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# YEAST AS AN EXTRINSIC FACTOR IN RELATION TO PERNICIOUS ANEMIA

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Wintrobe (1) recently stated that certain patients with typical pernicious anemia could be thrown into complete remission by oral treatment with dried, unautolyzed yeast, and he concluded that there was in the yeast some hematopoietic factor specific for the disease. As further argument for this belief, he stated that the addition of normal human gastric juice did not increase the potency of yeast more than it increased the potency of liver extract. Other workers have previously reported successful treatment of pernicious anemia with preparations of autolyzed (2) and unautolyzed (3) yeast.

In this report we give our observations on 2 patients with typical Addisonian pernicious anemia in relapse, who were treated with yeast in the manner outlined by Wintrobe. The response ob-

tained was then compared with the response from material of known hematopoietic activity. Both patients showed absence of free hydrochloric acid after subcutaneous administration of 1.0 gm. of histamine.

Patient C. W. was given ordinary brewer's yeast daily for 10 days (Figure 1). The attempt was made to administer 2 grams of yeast per kgm. of body weight, but the patient was not always able to take this amount. She never took less than 1.0 gram per kgm. of body weight, however, and consumed a daily average of 1.7 grams per kgm. of body weight over the 10-day period. During the test periods the diet contained no liver, meat, or eggs. On the sixth day, the reticulocyte count rose to 2.0 per cent. After 10 days, regular commercial ventriculin (Parke, Davis and Co.)

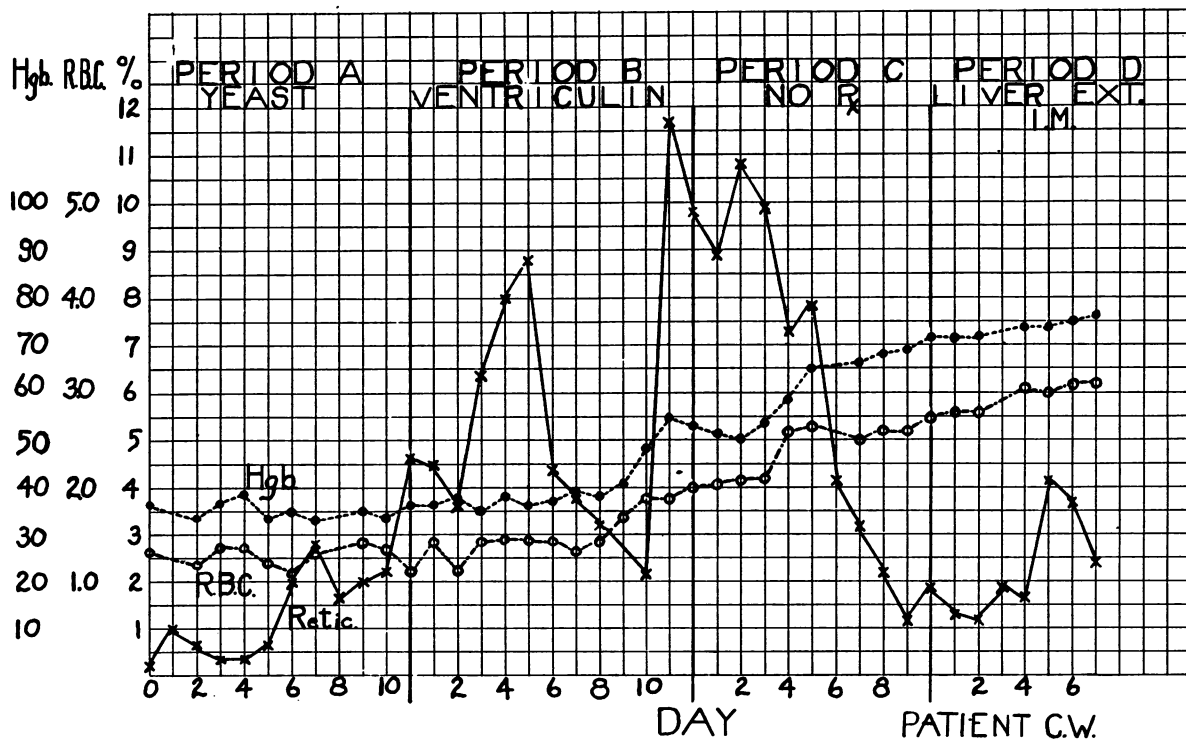


FIG. 1. PATIENT C. W. COMPARATIVE HEMATOPOIETIC RESPONSE TO YEAST, VENTRICULIN, AND PARENTERAL LIVER EXTRACT

was started, 15 grams daily (Period B, Figure 1). However, 14 days after starting yeast, the reticulocyte count rose to 8.8 per cent and the red blood corpuscle count and hemoglobin began to rise. Although this response occurred during administration of ventriculin, there can be no doubt that it was evoked by the yeast administered during the preceding period. This is proven by the fact that there was a subsidence of reticulocytosis followed by a second reticulocyte peak of 11.7 per cent on the tenth day after starting ventriculin. It is well known that two reticulocyte responses to continuous therapy with the same material in equal daily amounts do not occur (4). During the 10 days of Period C (Figure 1), no medication was given and the reticulocytosis subsided, although the red blood corpuscle count and hemoglobin continued to rise. In Period D (Figure 1), 5 cc. of liver extract (Campolon, Winthrop) were administered intramuscularly daily. On the fifth day there was a reticulocyte response of 4.2 per cent. From this it is concluded that the yeast evoked a partial hematopoietic response which was not as great as that following 15 grams of ven-

triculo daily. Further, the ventriculin, in the amount given, was not as effective as the parenteral liver extract, as evidenced by the further reticulocyte rise after parenteral administration of liver extract.

Patient C. H. received ordinary brewer's yeast during the 15 days of Period A (Figure 2), in doses of 2 grams per kgm. of body weight daily. He experienced no difficulty in taking the medication. He was on an ordinary house diet at the time, with the exception that liver was omitted, since it was desired to provide maximum opportunity for a response. The reticulocytes reached 5.9 per cent on the eighth day after starting yeast. During the next period (Period B, Figure 2) ventriculin was administered in doses of 15 grams daily. On the tenth day after starting ventriculin the reticulocyte count rose again to 5.2 per cent. In the last period, crude liver extract, 1 cc. derived from 5 grams of liver (Solution of Liver Extract, Lilly), was administered intramuscularly in doses of 2 cc. daily. On the eighth day of such treatment (Period C, Figure 2) the reticulocyte count reached 13.0 per cent and there was an increase in

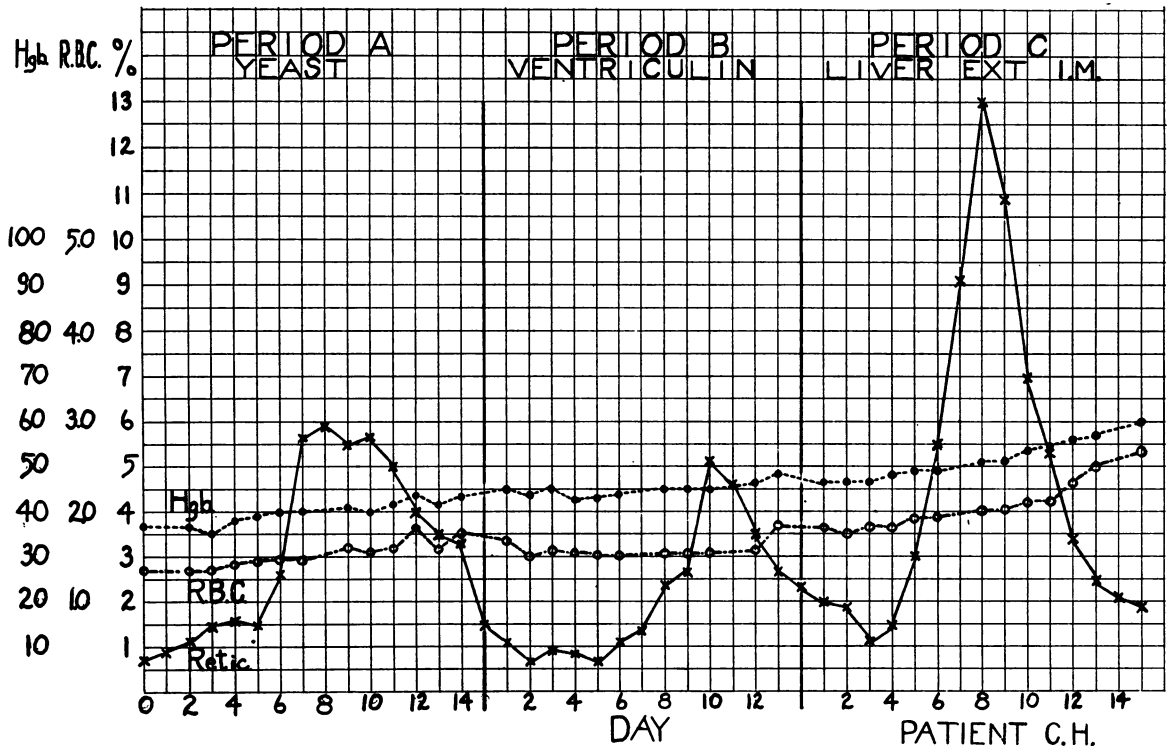


FIG. 2. PATIENT C. H. COMPARATIVE HEMATOPOIETIC RESPONSE TO YEAST, VENTRICULIN AND PARENTERAL LIVER EXTRACT

red blood corpuscles and hemoglobin. The fact that small doses of parenteral liver produced a considerably greater response than a theoretically minimal dose of ventriculin calculated to evoke a maximal reticulocyte response, argues that the patient was unable to respond fully to oral medication. This does not, however, invalidate the fact that a second response to the ventriculin followed a preliminary response to yeast, but it does indicate that the ventriculin was more potent than the yeast in the dosages employed. Parenteral liver therapy in the dosage employed was considerably more effective than either the yeast or the ventriculin.

#### DISCUSSION

Previous work (5, 6) has demonstrated that the intrinsic factor deficiency in pernicious anemia is quantitative rather than qualitative and that the gastric juice of patients with pernicious anemia, even in relapse, contains intrinsic factor, but in such small amounts that it will not prevent anemia in the patient. Thus, if an excess of extrinsic factor is supplied to such patients, it is conceivable that enough hematopoietic substance will be formed *in vivo* to prevent anemia or, at least, reduce the requirement for preformed hematopoietic substance. The response to yeast obtained in our cases is considered to be the result of supplying an excess of extrinsic factor in the presence of greatly diminished but not completely absent intrinsic factor. It is unnecessary to assume that yeast contains any hematopoietic substance specific for pernicious anemia. It supplies an abundance of extrinsic factor and certain patients with pernicious anemia may be thrown into remission without specific therapy if an excess of such extrinsic factor is supplied. In any event, the yeast, in

the dosage employed, was not as effective as small, daily oral doses of ventriculin or intramuscular liver extract.

#### SUMMARY

1. Two patients with pernicious anemia in relapse are reported. They obtained a response with ordinary dried brewer's yeast, but this response was neither as great as that evoked with a minimal amount of ventriculin calculated to give a maximal reticulocytosis nor with daily intramuscular injections of unconcentrated liver extract.

2. The response to yeast is due to the fact that pernicious anemia is a disease of quantitative rather than qualitative deficiency. Administration of large amounts of extrinsic factor with greatly diminished, but not completely absent intrinsic factor, will produce a response in certain patients with pernicious anemia.

#### BIBLIOGRAPHY

1. Wintrobe, M. M., The successful treatment of pernicious anemia by means of non-autolyzed yeast. *J. Clin. Invest.*, 1938, 17, 501.
2. Ungley, C. C., The effect of yeast and wheat embryo in anemias. I. Marmite, yestamin, and bemax in megalocytic and nutritional hypochromic anemias. *Quart. J. Med.*, 1933, 2, 381.
3. Ungley, C. C., and James, G. V., The effect of yeast and wheat embryo in anemias. II. The nature of the haemopoietic factor in yeast effective in pernicious anemia. *Quart. J. Med.*, 1934, 3, 523.
4. Minot, G. R., and Castle, W. B., The interpretation of reticulocyte reactions. *Lancet*, 1935, 2, 320.
5. Goldhamer, S. M., The presence of the intrinsic factor of Castle in the gastric juice of patients with pernicious anemia. *Am. J. M. Sc.*, 1936, 191, 405.
6. Goldhamer, S. M., The gastric juice in patients with pernicious anemia in induced remission. *Am. J. M. Sc.*, 1937, 193, 23.