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A very interesting paper showing elevation in FEP in infants is related to iron deficiency.

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Free erythrocyte porphyrins in cord blood

Red cell free erythrocyte porphyrin determinations were performed on cord blood specimens from 236 term infants and on capillary blood specimens from 63 preterm infants weighing less than 1,500 gm, during the first week of life. These results were contrasted with those obtained from 398 normal infants and children ages 1 to 6 years. The mean FEP value for the infants was significantly higher than that observed in the normal control subjects. In 10.5% of the term infants and 15.9% of the preterm infants, values in excess of 120 μg/dl RBCs, the highest value recorded in the normal subjects, were observed. Elevations in FEP values were not related to either blood lead concentration or hematocrit levels in the infants. Infants with elevated FEP values were found to have lower serum iron and transferrin saturation values than did infants with low FEP values. These findings suggest that elevations in cord blood FEP values may indicate a state of relative iron deficiency present at birth.

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THE MEASUREMENT of free erythrocyte porphyrin is now widely used as a sensitive screening test for the detection of both lead poisoning and iron deficiency anemia.[1-7] Several studies[8, 9] have demonstrated that some infants may be born with elevated cord blood lead levels. A study was initiated to screen cord blood specimens for the presence of intrauterine lead poisoning, utilizing FEP determinations. Many newborn infants had FEP values higher than those of normal children, and these elevations did not appear to reflect lead poisoning. The purpose of this communication is to describe our efforts to find an explanation for the elevated FEP values observed in newborn infants.

MATERIALS AND METHODS

Cord blood specimens were collected at the time of delivery from infants born at Community General Hospital and St. Joseph's Hospital, both in Syracuse, New York. Two cord blood specimens were collected from each infant, one in a heparinized tube and one in a tube with no anticoagulant (Vacutainer, Becton, Dickinson & Co., Rutherford, NJ 07070). FEP determinations were performed on 20 lambda specimens by the method of Piomelli[10] employing an Aminco-Bowman spectrofluorometer. Blood lead levels were measured by atomic absorption spectrofluorometry[11] in the New York State Laboratories. Serum iron and percentage of transferrin saturations were determined by the method of Jung and Parekh[12] by means of a Dupont Automatic Clinical Analyzer. Serum ferritin assays were performed through the courtesy of Dr. Peter Dallman of the University of California, San Francisco.

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Abbreviations used	
FEP:	free erythrocyte porphyrin
RBC:	red blood cells

RESULTS

Initially, cord blood samples from 236 term infants were analyzed for FEP levels and contrasted with concurrent samples obtained from infants and children 1 to 6 years of age and from 63 preterm infants during the first week of life (Table I). All infants and children (1 to 6 years of age) classified as normal had blood lead values of less than 30 μg/dl and were not iron deficient. All preterm infants had birth weights of less than 1,500 gm.

The mean FEP values in both the term and preterm infants were significantly higher than those observed in normal infants and children in the 1- to 6-year age range. Although the mean FEP value observed in the preterm infants was higher than that of the term infants, the difference was not statistically significant. It was found that 10.5% of the term infants and 15.9% of the preterm infants had FEP values above the highest value, 120 μg/dl

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RBC, that was recorded in the normal population of older infants and children.

Blood lead determinations were performed on 14 infants with the lowest FEP values and contrasted with similar determinations in 13 term infants with the highest FEP values (Table II). The mean blood lead values in these two groups were identical.

The FEP values of infants with low cord blood hematocrits were contrasted with those of normal infants (Table III). Considerable overlap in FEP values existed and there was no significant difference between these two groups.

After the initial study failed to reveal any relationship between either blood lead or hematocrit and elevations in FEP, 100 more infants were studied. Ten infants with FEP values in excess of 125 μg/dl RBC were identified. Serum iron and percentage of transferrin saturation values were contrasted with those of 20 infants with low FEP values (Table IV). This comparison revealed that infants with elevated FEP values had significantly lower values for both serum iron and percentage of transferrin saturation. Serum iron values in the high FEP group averaged 127 μg/dl. This is normal by conventional standards applied to older infants, children, and adults, but is well below the mean observed for the low FEP group. The value of 177 in this latter group is in close agreement with the mean values of 173 and 193 reported by Hagberg[13] and Sturgeon,[14] respectively.

Similarly, the transferrin saturation of 43.4% observed in the infants with the elevated FEP values would be considered normal by standards applied to older infants and children but is significantly lower than the value of 72.1% observed in the infatns with the normal FEP levels. Cord blood transferrin saturation has been reported to range normally between 65 and 80% in other investigations.[15, 16]

The total iron binding capacity averaged 316 μg/dl in the infants with elevated FEP values as contrasted with a value of 240 μg/dl in the infants with normal FEP values (Table IV).

Serum ferritin values were obtained in additional term infants with high and low FEP values (Table V). Only one infant was found with a ferritin level in the range considered diagnostic of iron deficiency. This value was less than 10 ng/ml and was observed in the infant with the highest FEP value.

DISCUSSION

Previous studies have suggested that porphyrin values may rise in red cells when iron supply is inadequate to meet the demands of intense erythropoiesis.[17-20] The level of free erythrocyte porphyrin has been shown to be increased in children with blood lead values in excess of 30 μg/dl.[1-3] In addition, children 1 to 6 years of age and adults with reduced serum iron values and transferrin saturations of less than 16%[1-3] usually have elevations in FEP. The measurement of serum iron and transferrin saturation alone, however, may not always be suitable for making judgments regarding iron sufficiency under such circumstances. The finding of elevated FEP values in newborn infants with seemingly adequate serum levels of iron may be an example of such a situation. The fact that serum iron values and transferrin saturations in infants with elevated FEP levels were significantly lower than those of normal infants is consistent with such an interpretation. The elevation in total iron binding capacity also supports the hypothesis that the elevated FEP reflects a form of relative iron deficiency rather than chronic intrauterine infection. FEP values may rise in chronic

Table I. Free erythrocyte porphyrin values in preterm infants, full-term infants, and normal subjects between 1 and 6 years of age

Group	No. of subjects	FEP (μg/dl RBC)		% of group with values in excess of 120 μg/dl RBC
		Mean*	Range	
Preterm infants	63	93.5 ± 48	46-306	15.9
Term infants	236	81.5 ± 28	33-200	10.5
Normal children (1-6 years of age)	398	54.0 ± 20	8-120	0.0

*Values expressed as mean ±1 SD.

Table II. Comparison of blood lead values in infants with "high" and "low" cord blood FEP values

Group	No.	FEP (μg/dl RBC)		Blood lead (μg/dl)	
		Mean	Range	Mean	Range
"Low"	14	57	45-64	11.1	7-13
"High"	13	146	125-199	12.0	10-15

Table III. Comparison of cord blood FEP values in infants with "high" and "low" hematocrits

Hematocrit	No.	Hematocrit (%)		FEP (μg/dl RBC)	
		Mean	Range	Mean	Range
"Low"	20	42	39-44	77.4	48-137
"High"	20	58	56-62	92.9	49-181

Table IV. Iron status of infants with "high" and "low" cord blood FEP values

FEP group	No.	FEP (μg/dl RBC) Mean	FEP (μg/dl RBC) Range	Serum iron (μg/dl) Mean	Serum iron (μg/dl) Range	Transferrin saturation (%) Mean	Transferrin saturation (%) Range
"Low"	20	44	33-54	177 ± 40.3	128-257	72.1 ± 19	49-92
"High"	10	156	126-200	127 ± 30.2	94-182	43.4 ± 20	5-70

Table V. Serum ferritin values in infants with "high" and "low" cord blood FEP values

Subject No.	"High" FEP: FEP (μg/dl RBC)	"High" FEP: Ferritin (μg/l)	"Low" FEP: FEP (μg/dl RBC)	"Low" FEP: Ferritin (μg/l)
1	156	110	38	> 200
2	177	77	48	175
3	178	89	52	68
4	231	151	73	53
5	376	5.9	77	91
Mean	224	86.6	58	117.5

inflammatory states,[21, 22] but in such situations the decrease in serum iron concentration is usually accompanied by a fall in the transferrin level.

In states of iron deficiency the levels of serum ferritin are low.[23, 24] The failure in our study to find significant differences in serum ferritin values between a small number of infants with high and low FEP values indicates the need for further studies to determine the clinical significance of an elevated cord blood FEP. Serial evaluation of such infants with respect to iron status may provide an answer.

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