Eight letters of Joseph (Lord) Lister to William Sharpey / by C. Robert Rudolf.

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EIGHT LETTERS OF JOSEPH (LORD) LISTER TO WILLIAM SHARPEY

BY

C. ROBERT RUDOLF.

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EIGHT LETTERS OF JOSEPH (LORD) LISTER TO WILLIAM SHARPEY.

By C. R. RUDOLF.

These eight letters written by Joseph Lister to William Sharpey were recently found by me in a second-hand bookshop in London. The bookseller was unable to say where he had obtained them. The first six letters submit Lister's ideas for Sharpey's criticism before offering his views to the Royal Society. These views, being approved by Sharpey, were embodied in various physiological papers which became well known to the scientific world. They led to Lister's recognition as an accurate and careful exponent of the processes of inflammation which had long exercised the minds of such thoughtful surgeons as Travers and Paget.

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11 Rutland Gate,
Edinburgh,
16*th November* /57.

My dear Dr. Sharpey,

I have received my paper for revision prior to printing in the transactions, and along with Mr. Stokes'[1] note was enclosed a report by Mr. Paget[2] on the paper. Of this I enclose a copy in case you may not have seen it; and now venture to trouble you for your advice on some points in Mr. Paget's suggestions, seeing that you are the "communicator" to whom he refers as the person through whom his suggestions should be conveyed to me: not to mention that your past kindness throughout this business, would have emboldened me to inflict myself upon you once more, even had you not occupied the position referred to.

First I must say that I am much impressed with Mr. Paget's care and candour in the matter, and, considering the position he occupies with regard to the subject, I think his remarks exceedingly handsome, and am much gratified by them. Mr. Goodsir[3] also mentioned to me his having read the paper and endorsed it with his recommendation for publication, and he too spoke in terms, I fear, considerably flattering regarding the production. I will now speak of each of Mr. Paget's suggestions and allude at the same time to Mr. Goodsir's remarks on the same points.

First as to omitting the account of the theories of previous writers. Mr. Goodsir also said, before he knew of Mr. Paget's report, that he thought the paper would be more classical without the historical sketch; although at the same time he said he thought it "excellent", supposing it necessary. But he did not think any such thing was required for a paper for the Royal Society. I am quite willing on these grounds that this part should be

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omitted, although, for the sake of the *general* reader, I should have preferred its being retained. I shall be guided entirely by you on the point. When writing this I do not know how much discretion is left to me. Mr. Stokes says " you will probably see reason to adopt " his (Mr. Paget's) " suggestions ".

As to the second part which Mr. Paget recommends me to blot out, viz., the discussion of vital affinities, etc., in the second section, Mr. Goodsir does not appear quite to agree with Mr. Paget. The former observed, " that is the opinion of a London man ". Now, unless you have seen the paper you could hardly form a judgment without my writing at greater length than would be expedient ; but I would ask you if there would be any objection to my retaining the mention of the observation of the absolute stillness of the blood in the capillaries and veins between the pulses in small frogs under the influence of chloroform. The fact that this state of things may continue for an unlimited time without any accumulation of corpuscles occurring in the vessels appears to me important, as the heart, though exceedingly weak, is then obviously the only cause of the movement of the blood. I would very much curtail my remarks on the bearings of the observation. It is not only in Edinburgh that persons think the vital affinities a cause of the blood's movement : witness Dr. Carpenter :[4] and here the opinion is rampant that [the] said affinities are the chief cause ? As to the discussion on the mode in which the constituents of the liquor sanguinis required by the various tissues for the purpose of nutrition find their way out of the capillaries, this I confess is very hypothetical and I am quite willing to expunge it. But it is not long, and, if there be no objection, it might be printed, and then if you thought well I would strike it out of the proof.

With regard to the expression about " paralysing " the concentrating and diffusing forces of the pigment cells, I feel seriously at a loss to know how to find a different mode of conveying my meaning. The facts are simply these. In the state of health the pigment cells exhibit the functions of concentration and diffusion of the granular portion of their contents under obedience to nervous influence. Also when a healthy limb is amputated concentration of the pigment (if previously diffused) takes place to the full degree and the pigment remains concentrated for some hours, after which a certain amount of diffusion again occurs, but if certain agents be applied to a portion of the web the pigment in that part ceases to manifest these functions. Not only is this the case when the limb is in connection with the body, but also when severed from vascular and nervous connection with the trunk. If the agent be applied to part of a dark limb just amputated the post mortem concentration does not occur in that part and again if the agent be applied when post mortem concentration is at the full, the subsequent diffusion does not take place in the spot operated on. In short, these functions of the pigment cells not only cease to vary in obedience to nervous influence, but also fail to exhibit the changes that ensue sooner or later after blood has ceased to circulate through the part : of which the post mortem concentration seems comparable to the post mortem rigidity of muscles. Now since I began to write this sentence I have been troubled with a difficulty that never occurred to me before, and which, I dare say, may be what Mr. Paget feels : and reflection upon this has detained this epistle two days. When speaking of

" paralysis of the concentrating and diffusing powers ", I convey the meaning that these powers not only cease to *vary* but cease to operate at all. Now I admit that this is by no means " proved " in my paper as it stands. There is good reason, I there state, to believe that the concentrating and diffusing forces are both in constant antagonistic operation, both being equally balanced except when either diffusion or concentration is occurring. Now all that I have shewn is that in the irritated part neither diffusion nor concentration occurs, and it may therefore be fairly argued that this does not prove more than that those forces cease to *vary* in *relative* amount under nervous influence, an effect which might result from paralysis of the extremities of the nerves, while the forces in the cells remained unaffected. But the consideration of all the facts with which we are acquainted regarding these pigment cells, including some which I have observed since the paper was written, seem to me to *prove* that the *cells* are affected independently of the nerves, and that this affection is one of paralysis. Now I am truly sorry to inflict this rigmarole upon you, but do not see how I can help it ; as I do not wish to run counter to Mr. Paget's opinion, and yet should be very sorry to give up the use of the term " paralysis " unless obliged to do so. You will remember that the German observers Brücke,[5] Wittich,[6] and Harless,[7] found that in the tree frog and the esculent frog concentration of the pigment resulted from the stimulus of light, from psychical excitement, from stimulation of the spinal cord, from stimulation of a branch of nerves leading to a particular portion of skin and from other stimuli. These observations tended to shew that concentration was the condition induced under the influence of stimuli applied through the nervous system, and that diffusion was the state with which the cells passed when left undisturbed by such stimuli. I have made similar observations on the frog of this country, which, however, is not nearly so sensitive to local stimulation, and I have also added the following fact lately. If I cut through all soft parts of the middle of the thigh except the artery, vein and nerve, the circulation goes on as usual and the leg retains the same colour as the rest of the body. But if I now cut through the nerve, the legs immediately become darker (if previously pale) and in a few hours the legs become black from full diffusion of the pigment, while the rest of the body may remain pale yellow. This very curious result is not *constant*, apparently in consequence of its being impossible to divide all the nervous filaments leading from the trunk to the limb, as proved by the fact that the arteries after a longer or shorter time regain their power of contraction, which is lost permanently if the brain and cord is removed. I have however induced this strange contrast of colour in three cases in which I performed the above operation. This experiment confirms the view that diffusion is the condition which occurs when nervous influence is removed.

An experiment by Wittich on the tree frog must be mentioned as illustrative of the same principle. He found that oil of turpentine when applied to a *moderately* dark tree frog caused the spot to which it was applied to grow pale, but after the oil had been removed the part not only returned to its former colour but became darker than other parts : the secondary diffusion of the pigment appearing comparable to the secondary dilatation of arteries after contraction from stimulation. So strongly did these facts impress the

German authorities that they considered them proof positive that concentration was the result of *contraction* of a cell and diffusion a relaxation of such contractile cell. Now I have shewn as you know, that this view is incorrect, as the cells do not change in form or size, but the pigment granules undergo changes of place in the fluid contents of the cells. And I have in the last few weeks made further observations on these curious processes, which shew that they are more complex than I had supposed. I have observed a cell in which slight diffusion was going on, and saw that the granules were moving in a very complex manner: one granule would be moving from the central dark mass of pigment while another was passing towards it. Sometimes a number of granules would start off together; then stop and some of them return, etc., etc. Shewing that diffusion is the aggregate result of a complicated set of movements of granules some towards, others from the centre. Sometimes one saw a single granule start off from the central mass and return to it after a circuitous course, as shewn in the diagram [omitted], where (a) is the central black mass of concentrated pigment, and the dotted line represents the course of a granule. Such movements reminded me of what one sees sometimes within the cells of vegetables.

This description of the movements of the granules you will say is a digression from the argument, and so it is, but I wish to mention it to you, in order to let you know that I have made some further progress. But, however complex the action of concentration and diffusion be, there nevertheless remain the facts shewing that concentration is what occurs in the cells when stimulated through the medium of the nerves, and diffusion is that which takes place when the influence of the nerves is withdrawn. Hence it appears to me clear that, as an agent which induces inflammation causes the pigment cells to remain in the state in which it found them (say that of medium diffusion) however much they may vary in other parts, this effect is something more than paralysis of the extremities of the nerves could cause. Paralysis of the extremities of the nerves would [nay], *must* lead to diffusion unless the cells themselves were affected. Then I think we need have no doubt whatever that the *cells*, independently of the extremities of the nerves, are affected in such a way that they no longer act as usual in obedience to stimuli, in other words that the cells have the functions of concentration and diffusion *paralysed*.

What I should like myself, therefore, would be to retain the expression "paralysis of concentration and diffusion", but to avoid the use of the expression paralysis of the concentrating and diffusing forces, or of the attractive and repulsive forces, as that implies what is incorrect regarding the physiology of concentration and diffusion, by giving the idea that during concentration the granules are all being attracted at once towards the centre, *and* vice versa.

One more point and one only: viz., regarding the publication of my supplement on the influence of the nerves on the arteries.

Mr. Goodsir has shown me a reference to Pflüger's[8] experiments on the large esculent frog, in which he found that division of the anterior roots of the spinal nerves causes relaxation of the vessels and stimulation of the same roots with galvanism causes the arteries to contract.

These are, I suppose, the experiments to which you had intended to refer me, but which I failed to find the account of. Had I been aware of them I dare say my experiments on this subject would never have been made; so that here, as in several other matters in this investigation, I have found myself anticipated. Yet at the same time I cannot but think some of my experiments deserving of publication, and it appears Mr. Paget thinks the same, but wishes me to make my results more precise. Now Mr. Goodsir agrees with me that experiments of the kind to which Mr. Paget alludes, viz., division of one half of the cord would be almost, if not altogether impracticable in the frog of this country. But I was aware of the possibility of making further observations regarding the seat of the nervous centre and have accordingly lately made some. In my paper I gave proof that a part of the cord as far forward as midway between the head and the caudal extremity does act as [a] nervous centre for the arteries after removal of the posterior half of the cord. What I felt might be further determined, but what I had not time to inquire into before the paper was read, was whether the posterior end in [the] tip of the cord is able to act as [a] nervous centre for the arteries after removal of the brain and the rest of the cord. Now this point I have since settled in the affirmative; I have found that after removal of the brain and all the cord except the posterior *tenth* part (in length) the arteries after a while recover their contractile and varying power. Now this seems to me of importance, as it proves that the portion of the cord which Waller[9] and Budge[10] found to be the "ciliary" centre, etc., etc., the nervous centre for the dilatation of the pupil, and which they also described as the centre for the contraction of the arteries of the face, is not the *only* part of the cord which has this office, at least for the lower limb. Thus this experiment along with my former ones proves that the posterior half of the cord contains throughout its length parts which act as nervous centres for the arteries of the feet. And other experiments render it probable that the same function is possessed by a part somewhat further forward. Now I believe this is about as much as can be made out on this point from the frog. I have also several times verified lately an observation I had made before viz., that after removal of brain and cord the arteries remain *permanently* relaxed, while on the other hand the experiment I related in speaking of the pigment, viz., dividing all the soft parts visible in the thigh except the artery and vein, after which recovery of contractile power on the part of the arteries occurs if the cord is entire, shews very strikingly how very slender a nervous communication between the cord and the arteries suffices to enable the former to influence the latter.

Now I believe I am not likely ever to carry this investigation much further, nor do I believe much good could be gained by so doing, I mean in the frog of this country, and Mr. Goodsir thinks that it would be well for the results I have got to be published to avoid the chance of being anticipated. If, therefore, you approve, I would rewrite this supplement on the influence of the nerves on the arteries, introducing my additional matter, and somewhat curtailing the old experiments perhaps. But I do not think it would be necessary to alter it so much as to require it to be published as a separate paper at a later period. It might simply be stated

that some new matter had been introduced with this part, the new parts being specified.

I find that there is yet *one* point Mr. Paget suggests that the supplement in the anatomy and physiology of the pigmentary system should be published as a separate paper *before* the essay on inflammation. My chief objection to this is that the chief illustration, i.e., figure of the pigmentary affair illustrates also a part of the "essay on inflammation". Also the last section of the paper is written as if the pigment subject was to be treated of in a supplement and I should prefer its remaining as such, if it might be so. This, however, is of small moment.

When must the paper be ready for printing? I am intending to be in London at Christmas for a week, and if that time would not be too late, I should very much like to consult with you personally as to the best way of getting the illustrations drawn. I should think that for the pigment cells, which require much delicacy of execution, Tuffer West[11] would be as good a man as could be found.

My father seems to think that some of the sketches on inflammation almost require the same kind of simple *colouring* that W. Jones'[12] plates in the bats wing in the Philosophical Transactions have. Certainly the plates would tell their tale much better, and the colouring would be only a *very* simple matter, viz., red for congested capillaries, pale red for arteries and arterial capillaries, and pale purplish for veins.

I am really exceedingly ashamed of this letter. I only hope you will not quite give me up as a bore.

Agnes unites in kind regards to Miss. Colville[13] and yourself with

Yours very truly,

JOSEPH LISTER.

W. SHARPEY, Esqr., M.D., F.R.S., etc.

11, RUTLAND STREET,
EDINBURGH.
28. *Nov*: /57.

MY DEAR DR. SHARPEY,

You will be wondering what has come over me that I have not long since thanked you for and replied to your most kind and to me highly satisfactory letter. Nothing indeed could have been more welcome to me. The reason of my delay in answering it has been the pressure of my present engagements, which have hardly left me any available leisure, except at times when the mind was too much fagged for work of such importance. To proceed, then to business. I mean to act on your suggestions from first to last. The section "on the state of the tissues in inflammation" will, I believe, be very much improved by remodelling it on the plan you have suggested, viz: speaking first of the facts actually seen in the pigment cells, viz: the "arrestment" of concentration and diffusion and then discussing the question of the "paralysis". That such "paralysis" really is present can, I think, hardly be doubted when the nature of the various agents which agree in causing

the "arrestment" is considered: for, while they differ among themselves exceedingly widely, they all have the common property of tending to destroy a part of the living body if maintained long enough in action upon it. It so happens, also, that the pigmentary tissue is a very delicate one, and is very apt to experience *permanent* injury without concomitant sloughing of the rest of the web. Thus if mustard be long enough applied, I find that the pigment cells begin to lose their sharpness of definition and appear to become disorganised. Similar effects on the pigment may also be seen in parts where mechanical violence has operated severely; and after some days the pigment in such parts becomes absorbed, and when once so removed is never replaced. There is one point on which you began to speak to me one evening at Millbank, but the conversation was in some way interrupted: viz. the change the blood experiences in the irritated part when its corpuscles become adhesive. You objected to my making use of such an expression as implied that the tissues in a state of health *exercise* an *active influence* over the blood in their vicinity, keeping the corpuscles from becoming adhesive. You said I might as well say that, because a man who was in good health when in a snug room grew rheumatic if exposed to the outside air or if holes were made in the walls, *therefore* the walls of the room *exercised* an *active influence* for good upon the man. I have often thought of that criticism and admit its applicability. But, at the same time, I must contend for activity *somewhere*, either in the blood or the tissues; just as the *man* in the room is active though the *walls* are passive, so, if the tissues are merely negative in their operation in health, the blood must have a positively active power. The *facts* seem to be these. In blood withdrawn from the body, the corpuscles, both red and white, are more or less adhesive; but within the vessels of a perfectly healthy part are quite free from adhesiveness. In the vessels of a part which has been acted on by some deleterious agent, (but short of actual disorganization or chemical decomposition) the corpuscles shew the same adhesiveness as when the blood is removed from the body. But this is not all. If the agent have acted so as to produce only a temporary effect on the tissues (as e.g. a powerful galvanic shock, which only temporarily "arrests" the changes of distribution of the pigment molecules) then as the tissues recover the blood also regains its natural healthy characters: the corpuscles previously viscid and closely packed, become non-adhesive again and are driven out of the vessels in which they had accumulated. Now I say this *recovery* on the part of the blood implies something active *somewhere*. We may either suppose that the *healthy* tissues exert a purely *negative* influence on the blood, which consequently does not suffer as it does when in contact with glass or any other dead matter, which must in such case be supposed to exert a disturbing influence leading to changes in molecular arrangement probably, an influence which would seem, very likely, synonymous with the "attraction of aggregation" which leads to crystalization, etc., etc.—or else we must suppose that glass, etc., has a negative influence and the healthy tissues an active one upon the blood. (I fear I am writing obscurely.) But supposing the former hypothesis be correct, and that blood in a healthy part has its corpuscles free from adhesiveness because *not* subjected to the action of disturbing forces such as are exerted on it by glass, sweet oil, atmospheric air, or paralysed tissues; then, I say,

the fact that, as soon as the paralysed tissues recover, the corpuscles return to their original state of non-adhesiveness implies that the blood has an independent power of recovery from its injured condition, (compare the case of the rheumatic man) so soon as the tissues cease to exert the said disturbing influence common to dead matter, and resume their healthy negative condition. Now at first this seemed to me very unlikely: viz. that glass, sweet oil, the atmosphere, and paralysed tissues should be the *active* agents (for evil) and that the healthy tissues should be merely negative in their operation on the blood, but I have been inclined to look more favourably upon this view from considering the phenomena of *coagulation* of the blood. I think it quite needless to allude to the simple facts which, to my mind, prove clearly that no *chemical* theory yet given accounts for the coagulation of the blood: for I believe you are quite satisfied of the insufficiency of these theories. In some way or other the healthy tissues (which may remain healthy as *tissues* for some time after death) *do not* make the blood undergo the changes which lead to coagulation which ordinary dead matter (such as glass, air, etc., etc.) and inflamed tissues (paralysed more or less) *do* induce these changes in the blood. The principle I am stating is well illustrated by the speedy coagulation of the blood at rest in an aneurismal sac, in contact *not* with healthy tissues but with mere coagulated fibrine or inflamed tissue. The contrast presented by such a case with the length of time that blood will remain uncoagulated after extravasation among healthy tissues is very striking. Again the same thing is seen perhaps even more remarkably exemplified by the fibrinous masses that accumulate about calcareous atheromatous spicula projecting into the aorta or other large vessels, when the "dead" matter determines coagulation of fibrine notwithstanding the rapid movement of the blood (though to be sure only on the *lee* side of the projecting mass, when the blood is, I suppose, more or less quiescent). Now, such cases as these look to me very much as if the "dead" matter with its ordinary "attraction of aggregation" was the *active* agent, the healthy tissues having a merely *negative* influence on the blood. Also the bulk of the masses of blood which may remain long free from coagulation after death (e.g., that in the auricles of the heart) but which coagulate so soon as exposed to the influence of the external world, seems to me inconsistent with the idea of the tissues exerting an *active* influence on the mass of blood, and so preventing coagulation. Now, if the influence of the tissues is purely negative as regards prevention of coagulation, this is a strong argument in favour of their being also negative as regards prevention of adhesiveness of corpuscles. Hence I mean to avoid the expression to which you objected.

I am glad to learn that you have verified the observation of the intermitting flow in the tadpole's gills. I alluded to Spallanzani's[14] observation in a note to my paper [p. 221], but did not lay very great stress upon it until I should be able to learn whether there is any *recoil* observed between the pulses. Can you inform me on this point? In the case of the young frog under chloroform there is certainly no recoil, only absolute quiescence, between the pulses. The case of the tadpole's gill seemed to me to differ from the adult frog's web in this respect that, as I suppose, there is only one auricle in the young tadpole as in the fish, or at least the right auricle is not brought into action for the

gills, and therefore the ventricle has to overcome the resistance of two sets of capillaries, the branchial and systemic, when driving the blood into the aorta. Now, it seemed to me that the resiliency of the elastic aorta beyond the gills might give rise to a recoil in the branchial capillaries, in which case the observation; though it would shew abundantly the superiority of the force of the heart to any other forces that might be conceived in operation, would not *prove* that no such forces did exist as causes of movement. With regard to the adult frog with weakened heart I have some doubt whether sufficient care has been taken to discriminate between the interruptions of flow due purely to weakness of that organ and such interruptions due partly to an unhealthy state of the blood with somewhat adhesive corpuscles. For I know that, unless attention has been specially directed to the matter, a very decidedly abnormal state of the circulation as regards the excess of slowly moving corpuscles may pass unnoticed.

One point I would ask your advice about is how the section "on the influence of the nerves upon the arteries" had better appear; whether as a supplement, as it now is, or as a separate paper. Mr. Paget says it should appear "if at all, as a separate paper", and Mr. Goodsir seems to think it forms such a distinct subject that it might be well to have it separate. In this matter I will be guided entirely by you. This only I would say, that if it be a separate paper it should appear, like that in the "pigment business" and in the same volume of the transactions, and, if possible, immediately before the others, or intermediate between them. I feel, for my own part, very indifferent about this, though I quite agree now that the *pigmentary* supplement will be better as a separate paper.

And now to reply to your question as to what things cause *concentration* and what *diffusion* of the pigment. First I would observe that there is this marked difference between the occurrence of concentration and diffusion under the influence of local applications, viz., that concentration occurs not only in the spot acted on, but in a greater or less area round about: in this respect concentration agrees with the contraction of arteries which occurs *round about* a part irritated, and both are obviously *reflex* phenomena, effected through the medium of the nervous system. Diffusion on the other hand occurs, as induced by a local application, only in the precise spot on which the irritant acts, e.g., beneath a little piece of mustard put on part of the web, but not at all beyond the limits of the mustard. Hence this diffusion is clearly due in some way to direct action of the irritant upon the part of the web on which it lies, and is not a reflex phenomenon. To this statement you will say I mentioned a contradictory fact in my last letter, viz., the *secondary* diffusion that Wittich observed after applying oil of turpentine to a moderately dark frog. This *secondary* diffusion *is* doubtless a reflex phenomenon, and is comparable to the secondary relaxation of arteries that occurs round about an irritated part. But I have never witnessed this *secondary* diffusion and possibly never shall in *our* frog, whose skin is far less sensitive to direct irritation than is that of the tree frog on which Wittich operated. Thus, oil of turpentine produces no primary concentration when applied to our frog, and its only effect on the pigment is to produce "arrestment" of concentration and diffusion. So little sensitive, indeed, is our frog to direct *stimulation*,

that the only cases in which I have observed concentration to occur from such local irritation are, 1st in an area round about a part pinched, 2nd beside the edges of a freshly cut wound, 3rd partial concentration has occurred in one leg in consequence of irritation of the roots of its nerves. The general rule respecting the operation of local irritants is that they deprive the part of the power of varying the distribution of the pigment, *leaves it just as it was*, whether fully concentrated, fully diffused, or in an intermediate state. To this general rule I have hitherto met with only three exceptions, viz., mustard, croton oil, and cantharides, which *before* they produce arrestment, produce a variable degree of diffusion in the spot on which they act. The effect is not always seen, and will be best seen when the agent acts least rapidly. Thus croton oil and cantharides act *extremely* slowly (not for one or two *hours*) and you will I believe always see some diffusion with them. But with mustard it is quite a matter of uncertainty, and if you use essential oil of mustard you are sure *not* to see any diffusion. "Arrestment" (paralysis) then takes place at *once*. But whether any diffusion occur[s] or not with mustard the ultimate effect (by the time stagnation occurs) is arrestment *both of concentration and diffusion*. As to the explanation of this variable degree of diffusion produced in the first instance by mustard, I am inclined to attribute it to paralysis of the extremities of the nerves occurring before the cells are fully paralysed, and so permitting a certain amount of diffusion to occur as always appears to do in health when the nervous influence is removed. That the extremities of the nerves are paralysed by the action of mustard is proved by the fact that if I put a bit of mustard on my own finger for an hour or two the spot loses its power of sensation.

By the way can you tell me if recent discovery has thrown any light on rigor mortis? Does it appear that the extremities of the nerves are concerned in its production? I am anxious to know this, in order to comprehend if possible, the remarkable post mortem concentration of the pigment.

Do you approve of the terms *concentration* and *diffusion*? They seem to me better than some others that might be used, because they imply not merely that the molecules are aggregated or dispersed, but also that they are collected with the centre of its cell or dispersed *throughout* the ramifying branches.

Many thanks as regard the colouring of the plates. I little intended so long a scrawl. Please forgive it if possible, and believe me, with kind regards to Miss Colville,

Yours very truly,

JOSEPH LISTER.

Many thanks for your kind proposal that I should make your house my town quarters at Christmas. Agnes desires me to unite her kind remembrances with mine. J. L.

11, Rutland Street,
Edinburgh,
3rd Dec. /57.

My dear Dr. Sharpey,

Among other things contained in the lengthy production which I last sent you was a request for information regarding the causes of rigor mortis. I now write to beg you not to trouble yourself to write on that point, as I have this morning obtained the information from Meissner's Bericht.

I also want to mention to you another set of observations I have made, which, though very simple, seem to me valuable with reference to the "paralysis" questions; which is, you know, a very important one as regards the essential nature of inflammation. It occurs to me that the cilia of the frog's mouth must perhaps be affected by agents which produce the "arrestment" of the pigmentary changes. I remembered your experiments with cilia, and recollected that your results were chiefly of a negative character, but then you had employed morphia and some other narcotics which, when applied to the web, do *not* cause inflammatory changes. I turn[ed] to your article in Todd's Cyclopædia, and found my recollections were in the main correct. I therefore proceeded to try the following experiment. Having cut off a small portion of the margin of a frog's tongue and placed it on a plate of glass under the microscope with just enough water around it to allow the cilia fluid to play in, I brought a piece of lint dipped in chloroform within about an inch of the object, so that the vapour might play upon it, while my eye was kept over the microscope. Almost immediately the cilia grew languid in their action and many stopped, reminding me of the speedy arrest of the flow of blood which occurs in the web when a drop of chloroform is applied to it. I then at once removed the lint, and soon the cilia resumed their action. I repeated this experiment several times. Then I tried strong liquor ammoniæ, proceeding in the very same way, having previously found that the pungent vapour playing for a short time on the *web* causes temporary arrestment of the pigmentary changes. The result was just the same, viz., almost immediate cessation of ciliary action, but recovery, *complete* recovery, after removal of the ammonia. I got similar results, but taking a longer time to develope themselves, by placing a piece of moistened mustard on the plate *near* the bit of tongue but not in the same water. I had previously ascertained that the pungent vapour of mustard will cause the pigmentary "arrestment", and that such arrestment may be only temporary. I also tried strong acetic acid, which readily induces inflammation of the web, operating as with the chloroform, so that its vapour might act on the bit of tongue. I only made one experiment with that agent, and it happened that the cilia were *permanently* arrested, I have no doubt because I applied the acid rather incautiously. For I must mention that the only difficulty in the experiment consists in applying the agents so delicately as only to cause *temporary* arrestment of the ciliary motion. There is no difficulty in making the cilia stop, but they will not recover their function unless you proceed very cautiously. I also found that the actual cautery brought near enough and not too near to the bit of tongue made the ciliary action languid without absolutely arresting it. The only one of your results which appeared at

variance with what I should have expected was that of the ciliary action going on in water impregnated with carbonic acid, for I had found that "aerated water" which I am assured contains nothing but carbonic acid, causes arrestment of the pigmentary changes. But then it occurred to me that very probably the carbonic acid might arrest the ciliary action also if *long enough* applied, just as the pigmentary arrestment and development of inflammatory stagnation of the blood require a considerable time of the action of the carbonic acid. And so it turns out. I put four bits of mucous membrane from different parts of the mouth and œsophagus of a frog in a glass of cold water, and four corresponding bits in a bottle of aerated water, and left both for about two hours. At the end of that time I found ciliary action in every specimen from the plain water, and not a trace of such action in any of those from the aerated water, although the cilia were distinct enough. There was, however, a great disposition to desquamation of the epithelium cells in the latter (from the carbonic acid water). I have since repeated this experiment on another frog with the same result. So far then, as I have tried, any agent that causes pigmentary arrestment when applied to the web causes also ciliary arrestment, and that not destruction of tissue, but suspension of function. Now there can, I conceive, be no doubt that the cilia, or the cells which bear them, are truly *paralysed* in these experiments, i.e., unable for the time being to act, and it is also *perfectly* clear that the effect is independent of nervous or any other influence from the rest of the body of the creature, for, as everyone knows, and as I saw abundantly in these experiments, the cilia continued to act after cells have been separated from the mucous membrane, *unless* you act upon them with one of these deleterious agents. The effect then is clearly a *direct* effect of the irritant on this form of extra vascular tissue. Do you not think that these simple experiments very much serve as experimenta crucis as regards the *nature* of the arrestment which irritants produce on the tissues, viz., that they paralyse. You see they do not in any way clash with yours, but it so happens that my former observations led me to try a set of agents which you had not employed. I see you found aether arrest the ciliary action; and I do not doubt it would excite inflammation if applied to the web. Hoping you will excuse me for thus trespassing again on your attention, I remain, with kind regards to Miss Colville, in which Agnes[15] unites,

Yours very truly,

JOSEPH LISTER.

W. SHARPEY, Esqr., M.D., F.R.S., etc., etc.

11, RUTLAND STREET,
EDINBURGH,
28th June /58.

MY DEAR DR. SHARPEY,

I heard the other day from Mr. Stokes to whom you forwarded my last to you, and his reply was in all respects quite satisfactory. Many thanks to you for procuring me the information it contained.

And now I must needs trouble you with another question: viz., whether a paper written now could have its abstract appear in the next number of the "Proceedings". I remember noticing in the number which contained the abstract of my inflammation paper that abstracts were given of some papers received after the Royal Society had ceased to meet for the season, some indeed as late as August.

I have been lately making some experiments in the so-called "hemmungs nervous system", a subject in which I have felt much interest from its connection with the origin of inflammation through the medium of the nervous system, as when the lungs inflame through long continued coldness of the surface of the chest. Some of my experiments with tepid water on the frog's foot had shewn that in the case of the *arteries*, relaxation of the muscular fibres in consequence of the application of an irritant to the skin is the result of the nervous centre (the spinal cord or those parts of it which preside over the arterial contractions) being thrown into a state of inaction. The very same stimulus whose *mild* action led to *action* of the nervous centre (with consequent contraction of the vessels) produced inaction of the same nervous centre when applied in a more intense degree. This was *proved* by the fact that the dilatation which occurs after contraction as the results of the application of tepid water of pretty low temperature gives place to contraction on re-application of water of the same temperature. Now—if the secondary dilatation was the result of any *action* of the nervous apparatus in consequence of the stimulus that dilatation would have been increased, instead of giving place to contraction, in repetition of the same stimulus. It is therefore clear that this secondary dilatation is the result of inaction of the nervous apparatus concerned. But it is quite impossible to draw the line between the dilatation which succeeds to contraction in consequence of a mild irritant, and that dilatation which occurs immediately, or, if you choose to assume it, after a "momentary contraction," after a stronger irritant, or the same irritant more strongly applied. Hence these experiments with tepid water lead to the remarkable conclusion that—given an afferent nerve, a nervous centre, and a motor nerve presiding over the contraction of unstriped muscular fibres—a very mild stimulus applied to the afferent nerve may (e.g., in the case of the arteries) lead to *action* of the nervous centre followed by muscular contraction, but a somewhat stronger stimulus applied to the afferent nerve may cause *inaction* of the nervous centre, and consequent muscular relaxation.

Having got this analogy to proceed upon I could hardly doubt that the same thing occurred in the so-called "hemmung system", viz., that if a mild enough stimulus were applied to the nerves, the contractions of the intestines and action of the heart would be increased instead of arrested. In order to put my ideas to the proof of experiment, I employed a coil battery, acting so feebly as to be only just appreciable to the tongue placed between its poles, and I have found the result such as I anticipated.

1st, as regard the intestines. I found the best mode of proceeding was to remove the skin and two layers of muscles from the abdomen of a rabbit, leaving the peritoneum and one layer of muscles, which are quite transparent enough to enable you to see any movements of the intestines, without the complication that the action of the air upon them involves. I found that

when a coil battery with its poles attached to the 6th and 12th dorsal spinous processes was put in action in the excessively mild manner I have mentioned, the writhing movement of the intestines became invariably greatly aggravated as long as the galvanic currents were acting on the cord, but as soon as the circuit was broken the former condition returned. But I also found that if the rods of soft wire were put into the helix, the "hemmung" action came into play and the intestines became relaxed and motionless: yet the action of the battery was very feeble, not even *unpleasant* to the tongue, when the rods were in. I also found that mechanical irritation of the spinal cord with a fine needle in the "dorsal region" (the same kind of irritation which I had always seen followed by contraction of the frog's arteries) produced increased contractions of the intestines. This I find from a paper to which Mr. Goodsir has referred me in Henle and Pfeufer's Zeitschrift for last year, has been observed also by a German, Spiegelberg[16] of Göttingen; and his observations are particularly satisfactory as they were only incidental to the subject of his enquiry, viz., the movements of the uterus, and made before he heard of Pflüger's "hemmung" experiment.

I have also found, and this is so far as I know a new observation, that the increased peristaltic action which comes on after death in consequence of the cessation of circulation, stops when the "hemmung" action of the battery is set on. If you wait many minutes after death you will not see this, as the spinal cord soon loses its vital powers. But an experiment of the same kind may be repeated almost as often as you please in the following way. Tie with a fine needle and thread two or three principal arteries in the mesentery leading to about four inches of the intestine of a rabbit (the intestine lying upon a plate covered with fresh olive oil) and very speedily the movements, analogous to the post mortem movements, occur in this part and nowhere else. Then set on the strong action of the battery, whose poles have been previously attached to the spinous processes, and immediately the movement ceases. This experiment may be several times repeated. Of course it is necessary to tie the little arteries very delicately so as to avoid as much as possible the little nervous filaments. This experiment is of double significance; first it proves very clearly that the increased peristaltic action that ensues on death is due simply to arrest of circulation in the part, for the "hemmung," on action of the battery, proves that the nerves have not been injured and therefore that the increased peristaltic action was not the result of injury of the nerves. 2nd, it proves that the arrest of the circulation does not *necessarily* produce peristaltic action, but that this post mortem peristaltic action, like that which occurs during life, requires that the nervous apparatus *in* the intestines should be in working order. I say the nervous apparatus *in* the intestine, for it is of course well known that the post mortem peristaltic action goes on after the mesentery has been cut off close to the gut. The existence of such a nervous apparatus distinct from the contractility of the muscular fibres is quite evident from the observation of Pflüger, which I have confirmed, that during the "hemmung" which results from powerful galvanic action through the cord, the intestines contract *at* any part irritated, though the movement does not extend to other parts; the muscular contractility is unaffected although the co-ordinating apparatus is thrown

out of action. I have added further proof of the distinctness of these two functions, muscular contractility and co-ordination of movement, in the observation that the faculty of contracting *locally* on irritation remains in the intestines of a dead animal for some time after the power of peristaltic action has ceased: the nervous apparatus dying before the muscular. Mr. Goodsir has, since these observations were made, pointed out to me Meissner's[17] discovery of ganglia in the submucous tissue of the intestines, recorded in the last part of the former series of Henle and Pfeufer's Zeitschrift (1857); shewing the mechanism by which, no doubt, this co-ordination is effected.

Again I have shewn that the ordinary peristaltic action which occurs during the life of the animal is affected by the apparatus within the intestine: for if you cut in the mesentery the fine nervous branches leading to a certain portion, say three inches, of the intestine, taking care not to injure the blood-vessels you find that the peristaltic action goes on as in adjoining parts quite unaffected by the operation, whereas, if the peristaltic action was produced through the influence of the solar plexus or other nervous centres distant from the intestine, it should cease when the nerves in the mesentery are divided. Then, to prove that the nerves leading to the piece of intestine have been thoroughly divided, you have only to set on the strong galvanic action through the cord, when you see perfect rest and relaxation of all parts except that to which the nerves have been cut, and that continues to move just as before. This is a very striking experiment, and further proves that the nerves leading from the cord to the intestine must be in a state of *action* as far as the intestine in order to produce the "hemmung". From these and other observations with which I need not bore you at present, it follows quite clearly that the "hemmung" of the movement of the intestines is produced by the action of the nerves leading to the intestines upon the nervous centres contained in the gut, but that this is not the only effect of the action of these nerves, a milder action of the same nerves increasing instead of preventing the action of the co-ordinating nervous apparatus of the intestine.

Next as regards the heart, I find that if after dissecting the vagus of one side from surrounding connections without injuring it by pinching or otherwise, and isolating it by a bit of glass placed between it and surrounding tissues, you apply to it the poles of the coil battery tipped with fine silver wire, the battery acting so feebly as scarcely to be appreciable to the tip of your tongue, the beats of the heart are increased in frequency instead of diminished, but that if the rods of the soft wire are put into the helix the action of the heart becomes diminished in frequency, gets irregular and at length stops. This shews, as in the case of the intestines, how very gentle a stimulus must be used in order to produce *increase* of action of the ganglia presiding over the action of the viscus. This, however, is quite consistent with the great effect produced by slight stimuli in many other cases: e.g., when a touch of the skin at one point induces horripilation over a large extent of surface. But had I not been led to do so by the analogy of the arteries, before alluded to, I should probably never have dreamed of using a battery so excessively feeble in action. I see that here too I have been anticipated; for Spiegelberg alludes to experiments by Schiff[18] recorded in Vierordt's archives (which I have not been able to get) by which he is said to have shewn that a

gentle stimulus applied to the vagus promotes, instead of arresting the action of the heart.

One experiment mentioned by Pflüger in his book on the "hemmung nerven system" (1857) seemed strongly in favour of a constantly operating controlling action on the part of the vagus over the heart's contractions; viz., That division of the vagi increased the frequency of the heart's beats: even doubled their frequency. At the same time it is said that this has not been seen in *frogs*, only in mammalia. On this subject I made the following experiment. The abdomen of a rabbit having been for ¾ of an hour open and the intestines out upon a plate covered with sweet oil, the beats of the heart not having been as yet at all affected as far as I could judge, but being about 42 in 10 seconds, I exposed both vagi in the neck, taking care not to pinch them, but isolating them so thoroughly from the sympathetic that I could at any time divide them with facility without injury to surrounding parts. Having thus counted the pulsations in a coiling artery of the mesentery and found them 42, I rapidly divided both vagi in the neck, each with a momentary act with a pair of fine scissors, and about a minute and a half after the operation, found the beats 40 in ten seconds. A minute or two later the beats were 38, and so on, the pulsations gradually diminishing till ¾ of an hour after the operation they were 28. When they had fallen to 32 I pinched one vagus with forceps, and within about a minute of the commencement of the pinching, and while the irritation was still continued, the pulsations were again 40 in the 10 seconds. Similar results followed from the irritation on subsequent trials, but in a less marked degree. Finally after the chest had been opened and respiration had ceased, I found that the same irritation which had before increased the heart's action, viz., pinching the vagus, diminished the number of beats: the ganglia of the heart being, I suppose, so feeble as to be thrown into diminished action by the same stimulus which had previously induced them to act more.

In this experiment the fallacies which may arise from opening the chest were avoided, and it proves of itself quite conclusively that there is not *always* in operation a controlling action of the vagus over the heart's action. On the other hand I have observed in the case of the intestines that *invariably* during a prolonged struggle of the animal the peristaltic actions cease; which seems to show that natural and normal actions of the nervous system *may* induce the "hemmung".

If you can find time to set my mind at rest as to whether I shall prepare this paper for the Royal Society or do it in a shabby way for the *Lancet* you would do me a very great kindness. Of course in a case of this kind, where so many persons are working at the subject, it would be very desirable to have a notice of this paper early: and the proceedings of the Royal Society would of course be the best medium.

I need scarcely say that if the paper does go to the Royal Society, what would please me best of all would be for it to be thought worthy of a place in the Transactions as well as the Proceedings.

Agnes joins in kind regards to Miss Colville and yourself with

Yours very truly,

Joseph Lister.

William Sharpey, Esq., M.D., Sec. R.S., etc.

11, Rutland Street,
Edinburgh,
7th July /58.

My dear Dr. Sharpey,

I fear my last letter to you must have arrived at a time when you were very much occupied, or else that you were very sceptical as to the trustworthiness of my observations. I suspect that the latter was the truth; for I admit that, considering the difficulty of the subject, and the variety of statement by different observers hitherto, anyone who goes to work at the "hemmungs nervous system" with a preconceived idea to support may be justly suspected of being unconsciously influenced, like the table turners, by his prejudice, and made to see things as he wishes rather than as they are. But I have endeavoured to bear fully in mind this tendency of the human mind, both in this and many previous observations, and, I trust guarded against it. Since I wrote to you I have made some additional experiments, two of which I will mention, for the sake of making you give some credence to those which I before related.

(1) It has been stated that division of the vagi produces in mammalia increased action of the heart. This, if true, would be strongly in favour of a constantly operating controlling action on the part of the vagus. I found it stated in Pflüger's book, however, that this effect had not been observed in frogs: and this seemed to me to throw doubt upon the alleged fact in mammalia. Accordingly I tested it by experiment. In 4 rabbits and a calf I have divided both vagi; I need not mention the details of the precautions used to avoid fallacy but may simply state, that in no single case was increase of the number of beats the result of division either of one or both nerves. Hence, even on the unlikely supposition that these were exceptional cases, these facts prove that there is not any *constant* controlling, i.e., checking influence exercised by the vagus over the heart's action.

(2) I had observed accidentally in one case in which I had been experimenting on the intestines after Pflüger's method (the poles of the battery being fixed to the 12th and 6th dorsal vertebræ) the vagi also having been both divided, the heart's action having grown very feeble was greatly improved by the application of galvanism to the cord. This shewed that the spinal system could influence the heart's action *otherwise* than through the vagi; and the same thing was proved by the frequently observed increase of the heart's action when the animal struggled, in cases where both vagi had been divided. Now it occurred to me that, if my view were correct, viz., that the nervous centres in the heart, intestines, uterus and probably other internal organs, were liable to "hemmung" from a little increase of action of the nerves (leading from the cord) whose *mild* action made these nervous centres more active; then the same kind of effects ought to follow from the irritation of other nerves proceeding from the cord to the heart as from irritation of the vagus; viz., increase of action with excessively mild stimuli, and "hemmung" with stronger stimuli. To test this I fixed the silver wire poles of my battery, one to the 6th dorsal spinous process, and the other to about

the 2nd or 3rd *cervical* spinous process, so as to transmit the currents through that part of the cord which sends off branches, through the sympathetic, to the cardiac plexus. I then found that when the action of the battery was the feeblest that I could recognize with the tip of my tongue placed between the fine silver wire poles, the heart's beats were increased by the galvanism so long as it continued in operation the number of beats in 10 seconds being raised 2 or 3, time after time, but after the circuit was broken and the action of the galvanism discontinued, the heart's beats fell to 5 or 6 beats below what they were before the galvanism was employed, and then after about 2 minutes regained their former number, e.g., in one case the beats were 37 or 38 before the galvanism was applied, 40 to 42 during the minute or two that the galvanism acted, then after it had ceased fell gradually but rapidly to 33, and then rose again to 37. These effects were observed time after time without exception; the increase in the beats during the galvanism being most marked at the commencement of the experiments, but the fall immediately after the cessation of the currents being as constant as it was striking. I could not but wonder that a degree of action of the battery so very faint should produce such effects. Then, when the rods of soft wire were put into the helix, or a little more acid into the jar, the action of the battery being still quite mild as felt by the tongue, the effect of connecting the circuit was to produce "hemmung", i.e., depression of the number of beats by about half a dozen *during* the action of the galvanism, and this time after time. I have experimented on two rabbits in this way, and in both found the results clear and satisfactory for a long time (about 2 hours), after which the galvanism failed to produce either increase or diminution of action of the heart; whether it was applied feebly as before or so powerfully as to elicit sparks from the parts of the tissues touched by the poles. It was quite evident that at these times the nerves concerned in conducting the stimuli to the cardiac ganglia were exhausted: and anyone repeating such experiments must be very careful not to use a strong action of the battery at first, or the exhaustion may occur very speedily, and then no effects upon the heart will shew themselves. I should mention that the counting of the beats of the heart with precision was greatly facilitated in my last experiment (done yesterday) by removing a portion of skin and pectoral muscle from the præcordial region of a half-grown rabbit, when the heart's action could be seen with the utmost ease through the transparent intercostal muscles and pericardium.

So this experiment confirms the general doctrine of the liability to diminished action of the part of the nervous centres seated in the viscera, in consequence of increase of the action of the nerves leading from the cord to them: and further shews how extremely delicate must be the stimulus applied to the cord or the nerves in order that the *increased* action of the nervous centres aforesaid may be developed. Also it shews how liable the nerves leading from the cord to these nervous centres are to lose their function in consequence of long continuance or excess of the stimulation. I expect to be in London at the end of this month, and, if you thought fit, would bring with me an abstract of a paper on this subject: for I really think I have now got facts enough to warrant me in publishing. If you do not approve of this

plan, I would send a paper on the subject to the *Edinburgh Medical Journal* for next month. The paper would have to be differently got up according to the medium in which it was to appear, so there seems no time to lose. May I then ask the favour of an early reply.

Yours very truly,

JOSEPH LISTER.

WM. SHARPEY, Esq., M.D., Sec. R.S.

11, RUTLAND STREET,

EDINBURGH,

28th Nov. /58.

MY DEAR DR. SHARPEY,

I am much obliged to you for the information conveyed in your kind note received this morning. I dare say my third (and last) paper might have been at the printer's before now, had not a recent letter from Tuffer West made me give up hope of getting it into the next part of the Transactions. Now, however, you may be sure, I will not waste a minute, for I am very desirous to get the job off my hands. Half the last paper is already fit for the press, and I will send it at once, and get the rest done in a few days.

One advantage this delay has had; viz., it has shewn that I was wrong, and you were right after all about the matter of the coagulation of the blood. Your view was that the reason of coagulation on removal from the vessels or on injury or disease of the vessels was a difference of *surface* in the surrounding objects. Mine had been that surrounding objects were neutral as regards the blood, but that the tissues of the vessels were active in preventing any tendency to escape of ammonia, etc., etc. My reason for this view was that I found that air freely admitted into the vessels along with the blood had no effect in causing coagulation. Hence, as exposure to air has been supposed by so many physiologists to have great effect in causing coagulation, I rashly inferred that because the atmosphere was neutral in its effect on blood within the vessels, therefore *all* dead matter was so, *solid* as well as gaseous. But by some recent simple experiments upon sheep's feet I have found that if a piece of fine silver wire, wax, hair, glass, etc., etc., be introduced into a vein, the fibrine deposits upon the solid and, if the mass be considerable, the clot may be large; although mere surrounding of a vein without introducing any extraneous solid does not cause coagulation except in the mouth of the wounded vessel. From these and other facts, which I must not detain you now with detailing, it seems to follow that the lining membrane of the vessels (and probably other tissues also) differs from any ordinary solid substances I have yet tried in being *neutral* as regards the tendency to cause deposition of the fibrine from solution, while silver, wax, etc., and the tissues themselves when diseased, attract the fibrine or in some way determine its precipitation, probably as a crystal does a solid in solution. Outside the body it appears that a certain small amount of ammonia is

necessary to keep the blood fluid, but within the vessels the ammonia seems not at all essential to the maintenance of the fibrine in solution. For it is easy to prove that most of the ammonia, if not all of it, escapes from the blood in the vessels of an amputated sheep's foot, when the foot has been kept a few hours or when a vein has been wounded. Under these circumstances the blood let out from a vessel coagulates immediately, so that I have seen evidence of the commencement of the process within 5 seconds of the shedding of the blood. This rapid coagulation must I imagine be attributed to escape of ammonia ; yet if the blood thus devoid of ammonia or nearly so be left in the wounded vessels it will remain fluid for any length of time, hours or days.

I have been induced to write you a much longer account of this matter than I intended, but I hope you will excuse this. Mr. Syme has returned safe and sound, and apparently well pleased with the results of the council meeting. He gives a good account of your health.

Agnes unites in kind regards to Miss Colville and yourself with

Yours very sincerely,

Joseph Lister.

Excuse great haste.

Willm. Sharpey, Esqr., M.D., Sec. R.S., etc.

11, Rutland Street,
Edinburgh,
26 *Oct.* /59.

My dear Dr. Sharpey,

Agnes wrote to you the day before yesterday enclosing my testimonials, and mentioning, I believe, the circumstances which induced me to send in my application to the Home Office. Of that application I received an acknowledgement from a clerk on Sir G. C. Lewis'[19] behalf; and I also know that the Lord Advocate has received his copy of the testimonials: so that I am now fairly in the field. And yet it seems again quite uncertain whether Lawrie has really resigned: at all events, if he has, neither the Glasgow Professors nor the Lord Advocate know anything of the matter. And yet I am well satisfied that I have sent in my application. Benjamin Bell,[20] who is kindly interested on my behalf, has seen the Lord Advocate, who told him that when he was in London (some months ago) Fergusson had pressed him very hard regarding Edwards, but he seemed anxious to have a further conversation with Mr. Bell, and also agreed to act on his suggestion that he (the Lord Advocate) should also refer to Allen Thomson and Douglas Maclagan. The latter is now fully on my side, Spence having retired from the field, and has great influence with Moncreiff, and, withal, is President of the College of Surgeons this year. Benjamin Bell says the Lord Advocate seemed quite open to conviction, and promised to read my testimonials carefully. So things look pretty favorable in that quarter.

Also Sir James Clark[21] called on Mr. Syme to-day, and had a conversation with him on the Glasgow business, and seems quite clear as to the superiority of my claims. I mentioned to Sir James (when I saw him for a minute or two) that I had stated in my letter of application to the Home Secretary that Sir James was willing to act as referee; and he quite approved. Whether or not he may be referred to is, however, quite uncertain, and I rather expect, from Sir James saying that "it would come best in that way", that he will not address the Home Secretary unless he be applied to. I have sent copies of the testimonials to the Glasgow Members of Parliament and also to the Professors, but beyond this I am keeping pretty quiet till the vacancy is distinctly declared. I have gone on talking about my own affairs in a way that would be hardly pardonable did I not know that you are interested in it.

And now my sheet being full, I had better conclude, remaining with kind regards from Agnes to you,

Yours ever most sincerely,

Joseph Lister.

W. Sharpey, M.D., Sec. R.S.

2, Rutland Street,
Edinburgh,
27th March /64.

My dear Dr. Sharpey,

Happening to be here at the time your letter to Mr. Syme arrived, I had the great pleasure of learning that you were the author of the remarks on Medical Education in this week's *Lancet*, and therefore that you approve of the plan of substituting class examinations for final examinations of degrees and licences in the Scotch schools. In Glasgow the Medical Faculty have unanimously agreed to adopt this principle, and the Senators at their last meeting acquiesced in the proposal. So we shall begin to work the new system this session, and I am sure it will prove an *immense* boon to the better class of our students. It will both act as a powerful incentive to work at each subject earnestly while they are engaged in it, and also leave their minds free to engage in the work by taking off from their shoulders the heavy load of the "cramming system". I was at one time afraid that the Assessors would have more work thrown upon them than they could accomplish; but it occurred to me that all that would be necessary would be for each Professor, when he has himself ascertained which of his students have exhibited sufficient attainment, to shew to an Assessor the written answers of these good students only. These will probably not be more than about a quarter or a third of the class, if so many, and thus the Assessor's labour will be greatly lightened. We are accordingly intending to act in this way: and it is a very fortunate thing that, thanks to the advice you gave me (which advice as coming from you was I believe a main means of enabling me to introduce the thing) we in Glasgow have for the last three years given our students class certificates of four different orders of merit. All that will be necessary will therefore be for the Assessors to look over the answers of those whom we think deserving of first and second class certificates, and then it will come to be understood that the receipt of such a certificate by a student exempts him from further examination. I believe that this system will so lighten the students' labour that any reduction of the curriculum will be quite unnecessary. For example, take even Botany. I think it will be anything but a disadvantage to a man to attend a course of Botany in the summer session of his first year, acquiring practical knowledge of plants by the excursions, etc., and learning habits of observation; *provided* that at the end of this course he can feel that the subject need not trouble him further. I concur most cordially in what you say about the essential thing being to get a man to work *really well* at a subject *once*.

The appointment of the Assessors was also a most happy thing for us. Without them we could not have worked this new plan of examination: which in truth will exercise a scarcely less beneficial effect upon the examiners than upon the students. For some of our Professors, I am sorry to say, did the examining duty in a very imperfect slovenly way, so that a student who only deserved a 4th class certificate might get a 1st and vice versa; which not only caused dissatisfaction in times past, but would have proved fatal to the proper working of the new system. Now, however, the Professors will take very good care that they do not send up to the Assessors answers from their

students of which they ought to be ashamed. And indirectly a good effect will also be produced upon our teaching, for it will not do for us to give hobbies too prominent a place or omit other matters of essential moment. I cannot tell you the happiness I feel in looking forward to this plan. I have been deeply impressed with the evil of having the student's mind occupied merely with a sort of unhealthy stuffing of the memory, to the utter neglect, if not destruction of the judgment, which is, I think, the most important faculty for a medical man. I think in Glasgow there has been a peculiar tendency to this: the very diligence of the students seeming often almost mischievous, from the slavish way in which they learnt what they were taught. And yet the poor fellows had no leisure for anything else.

With regard to the practical examination I must say I do not quite agree with you. As to anatomy there is no question of the immense advantage any more than of the practicability of the mode of examining, and Mr. Syme too is far from objecting to it there. But the case of Medicine and Surgery is altogether different. Letting alone the question of the propriety of using patients for the purposes of examination and (especially at a large school such as ours, where we expect 60 candidates to come before us at once on the next occasion) the practical difficulties in the way of carrying out the thing, the grand objection seems to me to be that you *cannot* expect students to be *practitioners* as they are *anatomists*. The best proof of this is that both in Edinburgh and Glasgow it is our *graduates*, and the very best among them, who take the offices of Residents in the Infirmary for the very purpose of doing that with reference to practical Medicine and Surgery which the student in the dissecting room does with reference to practical Anatomy. To be able to diagnose a case and decide at once upon the treatment requires a very high degree of practical attainment. I know for my own part, it was more by good luck than anything else that I was able to make anything like a decent appearance at the practical examination for M.B. at the London University. I never acquired anything *approaching* the sort of style that this examination professes to test till I came to be Dr. Walshe's assistant *after* my graduation. It may be said that it is very desirable to do anything you can to encourage practical work at the cases. But I believe that if the student is relieved from the labour of cramming and at liberty to look at his studies in some other light than merely as means for getting him through his examination, he will see the obvious importance of hospital work, and regard the clinical information he gains as having its own sufficient reward: being in fact the principle stock in trade for his future practice. Thus I confidently expect that under our new system hospital study will flourish with a healthy vigour far superior to that which could be fostered by any Clinical examinations: and I only wish I could clearly see a way in which the same system could be introduced in London.

I did not expect to have troubled you with so lengthy an epistle, which I only hope you will not think presumptuous, but believe that I remain as ever,

Yours with the greatest respect and gratitude,

Joseph Lister.

W. Sharpey, Esqr., M.D., Sec. R.S.

THE REPORTS OF THE TWO REFEREES (SIR) JAMES PAGET AND JOHN GOODSIR IN THE POSSESSION OF THE ROYAL SOCIETY.

Report on Mr. Lister's Paper on the Early Stages of Inflammation.

This communication consists of an introduction, four sections and two supplements, each of which requires separate notice.

The introduction contains some observations on the early phenomena of inflammation, intended chiefly to prove their similarity in warm and in cold-blooded animals: and an account of the theories of previous writers respecting the stagnation of blood in an inflamed part. Some of the observations, though simple, are I believe novel as well as instructive and should be published. The account of the theories may safely be omitted (pp. 6–10).

The first section "On the aggregation of the Corpuscles of the Blood" seems to me all worthy of publication.

The second "On the Structure and Function of the Blood-vessels" would be improved, I think, by the omission of all the discussion of vital affinities, etc., contained in pp. 22–25. The author appears to have laboured under the influence of recent discussions in Edinburgh, which, in both this and other parts of the paper has led him to give unnecessary extent to comparatively trivial and uncertain things. The rest of this section is valuable and necessary to the understanding of the parts following it.

The third section "on the effects of irritants upon the circulation" deserves publication entirely.

The experiments are simple and instructive—they confirm, with more evidence than has yet been published, the view that the stagnation of blood in the living vessels is not dependent on changes of size of the vessels, but, probably in molecular or vital changes in their walls, or in the tissues external to them.

The fourth section is the most valuable of all—the observations on the pigment cells of the frog's web give the best or only visible proof yet discovered, that in the early stages of inflammation in vascular parts, the tissues external to the blood-vessels are independently and even primarily affected by the stimulus applied. The whole of this section should, I think, be published, but I would suggest that the expressions about "paralysing" the attractive and repulsive, or the concentrating and diffusing, forces in the pigment cells imply much more than is proved and might be advantageously changed.

The concluding remarks, pp. 63–68, which seem to have been written under the influence already referred to, may be safely omitted.

Of the two supplements, the first, "On the influence of the nervous system on the arteries" should be published, if at all as a separate paper. And I should certainly recommend it for publication, but that I think the author could much increase the value, by increasing the precision of his results, if he would continue and extend his observations—. At present he has not attained to much more than the proof that the lower part of the spinal cord in the frog exercises an influence on the blood-vessels in the hind

feet similar to that proved by M. Brown-Sequard and others for the spinal cords of mammalia—. It would be interesting to imitate M. Brown-Sequard's experiments on sections of one lateral half of the cord, and to contrast the states of the vessels in the two webs: and by this and other experiments, I think, the author would discover more precisely than he has yet done, the seat of the nervous centre of the blood vessels. I would suggest, therefore, that instead of publishing this supplement in the Transactions, the communicator of the paper should be requested to recommend the author to extend this part of his enquiries.

The second supplement "On the Pigmentary System of the Frog" should, I think, be published entire, and as a separate paper, preceding the essay on inflammation.

JAMES PAGET.

July 30, 1857.

"Mr. Paget's Report on Mr. Lister's Paper"
July 30, 1857.

THE COMMITTEE OF PAPERS, ROYAL SOCIETY.

GENTLEMEN,

Having been requested by you to give my opinion regarding the eligibility of Mr. Lister's "Paper on the Early Stages of Inflammation" for publication in the Philosophical Transactions, I beg to state that while this paper contains observations and results, which, if verified, will have an important influence on the progress of the subject of which it treats, it would at the same time, in my opinion, as a paper on a pathological subject, be more suitable for the Philosophical Transactions if it had been more condensed, especially in the 'Introduction' and 'Concluding Remarks'.

I am, Gentlemen,

Your obed servt,

JOHN GOODSIR.

University of Edinburgh.
Oct. 4th, 1857.

COMMENTARY.

From the time that Lister as a medical student came under the influence of William Sharpey—the first Professor of Physiology at University College—he became his devoted friend and admirer. Under his tutelage was initiated a love of research that was to lead him from his early inquiries in microscopical science and the processes of inflammation to the culminating labours of his antiseptic treatment. It is on Sharpey's advice and with his introduction to James Syme that Lister arrives in Edinburgh, where the first phase of his career was passed and from which place these letters were written. In this correspondence through a number of years—physiology, the Glasgow election, medical education—everything is submitted with deference to his teacher and friend for whom affection and respect are everywhere apparent.

The first, second, third, and sixth of these letters deal primarily with the subject matter of his paper on "The Early Stages of Inflammation",[22] and its two supplements, which, as Lister was not yet a Fellow, were 'communicated' by Sharpey, their Secretary, to the Royal Society. They are also concerned with the criticisms of (Sir) James Paget and John Goodsir, the two referees chosen to decide on the suitability of the paper for inclusion in the *Philosophical Transactions*. The original MSS. is unfortunately lost, but the reports of the two referees are available and are reprinted above. Alterations in format, with the publication of the two supplements, each as a separate paper,[23] are adopted; but Lister is at issue with his critics on the question of 'vital affinities of the blood' and the physiology of the pigment cell. That these 'vital affinities' did, as he suggests, considerably exercise medical opinion at that time is supported by evidence at home and abroad. Alison[24] approves of the theory, and foreign physiologists, including Haller, Magendie, Kaltenbrunner, et al., contribute their observations to the contemporary press. Lister, however, is more concerned with the objection to his term 'paralysis' in relation to the concentrating and diffusive forces of the pigment cell. Writing to his father he says, "I felt it therefore to be by no means agreeable to have the correctness of the expression 'paralysis' questioned by Paget and Sharpey", supplying him also with a résumé of the experiments with which he sought to convince Sharpey. He successfully met both objections, and his views as originally expressed were ultimately incorporated in the *Philosophical Transactions*.[25]

Letters 4 and 5, dated June 28 and July 7, 1858, were the forerunners of his paper, "Preliminary Account of an Inquiry into the Functions of the Visceral Nerves, with Special Reference to the So-called Inhibitory System",[26] which appeared in the *Proceedings* of the Royal Society as a letter to Dr. Sharpey. In this form submission to referees could be dispensed with. There were others in the field and he was anxious to get his views into print, and but little more than two months were allowed to elapse between his first observations and the completed paper. To-day publication in the *Proceedings* is more sought after, but in the middle of the nineteenth century the *Philosophical Transactions* took precedence, its pages being reserved for original work of exceptional importance. It may, therefore, be conjectured that this paper of Lister's was not considered of sufficient moment to warrant, as he wished, its inclusion.

The concluding months of 1859 see Lister's stay in Edinburgh drawing to a close. In August he writes to his father[27] that Dr. Laurie is resigning his professorship in the University of Glasgow for reasons of health, and discusses his own possible candidature. By Oct. 12, it will be seen, he had definitely entered the field from which he emerged the chosen candidate early in the following year.

In 1864 the question of medical education was much to the fore. In Scotland, Syme and Lister led the way, and the Senates of Edinburgh and Glasgow Universities had already reorganized their system of teaching. In London proposals by Syme and Christison for modification of existing practice on similar lines were under consideration by the Medical Council. A series of articles on medical education appear in the *Lancet*,[28] where the

proposed innovations are critically examined. A note of antagonism by no means unusual in the polemics of the time is discernible in its Editorial wherein London teachers are exhorted to formulate their views before the assembling of the Council, whilst fears are entertained that "both the number and the decision of Scotch, Irish and University Members of the Council will give them a great advantage in enforcing their views." In the last of our letters Lister, least combative of men, deals with Sharpey's contribution to the *Lancet* with his usual serenity and good sense.

The original Lister letters are preserved in the Library of the Royal College of Surgeons.

I should like to acknowledge my indebtedness to Sir Arthur Keith for his kind advice, to Sir Edward Sharpey-Schafer for his note on Miss Colville, to Sir D'Arcy Power for his invaluable help in preparing these letters for the press, and to the Royal Society for permission to print the reports of Sir James Paget and John Goodsir.

NOTES.

[1] George Gabriel Stokes, Secretary of Royal Society from 1854 to 1885.
[2] Sir James Paget, 1814–99. Author of *Surgical Pathology*, 1853.
[3] John Goodsir, 1814–67. Professor of Anatomy at Edinburgh University.
[4] William Benjamin Carpenter, 1813–85. Author of *Principles of General and Comparative Physiology*.
[5] Emil Wilhelm, Ritter Von Brücke, 1819–95. Professor of Physiology at Vienna, 1849.
[6] Wilhelm von Wittich, 1821–82. Director of Physiological Institute at Bonn. Worked with Helmholtz.
[7] Emil Harless, 1820–62. Writes from Erlanger on the influence of gases on the blood, 1846.
[8] Eduard Friedrich Wilhelm Pflüger, 1829–1910. Director of Physiological Institute at Bonn.
[9] Augustus Volney Waller, 1816–71. Assistant of J. L. Budge (*see below*). Professor of Physiology, Birmingham.
[10] Julius Ludwig Budge (Senr.), 1811–88. Published his paper on the movement of the iris at Brunswick, 1855.
[11] Tuffer West. Well-known engraver of wood blocks; the business is still carried on by his successors.
[12] Thomas Wharton Jones, 1808–91. Experimental physiologist. Professor of Ophthalmology at University College.
[13] Miss Colville. Sir Edward Sharpey-Schafer writes: "Miss Colville was Dr. Sharpey's niece and kept house for him for a time at Hampstead, but she fell ill and died, I am not sure when. At any rate, as a result, he gave up housekeeping and went to live in lodgings in Torrington Square. She had a brother in either the Indian or Colonial Medical Service, Major Colville, who was stationed for many years at the Consulate at Baghdad and to whom I believe Sharpey left the greater part of his estate; but he did not long survive to enjoy it. He married after his retirement somewhat late in life. I know very well what a high opinion Lister always had of Sharpey."
[14] Lazzaro Spallanzani, 1727–97. Distinguished naturalist. Author of *Observations on the Circulation*, 1777.
[15] Agnes, elder daughter of James Syme and wife of Lister.
[16] Otto Spiegelberg, 1830–81. Professor of Midwifery at Göttingen.
[17] Georg Meissner, 1829–1905. Professor of Anatomy and Physiology at Basel.
[18] Moritz Schiff, 1823–96. Professor of Physiology at Basel.
[19] Sir George Cornwall Lewis, Bart., Home Secretary, 1859–61.

[20] Benjamin Bell, 1749–1860. Surgeon to the Edinburgh Royal Infirmary. Not related to Sir Charles Bell.

[21] Sir James Clark, 1788–1870. Physician-in-Ordinary to Queen Victoria, Physician to the Duke of Kent.

[22] "On the Early Stages of Inflammation", *Philosophical Transactions*, Part 2 for 1858, p. 645. (Read June 18, 1857.)

[23] "An Enquiry regarding the Parts of the Nervous System which regulate the Contractions of the Arteries", *Philosophical Transactions*, Part 2, for 1858, p. 607. (Read June 18, 1857.) "On the Cutaneous Pigmentary System of the Frog", *Ibid.* p. 627. (Read June 18, 1857.)

[24] Alison's *Outline of Pathology and Practice of Medicine*, 1843–4, p. 122. "These facts afford a strong presumption that in all these cases the impressions made on the capillaries and on the blood contained in them, solicit the flow through them on the *principle of a vital attraction of the blood*, rather than of relaxation of the vessels."

[25] Joseph, Baron Lister. *Collected Papers*, pp. 219–21, "Vital Affinities." *Ibid.*, pp. 250–1, "Paralysis of Concentrating and Diffusing Forces."

[26] *Proceedings of the Royal Society of London*, vol. ix, No. 32.

[27] *Lord Lister*, by Sir Rickman Godlee, p. 77.

[28] *Lancet*, 1864, March 12, 19, 26.

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