A discussion of nutritional anemia primarily due to iron deficiency is presented. The need for current information is stressed, with particular reference to infants and children in lower socioeconomic groups. Means of prevention are discussed.

THE USA TODAY—IS IT FREE OF PUBLIC HEALTH NUTRITION PROBLEMS?

ANEMIA

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Introduction

ANEMIA is generally defined as a condition in which the hemoglobin concentration or the volume of packed red cells (hematocrit) are lower than is considered normal. Such a definition, however, does not give insight into the mechanism of the development of anemia. Disorders in erythropoiesis or an increase in destruction of red cells may lead to anemia. Nutritional factors may be involved in both mechanisms, with deficiencies in folic acid, vitamin B_{12}, pyridoxine, ascorbic acid, copper and iron the leading causes of an erythropoietic disorder. It has been suggested that a deficiency in vitamin E leads to an accelerated destruction of red cells.

Anemia resulting from folic acid or vitamin E deficiency is chiefly associated with infants of low birth weight and is manifest primarily during the postnatal hospital stay. It constitutes a minor public health problem, assuming that these nutritional deficiency states are corrected prior to discharge of such infants from the hospital. With the exception of iron, lack of these other nutritional factors is rarely a cause of anemia.

There is much in the medical literature, however, to describe iron deficiency anemia as a significant public health problem among infants and young children. Its recorded frequency makes it seem reasonable to examine, in some detail, where we stand with respect to nutritional iron deficiency and compare current data with those available from years past. Have we made progress in eliminating this debilitating but usually not life-threatening disease?

Experience with nutritional deficiencies of sufficient magnitude to constitute public health problems has demonstrated that they can be managed through public health measures. By judicious enrichment programs, involving vitamins D and C, rickets and scurvy have been eliminated as public health problems. If nutritional iron deficiency is a particular threat to the health of our infant population, should we not attempt to eliminate it by assuring an adequate iron intake in the infant dietary?

Iron

Body Stores

About 75 per cent of the total iron in the infant body at birth exists as iron in hemoglobin. Iron in tissue, in enzymes, and in storage depots makes up the remainder. Since hemoglobin mass is a function of blood volume which, in turn, is a function of body weight, total body iron at birth is dependent on birth weight. Neonatal hemolysis in adjustment to increased availability of oxygen after birth provides additional stores of iron to be used in the hematopoiesis required to keep pace with growth. Maternal iron nutritional status appears to have little influence on the total body iron of the fetus. Delayed cord clamping, fetal-fetal or fetal-maternal transfusion, or excessive blood loss by the infant at delivery, are critical in establishing total body iron stores.

Growth with its concomitant expansion of vascular volume leads to dilution of hemoglobin mass. Even though much of the weight gain, in the first few months of life, is relatively avascular adipose tissue, this period of rapid growth creates demand for a supply of exogenous iron to maintain adequate hemoglobin synthesis.[1,2]

Low Birth-Weight Infants

Gorten and co-workers have demonstrated by labeled-isotope technique that low birth-weight infants absorb iron from a fixed intake, proportional to their rate of growth (Figure 1).[3] Utilization of absorbed iron for hemoglobin synthesis is dependent on bone marrow activity, as evidenced by reticulocytosis, which is apparently triggered by a reduction in hemoglobin concentration secondary to weight gain. These investigators have also shown a similarity in configuration between the age-related incremental growth curve and an age-related curve expressing iron absorbed from exogenous sources (Figure 2). Whenever a growth spurt occurs, as in the early school years or adolescence, an increase in iron absorption occurs.

The low birth-weight infant provides an excellent model to test the relationship between dietary iron, growth rate, and rate of iron utilization. His growth rate, accelerated beyond that of the normal birth-weight infant, creates a sharper demand for exogenous iron for hemotopoiesis. Studies of such infants in the Bronx, N. Y. C., and Baltimore, Md., indicate an incidence of anemia of 38 per cent among infants fed a formula that does not contain iron. When fed an iron-enriched formula, the incidence of anemia is reduced to 1.7 per cent (Table 1). Anemia can be prevented in low birth-weight infants by feeding a formula that contains iron.[4,5]

Gorten has studied this triad of dietary iron, growth rate, and rate of iron utilization in six groups of low birth-weight infants whose diets were

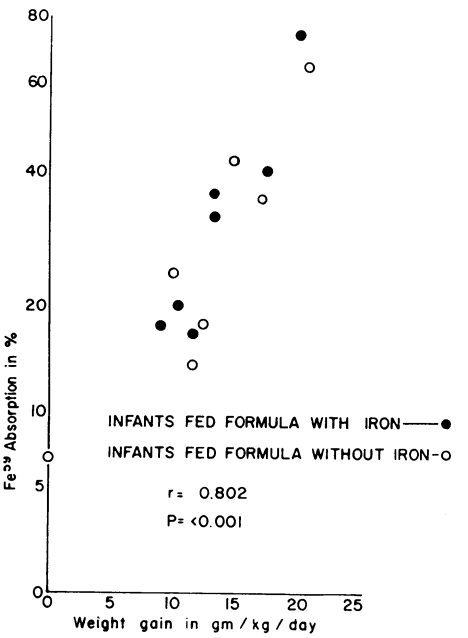

Figure 1—Iron absorption in relation to growth rate

supplemented with iron in a variety of ways from birth to 18 months (Table 2).[6]

Gain in weight, and length and rate of utilization of iron from birth to six months of age, are shown in Figure 3. Mean hemoglobin concentration and rate of iron utilization were highest for

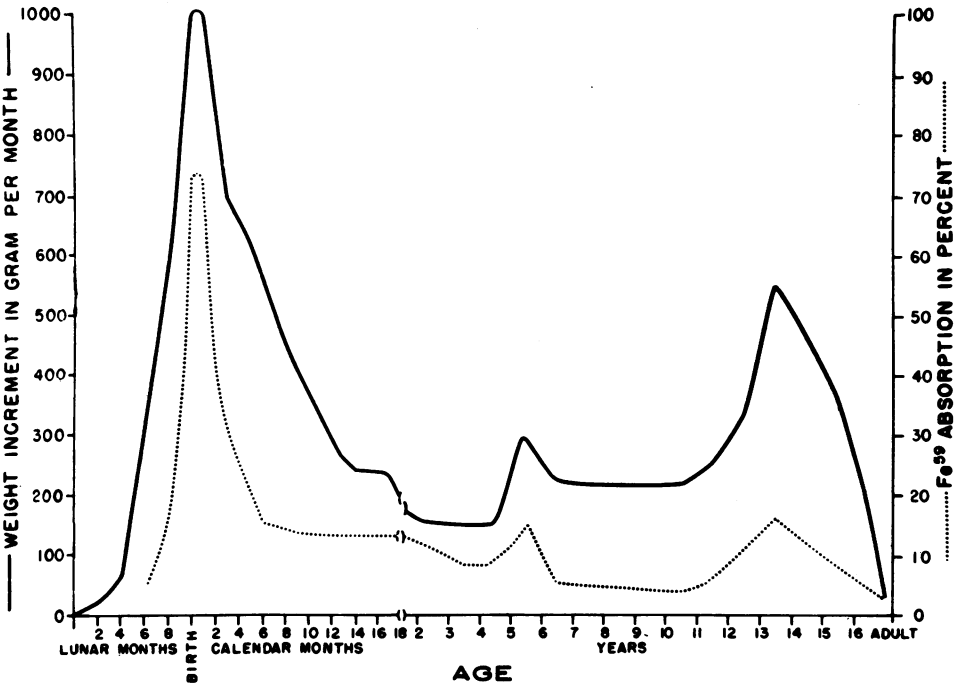

Figure 2—Relationship of rate of weight gain to Fe^{59} absorption from conception to maturity

Table 1—Incidence of nutritional iron deficiency anemia in low birth-weight infants

Investigator	Formula	Infants (#)	Birth Wt (Kg)	Infants Developing Anemia (#)
J. Schorr, Albert Einstein	☐ No Fe	19	1.32	15
IX Congress of International	▩ + Fe	21	1.35	2
Society of Hematology	☐	33	2.02	8
1:209, 1962	▩	25	2.05	0
M. Gorten, Univ. of Maryland	☐	76	1.89	25
J. Peds. 64:509, 1964	▩	69	1.84	0
Total	☐	128		48 (38%)
	▩	115		2 (1.7%)

Table 2—Low birth-weight infant-feeding plan

Group	A	B	C	D	E	F
Number infants	39	128	65	67	53	21
Formula	EM+CHO	EM+CHO	P*	P	P	P
Fe in formula (mg/quart)	Trace	Trace	Trace	12	5	8
Fe added (mg)	5 (supplied)	12 (prescribed)	None	None	None	250 (IM)

* P = Commercially prepared formula.

groups D and F. The former received prepared formula providing 12 mg of elemental iron per quart; the latter, 250 mg of iron by intramuscular injection between the third and fourth weeks of age, in addition to a formula providing 8 mg of elemental iron per quart.

From 6 to 12 months of age, anemia occurred in 54 per cent of infants in group C, fed a noniron-containing formula, and in 35 per cent of infants in group A, fed 5 mg of iron added to a formula made up of evaporated milk and carbohydrate. During this time period, the rate of growth of infants in group D was slightly greater than that of groups B and E. The rate of iron utilization and mean hemoglobin concentration was greatest in group D (Figure 4).

Between 12 and 18 months of age, infants in group D, fed a prepared iron-containing formula from birth, had a

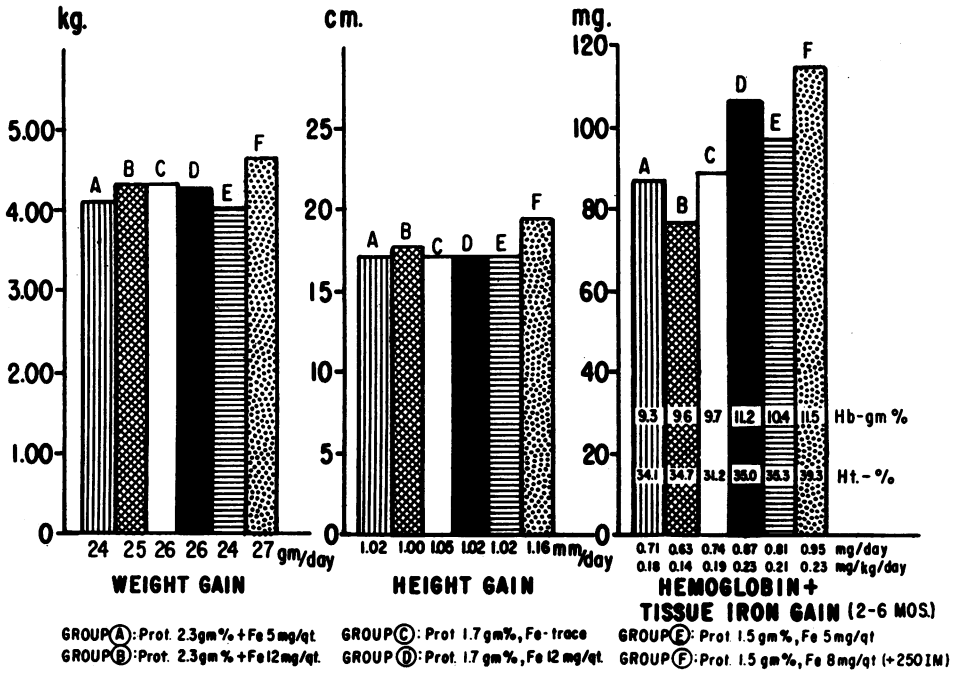

Figure 3—Relation of increase in weight and height, hemoglobin concentration and tissue iron to provision of exogenous iron birth to six months

greater mean concentration of hemoglobin and a greater rate of iron utilization than group B infants, for whom iron (12 mg/quart) was prescribed but not incorporated into the formula (Figure 5). By 18 months of age, 80 per cent of group B infants had developed iron deficiency anemia. None of group D infants were so involved. Gorten has concluded that the slower rate of growth manifest by group B infants was, in part, compensatory for a diet limited in available iron. For optimal growth of the low birth-weight infant, Gorten recommends that iron be supplied from the second week of life, incorporated in the formula, in a concentration that will insure a rate of utilization of 35 mg of iron per kilogram of body weight gain.[7]

Term Infants

In 1933, Elvehjem and co-workers reported hemoglobin concentrations for 750 children varying in age from birth to 5 years.[8] These were healthy infants and children who were followed in the child health centers of Madison, Wis. At one year of age, 10 per cent of these infants had hemoglobin concentrations lower than 10 gm/100 ml. When infants from this same population were given a daily supplement of 25 mg of iron as ferric pyrophosphate and 1 mg of copper as copper sulfate, the mean hemoglobin concentration was increased from 9-11 gm/100 ml to 12-13.5 gm.[9] This study is the first report providing information on the distribution of hemoglobin level

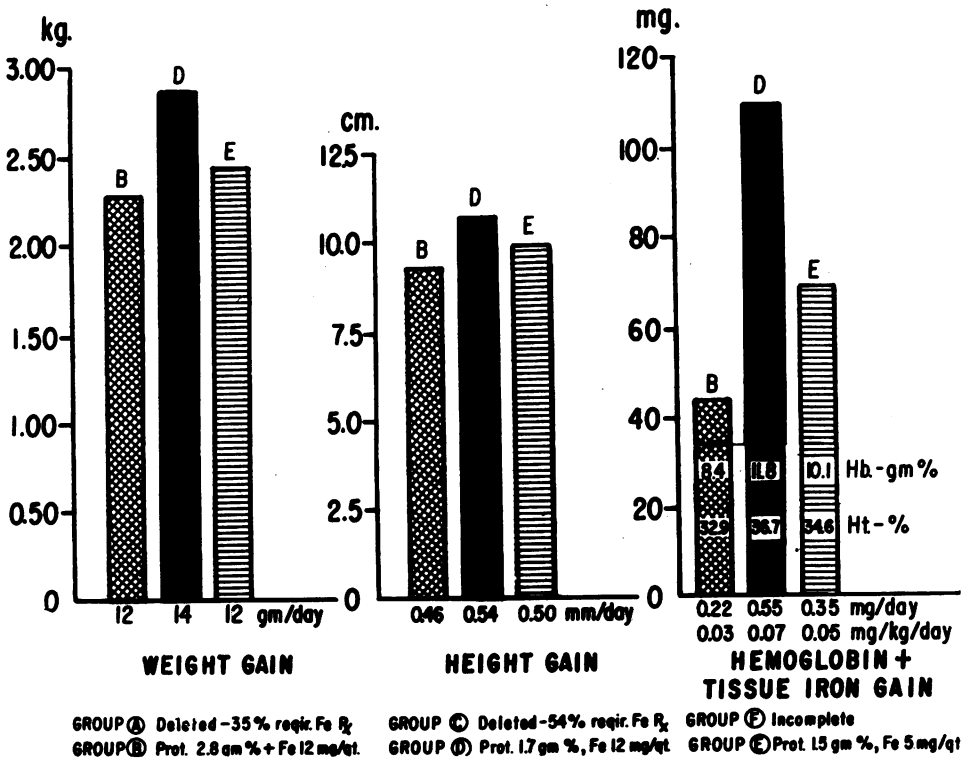

Figure 4—Relation of increase in weight and height, hemoglobin concentration and tissue iron to provision of exogenous iron 6 to 12 months

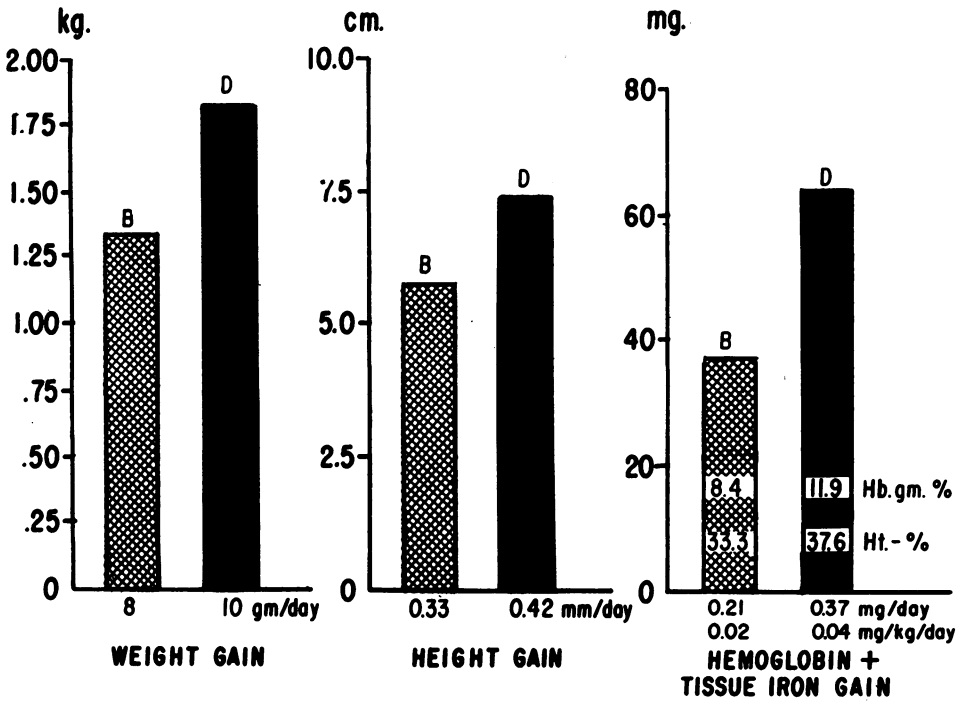

Figure 5—Relation of increase in weight and height, hemoglobin concentration and tissue iron to provision of exogenous iron 12 to 18 months

with age, from which one can estimate the incidence of nutritional iron deficiency among infants in the United States.

A study on iron requirements of infants reported in 1959 by Sturgeon indicates that approximately 7 per cent of term infants develop hemoglobin levels less than 10 gm/100 ml by 12 months of age.[10] All the infants followed in this study were under pediatric supervision and were permitted solid foods, including iron-fortified cereals. These infants were not considered underprivileged. Sturgeon concluded that advanced feeding schedules, with iron supplements of one kind or another, were required to bring and maintain the infant close to what appears to be his physiologic maximum for iron nutrition.

Haughton conducted a pilot study among an underprivileged population of New York City cared for in Child Health Stations.[11] At one year of age, 41.3 per cent of infants had hemoglobin levels lower than 10 gm/100 ml. Among 183 infants not more than three years old, 27.3 per cent had hemoglobin levels lower than 10 gm/100 ml.

Seventy-six per cent of term infants fed a noniron-containing formula, along with a recommended regimen of solid foods and followed for a period of 18 months in the Child Welfare Stations of the Eighth Health District of Chicago, developed iron deficiency anemia.[12] Under the same circumstances, except for receiving a prepared iron-containing formula for the first six to nine months of life, a study group of infants showed an incidence of anemia of 9 per cent (Figure 6).

Danneker has determined hemoglobin concentrations in children 6 to 36

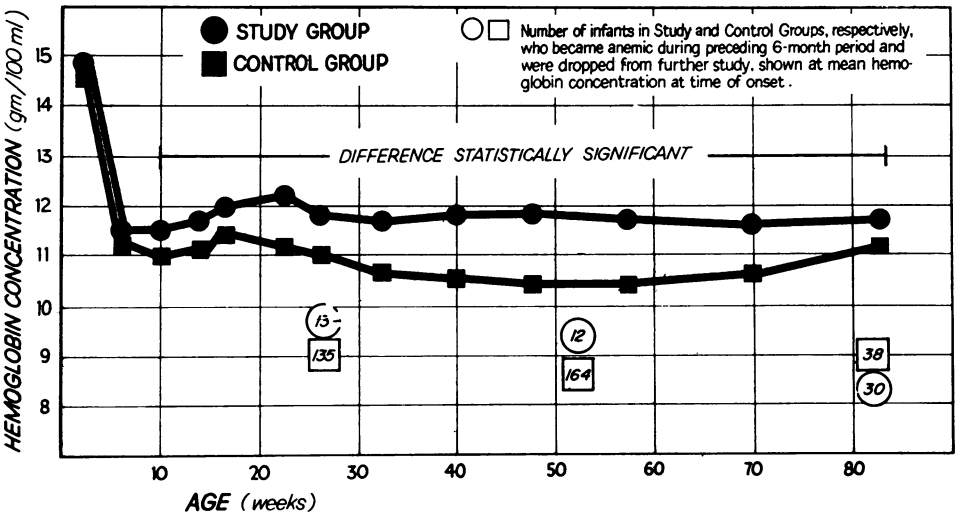

Figure 6—Mean hemoglobin concentration during the first 18 months of life for study group (fed iron-containing formula) and control group (receiving usual diet)

months of age followed in Child Health Conferences in Allegheny County (Pittsburgh), Pa.[13] In a population of 364 children, 16.4 per cent were found to have hemoglobin levels below 10 gm/100 ml. An incidence of 19.0 per cent was found among nonwhite children, approximately three times greater than that among white infants, at 6.8 per cent. Iron therapy with 25 mg of elemental iron per day for children whose hemoglobin concentration was less than 10 gm/100 ml raised hemoglobin concentration.

Gorten has reported observations on three large groups of term infants.[14] Two of these groups were studied in Baltimore, Md., the third in rural Pakistan. One group of United States infants was privileged in that they were raised in an ideal nutritional environment. The other group of United States infants, followed in a well-baby clinic, was supervised by the Baltimore City Health Department (Table 3).

Mean hemoglobin concentration as a function of age is plotted in Figure 7. The United States disadvantaged group

Table 3—Characteristics of infants surveyed

Group	A	B	C
Method of study	Longitudinal	X-sectional	X-sectional
Number of subjects	159	508	343
Observations	502	531	343
Environment	US privileged	US disadvantaged	Rural Pakistan
Formula	Prepared	EM+CHO	Human milk
Strained foods (initiated)	2.5 mo	3 mo	
Strained foods (full diet)	6 mo	advised 6 mo	12–18 mo

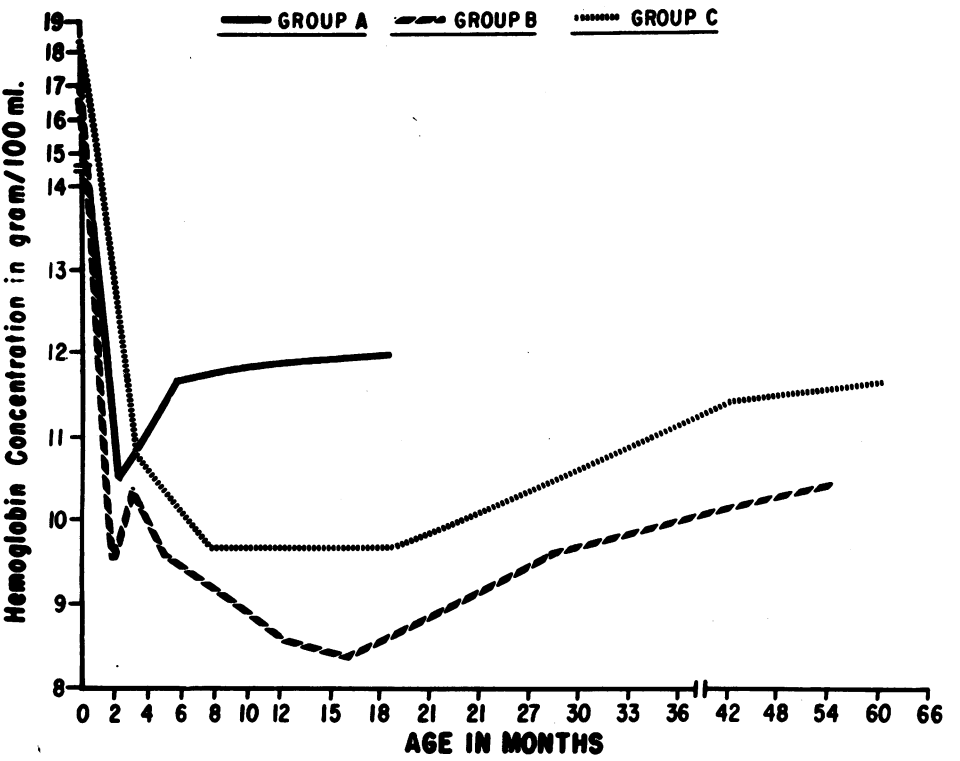

Figure 7—Hemoglobin concentrations for three groups of term infants: Group A—US privileged; Group B—US disadvantaged; Group C—Rural Pakistani.

shows a mean hemoglobin concentration that is lower than that obtained among rural Pakistani infants. Calculation of total body iron, however, indicates that the Pakistani infant has less than the United States disadvantaged infant (Figure 8). This calculation is dependent on body weight, and examination of growth curves indicates that the Pakistani infant grows along the lower third percentile for United States infants, during most of his first five years of life (Figure 9). The higher mean hemoglobin concentration of the Pakistani infant derives from a reduced rate of growth, due to lower caloric intake, that keeps him from diluting his hemoglobin mass to the same degree.

A small number of Eskimo infants, living near Nome, has been studied by Baker.[15] Hematocrit percentages lower than 30 occurred in 20.8 per cent of infants from 1 to 24 months of age, most of them between 6 and 18 months of age. The published results of the Interdepartmental Committee on Nutrition for National Defense (ICNND) Survey of the health and nutritional status of Alaskan Eskimos, conducted in 1958, are not detailed enough to permit comparison with the findings of Baker.[16]

Heller and co-workers have recently shown that average linear growth in the Eskimo infant, after six months of age, approximates the lower fifth percentile of that for white North American infants, as reported by Falkner.[17,18] Eskimo infants have been shown to have a ratio

of weight to height that is consistently higher than that of white infants.

Infant cereal products fortified with iron will maintain adequate hemoglobin concentrations for term infants, whenever they receive sufficient cereal to provide approximately 10 mg of elemental iron per day.[19] Analysis of one-day diet histories of 8,000 infants who were six months old indicates that 25 per cent of infants in the United States receive less than one-half the daily recommended intake of iron (Table 4).[20,21]

Hospitalized Infants

The incidence of nutritional anemia in infants 6 to 36 months of age admitted to hospitals in the United States has been subject to frequent study over the past 25 years (Table 5).

In 1957, Guest and Brown reported an incidence of nutritional anemia of 20 per cent among infants admitted to the Children's Hospital in Cincinnati during the years 1932 to 1942.[22] Twelve years later, Lahey found the incidence unchanged for infants in this hospital.[22,24] Comparable studies among hospitalized infants in Boston, Chicago, St. Louis, and Columbus, yield data consistent with the Cincinnati studies. While nutritional iron deficiency is primarily regarded as a deficiency state more prevalent among nonwhite infants and infants from a low socioeconomic background, its occurrence is not restricted to major metropolitan areas (Table 6).[27]

Preschool

Under Operation Head Start, several projects have investigated hemoglobin concentration among children of the pre-

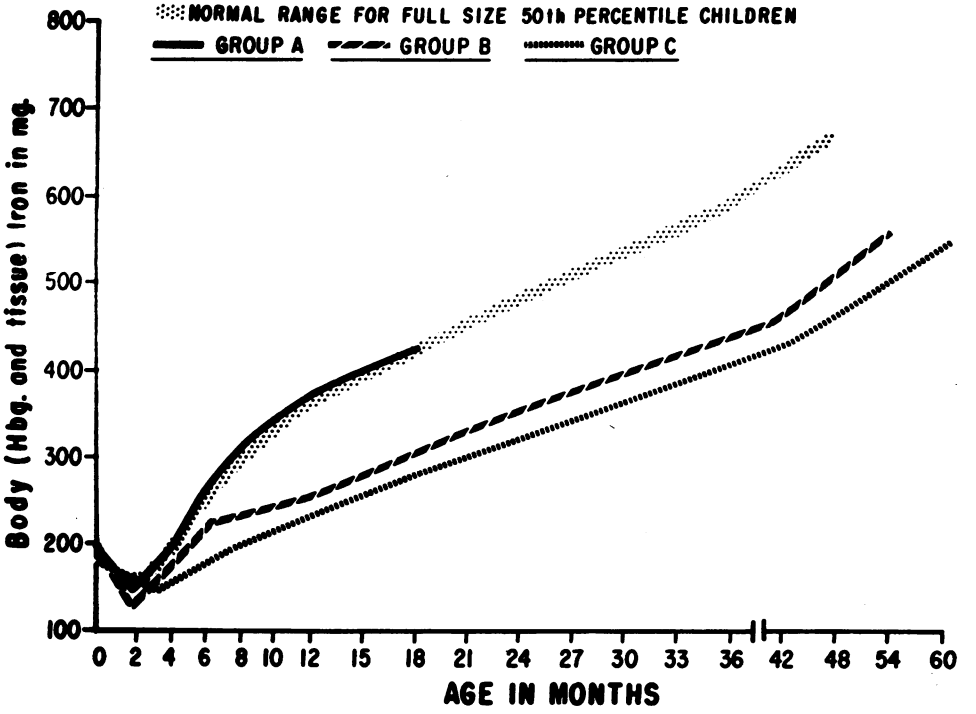

Figure 8—Calculated total body iron for three groups of term infants: Group A—US privileged; Group B—US disadvantaged; Group C—Rural Pakistani.

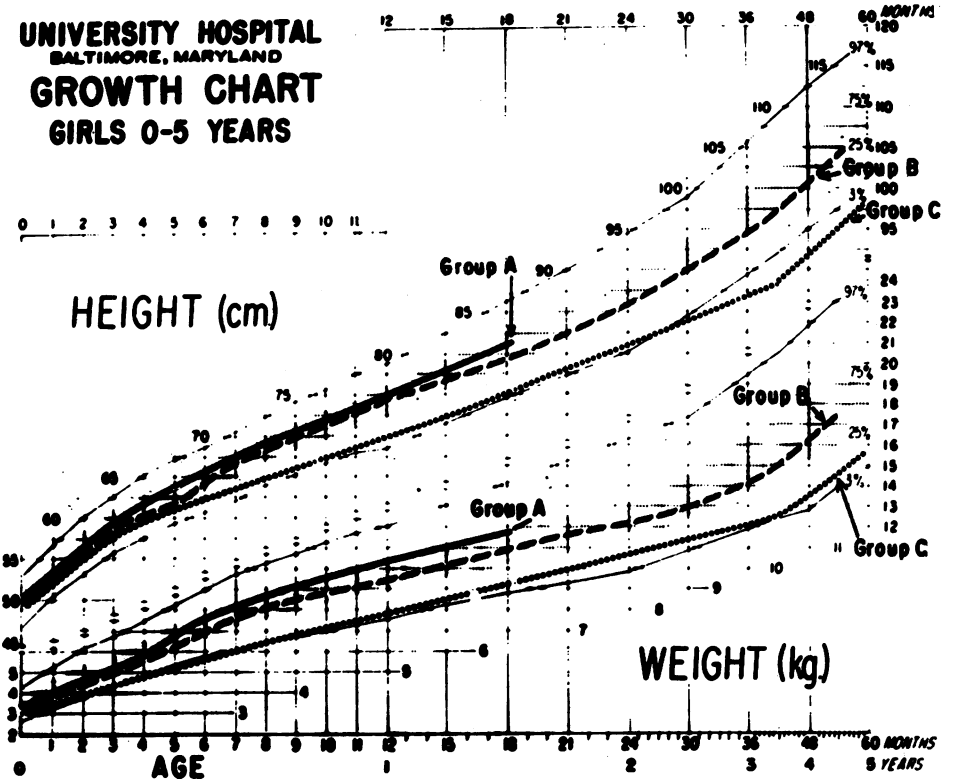

Figure 9—Mean growth of two US and one Pakistani groups of children

school age group. An early report from Chicago by Kravitz indicates that 8.5 per cent of these children had hemoglobin concentrations lower than 10 gm/100 ml.[28] For this age group a hemoglobin concentration of 11 gm/100 ml may be the better lower limit for nutritional adequacy. When this index is applied to the Chicago Head Start program, the incidence of anemia is found to be 31.6 per cent.

Pearson and co-workers have collated hematocrit percentages from project Head Start for a series of United States cities.[29] These data are summarized in Table 7. Children from Augusta, Ga., have lower hematocrit values than those determined for children residing in other major southern cities and in Chicago, Ill. Children from Chicago,

Table 4—Single-day iron intake of six-month-old infants (mg/day)

Sample	Percentile distribution 25	50	75
Total US	4.2	7.2	11.8
Urban	4.7	7.9	12.4
Rural	3.4	6.1	10.7
Education of mothers			
Grade	2.4	4.6	8.6
High	4.3	7.1	11.8
Past high	5.1	8.2	13.0
Annual income			
Less $4,000	3.4	6.0	10.4
$4,000–$7,000	4.4	7.5	12.2
More $7,000	5.2	8.3	12.9
Daily requirement 8 to 12 mg per day			

Table 5—Incidence of nutritional anemia in hospitalized infants (6 to 36 months of age)

Investigator	City	Year	No. of infants	Low Hgb* %
Guest[22]	Cincinnati	42	613	20
Diamond[23]	Boston	50	350	35
Lahey[22,24]	Cincinnati	54	314	22
Schulman[2]	Chicago	61	425	44
Holowach[25]	St. Louis	63	582	31
Robertson[26]	Columbus	63	797	25
Collins[27]	Iowa City	65	631	17

* Hemoglobin 9.9 gm/100 ml or less.

in turn, differ from those living in Houston, Tex., whenever hematocrit values are compared. As measured by hematocrit, some 1 to 8 per cent of infants of four to six years have anemia. Unfortunately, there are no data on this age group permitting comparison with the magnitude of anemia observed in previous years.

Kripke and Van Fossen have studied a group of preschool children in Cedar Rapids, Iowa.[30] These children from a low socioeconomic background do not differ appreciably in hemoglobin concentrations from those studied by Kravitz in Chicago. Among 81 children, 22 or 27.5 per cent had hemoglobin concentrations lower than 11.0 gm/100 ml. Oral iron administered at 120 mg/day for two weeks produced a change in mean hemoglobin concentration from 10.6 to 11.6 gm/100 ml, confirming a deficit of dietary iron.

Summary

Nutritional anemia in the United States is primarily due to a dietary deficiency in iron. Iron enrichment of the diet is necessary if nutritional iron deficiency is to be prevented in infants and children. Knowledge of the prevalence of anemia, due to iron deficiency, is primarily derived from studies conducted within the past 25 years. Since methods of study and dietary patterns have changed within recent years, it is essential that we obtain current information on the hematologic status of infants and children.

Nutritional iron deficiency, like scurvy and rickets, is preventable by a properly directed dietary enrichment program. Its occurrence among infants and children of lower socioeconomic backgrounds poses many problems to those working in public health. In this rather cursory review, no effort has been made to evaluate the secondary health gains that may arise from improved or adequate iron stores. Understanding of the magnitude of the problem and the location of individuals at risk throughout the country must precede consideration of ancillary benefits. Iron enrich-

Table 6—Anemia* among hospitalized infants 6 to 24 months of age

Hospital	All (infants) %	Race		Classification	
		White %	Nonwhite %	Private %	Indigent %
Childrens Hospital Columbus, Ohio	24.7	21.5	44.1	16.8	40.4
University Hospital Iowa City	21.0	19.5	50.0	14.3	26.1

* Hemoglobin 9.9 gm/100 ml or less.

Table 7—Hematocrit values for children four to six years of age

City	No. subjects	Hematocrit Mean	Hematocrit SD	% less than 31.0
Chicago	3,480	36.0	3.0	4.5
Jacksonville	662	36.7	2.9	2.8
Houston	1,750	36.6	2.6	0.6
Gainesville	477	35.1	2.3	1.7
Augusta	415	35.0	2.9	7.7

ment of certain foodstuffs poses few, if any, technical problems; thus, the means to eradicate the nutritional deficiency exist.

In the past 25 years, nutritional iron deficiency among infants has been well characterized. In spite of this information, little has been accomplished at the public health level to minimize the condition. Less information exists about the incidence of iron deficiency among older children. Head Start is providing some data. However scarce the data, we know that action programs must be initiated to correct this nutritional deficit.

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