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NOTE

ON THE

STATE IN WHICH FIBRIN EXISTS IN THE BLOOD.

BY

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It has for some time been the general opinion among physiologists, that the fibrin of the blood is liquid during life, and becomes solid only when that fluid dies; and this opinion is based on the well-known experiment, first performed by Müller, of filtering frog's blood before its coagulation, and thus obtaining the clot separate from the globules, which remain behind on the paper. At the meeting of the British Association at Glasgow, Dr. A. Buchanan exhibited a method of showing the same thing in human blood, by receiving it from the vein into a vessel of serum, in which the globules subside before coagulation.

The common notion of the change which takes place on coagulation has been well expressed as follows:—

$$\text{Living blood}\begin{cases}\text{Plasma}\begin{cases}\text{Fluid} & \text{Serum}\\ \text{Fibrin} & \end{cases}\\ \text{Globules} \quad — \quad \text{Clot}\end{cases}\text{Dead blood.}$$

From this opinion there have recently dissented M. Mandl* and Dr. A. Buchanan.† These gentlemen hold, that while of the corpuscles of the blood the *red* take no part in the coagulation, and are merely engaged as it were by accident in the clot, from which, by the above mentioned means, they may be artificially excluded; yet the *white* corpuscles and the *molecules* which exist in the fluid, really

* Anat. Microscopique, Art. Sang. 1842.
† Proceedings of the Glasg. Philos. Soc. 1843, p. 131.

constitute the fibrin: and that the coagulation consists simply in the aggregation of these previously isolated bodies. Dr. Buchanan's opinion to this effect is based, not upon the direct examination of the process of coagulation in the blood, but upon what he conceives to occur in the case of the fluid of blisters and of serous cavities, and to furnish an analogical argument of considerable weight.

Now, it is true that the fluid of blisters contains corpuscles like the white globules of the blood, and also that it coagulates on standing; and it may be likewise true, that the number of the corpuscles is in the ratio of the size of the clot: but I have carefully watched the fluid of a recent blister coagulating under the microscope, and find that the delicate clot forms independently of the corpuscles, as it is seen to occupy the whole area of the field of view, while at most two or three corpuscles may be scattered over it.

Again, it is true that in the very curious experiment which we owe to Dr. Buchanan, the mixture of the serum of blood and of that of hydrocele, exhibits after standing for some time a marked coagulum; but I submit that neither is this a proof that that coagulum is derived from the corpuscles existing in the fluid in which it forms; for I have divided such a mixture into two equal parts, and while leaving one untouched have separated by filtration all the corpuscles from the other, while still fluid, and tested their absence by the microscope, and yet the eye could detect no difference between the coagula subsequently formed in the two portions—nor, when aided by the microscope, any corpuscles newly formed.

But the *experimentum crucis* is the examination of the changes which occur in the plasma of the blood itself; and this may be effected by removing with a spoon a portion of the incipient buffy coat, (the whitish fluid which floats before coagulation on the surface of inflammatory blood,) and placing it under the microscope. This fluid is the blood *minus* the red corpuscles, which, as Mr. Wharton Jones has shown,* attract one another more strongly in inflammatory than in healthy blood, and sink rapidly in the fluid. Our view, then, of the changes which occur being no longer obscured by their presence, we watch the plasma swarming with molecules and white corpuscles, the latter always most abundant in inflammation, as may be seen even by placing a drop of the just abstracted blood under the microscope between two plates of glass, to which the white corpuscles stick because of their greater size, while the red (known by their smooth outline, their central nuclei, elongated profile, and, even under the microscope, pale yellowish colour,) rush beautifully past them, like fragments of floating things carried against a

* Ed. Med. and Surg. Journal, 1842.

buoy moored in a strong tideway. As we watch the plasma it has become partly solid, but no visible change appears; the corpuscles remain quite still, and it is only by drawing across the glass a needle, which carries the whole in a mass along with it, that we find that they are engaged in a thin coagulum. There is then no running together of the corpuscles; but so far we are still in doubt whether the clot may not be formed by their cohesion: the doubt is resolved by simply continuing to look: we have drawn aside the forming clot before its solidification was complete; and have left a clear fluid *perfectly free* from corpuscles of any kind, and yet in this again the coagulation takes place; it must, therefore, be from a solidification of the previously fluid fibrin.

So far my observations agree with those of Dr. Addison,* published after mine had been made; but he states that the fibrin solidifies in the form of fibres, and figures these of a somewhat stellate or spiculate appearance. In the existence of this sort of crystallisation I wholly disbelieve. I have repeatedly seen the whole field of view occupied uniformly by the extremely delicate clot, so fine and transparent as to be distinctly visible only when its edge was drawn across the glass with a needle, and thus contrasted with the remaining limpid fluid; and of which the structure was so faintly fibrous, that with the greatest difficulty, in a carefully modified light, there could, with a power of 600 diameters, be just traced, distributed equally over the whole surface, a most delicate striated appearance. It is true that afterwards the coagulum becomes fibrous, but this is the consequence of a subsequent contraction, the nature of which has not been satisfactorily explained, but of which I can say only this, that save its lessened size, and a slight increase of the fibrous appearance, no change, by motion or otherwise, could be observed in a coagulum prepared as above, and allowed to remain for twenty-four hours in a covered glass cell under the microscope, till it had fully contracted, and squeezed out all the serum from its interstices.

Moreover, I must differ in opinion from Dr. Addison, when he advances it as ascertained, that the fibrinous spontaneously coagulable liquid is formed within the white corpuscles, and appears on their rupture only: there is no doubt some inseparable connexion between the presence of these corpuscles and the existence of the fibrin of the blood, for in determination of blood, and in inflammation, the increase of the one keeps pace with that of the other: and it is possible that the corpuscles may have the function of converting the "reduced albumen"† of the food, and of the effete parts of the tissues,

* Trans. of the Prov. Med. Assoc. 1843. † Prout.

into organizeable fibrin, which appears first in the chyle along with these corpuscles, after that fluid has passed the mesenteric glands; and in all likelihood, first in the lymph after it has passed the lymphatic glands. Yet we find that in the mixed serums already spoken of, the solidification goes on for days gradually increasing, in the utter absence of corpuscles of any kind, and must, it hence appears probable, be owing to the progressive formation of fibrin, and not to the mere coagulation of that already formed; for *that*, as we see in the blood, is finished within a short time of the death of the fluid. Another proof of the essential difference between the white corpuscles of the blood, and its coagulable matter, is afforded by an elegant experiment, described by M. Donnè.* This consists in agitating the blood during coagulation: the fibrin is thus separated in stringy morsels, and on leaving the remaining part to stand for some time in a tall glass vessel, the white corpuscles are found forming a thin pale layer between the red globules below and the clear fluid, to the bottom of which they have subsided. The mode in which the change in the mixed fluids takes place is yet unexplained.

I believe with Dr. Buchanan, that the increased formation of fibrin in an inflamed part, takes place *within* the vessels, and therefore in the pure plasma of the blood itself; but that it is in all likelihood effected by the agency of the white corpuscles, which during inflammation become more numerous in the capillary blood-vessels, and adhere to their walls even more firmly than, in the state of health, they are wont to do; and thus throw an obstruction in the way of the red globules, which in health form a rapid current in the centre of the vessels.† Mere stasis does not produce the change, for in simple congestion, however much the blood may be delayed, there is no increase of fibrin—and in determination there *is* more fibrin formed, though there may be no obstruction, but rather a more rapid flow of blood: in the latter case, however, the vital nutritive action of the part is increased, in the former diminished, and this I take to be the true explanation of the increase of fibrin; holding it to be produced within the vessels by a greater activity of whatever organ (be it the white corpuscles or no) is in health charged to convert the "reduced albumen" to organizeable fibrin; an activity called into play by the increased demand for that material in the excited and over active part.

Thus, then, I think we must still believe that the coagulation of the blood forms an exception to the generality, contended for by Dr. Barry and others,‡ of the law that the living tissues are formed directly from cells.

* Cours de Microscopie, p. 84. 1843.

† Williams; Princ. of Medicine, p. 213. Travers; Pathology of Inflammation, &c. 1843.

‡ Various Papers, Phil. Trans. 1838, 1842, &c.

How the corpuscles of serous effusions are formed we cannot yet surely say: not, probably, as Dr. Addison * supposes, by the actual passage through the walls of the capillaries of the white corpuscles of the blood. The simplest effusion which takes place from vessels is pure water, as from the Malpighian bodies of the kidneys.† When there is more pressure or excitement, serum is effused, being water with albumen in solution, as in dropsy, or renal congestion;‡ if the local excitement still increase, fibrin is thrown out, and coagulates spontaneously when withdrawn from the body, as in the fluid of blisters;§ and a yet higher action of the part results in the throwing out of "lymph," or coagulable matter full of active cells, which, as in the inflammations of serous membranes, becomes rapidly organized. Dr. Addison would say that these cells are the white corpuscles of the blood, which have traversed the coats of the vessels, and go to form the plastic fibrin of the effusion; but then its plasticity ought to be in the ratio of their number, which is notoriously not the case: for pus, the most aplastic of all effusions, actually swarms with distinct corpuscles, very like those found in the blood, and yet contains no coagulating fibrin at all.

The opinion of Gendrin,‖ that the pus corpuscle is formed from the red blood globule, can scarcely now be held, except it be by Dr. M. Barry; and it is extremely improbable that bodies such as the white corpuscles, which are larger than the red globules of the blood, as 1-2600th to 1-3500th of an inch, should traverse the unruptured capillary walls while the latter are retained.

The nutrition of nonvascular tissue is effected** by the transudation of nutritive matter through the coats of the looped capillaries which encroach upon its edges; and we cannot suppose that white corpuscles, even if they too transuded, should make their way onwards to the centre of a solid mass of cartilage, for instance: we must suppose that it is the plasma alone which the tissue imbibes, and by which its living cells are nourished; and so in the case of effusion it seems most probable that what really occurs is simply a transudation of that plasma, nourished by which the corpuscles grow, whether they be descended from "germinal granules," or "cytoblasts," or in whatever way they originate.

The "molecules" and "granules," formed so abundantly in the buffy coat, exist also in healthy blood, in the serum of which they can be seen by the microscope; and in "milky" serum, such as occurs in renal inflammation, they are very abundant. Simon has shown††

* Loc. Cit. † Bowman, Phil. Trans. 1842. ‡ Robinson, Med. Chir. Trans. 1843.
§ Dr. Buchanan, loc. cit. p. 133. ‖ Sur les Inflam. ii. 472.
** Toynbee, Phil. Trans. 1842. †† Beitraege, &c. Lief. 1.

that it is in part to an albuminous, and not, as Prout and Christison* supposed, wholly to a fatty matter that such serum owes its opacity; and by the microscope it can be seen to swarm with particles resembling the molecules of the blood, rather than with the chyle globules which Gulliver describes,† though no doubt these may in certain cases exist. Dr. Andrew Buchanan‡ has discovered a method of separating this albuminous matter, and causing it to float on the surface of the fluid, when it puts on all the appearance of the amorphous substance found in what Hodgkin§ calls the nonplastic serous effusion. Do such effusions depend on the superabundance of this matter in the blood, as the more plastic forms are owing to increase in the coagulable fibrin, and is the well known action of mercury in making the plastic become the aplastic effusion, owing to some "reducing" action by which it tends to make the protein compounds of the blood less fibrinous, and more like common albumen?

It is evident that in the blood we have several forms of these compounds, deserving of much separate investigation, as:—

1. Albumen—coagulable by heating the serum.
2. "Serolin" remaining in the solution, mixed with urea, salts, &c. —and which Mulder, with what truth I know not, avers‖ to be a tritoxide of protein.
3. Fibrin—procured by agitating fresh blood.
4. White molecules—procurable by Dr. Buchanan's method from "milky" serum.
5. White corpuscles—probably procurable by a like method from the yet fluid buffy coat.
6. Hematosin dissolved out by water from the red globules.
7. "Globulin," or the coats and nuclei of these globules, which subside to the bottom when hematosin remains dissolved.

All these substances must be separately analysed, if we would perfect our knowledge of the blood: but it were an error to fancy that they must needs be exactly the same in all cases—even if in the same way procured. Mulder** tells us that the buffy coat is not pure fibrin, but a mixture of the deutoxide and tritoxide of protein: I cannot tell how this may be; but I know that it is not in the globules alone that we find a varying attractive or cohesive power. In inflammation, as Jones has shown,†† the mutual attraction of the red corpuscles is increased, so that they withdraw from the floating plasma; but the solidifying fibrin of that plasma contracts too with a

* On Granular Degen. of the Kidney.
† Notes to Gerber's Anat. ‡ Proceedings of Glas. Phil. Soc. 1844.
§ On Serous Membranes. ‖ Annalen der Ch. und Ph. 1843. ** Loc. cit.
†† Loc. cit.

varying power: in *sthenic* inflammation, when the system is otherwise in health, the coagulum shrinks during many hours, and the buffy coat forms a tough leathery covering to the clot. In *asthenic* or *specific* inflammation, as for example in the "ophthalmitis post-febrilis,"* occurring as a too frequent sequela of the fever lately epidemic in Glasgow, we have still the increased formation of fibrin and white corpuscles, still the greater mutual attraction of the red globules, and still the buffy coat; but it does not contract much, but maintains a gelatinous appearance, a state obviously owing to a vital power of the fibrin in some way diminished.

It remains for chemistry to tell whether the ultimate analysis of such a buffy crust differ from that of the more common kind; but from the difficulty of procuring material, it is probable the question may remain long unsolved.

But we have more: the red blood corpuscles have always a certain mutual attraction, clinging closely in death to one another; inflammation increases this, and likewise the quantity of fibrin and white corpuscles, and so the buffy coat is formed. But this takes place within a very few minutes: the subsequent *contraction* of the clot, by which the serum is squeezed from its interstices, is the work, *not of the globules but of the fibrin;* hence we find in one case a clot much contracted, though without a buff; in another buffy blood, of which the clot and even the buff itself are loose and soft; in still another the coagulum is soft and presents no buff; while there are also cases where the clot is small and dense, as well as clothed with a firm leathery coating.

The first occurs in sthenic states, where the fibrin is highly vitalised, but no inflammation is present—in plethora for instance: the second, where we have inflammation with an asthenic state of the system—as in the postfebrile ophthalmitis: the third, where much debility exists, without any local inflammation—as in fever: and the fourth, where, as in sthenic acute inflammation, there is a local disease, and an active state of the system besides.

These differences point at some element of the doctrine of the properties of blood, which it will go hard if chemistry alone can explain.

* Mackenzie.

FIG. 1.

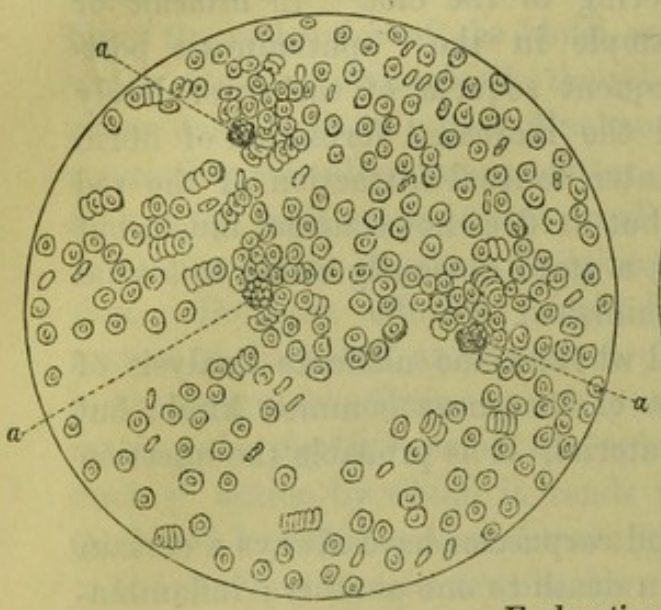
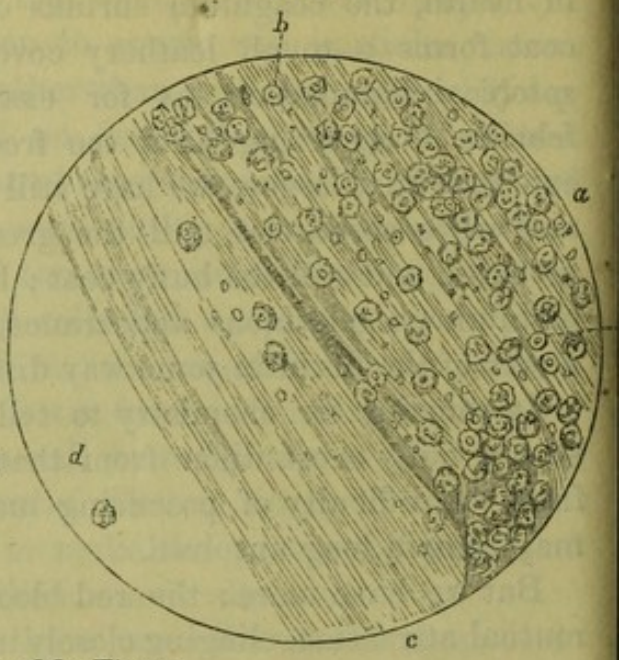


FIG. 2.



Explanation of the Figures.

Fig. 1.—Three white corpuscles (*a*, *a*, *a*,) are seen sticking to the glass in the field of view, while the red corpuscles rush rapidly past. (Inflammatory blood before its death.)

Fig. 2.—The coagulation of the buffy coat: *a*, the white corpuscles and molecules; *b*, a few red corpuscles; *c*, the striated coagulum, formed after the removal of the corpuscles; *d*, the clear space containing serum.

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