

indicate that insertion of the needle produces alteration of the viscosity of the protoplasm. Provided that the treatment is not too intense or too prolonged, effects appear to be reversible. More intense treatment results in local injury, and in extreme cases complete disorganization or even disruption of the cell.

Some time after this communication was submitted for publication, on April 28, our attention was called to a paper by Harvey and Loomis, published in *Nature* for April 21, entitled "High Frequency Sound Waves of Small Intensity and their Biological Effects." Although some of the observations therein described parallel closely results of some of our earlier, as yet unpublished experiments, we should like to point out that our method of affecting single cells differs distinctly from theirs; in our experiments, the supersonic effects are, for the most part, applied in definitely localized regions of cells by means of glass collectors pulled to micro-points. Data already in hand indicate that such localized disturbances may be followed by deep-set ontogenetic alterations.

4035

Effect of Liver Extract on Erythrocytes and Reticulocytes in Normal Individuals.

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The effect of liver extract in pernicious anemia may be analyzed from the point of view of the immediate reaction, as well as of the sustained reaction. The immediate reaction includes among other things 3 distinct morphological features: (1) the normoblastic response, (2) the reticulocyte response, and (3) the liberation of the mature erythrocytes.¹ It is a well established fact that the bone marrow in pernicious anemia is hyperplastic and contains large amounts of erythrocytes in various stages of development. In other words, there appears to be a difficulty in the maturation of the erythrocytes necessary for their discharge from the marrow into the circulation. This faulty maturation is in character probably morphological rather than chemical, for the cells in the marrow are completely filled with hemoglobin and products of hemoglobin have been deposited in the various tissues. Thus the hemosiderosis, in the classical interpretation of pernicious anemia looked upon as a proof of the hemolytic character of the disease, might indicate a destruction of erythrocytes in the foci where they were formed be-

¹ Watkins, Charles H., and Berglund, Hilding, *Proc. Soc. Exp. Biol. and Med.*, 1927, xxv, 206.

fore they were ever delivered into the circulating blood. When liver therapy is instituted, the bone marrow presumably is stimulated to mature and release the cells. A slight retardation in the maturation as compared with the discharge thus explains the 3 features of the immediate reaction. Experiments on the effect of liver extract upon normal individuals are here presented as a confirmation of the view of the mode of action of the liver extract to accelerate the discharge of cells into the circulation.

Six normal individuals (doctors and assistants in our laboratory) whose erythrocyte counts were between 4,500,000 and 5,800,000 were given 3 vials of liver extract (343 Lilly), or the equivalent of 300 gm. of raw liver, daily for a period of 10 days.

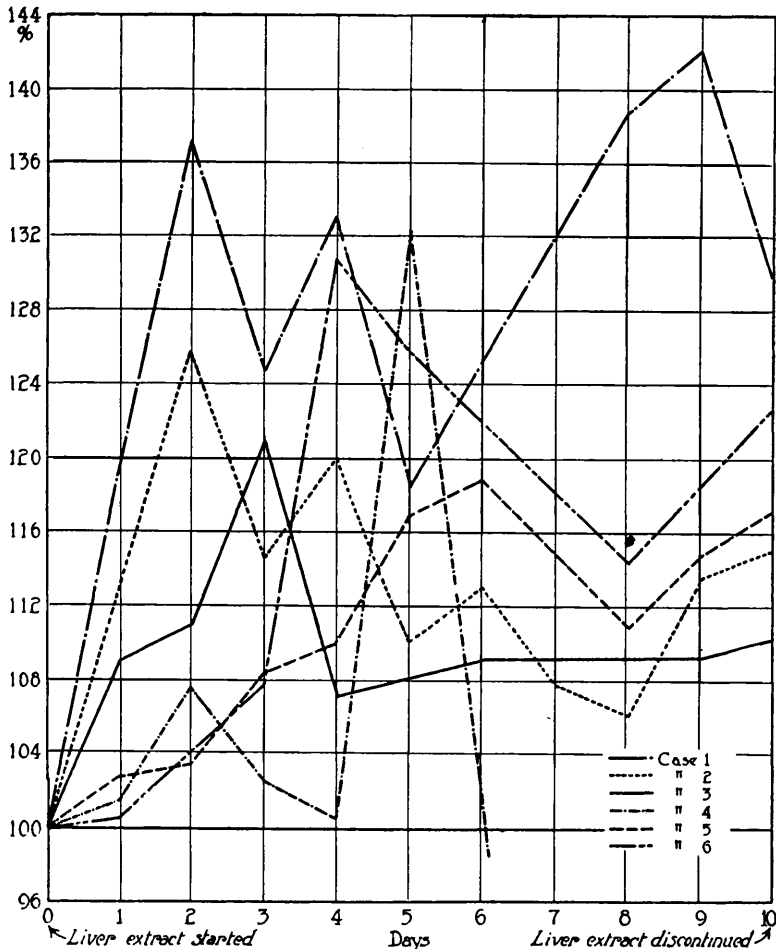


CHART 1.

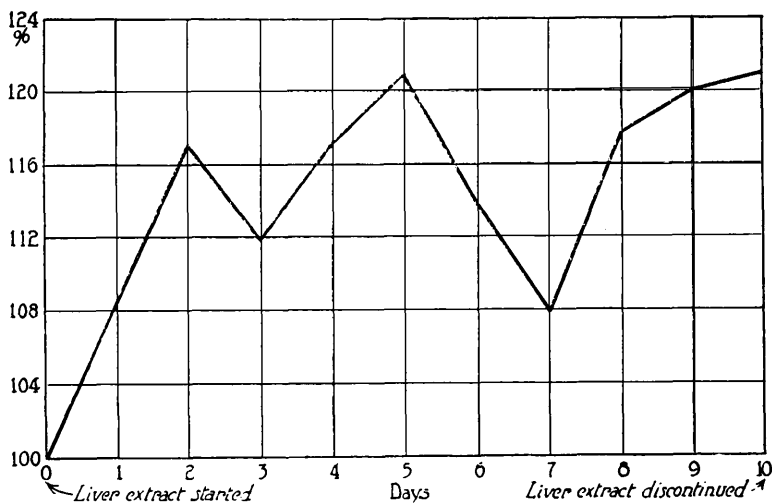


CHART 2.

Daily erythrocyte and reticulocyte counts were obtained. That the results might be reduced to a common base line, the original erythrocyte count of each individual was called 100% and the subsequent increase or decrease in erythrocytes was calculated in terms of the % of the original value.

Figure 1 is a field graph of the individual cases, in which the ordinate represents the percentage increment over 100% and the abscissa represents the days during which the liver extract was given. In each case there is an increase in erythrocytes, which is characterized by an irregular curve. In all cases but one there was a definite increase in erythrocytes at the 10th day.

In order to facilitate the interpretation of the results a numerical average of the percentage for each day was calculated and these values were plotted as represented in Fig. 2. From this graph it is seen that there is an increase from 100% to 117.1% on the 2nd day. Then there is a drop to 111.7% on the 3rd day. Following this the value rises to 120.9% on the 5th day, and again decreases to 107.8% on the 7th day. The percentage increases again to the value of 120.7% on the 10th day.

It is apparent that there is a definite increase in the erythrocyte count in all cases although the curve is quite irregular. The irregularity may be due to an attempt of the body to overcome the polycythemia.

In clear contradistinction to the occurrences in pernicious anemia, no increase in the reticulocytes took place in the normal individuals, the percentage remaining between 0.0% and 2.0%. There was

no change in the leukocyte counts. The hemoglobin followed the red count, but probably not in full proportion to the increase in red cells. In all cases the individuals developed some symptoms of polycythemia vera; thus varying degrees of headaches, epistaxis, acrocyanosis and abdominal distress were encountered. We call particular attention to the acrocyanosis.

We call attention to the immediate response in the normal individuals as compared with the delayed response in the discharge of mature red cells in pernicious anemia. If in the pernicious anemia we base our comparison on the occurrence of increased number of normoblasts, the first signs of response to the liver come as early in one group as in the other. Thus the liver extract in normal individuals, as in pernicious anemia brings about an immediate release of red blood cells into the circulating blood. In the normal individual the maturation of the cells is complete and the release rapid, in the pernicious anemia the maturation is retarded, discharge of incompletely matured cells occurs and precedes the discharge of fully matured ones; the process as a whole is prolonged.