

are significant, particularly in the light of the work of Beattie,^{3, 4} Cushing,⁵ Light,² and Ferguson.⁶

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Increased Potency of Liver Extract by Incubation with Human Gastric Juice.*

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(Introduced by G. H. A. Clowes.)

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Following the work of Castle and his associates,¹ Reimann² reported a marked increase in the potency of liver by its digestion in normal human gastric juice. Walden and Clowes,³ independent of Reimann, obtained a very active preparation by the incubation of liver and liver extracts with small amounts of hog gastric tissues. However, Barnett and Thebaut⁴ were apparently unable to increase the activity of liver by its digestion with normal human gastric juice.

The purpose of this paper is to report the results obtained by this laboratory when patients with pernicious anemia in relapse were fed daily a subminimal dose of liver extract No. 343 (that derived from 100 gm. of liver) which had previously been incubated at 40°C. for 4 hours with 100 cc. of normal human gastric juice obtained after histamine stimulation. During the control and test periods the diets

³ Beattie, *Proc. Royal Soc.*, 1930, B, 106.

⁴ Beattie, *Can. Med. Assn. J.*, 1932, 26, 278.

⁵ Cushing, *Proc. Nat. Acad. Science*, 1931, 17.

⁶ Ferguson, *Proc. Soc. Exp. Biol. and Med.*, 1932, 30, 328.

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¹ Castle, W. B., *Am. J. Med. Sci.*, 1929, 178, 748. Castle, W. B., and Townsend, W. C., *Am. J. Med. Sci.*, 1929, 178, 764. Castle, W. B., Townsend, W. C., and Heath, C. W., *Am. J. Med. Sci.*, 1930, 180, 305. Castle, W. B., Heath, C. W., and Strauss, M. B., *Am. J. Med. Sci.*, 1931, 182, 741. Strauss, M. B., and Castle, W. B., *New Eng. J. Med.*, 1932, 207, 55.

² Reimann, F., *Med. Klin.*, 1931, 27, 880.

³ Walden, G. B., and Clowes, G. H. A., *Proc. Soc. Exp. Biol. and Med.*, 1932, 29, 873.

⁴ Barnett, C. W., and Thebaut, W. M., *J. Am. Med. Assn.*, 1932, 99, 556.

of the patients contained no meat or eggs. The noon meal was given at 11:30 A. M. and the evening meal at 6:30 P. M. At 4:30 P. M. the material to be tested (after being brought to pH 5 by the addition of sodium hydroxide) was administered by mouth to the patients.

Case I received daily during the 10 day control period the amount of liver extract No. 343 derived from 100 gm. of whole liver. No response in the blood or improvement in the clinical condition of the patient resulted. This confirmed the findings of Zervas⁵ that this amount of liver extract No. 343 is insufficient to cause a reticulocyte response when fed by mouth to patients with pernicious anemia in relapse. During the following 10 day period the patient received daily the same amount of liver extract incubated with gastric juice as described above. Marked clinical and hematological improvement followed. Chart 1 shows the response of the blood to the medication.

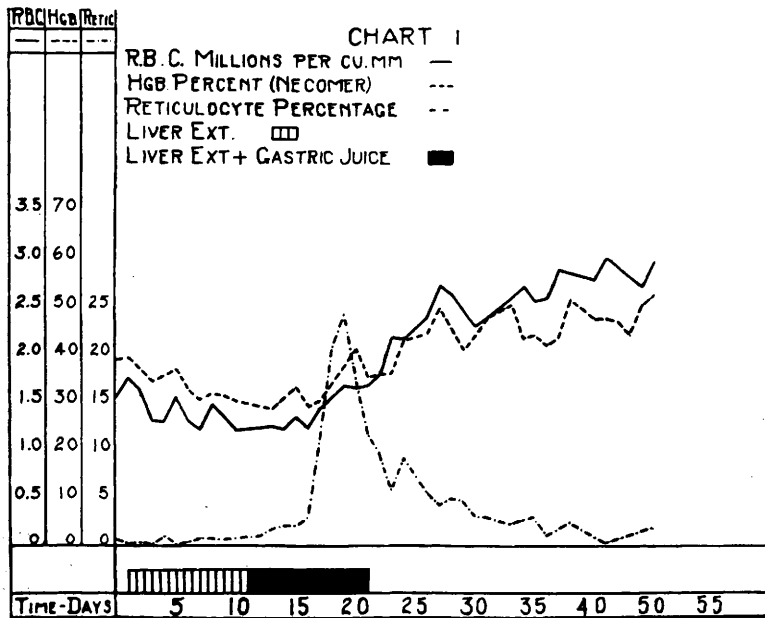


CHART 1.

Response of red blood cells, hemoglobin, and reticulocytes of Case 1 to the amount of liver extract derived from 100 gm. of liver and to the same amount of liver extract that had been incubated at 40° for 4 hours with 100 cc. of normal human gastric juice.

⁵ Zervas, L. G., *Arch. Int. Med.*, 1931, **47**, 135.

Case II during the 10 day control period received daily by mouth 150 cc. of normal human gastric juice which had been incubated for 4 hours and then adjusted to pH 5. No response in the blood of the patient was noted. This demonstrated that the response obtained in the first patient was not due to the effect of the gastric juice upon the food the patient ate during the experiment and confirmed the work of Castle and his associates that normal human gastric juice is ineffective in the treatment of pernicious anemia when fed by mouth. During the following 10 day period Case II received daily the liver extract-gastric juice preparation described above. Again a very good response in the reticulocytes and red blood cells (Chart 2) followed this medication.

In these experiments a known subminimal dose of liver extract No. 343 after incubation with human gastric juice (itself inactive) produced maximal reticulocyte responses and marked clinical improvement when administered daily by mouth to patients with pernicious anemia in relapse. These results are in harmony with and

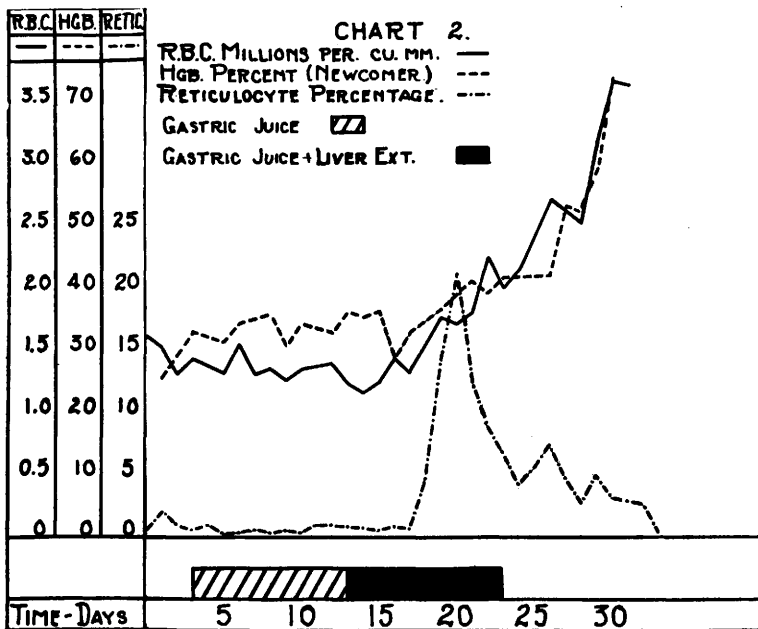


CHART 2.

Response of red blood cells, hemoglobin, and reticulocytes of Case II to 150 cc. of normal human gastric juice incubated at 40° for 4 hours and to liver extract No. 343 derived from 100 gm. of liver that had been incubated at 40° for 4 hours with 100 cc. of normal human gastric juice.

lend confirmation to the observations of Castle and his associates, of Walden and Clowes, and of Reimann. It still remains to be determined whether the enhanced activity which we have observed is due to an increase in the active principle originally present in the liver or to an effect of the type described by Castle and his associates when human gastric juice was allowed to act on beef muscle, beef muscle extracts and yeast.