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Hematopoietic studies in vitamin A deficiency[1-3]

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ABSTRACT Recent studies of experimental vitamin A deficiency in man led the authors to conclude that anemia may result from lack of vitamin A. A review of numerous nutrition surveys in underdeveloped countries enhanced the suspicion that deficiency of vitamin A does contribute to the prevalence of anemia. Preliminary studies of vitamin A-deficient rats confirmed previous observations that anemia may result from lack of this vitamin. The livers of these animals had very low concentrations of vitamin A but normal or increased concentrations of iron. The finding of anemia is in contrast with other reports that vitamin A deficiency may cause elevated values for hemoglobin and hematocrit. The authors suggest that loss of taste and smell as a result of deficiency may account for refusal of experimental animals to eat and drink enough to prevent inanitation and dehydration. The resulting hemoconcentration may mask the true hematological picture, which is one of anemia. *Am. J. Clin. Nutr.* 31: 876-885, 1978.

Human deficiency of vitamin A continues to be a significant problem, both in the developing countries (1) and in the United States (2). Recently we conducted a controlled study of vitamin A deficiency in a group of healthy middle-aged men (3-5). An unexpected finding in this group of subjects was the development of a moderate degree of anemia, despite seemingly ample dietary sources of all essential nutrients except vitamin A.

A review of publications relating to vitamin A deficiency occurring in both man and experimental animals disclosed a number of reports of hematopoietic changes. Many of these articles described an anemia associated with vitamin A deficiency (6-12), whereas others described polycythemia that may, in some instances, have resulted from dehydration and hypovolemia (8, 13-17).

These conflicting reports led us to evaluate this problem from three different aspects: a reevaluation of the hematologic aspects of our recent study of experimental human vitamin A deficiency, a review of data collected in many surveys of developing countries, and a new series of studies of vitamin A deficiency in rats.

Methods and results

Human studies

These studies were conducted in eight middle-aged men who volunteered to participate. The details of the diets fed, the experimental design, and the results of biochemi-

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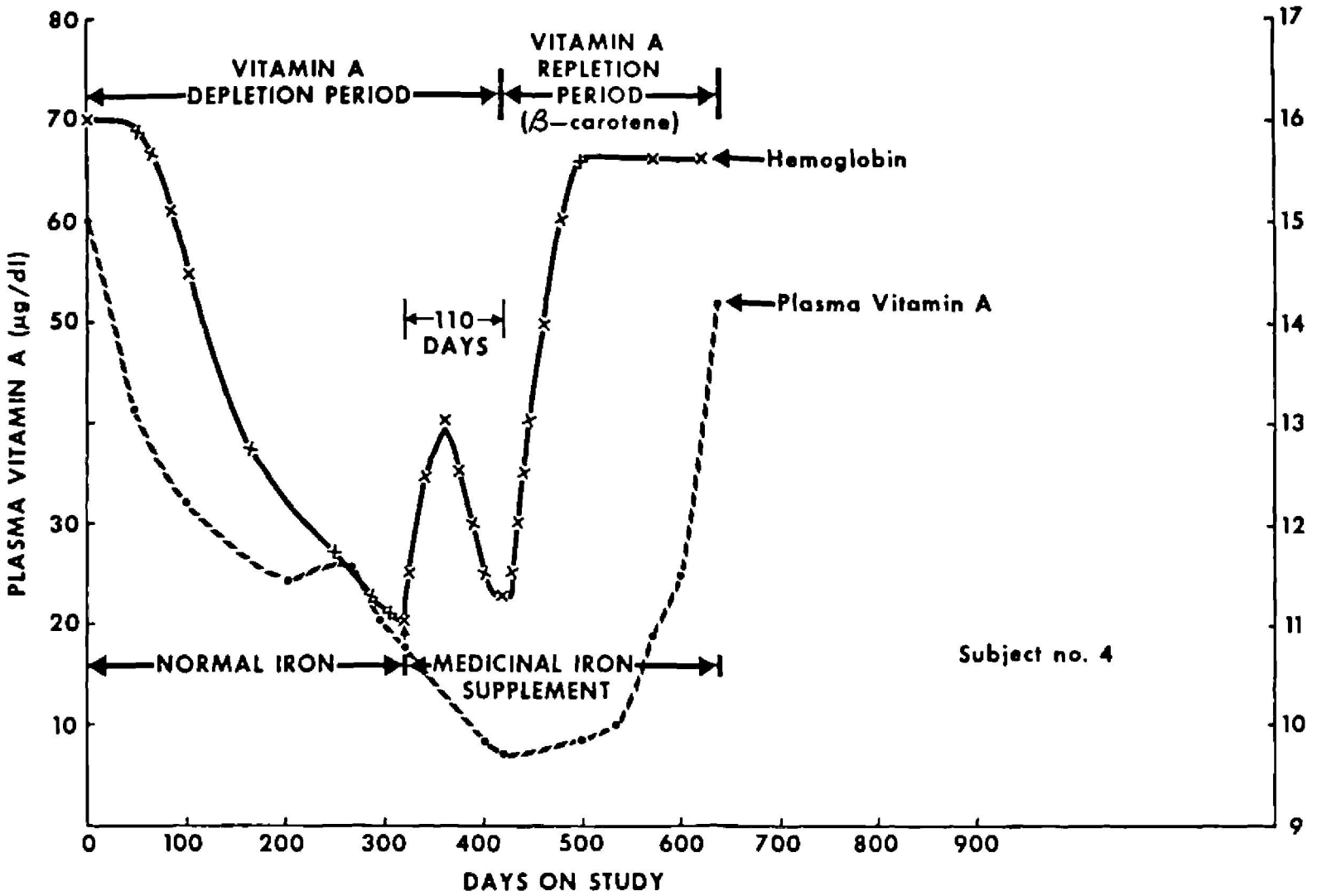

FIG. 1. Effect of vitamin A and iron supplements on plasma vitamin A and hemoglobin levels in a vitamin A depleted human volunteer.

cal, physiological, and isotopic studies are to be presented in a separate publication but the salient features have been published (4). The protocols and the approach were also similar to those described previously in studies involving other vitamin deficiencies in man (18–20). The vitamin A-deficient diets were of three major types: *1)* a liquid casein formula virtually devoid of vitamin A activity; *2)* a solid diet containing soy protein, selected vegetables, bread, and desserts, all low in vitamin A activity; and *3)* a diet composed of regular foods low in vitamin A. With all three of these diets the men were given vitamin and mineral supplements in amounts that equaled or exceeded the dietary allowances of the National Academy of Sciences (21).

As anticipated, the concentration of carotene in their serum fell rapidly and the concentration of retinol fell slowly. The vitamin A depletion time varied from 359 days for subject 5 to 771 days for subject 1. Despite a daily intake of 18 to 19 mg of iron in their diet, the men gradually began to manifest a mild degree of anemia (Fig. 1). During the early months of the study the amount of venous blood drawn for a variety of tests averaged about 70 ml/week. This would represent a loss of about 35 mg of iron weekly or about 5 mg daily. Measures were taken to reduce the amount of blood drawn to about 50 ml/week and to increase the amount of iron consumed daily, yet the anemia persisted. Another peculiar aspect of their anemia was the fact that, although the serum iron concentration was low there was not a corresponding increase in total iron binding capacity.

Vitamin A deficiency was arbitrarily defined as a condition in which the plasma retinol level fell to 10 µg/dl or less and dark

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adaptation became impaired by one log or more. Five of the eight subjects (1, 4, 5, 7, 8) fulfilled these criteria and a sixth subject (6) was "probably" deficient in vitamin A. Only the five deficient subjects were selected for evaluation of hematological data.

Determinations of hemoglobin, hematocrit, and red blood cell counts were performed using standard methods and equipment. Plasma vitamin A was determined by both the method of Bessey et al. (22) and Neeld and Pearson (23). Since the subjects became deficient in vitamin A at differing rates, comparisons of hematologic values were made in relationship to ranges of concentration of plasma retinol. We compared hemoglobin values for each of five subjects at times when their plasma levels of retinol fell within each of three categories: low (<20 μg/dl), adequate (20 to 30 μg/dl), and plentiful (>30 μg/dl). The results are shown in Table 1. The level of vitamin A in plasma correlates significantly with the concentration of hemoglobin in the blood, ($P < 0.01$).

During the active phase of the study, when it became apparent that the men were developing not only an anemia but also low serum levels of iron, they were given therapeutic iron orally. Customary doses of ferrous gluconate supplied 310 mg of elemental iron daily for varying periods during the latter half of the study. During this time and subsequently we continued to draw venous blood at a rate of approximately 50 ml/week. There was no cause for alarm since the men continued to feel well and were not severely anemic. Nevertheless, when all of the laboratory data had been evaluated, it was apparent that medicinal iron had been of little or no value so long as the men remained deficient in vitamin A. This is clearly shown in Figure 1 that depicts the hemoglobin and plasma levels of subject 4. He responded transiently to medicinal iron but relapsed despite continuing therapy. Soon after vitamin A repletion was started with β-carotene, he made a prompt and complete hemotologic recovery while continuing to eat the same diet. The other four subjects showed a similar rise in hemoglobin after they were given supplements of vitamin A or β-carotene (Table 2). The men were given varying doses of vitamin A or β-carotene for differing periods of time in an effort to establish the minimal effective dose and its rapidity of action. In all except one (subject 8), the final hemoglobin level was essentially the same as the initial value. Subject 8 was given the smallest repleting dose (75 μg/day of retinol) for 104 days. The other men were given varying starting doses ranging from 37.5 μg/day of retinol for 14 days (subject 1) to 150 μg/day for 82 days (subjects 5 and 7).

International surveys

Between 1954 and 1968 more than 30 nutritional and medical surveys were conducted in developing countries throughout the world, using essentially the same methods and procedures (24). Two of the most

TABLE 1
Comparison of levels of vitamin A and hemoglobin in men with experimental vitamin A deficiency[a]

Plasma vitamin A individual $\bar{x} \pm SD$ subject no.	Low (<20 μg/dl) hemoglobin g/dl	Adequate (20–30 μg/dl) hemoglobin g/dl	Plentiful (>30 μg/dl) hemoglobin g/dl
1	12.50 ± 0.35 (9)[b]	14.00 ± 0.53 (8)	15.95 ± 0.60 (10)
4	11.28 ± 0.26 (9)	12.25 ± 0.35 (10)	15.90 ± 0.52 (10)
5	11.19 ± 0.26 (9)	12.75 ± 0.71 (8)	15.45 ± 0.44 (10)
7	12.67 ± 0.50 (9)	13.90 ± 0.21 (10)	15.43 ± 0.56 (10)
8	11.62 ± 0.44 (8)	11.72 ± 0.36 (9)	15.50 ± 0.53 (10)
Group $\bar{x} \pm SD$	11.87 ± 0.72 (1)	12.92 ± 1.01 (2)	15.64 ± 0.55 (3)
	$P < 0.01$	$P < 0.01$	$P < 0.01$
	1 vs 2	2 vs 3	3 vs 1

[a] Hematological data from the five men who developed unequivocal deficiency of vitamin A were compared with plasma levels of retinol. These were grouped into low, adequate and high. Each group mean was significantly ($P < 0.01$) less than the other two. [b] (n).

TABLE 2
Effect of iron and vitamin A supplements on hemoglobin levels in vitamin A depleted men

Subject no.	Initial HB	Hb at point of iron supplement[a]	Days[b] + iron − vitamin A	Hb at point of vitamin A supplementation	Days vitamin A repletion	Average daily vitamin A supplementation as β-carotene	Average daily vitamin A supplementation as retinol	Hb at end of study
	g/dl			*g/dl*		*μg/day*		*g/dl*
4	16.0	10.9	110	11.3	193	360.6		15.6
5	16.0	11.0	50	11.5	493		365.7	16.0
6	16.0	11.0	50	11.5	496	194.5		16.0
7	16.3	13.0	198	12.5	149		304	15.9
8[c]	16.0	11.0	284	12.2	131		109.9	13.6[d]
Average	16.1[d] ± 0.13	11.4[e] ± 0.91		11.8[e] ± 0.52				15.4[d] ± 1.03

[a] 310 days after starting vitamin A depletion diet. [b] Indicates number of days each subject received medicinal iron before supplements of vitamin A were started. [c] Received only 75 μg retinol/day for 104 days and then 150 μg and 300 μg retinol/day for 10 and 17 days, respectively. [d,e] Comparisons between initial Hb and value at time of iron supplement were significant, $P < 0.01$. Similarly Hb at point of vitamin A supplement differed significantly ($P < 0.01$) from both initial and final values.

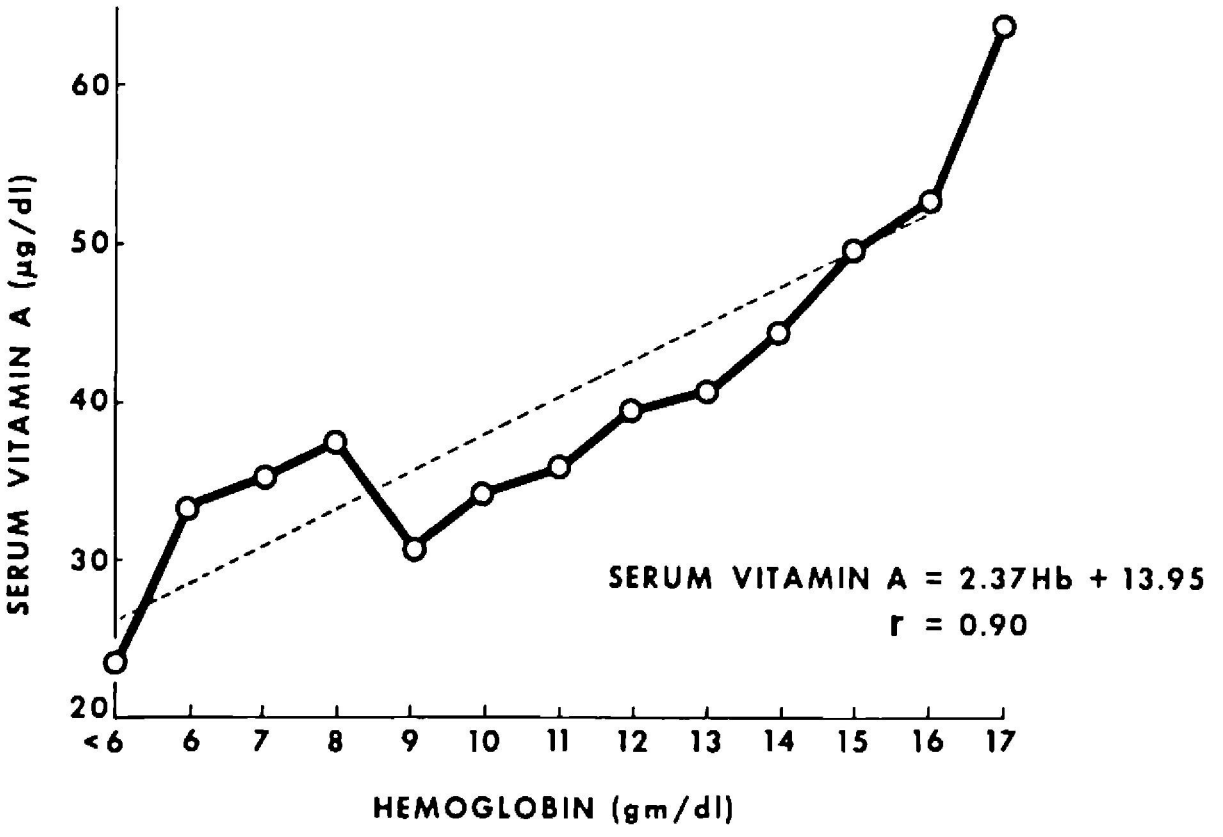

FIG. 2. Relationship of serum vitamin A levels to hemoglobin levels as observed in the ICNND nutrition survey of Paraguay (1967).

common findings were an inadequate intake of vitamin A and a high prevalence of anemia, especially in tropical and subtropical regions where the inhabitants depend largely upon rice or maize for the major share of their nourishment.

From these reports, we selected those which permitted a comparison between the average intake of vitamin A and the average levels of hemoglobin. The countries or regions selected were those where the average iron intake was reasonably adequate; 14 mg or more per day. Because women, during the reproductive years, are more likely to develop iron-deficiency anemia, we selected data from women between the ages of 15 and 45 years who were neither pregnant nor lactating.

The report of the Interdepartmental Committee on Nutrition for National Defense (ICNND) Nutrition Survey of Paraguay includes a graph (Fig. 2) which shows

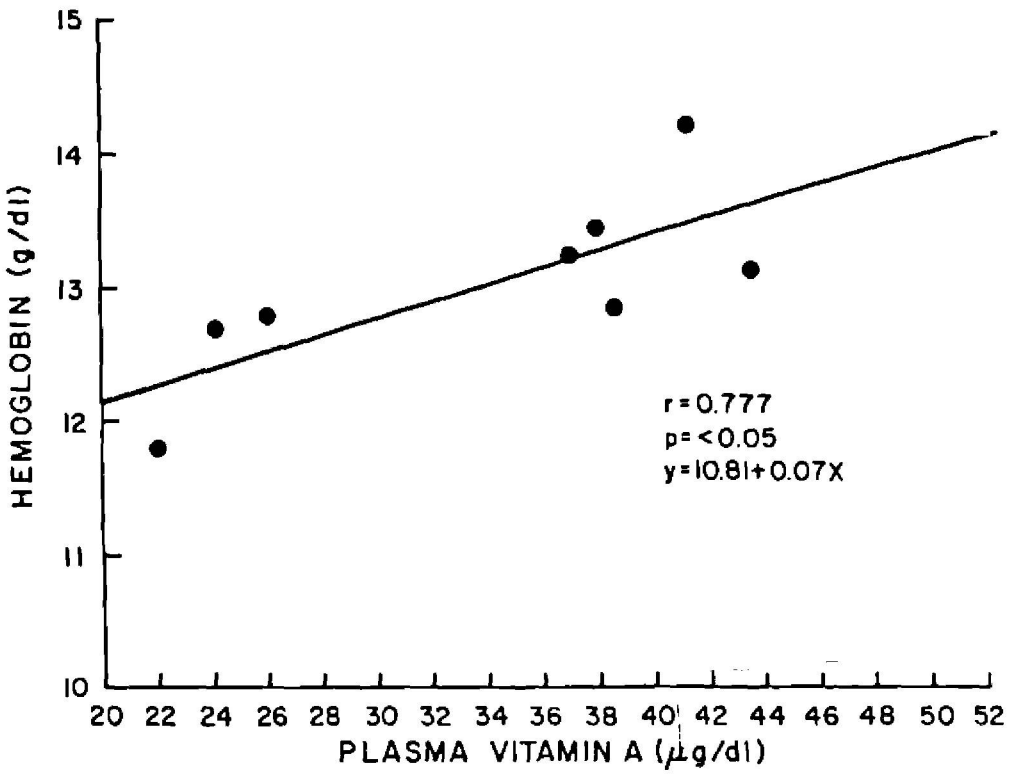

FIG. 3. Relationship of hemoglobin and plasma vitamin A as observed in several ICNND nutrition surveys (nonpregnant, nonlactating females, 15 to 45 years old). Correlation between plasma vitamin A and hemoglobin: $r = 0.777$ ($P < 0.05$), $y = 10.81 + 0.07X$.

TABLE 3
Hemoglobin levels, plasma vitamin A levels, and iron intake as observed in seven selected nutrition surveys[a]

Country	Hb	Plasma vitamin A	Iron intake
	g/dl	*µg/dl*	*mg/day*
South Vietnam	11.8	22.0	14.4
Chile	12.7	24.1	17.6
Northeast Brazil	12.8	26.2	17.4
Uruguay	13.3	37.0	14.7
Ecuador	13.5	38.0	17.1
Venezuela	12.9	38.6	16.0
Guatemala	14.3	41.2	14.3
Ethiopia	13.2	43.5	471.0

[a] Nonpregnant, nonlactating females, 15 to 45 years old. Note that iron intake in Ethiopia is about 30 times that of other countries. This has been verified by other studies.

a strong relationship between serum levels of vitamin A and blood levels of hemoglobin (25). This led us to study the survey reports of other nations having low or marginal average intakes of vitamin A. On this basis, seven ICNND reports (in addition to that of Paraguay) were selected for study (26), and the six countries surveyed by the Institute of Nutrition of Central America and Panama were included (27).

In the reports of surveys in eight countries; Vietnam, Chile, Northeast Brazil, Uruguay, Ecuador, Venezuela, Guatemala, and Ethiopia iron intake was adequate or nearly so but vitamin A intake was low. A comparison between blood levels of hemoglobin and plasma levels of vitamin A shows a direct correlation (Fig. 3). Furthermore, there is no relationship between hemoglobin levels and iron intake (Table 3). No data are available regarding plasma levels of folic acid and vitamin B_{12} and no studies were made to determine the extent of hookworm infestation in the populations surveyed.

Experimental vitamin A deficiency in rats

In an attempt to further evaluate the apparent relationships between vitamin A deficiency, iron metabolism and hemoglobin formation we conducted studies in 3 groups of weanling Sprague-Dawley rats (Simonson, Gilroy, Calif.), weighing approximately 40 g each. All three groups were fed a semi-purified diet, complete in all essential nutrients except vitamin A (Table 4). Control groups were given retinyl palmitate at a level of 6500 IU/kg of diet. The composition of this diet has been described by Lamb et al. (28). The control groups were fed the supplemented diet, either ad libitum or in restricted amounts so that their intake was the same as that of the deficient group (pair-fed) (Table 5). Hematological values were determined using standard methods. Hepatic vitamin A levels were determined spectrophotometrically

(29). The method of Roe (30) was used for determination of ascorbic acid in serum and liver. At approximately 50 days on the deficient diet and when weight loss was evident in the deficient animals, we gave a small supplement of vitamin A by allowing the animals to eat the complete diet for 1 day. Then after a transient spurt of growth, a new deficient state was attained. Ninety days later when evidence of vitamin A deficiency was obvious in the experimental group (failure to gain weight, rumpled fur, encrusted eyelids) all rats were killed and weighed. Livers were removed for measurement of retinol, ascorbic acid, and iron content. Blood was collected (some samples were lost due to technical error, or discarded when hemolysis was evident) for measurements of ascorbic acid, hemoglobin, hematocrit and red and white blood cell counts (Table 5).

Average body weight was lowest in the vitamin A-deficient group, intermediate in the pair-fed control group and normal in the ad libitum control group. In the vitamin A-deficient animals, however, there was significant evidence of anemia. Leukocyte counts remained normal.

Hepatic concentrations of retinol were very low and ascorbic acid concentrations were moderately reduced. Liver concentration of iron rose insignificantly in the deficient animals.

TABLE 4
Diet of rats

Composition of vitamin A deficient diet	
Ingredient	Percentage
Cerelose	61.0
Vitamin free-casein[a]	18.0
Vitamin mixture-sucrose[b]	10.0
Salt mixture[c,d]	6.0
Oil (olive oil)	5.0
DL-methionine	0.25

[a] Nutritional Biochemical, Cleveland, Ohio. [b] Provides the following mg/kg diet: cyanocobalamin, 0.02; biotin, 0.5; folic acid, 0.5; menadione, 0.60; thiamin, 5.0; riboflavin, 5.0; pyridoxine, 5.0; α-tocopherol acetate, 45.5; pantothenate, 50.0; nicotinic acid, 50.0; inositol, 100.0; choline chloride, 1000.0. The complete diet contained additional vitamin A palmitate (20 mg/kg diet). [c] J. Nutr. 103: 929, 1973. [d] Atomic absorption analysis of the whole diet showed it to contain 35.5 ± 6.7 ppm of iron.

Discussion

Previously published reports indicate that vitamin A almost certainly plays an important role in hematopoiesis. In 1922 Findlay and MacKenzie (6) reported that rats deficient in vitamin A developed patches of gelatinous degeneration in their bone marrow and that the animals surviving the longest had "almost complete replacement of haematopoietic tissue by fibrous tissue stroma." Wolbach and Howe (7), who stud-

TABLE 5
Body weight, liver and blood data of vitamin A-deficient rats as compared to ad lib and pair-fed controls, (means ± SD)

	Groups of rats		
	Ad libitum control	Pair-fed control	Vitamin A-deficient
Body weight (g)	463.5a[a] ± 71.5, n[b]=15	405.9b* ± 66.9, n=15	337.2c** ± 97.6, n=13
Liver vitamin A (μg/g wet wt)[c]	298.0a ± 70.5, n=15	307.9a ± 45.3, n=15	7.3b** ± 6.3, n=12
Liver vitamin C (μg/g wet wt)	268.4a ± 59.4, n=15	299.1a ± 51.1, n=15	204.0b** ± 35.9, n=14
Liver iron (μg/g wet wt)	219.4a ± 70.9, n=15	254.2a ± 92.0, n=15	318.4a ± 190.1, n=14
Whole blood vitamin C (mg/dl)	0.54a ± 0.13, n=10	0.55a ± 0.03, n=12	0.29b** ± 0.08, n=9
Hemoglobin (g/dl)	15.1a ± 1.4, n=8	15.0a ± 1.5, n=9	13.1b* ± 1.6, n=7
Hematocrit (%)	46.0a ± 2.4, n=10	46.0a ± 2.2, n=8	39.6b** ± 2.0, n=8
Erythrocytes × 10^6	7.2a ± 0.76, n=5	7.2a ± 0.44, n=6	6.3a ± 0.76, n=5
Leukocytes × 10^3	6.0a ± 2.4, n=5	7.0a ± 1.9, n=6	7.1a ± 2.3, n=5

[a] For each measurement, Means with different letters are significantly different, $^*P < 0.05$ or $^{**}P < 0.01$. [b] n, no. of animals. [c] Determination of liver vitamin A levels in animals of the same age as in the beginning of the experiment and under the same experimental conditions, revealed a liver vitamin A concentration of 15.3 ± 8.8 (n = 6) μg/g wet weight.

ied vitamin A deficiency in Wistar rats, noted cessation of growth, loss of ability to smell, and inability to eat. Careful histological studies of these animals disclosed almost complete disappearance of fat and "Reduction in numbers of cells concerned in hematopoiesis was apparent in a few marrows. . . ."

Koessler et al. (8) called attention to a phenomenon that may explain the disparity reported by various investigators regarding the hematological changes induced by a lack of vitamin A. Rats fed a diet deficient in vitamin A soon ceased to gain weight, then developed diarrhea, inability to eat, and dehydration. Erythrocyte counts and hemoglobin levels fell, then rose when the animals became dehydrated. Restoration of small amounts of vitamin A to their diets resulted in rapid improvement in weight but slower improvement in the blood picture. The stained blood film showed "very marked polychromatophilia and definite anisocytosis with many microcytes and macrocytes as well as erythroblasts of the normoblastic type." The authors also stated "Blood regeneration cannot take place without the presence of vitamin A." They suggested that "these experimental data seem to prove that the addition of a small quantity of vitamin A to the diet of an animal, long depleted in its vitamin A reserve, brings about rapid formation of new red blood cells."

Blackfan and Wolbach (9) reviewed 13 case reports collected in a span of 10 years. The diagnosis of vitamin A deficiency in these infants was based upon finding keratinized epithelial cells in seven cases and upon clinical findings (ocular keratomalacia) in the remaining six. Of these infants 12 died and necropsy was performed in 11. (No measurements were made of plasma vitamin A levels because a method had not yet (1933) been devised.) Hematological studies were reported for 11 of these 13 infants. Five had hemoglobin values of "70% or less" and six had erythrocyte counts of 4 million or less (including three of those with low hemoglobin levels). The authors called attention to a peculiar characteristic of vitamin A deficiency in human infants, rats and guinea pigs: there was hemosiderosis of the spleen and liver and ". . . in prolonged deficiencies . . . atrophy of the spleen and bone marrow." They also observed, "In animals, restoration of the diet (vitamin A) is followed by regeneration of the bone marrow, disappearance of the hemosiderin from the spleen and liver an outburst of erythroblastic activity."

Frank (10) also observed anemia in vitamin A-deficient rats and found similar changes in the blood of two infants with xerophthalmia. He too reported a prolonged bleeding time and a polymorphonuclear leukocytosis.

A study of experimental human vitamin A deficiency was reported by Wagner in 1940 (11). Ten men fed a diet deficient in vitamin A and carotene for 188 days became "deficient." Hematopoiesis was impaired, judging from hemoglobin levels and erythrocyte counts. They also noted poikilocytosis and anisocytosis of red cells.

O'Toole et al. (12) reported that vitamin A depletion in 11 rhesus monkeys resulted in "moderate to severe anemia" in "several of the animals." The most severely afflicted animal had a hematocrit value of 12% for several weeks while being treated with "liver, iron and whole blood." "Only after twice-weekly treatments of 5,000 IU of vitamin A were given did the hematocrit approach a normal level of 32%."

These articles seem to support the concept that vitamin A is essential for normal hematopoiesis. The observation that this type of abnormality of blood formation may be accompanied by hemosiderin deposition in liver and spleen suggests a possible mechanism. Hemolytic anemias usually are accompanied by accumulation of abnormal amounts of iron in the liver and spleen. The observation that erythrocytes may be abnormal in size, shape and staining characteristics suggest that the cells may be imperfectly formed—hence they may have a shortened survival time. If erythrocyte formation becomes impaired as a result of defective hemoglobin synthesis, one might anticipate an accumulation of the precursors of hemoglobin; iron and porphyrins or protoporphyrins. A well-known feature of vitamin A deficiency in the rat is the secretion of porphyrins from the Harderian gland of the

eye. Accumulation of iron in the liver may also suggest an alteration in the use and/or mobilization of iron. Vitamin A acid has also been shown to possess a potent mitogenic activity (33). Thus in vitamin A deficiency there may be a failure of cell division and differentiation of stem cells that could lead to an impairment of hematopoiesis. These are mere speculations that can be confirmed or denied by additional studies.

Studies that either failed to show anemia as a result of vitamin A deficiency or actually showed the opposite: polycythemia, should be evaluated. Sure et al. (13) described the effects of vitamin A deficiency in rats on their hematopoietic function. They noted that, with the onset of ophthalmia, there was a decrease in erythrocyte counts and hemoglobin concentrations but with progressive deficiency there was hemoconcentration and apparent polycythemia. They concluded; "After vitamin A deficiency has progressed to the ophthalmic stage, inanition complicates the blood picture so that high figures of hemoglobin and erythrocytes may be an expression of anhydremia, indicated by the concentration of total blood solids of the pathological animals as compared with normal animals of the same age and weight."

McLaren et al. (14) reported the results of two studies of vitamin A deficiency in Wistar albino rats. Growth rate slowed after 14 to 17 days and about 2 weeks later there was evidence of secretion from the Harderian gland of dark-colored porphyrin around the eyelids. By this time the experimental animals had significantly higher values for hematocrit, hemoglobin, and total protein. In a second study, McLaren weighed the animals daily and performed blood counts as soon as growth retardation occurred (25th to 45th day). Again he confirmed the finding of significantly elevated values for hematocrit, hemoglobin, and total protein. When hematocrit values were plotted on a log scale against body weight, a linear relationship was evident for both the control and experimental groups in both studies. The authors concluded that vitamin A requirement is a function of growth rate and that " . . . the vitamin A-deficient state exerts its effect, not directly on the hematopoietic tissues but indirectly, by affecting the growth of the body and reducing relatively the fluid compartment of the blood." In other words, the apparent polycythemia results from hemoconcentration.

A different type of report was published by Nockels and Kienholz (15) who studied the influence of vitamin A deficiency on the sexual development and on the hematocrit of cockerels. The deficient birds matured sexually at an earlier age than normal controls and their hematocrit values were significantly elevated. At the same time, their body weight was significantly less than that of controls. The authors suggested that increased androgen production could have stimulated hematopoiesis. An alternate explanation might be that the impaired rate of growth was accompanied by a reduction in circulating blood volume which gave an illusion of polycythemia.

In a carefully designed study, Amine et al. (16) compared the hematologic effects of iron deficiency and of vitamin A deficiency in rats. First they demonstrated that, whereas iron deficiency results in the familiar picture of microcytic, hypochromic anemia, deficiency of vitamin A resulted in microcytic hypochromic polycythemia. Deficiency of both iron and vitamin A produced normocytic, hypochromic anemia. Rate of growth was retarded in all three experimental groups.

Next, they studied absorption and retention of ^{59}Fe by vitamin A-deficient and by normal rats. They observed an increased rate of iron absorption in the vitamin A-deficient animals. Finally, they studied the effects of giving small supplements of either vitamin A or iron to animals deficient in both. Iron supplementation resulted in a prompt increase in growth and in hemoglobin and hematocrit values and erythrocyte counts. Supplementation of "double-deficient" rats with small doses of vitamin A resulted in further inhibition of growth, a significant fall in erythrocyte counts but an increase in hematocrit, mean cell volume and mean corpuscular hemoglobin. The authors considered several possible explanations but felt that hemoconcentration was not the most probable mechanism.

Subsequently, members of this same

group, Corey and Hayes (17), designed a model intended to elucidate the primary changes of acute vitamin A deficiency. Once again they observed the growth depression that occurs with vitamin A deficiency, and once again hematological values were elevated. These values were clearly related to changes in body weight and probably to shifts in water distribution. The authors stated that "Together these data suggest that the elevated hematocrit and weight loss (distinct from earlier depressed weight gain) may be due largely to water loss." They also called attention to prior studies which indicate that polyuria and polydipsia occur in vitamin A-deficient calves and that the renal glomerular filtration rate in ewes falls linearly with vitamin A depletion (31, 32).

These reports strengthen the concept that vitamin A deficiency probably interferes with erythropoiesis and that this effect may be masked at times by abnormal fluid losses that result in hemoconcentration.

The present report of anemia occurring in vitamin A-deficient men who failed to respond to medicinal iron is compatible with this theme. It is further supported by survey studies in developing countries where vitamin A deficiency is common amongst children. Of course, deficiencies of folic acid, vitamin B_{12}, and other nutrients must also be considered, and infestation with hookworm and other parasites cannot be ignored as a possible contributor to the anemia. Finally, preliminary rat studies confirm the fact that in vitamin A deficiency anemia can result. Elucidation of the mechanisms involved could lead to significant advances in the prevention and treatment of anemias throughout the world.

Summary

Data have been presented from three diverse sources to suggest that deficiency of vitamin A may result in anemia.

Studies of experimentally induced vitamin A deficiency in men disclosed the development of a moderate degree of anemia in five of eight subjects. This anemia did not respond to medicinal iron but it later responded to resupplementation with vitamin A.

A review of nutrition survey data from seven countries revealed in women of childbearing age, a significant correlation between plasma retinol levels and blood hemoglobin concentration. Furthermore, there was no correlation between iron intake, which was generally adequate, and hemoglobin levels.

Preliminary studies of vitamin A deficiency in weanling Sprague-Dawley rats confirmed the relationship between vitamin A deficiency and hematopoiesis. These animals became anemic but did not have significant changes in the concentrations of iron in their livers.

A review of previous studies of vitamin A deficiency, both in experimental animals and in human subjects supports the concept that vitamin A is essential for normal hematopoiesis. Deficiency of vitamin A will retard growth in young animals and may result in significant fluid losses with hemoconcentration that masks the presence of anemia.

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