tion in the state of things, and introduce necessarily into the consideration of the subject so much contentious matter. But the answer to such objection is obvious, and it is that no great reform has ever yet been brought about without difficulties of that sort being found to obstruct and block the way, but which lets and hindrances, as a rule, have only required time, energy, and determination to overcome.

What, therefore, we consider essential to the well-being of the service should be stated promptly, clearly, and without reservation. The demands would probably not be acceded to at first; but confident in their justice, we should continue to press them earnestly; and with increased knowledge of the facts of the case, the irresistible force of public opinion too enlightened to tolerate any longer the existing system, will, before long, peremptorily demand that a prompt remedy shall be provided for a condition of things which is at once a discredit and anachronism.

It has often been a matter of much surprise that the more than discreditable state of things to which I have drawn attention to-day, and which have been discussed lately in so comprehensive a manner in the *BRITISH MEDICAL JOURNAL* and the *Medical Press and Circular*, has not been dealt with before this by the authorities, who should, one would naturally have thought, have been the first to inquire into and take steps to remedy the abuses with which the whole system of public medical relief in Ireland is saturated. On the contrary, afflicted apparently with those intractable official ailments, voluntary amaurosis and deaf-mutism, they have, calm and unruffled, serenely pursued the even tenour of their ways, seemingly unconscious of the existence of a tyrannous treatment of a large section of our professional brethren throughout many of the rural districts of Ireland, that would be a lasting discredit to any civilised community. I fear this apathy on the part of the authorities is an illustration—one out of many that might be adduced—of the existing political powerlessness of our profession. But one thing is as certain as it is encouraging, which is, that with the rapidly increasing spread of education throughout the country, an ever progressing political development must come, which, increasing in power as it advances, like a great river that gets strength from every streamlet it receives, will then not only compel a more intelligent appreciation of scientific effort, and sweep away the vulgar sentimentality—always a motive force with the uncultured—which has proved so potent a factor in retarding research, but also the chronic apathy, indifference, and inaction among the authorities, which have caused eyes to be too long closed, and ears too long cruelly shut to the remonstrances and representations of our long-suffering and overworked professional brethren in the country.

There is no creature, Sir Walter Scott has said, "that works harder and is more poorly requited than the country doctor, unless, perhaps, it may be his horse." This is indeed true; but I would add that, notwithstanding his poorly-requited labours, the world may be challenged to find a body of men more brave, more unselfish, more generous in will and deed, or more steadfast and untiring in the discharge of their duties than the vast majority of dispensary medical officers. Surrounded often by influences the most depressing—woe, want, weariness, and wretchedness—they continue their work often denying themselves not merely the comforts, but even the necessities, of life, and only too often struck down by the disease they were combating, and before it was possible to make any provision for their families. In saying this I "speak what I do know," for it is not from hearsay, but from the knowledge I have acquired during the many years I have served on the Council of the Medical Benevolent Fund Society, and I can say truthfully I have given no coloured picture.

In Misery's darkest caverns known,
His useful care was ever nigh,
Where hopeless Anguish pour'd his groan,
And lonely Want retired to die.

CREMATION.—Application is to be made by the City Commission of Sewers in the ensuing session of Parliament for powers to construct a crematorium at their cemetery at Ilford. According to Mr. Thomas, the Chairman of the Sanitary Committee, which has the matter in hand, bodies are now dug up in many London cemeteries and burnt in order to make space for fresh bodies.

LECTURE ON NEUROLOGICAL FRAGMENTS.

Delivered before the Hunterian Society.

By J. HUGHLINGS JACKSON, M.D., F.R.C.P., LL.D., F.R.S.

I AM exceedingly obliged by the request to undertake the honourable task of giving the Hunterian Society's Lecture this year. It is for me a most pleasant thing to deliver it at the request of my greatly valued friend, Dr. Stephen Mackenzie, our late President.

I have often thought that the scientific investigation of insanities may be best begun in general hospitals, and especially by taking for study cases of delirium in such non-nervous maladies as pneumonia, and emphysema with bronchitis. These are not cases of insanity at all in the conventional sense of that word, but in a scientific regard, being departures from normal mental states, they are. After the late Dr. Monro I have urged that the mental condition in all insanities, short of dementia, is double—one of two opposite mental elements. In the hospital cases adverted to the insanity is named after the positive element—delirium; but with this there co-exists a negative element, if for convenience I may speak of a negative state existing. On this basis we may sometimes trace an increasing double departure from normal mentation. In cases of emphysema with bronchitis, we can observe a gradual losing touch with present surroundings (negative element), and a gradually increasing quasi-relation to organised experiences of former surroundings (positive element); or using popular, but not accurate, language, the patient gradually ceases to live in the real world, and comes to live more and more in a world of his own. A sack dealer was delirious during erysipelas. The house-surgeon opened a small abscess in one eyelid while the patient was in a strait jacket. The patient's account of these circumstances was that he had been to a public house, that the landlord fastened him down with two sacks, and then poked out one eye.

It is easy in this case to trace the substitution of unrealities, as we call them, for realities. I wish to urge that we have not only to take into account the patient's "pseudo-knowings"—that he had been to a public house, etc.—his delirium sampling a positive element, but also his "not-knowings"—that he was in hospital, etc.—sampling a co-existing negative mental element. We say that the patient's account was of a delusion ("pseudo-knowings"); there was a delusion for us, but in him a belief. To say that he believed in his delusion is the tautology of saying that he believed in his belief. The late Dr. Milner Fothergill gave an account of his delirium when ill with scarlet fever. It seemed to him most unreasonable that people should keep him in bed when he, a doctor, wished to go out to visit his patients. For Fothergill, when reduced to a lower mental state, it was, to use his words, "an interference with the liberty of the subject." By these remarks I wish to suggest that what we call the "disorderly" mental condition of an insane man—that sampled by his positive mental symptoms—is a mentation, having the same laws as the mentation of the patient's former sane, or, as we may say, entire, self.

Let us now look at the physical condition concomitant with insanities—the two abnormal cerebral states corresponding to the two abnormal mental elements. The negative mental state—the sack-dealer's "not-knowings"—signified loss of function of the highest range of his highest cerebral centres. (If anyone objects to the term "highest centres," he can substitute "certain cerebral centres.") The mentation remaining possible to him—his "pseudo-knowings"—signified increased activities of the intact lower ranges of those highest centres. We have here loss of function co-existing with over-function, and an illustration of a principle long ago put forward by Anstie and Thompson-Dickson. We have to bear in mind both the reduction (dissolution) and the range reduced to (the level of evolution remaining). The positive element of an insane man's mental condition signifies

evolution going on in lower intact ranges of his highest centres.

In the foregoing is illustrated a principle of importance—that, with obvious exceptions, there are in the symptomatology of nervous maladies in which there are negative lesions, not only the effects of those lesions, but other effects from activities of healthy parts. I have several times illustrated this principle by the symptomatology of cases of paralysis of ocular muscles. I now give an illustration from a case I published in the *Illustrated Medical News* of February 2nd, 1889—a case of paralysis of the lower part of the trapezius; there was malposition of the scapula; its lower angle was raised; it was nearer the middle line, and was “cocked out.” (Duchenne.) It is manifest that paralysis of the trapezius is not the cause, in a proper sense of the word cause, of such malposition. The displacement is owing to over-action, or unopposed action, of the levator anguli scapulæ, a part perfectly healthy. In the case of paralysis of the lower part of the trapezius, in a patient the subject of pseudo-muscular hypertrophy, there was not that malposition of the scapula; but in this case I found—and the observation was confirmed by Dr. James Taylor—that there was paralysis also of the levator anguli scapulæ. To return from this digression.

In hospital we can study degrees of insanity. Thus in some severe cases of emphysema and bronchitis there is delirium followed by coma, the coma or dementia being a greater degree, not of the delirium, but of the negative mental state coexisting with that positive or superpositive state. Referring to a former remark, the patient who gradually ceases to live in the real world, and comes to live in a world of his own, at length, when comatose, lives in no world at all (mentally, I mean). I attribute the “two degrees” of insanity in cases of emphysema partly to great supervenosity, to different degrees of it.

The neurologist is much interested in the effects of supervenous blood. Here I make some general remarks on the action of such blood. It is well known that it stimulates certain medulla centres, whether by excess of carbonic acid or by deficiency of oxygen does not for the present concern us. Most likely a slight degree of supervenosity is beneficial in cases of emphysema, by stimulating the respiratory centre, thus producing some degree of compensation. Traube and Cohnheim attributed the hypertrophy of the left side of the heart in some cases of emphysema to arterial constriction caused by stimulation of the medulla vaso-constrictor centre by supervenous blood. Such blood stimulates certain musculatures; here, perhaps, we see the reason why there are evacuations in some cases of nitrous oxide anæsthesia. Now for delirium with, and, as I think partly, if not mainly, from highly supervenous blood, in cases of emphysema and bronchitis, for example.

Since it is certain that such blood over-stimulates some lower (for example, medulla) centres, the obvious explanation of the delirium in cases of emphysema with bronchitis would be that it corresponds to over-stimulation of cerebral centres. But (Hitzig, Franck, Pitres) asphyxia renders the motor cortex inexcitable. Dr. Risien Russell has recently made for me a new research in this matter. He finds that the motor cortex of a dog is inexcitable in the third stage of asphyxia. It does not necessarily follow that because asphyxia annuls the function of the “motor area” that it renders the remainder of the cortex functionless. I, however, submit as an hypothesis that supervenous blood according to its degree of venosity diminishes or annuls the function of all parts of the cortex. If this be so it cannot be the cause of delirium, which evidently implies function going on. In a popular use of the word “cause,” as when it is said that opening floodgates causes water to flow, supervenosity may be called the cause of delirium. But speaking carefully, we can only say that it is constructively accountable for that positive mental element; it produces the negative functional state answering to the negative mental element coexisting with the delirium. I explain the relation of the two states on the same general principle as I did the condition in the sack-dealer’s case. The highest, the least organised, range of the highest centres is rendered functionless when the lower and more strongly organised ranges of those centres remain functionable; the lower ranges being now uncontrollable rise in activity, and during their activity delirium occurs (Anstie’s

principle). (The more complex and special nervous arrangements are the less organised, and thus they “give out” sooner to injurious influences.) When the supervenosity becomes very great the lower ranges of the highest centres also succumb, and then no sort of mentation, not even the “disorderly” mentation we call delirium, is possible. I have been speaking as if supervenosity were the sole agent; but since from highly supervenous blood there will be very great stimulation, and perhaps at length exhaustion, of lower (medulla) centres, the condition is probably more complex.

The study of degrees of insanity in relation to one another is very important. This can best be done by noting degrees of reduction (dissolution) of brain by alcohol. I, it may be supposed artificially, make three degrees of reduction (with sub-degrees). In considering these degrees of insanity we have to take note of the coexisting negative and positive states—of the reduction of the highest centres (dissolution) and of the range reduced to (evolution remaining)—until the third degree coma, acute temporary dementia, when the mental condition is seemingly entirely negative, and the reduction of the highest centres apparently total.¹

For purposes of practice we have to study alcoholic intoxication carefully. It is well known that men fatally ill from cerebral lesions are sometimes locked up in police cells for drunkenness. It needs insisting on that there may be from grave intra-cranial lesions, soon causing death, not only insensibility but manner and conduct, like that of a person partly intoxicated by alcohol. Dr. Stephen Mackenzie and I have recorded² a fatal case of meningeal hæmorrhage producing a condition which, without the history of onset, would, certainly by the non-medical, have been taken for drunkenness. The patient was violent, swore, and, what is more striking, there was a purposive action; the patient got the chamber utensil from under his bed and used it.

At the London Hospital we occasionally have under care men who, after sucking raw spirits out of a cask, are seemingly as deeply comatose as other men are after large and fatal cerebral hæmorrhage. Without history of circumstances and of mode of onset, the diagnosis of apoplexy produced by alcohol from that produced by cerebral hæmorrhage is very difficult and may be impossible.

For an hour or two after injuries to the head there may be a condition very like that of a man slightly drunk. This is an important matter. I was once consulted by letter on the case of a clergyman who was accused of drunkenness—a serious thing for a clergyman. I was able to say that the condition described might have resulted from an injury to the head the patient had had. It is to be borne in mind that after an injury to the head a patient may act elaborately, if foolishly, whilst “unconscious;” that is, on his recovery he remembers nothing of his strange doings—a thing evidently of medico-legal importance.

I have suggested³ that great supervenosity may cause loss of the knee-jerks, as when there is great cyanosis in severe cases of emphysema with bronchitis, and that possibly the absence of this tendon reaction in some cases of apoplexy is thus caused. Dr. Risien Russell was so good as to observe for me the state of the knee-jerks in an artificially asphyxiated dog; he found that they were increased during the earlier stages of asphyxia, and lost in the third stage. I suggested⁴ that the preliminary increase of the knee-jerks Dr. Russell observed was owing to lack of inhibition of lumbar centres by the motor cortex, and that the loss of the jerks in the third stage was owing to the more strongly organised lumbar centres succumbing later than the cortical motor centres. Dr. Russell⁵ brought forward interesting facts showing that my inference was at any rate hasty. Dr. Stephen Mackenzie, who has had a large experience of cases of anæmia, including many cases of “pernicious anæmia,” tells me that he has never found loss of the knee-jerks in any case. I mention this as supervenous blood may tell by deficiency in oxygen. Rapidly induced loss of oxygen is, however, a very different thing from slow loss of oxygen (loss of many oxygen carriers in anæmia).

¹ The neurologist will find in *Brain*, January, 1881, a most valuable paper, by Dr. Charles Mercier, on Degrees of Dissolution by Alcohol.

² *Med. Times and Gazette*, April 1st, 1871.

³ *BRITISH MEDICAL JOURNAL*, February 13th, 1892.

⁴ *Op. cit.*

⁵ *Physiological Society*, February 13th.

There is another complication. I have recorded⁶ a case of epileptiform seizure affecting mainly the left leg, in which, after the fit, the left knee-jerk was exaggerated; there was also foot clonus. Westphal, Gowers, and Beevor have noted temporary loss of the knee-jerks after epileptic fits. I suggested that the exaggerated knee-jerk in my patient was owing to exhaustion of fibres of the lateral column, whereby cerebral control was taken off the anterior horns concerned with the jerk.⁷ Dr. Gowers suggests that in the case of temporary loss of the knee-jerks after epileptic fits there is temporary exhaustion of the lumbar nuclei. As in the animal Dr. Russell experimented on there had been convulsion, we have to bear in mind that the loss of the knee-jerks may have been due, or partly due, to exhaustion of lumbar centres after their discharge. Dr. Beevor remarked on this point at the meeting above mentioned. His researches on the condition of reflexes after epileptic fits⁸ have to be carefully considered with regard to the question here raised.

I had the honour of reading a paper before this Society on Laryngismus Stridulus,⁹ when I submitted that the paroxysms are asphyxia fits analogous to those producible artificially in rabbits and dogs. I tried to show that the relation of rickets to these seizures (Elsässer, Jenner, Gee) is that the abnormally soft ribs render the action of the diaphragm inefficient (the infant's breathing being almost solely abdominal), and thus that, especially during sleep, when the attack commonly starts, there is overstimulation of the respiratory centre by supervenous blood, an excess of a "natural stimulant" and therefrom convulsions. Dr. Gay¹⁰ has very ably argued against the views I put forward. I do not here reply to his criticisms, but will mention some things bearing on my speculations.

When I wrote (1886), Horsley and Semon had discovered "representation" of the abductors but not of the adductors, of the vocal cords, in the medulla, and thus it seemed that there was no medulla mechanism by which (on my supposition of discharge beginning in the respiratory centre) the glottis could be closed in attacks of laryngismus. Semon and Horsley have since found that the adductors as well as the abductors of the vocal cords are represented in the medulla.

Asphyxia fits are easily producible in some lower vertebrates of the mammalian class by mechanical arrest of breathing; these seizures the physiologist tells us are owing to discharge beginning in the (medulla) respiratory centre, a discharge started by highly supervenous blood; the discharge there beginning no doubt spreads to other centres, or possibly they are discharged by the same stimulation.

(1) Convulsions are produced by clamping the trachea. (2) Curara in a certain dose paralyses the motor nerve endings to the respiratory muscles, and not those of the muscles of the limbs; asphyxia is produced, and there is convulsion of the limbs; the discharge of the respiratory centre in these circumstances is unable to effect anything upon the thoracic musculature. (3) Rabbits breathe almost exclusively by the diaphragm; Marcwald says that young rabbits "up to four months old, and even over that age, do not survive division of the phrenic nerves on both sides, but die, according to age, in a few minutes after the operation, showing strong convulsions and cyanosis, or in two or three days they die from asphyxia."¹¹ Probably the respiratory centres are stimulated by supervenous blood because it is deficient in oxygen.¹² For

⁶ *Medical Times and Gazette*, February 12th, 1881.

⁷ I have since learned from Dr. Waller that nerve fibres are practically inexhaustible; possibly the endings of fibres of the lateral column are alone exhausted in cases of post-epileptiform paralysis.

⁸ *Brain*, April, 1882.

⁹ *Brain*, April, 1886.

¹⁰ *Brain*, January, 1890.

¹¹ *The Movements of Respiration*, translation by Mr. Thomas A. Haig.

¹² Although, as is the custom, one uses the word "stimulation," the supposition is that, from lack of oxygen, there is such an anabolism of material of the respiratory centres that it becomes more "explosive," and thus katabolises on slight provocation, suddenly and excessively. There are convulsions in some cases of nitrous oxide anaesthesia. Thus Dr. Frederic Hewitt writes (*Med.-Ch. Trans.*, vol. 74): "The clonic contractions of the respiratory and extrinsic laryngeal muscles occur at or about the same time that clonic muscular phenomena in the extremities manifest themselves, and there can be little doubt that they are, like the latter, due to an absence of free oxygen. I have lately administered at the Dental Hospital of London for Dr. George Johnson pure nitrogen, as well as nitrogen with small percentages of oxygen, and the respiratory phenomena which have manifested themselves, as well as the general muscular movements, have so closely resembled those of nitrous oxide as to be indistinguishable from them." (No italics in original.)

(4) (Kussmaul and Tenner) fits like those produced by clamping the trachea are produced in rabbits by rapidly bleeding them to death. (5) Such fits come on when the medulla is deprived of arterial blood by tying the great arteries of the head. (6) Artificial respiration will not prevent asphyxial convulsions by a drug if that drug stops the action of the heart, and thus arrests circulation.¹³ "Stoppage of the heart, either by a ligature directly applied to it, or by action of drugs upon it, causes asphyxia and convulsions."¹⁴

Of course, it does not follow from anything I have just said that laryngismus stridulus in man (the infant human being) is an asphyxia fit, as I think it is. But it would be worth while to study in minute detail the onset and march of convulsions in laryngismus stridulus, especially when they become widespread or universal, in comparison and contrast with the onset and march of convulsions in artificially asphyxiated animals. The difficulties of this comparative study are obvious, but sometimes a medical man witnesses a fit of laryngismus.

Since, according to my hypothesis, in laryngismus stridulus the blood, when it has become rapidly supervenous, discharges the respiratory centre, and thus secondarily causes still more supervenosity by fixation of the thoracic cage, or some part of it, it may seem that the fit on that hypothesis would necessarily be fatal. Thus Dr. Gay says¹⁵ of my hypothesis: "Supervenosity initiates the paroxysm, which increases the supervenosity, and laryngismus would consist of a single and necessarily fatal gigantic respiratory spasm." My friend, Dr. Risien Russell, has been so good as to make experiments for me bearing on this matter; he clamped the trachea of three rabbits. He reports: "If the clamp was removed in the third stage, from 30 to 50 seconds after all convulsions (second stage) had ceased, the animal recovered without artificial respiration being performed, but if the clamp was not removed until a minute or more elapsed, the animal did not recover. The heart went on beating after all respiratory movement had ceased. An artificially-asphyxiated dog recovered without artificial respiration two minutes after all convulsions (second stage) had ceased."

A child, when seemingly dead after an attack of laryngismus may recover. Sir William Jenner¹⁶ reports a very striking illustration of this.

Not only is the opinion I hold of the pathology of laryngismus disputed, but the suggested localisation of the discharge on which the attack depends is also objected to. It is supposed by Horsley and Semon that fits of laryngismus are owing, not as I think to discharge beginning in a medulla (respiratory) centre, but to discharge beginning in a part of the cortex-laryngeal centre. They have certainly good reasons for this supposition. Krause, Horsley and Semon have discovered representation of the abductors of the vocal cords in the cortex, but have not discovered representation of the adductors in the cortex, except in the case of the cat. (The cat, Semon tells me, vocalises during inspiration). Discharge of the laryngeal centre of but one cerebral hemisphere will close the glottis (Semon and Horsley). This closure would, if kept up, cause asphyxia, but, as I learn from one of their experiments, the blood when it has, on this enforced closure of the glottis, become supervenous, so acts on the medulla as to bring the (medulla) abductor centre into activity. Horsley and Semon write, *BRITISH MEDICAL JOURNAL*, December 21st, 1889, "Unilateral irritation [of the laryngeal area of the cortex] produces bilateral effect. Thus, clinically, in any irritative unilateral affections of this area, spasm of the glottis, that is, bilateral adduction of the vocal cords, may occur, for example, in laryngismus stridulus. That this view is not purely theoretical is shown by the association, in severe cases of the last-named illness, of the glottis spasm with the so-called carpopedal contractions. This association is most easily explained on the assumption that we have any overflow of energy from the laryngeal to the neighbouring cortical areas for the limbs."

In some laryngeal crises (laryngismus of a different clinical kind from that already considered) there is asphyxia; there may be loss of consciousness and some degree of convulsion. I

¹³ Lauder Brunton, *Pharmacology*, ed. 3, p. 189.

¹⁴ Brunton, *op. cit.*, p. 289.

¹⁵ *Op. cit.*

¹⁶ *Lancet*, January 2nd, 1875.

have now under my care a tabid patient who has had twenty or thirty crises in the day with loss of consciousness, and four severer seizures in bed (one after urgent vomiting and three in sleep) also with loss of consciousness. The four attacks in bed, judging from the accounts given by the patient's wife, are not unlike epileptic fits. This patient has paralysis of the abductors of the vocal cords (Semon), no doubt from a lesion of their medulla centres. This ordinarily does not seem to embarrass the patient's breathing, he being quiescent. Semon tells me that he thinks that in laryngeal crises, with or without paralysis of the abductors, there is an "irritative" state of the (medulla) adductor centres. If so it is to occasional overaction of these centres, greatly narrowing or completely closing the glottis, that laryngeal crises are owing. I have never witnessed such severe laryngeal crises as, by description, my patient has had. Were I present at one of his seizures I should, if I could not abort the paroxysm by chloroform, very carefully note the state of his thorax, observe minutely any convulsions (eyes, hands, and face) there might be, note whether or not there was increased sweating, and inquire if there were evacuations of urine or fæces, and, if it were possible, test his knees.

Neurologists are much concerned with Regulation, and, in many maladies, with Unregulation. There is (1) nervous regulation which needs no illustration here; (2) mechanical regulation (elasticity of arteries, etc.); and (3) what for lack of a fit name I will call chemical regulation, stimulation of the respiratory centre by venous blood, for one example. Properly speaking there are three factors in regulation. In the case of the respiratory system (1) the (medulla) respiratory centre with its afferent and efferent nerves; (2) elasticity of the lungs and of the thoracic walls (recoil during expiration); (3) stimulation of the respiratory centre by venous blood. I shall speak almost solely of the third factor, the other two being taken for granted.

What is waste in one manufactory may be material for another. What is waste for one part of the body may be material for another (Treviranus and Paget). Thus I suppose that one factor in keeping up arterial tonus in health is stimulation of the vaso-constrictor centre by effete nitrogenous products—a "natural stimulant" of that centre. An excess of a natural stimulant is a poison. High tension in some cases of Bright's disease is probably owing to an excess of the natural stimuli mentioned, and perhaps also to the presence of unnatural stimuli of similar derivation. I have suggested that attacks of laryngismus are owing to a sudden excess of a "natural stimulant" of the respiratory centre. In some cases of simple jaundice the pulse becomes infrequent. This is ascribed to stimulation of cardio-inhibitory nervous elements by bile salts. It would be venturesome to speak of this as due to the action of an excess of a *natural stimulant*, since there is, I believe, no proof that bile salts exist in the blood of the healthy. There is one thing worth mentioning in this connection. Henoch says that he has never observed an infrequent pulse in the jaundice (catarrhal) of children under 7 years of age. He supposes that the excitability of the child's nervous system compensates for the retarding action of the bile acids. But may it not be that there is less for the bile salts to poison in persons so young? The cardio-inhibitory, and probably other inhibitory nervous arrangements (Soltmann), are presumably developed later than what may be distinguished as the directive (motor) nervous arrangements. (Perhaps this is only another way of saying that the child's nervous system is excitable). As bearing on the hypothesis I have submitted, it may be mentioned that both rabbits and young children tolerate large doses of belladonna; it is well known that in the rabbit section of the vagus nerves alters the rate of its heart but little.

In some cases of mitral valve disease ague is imitated, or at least well caricatured. I have long thought that the rigors, or sudden and temporary great rises of temperature, or both, are owing to the effects of disintegrated spleen from embolic infarctions.

We have a very complex problem in regulation—or, rather, in-unregulation—in cases of fracture dislocation of the spine, crushing the cervical cord across below the emergence of the phrenic nerves. The nervous mechanisms of the digestive, circulatory, respiratory, and animal heat systems—the "four

systems"—are mutilated; there is constipation with "distension" of the abdomen; the pulse is infrequent; respiration is diaphragmatic only; temperature is often very high. For the methodical analysis of this compound confusion of regulation we have to take into account not only centres of the Lowest Level, which are Ulterior (peripheral-wards) of the lesion, but also those of this level which are Citerior (brain-wards) of the lesion. It is, I think, not going too far to say that the whole symptomatology is, in late stages, traversed by supervenosity. There is in the spinal fracture case as certainly an anatomico-physiological problem as there is in the case of subphrenic section of the cervical cord in a dog or a rabbit. Surgeons and physicians would gain much from the co-operation of a well-trained physiologist in the investigation of the effects of such a very local spinal cord lesion in man compared and contrasted with those in the dog and especially with those in the very different vertebrate, the rabbit, similarly mutilated. In some cases in man there is delirium: an example of a healthy brain failing consequent on a very local spinal cord lesion—consequent on that lesion in a roundabout way—directly owing to the results of imperfect working of the "four systems" mentioned. Hence, in the spinal fracture case, in which the central nervous system is cut in two at a critical place, we have to take note of all centres of the nervous system. Further, as it is said that supervenous blood excites certain musculatures apart from nervous agency, we have to take also into account many, perhaps all, parts of the body.

Taking, quite artificially, but one symptom, great rise of temperature in some cases of fracture dislocation (subphrenic cervical cord), we find it very difficult of interpretation. The greater rate of emission of heat may not signify greater thermogenesis. Very many of the muscles—the main heat-producing organs—are "paralysed;" and thus it may be supposed that there is less thermogenesis. We cannot make calorimetric researches on our patients. Paralysis is an indefinite word. In the case of a dog poisoned by curara, all the skeletal muscles are cut off from the motor influence of the whole central nervous system; an animal thus poisoned becomes "cold blooded." But in the fracture dislocation case muscles are "paralysed" in a very different way; they remain connected with their anterior horns, and it is fair to speculate that they may not only continue to produce heat, but that, being cut off from higher inhibitory heat centres, they may produce more than normal. I have been speaking of "paralysis below the lesion;" there is no doubt, from destruction of grey matter of the part of the cord crushed, some "paralysis at the lesion;" but the amount of muscle thus cut off from the influence of the central nervous system is a negligible quantity. If the "muscles below the lesion" cease to produce heat, then, as Hutchinson has said, they become refrigerators—have to share in the heat produced by "muscles above the lesion." A patient of the late Mr. Hilton lived fourteen years after a fracture dislocation crushing the cervical cord across below the emergence of the phrenic nerves. Did not the "muscles below the lesion" in this man produce heat when they were "paralysed?" If they did not, they would have had to share the heat produced by the "muscles above the lesion" (and of course by other parts of the body); and would thus be refrigerators.

A question in neurology—one of great physiological interest and clinical importance—is raised by certain researches of Charlton Bastian.¹⁷ He showed that in some cases of an absolutely complete transverse lesion of the cord above the lumbar enlargement the knee-jerks were absent and the legs flaccid up to the time of death three or four months later. This is quite contrary to current doctrine. So far as I have observed in cases of fracture dislocation crushing the cervical cord completely across, the knee-jerks are lost—to take that one symptom for illustration. I am greatly interested in this matter, since Bastian's conclusions harmonise with a hypothesis I have put forward as to cerebral and cerebellar influxes. It may be said that did the patients referred to live long enough their knee-jerks would return. In some dorsal cases under my care the knee-jerks have returned, in one case after being absent for thirty-eight days, and in another for two years; there is in neither case any return of sensation or motion in the legs. But granting for the sake of argument

¹⁷ *Med.-Chir. Trans.*, 1890, vol. 73.

—and for the sake of argument only—that there has been no re-establishment of lines of connection in these cases, we have still to explain the absence of the jerks for weeks and months, in conditions where shock was out of the question. If Bastian has only shown that the knee-jerks are absent for weeks or months he has made a valuable contribution to clinical medicine; I should still think that the doctrine of cerebellar influx is countenanced. The situation is not so simple as it has been supposed to be. In many such cases (Bowlby) the superficial reflexes are present or if absent at first may return. It has been said that when in chronic cases the knee-jerks are absent, there are set up secondary morbid changes in centres below the lesion and perhaps in peripheral nerves; we have, however, to explain not only the loss of the tendon reaction but also the presence of the superficial reflexes. There is priapism in cases of fracture dislocation of the cervical spine; it may be (Hutchinson) present in “shock.” Does not this show overaction of some elements of Stilling’s nucleus? Moreover, those who suppose that secondary morbid changes set up in centres below the lesion cause loss of the knee-jerks for months have to account for the return of these tendon reactions in some cases. Are those morbid changes reversed or in part reversed? We have, with regard to the doctrine of cerebellar influx, to bear in mind that in many cases of tumour of the middle lobe of the cerebellum the knee-jerks are absent. I may mention a case (necropsy) of hæmorrhage into the left lobe of the cerebellum (observed by Dr. Penberthy, my late house-physician) in which the right knee-jerk only was lost; I say nothing as to the bearing of this case.

I have applied the doctrine of non-antagonised cerebellar influx in the explanation of athetosis and paralysis agitans, supposing that in both upon loss of cerebral influence there is preponderance of cerebellar influence. It is right that I should state facts counter to this application of the hypothesis. Victor Horsley, by removing the “arm area” of one of his patients, put a stop to athetosis. There is on record¹⁸ a case of cerebral hæmorrhage occurring in a patient the subject of paralysis agitans; the tremor ceased on the side of the body paralysed, continuing on the other.

The symptoms of disorder (unregulation) of the organic systems—very strikingly of the respiratory—are most important. When death occurs in apoplexy from cerebral hæmorrhage it is with failure of the respiratory system, and, presumably, of the other organic systems. These failures may be put down to lack of so much brain, but not rarely do we see patients who live for years with much more extensive destruction of brain than that by a hæmorrhage which may kill in a few hours. They may be ascribed to the wider abnormal state of the brain which answers to loss of consciousness or perhaps to pressure indirectly transmitted to the medulla oblongata. I have to suggest a different interpretation.

In some cases of cerebral hæmorrhage, where there has not been loss of consciousness at first and in which respiration, circulation, and temperature have been apparently normal for some time, disorder of these systems ensues later on. There is, what many years ago I used, after Trousseau, to call “cerebral fever.” In such cases it seems to me that the “fever” depends, not on the immediate effects of the effusion, but on secondary effects the clot produces in medulla centres. To consider methodically the question here raised we should study cases of other “foreign bodies”—tumours, abscesses, and other masses in the brain. In these cases it is notorious that there is one distant effect. Optic neuritis is nearly always set up, and I submit that, adopting the principle of an hypothesis put forward by Buzzard,¹⁹ that there are other “distant effects;” that morbid changes akin to those of optic neuritis are set up in medulla centres. We certainly have, in very many cases of optic neuritis from cerebral tumour, to explain the urgent “purposeless” vomiting. Moreover, in such cases there may be a chronic illness with occasional vomiting, infrequent pulse, constipation, and emaciation.

In a few cases of cerebral tumour there is an acute illness very like tuberculous meningitis. Further, it is notorious that some patients who have cerebral tumour die suddenly. It is not at all likely that death occurs from the destruction of the tumour causes directly, or by the softening induced round

about; it is not likely that it occurs from mere lack of so much cerebral hemisphere. Again, as the late Hilton Fagge first pointed out, death occurs rapidly in some cases of intracranial tumour by respiratory failure. It may be asked, “Why does respiration in such cases fail rapidly?” I can only suggest an analogy. It is well known that sight may be good in optic neuritis for a long time, and then rapidly fail. So I imagine that in the cases mentioned, morbid changes are slowly produced in the respiratory medulla centre, and that that centre fails rapidly, perhaps having worked inefficiently some little time before.

After irruption of blood in the brain that blood becomes a clot, acts as a “foreign body,” produces a local encephalitis, and by intermediation of this there are set up secondary morbid changes, changes in centres (respiratory among them) of the medulla. This is, of course, hypothetical. At any rate, in a case of large cerebral hæmorrhage, it is at least convenient to distinguish several modes of action of the escaped blood: (1) it destroys, and thus produces such symptoms as hemiplegia; (2) according to the rate of its escape it causes “shock;” (3) according to its bulk it squeezes, and thus, in addition to (2), it produces loss of consciousness; (4) in its character as a “foreign body,” it may produce encephalitis, and thereby, hypothetically, “cerebral fever” by changes induced in medulla (regulating) centres. But this is not all; (5) in some cases of cerebral hæmorrhage, in which consciousness, if defective, has not been lost at the onset, delirium may occur. I submit that this is mainly a “return effect” on the brain, a consequence of imperfect working of the respiratory and other organic systems, a state of things analogous to that in the delirium of some cases of emphysema with bronchitis, and in some cases of cervical fracture dislocation of the spine.

Dr. Charlton Bastian many years ago expressed the opinion that the posterior lobes are the most important parts of the brain for intellectual purposes. Agreeing in this, I have supposed that disease of the right posterior lobe produces greater mental defect than disease of the left does; at least, in some cases of tumour of the right posterior lobe there has been what I have called Imperception—defect or loss of recognition. Imperception is psychologically the corresponding opposite of Inexpression; the latter is a name I would give to the condition in cases of what is called “motor aphasia.” It is true that disease of certain centres of the left cerebral hemisphere produces those highly special forms of Imperception which are called “sensory aphasia” (word blindness and word deafness); but in some cases of disease of the right posterior lobe there is, I think, general Imperception, an inability or a difficulty in the recognition of objects, places, and persons.

I have suggested²⁰ “that mental defect (imbecility) sometimes occurs with hemiplegia, in which the leg suffers more than the arm, and I believe that it occurs oftener when the left is the side paralysed.” I remarked this as one reason for being careful to note the side of the body in which spasm starting in one leg sets in. I have, however, since that was written, not taken up the question for special investigation. I now refer to cases of right hemiplegia, the arm suffering less than the leg. Trousseau,²¹ speaking of those cases of hemiplegia in which the arm recovers more rapidly than the leg does, remarks that the patient is worse off than when the reverse obtains. It is not quite clear that Trousseau refers to failure of intellect. I think he does, for he relates in illustration the case of a man—hemiplegic (right)—who died in a state of perfect imbecility, and he predicted that the woman whose case was the text of his lecture would die within the year “a thorough imbecile.” It is important to observe that the man had excruciating pain in the paralysed side, especially in the leg, and this symptom, also, Trousseau believed would follow in the woman’s case. The late Dr. Bazire, in a footnote to Trousseau’s lecture, speaks of the case of a patient who was seen in private practice by Dr. Ramskill, for right hemiplegia like that Trousseau spoke of. In less than a year this patient died “completely demented.”

I have thought that in cases of hemiplegia, I will say left for illustration, there is some very slight weakness of the lower part of the erector spinæ muscle on the right side, the

¹⁸ Raymond, *Hemic chorea*, 19 *Trans. Ophth. Soc.*, vol. 1, 1881, p. 98.

²⁰ *St. And. Grad. Assn. Trans.*, vol. III, 1870.
²¹ *Clinical Medicine*, vol. 1, p. 16; *New Syd. Soc. Trans.*

side of the cerebral lesion. Dr. Risien Russell and Dr. James Taylor have joined me in examining hemiplegic patients with regard to this question. We do not, however, as yet speak confidently on the matter. The examination is very difficult, and sources of fallacy are many. I state the hypothesis because I imagine that the muscle mentioned is supplied (I mean in part, of course) by intermediation of Turck's column from the same (right) half of the brain. In many cases of Friedreich's disease there is lateral curvature, presumably owing to paralysis of some region of the erector spinæ. In some cases of Friedreich's disease degeneration of Turck's column has been found. The cases of this malady reported on by Dr. Ormerod do not, however, show that this degeneration has been especially discovered, in those cases where there has been spinal curvature. I admit a serious discrepancy, and thus I do not conclude but merely state the hypothesis that that curvature is owing to paralysis of the erector spinæ from lesion of Turck's column.

A DISCUSSION ON PHAGOCYTOSIS AND IMMUNITY.

At the Pathological Society of London, March 1st, 1892.

The discussion on Phagocytosis and Immunity, which was adjourned from the last meeting, was resumed (Sir GEORGE MURRAY HUMPHREY, F.R.S., President, in the chair) by

V.—J. SYER BRISTOWE, M.D., F.R.S.,

Senior Physician and Joint Lecturer on Medicine at St. Thomas's Hospital.

DR. BRISTOWE approached the subject from a clinical point of view; he showed that the resistance of the body to the invasion of infective diseases was provided for in various ways: (a) mechanical, as the opposition of the skin and mucous membranes; (b) by inflammation with subsequent encapsulation or suppuration; (c) by active warfare or phagocytosis; (d) by unfitness of soil, etc. With regard to (c), he agreed with Dr. Burdon Sanderson's position as stated at the last meeting. Should the infective principle succeed in getting past these first barriers, they would enter the system along the blood vessels, or more commonly along the lymphatics as far as the first group of glands. He thought that cure occurred by the infective principle getting beaten at the mucous membranes or at the lymphatic glands; but these modes of spontaneous cure would not include the cure of the exanthemata after their generalisation, and it was in these cases especially that immunity most frequently arose.

He then contrasted various types of infective diseases, taking tubercle, diphtheria and typhoid, and small-pox as types of the different varieties. Local skin tubercle or lupus, instead of producing general tuberculosis, seemed to prevent it. In diphtheria and typhoid the chief symptoms were associated with the local lesions rather than with the generalised poison, which as a rule produced its effects after the subsidence of the local lesions. With small-pox and the other exanthemata the conditions were wholly different. Taking inoculated small-pox as an example, the poison appeared to be developed for nine days, with formation of the pustule and enlargement of neighbouring glands; then the generalised condition set in, with eruption on the third day. Immunity seemed to be acquired in the earlier stage of the disease, as it was remarkable that whilst the pocks were developing the poison from them was not absorbed by the body. Probably the pocks were really cut off from communication with the rest of the body by phagocytosis and by the inflammation which surrounded them. By vaccination the generalised disease that was produced and which gave immunity was comparable to the invasion period of small-pox, but he could not say how the immunity was caused. He suggested that it might be possible to avoid the local ill effects of vaccination by injecting the lymph deeply into the tissues or into the glands.

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PART I.—FACTS RELATING TO IMMUNITY.

BEFORE discussing the probability of one or other doctrine, it is well to have the facts clearly before our minds. The facts, then—to take the simplest case—are briefly these: that in non-protected animals virulent bacteria inoculated subcutaneously produce little or no local change, grow unhindered, and cause general infection; while in protected animals inoculation of the same bacteria is followed by a local leucocytosis at the point of injection, a certain degree of inflammation is set up, and general infection is prevented.

In virtue of some change in the body, that which was formerly capable of setting up a general disease can now only set up a local affection. What is the nature of this change? On the one hand, we have the bacteria with their powers of forming poisons undoubtedly capable in many instances of affecting the organism most injuriously. These poisons are of two kinds: (1) easily-diffusible substances of alkaloidal nature—toxines—whose mode of action on the organism is analogous to that of the vegetable alkaloids; and (2) less diffusible substances of proteid nature, whose nature is still very imperfectly known. So far as is known, however, their action resembles more that of ferments than of ordinary chemical poisons, inasmuch as it is lost on heating to a temperature of 50° or 60° C., at which the active properties of ferments generally are destroyed. Both these classes of poisons stand in the same relation to the bacteria, in so far as they are the special products of their activity, in the same way that nitrogenous products such as urea, or active proteid substances such as ptyalin or pepsin, are the products of the activity of cells of higher organisms.

In addition to these two groups of metabolic products formed by bacteria, there is another class, differing both in origin and action from the foregoing. These are also proteid bodies, having, so far as is known, the character of albumoses. These are substances—first described by Nencki in 1880—derived from the bodies of the bacteria themselves, so-called "proteins," for a knowledge of whose action we are indebted, perhaps, most of all to Buchner. They resist in a remarkable way the action of heat, withstanding when in a moist condition even boiling temperatures. Their most remarkable property, however, is their chemiotactic power, the power of attracting wandering cells, and inducing, therefore, a greater or less degree of leucocytosis wherever they happen to be present. Their action in this respect I hope to illustrate to you later on.

It is to be noted as a further difference between these two classes of bacterial products, the toxines and toxalbumins on the one hand and the proteins on the other, that the former are only formed, and are formed most abundantly, when the bacteria are active, the latter only, and most abundantly, when the bacteria are dying.

A further difference—an important physiological one—may be noted, namely, that while the former are responsible for the general symptoms of disease, the action of the latter is, in the first instance at least, mainly a local one. Without being entirely confined to the part where they are formed, the most important action of these proteins and the one which lends them their chief interest is the chemiotactic power above mentioned.

When we turn now from the invading bacteria to the organism thus attacked, we find that the means it has at hand to defend itself are of a twofold character. On the one hand there are the cells—especially those free lances of the body, the wandering leucocytes—having the power of seizing upon everything, animate or inanimate, possessing a less power of resistance than themselves, and, in virtue of this power, doing undoubtedly much useful work for the organism both in health and disease. The theory of phagocytosis, so beautifully and skilfully elaborated by Metschnikoff in the first instance, assumes, on the basis of many observations whose accuracy cannot be seriously called in question, that this power is exercised in a special degree by the cells in defending or protecting the organism against bacteria.

This is admittedly, however, not the only weapon possessed