lineage-restricted pattern of antigen expression may thus be useful for the immunophenotypic subclassification of leukemias.

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References

1. Kristiansen M, Graversen JH, Jacobsen C, et al. Identification of the haemoglobin scavenger receptor. Nature. 2001;409:198-201.
2. Radzun HJ, Kreipe H, Bödewadt S, Hansmann M-L, Barth J, Parwaresch MR. Ki-M8 monoclonal antibody reactive with an intracytoplasmic antigen of monocyte/macrophage lineage. Blood. 1987;69:1320-1327.
3. Backé E, Schwarting R, Gerdes J, Ernst M, Stein H. Ber-MAC3: new monoclonal antibody that defines human monocyte/macrophage differentiation antigen. J Clin Pathol. 1991;44:936-945.
4. Pulford K, Micklem K, McCarthy S, Cordell J, Jones M, Mason DY. A monocyte/macrophage antigen recognized by the four antibodies GHI/61, Ber-MAC3, Ki-M8 and SM4. Immunology. 1992;75:588-595.
5. Pulford K, Micklem K, Law SKA, Mason DY. CD163 (M130 antigen) workshop panel report. In: Kishimoto T, Kikutani H, von dem Borne AEGK, et al, eds. Leukocyte typing VI: white cell differentiation antigens. New York, NY: Garland Publishing; 1997:1089-1091.
6. Kinney MC, Lukens JN. Classification and differentiation of the acute leukemias. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, eds. Wintrobe's Clinical Hematology, 10th edition. Baltimore, MD: Williams & Wilkins; 1998:2209-2240.
7. Schaer DJ, Boretti FS, Schoedon G, Schaffner A. Induction of the CD163-dependent haemoglobin uptake by macrophages as a novel anti-inflammatory action of glucocorticoids. Br J Haematol. 2002;119:239-243.
8. Greer JP, Baer MR, Kinney MC. Acute myelogenous leukemia. In: Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM, eds. Wintrobe's Clinical Hematology, 10th edition. Baltimore, MD: Williams & Wilkins; 1998: 2272-2319.
9. Ball ED, McDermott J, Griffin JD, Davey FR, Davis R, Bloomfield CD. Expression of the three myeloid cell-associated immunoglobulin G Fc receptors defined by murine monoclonal antibodies on normal bone marrow and acute leukemia cells. Blood. 1989;73:1951-1956.
10. Fehr J, De Vecchi P. Transcobalamin II: a marker for macrophage/histiocyte proliferation. Am J Clin Pathol. 1985;84:291-296.

To the editor:

Is iron gluconate really safer than iron dextran?

Parenteral supplementation of iron is required in some patients with iron deficiency, including those with oral iron intolerance, chronic uncorrected bleeding, malabsorption, gastrointestinal inflammatory disease, dialysis dependence, or failure to take prescribed oral iron. A more rapid increase in hemoglobin production occurs after intravenous administration, which may be valuable in anemic patients and chronic bleeding patients. Unlike oral iron, the full dose of intravenous iron is delivered to the bone marrow and saturates tissue stores.[1,2]

The 2 popular forms of available parenteral iron in the United States are iron dextran and iron gluconate. Despite their value, intravenous iron therapy carries the potential for serious allergic reactions. In 1980, Hamstra et al examined over 2000 infusions of iron dextran among 481 patients and reported that 26% of patients experienced side effects, of which the majority were mild and self-limited. Of the reactions, 2% were considered "severe" allergic and 0.6% were classified as anaphylactoid. Most reactions were reported to occur immediately during the infusion of a test dose. As a result, administration of a test dose is now recommended to monitor patients for reactions.[1]

In contrast, iron gluconate is considered to have a lower reaction rate and a test dose is not recommended by the manufacturer. During the years of 1992 to 1996, Faich and Strobos reported 3.3 allergic events per million doses per year with iron gluconate and 8.7 allergic events per million doses per year with iron dextran.[3] No fatalities were associated with iron gluconate between 1976 to 1996. However, 31 fatalities among 196 allergy/anaphylactic cases were recorded between 1976 to 1996 for iron dextran, translating into a case fatality rate of 15.8% for iron dextran.[3] Other studies have reported similar high rates of allergic reactions for iron dextran.[4-6] As a result, several authors have advocated the use of iron gluconate over iron dextran, in order to avoid serious reactions. For example, The University of Iowa Health Care Center uses only iron gluconate despite the need for multiple dosing.[7]

Table 1. Reactions to iron dextran versus iron gluconate

	Iron dextran* (%)	Iron gluconate† (%)
Severe reaction	1 (2.6)	0 (0)
Moderate reaction	3 (7.7)	1 (3.8)
Mild reaction	4 (10.3)	5 (19.2)
No reaction	22	20
Total no. reactions	8 = 20.5% of infusions	6 = 23% of infusions

*Total 39 infusions; 32 patients.
†Total 26 infusions; 4 patients.

We report here a chart review of recorded reactions over the past 3 years (1999-2002) to intravenous infusions of iron dextran and iron gluconate administered in the outpatient Blood Transfusion Center at Massachusetts General Hospital, Boston. A total of 65 infusions of either iron dextran (INFeD, Schein) or iron gluconate (Ferrlecit, Schein, Morristown, NJ) were performed among 35 patients over the 3-year period. All patients were directly observed for allergic reactions and reactions were recorded.

We grouped the resulting reactions into 3 categories: severe (reactions such as anaphylactoid, shock, and cardiovascular collapse); moderate (reactions such as dyspnea, severe urticaria, and neck and back spasm in which the infusion was stopped and patient did not tolerate further infusion); and mild (reactions such as headache, dizziness, tachycardia, and hypertension in which the infusion was stopped but the patient subsequently completed the infusion). Over the 3-year period, an average of 21.5% (14/65) of infusions demonstrated some form of mild, moderate, or severe reaction. Of these reactions, only 1 reaction was severe, 4 were moderate, and the remainder were mild. As shown in Table 1, the rate of acute allergic reactions was comparable with the 2 preparations.

As previously reported by others, our data suggest a high rate of acute reactions to intravenous iron. When compared with other commonly prescribed medications, intravenous iron has an extremely high rate of adverse events. In contrast to previous reports, we have found that acute allergic reactions appear to be as common with iron gluconate as with iron dextran. Our findings are not explained by a selection bias (use of iron gluconate in patients with prior reactions to iron dextran) because only one patient who reacted to iron gluconate had had a prior reaction to iron dextran.[7] Our results challenge the notion that iron gluconate, which requires 8 infusions in place of the single infusion of iron dextran, is a safer

alternative treatment to iron dextran. Because our data set is small, further studies are needed to determine more conclusively the rates of reaction to different iron preparations.

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References

1. Hamstra RD, Block MH, Schokert AL. Intravenous iron dextran in clinical medicine. JAMA. 1980;243:1726-1731.
2. Andrews NC. Disorders of iron metabolism. N Engl J Med. 1999;341:1986-1995.
3. Faich G, Strobos J. Sodium ferric gluconate complex in sucrose: safer intravenous iron therapy than iron dextrans. Am J Kid Dis. 1999;33:464-470.
4. Burns DL, Pomposelli JJ. Toxicity of parenteral iron dextran therapy. Kidney Int Suppl. 1999;69:S119-S123.
5. Michael B, Coyne DW, Fishbane S, et al. Sodium ferric gluconate complex in hemodialysis patients: adverse reactions compared to placebo and iron dextran. Kid Int. 2000;61:1830-1839.
6. Fishbane S, Kowalski, EA. Comparative safety of intravenous iron dextran, iron saccharate and sodium ferric gluconate. Semin Dial. 2000;13:381-384.
7. Schrand LM, Johnson SJ, Berkowski SS. New intravenous iron products: increasing safety at UIHC [letter]. P T News. 2001.