ORIGINAL COMMUNICATIONS.

ON THE EFFECT OF CERTAIN MORBID AGENTS IN PRODUCING COAGULATION OF THE BLOOD IN THE LIVING BODY.

By HENRY LEE, F.R.C.S., Surgeon to the Lock Hospital, Assistant Surgeon to King's College Hospital, etc.

[Read before the Medical Society of London, Feb. 3rd, 1855.]

On the 19th of November, 1853, I brought under the notice of the Medical Society the case of a gentleman who had some time previously suffered from most violent paroxysms of dyspnoea. The notes of the case, entered upon the minutes of the Society at that time, state that "the paroxysms were so violent as to threaten immediate death. There was bloody expectoration, but no fever, nor any evidence of inflammation. The stethoscope revealed the existence of a patch of lung in which respiration had ceased; and Mr. Lee thought this arrest of function was to be attributed to a plug in the pulmonary vessels. The case did well by the use of stimulants."

The following are my own notes of this case, taken in 1851 and 1852.

"CASE OF SUPPOSED OBSTRUCTION OF THE RIGHT PULMONARY ARTERY: RECOVERY. W. M., Esq., a gentleman of florid complexion, relaxed muscular fibre, and about 60 years of age, had for some time past been occasionally subject to active congestion of different parts. Four or five years previously, his throat had become affected, and he was deaf for several weeks. The mucous membrane of the throat was then of a deep purple colour, much swollen, but unattended with pain. This attack was most obstinate in its character, and did not yield to ordinary remedies: it ultimately was relieved by a short sea voyage. After an interval of two years, some boils formed in different parts, and manifested the same indolent character. During the spring of 1851, he suffered from a severe attack of hæmorrhoids, which yielded to no local applications, and for which an operation was ultimately performed. Whenever this gentleman was indisposed, the skin would assume a dusky yellowish hue; and the conjunctivæ of the eyes would become of a light yellowish brown colour. The urine at the same time was often loaded with red or yellow sediment. He speedily recovered, and remained perfectly well after the removal of the hæmorrhoidal tumours. In the beginning of the year 1852, however, he experienced some difficulty in walking up hill, and found that he became sooner tired than formerly. After a time, there was some dyspnoea on taking exercise; and at length the same inconvenience was felt quite independent of any exertion. The difficulty of breathing now evinced a tendency to recur in paroxysms, which at first recurred at intervals of two or three weeks, but gradually became more and more frequent. He always recovered from his attacks in the evening, after dinner.

"On the 24th of March, the difficulty of breathing had become almost constant, and was occasionally accompanied by distinct jugular pulsation, and an irregular, intermittent, but not accelerated pulse.

"The sounds of the heart were ordinarily indistinct, but afforded in other respects nothing remarkable. When the pulse intermitted, a 'reduplicate' action of the heart might often be detected. Immediately to the right of the right nipple, no respiratory murmur could be detected for the space of three or four square inches. There now appeared a very remarkable insensibility of the lung to the want of air. As soon as the patient fell asleep, the respiration would gradually become slower, and at length would completely stop. After the lapse of something less than a minute, the countenance would become livid, and he would awake with an anxious and extremely distressed expression. The struggle for breath which followed was most painful to

witness: a number of forced inspirations would succeed each other with great rapidity, and by degrees the lividity of the countenance would disappear. The patient would then occasionally for a time appear tolerably comfortable. Whenever he attempted to sleep, the same train of symptoms invariably followed; and he was consequently prevented from sleeping more than a minute or two at a time. This peculiar condition lasted for three days and nights, at the expiration of which he was much exhausted for want of rest. In order to relieve the excessive distress occasioned by these attacks, the plan was now adopted of keeping up artificial respiration by means of pressure on the front and sides of the chest. The patient was so sleepy that he did not appear at all disturbed by this process, and for the first time got comfortable sleep for half an hour. For several days following, this plan was occasionally followed, and generally with success. It sometimes, however, happened that the attacks of dyspnoea would recur during the period that the artificial respiration was being maintained. They then appeared to be connected with ineffectual attempts at expectoration. The matter brought up was at first small in quantity, and composed of frothy mucus; but it rapidly became increased in amount, and of a firmer and more tenacious consistency. It was from the first deeply stained with blood. Up to this time, no symptoms of general fever had presented themselves; nor was the pulse ordinarily much above its natural standard. The patient's appetite continued good; and all the natural functions, with the exception of those above mentioned, were regularly performed. The respiratory murmur, which had been noticed to be absent on the right side of the chest, had again in a great measure returned, when a change in the symptoms was observed. The urine now deposited a bright pink sediment; the pulse rose to near 100; and the legs became oedematous. There was at the same time some pain in the lumbar region, which was tender upon pressure. The patient rather suddenly lost his voice, so that he could speak only in a whisper. The cause of this did not at first appear; but in two days the mucous membrane at the back of the throat became covered with aphthæ. These gradually extended over the whole of the tongue and inside of the cheeks. Some fresh congestion appeared at the same time to have taken place at the lower and back part of the right lung. The expectoration was considerably increased in quantity, and was loaded with blood. The swelling which had commenced about the ankles gradually extended up the legs and thighs, and the whole of the lower extremities became affected. The back of the right hand and arm also for a few days became puffy and oedematous. There was occasionally some faintness, and he experienced a sensation as if the 'room ran round'; but, at other times, the muscular power was very little impaired. The skin, which from the first had been cool and moist, was now occasionally bathed with perspiration. This was particularly the case at night.

"On the 3rd of April, after having expectorated an unusually large quantity of thick gelatinous matter, he slept comfortably for an hour and a half. During this time the breathing was quite regular and unassisted; the inspirations were deep and heavy. He awoke confused, and took some medicine without knowing it. Shortly afterwards he had a most severe paroxysm of general distress, during which he shrieked so as to be heard over the whole house. The discomfort did not upon this occasion appear to proceed from any want of breath, but from an ill-defined and most painful general sense of oppression. The attack lasted about fifteen minutes, and left him feeling 'giddy and queer'.

"The symptoms now generally became somewhat relieved; and, on the 6th of April, the dulness had subsided. There was still, however, a dry cough; after which the breathing was quicker than natural. The perspiration was greater than before. The swelling of the legs and thighs was in some degree relieved.

"On the 10th, a decided improvement had taken place. There was less cough, and he breathed more naturally.

"On the 16th, the expectoration had ceased, and the respiration was natural. The voice, which had been affected ever since the appearance of the aphthæ on the mucous membrane of the throat, had not yet quite recovered its usual character. The swelling of the legs now rapidly subsided.

"On the 26th, the wind having for several days been in the north-east, a slight attack of erysipelas made its appearance at the back of the neck: it commenced in the immediate neighbourhood of an issue which had been made a month before, and had been kept open ever since. The erysipelas was of the erratic character, and evinced a disposition to return again after the expiration of a few days.

"At the end of May, this patient went to the sea-side, all his symptoms having disappeared.

"On the 12th of June, he continued well, and could take his usual exercise without any inconvenience.

"On the 6th of July, I heard from the usual medical attendant of this patient that he had returned from the sea-side apparently well, and without any remains of his former indisposition."

These were the notes which I took of this case during the years 1851-52, and I then considered that recovery had taken place. This patient continued to enjoy his usual health until August 1854. He now again began to complain of shortness of breath. Upon examination, the dulness was still perceptible where it had formerly existed, at the base of the right lung; and a slight cooing sound was heard upon each inspiration. The symptoms increased in severity during the month of September, and evinced the same disposition as formerly to recur in paroxysms. Towards the end of this month, the difficulty of breathing had again become very great, and constituted the marked and prominent feature of the case. The pulse was now very irregular both in force and frequency, sometimes scarcely to be felt, at other times beating without much force as many as 150 in a minute. Alarming attacks of syncope occasionally occurred; there were copious fetid evacuations, and most profuse perspirations. The superficial veins of the skin of the face were habitually congested. Whenever he fell asleep, the breathing would become slower and slower, and at length it would cease for a quarter or half a minute. The whole countenance would then become somewhat livid; the patient would awake in great distress; and a number of forced and deep inspirations would succeed each other in rapid succession, as in the former illness. The lower extremities at the same time became oedematous, although not to the same extent as formerly. The tongue was generally clean, although it sometimes was whiter than natural. There was now no expectoration of any kind. The appetite continued good till the last. Three days before the death of this patient, a change in the symptoms occurred: the difficulty in breathing, and the consequent want of rest, continued, if possible, with greater distress than before; but he complained, in addition, of pain above the pubes. There was at the same time suppression of urine; and the attendants distinctly described a pulsation in the lower part of the abdomen, synchronous with the pulse. A catheter was introduced; but the bladder did not contain any urine.

This patient died on the 3rd of October; and on the following day, in conjunction with Mr. Robinson, the ordinary medical attendant, I examined the body.

Expecting to find the heart and large vessels obstructed by fibrinous coagula, these were opened *in situ*. The right auricle presented, firmly attached to its internal surface, a small tough fibrinous mass, terminating somewhat abruptly. This was so firmly incorporated with the walls of the auricle, that it appeared as if it could not have been of recent formation. The abrupt way in which it terminated led to the idea that it had at some time been longer, and that its extremity had been detached. Such a supposition would coincide with and account for the attack of extreme distress which was witnessed on the 3rd of April, 1852; and also for the jugular pulsations observed previously to that date. As found after death, this

fibrinous concretion could not interfere with the action of the tricuspid valve; but, if longer, its extremity would necessarily have been carried by the current of blood through the auriculo-ventricular opening on the right side of the heart, and would thus have prevented the valves in this situation from closing. I therefore think it probable that, as long as this condition existed, the imperfect action of the tricuspid valve led to the jugular pulsation which had been noticed; and that, when a portion of the concretion became detached, other symptoms were induced, but that the valve resumed its natural action.

On opening the right ventricle, a firm white rounded mass of fibrin was found intimately connected with its internal surface. This round cord extended up through the semilunar valves into the pulmonary artery, and, dividing at its bifurcation, was continued along its subdivisions into the lungs. At the point at which this prolongation of fibrin passed the semilunar valves, it had received, and even now retains, an accurate mould of them. So firmly was this deposit united to the ventricle of the heart, that a portion of the latter, when removed, was accidentally allowed to fall out of the hand, but was caught and held by the fibrinous cord, without any separation taking place.

The left ventricle contained a membranous layer of fibrin, an inch and a half in length. The aorta contained tough and branched fibrinous coagula; these were of a size to fill some of the largest branches given off from the aorta; but when that vessel was opened, they were removed, without its having been ascertained into which vessels they had extended. The pulsation observed a few days before death in the abdomen may, I should imagine, be associated with the obstruction to the circulation caused by the presence of these coagula, which had probably found their way, more or less completely formed, from the left ventricle into the aorta.

Both lungs were found greatly loaded with frothy mucus, and congested. A small collection of white fluid existed in the upper part of the left lung. The lower part of the right lung was puckered up in a very peculiar manner; it was firm and elastic, and, when pressed between the fingers, gave something like the sensation of a soft leather ball. Portions of it sank when placed in water; but this did not appear to arise from the presence of any inflammatory product, but from the collapsed and puckered condition of the pulmonary tissue. Both sides of the chest, but especially the right, contained some serum.

The different organs in the chest and abdomen were examined, but the only disease which could be discovered, with the above exceptions, was in the situation of the suprarenal capsules. Here on each side a large mass of brown substance presented itself, easily torn, and having somewhat the appearance and colour of gingerbread. My friend Dr. Druitt, to whom I sent a portion of this substance for examination, without telling him whence it was derived, wrote me word that the specimen sent looked "just like the fat in the neighbourhood of the kidney of a fœtus: part of it seemed of a healthy pink, part of a dead cheesy yellow. On examination by the microscope, the healthy-looking portion was seen to be composed of ordinary fat-cells and delicate cells of white fibrous tissue. The yellower portion looked like fat in a state of fatty degeneration, if such a term may be used. The fat-cells were broken down into a mass of oil-globules, which floated about in the water in which the specimen was dissected; and the filamentous tissue was confused and oily."

As this was the only diseased structure which, upon a careful examination, could be discovered, it becomes a question of interest to consider whether it might in any way have been connected with the extensive fibrinous deposits which caused such severe, protracted, and fatal suffering. Without attempting to determine this question in reference to this particular case, there appears to be some, though not at present very conclusive, evidence to show that fatty matter introduced into the blood has a tendency to determine the coagulation of this fluid within the living body.

The following experiments, performed by M. Gaspard, are in point:—

EXPERIMENT I. Half an ounce of chicken's fat, refined and melted, was injected into the jugular vein of a very large dog. The animal was immediately affected with extreme dyspnoea, faintness, and prostration of strength, accompanied by a very slow pulse and inability to stand. These symptoms were followed, in the course of an hour, by fever, shiverings, indications of pain in the chest, and a frequent pulse. On the third day, the animal was enabled to get up and walk, although with a very unsteady gait; and, on the 6th of May, he was convalescent.

Two days after this, about a drachm of mercurial ointment was injected into the opposite jugular vein. There was immediate prostration of strength. The body was rendered immoveable, and the pulse was reduced to twenty-four beats in the minute. The respiration became very slow and short. There was subsequently extreme dyspnoea; and the animal died an hour and a half after the injection of the ointment.

The lungs were found inflamed and hepatised from the first experiment. The branches of the pulmonary artery were obstructed with a dark, concrete, fibrinous, and elastic clot. This had moulded itself to the branches of the pulmonary artery, and had followed its ramifications.

EXPERIMENT II. Three drachms of olive oil, warmed, were injected into the jugular vein of a fox. As in the former experiment, there was complete loss of power. The respiration was interfered with, and the pulse faltered. The animal died at the expiration of twenty minutes.

The body was examined four hours afterwards. Some bloody fluid was contained in the bronchi. The venous system, the right cavities of the heart, and the lungs, were greatly gorged with blood. The pulmonary tissue, for the most part, no longer crepitated upon pressure; and portions of it sank when placed in water. Some drops of oil could be distinguished exuding from its structure, after handling which an oily feeling was left upon the fingers.

These experiments appear to indicate not only that the introduction of some kinds of greasy matters into the circulation will communicate to the blood an unnatural tendency to coagulate in the living body, but that, when such a result has taken place in the lungs, the affected portions may become impervious to air; and that a bloody fluid may be exuded from the lining of the bronchi, quite independent either of inflammation, or of disease of the heart.

It may form an interesting subject of inquiry to ascertain how far portions of separated fibrin, when carried into the substance of the lung, may tend in their contraction to cause a puckering of that organ, and to render its structure inexpandible, as it was found to be in the preceding instance. This case furnishes, as I conceive, a good example of the length of time that the fibrin, separated from the blood, may remain in the living body without undergoing those changes, accompanied by softening and cell-formation, which so speedily take place when the separation of the fibrin has been caused by the presence in the blood of purulent or putrid fluids.

Analogous to the results above recorded, as far as the coagulation of the blood in the lining vessels is concerned, appear to be the effects produced in certain instances of strumous disease. The following very interesting case is related by M. Charcot in the *Medical Gazette* of Paris for the 21st of February, 1852.

CASE II. Louis Arnold, aged 29, was admitted into St. Michael's Hospital on the 10th of June, 1850, and died on the 6th of July following. In early life, this man was subject to oppression in breathing, palpitations, and some cough. At the age of twenty, he became a soldier in Africa, but was still occasionally subject to cough and oppression at the chest, and was attacked with a tertian intermittent fever. This recurred several times, but was not followed by any dropsical affection. After his return to his native country, he followed a laborious occupation for three years, and during the whole time was very irregular in his habits. He was not subject to any return of fever,

to any nocturnal perspirations, nor to hæmoptysis; but the cough and the oppression of the chest increased. He very soon became tired, even without sufficient cause; but did not lose his flesh.

Four months before his admission into the hospital, without any apparent cause, and in a single day, the eyelids and the cheeks became considerably swollen. The lower extremities and the forearms became at the same time œdematous. No rigor occurred at this time. The affection was preceded only by apathy and considerable lassitude. He, however, continued to work for a fortnight, when, the sense of fatigue having increased, and the scrotum having become swollen in addition to his previous symptoms, he sought admission into the hospital, where he continued for two months. He now left the hospital, and remained at home without treatment for two weeks, after which he was admitted into *La Charité*. There was then a soft murmur with the first sound of the heart, heard principally at the base of the organ. A double murmur was heard in the vessels of the neck, and the surface generally was pale, and of a yellow tinge. The upper and lower extremities and the scrotum were œdematous; the face was puffy; and there was some fluid in the peritoneal cavity. There was constant cough, especially at night. The expectorations were green, large, round, and puriform; sometimes russet-coloured, and streaked with blood. He complained of a sense of oppression. The voice was feeble, but not hoarse. For two days previous to death, he suffered the greatest distress from dyspnoea.

Upon a *post mortem* inspection, there was no cadaveric rigidity. The right lung was found adhering to the thoracic parietes. The pulmonary tissue presented a greenish hue; it was hard, homogeneous, and crisp; it presented several large cavities, some of which communicated together. These excavations contained very little puriform matter. Some craccaceous tubercles were found at the apex of the lung.

The left lung was a little congested at its back part, and throughout was but slightly crepitant. On making a section, a very large quantity of clear frothy liquid escaped. The vessels of different diameter were observed completely filled with concretions having the form of ramified cylinders, which extended through the pulmonary artery into the right ventricle of the heart. These concretions were white, or of a russet colour, solid, and resisting; they were exactly moulded to the vessels in which they were contained; they adhered but very slightly here and there to the lining membrane of the vessels, and were, in some parts of the pulmonary artery and its larger branches, surrounded by a layer of semi-fluid black blood.

The anterior surface of the heart, and the corresponding surface of the pericardium, were covered by a great number of very minute fibrous vegetations, which caused a slight adhesion of the opposite surfaces. The left ventricle contained a coagulum of a fibrous structure, and slightly adhering to the apex of the heart; it extended on the one hand into the left auricle, and on the other into the aorta; it here terminated in a point, being capped by some black semi-coagulated blood. The section of the clot showed no softened spot in its centre.

The right ventricle, which appeared slightly distended, was occupied by a conical concretion, having no adhesion except near the apex of the heart. Above, this concretion divided itself into two; one portion extended into the pulmonary artery; the other into the right auricle, from whence prolongations were continued into the venæ cavae. At the point at which the coagulum came into contact with the semilunar valves of the pulmonary artery, it was constricted by them, and presented three rounded eminences, exactly moulded to these cavities. In the right ventricle, as in the lungs, the concretion was pale, fibrous in structure, and streaked longitudinally with blood.

In dissecting the concretion found in the right ventricle, it was found homogeneous in the greater part of its extent; but at its inferior portion, near its point of adhesion, were two cysts; the one as large as a filbert, the other of the size

of a small pea. These two cysts had a lining very distinct from the surrounding fibrin, both in colour and texture: they contained a thick greenish fluid.

The internal surface of the right ventricle was studded with a number of similar cysts: these were situated in the interstices of the columnæ carneæ. In some instances, they were almost concealed; but in others they projected, to a greater or less extent, into the cavity of the heart: they varied in size from a pea to a nut. That portion of them which projected into the ventricle was smooth, rounded, and globular, sometimes presenting half a sphere, and sometimes nearly a complete sphere. Each of these cysts was prolonged by a fibrous pedicle, more or less compressed, and passing beneath the columnæ carneæ. The concealed portions of the tumours adhered but very slightly to the heart: often two tumours would have one pedicle. The colour of the pedicles, as of the cysts, was green. The cysts presented a fluctuating feeling; and, on opening them, a puriform fluid escaped. In the larger ones, the parietes then collapsed. The cavity of the cyst was usually continued into the pedicle. The internal surface of the ventricle and of the pulmonary artery appeared healthy. On examining the contents of the cysts by the microscope, they appeared to contain—1, an amorphous substance, apparently disintegrated fibrin; 2, a very great number of granular molecules; 3, a certain number of rounded globules, pale, and rather larger than the globules of the blood. None of the globules presented the distinctive characters of pus.

For the notes of the following case, I am indebted to Mr. Conway Evans, at present the House-Physician to King's College Hospital.

CASE III. James Hunter, aged 44, was admitted into King's College Hospital, under the care of Dr. Todd, on the 1st of June, 1854. He had been ill for seven or eight months; but, upon the 26th of May, he had been seized for the first time with extreme dyspnœa. This symptom was so distressing that it precluded the possibility of his sleeping even for a few minutes. He sat up all night, and laid his head upon a table; this being the only position in which, as he said, he could get any ease. He complained only of the difficult respiration, and consequent loss of sleep, accompanied by a peculiar sensation, which he described as "anguish," about the præcordial region. When admitted into the hospital, he said that he had had no sleep for four days and nights.

On the evening of the 4th of June, it was noticed that the left foot was cold and livid. On the 5th, no pulsation could be felt in the dorsal artery of the foot. He died upon the 8th, thirteen days after the first attack of dyspnœa.

The body was examined fourteen hours after death. The left foot and lower half of the left leg were of a livid blue colour. Upon cutting open the ventricle of the heart, a quantity of thick discoloured fluid flowed out. Besides this fluid, the left ventricle contained many clots of semi-solid fibrin, in various stages of softening. The left common femoral artery contained a dirty white fibrinous clot, which quite filled up the canal of the vessel, but which was not the least adherent to the inner coat. The popliteal artery contained a mottled coagulum, an inch and a half in length, firmly adherent to its inner coat, and completely blocking up its canal. The lining membrane of the vessel was here very red. The popliteal vein corresponding to this portion of the artery was obstructed by a coagulum; and the tissues surrounding both vessels were infiltrated and condensed. The coagulum in the artery was so firmly adherent to its lining membrane, that a stream of water, allowed to fall upon it from the height of from eight to twelve inches, did not in the least detach it. This coagulum, and the corresponding portion of the popliteal artery, are shown in the accompanying preparation. The right lung in this case contained some tubercles. The liver, upon a section, and examined by the microscope, was found loaded with oil. The kidneys were diseased, and

contained a few spots of yellow deposit in their cortical substance. This deposit, upon a microscopical examination, appeared to consist chiefly of fatty matter.

REMARKS. In all the cases now related, difficulty of breathing, of a very peculiar character, was the great and prominent symptom; and, as these cases had no particular points in common in a pathological point of view, with the exception of the formation of the fibrinous coagula found in the heart and large vessels, we must, I think, regard these coagula as the immediate cause of this peculiar difficulty of breathing, and this symptom as in some degree diagnostic of this particular affection. The absence of any disease in the vessels in any of the cases (with the exception of such as might reasonably be expected to have been communicated to them through their stagnant contents), and the extensive coagulation of blood which had taken place in those vessels, alike indicate that this disease had its origin in the blood.

The preceding cases and observations may be further illustrated by the following experiment, which shows how extensively the blood may coagulate in the living body from the admixture of a morbid product, independently of any disease in the vessels themselves.

EXPERIMENT. Some pus was obtained from an acute abscess in the breast of a young unmarried woman. About six hours afterwards, a trocar was introduced into the jugular vein of a donkey, which had been kept for the purpose, and was in excellent condition. A common glass syringe full of the pus, which was very viscid and tenacious, was now injected through the canula into the vein: almost immediately the animal became oppressed, and extended its head in a very peculiar manner. Extreme distress in breathing followed. The respirations were very rapid, and accompanied by much heaving at the flanks. This formed the great and prominent symptom, and continued until the animal died, which it did three hours after the injection of the pus.

Upon a *post mortem* examination, the right ventricle was found to contain an extremely firm white fibrinous clot. This was continued on the one hand into the auricle and right jugular vein, and on the other into the pulmonary artery and its branches.

A few of the larger pulmonary vessels were slit up, and the coagulum was removed, and placed upon a piece of paper, and allowed to dry.

Both lungs, but especially the right, were found to contain filamentous prolongations of decolorised fibrin, which no doubt had been continuous with the fibrinous clots which had been removed. The prolongations often terminated in thicker black rounded coagula. The portions of the lung in which they were most numerous were firmer to the touch than the rest.

The coagula which were removed from the right ventricle, pulmonary artery, and its branches, although of much larger size, resemble in general disposition those removed from the first case which I have related. The similarity in the effects produced by the natural and by the artificial disease, allowing for the difference in the size of the vessels in the two cases, is sufficiently striking.

From the whole of the observations now made, it appears to me to be demonstrated that different morbid products have the power of determining the coagulation of the blood in the vessels of the living body; that among these may probably be classed fatty and tuberculous matter, and particularly pus, when it is the product of acute inflammation: and that whenever, from any of these causes, coagulation of the blood occurs in the heart or large vessels, difficulty of breathing will be a most urgent and prominent symptom.

Dover Street, February 1855.