

SOME EXPERIMENTS ON THE EFFECTS OF LIVER SUBSTANCE
ON THE URIC ACID CONTENT OF THE BLOOD

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Liver substance, as it is known, has been made previously, but not until August, 1925, was it placed on the market as a substance which would reduce blood pressure. The liver substance which was used in these tests was furnished by Swan-Meyers Biological and Pharmaceutical laboratories of Indianapolis, Indiana. This substance, as manufactured by them, is prepared by a process of acid hydrolysis. Each c. c. of the solution represents 25 gms. of fresh liver tissue. It contains a minimum of nucleo-protein, no cholin, and gives a slight test for histidine and histamine. The solution is given in doses of 1 c.c. subcutaneously or intramuscularly, every second or third day. In these experiments this routine was not exactly followed.

In summarizing the work that has been done with this substance very little can be said; for work upon this has been done very recently and by only a few workers. In 1895, Olin and Schaefer made aqueous and glycerine extracts of thryoid, spleen, parotid, and submaxillary glands, and found that they reduced blood pressure. They reported nothing concerning the effects of these substances on the uric acid content of the blood, nor upon any other chemicals in the blood. Recently MacDonald, of St. Catherines, Ontario, did some work with liver substance on high blood pressure. He conceived the idea that the liver secretes a substance which plays an important part in controlling the uric acid content of the blood. He further conceived that if such a substance could be produced, that it might be a cure for cancer, since Killian and Kast have found that in 80% of the cases of cancer studied that there is a high percentage of uric acid in the blood. Fishberg has shown that there is a high percentage of uric acid in the blood of patients with arterial hypertension.

C. X. Williams has shown that an increased destruction of leucocytes is attended by an increased excretion of uric acid in the urine. His studies apparently prove that is cases in which a rise in the phosphoric acid curve follows a fall in the leucocyte curve and in the number of glandular cells, especially, this rise corresponds with a rise in the uric acid. It is true that in all cases of hypertension there is an increased amount of uric acid in the blood. This may be remedied by placing the patient on a diet free from protein. There are very few diseases which are directly caused by uric acid. Perhaps the one which is of most importance is gout.

In gout there is an increased amount of uric acid found in the blood. It has been thought that sometimes it is due to the inability of the kidneys to excrete this uric acid. Decosta* advises that diseases in which the symptoms point to a disorder of metabolism, water and salt solutions should be used. This statement has been contradicted by Cushny** in his Pharmacology. He says: "As a matter of fact, the more recent work in this direction shows that large quantities of water and diluted salt solutions have little or no effect on the uric acid excretion, which was formerly believed to

*DeCosta 2 ed .pp. 263.

**Cushny Pharmacology and Therapeutics of the Action of Drugs pp. 518.

be diminished. This fact does not necessarily involve the influence that the treatment is erroneous, for it is now generally recognized that gout is not really due to the failure of uric excretion."

All uric acid determinations were made by the Folin-Wu method which was perfected by Benedict. The Folin-Denis uric acid reagent was used. These methods are well enough known that they need no further explanation.

In every case of blood pressure tests a dog was used. High blood pressure was obtained by using adrenalin chloride. In a few experiments liver substance was mixed with the blood of various animals, which was then examined.

A 7 kilogram dog was used for the experiment. The dog was not placed on a strict diet but was fed on ordinary rations. For one week, 1 c. c. of liver substance was injected intramuscularly each day and a test for the uric acid content of the blood was taken each day, blood being drawn directly from the heart by means of a syringe. The highest content of uric for this period was 2.66 mg. per 100 c. c. of blood, and the lowest, which occurred at the end of this period, was 1.43 mg. per 100 c. c. of blood. The average for this period was 2.088 mg. per 100 c. c. of blood.

For a period of 10 days, 2 c. c. of the liver substance was injected intramuscularly each day and a test for uric acid taken each day. During these tests the animal was kept on a protein diet. The uric acid content fluctuated between 1.12 mg. and 1.42 mg. per 100 c. c. of blood. The average content for this period was 1.295 mg. per 100 c.c. of blood.

Following these periods 3 c. c. of liver substance was injected each day and a test taken at the end of a week. The blood tested 1.05 mg. of uric acid per 100 c. c.

The same dog that was used in the above tests was not injected for two weeks and then the blood was again tested for uric acid. The blood tested 1.52 mg. per 100 c.c. To 6 c.c. of the above blood 1 c.c. of the liver substance was added. This showed a uric acid content of 1.72 mg. per 100 c. c. Another test in which 4 c. c. of the blood was mixed with 2 c. c. of the liver substance showed a uric acid content of 2.66 mg. per 100 c. c.

Horse blood was tested for normal uric acid content and was found to be 2.67 mg. per 100 c. c. 2 c. c. of liver substance was added to 5 c. c. of blood filtrate and the uric acid was 2.84 mg. per 100 c.c. Then 3 c.c. of liver substance was added to 5 c. c. of horse blood filtrate and the uric acid test was 3.6 mg. per 100 c.c. of blood.

Rabbit blood was used and tested for normal uric acid content and was found to contain 2.56 mg. per 100 c.c. of blood. 1 c.c. of liver substance was added to this blood filtrate and the uric acid tested 5.6 mg. per 100 c. c. of blood. The normal readings for uric acid in the blood of the dog before the liver substance was injected showed an average of 2.224 mg. of uric acid per 100 c. c. of blood, and at the end of the periods of injection the uric acid content tested 1.05 mg. per 100 c. c. of blood.

In every case in which liver substance was injected there was a fall in blood pressure of at least 60 mm. of mercury, but in no case was there a decrease in the uric acid content of that blood.

When the substance was injected into the dog the uric acid content gradually fell, but when the liver substance was mixed directly with the

blood there was an increase in the content of uric acid. In view of the two contrasting observations, I concluded that the liver substance does not directly cause the decrease in the uric acid content of the blood, and that the increase of uric acid in which the liver substance and blood were mixed directly is due to the fact that the liver gives off urea which is formed by decomposition of the uric acid; consequently the liver substance must have contained some uric acid in some form. There is no reason to believe that high blood pressure is caused directly by an increase of uric acid in the blood.

Liver substance is dangerous in large doses and must be administered very cautiously in order that there be no harmful results. Injected in large doses causes an element of drowsiness and soreness in the parts in which it was injected.