Minnesota Branch.

University of Minnesota, May 31, 1928.

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Rapid Stimulation of Hemoglobin Synthesis in Secondary Anemias After Feeding Fetal Calf's Liver.

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Observations by different workers show that in patients afflicted with some form of secondary anemia there is as a rule no response to the feeding of calf's liver or of the Cohn-Minot liver extract. To the well known response of patients with pernicious anemia to this extract has recently been added the definite but peculiar type of response, which normal individuals show to the same extract. It is being assumed that the nature of the effect of the extract is to bring about a maturation or discharge into the circulation of erythrocytes or a combination of both these processes.

It is generally recognized that it is not the erythropoesis which is primarily at fault in socalled secondary anemia but the ability to synthesize enough hemoglobin to give the proper hemoglobin concentration in the erythrocytes that are being formed. The lack of effect of liver or liver extract upon secondary anemia is in harmony with this view.

The appearance of abundant amounts of hemoglobin already during the early stages of the development of the primitive erythrocyte was considered as a significant fact during our search for a way specifically to stimulate hemoglobin synthesis. The important rôle which the fetal liver takes in the next stage of erythropoesis led us to the attempts to be communicated in this paper.

We have adopted the feeding of fetal calf's liver as a mode of treatment of certain types of secondary anemia. Characteristic features of these anemias are their prevalence in women between the age of 25 and 45, marked chronicity and failure to respond to treatment with iron or chlorophyll-rich diet as well as to ordinary calf's liver or liver extract. The apparent lack of any causative

agent makes these cases stand out more or less as primary or essential anemias of the type one hematologically characterizes as secondary. One of the curves in our charts represents a boy, age 10, with an almost aplastic anemia of secondary type. The other curves are from women of the type just indicated.

The livers, which have been used so far, have been from calf fetuses measuring 40 cm. or more from the tip of the nose to the ischial tuberosities. Recent therapeutic observations have led us to a somewhat different selection, the fetuses not to exceed 70 cm. in length and with a preference for the smaller ones. Microscopic sections of livers from fetuses of different length reveal in an 18 cm. embryo the blood forming islands almost as prevalent as the liver structure proper, in a 77 cm. fetus only a few islands of normoblasts and in a 112 cm. calf (full term) practically no signs of intrahepatic blood formation. The livers have been removed from the fetuses within 4 hours after the animals have been killed, ground through a meat chopper, dried in a hot air current, the material suspended about an inch above a hot plate, the dried material powdered and administered either as powder or made into tablets. The equivalent of about 300 g. of liver has been fed daily.

Chart 1 demonstrates in 4 representative cases the increase of hemoglobin during fetal liver feeding in percentage of the initial values, these having been calculated as unity. The actual hemoglobin values at the beginning and end of the experiment are

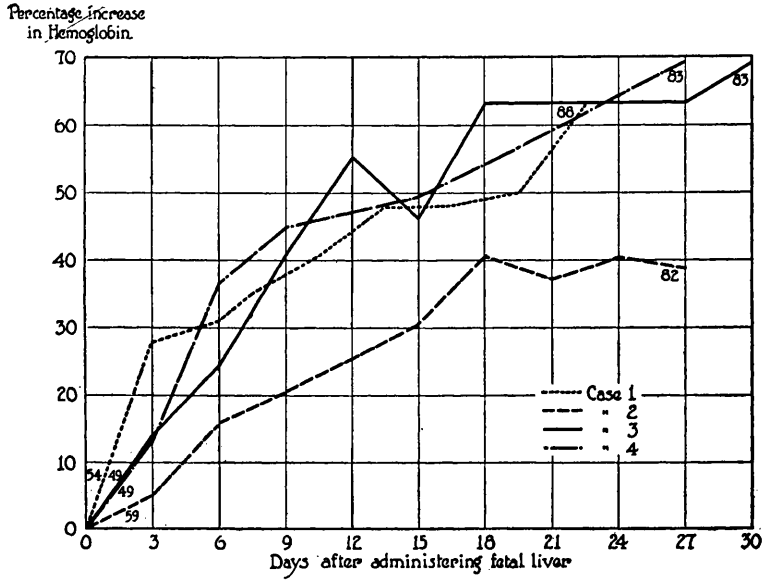

CHART 1.

attached to the individual curves. The hemoglobin values, determined according to Sahli against permanent standards have been read after 15 minutes, when the curve for the color development has

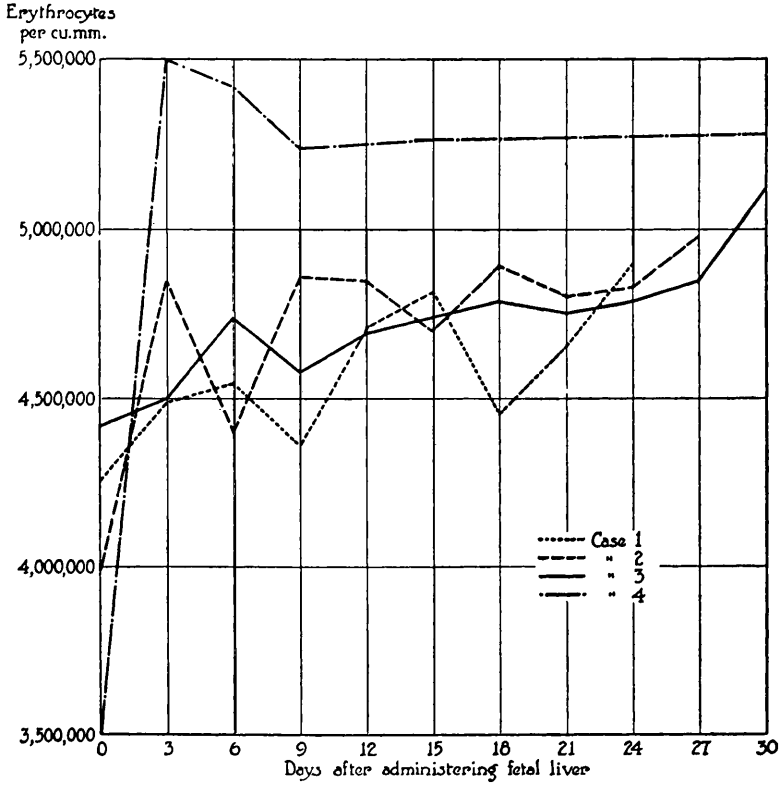

CHART 2.

flattened out, instead of after 2 minutes. Chart 2 gives the corresponding curves for the number of erythrocytes. Chart 1 shows in all cases a uniform increase in the hemoglobin content, in 3 of the 4 cases amounting to from 60% to 70% of the initial values within 22 to 30 days, and in all cases leading up to practically normal absolute figures. A comparison between Chart 1 and Chart 2 fails to reveal any correspondence between the curves for the number of erythrocytes and for hemoglobin content. Particularly elucidating are the curves labeled 4. Here a rapid discharge of hypochromatic erythrocytes brings the blood count to a high normal level, only slightly altering the hemoglobin content The hemoglobin curve then continues to rise, with the erythrocyte curve remaining level. As an approximately correct expression one might state that the time required to bring about a normal hemoglobin content in a

hypochromatic type of anemia is the time required not only to raise the erythrocyte count to normal but to replace the erythrocytes present in the circulation at the onset of treatment with new erythrocytes of normal hemoglobin content. This is in fundamental contradistinction to the situation in pernicious anemia.

At no time during the treatment with fetal liver was there any increase in the number of reticulocytes.

Conclusion: A procedure to accelerate the hemoglobin synthesis in secondary anemia through the feeding of fetal calf's liver has been carried out successfully.

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Effect of Cholesterol Exposed to Roentgen Rays on Rachitic Rats.

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Hess and Weinstock[1] state that cholesterol, which has been irradiated with roentgen rays, does not cure rickets, and also that the absorption spectrum in the ultra violet of cholesterol is not changed by this kind of radiation. On the other hand, Reinhard and Buchwald[2] found that a definite change takes place in the absorption if cholesterol is irradiated in chloroform solution. This change in the absorption was similar to the change that is produced by irradiation with ultra violet. If commercial cholesterol is exposed for a short time to ultra violet radiation from a mercury arc, it obtains a curative effect on rickets and there seems to be a correlation between the activity and the change in the absorption. It seems, therefore, that cholesterol in a chloroform solution might obtain anti-rachitic properties by being exposed to roentgen radiation.

After some preliminary tests with the production of rickets in rats, the following experiment was carried out. Through the courtesy of Dr. Cornelia Kennedy a litter of 8 rats was obtained after weaning, at the age of 28 days. The mother rat had been fed on Steenbock's diet[3] which is poor in vitamine A. The eight rats were put on Steenbock and Nelson's diet No. 2966[4] free from vitamine

[1] Hess, A. F., and Weinstock, M., *J. Biol. Chem.*, 1925, lxiv, 1923.

[2] Reinhard, M. C., and Buchwald, K. W., *J. Biol. Chem.*, 1927, lxxiii, 383.

[3] Steenbock, *Science*, 1923, lviii, 449.

[4] Nelson, E. M., and Steenbock, H., *Am. J. Physiol.*, 1925, lxxiii, 341.