On spontaneous gangrene from arteritis and the causes of coagulation of the blood in diseases of the blood-vessels / by Joseph Lister.

With the author's best respects

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ON

SPONTANEOUS GANGRENE FROM ARTERITIS

AND

THE CAUSES OF COAGULATION OF THE BLOOD IN DISEASES OF THE BLOOD-VESSELS.

By JOSEPH LISTER, Esq., F.R.C.S., Eng. and Edin.,
ASSISTANT-SURGEON TO THE ROYAL INFIRMARY OF EDINBURGH.

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Mr President and Gentlemen.—The case which I have the honour to bring before you this evening is one of spontaneous gangrene in a child. The patient was a girl, six years old, who, having had scarlet fever nine months previously, and afterwards suffered severely from dropsy, was seized about the middle of July last with deadly whiteness and coldness of both lower limbs up to a little above the knees. Her mother describes them as having resembled wax in appearance. She and her neighbours rubbed the legs perseveringly, and, after an hour or two, the left limb recovered its warmth and usual aspect, but the other continued in the same state for about two days, when the mother observed some pale blue discoloration between the ankle and the calf. This increased, spreading downwards to the foot; and, at the same time, undergoing various changes of tint to pink, red, and green, till, at the end of four weeks, the limb presented the appearance depicted in this sketch. [Not here reproduced.] At this time she was brought to the Royal Infirmary, and was admitted into one of the senior surgeon's wards, where, in the temporary absence of Mr Spence, she came

under my care. Her general health appeared remarkably good, considering all that she had gone through: her tongue was clean and moist, and her appetite good, and though her pulse was very quick, viz. 148, this was not to be regarded as a serious symptom in one so young, with such a source of irritation present. Accordingly, three days later, a line of demarcation having distinctly declared itself, I performed amputation immediately above the knee. Very little blood was lost in the operation, which did not accelerate the pulse or impair the appetite even for a day. Three days later, the constitution was evidently experiencing relief from the removal of the disease: the pulse was reduced to 112, and her general aspect improved. The stump healed kindly, and the result was in all respects satisfactory.

The amputated limb having been laid open on its posterior aspect, the gangrene was found to have extended somewhat higher in the deep parts than in the skin; the mortified tissues, including the posterior tibial nerve, were congested in a manner closely simulating inflammation, but of a duller tint, and exactly as far as this congestion extended, the posterior tibial venæ comites were turgid, and evidently contained coagulated blood. In the upper part of the limb the veins were flaccid and empty, and all the tissues appeared healthy, except that the popliteal artery, for an inch and a half from its lower end, was the seat of intense congestion, which also implicated slightly the cellular tissue about the vein and nerve. [These appearances were represented in a coloured drawing.] On laying open the vessels, the vein was found pervious and healthy, except that its coats seemed a little thicker than natural, but the artery was filled at the congested part with a coagulum, an inch and a quarter in length, partly pinkish and partly dark in colour. There was no appearance of any inflammatory exudation having taken place into the interior of the vessel, but the clot lay everywhere in contact with the internal coat, to which it was firmly adherent, so much so, as to tear away a portion of it when removed. Beneath the lining membrane were to be seen transverse red streaks, which appeared due to congestion of the circular coat of the vessel. [A sketch of the vessel and its contained clot was now exhibited.] The coagulum extended down the anterior tibial artery as far as to the commencement of the gangrene, but the companion veins were empty and perfectly natural in appearance, as also was the posterior tibial artery.

These pathological appearances clearly indicate that the primary disease was inflammation of the arteries, accompanied by coagulation of the blood within them, obstructing the supply of the nutrient fluid, and so inducing death of the lower part of the limb. This conclusion is in harmony with the previous history, which was from the first that of arterial obstruction.

This case is of practical interest, as illustrating the principle that spontaneous gangrene may be entirely local in its cause, and that in such cases the greatest benefit may be anticipated from removal of

the mortified part, provided the constitution be in a state fitted, as regards age and in other respects, for bearing the operation.

But my chief reason for bringing the case now before the Society is, because it appears a distinct example of inflammation of the coats of a vessel determining coagulation of the blood within it, without the exudation of lymph into its interior. Not that there is any novelty connected with such an occurrence, but because this effect of arteritis and phlebitis, long recognised by all sound pathologists, appears to be of peculiar interest at the present juncture, in connection with the recent publication of the last Astley Cooper Prize Essay, in which Dr Richardson of London propounds the theory, that the coagulation of the blood is due to the escape of a minute quantity of ammonia, which he believes holds the fibrine in solution. I propose, therefore, on the present occasion, to consider how far this new theory accounts for the phenomenon of coagulation in inflammation and other diseases of the blood-vessels.

So short a time having elapsed since the publication of the volume alluded to, it may be well to mention, as briefly as possible, the main facts by which the arguments of the author are supported:—And first I may relate the startling observation made by Dr Richardson, that if a current of air is passed through two successive portions of freshly drawn blood, contained in two Wolfe's bottles, while that in the first bottle, as might have been expected, has its coagulation accelerated, that in the second bottle is prevented from coagulating for several minutes after the time at which it would have solidified, had it been left in the vessel without interference. In other words, the air has had its properties so modified in passing through the first mass of blood, that it afterwards retards instead of promoting coagulation; whence Dr Richardson infers, that it has obtained in its passage some volatile solvent of the fibrine. Secondly, Dr Richardson has discovered that a very minute quantity of ammonia added to freshly drawn blood keeps it fluid for an indefinite period in a stoppered bottle, but that if exposed to air it coagulates as usual, though at a later period, in proportion to the amount of ammonia employed. He also finds that, by careful management, a fresh clot may be redissolved by means of ammonia, and that after the escape of the ammonia it will again coagulate, and afterwards contract in the usual manner, though more feebly. Next, he finds that ammonia is always to be obtained from the halitus of freshly drawn blood, and although the alkalinity of the blood through soda renders the ammonia excessively prone to escape, so that a good deal is necessarily lost from unavoidable exposure to air, yet he has succeeded in collecting about a third by weight of the smallest amount which he has found sufficient to keep the blood permanently fluid outside the body. Lastly, he has observed that all those circumstances which are known to promote the coagulation of blood outside the body, such as an elevated temperature, free admixture with air, a vacuum, etc., also hasten the process in blood mixed with ammonia, or, in other words,

favour the escape of the volatile alkali; while, on the other hand, those things which check coagulation, such as cold and occlusion from air, prevent or retard the evolution of the gas. To the latter class he has added the remarkable fact, that blood remains fluid for many hours under a high mercurial pressure, but coagulates when relieved from it. I confess that, although I was by no means prepossessed in favour of this theory, these facts appear to me to prove irresistibly that the cause of the fluidity of blood, after it has been drawn from the body, is a minute portion of free ammonia holding the fibrine chemically in solution, and that the coagulation of such blood is the result of the escape of the alkali. The only point on which the evidence appeared deficient was the effect of occlusion from air in tubes of dead matter, and this defect I endeavoured to supply by the experiment which I mentioned at last meeting of the Society, by which I succeeded in keeping the blood of a sheep fluid for three hours within a vulcanised Indian rubber tube, the blood coagulating in about two minutes when let out just as if freshly drawn from the veins of the animal.[1] Hence it appears to me that the medical profession is deeply indebted to Dr Richardson for his laborious and able investigations, which have, as I think, removed much mystery from this long vexed question.

But Dr Richardson aims at much more than the explanation of coagulation outside the body. He believes that the fluidity of the blood within the healthy living vessels is due simply and solely to the presence of free ammonia, which he supposes to be generated either in the systemic or pulmonary capillaries, and he denies that the walls of the arteries or veins have any effect on the blood by virtue of their vitality, or exercise any other influence upon it than that of checking

[1] This experiment was performed in the following manner:—One of the jugular veins of a sheep having been exposed, it was emptied of blood by passing the finger along it while pressure was applied by an assistant at its anterior part. The vessel was then opened at two places about three inches distant from each other, and into each opening was tied one end of a piece of vulcanised India rubber tube, a quarter of an inch in diameter, and about eighteen inches long, filled with water, to prevent the introduction of air into the circulation. The pressure was then removed from the upper part of the vein, so as to allow the blood to flow through the tube. It was now easy to ascertain, by observing the collapse of the lower part of the vein, when a part of the tube was momentarily obstructed by pressure, that the circulation was going on freely through the new channel. This having been determined, ligatures of waxed string were tied as tightly as possible round the tube, at intervals of about two inches, beginning at the end next the head and proceeding backwards, so as to avoid all tension upon the enclosed blood, which was, of course, displaced freely in the direction towards the thorax. By this means a number of portions of blood were obtained enclosed in receptacles nearly, though not absolutely impermeable to gases. The various compartments were opened at different intervals, and up to three hours some of them contained fluid blood which coagulated on exposure, whereas there was in others a considerable portion of coagulum. After four hours, coagulation was almost complete, but a slender thread of fibrine was still obtained from the fluid part in one of the divisions a few minutes after it had been let out.

the evolution of ammonia, just as would be the case were they tubes of dead matter of the same degree of permeability. And all cases of coagulation within the living body are supposed, by him, to be explicable on simple chemical principles. Here, however, I find myself quite unable to follow him. Thus, he believes that the coagulation in an aneurism is the result of the blood which is at rest in the tumour giving up its ammonia to the current which is flowing past the mouth of the sac. This theory was suggested to him by the following circumstance:—In one of the experiments of transmitting air through successive portions of blood, the longer tube in the last Wolfe's bottle was accidentally too short, so that it did not reach farther down than to about an inch from the bottom of the vessel. The result was, that while the upper part of the blood in this last bottle was retained fluid for a considerable time, that below the level to which the tube reached speedily coagulated. Dr Richardson infers that the lower portion of blood gave up its ammonia to the air which was bubbling through the upper part sufficiently charged with the alkali to retain that part in a state of fluidity. But, surely, this implies a mistake in chemistry. The lower portion of blood coagulated, I imagine, for the same reasons that it would have done had it been put in a stoppered bottle[1] after passing through the air, though probably not quite so rapidly, while the other part was prevented from coagulating by the ammoniacal vapour bubbling through it.

But if the ammonia theory fails to explain the coagulation that occurs in aneurism, still more inadequate does it appear to account for the phenomenon in arteritis or phlebitis. How can the fact that the wall of the vessel is inflamed determine, on simply chemical principles, the evolution of ammonia from the blood within it? Being convinced that in these and other cases of coagulation of the blood in local diseases of the vessels something remained quite unexplained, I have, during the last fortnight, made several experiments, with a view to throwing further light upon the subject, and will now communicate to the Society the results at which I have arrived.

In reflecting upon the matter, some circumstances in physiology and pathology appeared to me to indicate that, on the hypothesis that the blood does contain free ammonia in the living body, the healthy vessels must have a special power of preventing its escape. Thus, the blood in the capillaries of the lungs, is separated from the air in the air-cells only by an excessively thin partition of permeable living tissue; yet Dr Richardson's experiments have shown that there are times in the day, as, for instance, early morning, in which not a trace of ammonia is given off in the breath. Again, in surgical emphysema, the tissues of the body may be enormously distended with air, without any special tendency to coagulation of the blood in the vessels, such as might be anticipated unless

[1] This occurrence I have frequently observed.—J. L.

their parietes have a special power of preventing the escape of ammonia. It is true that in this case, the blood being in constant circulation, a perpetual supply of lost ammonia might be maintained from the capillaries; but it occurred to me that some information might perhaps be gained upon the point in question, by producing emphysema artificially in a limb in which the circulation had been arrested. For this purpose I applied a tourniquet firmly to one of the fore legs of a sheep, just above the elbow, and then injected air, by means of a condensing syringe, into the tissues of the lower part of the limb. The struggling of the animal, however, caused repeated displacement of the tourniquet, which I did not succeed in retaining in position for longer than an hour at a time. But, though the experiment was so far a failure, it yielded fruit in an unexpected manner. Having amputated the limb and preserved it, though with little expectation of learning anything from it, I was surprised to find, on examining it six hours later, that, although the cellular tissue about the vessels was still fully distended with air, the blood within them was perfectly fluid, and coagulated in about two and a half minutes, when shed into a saucer. Still greater was my surprise on finding next day, sixteen hours after the amputation, that the blood was still fluid in the vessels; and though it took longer to coagulate when let out from them, viz. five minutes, did so as fully as before. The muscular irritability, as tested by a powerful galvanic battery, had been found, on the previous evening, to be entirely lost. I next obtained four other feet, with the veins turgid with blood, by applying bandages firmly to the limbs below the joints where the butcher removes them, and amputating above the constricting band, after the sheep had been killed in the usual manner, by the knife. I examined veins in these limbs, day after day, till all the vessels were exhausted, and found at the end of the sixth day after their severance from all connection with the vascular and nervous centres, that the blood from a deep vein was still perfectly fluid, and coagulated when shed, though the time occupied by the process was now half an hour,—the length of the period having gradually increased, from day to day, since the time of the amputation. The feet, in the meantime, continued perfectly sweet, the coldness of the weather at the time being very favourable for the experiments. Some blood from a subcutaneous vein of the same foot, where decomposition might be expected to occur somewhat earlier, contained, at the same period (the end of the sixth day), some minute portions of coagulum. The fluid part of this blood remained liquid for an hour, but then coagulated well. Hence it was evident that so long as the tissues retained their freshness, the blood within the vessels was kept in a state of fluidity by some agency utterly inexplicable by the ammonia theory. I also found that the same thing occurs in the cat. In one such animal, killed under chloroform, by a knife passed into the great vessels of the neck, the blood in the veins of the extremities remained perfectly

fluid after forty-eight hours, and coagulated when shed. In another cat, killed by asphyxia, the same was the case as regards the posterior extremities; but the veins of the fore legs contained particles of coagulum, like the subcutaneous vessel of the sheep's foot. This difference I am inclined to attribute to the fact, that the animal made violent and protracted exertion with the fore legs during the death struggle, thus exhausting their vital energies more than those of the other limbs. After four days, however, the blood in the hind legs, though still fluid, with the exception of very minute particles of coagulum, had lost its power of coagulation. This increasing slowness and final absence of coagulation in blood long kept within the vessels, is curious, and must, I imagine, depend upon some gradual change in the properties of the fibrine.

We have seen that in two classes of the higher animals, differing from one another as widely as the carnivora and herbivora, and after modes of death so various as hæmorrhage, asphyxia, and an operation performed under chloroform, the blood remains fluid in the vessels, though perfectly at rest, for days after death. It may appear almost incredible that a fact of such fundamental importance, and at the same time so easy of demonstration, should have escaped the observation of all the eminent men who have made the coagulation of the blood a subject of special study; yet such appears to be the case. Dr Richardson speaks of occasional instances of fluidity of the blood after death, and coagulation on exposure, but considers it quite essential for such an occurrence that the vascular system should not have been opened by wound, though it is difficult to see how such a circumstance could affect the question, according to his theory, except on the supposition that the blood vessels were impermeable to gases in solution. Again, Dr Davey, in his "Researches," writes as follows:—"The blood, after death, I have often found liquid, and that many hours after death, when cold, but still retaining its power of coagulating;" but he had no idea of fluidity and coagulability lasting for days after death, or even for hours, except in rare instances. The nearest approach which I have been able to find to such an observation is contained in that inexhaustible treasury of original observation and profound reflection, the works of John Hunter, where the following passages occur:—"As a proof that blood will not coagulate in living vessels, in a perfect and natural state, and ready to act when powers were restored to it, I found that the blood of a fish, which had the actions of life stopped for three days, and was supposed to be dead, did not coagulate in the vessels, but, upon being exposed or extravasated, soon coagulated." "The blood of a lamprey-eel, which had been dead to appearance some days, was found fluid in the vessels, because the animal was not really dead: there had, however, been no motion in the blood, as the heart had ceased acting; but upon its being exposed, or extravasated into water, it soon coagulated." (*Palmer's Edition*, vol. iii., p. 32.) Hunter, however, does not

seem to have drawn any inference with regard to the higher animals from these cases. He speaks of "the very speedy coagulation of the blood which usually takes place in all the vessels after death" (vol. iii., p. 27); and though he believed that "where there is a full power of life, the vessels are capable of keeping the blood in a fluid state," he also supposed that some motion, though "very little, is required to keep up its fluidity" (ib., p. 32). Indeed, the expression, "full power of life," just quoted, is quite inconsistent with the state of a sheep's foot, six days after muscular irritability has been lost. I had myself frequently made experiments on inflammation upon the amputated limbs of frogs, and observed that the blood remains fluid for more than twenty-four hours after death; but muscular irritability, ciliary action, etc., also last in those creatures to a very much later period than in the higher animals, so that I never ventured to infer that fluidity of the blood was likely to continue long after death in mammalia.

Further observations on the feet of the sheep and limbs of the cat, proved even still more strikingly, the influence of the vessels upon their contained blood. If the skin be reflected from over a subcutaneous vein full of blood, and lightly replaced, so as to protect the subjacent parts from evaporation, without excluding the air, the vessel will be found, in two or three hours, changed from a dark venous colour to a scarlet arterial tint; yet no coagulation will occur in the blood, although the oxygen of the atmosphere has evidently penetrated freely through the coats of the vessel, showing that abundant opportunity has occurred for evolution of ammonia, provided any tendency to such an occurrence existed. Again, if such a vein be cut across with fine sharp scissors, without disturbing its connections, or inflicting much injury on its coats, the blood will be found, after about six hours, perfectly fluid in the vein, up to within perhaps 1-20th inch of the wound, where a small clot is perhaps seen, utterly insufficient to obstruct the progress of ammoniacal vapour. Hence it appears to me to follow, as a matter of demonstration, that, if free ammonia really exists in the blood within the vessels, the circumstance of its being in those vessels deprives it entirely of its volatility; and that, whether the ammonia be free in the blood or not, its chemical tendencies, such as it exhibits outside the body, are in some manner entirely modified by the vicinity of the vascular tissue. With regard to the nature of the modifying influence, no other explanation appeared to offer itself than that it depended upon residual vitality in the tissues.

In order to prosecute the investigation of the cause of coagulation in arteritis or phlebetis, I endeavoured to produce artificially, as nearly as practicable, in a living animal, the condition in which the vessels are when inflamed. Having proved, as I think I may venture to say—by investigations an account of which will shortly appear in the *Philosophical Transactions*—that inflammation consists in an impairment of the vital energies of the tissues of the part

affected, I resolved to destroy the vitality of a vein, and then permit the blood to flow through it for some time, and ascertain whether coagulation would occur in spite of the current, as it must do in phlebitis.[1] The agent which seemed best adapted for inflicting the lesion was strongest liquor ammoniæ, both on account of its rapid action, and also from the circumstance that, as Dr Richardson has shown, its chemical effect upon the blood, whether applied concentrated or diluted, is to prevent coagulation. On the 8th inst., having exposed one of the jugular veins of a sheep, and isolated it from surrounding connections for six inches of its length, carefully avoiding even momentary obstruction of the flow through it, I placed a plate of glass beneath the vein, to protect the neighbouring tissues from the action of the alkali, and at 3·13 P.M., emptied the portion of vein of its blood, by stroking the finger along it, while an assistant exerted gentle pressure on the anterior part, and then at once applied the liquor ammoniæ thoroughly, with a camel's hair brush, to all sides of the vessel throughout the length exposed. The application of ammonia occupied three quarters of a minute, and three quarters of a minute later the blood was again allowed to flow through the vessel, having been arrested altogether a minute and three quarters. A short time having been allowed for the evaporation of the ammonia, the edges of the wound were brought together with stitches. At 4.58, or an hour and three quarters later, the wound having been opened, the flow was again obstructed as before, and the vein was rapidly slit up. A small amount of dark coagulum escaped with the fluid blood. The interior of the vessel was now immediately examined. A valve with three flaps, about the middle of the opened portion, was rendered conspicuous from the fact that a black coagulum existed between each of the flaps and the wall of the vessel; and on careful observation of the lining membrane of the vein in other parts, it was seen to be dotted over in patches with fine granular deposits of pink fibrine, which could only be detached by firmly scraping with the edge of the knife, reminding me precisely of the close adhesion of the clot which occurred in the popliteal artery in the case which I related at the commencement of this paper, and which is known to be characteristic both of arteritis and phlebitis. Here it is clear that the coats of the vessel having been deprived of their vitality, the blood flowing through it assumed the same chemical tendencies as we have seen it to possess when removed from the body; and those parts of the fluid which re-

[1] Sir Astley Cooper performed experiments to show the effect of mechanical injury of the coats of a vein upon the coagulation of the blood at rest within a portion of the vessel contained between two ligatures; and he came to the general conclusion, that loss of vitality in the vessel greatly accelerated the process of coagulation. Dr Richardson alludes to these experiments, but says they have been invalidated by subsequent investigations by Scudamore. I have not as yet seen Sir Astley's own account of his researches on this subject; but, from a notice of them by Palmer, in his edition of Hunter's works, I suspect that they do not deserve to be set aside so lightly.

mained at rest under these conditions, namely, the motionless layer of liquor sanguinis next to the lining membrane, and the portions of blood in the sinuses of the valve, underwent coagulation, yielding up their ammonia through the permeable coats of the vein. And I think we need not hesitate to admit that similar occurrences take place in the early stages of arteritis and phlebitis, the coats of the vessels being in those cases not dead, but impaired in vital energy by inflammation.

A similar explanation appears to account for the early formation of coagula in the vicinity of a ligature placed upon an artery. It has been seen how utterly the usual explanation, that of the quiescence of the blood, fails to account for the phenomenon; but the fact that lymph is afterwards exuded from this part of the vessel, shows that the case is really one of limited traumatic arteritis.

But if the coagulation within inflamed vessels thus receives a solution from the results of the last mentioned experiment, still more unequivocally, at least to most of my hearers, is the coagulation in gangrene explained, such as occurred, for instance, in the case which has been described.

Again, it is well known that contused wounds bleed very little, the ends of the divided arteries becoming speedily plugged with a long coagulum. The only explanation which Sir Charles Bell could offer of this remarkable provision of nature was, that the living vessels had a special faculty of preventing the blood from exercising friction upon their lining membrane, but that the contused artery, having lost its vitality, the blood became arrested by friction, and coagulated. We now see that there was much more truth in this theory than has been generally supposed, though the loss of vitality in the vessel does not operate in the manner which Sir Charles imagined.[1]

It has been found difficult to understand why the fact of the arteries being converted into calcareous tubes should impress upon the blood within them a tendency to coagulate in atheromatous degeneration of the vessels. The impairment, or entire loss of vitality connected with such a condition, will now be found a sufficient explanation.

The coagulation in aneurism is now equally comprehensible, the walls of the sac consisting either of degenerated or torn coats of the vessel, of inflamed surrounding tissues, or of layers of fibrine, each of these constituents being in a state of very low vitality.

The rapid coagulation of lymph, which appears to be neither more nor less than the fibrine of effused liquor sanguinis, contrasts,

[1] I find I have not done justice to Sir C. Bell's views upon this subject. In his later works he expresses the opinion that the lining membrane of the living vessels possesses the power of "preserving the blood fluid," and that the cause of coagulation in a contused artery is the loss of this power in consequence of the injury.—*Vide* Sir C. Bell's *Institutes of Surgery*, vol. i., p. 52, and vol. ii., p. 277.

in a very striking manner, with the lengthened period during which blood extravasated into the cellular tissue may retain its fluidity. But the fact that the liquor sanguinis is exuded among tissues that are in a state of inflammation, and so impaired in their vital energies, renders the circumstance in question easily intelligible.

With regard to the nature of the influence exercised by the living vessels upon the blood within them, it might be conceived to be either of a positive or negative character. It might be imagined, either that the blood has a natural tendency within the vessels to comport itself as it does when outside the body, and that this tendency is counteracted by an active operation of the living tissues, or, that the vital fluid tends to no such change except when prejudicially acted on by surrounding objects, which in that case might be supposed to exert upon it attractive forces such as tend to group the molecules of dead matter together in aggregation, while the living tissues were destitute of such action, and simply neutral in their conduct towards the blood. Of these, the former has always appeared to me the more likely, *a priori*, but I had not expected to have met with any facts to give distinct evidence either in one direction or the other upon a subject so recondite. A simple observation, however, made on the sheep's foot, appears to throw clear light on the matter. I have frequently observed, that when a vein has been opened and has remained patent, the blood has continued fluid in the aperture for a very much longer time than is necessary to produce coagulation of a portion of that blood placed in a saucer. When the wound in the vein has been a narrow one, I have seen the blood remain fluid between its lips for three hours together, though perfectly at rest. I have even observed where a portion of fluid blood has been pressed from a vein into a groove in the tissues, formed by muscle below, periosteum on one side and tendon on the other, this portion of blood has remained fluid for an hour, while another drop removed into a saucer at the same time from the same vein, has coagulated in a quarter of an hour. Now, in all these cases the blood was fully exposed to the influence of the atmosphere; and if the air had been an active agent, promoting the tendency to coagulate, and the tissues merely neutral in their operation, coagulation must have occurred rapidly. On the other hand, if we admit that the tissues exert an active influence on the blood, and that air, oil, and other inorganic matter is inert with regard to it, the retarded coagulation follows naturally.[1] Here, then, it appears to me, we

[1] Since this paper was read, I have obtained further evidence which will, I trust, appear quite conclusive regarding the entirely negative influence of the atmosphere upon the blood, with respect to promoting the tendency to coagulation. Just forty-eight hours after the death of the sheep which furnished preparations exhibited to the Society, I exposed a vein of one of the feet and injected air forcibly into it, by means of a condensing syringe with a fine injection pipe adapted to it. Seven hours later I again examined the foot, and on reflecting the skin from the opposite aspect of the limb, found there a large subcutaneous vein distended with a mixture of blood and air; the latter, which

have a sure, though imperfect glimpse, of the operation of mysterious but potent forces, peculiar to the tissues of living beings, and capable of reversing the natural order of chemical affinities; forces which I suspect will never be fully comprehended by man in the present state of his existence, and the study of which should always be approached with humility and reverence.

Having thus obtained evidence of the active operation of the living tissues upon the blood, it occurred to me that the walls of the vessels might probably act to greater advantage upon their contents when of small than of large calibre, and that, in that case, the blood might be found fluid in the small vessels of the human body after death, although coagulated in the heart and large vessels. Accordingly, I have examined three human bodies with regard to this point, and in every case have found my idea confirmed. One of these was a woman, aged 70, who had been a patient under Dr Gillespie's care at the Infirmary, with senile gangrene. The right cavities of the heart were full of blood, and contained large clots buffed on their upper surface, and the large vessels also contained abundant soft coagula, but a small vein from one of the thighs yielded fluid blood, which coagulated slowly in a saucer. The body was examined about thirty-six hours after death. The other two had been patients under Dr Gairdner's care, also in the Royal Infirmary. One of these was a man about 30, who had died of meningitis. The heart had been removed before I saw the body, but the large vessels, such as the external iliac vein, contained coagula, whereas all the small veins which I observed contained perfectly fluid blood, which, however, had lost the power of coagulation. The third case was that of a young man, aged 21, who died of a complication of medical and surgical complaints, nearly forty-eight hours before the body was examined. The corneæ were perfectly clear, and there was no appearance of any incipient decomposition. This case was investigated very carefully; and as the subject is novel, it may be well to give the results in detail:— I was not present when the heart was removed, but Dr De Fabeck

had evidently passed through an anastomosing channel, being present in the form of very numerous large and small bubbles. Having secured the ends of a long piece of this vein, I dissected it out and shed its blood into a saucer. Not a particle of clot existed in the vein, and complete coagulation took place within a quarter of an hour. The vein which had been exposed, in order to inject the air, contained here and there portions of clot in the exposed part, the vitality of the vessel having doubtless been impaired by the mechanical violence to which it was subjected in the dissection, or by the drying influence of the atmosphere.

In order to illustrate the effect of mechanical violence applied to a vessel in promoting the coagulation of the blood within it, I pinched a vein of the same foot severely with dissecting forceps in about an inch of its length, at the same time that I injected the air into the other vein. On examining the foot, seven hours later, the vein which had been pinched contained coagulum in the part which had been so treated, but fluid blood in the rest of its extent, both above and below the injured portion.—J. L., 19th March 1858.

(resident physician under Dr Gairdner) informs me that the cavities contained coagula buffed on their upper surface. The vena cava, the right iliac veins (common, internal and external), and the femoral vein for about four inches down the thigh, contained soft coagula, mixed with thick dark fluid blood. The upper part of the axillary vein and the internal jugular of the same side, also contained some soft dark coagula, but the deep epigastric, the femoral vein below the part before mentioned, the internal saphena, and a smaller venous branch in the thigh, the axillary, except at the upper part, the cephalic and a subcutaneous vein of the throat, all contained fluid blood, which coagulated in about half an hour after being shed; and I noticed in the thigh that the blood from a small venous branch coagulated more quickly than that from the saphena. In the veins of the lower limb, both large and small, there were curious strings of highly elastic tawny fibrine, but these had evidently been deposited long before death. Similar threads were also present in the veins of the neck and in the aorta, external iliac and femoral arteries, which, however, contained but little blood, and no *post mortem* coagula. I did not test the coagulability of the blood in the arteries, nor in a branch of the internal iliac vein, which also contained fluid blood.

I am aware of one source of fallacy in these experiments, namely, that the abdominal viscera are subject to decomposition before the limbs; and as soon as decomposition does set in, the blood coagulates in the parts which are the seat of it; as, for example, in small veins of the intestines. This cause of error was, however, I think, guarded against in the last case;[1] and considering the almost universal occur-

[1] Through the kindness of my friend Mr John Gamgee, of the New Veterinary College, I have had the opportunity of making further observations regarding this point, upon an animal with very large blood-vessels, so soon after death as to avoid the risk of incipient decomposition. A healthy horse having been killed by pithing, at 11·30 P.M. on the 22d inst. (March 1858), I examined the body just twelve hours later, while it was still warm. The cavity of the thorax, when opened, smelt perfectly fresh. Both auricles contained large masses of coagulum, buffed on their upper surface. There were also soft dark clots in both ventricles, together with a good deal of fluid blood, which, however, scarcely coagulated at all, a considerable portion from the right ventricle yielding, after many minutes, only a minute thread of fibrin. I suspect this was chiefly serum and corpuscles, which had passed in from the auricles on relaxation of the ventricles. There was a considerable amount of firm coagulum in the aorta, and the large veins at the anterior part of the chest were loaded with firm buffed clot. A small branch beneath the pleura, where it is reflected over the pericardium, contained perfectly fluid blood, as also did a coronary vein of the heart, about as large as the saphena of the human thigh; whereas the concomitant artery, which was very large (bigger than the human femoral), had the blood a good deal coagulated. That from the coronary vein having been shed into a saucer, yielded, after some time, threads and lumps of fibrine. An intercostal vein, from beneath the pleura, as big as a crow-quill, furnished fluid blood, which coagulated. The superficial veins of both fore-legs yielded perfectly liquid blood, which began to coagulate in about four minutes, and set into a solid mass. But, just below the axillary, small portions of

rence of coagulum in the heart of the human subject twenty-four hours after death, compared with the universal absence of it in the small veins of healthy parts, so far as I have yet examined them, both in man and the lower animals, I think the fact must be admitted, that where a large mass of blood exists within a cavity of the heart or a blood-vessel, it experiences coagulation sooner than if in a small vessel of the same body. If this be admitted, it becomes a strong argument in favour of the active operation of the tissues, for the blood is more exposed to the influence of the air in a subcutaneous vein than in the heart, and the only conceivable reason for the greater persistence of fluidity in the latter than in the former, is that the influence of the tissues operates to greater advantage upon the smaller mass of blood.

Again, supposing it to be admitted that free ammonia exists within the blood vessels, maintaining the fibrine in solution, a hypothesis which, I confess, appears to me very probable,—granting the ammonia theory, I say, as far as it can possibly be granted, it is clear that no merely neutral action of the tissues could check the evolution of the alkali in the manner above described; and nothing can tend to convince us more of the potency of the vital forces than to consider what new powers must be impressed upon the chemically inert constituents of the tissues, in order to enable them securely to chain down the alkaline gas, in spite of its excessive volatility.

There is one other experiment upon the sheep's foot which I do not like to omit mentioning. Having exposed a subcutaneous vein, six hours after the death of the animal, I pressed out the blood from an inch of it, and treated the empty part with caustic ammonia, the adjacent parts being protected by olive oil. When the smell of ammonia had passed off, I let the blood return, and, two or three hours after, found that the portion which had had its vitality destroyed by the ammonia, was full of clot, while the blood in the adjacent parts of the vein was fluid, and coagulated on exposure.[1]

This, however, was not the only result of the application of the ammonia. The surrounding tissues had not been thoroughly protected from its action by the oil, and next morning all the parts on which it had acted were the seat of the most intense congestion, accompanied with exudation of glary matter into the cellular tissue; in fact, there were all the appearances of the most severe inflammation. Some of the exuded matter had trickled down on a board beneath, and had there coagulated, showing that genuine exudation

coagulum made their appearance in the vessels, which here attained a size about equal to the femoral in man; and both the axillary trunks were plugged with firm clot.

[1] Two feet of a sheep, killed six hours before the Society met, were exhibited in illustration. One of these was prepared in the manner described in the text. The portion of vein which had been treated with ammonia, contained a cylindrical coagulum, while the blood in the adjacent parts of the same vessel was fluid. The other foot was for the purpose of showing the fluidity of the blood so many hours after death. A considerable amount having been shed into a saucer in the liquid state, soon assumed the solid form.

of lymph had been the result of this *post mortem* inflammation, then, I believe, for the first time observed in one of the mammalia.[1] I cannot avoid expressing the satisfaction that it has given me to find what I had inferred from other circumstances, in my investigations on inflammation, now established as a matter of observation. I had found that the blood-corpuscles, both red and white, were perfectly free from adhesiveness within the vessels of a healthy part, but that in an inflamed region they stuck together just as they are seen to do between two plates of glass. Having thus observed that the corpuscles of the blood comport themselves in an inflamed part in the same manner as in blood drawn from the body, I inferred that the liquor sanguinis was, in all probability, similarly affected, although coagulation is not observed in the capillaries, in consequence of the movement of the blood; and I gave the same explanation of the speedy coagulation of lymph, and of the formation of clots in inflamed vessels, as has been substantiated by independent facts this evening. In the paper before alluded to, the following passage occurs :—"The non-adhesiveness of the red and white corpuscles, and the fluidity of the blood, seem to be due to one and the same mysterious and wonderful agency,—the tissues of a healthy body appearing to extend over the blood near them, a part of the same influence by which they are themselves protected from the action of chemical affinities tending to their decomposition." We now see that when an agent capable of producing inflammation acts upon a part in which the blood is at rest, coagulation of the blood does really occur in the vessels.

There is an error of observation into which Dr Richardson has unaccountably fallen, which it appears important to correct. In speaking of the coagulation of a portion of blood enclosed between two ligatures in the jugular vein of a dog or cat, he mentions the formation of a large bubble of air within the vessel, a little prior to the occurrence of coagulation. I have frequently seen the pellucid appearance he describes, but find that it is in no way connected with coagulation, but is due to the subsidence of the red corpuscles, leaving a layer of clear liquor sanguinis at the top. If two ligatures be applied, about an inch apart, upon a subcutaneous vein of one of the legs of a cat, care having been taken not to disturb the connections of the vessel, or inflict injury upon it, and the leg be suspended by the paw in the vertical position, the clear appearance will begin to show itself below the upper ligature within five minutes. If now the limb be left for several hours, the skin having been carefully replaced so as to prevent evaporation, the clear colourless upper layer will be found to occupy nearly two-thirds of the length of the portion of vein, and to be sharply defined from the black lower layer which contains all the red corpuscles. If now the upper part be

[1] Tension upon the blood in the vessels, resulting from the bandage, supplied, I imagine, the place of the force of the heart in squeezing out the liquor sanguinis through the walls of the capillaries, deprived of their usual power of retaining it.

punctured, the clear liquor sanguinis will flow out, and coagulate upon any object held to receive it.[1]

Some of the observations above described will have a bearing upon medico-legal inquiries, showing, as they do, that not only ecchymosis, which some have denied, but even inflammation may be developed *post mortem*, provided that the return of blood by the veins is in some way prevented.

There are other bearings, both upon pathology and practice, to which I cannot even allude on the present occasion; but I thought it best to place the facts at once before my professional brethren, confident that they will receive from them all the attention that they may deserve.

In conclusion, I have to express my thanks to my friend, Mr Craig, for the kind and able assistance which he has afforded me throughout this investigation, and also to my friends, Drs Gourlay and Hill, who have on several occasions lent me most valuable aid.

[1] *Post mortem* congestions simulating inflammation, are, I suspect, due to this gravitation of the red corpuscles of the still fluid blood into the vessels of dependent parts.

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