The Role of Zinc, Copper and Calcium in the Etiology of the “Meat Anemia”

By Karl Guggenheim

A severe anemia in mice which had been kept on a diet of meat only has recently been described. The anemia, which was mainly macrocytic and slightly hyperchromic, could not be cured or prevented by any of the hematopoietic factors such as iron, pyridoxine, folic acid or vitamin B12 alone or in combination. Replacement of one-quarter of the muscle meat by liver prevented the anemia completely. Liver contains more copper than muscle, and since the addition to the meat of an amount of copper equal to that present in the added liver also prevented the anemia, it was assumed that “meat anemia” of mice is a dietary copper deficiency anemia.

Further experiments threw some doubt on this assumption. Mice fed a milk diet which did not provide more copper than meat did not become anemic within a period of 6 weeks, although the meat diet did cause a severe anemia within this period. The milk diet would probably have caused anemia if the observation period had been extended. The fact that feeding meat results in a severe anemia so quickly suggests an etiology other than simple dietary copper deficiency.

Interrelationships between zinc and copper have been reported. Dietary excess of zinc induces signs of copper deficiency, including anemia, which can be prevented by adding copper to the diet. The possibility that the “meat anemia” of mice is due to a high intake of zinc which is insufficiently counteracted by the small amounts of copper present in muscle meat was therefore considered. The experiments described in this paper were designed to investigate this possibility.

METHODS

Animals. The animals used were male Swiss mice, 3 weeks old, or male rats of a local strain, 4 weeks old. The experimental animals and their mothers were fed a previously described stock diet till they were used.

Diets. The experimental diet consisted either of raw beef muscle or of a semisynthetic diet of casein 18, glucose 75, vegetable oil 5 and salts 2. The salt mixture was devoid of calcium and had the following composition: potassium phosphate (dibasic) 44, magnesium sulfate 24, sodium phosphate (monobasic) 18, sodium chloride 8 and ferrous sulfate 6. This diet was supplemented with the following vitamins (mg. per 100 Gm. ration): thiamine 0.2, riboflavin 0.3, pyridoxine 0.2, calcium pantothenate 1.6, and choline chloride 100. Each mouse received 50 I.U. vitamin A and 2 I.U. vitamin D twice weekly. When calcium was to be included in the diet, 2 parts of glucose were replaced by calcium.

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786

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ZINC, COPPER AND CALCIUM IN "MEAT ANEMIA"

Analytically pure copper sulfate (CuSO₄·5 H₂O) or zinc chloride (ZnCl₂) was incorporated into the minced meat or the semisynthetic diet in varying amounts as indicated in the tables. When liver was added to meat, one-quarter of the muscle meat was replaced with liver.

**Chemical examinations.** Hemoglobin was determined by the cyanmethemoglobin method. Copper was determined as previously described and zinc was determined colorimetrically. A sample containing 3–10 µg. of zinc was digested in 5 ml. of concentrated nitric acid and 2 ml. of concentrated sulfuric acid until a colorless or a very pale yellow liquid was obtained. Cooling water was then added and the digest was heated to boiling to evaporate the fumes. For separation of copper, the solution of the decomposed sample was neutralized with ammonium hydroxide and sufficient hydrochloric acid was added to make its concentration 0.05 N. Then water was added to make 50 ml. The cold solution was transferred in a separatory funnel and copper was extracted by shaking with 5 ml. of 0.01 per cent dithizone in carbon tetrachloride. This procedure was repeated until the color of the dithizone solution remained unchanged. To 10 ml. of the aqueous phase remaining in the separatory funnel, 5.0 ml. of acetate buffer solution (pH 4.75) and 1.0 ml. of a 25 per cent solution of sodium thiosulfate were added. Care was taken to remove reacting heavy metals from the acetate buffer by shaking with 0.01 per cent dithizone solution. Then 5.0 ml. of 0.001 per cent dithizone in carbon tetrachloride were added to the separatory funnel and shaken vigorously. After separation, the dithizone solution was collected and absorption at 620 mμ was measured in a Klett apparatus.

**RESULTS**

The zinc and copper content of muscle meat and liver. In five samples of fresh beef muscle, 65 (47-75) mg. of zinc per Kg. and 1.34 (1.22-1.67) mg. copper per Kg. were found. The zinc-copper ratio (Zn/Cu) was thus 50. In five samples of fresh beef liver, 38 (31-56) mg. zinc per Kg. and 22.1 (20.0-25.3) mg. copper per Kg. were found, the Zn/Cu ratio being 1.7. The mixture of 1 part liver and 3 parts muscle meat which was found previously to prevent anemia had, therefore, a Zn/Cu ratio of 9.

Supplementation of muscle meat with liver, zinc and copper. In the first series of experiments, beef liver or various amounts of copper and zinc were added to muscle meat. The ratio Zn/Cu in the resulting diets ranged between 10 and 86. Nine groups of mice were used in these experiments. Their initial weight was 10–12 Gm. and their hemoglobin 14–16 Gm./100 ml. As in a previous publication, only the changes observed in 6 weeks will be reported.

Data in table 1 confirm that severe anemia develops in mice fed a meat diet and that it can be prevented by adding liver or copper to the meat (Exp. 1, 2, 7). Generally, diets with a Zn/Cu of 24 or less do not produce anemia (Exp. 2, 5, 7, 8) whereas a Zn/Cu of 50 or more produces a more or less severe anemia (Exp. 1, 3, 4, 6, 9).

Supplementing meat with liver or copper improves the weight gain of the mice considerably, whereas growth is markedly impaired with the unsupplemented meat diet. Addition of 200 or 500 mg. Zn to meat supplemented with liver or copper also has a marked growth-depressing effect. Over 50 per cent of the animals in series 4, 6, and 8 died within 6 weeks. The death rate in the other series was much lower (the figures in table 1 and in the following tables refer to survivors only).

**Supplementation with calcium and vitamin D.** Various calcium salts have
Table 1.—Effect of Supplementation of a Meat Diet with Liver, Copper and Zinc on Hemoglobin and Weight Increase of Mice
(Means ± standard errors)

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>No. of Mice</th>
<th>Supplements</th>
<th>Change of Hemoglobin Gm./100 ml.</th>
<th>Weight Increase Gm.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>- - -</td>
<td>50</td>
<td>-10.2 ± 0.94</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>- - 20</td>
<td>20</td>
<td>-1.0 ± 0.30</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>- 100</td>
<td>50</td>
<td>-5.2 ± 0.78</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>- 200</td>
<td>80</td>
<td>-8.0 ± 0.89</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>- 10</td>
<td>10</td>
<td>-0.7 ± 0.26</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>- 500</td>
<td>90</td>
<td>-7.6 ± 0.82</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>250 -</td>
<td>9</td>
<td>0 ± 0.36</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>250 - 500</td>
<td>24</td>
<td>-0.3 ± 0.27</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>250 - 500</td>
<td>86</td>
<td>-5.5 ± 1.42</td>
</tr>
</tbody>
</table>

Table 2.—Hemoglobin and Weight of Mice Sustaining on a Meat Diet Supplemented with Calcium, Copper and Zinc
(Means ± standard errors)

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>No. of Mice</th>
<th>Supplement (mg./Kg.)</th>
<th>Change of Hemoglobin Gm./100 ml.</th>
<th>Weight Increase Gm.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>3600 - - 50</td>
<td>-0.1 ± 0.70</td>
<td>13.4 ± 0.83</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>3600 - 2 100 500</td>
<td>+1.1 ± 0.35</td>
<td>9.8 ± 0.42</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>3600 - 2 200 80</td>
<td>+0.2 ± 0.43</td>
<td>10.9 ± 0.76</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>3600 - 200 204</td>
<td>-12.4 ± 0.54</td>
<td>7.2 ± 1.17</td>
</tr>
<tr>
<td>5</td>
<td>19</td>
<td>7200 - 200 204</td>
<td>-9.1 ± 0.83</td>
<td>5.4 ± 1.07</td>
</tr>
</tbody>
</table>

been shown to prevent "meat anemia" when incorporated into the meat diet. In a further series of experiments (table 2), it was found that mice maintained on diets with a high Zn/Cu ratio (50 or 80) did not become anemic when calcium (as calcium carbonate) was also added. Calcium appears, therefore, to counteract the effect of a high Zn/Cu. It had, however, no effect with the Zn/Cu was high (over 200). Even large amounts of calcium (7.2 Gm./Kg.) did not prevent the fall of hemoglobin and the depression of growth produced by this very high Zn/Cu ratio.

In an attempt to elucidate the mechanism of action of calcium, the question as to whether it acts in the intestinal tract or after its absorption was studied. Calcium gluconate and levulinate were subcutaneously injected into mice in the same amounts as were consumed with the calcium-supplemented diet. However, even when highly diluted and administered in three doses each day, both compounds were toxic, and the animals died after a few days of treatment. Since vitamin D improves intestinal absorption of calcium, it was reasoned that it would prevent anemia if calcium acts after its absorption. But if vitamin D was found to have no effect on the development of anemia, it may be concluded that the site of action of calcium is within the intestinal tract. The meat diet was therefore supplemented with 1000 I.U. vitamin D per Kg. (table 3). This supplement did not prevent anemia. Nor did it intensify the action of calcium when it was added to meat together with an amount of the mineral (180 mg./Kg.) which was in-
sufficient in itself to prevent the anemia. It may, therefore, be concluded that calcium counteracts the anemia-producing action of a high Zn/Cu ratio in the intestine, possibly by inhibiting the absorption of zinc.

Experiments with a semisynthetic diet. In further experiments a semisynthetic diet which, like meat, was rich in phosphorus and poor in calcium was used. It contained (per Kg.) 2.2 Gm. phosphorus, 9 mg. zinc, 1.8 mg. copper and only traces of calcium. By addition of 20 Gm. of calcium carbonate and/or 80 mg. of zinc and 2 mg. copper, five variations of basal diet were made (table 4). Twenty-one mice were maintained on the unsupplemented diet (Zn/Cu ratio = 5) for 6 weeks (Exp. 1). Their growth was very poor and hemoglobin determinations carried out on them gave erratic results. Seven of these mice did not become anemic, but severe anemia developed in nine mice and a moderate anemia in five. The mean decrease of hemoglobin (−5.3) indicated a moderate anemia with a high standard error (3.26). Addition of calcium carbonate to this diet prevented the anemia (Exp. 2).

In another experiment, 2 mg. of copper and 80 mg. of zinc were added to the diet giving a Zn/Cu ratio of 24 (Exp. 3). In spite of the relatively small amount of zinc added and the low Zn/Cu ratio, the diet proved to be toxic. Mortality in 6 weeks exceeded 50 per cent and growth stopped completely. This high toxicity of zinc could be prevented by calcium (Exp. 4). Supplemental zinc without copper added (Exp. 5) resulted in a similarly high toxicity which, however, could only partly be counteracted by calcium (Exp. 6).

It appears, therefore, that mice are more susceptible to zinc poisoning when maintained on the semisynthetic diet than when fed meat only. Here
Table 5.—Experiments on Rats (Means ± standard errors)

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>No. of Rats</th>
<th>Diet</th>
<th>Supplement (mg./Kg.)</th>
<th>Zn/Cu Ratio</th>
<th>Change of Hemoglobin Gm./100 ml.</th>
<th>Weight Increase Gm.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>meat</td>
<td>Ca - 50</td>
<td>-</td>
<td>+1.8 ± 1.18</td>
<td>86 ± 5.0</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>meat</td>
<td>Ca - 100</td>
<td>200</td>
<td>-0.3 ± 0.90</td>
<td>88 ± 8.6</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>meat</td>
<td>Ca - 50</td>
<td>200</td>
<td>-1.5 ± 0.95</td>
<td>90 ± 8.0</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>meat</td>
<td>Ca - 50</td>
<td>435</td>
<td>-6.1 ± 0.93</td>
<td>33 ± 6.4</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>semisynthetic</td>
<td>Ca - 50</td>
<td>5</td>
<td>+1.2 ± 1.02</td>
<td>34 ± 4.4</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>semisynthetic</td>
<td>8000</td>
<td>5</td>
<td>+1.3 ± 0.40</td>
<td>70 ± 5.8</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>semisynthetic</td>
<td>500</td>
<td>5</td>
<td>-1.1 ± 0.81</td>
<td>32 ± 3.5</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>semisynthetic</td>
<td>8000</td>
<td>500</td>
<td>+1.6 ± 0.94</td>
<td>77 ± 1.8</td>
</tr>
</tbody>
</table>

again the antagonistic effect of calcium could be demonstrated. Calcium had a distinct effect in the prevention of anemia.

Experiments with rats. In a previous publication it was reported that rats are rather insensitive to the anemia-producing effect of meat. We therefore investigated whether they are more resistant to the toxic effects of zinc on hematopoiesis than mice. Six groups of rats were kept on meat or on the semisynthetic diet to which calcium and/or zinc were added (table 5). Their weight at the beginning of the observation period was 30–40 Gm. and their hemoglobin 12–14 Gm./100 ml.

It can be seen that neither meat alone nor meat supplemented with 100 mg. zinc per Kg. affected hemoglobin concentration or growth (Exp. 1 and 2). Addition of 200 mg. zinc (Exp. 3) produced a slight fall in hemoglobin without impairing growth. Only when 500 mg. zinc were added and the Zn/Cu ratio exceeded 400, did anemia result. This amount of zinc proved to be toxic as evidenced by the high mortality (over 50 per cent) and the depression of growth. Rats thus appear to be less susceptible to the toxic effect of zinc than mice.

The same conclusion could be drawn from experiments with the semisynthetic diet. When no calcium was added, growth only was impaired whereas hemoglobin levels were not affected (Exp. 5 and 6). But even addition of 500 mg. zinc produced a slight fall only in hemoglobin which could be prevented by calcium (Exp. 7 and 8). The difference proved to be statistically significant.

Discussion

Our suggestion that the "meat anemia" of mice is the result of an excessive intake of zinc accompanied by a dietary lack of copper does not lend itself to a direct proof, since it is impossible to remove zinc from meat. The indirect evidence seems to be compatible with this suggestion.

1. Muscle meat was shown to contain more zinc and less copper than liver. It has a Zn/Cu ratio of 50. The anemia-preventing mixture of 1 part liver and 3 parts meat has a much lower Zn/Cu ratio (9) than meat.

2. Supplementation of meat with copper or liver which reduces the Zn/Cu ratio protects against anemia whereas increasing the Zn/Cu ratio to 50 or more by the addition of zinc invariably leads to anemia. However,
feeding unsupplemented meat with a Zn/Cu ratio of 50 causes a more severe anemia and growth depression than the same Zn/Cu ratio produced by supplementation of meat with both copper and zinc. It is, therefore, possible that the relative contents of zinc and copper of meat are not the only determinants in the etiology of the “meat anemia.”

3. Calcium prevented “meat anemia” even when the Zn/Cu ratio was high. This effect is not the result of an improvement of the intestinal absorption of copper. Since vitamin D, which improves absorption of calcium, does not prevent “meat anemia,” it was concluded that the calcium effect is probably due to an interference with intestinal absorption of zinc. The growth impairment caused by meat diets with high Zn/Cu ratios generally paralleled the severity of the anemia. Addition of calcium to meat resulted in normal growth, even when the Zn/Cu ratio was as high as 50 or 80 (table 2). The antagonism of calcium and zinc is well known. Vallee in his review on zinc mentions that paraceratosis of hogs resulting from dietary deficiency of zinc is aggravated when the level of calcium in the diet is increased. Conversely, addition of EDTA to the diet increases the availability of zinc for turkey poults. These findings and our own lend support to the view that calcium impairs the absorption of zinc. It seems, therefore, that the anemia preventing effect of calcium is due to its interference with the availability of zinc.

4. Our experiments with the semisynthetic low-calcium diet point in the same direction. Dietary manipulations which raised the Zn/Cu ratio led to anemia which could be partly or completely prevented by calcium. However, mice kept on the semisynthetic diet were more susceptible to zinc toxicity (anemia, growth depression, mortality) than those maintained on meat.

Anemia resulting from dietary excess of zinc and its prevention by the simultaneous administration of copper has already been reported. The “meat anemia” of mice is mainly macrocytic and slightly hyperchromic, as mentioned above. The morphologic characteristics of copper-deficiency anemia seem to vary rather widely in different species. In rats, rabbits and pigs, the anemia has been described as hypochromic and microcytic, indistinguishable from iron-deficiency anemia. In Australia and New Zealand, the anemia observed in cattle grazing on copper-deficient pastures has been stated to be macrocytic and hyperchromic, and in sheep it has been found to be hypochromic and microcytic in the lambs but macrocytic in the ewes. In dogs, on the other hand, Van Wyk, Baxter, Akeroyd and Motulsky have shown the anemia of copper deficiency to be normocytic and normochromic.

Rats appear to be less susceptible to the toxic effects of zinc, and are therefore more resistant to the anemia-producing effect of the meat diet. Moore, however, using piebald rats, reported anemia in these animals when they were fed on meat. The discrepancy between his findings and ours points to the existence of genetic factors involved in the development of “meat anemia.”

“Meat anemia” of mice seems, therefore, to be mainly due to the presence in meat of insufficient amounts of copper accompanied by an excess of zinc.
whose effects are accentuated by a concomitant lack of calcium. It results from an imbalance of three elements. Genetic factors which determine the particular sensitivity of the animal to zinc seem to play an important role as well.

**Summary**

The suggestion that the “meat anemia” of mice is due to a dietary lack of copper accompanied by an excess of zinc in meat was investigated.

Muscle meat contains small amounts of copper and much more zinc whereas liver which protects against “meat anemia” contains more copper and less zinc than muscle. Supplementation of meat with copper or liver, which reduce the zinc-copper ratio of the diet, prevents anemia. Addition of zinc, which increases the zinc-copper ratio, leads to anemia.

Calcium prevents anemia even when the zinc-copper ratio is high. Treatment with vitamin D does not protect against anemia. It is concluded that calcium acts before its absorption in the intestinal tract, probably by interfering with the absorption of zinc.

Anemia also develops in mice which are maintained on a semisynthetic low-calcium diet with a higher content of zinc than of copper. Supplementation of this diet with calcium likewise alleviates the anemia.

Rats, which are resistant to “meat anemia,” are less susceptible to the toxic effects of zinc than mice.

“Meat anemia” of mice seems, therefore, to result mainly from the presence in meat of insufficient amounts of copper accompanied by an excess of zinc, the effects of which are accentuated by a concomitant lack of calcium. Genetic factors determining the particular sensitivity to zinc seem to play an important role as well.

**Summario in Interlingua**

Esseva investigate le conception que le “anemia a carne” de muses es causate per un manco dietari de cupro, accompaniante de un excesso de zinc in le carne.

Carne de musculo contine micre quantitates de cupro e multo plus zinc, durante que carne de hepate, que protege contra le “anemia a carne,” contine plus cupro e minus zinc que carne de musculo. Le supplementation de carne con cupro o con hepate, que reduce le proportion zinc:cupro del dieta, preveni le anemia. Le addition de zinc, que augmenta le proportion zinc:cupro, induce le anemia.

Calcium preveni le anemia mesmo quando le proportion zinc-cupro es alte. Tractamento con vitamina D non preveni le anemia. Es conclude que calcium age ante su absorption in le vias intestinal, probablemente per interferer in le absorption de zinc.

Anemia se disveloppa etiam in muses mantenite con un dieta semisynthetic a basse contento de calcium con plus zinc que cupro. Le supplementation de iste dieta con calcium allevia le anemia.

Rattos, que es characterisate per lor resistentia contra le “anemia a carne,”
es minus susceptibile de sufrir le efectos toxic de zinc que muses.
Il pare, per consequente, que le “anemia a carne” de muses resulta pri-
marimente del presentia in le carne de insufficiente quantitates de cupro ac-
companiate de un excesso de zinc, e le effectos de iste factores es accentuate
per be concomitante carentia de calcium. In plus, factores genetic, que de-
termina le sensibilitate particular pro zinc, etiam pare haber un rolo im-
portante.

ACKNOWLEDGMENTS

The skilled technical help of Mrs. A. Vogel and Mr. E. Tal is gratefully acknowledged. The determinations of zinc were performed by Dr. A. Goldberg.

REFERENCES

1. Adler, S.: The effect of a meat diet on the course of infection with Plasmod-

2. Ilan, J., Kende, M., and Guggenheim, K.: On the etiology of the “meat ane-

3. —, Guggenheim, K., and Ickowicz, M.: Characterization of the “meat ane-
mia” in mice and its prevention and cure by copper. Brit. J. Haemat. 9:

4. —, and —: Effect of feeding animal tissues on “meat anemia” in mice.


trition. VIII. Copper as a supplement to iron for hemoglobin building in
the rat. J. Biol. Chem. 77:797, 1928.


8. Van Reen, R.: Effects of excessive dietary zinc and in the rat and the in-

9. Duncan, G. D., Gray, L. F., and Dan-
ield, L. J.: Effect of zinc on cyto-


11. Ritchie, H. D., Luecke, R. W., Baltzer,
B. V., Miller, E. R., Ullrey, D. E.,
and Hoefer, J. A.: Copper and zinc interrelationships in the pig. J. Nu-

12. Hill, C. H., Matrone, G., Payne, W. L.,
and Barber, C. W.: In vivo interac-
tions of cadmium with copper, zinc

13. Crosby, W. H., Munn, J. F., and Firth,
F. W.: Standardizing a method for
clinical hemoglobinometry. U. S.

14. Sandell, E. B.: Colorimetric Determina-
tion of Traces of Metals, 2nd ed.
New York, Interscience Publishers,

15. Vallee, B. L.: Biochemistry, physiology
and pathology of zinc. Physiol. Rev.

16. Kratzer, F. H., and Starcher, B.: Quanti-
tative relation of EDTA to availa-
bility of zinc for turkey poults. Proc.
Soc. Exper. Biol. & Med. 113:424,
1963.

17. Smith, S. E., and Medlicott, M.: The
blood picture of iron and copper de-
ficiency anemias in the rat. Am. J.
Physiol. 141:354, 1944.

18. —, —, and Ellis, G. H.: The blood
picture of iron and copper deficien-
cy anemias in the rabbit. Am. J.
Physiol. 142:179, 1944.

19. Lahey, M. E., Gubler, C. J., Chase, M.
S., Cartwright, G. E., and Wintrobe,
M. M.: Studies on copper metabo-
ilism. II. Hematological manifesta-
tions of copper deficiency in swine. Blood
7:1053, 1952.

20. Bennets, H. W., Beck, A. B., Harley,
Karl Guggenheim, M.D., Associate Professor of Nutrition and Head of the Laboratory of Nutrition, Hebrew University-Hadassah Medical School, Jerusalem, Israel.


Scorbutic guinea-pigs showed normocytic anemia with neutropenia and lymphopenia. Plasma iron and total iron binding capacity decreased with decrease of ferritin of liver. An increase in erythrocytic protoporphyrin content, a low sideroblast percentage and a high hemosiderin content were recorded in the bone marrow. All the defects could be ameliorated by feeding ascorbic acid.—J. B. C.


Patients with Addisonian pernicious anemia given four injections of 1000 μg. hydroxocobalamin on alternate days showed a more prolonged elevation of the serum B12 level than patients given similar injections of cyanocobalamin. The increased binding of hydroxocobalamin to serum as compared with cyanocobalamin was confirmed by separation of the free and bound forms on a sephadex G25 column.—I. C.
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