REMARKS ON THE REPORT OF THE SECOND HYDERABAD CHLOROFORM COMMISSION.

By JOHN G. MCKENDRICK, M.D.,
Professor of Physiology in the University of Glasgow;

JOSEPH COATS, M.D.,
Pathologist to the Western Infirmary, Glasgow;

AND

DAVID NEWMAN, M.D.,
Surgeon to the Western Infirmary (Outdoor Department) Glasgow;
Members of the British Medical Association Committee on Anesthetics.

The Work of the Commission.—The Dangers of Chloroform.—Its Action on the Heart.—Liability to Sudden Fall of Blood Pressure.—Gradual Fall constantly observed.—Chloroform or Asphyxia?—The Relative Importance of Heart and Respiratory Failure.—Points of Agreement.

1. We desire, in the first instance, to congratulate the members of the Hyderabad Chloroform Commission on the completion of an investigation of great importance to humanity. It reflects much credit not only on the members of the Commission who carried out the experiments, but also on the Government of His Highness the Nizam, his Prime Minister Sir Asman Jah, and especially on Surgeon-Major E. Lawrie, whose zeal and energy originated and successfully carried out the Commission. The completion of a scientific investigation of such magnitude, and with the aid of all the refinements of a modern physiological laboratory in the capital of the largest native Indian State, is an event of historical importance, and may be regarded as an earnest of the time when East and West will co-operate for the advancement of science.

2. The report of the Hyderabad Chloroform Commission appeared in the *Lancet* of January 18th, 1890 (vol. i, 1890, p. 149). The Reports of the British Medical Association's Committee was printed in the *JOURNAL*, vol. i, 1879, pp. 1, 103, and 921; and in vol. ii, 1880, p. 957.

3. We have to thank Dr. Lawrie for kindly submitting to our inspection the kymographic tracings of blood pressure taken by the Hyderabad Commission. These convey an idea of the enormous amount of work done by the Commission, work involving great expenditure of time and energy, and demanding high technical skill. We delayed the present remarks till we should have the opportunity of examining these tracings, and we have made the examination with a view to adjusting our points of difference and bringing out our points of agreement.

4. The main point of difference between the Commission and the British Medical Association Committee has reference to the action of chloroform on the heart. This will be taken up afterwards; meanwhile, we may note that in our report we fully recognised the danger from failure of the respiration,—a fact which the Hyderabad Commission has omitted to allude to in referring to our report. Thus, in our report we say: "Chloroform may cause death in dogs either by primarily paralysing the heart or the respiration." "In most cases respiration stops before the heart's action." "The danger of death from stoppage of the respiratory functions must be borne in mind in every case in which anesthetics are given," etc. These sentences show that we recognised the danger to respiration. At the very beginning of our report we state: "Without going into detail, we may say that it soon became apparent to us that chloroform administered to dogs and rabbits has a disastrous effect on the respiratory centres; it is easy to kill one of these animals by pushing the chloroform till respiration is paralysed. In observing the rate of the heart during these experiments, it could often be determined by auscultation that its contractions were maintained after respiration had ceased. It was apparent, however, that even when failure of respiration was more directly the cause of death, the heart was to some extent simultaneously affected; and there were even cases in which the heart appeared to fail at least as soon, if not before the breathing."

It is evident from this that we regarded the danger to respiration as a proved, and, indeed, a well-recognised fact; and our special object was to investigate the question of how far chloro-

form was dangerous to the heart. The result of our inquiries was to convince us that danger to the heart is at least an occasional occurrence, and one to be kept in mind in watching a patient under the influence of chloroform. In summing up, we put the matter thus: "The chief dangers are (1) sudden stoppage of the heart; (2) reduction of the blood pressure; (3) alteration of the pulse-respiration ratio; and (4) sudden cessation of the respiration." In this enumeration we did not intend to place the phenomena in the order of their relative frequency or importance, although we admit the sentence might bear this interpretation were it not taken in connection with the statements quoted above from the beginning of the report. The question, then, narrows itself down to this. Does chloroform ever kill by paralysing the heart? We assert that it may do so; the Hyderabad Commission hold that it never does so, and that it always kills by paralysing the respiratory centres, or, in their own words, referring to experiments without recording apparatus: "In every case in which chloroform was pushed the respiration stopped before the heart."

5. Before entering on an examination of the Hyderabad observations, we may reiterate some of the points which our experiments seemed to bring out:—

(a) We showed that chloroform vapour has a paralysing effect on the muscular tissue of the heart, and indeed on all kinds of protoplasm, when directly applied. When the heart of a frog was exposed to the direct action of chloroform vapour, it "became rapidly weaker till it ceased beating." As regards the action on the mammalian heart, we make the following quotation from our report: "With a similar view, a method was devised for warm-blooded animals. Rabbits were first used, and afterwards dogs. The animal was anaesthetised, then the trachea was opened, a tube introduced, and artificial respiration begun by means of a double-acting pump (one cylinder forcing air in and another sucking it out). By an arrangement of india-rubber tubes, chloroform or any other anæsthetic could be introduced in the circuit between the pump and the trachea. It is to be understood that, in these experiments, the air passing into the animal's lungs was saturated with the vapour of the substance used. After artificial respiration had been set going, the heart was exposed by an incision in the middle line, which was carried by a pair of blunt scissors or bone-forceps through the ensiform cartilage and lower part of the sternum. This was effected generally with no serious bleeding. It soon became apparent that, when chloroform is given in this way, there is at once a most serious effect on the heart; the right ventricle almost immediately begins to distend, the heart presently stops, with the right ventricle engorged with blood. The heart has often, in the case of rabbits, virtually come to a standstill within a minute of the introduction of chloroform by the method described. The contrast was most striking when ether was used instead of chloroform, the other steps in the experiment being the same. Ether may be given for an indefinite period without interfering with the heart. We kept up artificial respiration with ether in the circuit for an hour, not including twenty minutes occupied in producing anaesthesia, and at the end of that time the exposed heart was beating as vigorously as at first."

It might be objected to these experiments that the dilatation of the heart, especially of its right cavities, may be due to asphyxia, but the fact that the heart is not affected in the same way by ether as by chloroform, although the other conditions of the experiment are precisely similar, meets that objection.

(b) During the operation of registering the blood pressure either by the mercurial or by the spring kymograph, we observed in several instances, both in rabbits and in dogs, and especially in dogs, even when the blood pressure was not very low, a sudden failure of the heart's action. This effect was a common occurrence during the administration of chloroform, especially in the earlier stages or when the animal was recovering; it rarely happened with ethidene, and we never observed it with ether. This effect is well seen in the blood pressure tracings from the rabbit, G and H. During deep narcosis, these sudden variations do not occur. We were quite aware of the fact that these effects might be held to be due to a reflex mechanism, irritation of sensory nerves of the outer openings of the respiratory passages stimulating the inhibitory centre of the vagi in the medulla, and thus retarding or even arresting the action of the heart. Whatever may be the explanation, the fact remains that at certain stages in chloroform narcosis there may be sudden falls in blood pressure due to interference with the heart's action, and no one will deny that this is a serious state of matters.

(c) We have seen in more than one instance the blood pressure of the dog become enormously reduced, and the pulsations become so infrequent as to be virtually ineffectual while respiration continued. A record of this experiment produced the "Glasgow trace," as it is termed by the Hyderabad Commission.² The explanation of this trace is of great importance, and on this point we venture to differ from the Hyderabad Commission, as will appear further on.

6. The principal points in which the Hyderabad Commission differ from us are (i) the question of how death occurs under the administration of chloroform, whether the danger is only of failure of the respiration, or whether there is danger also on the side of the heart; (ii) the explanation of the sudden effect on the heart sometimes occurring under the influence of chloroform, and observed equally by the Hyderabad Commission and by us, but ascribed by the Commission to asphyxia and by us to a peculiar, and apparently capricious, influence of chloroform.

(i) In the report of the Hyderabad Commission it is stated that chloroform "causes a gradual fall in the mean blood pressure..... As this fall continues the animal first becomes insensible, then the respiration gradually ceases, and, lastly, the heart stops." This is regarded as the normal course of events, and in confirmation of it reference is made to Experiments 168, 169, and 170. We have carefully examined these tracings, and others of a similar character. Like our own tracings, they show that, under the administration of chloroform, the blood pressure is continually lowered, and that when chloroform is pushed the depression is apt to assume what the Hyderabad Commission admit to be a "dangerous" degree. These tracings seem to us in themselves to show that chloroform when pushed has a disastrous effect on the heart as well as on the respiration.

In most of the experiments two different kinds of tracings were taken, one by Ludwig's and another by Fick's apparatus. The Ludwig curve shows more particularly the blood pressure, while the Fick tracing, taken while the Ludwig tracing is suspended, shows specially the excursions produced by the individual pulsations of the heart. What we notice, especially in 169 and 170, is that there is a gradual fall of the blood pressure, occupying four minutes in the one case and five and a half in the other. Fick tracings, taken at intervals, show not only a reduction of pressure, but a very striking diminution in the force of the pulsations. By the time the breathing stops the pressure is reduced almost to zero, and the Fick tracings, taken immediately after the cessation of the breathing, show the merest indication of movements in the heart; whose pulsations are reduced in number to less than half. So far as the efficiency of the heart is concerned in carrying on the circulation, it has virtually ceased to act by the time the respiration has stopped, and we are inclined to believe that the inefficiency of the circulation may be, at least in part, the cause of the cessation of the respiration—this opinion being based on the fact that the fall in blood pressure is so extreme before the respiration stops as to interfere with the proper nutrition of the respiratory centres.

(ii) In paragraph 30, section (8) of the Hyderabad Report it is said that "the effect of involuntarily holding the breath..... is much more remarkable, the pressure often falling with great suddenness, while the heart's action is markedly slowed." Further on, in Section (12), they say: "Complete, or almost complete, asphyxia, as by forcibly closing the nose and mouth, or closing the tracheal tube after tracheotomy, has an effect similar to but more marked than that produced by holding the breath, and the character of the tracing corresponds precisely to that produced by irritation of the peripheral end of the cut vagus. The pressure falls extremely rapidly, sometimes almost to zero, and the heart's action becomes excessively slow, or even stops for a few seconds. If the Fick trace of Experiment 148 be compared with the photographic reproduction of Trace A of the Glasgow Committee it will be seen that they are identical, and that the slow action of the heart with great fall of pressure, which the Glasgow Committee attributed to some capricious action of chloroform upon the heart, was undoubtedly due to asphyxia." A number of tracings are adduced by the Hyderabad Commission in confirmation of these statements, and these we have carefully examined, with results different from those arrived at by them.

In the first place, in Experiments 103, 119, and 157, quoted in Note 10 of *Lancet* Report, we have sudden falls of pressure; and opposite some of these, not all, there is the note "holding breath." Thus, in 103 (Ludwig), between Fick 20 and 21, there is a very sudden fall, at the bottom of which is noted "holding breath."

² See Trace A, *JOURNAL*, vol. ii, 1880, p. 962, which we have here reproduced.

Again, Trace 119, Fick 2, shows a sudden fall, and in the Ludwig trace we have a similar note. It is the same with 157, Fick 2, (not Fick 4, as in Report of Commission). But these sudden falls of pressure are not confined to occasions when the animal holds its breath.

An examination of Trace 157 is very instructive in this respect. Soon after the commencement of this tracing there is, as shown in the Ludwig trace, a sudden fall of blood pressure, with the note, "taking off gag he suddenly held his breath, and pressure fell." There was then a slight recovery of pressure, and trace Fick 2 was taken, which starts from a low pressure, and shows a tracing somewhat like our A. Further on in the tracing comes Fick 4, which is very like that of Fick 2, so like that the Commission in their Report have misplaced the numbers, but the animal is distinctly noted as "struggling, but not holding breath." It is noted, however, that chloroform is being given "with the cap closely applied." If we add to this that in the cases noted the fall of blood pressure seems to have been almost simultaneous with holding the breath, the effect on the heart can hardly be regarded as the result of asphyxia, as asphyxia is well known to induce reduction of blood pressure only after a considerable time. (See further on.)

Turning to the experiments referred to in Section 12, where the breathing was artificially interrupted, we have been astonished to find that the traces do not bear out the statement of that paragraph. For example, take Experiment No. 150. The following facts are noted in regard to it. (a) Near the beginning of the trace we find that "holding nose and mouth" produces a distinct fall, not nearly so abrupt or great as in our A, or as in observations under "holding the breath." (b) Again, at 11.55, pressure has greatly fallen under the influence of chloroform, which has rendered the animal insensitive, before the nose and mouth are stopped; the fall continues, but not with any approach to the rapidity of those previously mentioned under "holding the breath." (c) Further on, at 12.5-30, after the animal had partly recovered, and when chloroform is being given with "lots of air," and with the animal "just insensitive," stopping the nose and mouth produces a much more gradual fall than in the previous two occasions, apparently because the animal is less affected by the chloroform. (d) Again, at 12.9 30, the chloroform is pushed with the cap crammed over the nose, but the respiration is not obstructed, and there is a fall similar to that in b. (e) Still further on, at Fick 7, we have "mouth and nose closed," but there is scarcely any effect on the blood pressure, and very little on the pulsation. (f) At Fick 10, chloroform having been stopped awhile, holding mouth and nose produced little effect on the pressure, but distinct slowing of the pulse. After this the vagi are cut, and the experiment need not be followed further.

No. 151 brings out similar facts, namely, that when chloroform is pushed, whether the nose and mouth be held or not, the blood pressure falls, and there is the additional fact that this seems to depend very little on the action of the vagi. Thus, soon after the beginning of the trace there is the note "stop nose and mouth," which is followed by a slight fall. One minute after this the Fick tracing 3 shows great slowing of the pulse. Then the vagi are cut. Chloroform is given at 3.55, and there is the usual fall, to be followed by a rise when the chloroform is stopped. The pressure rises till 3.58, when Fick 4 is taken. After this the nose and mouth are again held, but there is little effect on the pressure for more than two minutes, after which the fall is somewhat rapid (from Fick 4 to Fick 6) till the nose and mouth are again set free. This shows the true asphyxia curve, the fall in pressure not occurring for two minutes after the respiration was obstructed.

No. 148 is mentioned as an example of asphyxia by obstructing the nose and mouth, and the tracing is described as "identical" with our A. We recognise a resemblance to our trace in the Fick tracings 2 and 6, but in these the chloroform is being pushed, and there is no obstruction to the respiration. The place where there is such obstruction is before Fick 17. At 3.54.15 we have "asphyxia by holding mouth," and there is a gradual fall for three-quarters of a minute, when Fick 17 is taken. The Fick tracing does not show the fall, and has no particular resemblance to our A, while the Ludwig trace shows that the fall here is, as in other cases of asphyxia, greatly slower than ours, taking three-quarters of a minute to accomplish a less fall than was attained in ours in about seven seconds. (Note that the drum in our observations revolved very much faster than in theirs. The time is given by a chronograph showing half-seconds in our Trace c.)

We turn now to our own tracings, from the examination of which the Hyderabad Commission infers that the sudden fall in blood pressure is due to asphyxia. It has been indicated above that the fall in blood pressure due to asphyxia is not sudden, but follows some time after the interruption to the respiration. This applies to our tracings; but, besides that, they show in their very form that there was here no asphyxia. In order that our statements may be followed we reproduce the Tracings A and C.

In Trace A it will be observed that the beginning of the fall is associated with what we take to be a respiratory curve, that is to say, after the fall has begun, as shown by the sudden dip, there is a gradual rise with five pulsations of the heart which is clearly identical with the respiratory curves further on in the trace, when the pressure is beginning to rise (see A, continued). It is to be noted that this tracing was taken at a time when the administration of chloroform had been stopped for two minutes.

If any doubt exists as to Trace A, none can exist as to Trace C. This records an observation on the same dog as Trace A, made on the same day after a partial recovery of the animal, and it forms a continuation of the same tracing. Two things will be observed in this tracing. In the first place, it is definitely noted on the sheet "Respiration Continues," although the heart is at a standstill. But, in the second place, the curve itself shows that there was no asphyxia. In the second block of C, there are the most obvious respiratory variations in the curve, and these continue right on till the rapid fall sets in. This tracing is so important that we may repeat here our original remarks on this observation:

"It is to be remembered that this animal got chloroform in the usual way, by a cloth saturated with the agent being held over his mouth and nose. He received no overdose, and the administration only lasted seventy seconds. As bearing on at least one mode of death under chloroform, the relation of the heart's action to respiration is of particular significance. The blood pressure is enormously reduced, and the pulsations have become so infrequent as to be virtually ineffectual, yet respiration continues. But respiration stops forty seconds after the heart has resumed, the pulsations being still, however, so ineffectual that the pressure is even *minus*. We believe that the legitimate inference to be drawn is that the stoppage of respiration was not due directly to the chloroform, the inhalation of which had ceased for about forty-eight seconds. It seems likely that the failure of the heart in the first instance, and the insufficiency of its subsequent pulsations, were the cause of the failure of respiration. In such a state of the circulation, the respiratory centres would probably be insufficiently supplied with blood, and be consequently liable to cease acting. In this case, if death had occurred, it would only apparently have been due to the failure of the respiration, the primary failure being that of the heart. To what extent this may apply to human cases we do not venture to speculate."

7. We now come to a very interesting point, namely, that of determining the relative effects of a diminished activity of the heart or a diminished activity of respiration in bringing about a fatal result. In this connection, the report of the Hyderabad Commission contains many valuable suggestions. We both observed that there is still a fall of pressure after the animal had ceased to inhale chloroform. Thus, in the first recorded experiment of the British Medical Association Committee, it is noted: "Chloroform was given, and during deep anaesthesia a cannula was introduced into the carotid artery, and connected with the kymograph. By the time connection with the kymograph was established, no chloroform had been given for about two minutes. On first making the connection, the pressure registered 104 millimètres, which may be regarded as nearly normal; but now, without any fresh dose, the pressure rapidly fell to zero, with a remarkable retardation of the heart."³ We quite agree with the Hyderabad Commission in the view that "this after-fall is probably due to absorption of a portion of the residue of chloroform in the air passages after the stoppage of the inhalation." The Hyderabad Commission, however, hold that "slowing or temporary stoppage of the heart in chloroform administration is not dangerous," and that the "controlling influence of the vagus on the heart is a safeguard, and that it is the exhaustion of the nerve which is dangerous." Their theory is that when the inhibitory action of the vagus (which is known to be intermittent and not continuous) is called into play, the heart does not beat so quickly nor so strongly, that less chloroformed blood is transmitted to the respiratory centres, and that, consequently, these centres are not then in danger of sudden

arrest. Further, that if the vagus irritation ceases, or if the vagus becomes exhausted, the heart "bounds on again," and "the blood then becomes quickly saturated with chloroform, and an overdose is at once conveyed to the nerve centres." This ingenious view has much to support it, and we think that much credit is due to the Hyderabad Commission for its suggestion, as it undoubtedly explains the beneficial action of atropine as an adjunct to chloroform administration. We would remark, however, that in our opinion the Hyderabad Commission attach too much importance to it, and that it does not account for the facts in each case. For example, we observed in one case, after stoppage of respiration, while the heart continued beating, that respiration was spontaneously resumed; and we supposed that by the cessation of respiration, less chloroform was taken into the blood, so that in a short time the respiratory centre recovered. In this case the heart was pulsating vigorously after stoppage of respiration, but, as the chloroform in the air passages was taken up and quickly eliminated and decomposed in the blood, the respiratory centres recovered. When, however, they recovered, breathing recommenced, more chloroform was introduced, and again there was danger to the respiratory centres and to the heart. Chloroform, no doubt, is taken from the pulmonary air cells by diffusion, and this will be facilitated by inspiration, possibly by expiration; at all events, the rapidity of absorption will not be the same when the pulmonary air cells are quiescent as when they are expanding and contracting in inspiration and expiration. Thus the movements of respiration will affect the amount of chloroform absorbed, and, if respiration becomes feeble, or even ceases, less chloroform will be taken up and time may be allowed for both the respiratory centres and the heart to recover. Thus the number and volume of the respiratory movements affect the quantity of chloroform absorbed and the number and volume of the heart beats affect the quantity of chloroform sent to the nerve centres. It is clear, therefore, that the problem is more complicated than as stated by the Hyderabad Commission, and that the physiological action will depend on so many factors as to make it extremely unlikely that the course of events will be the same in each case. Thus we have (1) the condition of greater or less asphyxia, as effected by the quantity of air mixed with the chloroform vapour; (2) the occurrence of any inhibition of the vagus, as affecting the number and volume of the heart beats, and thus the amount of chloroform reaching the nervous centres; (3) the number and amplitude of the respiratory movements, as affecting the amount of chloroform absorbed into the blood; (4) as we hold, the specific action of chloroform on the muscular structure and intrinsic nervous mechanism in the heart; and (5) the influence on the vasomotor centre, as a factor in producing the great fall in blood pressure. We think the Hyderabad Commission attach too much importance to one common mode of death, failure of the respiratory centres, and while we agree generally with their conclusions, which in many respects are similar to our own, we consider it unwise and unsafe in practice to pay no attention to the state of the circulation, and to observe respiration alone. We also consider it unwise to convey to the public, even through the profession, the notion that the administration of chloroform is a proceeding in which there is practically no danger. At the same time, we thankfully admit that the number of deaths following the use of so potent an agent has been remarkably small, even in the hands of those who pay little or no attention to the condition of circulation. As a matter of common prudence, and especially seeing that when respiration fails we can employ artificial means for its restoration, while if the heart fails, little or nothing can be done to avert a fatal issue, it is incumbent on every one giving chloroform to watch both the pulse and the breathing.

It may here be noted that our observations are in complete accord with those recorded by Drs. Wood and Hare, of the University of Pennsylvania, published in the *Medical News* of February 22nd, 1890, and reprinted in the *Provincial Medical Journal*, April 1st, 1890. The results of numerous experimental observations are embodied in the following paragraph:

"The experiments which we have given show that chloroform acts as a powerful depressant poison upon both respiration and circulation, that sometimes the influence is most felt at the heart, and death results from cardiac arrest; that in other cases the drug paralyzes primarily the respiratory centres, whilst in other instances it seems to act with equal force upon both medulla and heart. So far as practical medicine is concerned, it makes little difference whether the heart stops before or just after respiration, so that those cases in which cardiac and respiratory arrest are

³ JOURNAL, vol. ii, 1880, p. 962.

almost simultaneous are, for the purposes of the clinician, the same as those in which heart arrest precedes respiratory paralysis. Finally, the general results of our new experiments also coincide with our previous experience in the laboratory, and with what we believe to be the general belief of physiologists—that cardiac arrest is specially prone to occur when chloroform is administered rapidly and in a concentrated form.”

8. It will probably serve a useful purpose, seeing that the points on which we disagree with the Hyderabad Commission have been set forth in some detail above, if we now state in a summary form the more important matters on which we are agreed.

(I) We are agreed that death from chloroform occurs by failure of respiration, and that this is probably the most frequent mode of death.

(II) We are agreed that chloroform causes a gradual fall in the blood pressure as registered by kymographic tracings from the carotid artery. This is the normal effect of chloroform.

(III) We are agreed that when chloroform is pushed this gradual fall may be so great as to become in itself “dangerous.” This is admitted in Paragraph (8) of the Hyderabad Report, where they state that after an animal has been involuntarily holding its breath “the gasping respiration which succeeds then causes very rapid inhalation of chloroform, with immediate insensibility and a rapid fall of blood pressure, which quickly becomes dangerous.” (The italics are ours.)

(IV) In addition to this, which we may call the normal effect of chloroform on the heart and blood pressure, both of us observed peculiarly sudden and unexpected falls of pressure, with slowing of the heart. We are agreed that this phenomenon occurs, and the Hyderabad tracings show that it is frequent. We differ as to the cause of its occurrence, the Hyderabad Commission ascribing it to asphyxia, while we contend that neither in the time of its occurrence after holding the breath nor in its general characters does it correspond with the fall of pressure due to asphyxia. Whatever be the explanation, the occurrence is in itself sufficiently serious, and should not be minimised as forming one of the sources of danger in the administration of chloroform.

THE CROONIAN LECTURES ON CEREBRAL LOCALISATION.

Delivered before the Royal College of Physicians of London.

By DAVID FERRIER, M.D., LL.D., F.R.S.,

Physician to King's College Hospital, and to the National Hospital for the Paralysed and the Epileptic, Queen Square.

LECTURE II.

MR. PRESIDENT AND GENTLEMEN.—I will now invite your attention to a brief consideration of the phenomena of electrical irritation of the brain of the monkey, more especially as determined by my own experiments, and those of Horsley, Schäfer and Beever, which, though in all essentials confirming mine, have been worked out with more elaborate detail and minuteness.¹

Beginning anteriorly we find that what is generally termed the prefrontal lobe—that is, all in advance of a line drawn at right angles to the anterior extremity of the precentral sulcus—gives no, or very doubtful, response to electrical stimulation.

Between this line and that of the precentral sulcus continued upwards to the longitudinal fissure, there is a region or area (1, 2, Fig. 5; Figs. 6 and 7, head), stimulation of which causes opening of the eyes, dilatation of the pupils, and movements of the head and eyes to the opposite side. This area has been further differentiated by Beever and Horsley, according to the primary movements which result from minimal stimulation of the points indicated on their diagram (Fig. 8). The corresponding region in the brain of the dog is (12, Fig. 9). No similarly differentiated centre is seen in the cat (Fig. 10) or rabbit (Fig. 11).

At the upper extremity of the central convolutions (ascending frontal, ascending parietal, and postero-parietal lobule) (1, 2, Fig. 5; leg Figs. 6 and 7), and extending over the margin of the hemisphere into the posterior part of the marginal convolution, or paracentral lobule, electrical stimulation causes movements of the lower extremity. The movements vary according to the position

of the electrodes on this area. Behind the fissure of Rolando the movements are chiefly, or exclusively, of the foot or toes. Anterior to the fissure of Rolando they are combined with flexion of the leg and thigh. With minimal stimulation the movements may be still further differentiated (Fig. 8), and, in particular, the great toe can be excited to movement separately by stimulation at the upper extremity of the fissure of Rolando. The corresponding region in the brain of the dog, cat, and rabbit, is indicated by 1, Figs. 9, 10, 11.

Below the leg area, and partly in front of it, and occupying the middle third, or rather two-fourths of the central convolutions, there is a region stimulation of which causes movements of the upper extremity (3, 4, 5, 6, a, b, c, d, Fig. 5, and arm, Fig. 6). In this area it is possible to differentiate, more or less completely, movements of the upper arm (protraction and retraction); movements of the forearm (flexion, supination, etc.); and of the wrist, fingers and thumb. The proximal movements are represented most in the upper part of this region; the distal movements, that is, those of the fingers and thumb, most at the lower part.

By minimal stimulation at the lower extremity of the intraparietal sulcus the thumb may be individually thrown into the action (Fig. 8). The corresponding region in the brain of the dog is that indicated by the numerals 4 and 5 situated on the post-crucial division of the sigmoid gyrus (Fig. 9), and by the same numerals on the brain of the cat (Fig. 10), together with a situated on the anterior extremity of the second external convolution. Stimulation of this latter point causes protrusion of the claws; an action comparable to the movements of the wrist and fingers excited from the lower part of the ascending parietal convolution in the monkey. The corresponding region in the brain of the rabbit is indicated by the same numerals (4, 5, Fig. 11).

Fig. 5.—The left hemisphere of the monkey. 1. The opposite hind limb is advanced as in walking; 2, flexion with outward rotation of the thigh, rotation inwards of the leg, with flexion of the toes; 3, the tail; 4, the rotation inwards of the leg, with flexion of the toes; 5, the tail; 6, the opposite arm is adducted, extended, and retracted, the hand pronated; 7, extension forwards of the opposite arm; a, b, c, d, movements of the fingers and wrist; 8, flexion and supination of the forearm; 9, retraction and elevation of the angle of the mouth; 10, elevation of the ala of the nose and upper lip; 11 and 12, opening of the mouth, with protrusion (9) and retraction (10) of the tongue; 13, retraction of the angle of the mouth; 14, the eyes open widely, the pupils dilate, and head and eyes turn to the opposite side; 15 and 15', the eyes move to the opposite side; 16, pricking of the opposite ear, head and eyes turn to the opposite side, pupils dilate widely.

Below the arm area, and occupying the lower third of the central convolutions, there is a region stimulation of which causes movements of the face, mouth and tongue. In the upper part of this area can be differentiated centres for movements of the upper facial muscles (7, 8, Fig. 5) in front of, and platysma (11) behind the fissure of Rolando. The corresponding region in the brain of the dog, relatively much larger than in the monkey, is indicated by the numerals (7, 8, Fig. 9), and the same indicate the homologous regions in the brain of the cat (Fig. 10), and rabbit (Fig. 11). In the lower portion excitation causes movements of the mouth and tongue; protrusion of the tongue being generally caused by stimulation anteriorly (9, Fig. 5), and retraction by stimulation posteriorly (10, Fig. 5).

It has further been demonstrated by Semon and Horsley² that excitation of the lower extremity of the ascending frontal convolution causes phonatory closure of the vocal cords. The phonatory closure of the vocal cords was first demonstrated ocularly in the dog, on irritation of the pre-sigmoid region, by Krause,³ though I

² On the Central Motor Innervation of the Larynx, JOURNAL, December 21st, 1889.

³ Pflüger's Archiv., 1883.

¹ Horsley and Schäfer, *Phil. Trans.*, B. 20, 1883; Beever and Horsley, *Phil. Trans.*, B. 1890.