

## LIVER EXTRACT IN THE TREATMENT OF THE ANEMIAS OF SPRUE.

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The investigations, of which the present preliminary note is a summary, were begun in January 1928 when I received from the Eli Lilly Company, on the request of Dr. George Minot with whom I had been in correspondence, a quantity of liver extract sufficient to test its effect on four cases of anemia of the pernicious type associated with tropical sprue. A little later the extract was placed on the market in San Juan and I was enabled to study its action in 20 additional cases.

On the 24 cases investigated, 20 were examples of typical sprue. Of these, 14 showed an anemia of the primary type, and 6 the secondary type. The 4 remaining cases of the series were examples of secondary anemia not associated with sprue.

Of the 20 sprue cases, 14 were given three to six vials of the extract daily, along with my own diet; four were treated by the diet alone; one received the diet and *Monilia psilosis* vaccines, and one was given the vaccines without liver extract or dietary restriction.

The sprue diet referred to is abundant in animal proteins, fresh vegetables and fruits, extremely limited in fats, and free from sugar of commerce and cereals.

The vaccine consisted of one per cent suspension of killed cultures of *M. psilosis*. Weekly injections were given, beginning with 0.1 cc. and increasing each injection by 0.1 cc. until a dose of 1 cc. was reached.

The progress of the 24 cases was noted daily, or every other day, with particular reference to changes in the blood. Hemoglobin and erythrocyte counts were made in addition to a careful enumeration of the reticulocytes.

Reticulocytes, it may be pointed out, are immature red cells, recognized by their specific staining with cresyl blue. In the normal healthy adult they are present in very small numbers, generally only 1-5 per 1,000 red cells. In 23 controls which I investigated the average percentage was only 0.18, which is probably not far from



the normal for the healthy population of San Juan. Minot and others have shown that liver extract in pernicious anemia induces within a few days a veritable shower of these immature cells, followed by a marked and rapid rise in both the hemoglobin and red count. And any extract may be tested by administering it to such cases, its potency being directly proportionate to the reticulocyte reaction induced.

The results of the use of the extract in the 24 cases referred to above may be briefly stated:

Of the 10 sprue cases with a primary of pernicious type of anemia treated with extract, five responded with a reticulocyte shower. In these five cases the average number of red cells at the beginning was 1,160,000 or 23.2 per cent of the normal, while the average hemoglobin was 35.8, giving a color index of 1.55. After nine weeks of treatment the corresponding figures were 71.8 and 93, a color index of 1.30. The reticulocytes rose from an average of less than ten per 1,000 red cells, to 162 per 1,000 (16.2 per cent), the peak being reached after about twelve days. The reticulocyte rise began one to six days after the extract was first administered.

Of the five remaining cases with a primary type of anemia, the average red cell count was 2,950,000 or 59 per cent of the normal, at the beginning and the average hemoglobin was 66.8, giving an average color index of 1.30. After forty days these figures reached 70 and 81, respectively, an average color index of 1.16. No reticulocyte shower was observed in any of the cases.

Of four cases of sprue showing a secondary type of anemia none showed the slightest reticulocyte reaction following the administration of liver extract.

Of the four cases of sprue treated by diet alone, one had a mild grade of secondary anemia, two had a remittant pernicious type of anemia, with red-cell counts of over 2,000,000. The fourth was a young woman with a severe anemia of the pernicious type. Her hemoglobin was 25 per cent with 824,000 erythrocytes and 1.8 per cent reticulocytes. On dietary treatment alone her reticulocyte percentage started to rise on the fifth day and reached 10.4 per cent on the eleventh day. The reticulocyte curve corresponded closely to that seen after the administration of liver extract, falling to the original point after about twenty-one days. The patient's general condition was greatly improved.

The two cases of the sprue series remain. One was treated with diet and vaccines, the other with vaccines alone. In the first, the type of anemia was secondary and no rise of reticulocytes was seen



or expected. The anemia in the second case was definitely pernicious in type. The hemoglobin was 44 per cent erythrocytes, 1,600,000 or 32 per cent of normal (color index, 1.4), and reticulocytes 0.5 per cent. Throughout the course of treatment, which consisted of ten inoculations, there was a series of reticulocyte rises which may or may not be ascribed to the therapy. The patient improved, however, and within two months the hemoglobin was 60 per cent and the erythrocytes 1,776,000. The patient was never restricted in her diet. On the contrary she was encouraged to eat everything.

The four non-sprue cases which served as controls were all instances of secondary anemia. They were treated with liver extract over an average period of 22 days. No reticulocyte rise was observed at any time.

#### CONCLUSIONS

The anemias of sprue with a high color index and less than 2,000,000 erythrocytes are fairly certain to respond to the administration of a potent liver extract with the typical reticulocyte reaction seen in Addisonian anemia. The failure of certain cases to respond is probably due to an aplastic state of the bone marrow which autopsies have shown may be present in sprue.

Cases in sprue with erythrocytes over three millions have so far shown no reticulocyte response to liver extract even though the anemia was primary in type with a high color index.

Dietary treatment alone, without liver, may bring about a reticulocyte response in sprue when the anemia is marked and of the primary type. Such a case treated by the author's diet showed a reticulocyte curve which differed from that produced by liver extract in similar cases only in being sustained longer, with a more gradual ascent and descent.

Thus far no cases of secondary anemia among either sprue or non-sprue cases have shown any reticulocyte response to liver extract.