritin values of the other 16 patients (8 with liver disease, 5 with renal failure, 2 with Hodgkin's disease and 1 with multiple myeloma). Hence we have confirmed previous conclusions that a normal serum ferritin value cannot be used to exclude iron deficiency in the presence of hepatic, malignant or inflammatory conditions.[8-11]

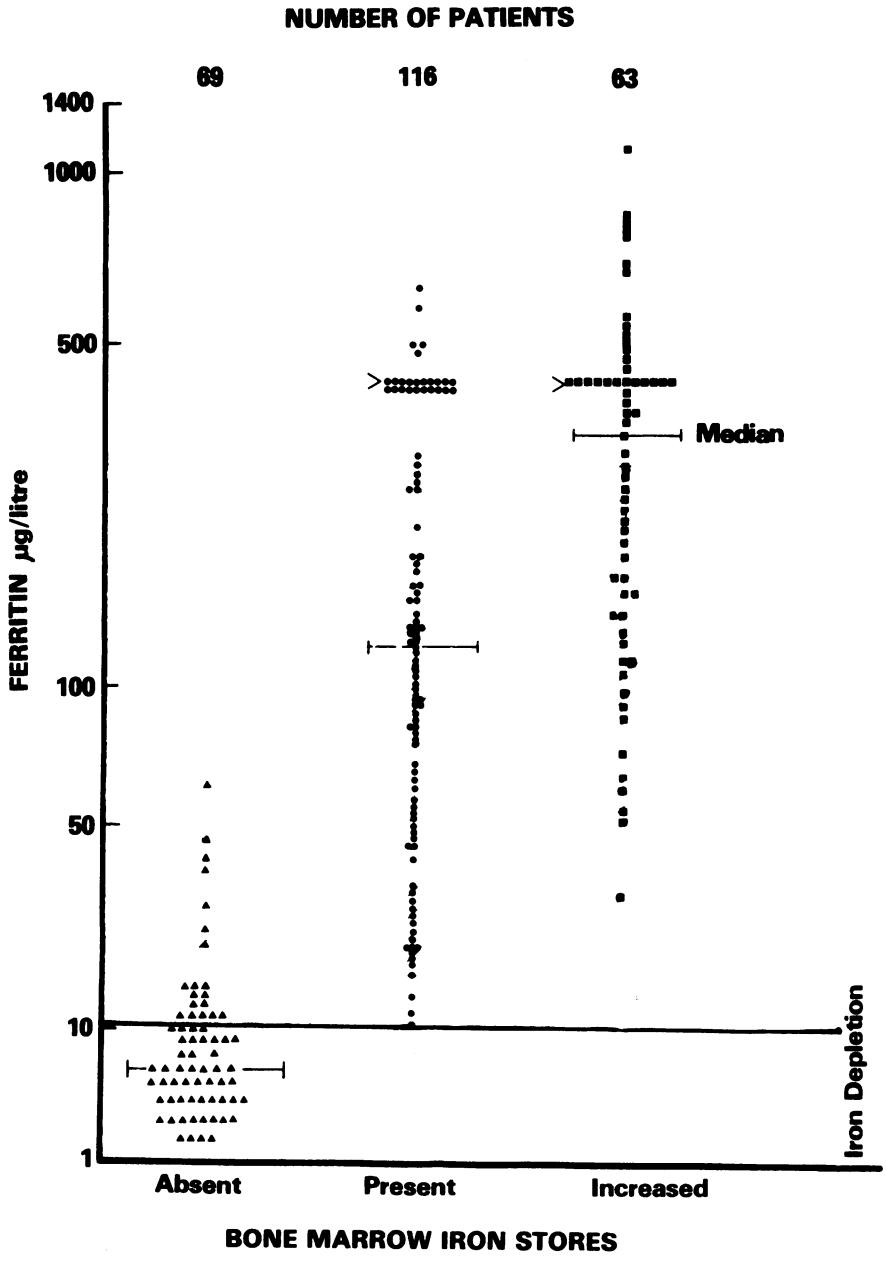

FIG. 1—Relation between status of bone marrow iron stores assessed histologically and serum ferritin concentration in 248 hospital patients.

References

1. ALFREY CP JR, LYNCH EC, WHITLEY CE: Characteristics of ferritin isolated from human marrow, spleen, liver and reticulocytes. *J Lab Clin Med* 70: 419, 1967
2. WALTERS GO, MILLER EM, WORWOOD M: Serum ferritin concentrations and iron stores in normal subjects. *J Clin Pathol* 26: 770, 1973
3. ADDISON GM, BEAMISH MR, HALES CN, et al: An immunoradiometric assay for ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. *J Clin Pathol* 25: 326, 1972
4. JACOBS A, MILLER F, WORWOOD M, et al: Ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. *Br Med J* 4: 206, 1972
5. LIPSCHITZ DA, COOK JD, FINCH CA: A clinical evaluation of serum ferritin as an index of iron stores. *N Engl J Med* 290: 1213, 1974
6. DACIE JV, LEWIS SM: *Practical Haematology*, 5th ed, Edinburgh, Churchill Livingstone, 1975, p 137
7. LUXTON AW, WALKER WHC, GAULDIE J, et al: Radioimmunoassay for serum ferritin. *Clin Chem* 23: 683, 1977
8. COOK JD, LIPSCHITZ DA, MILES LEM, et al: Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nutr* 27: 681, 1974
9. VALBERG LS, SORBIE J, LUDWIG J, et al: Serum ferritin and the iron status of Canadians. *Can Med Assoc J* 114: 417, 1976
10. JACOBS A, WORWOOD M: Ferritin in serum. Clinical and biochemical implications. *N Engl J Med* 292: 951, 1975
11. ELIN RJ, WOLFF SM, FINCH CA: Effect of induced fever on serum iron and ferritin concentrations in man. *Blood* 49: 147, 1977