ON THE
DEPOSITION OF FIBRIN
ON THE
LINING MEMBRANE OF VEINS.

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Received Jan. 28th.—Read April 27th, 1852.

M. GENDRIN, in his '*Histoire Anatomique des Inflammations*,'¹ cites an experiment upon which much stress has been laid by subsequent writers, and from which the existing theory respecting the mode of formation of lymph in inflamed vessels has derived much of its support.

If, says M. Gendrin, an irritating injection be thrown into a portion of an artery included between two ligatures, emptied of its blood, and washed, the inflammation which follows is characterised by the formation of a plastic layer, which lines the internal membrane, and ultimately fills up the cavity of the vessel. This is accompanied by an obscure redness of the lining membrane, which is not under the circumstances stained of a violet red colour by the imbibition of the colouring matter of the blood, as happens when the vessel is filled with the coagulum.²

In repeating his experiments upon veins, M. Gendrin arrived at similar results, but found that the lining membrane of these vessels increased in thickness to a greater extent than that of the arteries, that they suppurated more

¹ Paris, 1826.

² Tom. ii, p. 13.

quickly, and that they always afforded readily a concrete layer of lymph, which obliterated the vascular canal.¹

Hassé, in his 'Pathological Anatomy,' has followed Gendrin, and believes that the induration of inflamed veins depends partly upon the coagulated blood which they contain and partly upon the lymph secreted from the lining membrane into their interior.

English pathologists have generally adopted the same view, and coagulable lymph is spoken of by them as capable of being effused as readily on the lining membrane of veins as upon the peritoneum or pleura. The writers who have thus regarded the internal surface of the veins as analogous, in a pathological point of view, to a serous cavity, are so numerous that it might seem superfluous to refer to any individual treatises upon the subject; but, if necessary, quotations might be taken from works of pre-eminent authority, not only in this, but in every country of Europe. Thus, in the first sections upon diseases of the veins in Mr. Hodgson's most justly celebrated work, it is stated that "the veins are liable to all those morbid changes which are common to soft parts in general; but the membranous lining of these vessels is peculiarly susceptible of inflammation. . . . This inflammation sometimes produces an *effusion of coagulating lymph*, by which the opposite sides of the vein are united, so as to obliterate the tube; in this manner, a great extent of the vessel is occasionally converted into a solid cord."

Again, in Mr. Travers's most valuable treatise on Inflammation, the existing theory is summed up in the following words:—"The false membrane, as it is called, within the visceral chambers, canals, and blood-vessels, are depositions of fibrine *secreted by the capillary vessels under inflammation.*"

Finally, in a very able article now in the press for the 'Cyclopædia of Anatomy and Physiology,' I have reason to believe that similar views are maintained. In the face of so much traditional authority, no small degree of responsibility is involved in stating an opinion to this Society in any

¹ Tom. ii, p. 15.

degree at variance with that which has hitherto been maintained upon the subject; nor should I venture to do so had I not direct observation and experiment to appeal to.

In the year 1848 I was first led to suspect the correctness of the current explanation of the pathological appearances observed in cases of phlebitis, by noticing that no irritation or inflammation occurred (in cases where it might have been expected) if the blood were prevented from stagnating in the vessels. An animal, for instance, had some pus injected into its brachial vein, and was killed on the third day. The vitiated blood had, at the time of the experiment, been prevented from lodging in the vessel by mechanical pressure in the course of the circulation. On examining the vein after death, its lining membrane was found of its natural smooth, polished, and lubricated appearance. The opening that had been made in the experiment was filled by some brownish granular matter, and no other local morbid appearance presented itself. About the same time a case occurred where a man had received a spike wound at the back of the head, which penetrated into the lateral sinus. This patient died of repeated hæmorrhage, several days after the accident. Although different styptics had been during his life introduced to the bottom of the wound, yet was there no inflammation of the vein produced. The lining membrane presented its natural polished surface. In another case, a patient died of symptoms of poisoned blood, after the operation for hæmorrhoids by ligature. On examining the parts, a vein was found terminating upon the wound produced by the operation, but its lining membrane presented nothing remarkable.

In these instances, no coagulum had formed in the wounded vessels. The blood, which was found fluid after death, had flowed through them in its natural course; and it appeared to me probable that, where coagulation of the blood did not take place, lymph was not so readily produced upon the lining membrane of veins as was generally believed.

In pursuing this subject, it was found that even a small

quantity of purulent matter introduced into a vein would determine the coagulation of the blood which it contained, if not prevented by mechanical interference. The examination of such cases afforded the strongest contrast to those above mentioned. Large fibrinous clots were found obliterating the cavities of the veins, the coats of which presented the well-known marks of having been acutely inflamed. These fibrinous plugs were in some parts composed of blood, which, in becoming firm, had moulded itself to the shape of the vessels; but in other parts the fibrin was entirely deprived of its colouring matter, and adhered firmly (as in preparation No. 3) to the sides of the vein.

The cellular membrane around the veins was found in these cases loaded with serum, lymph, and pus, the results of inflammation which had evidently been excited by the morbid matter detained in them by the coagulated blood.

In examining the specimens contained in the different museums of London, it will be difficult to find an instance where lymph has been deposited upon the lining membrane of a vein, and where the blood has not coagulated in the vessel. In many cases (and I may instance particularly some of Dr. Lee's beautiful preparations in the museum of St. George's Hospital) the same vein will be seen inflamed where a coagulum has adhered to it, but presenting its natural smooth and polished surface where this has not been the case. On finding, therefore, fibrin adhering to the lining membrane of veins only when coagulation of the blood had taken place, a doubt was raised whence this fibrin was derived; and it became a point of much interest to endeavour to determine whether it was really the product of inflammation, or whether it might not be deposited directly from the blood by a modified process of coagulation.

The results obtained by M. Gendrin above referred to, which have been so generally received, would appear directly to support the former theory, and, if made with sufficient care, must have finally determined the question. But from the description he has left, a source of fallacy appears not to have been guarded against in his experiments. It is not

stated that any means were used to prevent hæmorrhage into the cavity of the vessel between the two ligatures. Such hæmorrhage might occur after the operation, either from the divided vasa vasorum in the case of an artery, or from some collateral branch, or from the vasa vasorum which open into its cavity, in the case of a vein. The observations which I had made led me to suspect that the results which M. Gendrin had obtained depended upon this cause, and that the fibrin had been deposited from blood which had gained admission to the vessels after the ligatures had been applied. I therefore determined to repeat M. Gendrin's experiment, and to observe whether, if the blood were carefully excluded from the cavity of the vein, lymph would still be effused upon its lining membrane.

By the kindness and liberality of Mr. Mayer, veterinary surgeon, every convenience and assistance were afforded me for performing the experiment; and the results obtained it is my principal object now to lay before this Society. The left jugular vein of a donkey was exposed, and two ligatures were placed upon it at an interval of something less than four inches. The vein was open for about an inch, near the centre of the exposed portion, and all the blood which it contained was carefully removed. The cavity of the vessel included between the two ligatures was now filled with cotton wadding. This was introduced piece by piece, and was pressed tolerably firmly towards the lower or sternal extremity as far as the ligature. Some of the cotton wadding was also introduced, but in less quantity, towards the upper ligature. The vessel was then carefully closed, its divided edges being sewn together with a needle and thread. Finally, the lower or sternal ligature was removed, and the wound in the integuments closed by a number of stitches. The lower ligature was removed in order to leave the circulation in the outer coats of the vessel as free as possible, the plug of cotton wadding being deemed sufficient to prevent any regurgitation of blood into its cavity. Immediately after the completion of this operation, a small portion of the cotton wadding was carefully introduced into the peritoneal

cavity, and the wound made in the abdominal parietes closed by suture.

The means were thus afforded of testing the difference which would be produced by the irritation of cotton wadding, in contact with the peritoneum and in the cavity of the vein, and of observing whether these parts were really analogous in their morbid actions. The animal was killed at the expiration of forty-four hours. On opening the abdomen, the peritoneal cavity was found to contain a considerable quantity of serum, and the peritoneum itself was much injected in different parts. The piece of wadding was found completely enveloped in a thick coating of lymph. The omentum, and a portion of the colon with which it was in contact, were injected to a high degree, and the latter especially presented a very large number of spots of a bright red colour. These appearances have been represented in the accompanying drawing by Dr. Westmacott.¹ On examining the neck, the parts about the lower portion of the jugular vein were much swollen and infiltrated with serum. The coats of the vein were found somewhat thickened for some distance below the seat of the operation. On slitting open the vein, some loose fibrin of a greyish white colour occupied its cavity below the cotton wool. Portions of this could be separated with the slightest force from the lining membrane of the vein, which was then left of its natural smooth, polished, and lubricated appearance. Immediately in contact with the wadding in this situation were some very small coagula of blood. These imperceptibly lost their colour, and faded into the appearance of the lymph with which they were, in substance, evidently united. Between the upper ligature and the head, the vein was of its natural appearance. The blood which it contained was fluid, with the exception of a loose unattached coagulum which floated in it. The point at which the upper ligature had been applied was thickened, and the circumference of the vein was here marked by an opaque white ring, about a line and a half in breadth.

¹ See also Preparations I, I.

The part of the vein included between the two ligatures is that to which I wish particularly to direct attention. The lining membrane here was of rather a deeper colour than natural, *but in no point did it present any trace of effused lymph.* The results of the irritation here afforded the most marked contrast to those produced by similar means in the peritoneal cavity. The whole of the lining membrane of this portion of the vein presented a smooth and polished surface, and the valves which it contained were not perceptibly thickened.

The point at which the effusion of decolorised fibrin, observed in the sternal portion of the vein, terminated, was defined with the greatest exactness. This was exactly where the lower of the two ligatures had been applied.

On removing the vein from its bed, it was observed that suppuration had distinctly taken place in some circumscribed portions of the surrounding cellular tissue.

The principal conclusion to be drawn from the preceding experiment and observations is, that the analogy which has been supposed to exist between the lining membrane of blood-vessels and the closed serous cavities of the body cannot be maintained, with regard to their morbid processes; and consequently that the mode of treating inflamed veins which has been based upon the supposed resemblance is not founded upon sound physiological principles.

Another point of secondary importance, but by no means devoid of interest, is the power which the blood is shown to possess of separating directly from itself a fibro-albuminous element, without the intervention of any membrane and independent of any inflamed surface. The true pathology, and consequently the rational treatment, of obstructed veins cannot, I apprehend, be arrived at, without considering the proximate cause of the changes observed upon post-mortem inspections in the contents of the vessels and in the surrounding parts. That violent irritation is often produced in such cases, the amount of pain, swelling, and effusion abundantly testify. But in what part are the effects of this irritation first apparent? Not in the lining membrane of

the vein, but in the surrounding areolar tissue. In the experiment above related, the internal coat of the vein was scarcely changed in appearance; the outer coverings were slightly thickened, but the surrounding cellular membrane had actually suppurated. Here, then, was the seat of the inflammation; and for what ulterior object was it established? Evidently for the purpose of getting rid of a foreign substance lodging in the vein.

The process here observed is quite analogous to that which takes place when any vitiated secretion finds its way into the circulation, and is retained in a vein. The surrounding areolar tissue will become inflamed, loaded first with serum, and then with lymph and pus, before the coats of the vein have taken on any similar actions. The process by which, in either case, the morbid matter is to be eliminated, extends *to* the lining membrane of the vein, and not *from* it.

During the time that this surrounding inflammation is being established in ordinary cases of phlebitis, still more important changes, although of a different nature, are taking place within the vein. Its contents, as I have attempted to show, almost invariably become solid before its coats are thickened, and even before the surrounding parts have begun to inflame. The proximate cause of this, it is not difficult to conceive or to illustrate by experiment. The effects produced by the admixture of pus with blood previously referred to, evidently show a latent sensibility in the blood ever ready to be called into action for the preservation of the system. Foreign matter, which would otherwise be carried in the course of the circulation, is by this means confined to one part, and produces only a local irritation. When morbid matter is thus detained in a vein by the coagulation of the blood, the inflammation of that vein will be much greater than if the vitiated matter could, in part or altogether, escape into the general circulation. This is quite in accordance with the wisest economy of nature,—an economy which we cannot too much admire, by which, when her intention is not frustrated, a part is sacrificed for the preservation of the whole. After diseased fluids have in this way entered

into a kind of combination with the blood, further changes take place.

If the proportion of morbid matter be large, the whole coagulum will rapidly soften, and present to the naked eye the appearance of pus more or less discoloured. But if the quantity, which has become mixed with the blood, be small, the coagulum will retain its consistency and become adherent to the sides of the vessel. Under these circumstances the coagulum will adhere to one side only of the vessel, and as it contracts, the diameter of the vessel will be restored to its original size. In other cases the outer layer of the coagulum will become adherent to the whole circumference of the vein, and the inner portions, which are always the least consistent, will become softened and broken down. A complete cylinder of fibrin may, in this way, be formed in the interior of a vein, through which (when the fluid portions of the coagulum are removed) the blood will circulate. It is worthy of remark that when plugs of fibrin are thus formed, the adjacent lining membrane of the veins are coloured in exact proportion to the quantity of colouring matter contained in the coagula. In a preparation on the table, the vein may be observed to be deeply blood-stained where in contact with the dark coloured clot, but to retain its natural appearance where its contents are decolourised. The changes which take place in the interior of veins now mentioned, may be referred, I conceive, entirely to actions in the blood itself, so long as the lining membrane of the vessels remains entire. The adhesion of the coagulum, and the changes which it undergoes, are no way dependent upon secretion from its lining membrane.

This opinion is quite in accordance with what is known of the minute anatomy of the blood-vessels. In no case have vessels, I believe, been observed on the delicate fenestrated membrane which lines the veins either in health or disease. There would, in fact, be no object in providing a surface with blood-vessels which is already in contact with the blood. This fact alone might lead to the inference, that the results of inflammation in a vein would be different from those

observed in serous membranes; and especially might it, *a priori*, induce us to believe that the deposits, under such circumstances, on the lining membranes of veins, would differ from the ordinary products of inflammation in their origin and mode of formation.

The opinion, that the material found in obstructed veins is derived directly from the blood, is further supported by the fact, (which was well illustrated by preparation No. 2, when in a recent state,) that where a coagulum is formed, and becomes incorporated with the coats of a vein in one part, the lining membrane of the vessel in its immediate neighbourhood may, nevertheless, present its natural shining appearance. Did the union, in such a case, depend upon lymph effused by inflammation, the alterations in appearance of the lining membrane would not be limited exactly and precisely, in the first instance, to the points of adhesion, and be found in no other part.

Again, we should naturally expect that a secretion, derived from the lining membrane of a vein, would adhere equally to every part of its circumference; but in the case we are considering this does not usually happen. Adhesion will take place upon one side only of the tube, and the lining membrane will, in other parts, present its natural appearance.

The process which here takes place is quite analogous to that which occasionally occurs when blood is effused in the serous cavities of the body, and which has been so admirably illustrated by Mr. Hewett in vol. XXVIII of the 'Medico-Chirurgical Transactions.'

When blood is effused in the arachnoid cavity, Mr. Hewett has shown that a smooth and polished layer will form upon its surface; and that this newly-formed substance will present the external characters of a serous membrane. Such adventitious layers were long supposed to be formed by lymph secreted by the serous membranes in which they were found;—a supposition which has also long been maintained with regard to similar formations in the cavities of veins. But it must be evident in either case, that if these membranes were

formed by lymph the product of inflammation, they would adhere to all the surfaces with which they are in contact ; whereas the greater part of their circumference is generally found smooth, polished, and lubricated.

Finally that the material which, in the first instance, lines the cavities of obstructed veins, is derived exclusively from the blood, appears to be directly proved by the experiment which has now been laid before the Society.

The point of the vein most irritated, but to which the access of blood had been derived, contained no deposit or secretion of any kind, although exposed to the contact of foreign matter for forty-four hours previous to death.

I have been the more careful in endeavouring to establish this point, inasmuch as the treatment of phlebitis has necessarily been influenced, in a great measure, by the ideas which have been entertained of its pathology.

Attempts have usually been made to subdue the prominent inflammatory symptoms by bleeding, either general or local, or by the administration of calomel and opium. M. Cruveilhier even ventures to assert that every case of phlebitis may be cured by the application of a sufficient number of leeches, often enough repeated in its incipient stage. There can be no doubt that the patients thus treated often survive both the disease and the remedies, still oftener are the prominent symptoms apparently relieved. But if the view which has now been taken of the real nature of this disease be correct, what does the sudden disappearance of the local symptoms imply? Experience proves that but too often they subside in one part only to manifest themselves in another ; and it not unfrequently happens that a day or two before death, the local symptoms have attracted less attention than at any other period of the disease.

How constantly do we see that an inflammation in the arm after bleeding will subside only to develop itself in the opposite arm, or in one of the lower extremities, if not in some internal organ ! We have here the explanation of the recorded description of cases in which it is stated that the patient was often bled, and every time with much advantage ;

but that, unfortunately, a day or two before death, his strength had so far given way, as to require the use of cordials.

It were wiser, in my opinion, to adopt and follow out the hint given us by the yet unimpaired powers of life, in combating this disease.

Unaided by medical assistance does the blood itself fix the morbid matter which threatens the constitution to one point of the vascular system. Here it produces an irritation, the object of which is to expel the foreign matter. Bleeding and calomel will perhaps prevent the development of the inflammation established for this purpose; and they do so, I conceive, *by destroying that power in the blood which tends to localise the disease.* Calomel loosens newly-formed adhesions, and bleeding renders the coagulating power of the blood feeble; and under their influence, any morbid secretion retained in a vein would be likely to be translated to some other part of the system. When this occurs the constitution may still have power to throw off the diseased matter which has excited the irritation, and this is often done by the secretions of the bowels and liver. But in severe cases, I cannot but doubt the propriety of putting *the powers of the constitution to this test.*

The second point which I wish briefly to notice, with regard to the preceding experiment, is the similarity in the appearance of the lymph secreted from the peritonæum and the fibrin deposited from the blood. The two presented, as nearly as possible, the same colour and external aspect, but differed materially in consistence. The lymph adhered on all sides firmly to the surrounding parts, whereas the fibrin could be detached with the slightest force.

That the deposit in the vein was really fibrin, is evident from its having taken place only when the blood came in contact with the cotton wadding and the vein; from the facility with which it could be detached from the lining membrane of the vessel, which was then left of its natural appearance; and, lastly, from portions of the fibrin being continuous, and united with small coagula unchanged in colour.

It would thus appear that the blood has the power of separating from itself, independent of the intervention of a membrane, a fibro-albuminous element resembling lymph in its characters : and the observations previously made show, I think, that this is the material which lines the cavities of inflamed and obstructed veins, so long as the lining membrane remains entire. It is found sometimes in rounded masses, having more or less the shape of a coagulum of blood ; at other times it is expanded into membranous layers ; and there can be little doubt that occasionally it becomes softened, broken down, and discharged, either into the current of the circulation, or externally from the vein together with the pus from surrounding parts. An attempt to prevent the deposition of this fibrin on the internal coats of diseased veins, by bleeding and antiphlogistic remedies, must be as futile as it is unphilosophical. And even could this be accomplished, it would be at the expense of the reparative processes which are taking place. It would deprive the parts of the very means used by nature for the reparation of local disease, and for the preservation of the system.