

Beeturia

A Sign of Iron Deficiency

Walter W. Tunnessen, MD;
Charles Smith, MD; and
Frank A. Oski, MD, Philadelphia

BEETURIA is a term applied to the deep red or pink coloration of urine which may occur after the ingestion of beetroot. The color is due to the presence of betanin, a red pigment which is chemically different from the anthocyanins, the reddish violet pigments of most plant species. Beeturia is often misinterpreted as hematuria by the unsuspecting.

Beeturia has repeatedly been noted in a small percentage of the population. It has variously been attributed to a genetic trait¹ or to beet allergy.² Watson and associates³ were the first to observe that it occurred with increased frequency among adults with iron deficiency. Because beeturia is not an uncommon pediatric problem, its relation to iron deficiency in children was studied.

Materials and Methods

Patients selected for study were in-patients on the pediatric ward of the Hospital of the University of Pennsylvania. All patients at the time of study were either recuperating from an acute illness or hospitalized for evaluation of non-hematologic problems. The patients ranged in age from 5 months to 7 years.

In each patient selected for study hemoglobin, hematocrit, serum iron level, and serum iron binding capacity were determined. The serum iron level and the iron binding capacity were determined by the method of Ramsay.^{4,5} Where appropriate, sickle cell preparations, brilliant cresyl blue preparations, hemoglobin electrophoresis, and red cell glucose-6-phosphate dehydrogenase assays were also examined.

On the morning of study the first voided urine was collected and then the fasting patient was fed 6 tablespoons of homogenized beets, prepared from canned sliced beets (Great Atlantic and Pacific Tea) which had been homogenized in a blender. The next two voided samples were then collected separately. During the first two

Received for publication June 12, 1968.

From the Department of Pediatrics, Hospital of the University of Pennsylvania and the University of Pennsylvania School of Medicine, Philadelphia. Dr. Oski is a recipient of the Public Health Service Research Career Development Award.

Reprint requests to Hospital of the University of Pennsylvania, 3600 Spruce St, Philadelphia 19104 (Dr. Oski).

hours of the collection period the child did not receive other foods or fluid by mouth.

The urines were examined visually and compared with the fasting specimen and then scored on a 0 to 3+ scale. The urine was not acidified prior to examination. Preliminary studies quantitating the beeturia by examining the urine's absorbance photometrically at 530 μ on a spectrophotometer demonstrated good agreement with the simpler visual estimation and thus precise quantitation was not employed for the major portion of the study.

Results

A total of 41 patients were studied. The patients were subdivided into five groups for purposes of evaluation. The five groups were as follows:

1. Anemia and hypoferremia. Hemoglobin was less than 10 gm/100 ml; serum iron less than 75 μ g/100 ml; and serum iron binding capacity less than 20% saturated.

2. Hypoferremia without anemia. Hemoglobin was above 10 gm/100 ml; serum iron less than 75 μ g/100 ml; and serum iron binding capacity less than 20% saturated.

3. Equivocal hypoferremia without anemia. Hemoglobin was above 10.0 gm/100 ml; and either the serum iron was below 75 μ g/100 ml or the iron binding capacity was less than 20% saturated.

4. No anemia or hypoferremia.

5. Anemia without hypoferremia.

In the Table it can be seen that only the patients in group 1, those with anemia

and hypoferremia, demonstrated significant degrees of beeturia. Of the 19 children in this group, 12 had 2+ or 3+ beeturia. Only two children in this group had negative urine test results, and one of these patients was subsequently demonstrated to have sickle cell anemia and stainable marrow iron despite the presence of a low serum iron level. There was no apparent relation between the degree of beeturia and the patient's age within this small group.

In group 2, infants and children with hypoferremia but no anemia, three of the six patients had minimal beeturia, while only one of five subjects in group 3, those with questionable hypoferremia, demonstrated beeturia.

Two of the seven normal subjects in group four demonstrated 1+ beeturia, while none of three patients with sickle cell anemia not associated with hypoferremia had pigmenturia.

Thus of 12 patients with easily visible beeturia (2+ or 3+), all were anemic and iron deficient. Of the 12 subjects with no trace of beeturia, 10 were either not iron deficient or had equivocal evidence of iron deficiency.

Comment

Watson et al³ observed a 13.8% incidence of beeturia among normal adults and an incidence of 48.6% among patients with iron deficiency although they did not grade the degree of pigmenturia.

Relation of Hemoglobin and Iron Studies to Beeturia *

Group No. (No. of Patients)	Hemoglobin (gm/100 ml)	Serum Iron (μ g/100 ml)	Serum Iron Binding Capacity (μ g/100 ml)	Saturation (%)	Beeturia Score				
					0	$\pm$	1+	2+	3+
1 (14)	7.6 (3.6-9.8)	39.8 (16-70)	441 (234-600)	9.9 (3.0-19)	2	0	5	7	5
2 (6)	11.0 (10.5-11.6)	44.0 (29-65)	398 (355-466)	10.8 (7-14)	1	2	3	0	0
3 (5)	11.4 (10.2-12.6)	71.0 (61-86)	358 (270-465)	19.9 (18-23)	3	1	1	0	0
4 (7)	11.7 (10.7-13.4)	102 (92-115)	365 (318-417)	28 (21-35)	4	1	2	0	0
5 (3)	8.3 (7.7-8.8)	83 (73-92)	309 (263-754)	24.6 (22-28)	2	1	1	0	0

* Numbers given are the means, with range in parenthesis.

When these authors subdivided their group of iron deficient patients into those that had and had not received iron therapy, they noted that 80% of the untreated patients had positive test results, while only 6.7% of the treated patients demonstrated beeturia. In patients in whom repeated testing was performed, the beeturia disappeared or markedly decreased during iron administration. In a single patient in whom we performed serial studies the beeturia decreased from 3+ to 0 within two weeks of orally administered iron therapy. During this period the hemoglobin rose from 3.6 to 7.1 gm/100 ml suggesting that the beeturia disappeared as a consequence of iron therapy rather than as a result of the correction of anemia.

Based on the previous experiments of Horwitt⁶ and their own experimental data, Watson and associates³ concluded that beeturia was a consequence of enhanced absorption of the betanin pigment rather than a consequence of alterations in the renal excretion of the material. Intravenous administration of the pigment invariably produced beeturia while oral administration did not. The authors proposed that beeturia resulted from increased gastrointestinal absorption of the betanin pigment in the iron deficient subject because the apoferritin carrier system in the gut mucosa could not distinguish between this pigment and iron.

Iron absorption is recognized to be markedly increased in subjects with iron deficiency because of desaturation of the transport system.⁷

An alternate explanation is that the beeturia may reflect the abnormal gastrointestinal function and permeability recognized to be present in many children with iron deficiency.^{8,9} Although the precise pathologic mechanism responsible for the increased absorption remains undefined, the finding of a nearly 66% incidence of significant beeturia in iron deficient infants and children should alert the physician to this diagnostic possibility whenever a history of beeturia is elicited or the phenomenon observed.

Summary

The relationship of beeturia to iron deficiency was studied in a group of 41 infants and children. After the ingestion of 6 tablespoons of pureed beets, 12 of 19 patients with iron deficiency anemia showed marked beeturia. The incidence of minimal beeturia was increased in those with hypoferrremia without anemia but was not as marked as those in the former group. It is concluded that a history of, or the observation of, beeturia in an infant or child should alert the physician to the presence of an associated iron deficiency anemia.

This study was supported in part by Public Health Service Research Career Development Award 3-HD-38 600 (Dr. Oski).

References

1. Allison, A.C., and McWhirter, K.G.: Two Unifactorial Characters for which Man is Polymorphic, *Nature* 178:748-749 (Oct 6) 1959.
2. Zindler, G.A., and Colovos, G.C.: Anthocyaninuria and Beet Allergy, *Ann Allergy* 8:603-617 (Sept-Oct) 1950.
3. Watson, W.C.; Luke, R.G.; and Inall, J.A.: Beeturia: Its Incidence and a Clue to its Mechanism, *Brit Med J* 2:971-973 (Oct 19) 1963.
4. Ramsay, W.N.M.: The Determination of Iron in Blood Plasma or Serum, *Clin Chim Acta* 2: 214-220 (July) 1957.
5. Ramsay, W.N.M.: The Determination of the Total Iron-Binding Capacity of Serum, *Clin Chim Acta* 2:221-226 (July) 1957.
6. Horwitt, M.K.: Observations on Behavior of the Anthocyanin Pigment from Concord Grapes in the Animal Body, *Proc Soc Exp Biol Med* 30: 949-951 (April) 1933.
7. Conrad, M.E., Jr., and Crosby, W.H.: Intestinal Mucosal Mechanisms Controlling Iron Absorption, *Blood* 22:406-415 (Oct) 1963.
8. Naiman, J.L., et al: The Gastrointestinal Effects of Iron Deficiency Anemia, *Pediatrics* 33:83-99 (Jan) 1964.
9. Guha, D.K., et al: Small Bowel Changes in Iron Deficiency Anaemia of Childhood, *Arch Dis Child* 43:239-244 (April) 1968.