On a new constituent of the blood and its physiological import / by L.C. Wooldridge ; communicated by M. Foster.

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"On a New Constituent of the Blood and its Physiological Import."

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In a paper on the Origin of the Fibrin Ferment, published in "Proc. Roy. Soc.," vol. 36, I showed that there exists, dissolved in the plasma, a body which can give rise to fibrin ferment.

I have proceeded with my investigations, and have succeeded in making some additions to our knowledge of this subject, which I here describe. As my researches are not complete, I confine myself to as brief an account as possible.

The subject is best studied in the blood of peptonised dogs. But as I showed in the above quoted paper, similar results are obtained from normal salt plasma, so that the results are not peculiar to pepton blood. The body, the presence of which gives rise to fibrin ferment, can be isolated from pepton plasma in the following very simple manner:—The plasma having been completely freed from all corpuscular elements by means of the centrifuge, is cooled down to about 0°. The plasma, which was previously perfectly clear, becomes rapidly turbid, and after standing for some time in the cool, a very decided flocculent precipitate forms. I have already described this observation in a short note, "Ueber einen neuen Stoff des Blut-Plasmas," in du Bois Reymond's "Archiv für Physiologie," but it is necessary for me to allude to it here.

Now it is this body which gives rise to the fibrin ferment. So long as the former is present in considerable quantity the latter clots readily on passing through it a stream of carbonic acid, or on dilution, and at the same time a very considerable quantity of fibrin ferment makes its appearance.

By prolonged cooling the greater part of this substance can be removed, and with its gradual removal the plasma clots less and less readily with CO_2, and less and less ferment is formed, till finally it becomes practically incoagulable, *i.e.*, forms only a faint trace of fibrin after several days. If some of the substance be again added to the plasma, it regains its power of clotting with CO_2.

(The substance must be added before it has stood very long: see under.)

It must be understood that the plasma, previous to the passage of the CO_2, is quite free from fibrin ferment, so that there can be no question of the ferment being mechanically removed by the precipitate.

Moreover, that it is really the body removable by cold which gives rise to the fibrin ferment, and not any second body which is mechanically carried down with the former, is shown by the fact that the diffusion of a large quantity of inert finely-divided precipitate through the plasma, and its subsequent removal by the centrifuge, does not in any way do away with the power of the plasma to clot.

It is therefore justifiable to assume that when pepton plasma clots readily and completely with CO_2, it must contain this new body in some quantity, and that when it will not clot, or only very imperfectly, after *repeated* treatment with CO_2 or dilution, this new body must be present in very small quantity.

Now I have found that the behaviour of pepton plasma with CO_2 varies very considerably with the diet on which the animal is fed, and whether the animal is fasting or has recently been fed. In some cases it clots readily, in others practically not at all.

Out of eight dogs fed on very lean meat only one gave a plasma which clotted at all fully, and in this case the clotting went on for two days. From all the others the plasma, in spite of repeated treatment with CO_2, only gave rise after two or three days to a scarcely perceptible fibrin membrane. The animals were killed about eighteen hours after the last meal.

Of six dogs fed on fat and meat for several days all gave a plasma which clotted rapidly and fully in from twenty minutes to one hour after the CO_2 treatment. The animals were killed about eighteen hours after being fed.

Of two dogs fed on bread and meat both gave a readily coagulable plasma.

One day's feeding on fat does not produce any effect; that is the blood of a dog thus fed behaves like that of a dog fed on a lean meat.

A dog fed for some days on fat and meat, was for five days previous to being killed put on fat alone; as a consequence it practically starved, as it ate scarcely anything. The blood from this dog clotted very incompletely.

Simple starvation for three days did away with the influence of fat in another case.

These results only hold good for dogs in health. In a dog with a suppurating wound, kindly placed at my disposal by Mr. Horsley, the plasma, in spite of a lean meat diet, clotted with very great rapidity, and contained an enormous quantity of the new body. All the other dogs were healthy, but were badly nourished when they came into my hands.

It is necessary for these experiments that the peptonisation should be complete.

For the complete understanding of these results, I must return to a further consideration of this new constituent of the plasma.

The turbidity which appears on first cooling the plasma, if examined microscopically, is found to consist of a great number of minute pale transparent bodies of a rounded shape, much resembling small organised bodies, such for instance as the stroma of the red corpuscles, except that they are of very various size, but generally much smaller than red corpuscles. They have a great tendency to run together into granular masses.

At first the precipitate is soluble on re-warming the plasma slightly, but it soon undergoes change, and loses the power of redissolving by heat. If the substance be collected by means of the centrifuge it forms a disk or thin membrane at the bottom of the tube, much reminding one of fibrin, but closer examination shows that it presents marked differences from the latter, and that, in truth, it much more closely resembles the peculiar viscid body obtained by destroying leucocytes with dilute alkalies, &c.

On longer standing, however, it becomes in most cases still further changed, and is then undistinguishable from ordinary fibrin, swelling in dilute HCl like the latter. For further details as to the properties of this substance, I refer to my paper quoted above.

We have already seen that this substance gives rise to fibrin ferment, but it does more than this in inducing coagulation.

Pepton plasma is not coagulable with fibrin ferment. If we take some plasma rich in this new substance, and by means of CO_2 induce coagulation, we obtain, on removing the clot, a serum which has the power of inducing exceedingly rapid coagulation in a new portion of plasma, and this, when the serum has regained its alkalinity. This serum contains ferment, but inasmuch as ferment is not sufficient to induce coagulation, it must also contain some other substance. Now leucocytes have exactly the same power. They give rise to ferment, but they also give rise to the other substance necessary for coagulation.

We see, therefore, that we have dissolved in the plasma a body exerting the same influence on the induction of coagulation as the leucocytes.

I think this is the strongest chemical proof that can be brought that the leucocytes break down to make, at any rate, a part of the proteid constituents of the plasma, and have shown above the influence which diet, &c., has on the extent of this process, a fact of obvious interest for the question of assimilation.

There is, however, another important conclusion to be drawn from these observations, viz., that one must admit, in addition to the

ordinary fermentative fibrin formation, that fibrin may be deposited from blood by simple physical means, without any ferment process; for this new substance becomes, as I have stated, true fibrin, and yet the plasma does not contain ferment. Possibly this mode of fibrin formation is of importance in the formation of a thrombus.

The peculiar microscopical characters should also be noted, as possibly affording an explanation of the observations made by Osler, Bizzozero, Hayem, and others. I refer of course to the granules, Blutplättchen, hæmatoblasts, described by these authors.

As I am actively engaged on this subject, and as I hope before long to produce a complete account of my researches on the coagulation of the blood, I have purposely confined myself to the briefest outlines.

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