

SOME SUBSTANCES EMPLOYED IN THE TREATMENT OF PERNICIOUS ANÆMIA AND DIABETES MELLITUS.

Notes from two of a series of lectures on "Drug-like Actions of some Foods," given at the Royal Institution on March 24th and 31st, 1936, by Professor Mellanby, M.A., M.D., F.R.S., F.R.C.P.

(a) Anahæmin—an active principle of liver.

(b) An active substance in stomach mucous membrane. The stimulant action of these substances on the formation of red blood corpuscles, with special reference to their use in pernicious anæmia.

(c) Insulin—an active principle of the pancreas. Its effect on carbohydrate metabolism with special reference to the treatment of diabetes mellitus.

(d) Protamine insulate.

ANAHÆMIN.

Anahæmin is the alkaloid of liver which is responsible for the cure of pernicious anæmia.

The Anæmias.

1. Hæmorrhagic anæmia is due to loss of blood and may be either primary or secondary.

2. Chlorosis is a type of anæmia formerly very common among young women between 16 and 30 years of age, but it has now practically disappeared from this country.

3. Nutritional anæmia is due to some lack in the quantity or quality of food. This type is sometimes seen in pregnant women and is caused by the drain upon the mother by the growth of the foetus.

4. Certain poisonous substances give rise to anæmia.

5. Aplastic anæmia is due to the breakdown of the red-blood-cell-forming tissue of the bone marrow. It is a very grave condition and so far no cure has been found.

6. Pernicious anæmia. In this disease changes take place in the composition of the blood, but there is nothing wrong with the bone marrow or the liver.

The blood picture in pernicious anæmia.

Large nucleated cells of the type called megaloblasts are found in the blood. These are normally confined to the bone marrow, where they develop into normoblasts and then into red blood cells. The red blood cells also are larger, on the whole, than the normal. The hæmoglobin content of the blood may be as low as 20 per cent. At certain periods of the disease there occur blood crises when an unusually large number of megaloblasts are poured into the blood stream. These crises are a serious indication of the prognosis of the disease.

Experiments to find a diet for pernicious anæmia.

The old treatment consisted in bringing the patient into hospital and administering arsenical preparations. After the first attack the patient might go home considerably better, but soon had to come back and with each return the treatment had less effect. The average life after the onset of the disease was from one to two and a half years. The first experiments with diet showed that milk, white meat, bread, bone marrow had no effect upon the patients. With fruits, such as apples, prunes and so on there was a little improvement. Beef,

kidney and especially liver seemed to give the best results. In 1926 Doctors Minot and Murphy published the results of the liver diet which they had worked out. At this time half a pound of raw liver was administered daily. The next problem was to find a more palatable method of giving the diet, which was apt to be nauseating after a time. Minot and Cohn prepared a substance "extractum hæpaticum siccum" of which 20 grammes is equal to half a pound of raw liver. They also discovered that this liver extract, given intravenously, was from 30 to 100 times more effective than when given by mouth. Experiments have now been fruitful in the discovery of the active principle of liver which cures pernicious anæmia, anahæmin. One ounce of this substance has a marvellous effect upon the most advanced cases, 100 millegrammes of it being equal to 20 lb. of raw liver. The effects of anahæmin upon the general condition of the patient are soon apparent. The sore tongue, which is common in this disease, disappears, the skin takes on a smooth appearance instead of being dry and sagging, the weight goes up, not because more fluid is being taken, but because the body can retain more and the patient begins to feel much better.

Effects of anahæmin on the blood picture.

The megaloblasts almost immediately begin to give place to normoblasts, the hæmoglobin content of the blood goes up from, perhaps, 20 per cent. to 80 per cent. and the red blood cells from below 1,000,000 to over 4,000,000. The colour index, likewise, approximates to the normal. The first effect which is apparent upon the blood is the rapid increase of reticulocytes. This begins to show between the seventh and tenth days after the commencement of the treatment. If there is a large increase early it is an indication that a good reaction is going to take place. The amount of reaction is inversely proportional to the number of red-blood cells present at the beginning of the treatment.

What is the cause of pernicious anæmia?

It is neither the bone marrow nor the liver of these people which is at fault. The disorder probably commences in the stomach. Hydrochloric acid is absent from the gastric juice, and, indeed, there is very little gastric secretion at all. Experiments were made with this fact in view and it was discovered that meat digested in gastric juice had a good effect upon pernicious anæmia. It was next assumed that there was an extrinsic and an intrinsic factor responsible for the disease, the intrinsic factor being something in the stomach. The next discovery was that dried pig's stomach produced much the same effect as liver extract, but this was found to lose its power if subjected to heat. It has been assumed that the factor in the gastric juice is an enzyme, "hæmopietin," which is supposed to act by its effect upon protein, thereby producing a substance which works in the same way as the anahæmin of the liver. We do not yet know the connection between these two substances. They are important, not only in connection with this disease, but because they may be signposts pointing in the direction of new fields in pathology. We may, for instance, know before long why people who suffer from pernicious anæmia are particularly prone to develop sub-acute combined degeneration of the spinal chord.

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