upon a chain of circumstances, the sum-total of which leads to the ultimate production of such an intractable malady.

Either Colonel Cowan or Dr. P. O. Ellison kindly carried out the bacteriological and biochemical investigations referred to in this paper.

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THE ACTION OF HISTAMINE ON THE VEINS:

A METHOD OF DIFFERENTIAL PERFUSION: NITRITES IN THE PREVENTION OF HISTAMINE SHOCK.

(Preliminary Communication.)

BY

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DALE and LAIDLAW¹ have shown that in histamine shock there is capillary dilatation, with fall in blood pressure and respiratory failure within a very short time of the injection of the drug. They conclude that histamine produces an active dilatation of capillaries, and dismiss the possibility of active constriction of veins. I have devised a method of perfusion which differentiates between the action of a drug on arteries and on veins respectively.

Method.

Cannulae are inserted into the artery and vein of the organ; bleeding points are ligatured, and the organ after excision is perfused for a short time in the ordinary way with warm oxygenated Ringer's fluid under hydrostatic pressure, in order to wash out the blood and to determine there is no leakage. An incision is made in the organ, avoiding large vessels, or the surface may be scarified. For perfusion of the veins the Ringer's fluid is led to the cannula in the vein and the artery is occluded. The perfusion fluid now passes backwards through the veins and escapes by the incision, and the rate of flow is measured. For arterial perfusion the reverse process is adopted—the vein is occluded and the fluid from the arteries escapes as before. A fresh preparation must be used for arteries and for veins, because after the tissues have been perfused with the drug by the one channel they are so affected that only a small effect may be obtained if perfused afterwards by the other channel.

Certain details of procedure may be briefly indicated for particular organs. For the small intestine cannulae are inserted distally in the portal vein and superior mesenteric artery. The incision in the isolated loop of gut is made longitudinally on the opposite side to the attachment of the mesentery. In the liver a cannula is inserted in the portal vein directed towards the liver; another cannula is placed in the inferior vena cava in the thorax, directed tailwards, and the diaphragmatic veins are ligatured. The liver is then removed after a ligature has occluded the inferior vena cava and hepatic artery in the abdomen. After scarification of the liver separate perfusions of the portal ramifications in the liver and of the hepatic vein may thus be obtained.

For the hind limbs the usual preparation is made, and after skinning the limbs the fascia lata is removed and the superficial fibres of the thigh muscles cut away with scissors. The perfusion fluid exudes from the raw surface thus exposed.

In the lung a cannula is inserted into the pulmonary artery through the right ventricle; another cannula is inserted into the left auricle through the mitral orifice. The remains of the heart are cut away and the lungs with the trachea removed from the body. Into the trachea a small quantity of warm liquid paraffin is introduced, and the lungs are inflated to about their normal volume in the chest and the trachea ligatured. In this way air-locks are made in the bronchi. The surface of the lungs is then scarified to provide exit for the perfusion fluid. The air-locks prevent the lungs from collapsing, and the scarification allows the pulmonary artery and veins to be perfused separately.

By this method of perfusion it was found that after histamine both venules and arterioles were constricted in the isolated limbs and lungs of both cats and rabbits, and constriction of both portal and hepatic veins occurred in the liver of these animals. In the isolated intestine of the cat a similar constriction of venules and arterioles was observed. The rabbit's intestine, however, showed no constriction of mesenteric venules but only the arterial constriction. Ring preparations of the portal vein and mesenteric artery of the pig (from the slaughterhouse) also showed tonic constriction by histamine. It would appear that constriction of venules is an important action of histamine, leading to capillary engorgement and consequent oedema. In view of the above observations the shock induced in the cat, and its absence in the rabbit, would appear to be largely due to the difference in the reaction of the splanchnic veins to histamine in these animals.

These experiments suggested that a preliminary treatment by nitrites in order to dilate the veins, followed by the infusion of a sufficient quantity of Ringer's solution into the veins to fill the dilated vessels, might prevent death in the cat after a toxic dose of histamine.

A cat of 1.9 kilos anaesthetized with urethane received an intravenous injection of 16 mg. of sodium nitrite in 1 per cent. solution; Ringer's solution was then intrafused under 20 cm. water pressure into the vein; 6 mg. of ergamine (B. W. and Co.), containing approximately 2 mg. histamine base, were injected intravenously. The animal did not require artificial respiration, and was alive one and a half hours after the injection of the histamine; the blood pressure and respiration improved considerably within half an hour.

Further experiments on these lines are in progress; a method of treatment after the induction of histamine shock is being attempted.

These experiments suggest that the wheal described by Dale and Laidlaw which arises at the point of local application of histamine may be due to intense local constriction of venules leading to local congestion and consequent oedema. This may be a protective response on the part of the organism to prevent the admission of histamine into the general circulation. If histamine shock be regarded as a generalized extension of such a response it is clear that for treatment the venules must be dilated sufficiently to provide an adequate circulation in the organism, but the oedema must be encouraged in order to assist the elimination of the histamine from the blood.

The regulation of the flow of blood through the veins would appear to be important. Gunn² has shown already that veins are constricted by adrenaline.

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A SIMPLE DIET TABLE.

BY

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THE following table has been in use in both hospital and private practice for nearly twelve months; the results obtained have been so satisfactory that I venture to think that it may prove of value to others who have to undertake the dietetic management of various metabolic disorders.

Most food analyses are expressed in percentage values of carbohydrates, fats, proteins, water, and salts, the quantity of food itself being given a unitary or workable value. In clinical work, on the other hand, it is obvious that what is required is a unitary value for the specific carbohydrate, fat, or protein content, and with this end in view I was led to devise this simple table. The factors which determine the success and accuracy of any particular diet would appear to be the ease of original construction, an elasticity which allows, if necessary, of a daily change, and a small demand only on the time and intelligence of helpers and patients. This table has been found to meet these requirements, the only other essential being a small pair of scales. The specific contents have been worked out from the excellent tables given by Joslin¹ and Cammidge² and from other sources; the quantities are not strictly accurate, as the unit idea was kept mainly in mind, in view of the ordinary conditions under which patients arrange their own dietary. The scheme has been principally used in the dietetic management of chronic nephritis, diabetes mellitus, hyperchlohydria, and achylia gastrica. In these conditions, where specific intolerance of carbohydrates, fats, proteins, or their derivatives is often manifested, a simple control of intake has been obtained by the use of this table; determinations of output or utilization have been made in the case of carbohydrates by glucose estimations in blood and urine, in the case of proteins by determination of urea in the blood and of total nitrogen and urea in the urine, and in the case of fats by the ordinary methods of detecting the onset or degree of acidosis. By these means it has been found that growth or loss of tolerance for carbohydrates and proteins is readily observed and that the onset of acidosis is easily controlled.

The following chart may serve to illustrate the simple method of prescribing food, quantities of which are shown daily; growth of tolerance for carbohydrate (without fasting or the use of "ladder" schemes) and maintenance of nitrogenous equilibrium are also clear. The case is one of a woman of 26 suffering from diabetes mellitus. Blood sugar