ON CERTAIN TREMORS IN ORGANIC CEREBRAL LESIONS.

BY GORDON HOLMES, M.D.

Resident Medical Officer, National Hospital.

THERE is perhaps no symptom in neurology whose anatomical basis or the physiology of whose production is less understood than those involuntary movements which, though varying in their character and accompanying conditions, are collectively known as tremors. Their occasional association with various gross organic lesions of the central nervous system has been recognised and described for years, but, on the one hand, indefinite and incomplete clinical characterisation, and on the other unsatisfactory and often defective description of the localisation and nature of the pathological lesion, has made a study of the cases unproductive of tangible results.

Owing to the loose way in which the term tremor has been employed in the literature of the subject, it seems advisable to offer at once such a conventional definition as will serve as a basis for the more detailed description of its several characteristics. I would suggest that the term tremor be used to denote a clinical phenomenon consisting in the involuntary oscillation of any part of the body around any plane, such oscillations being either regular or irregular in rate and in amplitude, and due to the alternate action of groups of muscles and their antagonists. If such a definition be accepted it becomes obligatory in describing the symptom to note the regularity or irregularity of the range and of the rate of its component oscillations. Here, too, emphasis must be laid on the importance of detailing exactly what movements are comprised in a particular tremor. A tremor may be simple or compound; in the former case only one group of muscles and its antagonists

being involved, in the latter the resulting movement being the effect of the action of several groups and their antagonists. For instance, flexion and extension of the fingers may coincide with pronation and supination of the forearm. In such cases the study of the condition evidently resolves itself into the study of the individual simple movements.

The graphic representation of the oscillations as first employed by Gowers, or of the muscular contractions by some form of ergograph, is advisable, generally almost necessary, for a complete study of all clinical tremors, and direct tracing of the movements is when possible preferable to tambour records as being more accurate. This method has been employed in the examinations of all the cases here recorded as well as in that of a number of other cases which have been carefully studied for the purpose of contrast and comparison. When the tremor is compound it is necessary in taking a tracing to mechanically check all but the one movement which is being studied, or to adopt some device to exclude the complications introduced by other movements.

In addition to the detailed description and graphic record of the movements of which the tremor is composed, it is important to note the influence of volitional movement, of attempted voluntary inhibition, of sleep, and of psychical rest and activity.

The cases recorded in the paper presented clinical symptoms of considerable similarity, and the evidence thus afforded suggested a common site for their pathological lesions, a suggestion which was verified in the two cases examined *post mortem*. The aim of the paper is to give a concise clinical description of the cases, to ascertain from direct and indirect evidence the nature and position of the lesions, to attempt to exactly define the essential factor in the lesion, to discuss the possible pathogenesis of the tremor, and finally, to compare and, contrast the cases with identical or similar ones collected from the literature.

I must first express my indebtedness to Dr. Buzzard, Dr. Hughlings Jackson, Dr. Ferrier, Dr. Ormerod, Dr. James Taylor, and Dr. Risien Russell, for permission to use the cases I have observed under their care in the National

Hospital, and to Dr. Farquhar Buzzard for having kindly supplied me with the description of the lesions which he, as pathologist, found in the cases which were examined *post mortem*.

Case 1.—R. E., the first case observed, was a healthy-looking woman of 59 years, with an excellent family history, and no history of previous illness, who came under the care of Dr. Ormerod in July, 1903. Four months previously she suddenly and without loss of consciousness became unable to walk and found her left arm useless. She was taken to an infirmary, where she slowly regained the power of walking, but has never since been able to get about as she formerly could. She also complained of the left arm having remained "useless," though she was able to move it about quite well, that it became quite unsteady when she attempted to do anything with it, and that when even at rest it frequently shook. She had not been able to read since the onset of this condition, and has had diplopia. There was no headache, vomiting, or other symptom in the history of her illness which could raise the suspicion of cerebral tumour.

On examination her visceral organs were found normal, but her pulse tension was unnaturally high, though no other evidence of renal disease could be detected. There was no psychic impairment, but she was abnormally emotional, and frequently burst into tears or laughter without adequate cause. Her vision was fair and the visual fields were uncontracted, but she was unable to read owing to paralysis of accommodation. There was also complete paralysis of the upward movement of both eyes, and the downward movements were defective, but the range of lateral excursion and convergence remained good. There was also marked bilateral ptosis, with compensatory wrinkling of the forehead in the attempt to look up. Both pupils were inactive to light stimulation, and contracted very little and sluggishly on convergence. Since then there has been slight return of the upward movement of the left eye, but the palsy of the levators of the right remains complete. The range of downward movement is much increased; at present it is almost normal. Her face was stiff, fixed and expressionless, and there was little change of expression as she conversed, but the voluntary movements were all perfect, and the associated movements good. There was, however, very little movement as she attempted to smile, and those which occurred when she laughed or wept were slow and stiff. The speech, too, was monotonous and expressionless. The mask-like facial expres-

sion and the monotonous and toneless articulation gave to the case, as many who saw her remarked, the appearance of paralysis agitans.

When she first came under observation there was definite paresis of the left limbs, with some rigidity, brisk deep reflexes, and an extensor plantar response on the same side. The right limbs were then normal in every respect, and of good power. The left hemiparesis soon disappeared. and the plantar extensor response was replaced by one of the normal flexor type, but the slight degree of rigidity has remained unaltered.

In walking both limbs and trunk were held stiff, without any swing or play of movement; she shuffled along with short steps in an uncertain manner, and turned *en bloc*, so that her gait, though neither reeling nor ataxic, appeared affected out of all proportion to the slight impairment of power of the lower extremities. The left hand was generally held in the interosseal position, the fingers extended at the distal and partially flexed at the metacarpo-phalangeal joints, with the thumb opposed to the index finger. There was no other peculiarity in the position of the limb. The whole arm was slightly rigid; there was almost uniform and constant resistance to passive movement through its whole range. The voluntary power of the various movements was, as compared to the corresponding of the right limb, only little feebler.

Except when the limb was at perfect rest and so supported that each segment bore its own weight, there was constantly slow clonic tremor of one or other part of it, but more marked at the distal than at the proximal joints. Frequently the adducted fingers were flexed and extended at their basal joints, the index finger rubbing against the opposed thumb, which was in synchronous tremor. Often it was flexion or extension of the hand at the wrist, or flexion and extension, but more frequently pronation and supination, at the elbow. Movements were less frequently visible at the shoulder.

Similar tremor was occasionally to be observed in the left lower extremity, and, as in the arm, more frequently at the distal than at the proximal joints. It most often took the form of extension and flexion of the foot.

The character of the tremor was constant, no matter in which portion of either limb it was observed. It was remarkably regular in rate, and varied very little in amplitude, so that the movement of the limb, as long as only one group of muscles was involved, was essentially regular and rhythmical, but as more than one group was frequently at one time in action, the resultant

movement was often a compound tremor. It was slow in rate, from 2½ to 3 oscillations per second, and of considerable amplitude. (Tracing I.)

It always ceased during sleep and when the limb was allowed to lie at rest, so supported that each portion bore its own weight. If any part of the limb was allowed to hang passively (as the hand when the limb was held up by the forearm), the tremor immediately began at the most proximal joint of the unsupported portion. It was increased by any excitement or agitation on the part of the patient, and by movement of the opposite limb. The movements could only be inhibited for a very short time. Voluntary movements of the limb were complicated by wide irregularities of the intention tremor type, but there was no other affection of co-ordination. There was no alteration of any form of sensation. The patient's condition still, now fifteen months after the onset of the illness, remains practically unaltered.

Diagnosis.—The existence of such definite ocular palsies indicates disease in the mid-brain, and the sharp differentiation of the movements affected points to direct involvement of the oculo-motor nuclei, the lesion extending more to the right than to the left of the middle line. The sudden onset of the condition indicates a lesion of vascular origin.

Case 2.—A. R., a woman aged 37 years, came under the care of Dr. Ormerod in November, 1903, complaining of uselessness of the right limbs, affection of gait and double vision. Her family history and previous health were good. Four months previously she had fallen down a flight of stairs, bruising and cutting the left side of her head over her ear. She lay unconscious for two hours, and had to keep her bed for a few days. Then she noticed diplopia on looking below the horizontal, the images being one above the other. Since then, too, her right arm has been more or less useless; "she didn't seem to have the power to do anything with it;" she has not, for instance, been able to use it in dressing her children, though there was no loss or limitation of any movement. Three weeks after the accident the right upper extremity began to shake, and all its movements became very irregular. The tremulousness of this limb has gradually increased till the present.

It was a month after the accident that her walking first was affected, and since then it has rather rapidly become worse. She also complains of the right leg shaking. There have not been any aphasic symptoms associated with this right-sided affection. She spontaneously remarks that she has been very low-spirited, and has frequently wept without cause during the illness.

The patient is a dull, stupid woman, poorly educated but extremely emotional, frequently weeping without adequate or any cause, and in the same way occasionally bursting into uncontrolled laughter. Her visceral organs were normal. She occasionally suffers with headache, but there was no optic neuritis or history of vomiting.

Her distant vision was normal, but there was paralysis of accommodation of the left eye, so that she could not read with it as she formerly could. On looking up, the left eye evidently did not move so well as the right, and there was diplopia, due to weakness of both elevators. The downward movement of the left eye was also affected, and the patient had diplopia on looking below the horizontal plane.

The lateral movements were unimpared, there was no ptosis and the pupils, which were equal, reacted well to light and on accommodation. There was no appreciable difference between the two sides of the face when at rest or in voluntary movement, but in emotional expression the right side moved distinctly less than the left. Both sides of the face were, however, rather fixed and expressionless as she conversed. The musculature of the limbs was fairly well developed for a woman of her size, and the left limbs seemed normal in all respects. On the other hand there was slight rigidity and relative weakness of the right limbs, but no limitation of the range of movement. There was also a marked slowness in starting every voluntary movement, and in exerting the full possible force, which was then not well maintained.

Both right limbs were affected by tremor when they did not lie at perfect rest with their muscles completely relaxed, but it also came on when each portion of the limb was not so supported as to bear its own weight. Thus, it was rarely to be observed as the limbs lay in bed and the patient was quiet and unexcited. It might occur at any joint, but in both arm and leg was more frequent at the distal. The most constant movement was flexion and extension of the hand or of the fingers at the metacarpo-phalangeal joints, but there was also often adduction and abduction of the fingers, and occasionally the thumb might be moved against and simultaneously with the forefinger. In the leg flexion and extension of the ankle was most frequently observed, also similar movement of the toes, but various movements at the more proximal joints were often present.

The tremor was generally compound, that is, it was rarely limited to one group of muscles and their antagonists, so that the limb was as a rule simultaneously moved at two or more joints.

It never persisted for long in any group of muscles. The clonic contractions of each group of muscles involved were essentially regular in rate but relatively slow, from 3 to 3½ per second, and the range of the movements was more or less regular but considerable, *i.e.*, the tremor was slow and coarse. It ceased everywhere during sleep and was increased in amplitude but not in rate by excitement or agitation and by forcible movement of the fellow limb. The patient was unable to check it voluntarily except by allowing the limb to fall relaxed in perfect rest. There was marked intention-tremor of both right limbs, *i.e.*, abrupt deviations from the direct line of movement increasing towards the completion of the voluntary act.

When admitted to hospital she was unable to walk alone, though the strength of each lower limb was good enough to permit it, but she was soon able to get about the ward without assistance. Then she walked with short shuffling steps and body bent forward and held remarkably stiff. Though there was practically no tendency to fall, she was very reluctant to walk without support or assistance, being apparently afraid to trust her weight on her right foot, though she could to order stand on it alone for a considerable time. She did not reel or stagger or drag either foot. There were no definite sensory changes. The deep reflexes were exaggerated in the right side and extension of the great toe resulted from stimulation of the right sole.

Diagnosis.—In this case the hemiplegia alternans superior, right hemiparesis with affection of part of the left oculo-motor nerve, indicated a lesion in the left side of the mid-brain, which, from the mode of onset and course, was probably of vascular origin.

Case 3.—R. T., a strong aud robust-looking man of 21 years of age, was admitted under the care of Dr. Buzzard, in February, 1904.

His health had been excellent until eight weeks previously, since when he had suffered with intense occipital headache and vomiting, and had staggered like a drunken man, always stumbling and falling to the left. Some time later his left arm became unsteady when he tried to use it, and his sight began to deteriorate. Diplopia also developed, and he was noticed to have a squint, "the left eye turned in." He also complained of attacks of giddiness for some weeks, in which he felt inclined to fall to the left, and had the sensation of translation of objects in front of him from left to right (clockwise).

He was found on admission to be in a very weak, almost collapsed, state, and was very drowsy and inattentive, and consequently difficult to examine.

His hearing was not affected, though he complained of tinnitus in his left ear; his vision was very much deteriorated, and he had extremely intense optic neuritis evidently of considerable duration. There was complete paralysis of the left external rectus, and considerable weakness of the right. The inward and downward movements of the eye-balls were unaffected, but the upward movements of each eye were considerably limited. Coarse nystagmus resulted on lateral movements, slower and coarser in the attempt to look to the left than to the right. There was slight paresis of the left side of the face, but no interference with the functions of the other cranial nerves.

The left limbs were definitely weaker than the right, and were, in addition, wildly ataxic in voluntary movements. He was unable to walk alone, with support reeled and staggered about. All deep reflexes were absent, and plantar stimulation gave flexor responses. Sensation was not affected in any part of the body.

From these symptoms a tumour of the cerebellum, chiefly in the left lateral lobe, was diagnosed, and Sir Victor Horsley, who was called in, decided to make an attempt to remove it two days after the patient's admission to hospital. There was found to be enormous increase of the intracranial pressure, but no tumour could be found in exploring the cerebellum. As, however, the pressure suddenly fell and the brain, which was exposed, collapsed and some fluid escaped on cutting into the left lateral lobe of the cerebellum, it seemed probable that a cyst had been ruptured. The patient's condition improved very much after the operation, and most of the neuropathic signs began to disappear.

Three weeks later, however, he again became drowsy and weaker, and a new symptom slowly developed. From this time till his death, about three weeks later, there was almost constantly tremor in all four limbs. It only ceased during deep sleep, or when the muscles were quite relaxed and the limbs so supported that each segment bore its own weight. The tremor commenced at once when any of the muscles were put in tension or brought into action, as when part of either limb was allowed to hang over the edge of his bed, or when it was held up in the observer's hand. It was easily made out that the series of oscillations were due to alternate contraction of the one group of muscles and its antagonists, *i.e.*, that the movements comprised a true tremor. If the limb were left in a suitable position it seemed as if the tremor

would persist indefinitely. It was forcible and not easily checked, and showed very little tendency to overflow into other groups of muscles when passively stopped in one set. As two or more movements might simultaneously occur, the resultant movement of the limb was often compound. The upper extremities were more affected than the lower, and the left limbs very much more than the right. In the upper limbs the movements most frequently observed were flexion and extension or pronation and supination of the elbows, flexion and extension of the wrists, and flexion and extension or abduction and adduction of the fingers, which generally remained extended at interphalangeal joints. In the lower extremities flexion and extension of the ankles and similar movements of the toes were the most frequently present, but there was also often similar oscillations of the thigh round the hip joint and of the leg at the knees.

The tremor was in every part regular in rate, about five to six oscillations per second, and the rate did not seem to vary, no matter what part of any limb was affected. It may be described as coarse, *i.e.*, of large amplitude, and the range of oscillation often changed in a more or less rhythmical manner, *i.e.*, the range of successive oscillations would slowly increase to a certain point and then slowly decrease. (Tracing II.). Consequently the tremor must be described as irregular in range. He was unable to voluntarily inhibit the tremor, and its amplitude was increased by any excitement or agitation, or by forcible movement of the opposite limbs. The finer voluntary movements, too, were complicated by ataxia and irregularity of the intention-tremor type, so that he scarcely found it possible to bring his hand to his face.

With the increase of the drowsiness and general feebleness all his limbs became weaker, the left more so than the right, and at the same time rigid or rather stiff, so that they offered considerable resistance to passive movement. Some general loss of sensation on both sides of the body was also observed, and later Babinski's sign was obtained on plantar stimulation.

Some difficulty in swallowing developed towards the end, his articulation became almost unintelligible, and he slowly lost all power of movement of the eye balls. As the general weakness progressed the tremor became more feeble, yet it persisted in some degree till his death.

Diagnosis.—When the patient first came under observation there was every justification for the diagnosis of a left-sided cerebellar tumour, but the later bilateral spastic symptoms and involvement of the oculo-motor nerves pointed to extension of the growth to the mid-brain.

At the autopsy a large tumour was found lying in the dorsal half of the mid-brain which extended into the thalamus, destroying the dorsal and medial nuclei of each side in their caudal halves more extensively on the left than on the right side. There it extended a short distance into the hippocampal gyrus, but on neither side reached farther forwards than the middle commissure.

Posteriorly its end lay in and almost filled up the upper half of the fourth ventricle, and extended into and involved the left lateral lobe of the cerebellum and the neighbouring portion of the middle lobe.

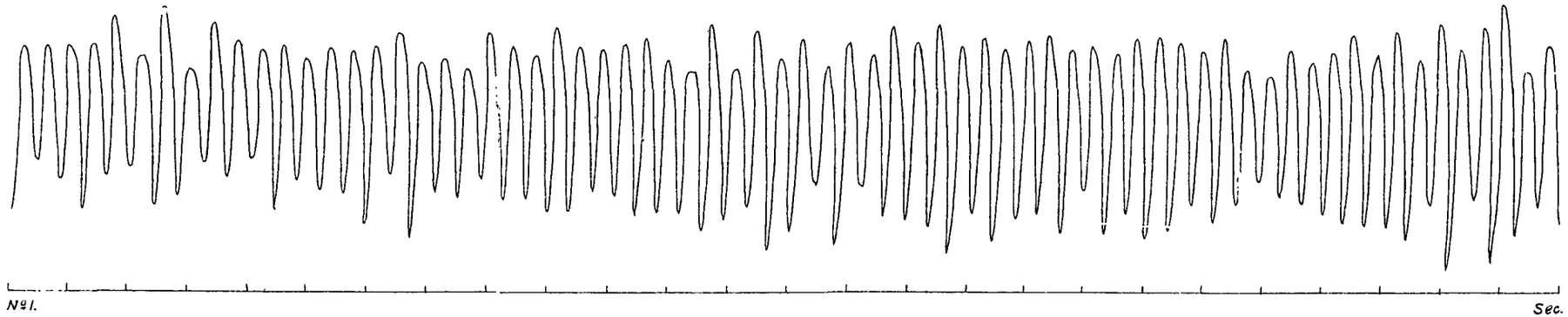
The tumour was well limited and did not infiltrate the structures neighbouring those it destroyed. It did not reach nearer than 1 cm. to the pyramidal tracts in any part of their course.

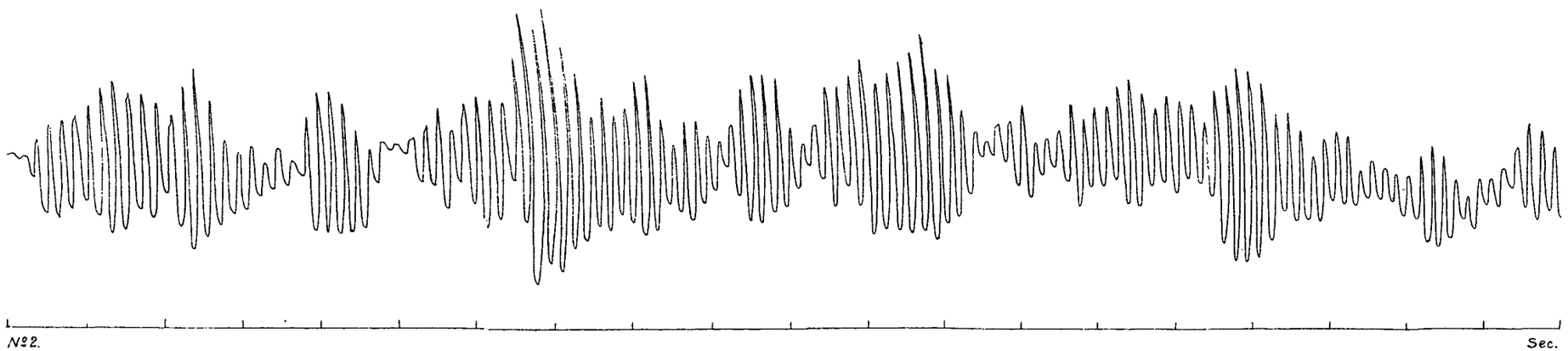
In the thalamus the internal and dorsal nuclei were alone destroyed, the ventral and lateral and the internal capsule apparently remaining intact. The greatest amount of destruction was in the mid-brain, where practically nothing remained of the tegmentum and tactal region. It seemed as though the tumour lay in the aqueduct of Sylvius and destroyed the surrounding tissues by expanding, but the pes pedunculi, though flattened out, appeared unaffected. Thus it destroyed the dorso-caudal part of each thalamus, the tectum and tegmentum of the mid-brain, including superior cerebellar peduncles and red nuclei, which were unrecognisable, and posteriorly involved the left lateral lobe of the cerebellum and the adjacent portion of the vermis.

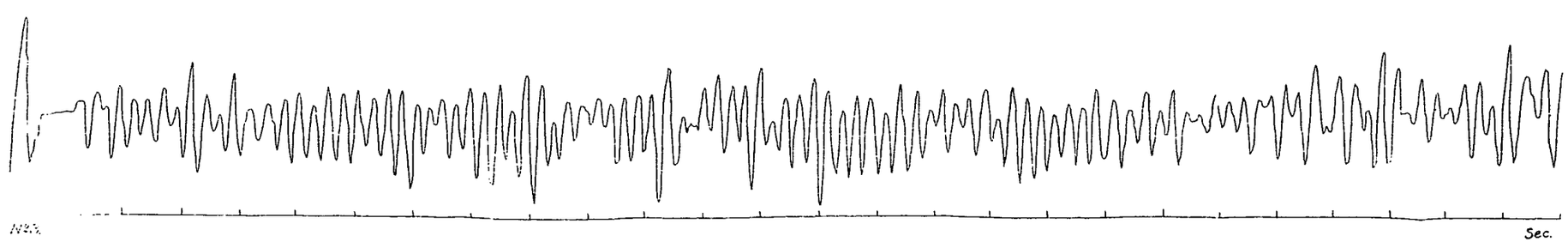
The pons varolii, medulla oblongata and spinal cord were investigated by Marchi's method. At the level of the lower part of the pons there were very few degenerated fibres in the pyramids, but considerable degeneration marked the position of the rubro-spinal tracts. Sparse, scattered black spots indicated a slight degree of diffuse degeneration, probably pressure effect.

In the medulla there was only degeneration in the position of the rubro-spinal tracts, and in the cord some degeneration of large fibres, probably of the same origin, was visible in the lateral columns, and, in addition, degeneration in the dorsal columns of the type frequently met with in cases of cerebral tumour.

Case 4.—J. R., a boy of 6 years, was admitted under the care of Dr. Ferrier, in September, 1903. There had been gradually progressing weakness of the right limbs of three months' duration, with consequent difficulty in walking and reluctance to use the right hand. No facial weakness or







Hale and Danielsson, Ltd., Del. and Lith.

abnormality was observed, but a squint was noticed six weeks previous to admission.

Since the weakness of the right arm became marked his mother had noticed that it was very unsteady and tremulous in voluntary movement, and that it occasionally would shake even when at rest. He had suffered much with headache, generally referred to the back of the head, and frequently vomited during the course of the illness. There had not been any affection of speech and no fits.

He was found to be a strong and healthy-looking child and bright and intelligent. His sight and visual fields were good, but intense optic neuritis was present. His head was constantly held inclined to the right and rotated to the left, so that the right occiput approached the right shoulder, while his eyes were generally in conjugate deviation to the left. It was very difficult to make him look to the right, and in so doing some weakness of the right external rectus became visible, and apparently diplopia resulted, as he tried to cover one eye with his hand. Movement of both eyes to the left was fully possible, and the vertical movements and convergence were also good, but there was coarse nystagmus on looking to the left. The pupil reflexes were normal. The right side of the face scarcely moved so fully as the left on voluntary effort, and there was some relative weakness of the right limbs but without any rigidity. All movements of the right arm were very irregular and ataxic, and some coarse and rapid tremor affecting one or any group of muscles appeared when the limb was handled or when he was asked to perform any strong movement with the left arm. The tremor was rapid: from tracings the rate seemed to be about 4 or 5 oscillations per second, and while it was limited to one group of muscles regular in range.

The distal and proximal muscles were about equally affected. The child was unable to check it voluntarily, and it was always much increased by any excitement or agitation, as when he wept. There was a slight degree of right hemianæsthesia, but the deep reflexes were about equal on the two sides, though a typical Babinski's sign was obtained on the right.

The child became drowsier while under observation, suffered considerably with headache and vomited almost daily. Within a fortnight the upward movements of both eyes were lost, and the pupillary light reaction became very slugglish, and a few days later could no longer be obtained. The right limbs also became weaker, and the above-described tremor was more frequently present. About a month after admission it began to affect the

right lower extremity. As in the arm, it always appeared or was increased when the boy was agitated, or when he moved the left limbs against resistance. The right-sided hemianæsthesia also became much more definite.

Later, the downward movements of the eyes became deficient, the upward movements completely lost, and he was no longer able to converge. The pupils remained inactive to light, and the contraction on accommodation became sluggish. The weakness of the right side of the face on voluntary movement became more marked, yet this side seemed to move the more on smiling. As the paresis of the right limbs increased, the tremor began to disappear, and finally was only to be observed when the child was very agitated, as when he sobbed or cried.

The child became weaker and more drowsy, and died about two months after admission to hospital.

Diagnosis.—The right-sided hemiplegia and hemianæsthesia, with the above-mentioned ocular symptoms, lead to the diagnosis of a lesion of the left side of the mid-brain being made, and from the general symptoms, the headache, vomiting and optic neuritis, this lesion was evidently a neoplasm.

The diagnosis was fully confirmed in the autopsy, for a small tumour, which on microscopical examination was seen to be gliomatous, was found in the left side of the mid-brain. The tumour, which was almost quite spherical and about the size of a hazel nut (1·7 cm. in cross section), lay in the lower part of the left tegmentum and largely infiltrated the left pes pedunclei at about the level of the left oculo-motor nerve, completely destroying the structures immediately dorsal to it, including the substance nigra and the nucleus ruber.

Posteriorly, dorsally, and laterally this tumour was limited by a cystic cavity which contained clear, viscid, greenish fluid. It was considerably larger in all dimensions than the tumour, and caused marked displacement of the neighbouring structures. Its effect extended posteriorly into the tegmentum of the pons and frontalwards to the posterior part of the thalamus, without, however, invading either. It practically destroyed the left corpora quadrigemina, and to a great extent also the right, but its chief effect on the various structures was merely displacement. The pons varolii, medulla oblongata and spinal cord were examined by Marchi's method, but the degeneration present was limited to the pyramidal tract and Monakow's bundle (tractus rubrospinalis) on the right side, and was relatively slight in the former. The latter followed the typical course described by Collier and

Buzzard. The amount of secondary degeneration was, as is generally the case from gliomatous tumours, remarkably small in contrast to the size of the lesion.

Case 5.—E. W., a boy of five years of age, was admitted under the care of Dr. Ferrier in December, 1903. His health previous to this illness was good, but one brother had tubercular joint disease. He was a healthy and bright child till three months before he came under observation, when he began to vomit very frequently and to suffer severe headache. A short time later it was noticed that the child was reluctant to use the right arm and limped on the right leg, and about two months from the commencement of his illness the right arm began to shake and tremble when he moved it, when it lay in any "uncomfortable position," or even at apparently perfect rest when the child was excited or agitated. This tremor, or unsteadiness of the arm, slowly increased till a few days prior to his admission to hospital. Then one day he fell down unconscious, and since then has scarcely been able to move either of the right limbs.

On examination the child was found to be bright and intelligent, his visceral organs were normal, and no evidence of tubercular disease could be detected. His sight was considerably impaired, there being intense optic neuritis, and there was right hemianopia reaching almost up to the vertical line through the fixation point. Wernicke's hemianopic pupillary reaction test was positive, that is, the pupils did not contract to rays of light thrown in from the blind halves of the visual fields.

There was slight weakness of the left external rectus, and some difficulty in the conjugate movements of both eyes to the right. Though there was no visible difference between the two sides of the face while they were at rest, there was slight weakness of the right side, practically limited to its lower half, on voluntary movement. In a spontaneous smile, on the other hand, there was practically no movements of the right side of the face, though that of the left side was free, and by contrast apparently exaggerated. Some movement of the right side occurred when the child laughed aloud, or wept, but much less than of the left side. There was no paresis of the tongue or palate, and no affection of phonation or deglutition.

The constancy with which the head was held in an unnatural position was striking. It was always to be seen slightly inclined to the right and rotated to the left, so that the right side of the occiput was approximated to the right shoulder, but voluntary movement in each direction was free and strong.

The muscles of the limbs were fairly well developed, and the strength of the left pair was relatively good and their voluntary movements well co-ordinated. When, however, the child was agitated, rather fine tremor of medium rate and regular in amplitude and rate was observed in both the left arm and leg. This was never visible when the child was composed and at rest, and as it only occurred under the above-mentioned condition, and never persisted for long, its further character could not be studied. The right arm lay quite powerless and flaccid as he first came under observation, and no tremor of any part of it was observed. The right lower extremity was also very weak, but not so severely affected as the arm. He was then unable to walk alone, and with support reeled and staggered. There was no trace of aphasia associated with this right hemiplegia, even though the boy was right-handed. There was also considerable diminution of all forms of sensation on the right side of the body, the loss of the sense of position in the right limbs being relatively the greatest. All the deep reflexes were absent, stimulation of the soles of the feet gave an extensor response on the right side, but on the left flexor.

While under observation in hospital the right limbs became more rigid and there was some return of power. The voluntary movements possible, however, were complicated by an irregularity of the intention-tremor type, and spontaneous tremor was frequently observed in the right arm when the child was in any way excited or agitated, as if abruptly wakened from sleep. He apparently had no power to check or control this tremor, which, while it lasted, was of medium rapidity—about four oscillations per second, and regular in rate. It was fairly coarse, but not quite regular in amplitude. It generally resulted from forcible movements of the opposite limb, and ceased when the child was composed and the limb lay at rest.

The presence of hemianopia with Wernicke's reaction was repeatedly confirmed, till the child finally became almost quite blind, with subsidence of the optic neuritis into atrophy.

Some weakness of the upward movement of the left eye also developed while the patient was under observation.

The voluntary paresis of the right side of the face diminished, but the defect of expressional movement became more pronounced, in fact, the right side of the face was generally described as immobile on smiling.

The deep reflexes soon returned. The patient's general condition improved and the headache and vomiting ceased. The

patient finally left hospital almost blind, unable to walk, but with fair range and power of movement of the right limbs.

Diagnosis.—This case so much resembles Case 4 that the same arguments serve to indicate the localisation of the lesion. The defective upward movement of the left eye, which developed while he was under observation, and the paresis of the right side of the face in expressional movements, tend to confirm the diagnosis of a lesion in the left side of the mid-brain.

Case 6.—F. H., a boy of 15 years of age, was admitted under the care of Dr. Ormerod, in October, 1903. He came of healthy parentage and has not had any serious illnesses. Two months previous to admission his left arm was first noticed to become weak, or "useless" as he described it, so that he could not employ it properly in his work, and he became unable to perform finer movements with it. This affection was from the first slowly progressive, and about a month or six weeks later the limb began to shake on movement or even during rest. For six weeks his gait had been affected, and his sight had not been so good as it formerly was. During the whole period of his illness he suffered very much with severe headache, and frequently "felt sick," though he rarely vomited.

On examination, hemianopia to the left extending up to the vertical line through the fixation point was found, and Wernicke's hemianopic pupillary reaction was present, *i.e.*, the pupils did not react to rays of light thrown into the eyes from the left side. There was no limitation or weakness of any of the ocular movements, and no paresis or loss of function of any of the other cranial nerves.

The muscles of the limbs and of the trunk were well developed for a boy of his age, but there was a very slight degree of rigidity of the left limbs. The left arm was very slightly weaker than the right, but the paresis of the left lower extremity was proportionately greater, indeed, practically no voluntary movement of the foot or toes was possible.

The most striking symptom of the case was the presence of involuntary movements, in the form of a tremor of the left limbs, but much more frequently and constantly observed in the upper than in the lower extremity. Neither the face nor tongue was ever affected by this, and it never spread to the right limbs. When the left arm was moved, or when it did not lie at perfect rest, each segment of the limbs supporting its own weight, there was constantly coarse tremor of one or other part of it whose rate, counted from tracings, was always about $3\frac{1}{2}$ oscillations

per second. All groups of muscles were involved, but the distal more frequently than the proximal, and in the latter the tremor was always coarser. Flexion-extension or pronation-supination of the elbow, flexion-extension of the wrist and flexion-extension of the fingers at the metacarpo-phalangeal joints, were the most frequent movements. Though more or less rhythmical the range of the oscillations was seldom constant for long, but their rate did not tend to vary. The amplitude was increased by bringing the muscles into action, or by placing the limb in such a position that they were in a state of strain, by excitement or agitation of the patient, and by strong action of the fellow limb. It only ceased during sleep, or when the limb lay at perfect rest. Voluntary movements were complicated by ataxia and irregularity of the intention-tremor type, *i.e.*, the range of deviation from the direct line increased towards the completion of the action. Similar tremor under similar conditions was occasionally observed in the lower extremity, with a predilection to the distal joints, but the voluntary movements of the limb which were possible were fairly accurately executed. His gait was only affected by the weakness of his left limb, which, as the foot could not be fully dorsi-flexed owing to weakness, was raised high to allow the toes to clear the ground, and thrown somewhat outwards as it was advanced. There was a slight degree of left-sided hemianæsthesia, tactile sensation being the most defective. The deep reflexes were increased in the left side, and the left plantar reflex was of the extensor type. His condition has remained practically unchanged since he first came under observation, excepting that the headache and general cerebral symptoms have abated.

Diagnosis.—The left hemianopia and the presence of Wernicke's reaction indicates involvement of the right optic tract before its termination in the primary optic centres, or of the quadrigeminal region, and the left-sided hemiparesis and hemianæsthesia, associated with it, points to a lesion of the right side of the mid-brain, probably by a tumour growing from its lateral surface medianwards.

Case 7.—C. S., a woman of 37 years of age, was admitted under the care of Dr. Hughlings Jackson, in September, 1903. She complained of uselessness of the right limbs and of occasional attacks of headache and vomiting. She came of tubercular stock, and her antecedent history gave rise to the suspicion of syphilitic infection.

The affection she complained of had then lasted nearly two years, and had developed slowly after a fit, which was preceded by

some vertigo. During the next week or so the right arm slowly became weaker, and about six weeks later it first became shaky and tremulous when she attempted to use it. The tremor of the right arm has slowly increased since then, and she has now for eighteen months not been able to use this limb in taking her food. She spontaneously emphasises that it is rather "uselessness" than weakness which affects this limb. She cannot pick anything up with the hand, but is able to nurse and carry her baby on this arm when she has placed him in it with the left hand.

Her gait became affected only nine months after the commencement of the illness. First the right leg felt weak and gave way under her, and soon she began to walk so unsteadily and uncertainly that she was reluctant to go out of doors lest it should be thought she was drunk. Since then she has taken very short, shuffling steps. For two months she has been troubled with difficulty in reading: the letters now run into one another and she has had double vision.

On examination, her visceral organs were found to be normal, and, though an uneducated woman, she was clear and intelligent with a good and reliable memory. She was very emotional and frequently burst into tears or laughter without adequate cause, saying she could not help it.

Her vision was good and there was no contraction of the visual fields or optic neuritis. Although she complained of diplopia there was no visible paresis of any ocular muscles, but marked nystagmus on lateral deviation, and slighter accompanying the vertical movements was present; even on fixation the eyes were unsteady. The pupils were equal and reacted well to light and on accommodation. The face seemed rather fixed and expressionless, but there was no visible paresis in voluntary movement, though in emotional expression movement was limited, slow and rather constrained. The muscles of all limbs were well developed and of good strength, with but little difference between the power of the two sides, yet it was of uselessness of the right limbs that she most complained. In the right, however, there was marked tremor of a coarse and more or less irregular character, definitely rhythmical, with frequent increase of amplitude, but from numerous tracings taken it is apparently constant in rate, about four oscillations per second. (Tracing III.). This tremor ceased during sleep and when the limb lay at perfect rest in bed, but at once commenced when she was at all excited, or even when she comes under observation, when the limb is moved about either passively or

actively, or when the muscles are in any way put in a strain, as, for instance, when the limb hangs by her side. The tremor was not so regular in the amplitude of its oscillations as that of the preceding cases, but regular, clonic contractions of one or other group of muscles might be observed persisting for a considerable time under favourable conditions. This was not at first apparent, the movements of the limb being generally irregular owing to the simultaneous presence of several tremors affecting different groups of muscles. It was a true tremor, in that it was due to the alternate contractions of one or more muscles and their antagonists, and might affect any group in the limb, but showed a preference to the distal. Voluntary movements, but especially the finer, were complicated by an accentuating tremor of the intention-tremor type, so that she was unable to use this limb in taking her meals and could not hold one finger in apposition to her nose. Similar tremor has not been observed in the lower extremity, but its voluntary movements are jerky and irregular.

Her gait was very peculiar; she advanced with slow, shuffling steps, but it was neither ataxic nor spastic, for she neither staggered nor dragged her feet, but took very short steps as though afraid to trust her weight on the right limb, consequently advancing the left foot as quickly and as short a distance as possible and in the next step unable to move the right foot fully forwards. She could stand, however, easily on either foot, and did not reel with her feet together and her eyes closed.

There was, besides, a definite degree of right hemianæsthesia, which extended up to the middle line, and a more marked loss of the sense of position in the right limbs. The deep reflexes were slightly brisker on the right than on the left side, but both plantar reflexes were of the normal flexor type. There was no trace of aphasia or other affection of speech. The patient remained about six weeks in hospital, but is still under observation. She is so far unimproved.

Diagnosis.—Even though the cardinal symptoms—headache, vomiting, and optic neuritis—were absent, there can be little doubt that in this case the lesion is a tumour which has been of very slow growth and has been, perhaps, for some time latent. The marked hemianæsthesia, with ocular symptoms and but slight hemiparesis, makes a mid-brain lesion of the opposite side probable, and this localisation is supported by the emotional state.

Case 8.—A. B., a man of 47 years of age, had been under the observation of Dr. Risien Russell for five years in the out-patient department of the hospital. His illness had a sudden onset during

sleep, six years ago. For the next three weeks he was in a dazed condition, but not unconscious, and suffered with severe headache and vomiting. From the onset he was able to move all his limbs about in bed, but noticed that the movements of the right arm and leg were weaker than they had previously been, and were, in addition, very awkward and irregular. He had no difficulty in speaking, but people were not able to understand him easily for some time. He had, however, no difficulty in swallowing. On leaving bed he found that his gait was extremely ataxic; he reeled about like a drunken man, had to learn like a child to walk again, but it rapidly improved. His right arm has remained very ataxic; he described it as "useless," recognising that he had sufficient power to move it in any way he pleased, but that he was unable to correctly regulate its movements. Besides this defect in the co-ordination of movements, he describes a trembling of the right arm which came on when he allowed it to lie in any uncomfortable position or held it up. This tremor has been most marked when he was [illegible] excited, or tired. It first appeared two or three months after the beginning of his illness, and not, as the ataxia, immediately after the onset. During the first three or four months of his illness he had diplopia, especially, he thinks, on looking down, the images being separated both horizontally and vertically, and tended to cross one another. He has never had ptosis or any affection of co-ordination.

No diplopia can now be made out, but, on looking down, the left eye moved slightly less fully than the right; otherwise his vision and ocular movements were unaffected. There was a very slight trace of voluntary paresis of the right side of the face, but the difference between the two halves was more marked in expressional movements, and as he conversed he elevated only the left eyebrow. No involuntary movements have been observed on either side of his face or in tongue. There was but little difference between the strength of the right and left limbs, the former being only slightly weaker, but there was a relatively greater degree of irregularity. The voluntary movements of both right arm and leg were very irregular, the irregularity being of the type of intention-tremor. His gait is at present almost quite natural, but he says that he must be careful and slow in going up and down stairs, as the right leg trembles. Besides this intention-tremor, there was some tremor of the right arm when he held it extended in front of him or kept it in such a position that each part did not bear its own weight. The movements may occur at any joint, but more frequently at the distal than at the proximal. It only

remained a short time limited to any one group of muscles, but while it persisted was regular in rate and in amplitude, of medium rapidity, about four oscillations per second, and fairly coarse in range. He was unable to voluntarily inhibit it for any time, and on movement the intention-tremor above described appeared.

It was increased by any excitement or agitation, and constantly came on when he attempted to perform forcible actions with the left arm. It ceases when he is at perfect rest.

No affection of any form of sensation could be determined, and the reflexes were practically equal in the two sides. His gait presented no abnormal features.

There was no evidence of vascular disease, but the patient had syphilis in youth.

Diagnosis.—This rests mainly in the definite history of diplopia with vertical separation of the images, and the slight defect of downward movement of the left eye which is still apparent. These indicate a mid-brain lesion affecting part of the left oculo-motor nucleus or nerve. The sudden onset of the condition suggests that it was of vascular origin.

Case 9.—J. L., a man of 57 years of age, came under the care of Dr. Risien Russell two weeks after the onset of his illness. According to his history he retired to bed one night as well as usual, but woke up at an early hour conscious that something had happened to him. On attempting to leave bed he found he was unable to stand, and though able while lying down to move his legs about, they seemed too weak, and especially the left, to bear his weight; in his own words, he "seemed to have lost control over them." He had also tingling and numbness of all four extremities, subjectively more intense on the right than on the left side of the body. There was also when he moved severe vertigo, with translation of the objects he looked at from left to right, but there was no subjective or objective auditory disturbance. When brought a drink he found he was unable to bring it to his lips, as he had also lost control of his hands, they were very unsteady, and he was unable to direct their movements accurately. His articulation was also at the time so much affected that his speech was unintelligible. He felt very ill, had severe headache and vomited persistently for the first twenty-four hours.

The more acute symptoms disappeared after the first few days, and in the course of a week or so his right limbs were again normal, his speech was quite easily intelligible, though not natural, the vertigo had ceased, and he had no longer any paræsthesia in his limbs. The weakness and uselessness of the left limbs, however,

has persisted, the arm is so unsteady that he cannot employ it in any work, and the leg so weak that he is afraid to trust his weight on it when walking.

From the onset of his illness till he came under observation he was troubled with diplopia, especially on looking down or in front as he lay in bed. He gave no history of involuntary movements of the limb, except the irregular excursions associated with voluntary movement.

On examination he was found to be a healthy-looking, well-preserved man for his years, but his arteries were tortuous and rigid, and he admitted syphilitic infection some years previously. His special senses were unaffected, but on investigation of the ocular movements, there was found to be some defect in the downward movement of the right eye and diplopia, indicating weakness of the right inferior rectus. There was no affection of the functions of the other cranial nerves.

The musculature of the limbs was fairly developed, and there was practically no difference between the strength of the right and left limbs, nor was there any rigidity on either side. All movements of both left arm and leg were, however, very ataxic, the inco-ordination closely resembling that due to unilateral cerebellar lesions, and this was equally marked in bringing his finger to his nose and in touching a foreign object. There was also a very slight degree of diadokokinesia in the left arm. His gait, which, from his own account, resembled that of a drunken man during the first fortnight of his illness, was no longer ataxic when he came under observation, but he walked with short, uncertain steps, holding the left leg too stiff and bringing the foot too forcibly to the floor. For the first few days of his stay in hospital there was slight left hemianæsthesia, but it quickly disappeared. The left deep reflexes were brisker than the right, and the left plantar reflex was of indefinite character.

His general condition, and especially his gait, improved after he came under observation; but about six weeks after the commencement of his illness a new symptom developed. This was tremor of the left upper extremity, which at first was only very occasionally to be observed, but became more frequent. It showed predilection to affection of the more proximal groups of muscles, as adduction-abduction of the shoulder, with occasional rotation, flexion-extension of the elbow; but flexion-extension of the wrist and cigarette-rolling movements of the fingers and thumb were often observed. It only came out after some movement of the limb, if this lay in a constrained position, if the patient were at

all agitated, or when he moved the right arm forcibly against resistance. It was fairly rhythmical in character, slow (about 3½-4 oscillations per second), and regular in rate, with some tendency to slow accentuation and decline of amplitude, which was otherwise regular. It never persisted for long. The patient was unable to voluntarily arrest it, and it increased on any excitement or exertion. While earlier the defect of co-ordination of the movements of the left arm was of the cerebellar type, it slowly became identical with the intention-tremor of disseminated sclerosis, so that on trying to bring a finger to the tip of his nose it would strike the nose repeatedly in the vain attempt to keep it in position.

Diagnosis.—The existence of a partial palsy of the right oculo-motor nerve, with contra-lateral limb symptoms, indicates disease of the right side of the mid-brain. The sudden onset makes a vascular lesion probable.

In this series of cases, dissimilar though they be in their general appearance and in many of their clinical characters, there is one constant symptom. This symptom is tremor, which, it will be seen from the clinical and anatomical descriptions given above, has been observed in two classes of cases, in chronic and unprogressive cases in which the lesion is probably either of vascular origin as in Cases 1, 2, 8, 9, or, for the time being, latent tumour, as in Nos. 5, 6 and 7; and in rapidly progressive and early fatal cases of intracranial neoplasm, as Cases 3 and 4. In spite of this the tremor in all cases is very similar, or at least has constantly such characteristics as will allow of it being regarded as a definite symptom and clinical entity.

In recapitulating from the history of the individual cases, it may be described as consisting in a series of involuntary oscillations of any part of a limb, due to the alternate contractions of one group of muscles and its antagonists, of slow rate, varying in rapidity from 3 to 5 oscillations per second, in all cases more or less regular in rate while limited to any one group of muscles, in some cases (1, 3, 4) absolutely so; generally coarse, *i.e.*, of large amplitude, and either quite regular in the range of amplitude, as 1, 3, 4; with a periodical rhythmical increase and decrease of the range, as 8 and 9; or irregular, as Cases 6 and 7.

In some instances there was a remarkable tendency for the tremor to persist, apparently indefinitely, limited to the one movement if the position of the limb and other conditions remained unaltered; while in other cases it would involve various groups of muscles for short periods in succession or even simultaneously, the resulting movement of the limb being in the latter case compound and irregular, as the various oscillations were not synchronous in rate or equal in range.

In every case it was found that the patient was unable to voluntarily check the movement for more than the shortest space of time, and often the attempt to inhibit it only resulted in increase or accentuation of the range. In addition to the tremor proper, which may be described as static, as it occurred independently of voluntary or reflex movement of the part, volitional movement of the limb affected was in every case complicated by an irregularity of the intention-tremor type as met with in disseminated sclerosis, that is, the range of deviation from the direct line of the movement increased as the completion of the act purposed was approached.

In no case did it persist during sleep, though in Case 3 the patient was, during the greater part of the time that it was observed, in a semi-comatose state. It also ceased when the limb involved lay at complete rest, so supported that each of its segments was individually supported. In each case the influence of gravity on its production and existence was emphasised; any part of the limb allowed to hang unsupported was in some cases invariably, in all cases frequently, affected by tremor. This would seem to point to a certain condition of tone of the muscles being essential to, or at least concerned in, its pathogenesis, and opens up an interesting field for discussion and study of the relation of the two conditions. This, however, is avoided here with the excuse that we are still too ignorant of the full nervous mechanism concerned in the production and maintenance of muscle tone to profitably allow it.

In each case, too, it was observed that the psychical state exerted considerable influence on the intensity and

character of the tremor; it always increased with any agitation or excitement of the patient, and diminished as the patient again became composed and calm. Another factor which increased the tremor was forcible movements of the opposite limb, and even the more finely co-ordinated purposeful ones. It is noteworthy that in every case it only developed some weeks after the initial onset of the illness.

Each case of this series presents other symptoms worthy of more special notice. These may be roughly, though not perhaps accurately, grouped as those associated with the symptom-complex, but not invariably present, as rigidity, paresis and uselessness of the limbs, affection of co-ordination and an emotional state; and those merely casually related or coincident, as marked loss of voluntary power, sensory disturbance, the change in the reflexes, and the affection of the ocular movements, or of the functions of other cranial nerves. At present it is only the former group which will be dealt with, as the members of the latter are chiefly of interest in determining the anatomical site of the lesions.

The rigidity presented no special character. That which is described as belonging to the symptom-complex was, in all probability, not due, as the rigidity of the usual spastic states, to involvement of the cortico-spinal tracts in the lesion, for neither the condition of the reflexes nor the general character of the limbs warranted this conclusion. Unlike the late rigidity of hemiplegia and other spastic states, it was never associated with organic contractures. It was slight in degree, and is perhaps better described as a stiffness and a constant resistance experienced in the passive movement of the limb through the whole range of the movement. This resistance was not more marked at the commencement of the movement, and remained constant through it, and in these and other particulars was dissimilar from the rigidity of spastic paralysis. Associated with it was often a marked slowness in performing, and especially in initiating, voluntary movement.

Though the patients complained of weakness and "use-

lessness" of the affected limbs, there was in several of the cases no paresis or scarcely any in contrast to the power of the normal limbs, that accompanying the onset of the condition in the vascular cases rapidly passing off and leaving no definite evidence of affection of the cortico-spinal tracts. This weakness of which they complained was then, in great part, merely subjective. In some cases it may have been due to the accompanying sensory loss, but where this explanation does not serve, as will be more fully discussed below, it is probably to be largely attributed to interference with other systems than the cortico-spinal. Being largely subjective it is perhaps best described by using the term employed by so many of the patients—"uselessness.' Further, it is to be noted that in all probability it was not entirely due to the affection of the co-ordination of the volitional movements.

The emotional state of some of the cases also deserves some attention. This was particularly marked in Cases 1, 2 and 7, and to a lesser extent in Cases 8 and 9. These patients all remarked spontaneously or to leading questions that their temperament had changed, and laid special emphasis on a troublesome tendency to burst into uncontrollable attacks of laughing or of tears without an adequate cause, and often quite irrelevantly to the situation. Indeed, this symptom appeared so frequently that it came to be of the greatest annoyance to the patients themselves and to their neighbours. Case 1 was often continually in laughter while being examined, and Case 7 was frequently found in tears, yet both on questioning denied any knowledge of the cause or reason of their states, and might assert that their frame of mind was in quite the reverse condition. The first three cases cited, however, occasionally complained of feeling very depressed and sad, admittedly without reason. On conversation they were found to be unnaturally dull and apathetic, a change which was also observed by their friends. They took little interest in their surroundings and exhibited a marked disinclination to exert themselves in any way, and they generally preferred to remain in bed than to mix with the other patients of their wards. There was also apparent

a slowness in replying to questions or carrying out any command, a tardiness in initiating thought and action. With this psychical state some of the patients, Cases 1, 2, 4, 5, 7 and 8, exhibited a corresponding corporeal symptom. This was marked, or at least definite, paresis of the expressional or emotional movements of the face while its voluntary movements were intact or only relatively slightly affected. In Cases 1, 2, 7 and 8 the face remained remarkably placid and mask-like during conversation, with scarcely a change of expression or play of emotion, except when the patients laughed or wept, and then the movements were slow, stiff and imperfectly regulated. The affection in these cases was bilateral. In Cases 4 and 5, however, it was limited to the one side of the face, that corresponding to the limbs affected, and was by force of contrast remarkably apparent. As the children's interest was engaged or when they smiled it was seen that the movement was limited to one side of the face, and yet on voluntary effort there was little or no paresis visible. The mental state described above was not present in these two cases.

The symptoms which may be regarded as merely coincident with the symptom-complex described, are chiefly of interest as indications of the localisation of the lesions in the various cases. They deserve to be briefly discussed individually.

While, as above-mentioned, the weakness and "uselessness" of the limbs of which the patients complained were more subjective than objective in several of the cases, in others there was marked motor paresis in the form of hemiplegia. Cases 4, 5 and 6 resembled in this respect ordinary hemiplegia of considerable severity, in Case 2 there was only slight relative weakness, with an extensor plantar response when she first came under observation, and in Case 3 the only definite evidence of involvement of the cortico-spinal tracts was Babinski's sign during the last few days of life, though examination of the cord failed to reveal any degeneration of the pyramidal tracts, they having probably become affected at too recent a date for secondary degeneration to have taken place. Thus, from the descriptions of the

cases, it may be seen there are two varieties of weakness, that with extensor plantar response and the other signs of organic hemiplegia, and a variety, always much less intense, without accompanying signs of organic spastic paraplegia save the rigidity above discussed.

The strange character of the gait in Cases 1, 2, and 7 was very striking. Though there was little if any weakness of either limb, each of these women was reluctant to walk alone without some support or assistance, and even with it took short, shuffling steps, advancing each foot but a little distance. Each, too, kept her body bent forwards like a prematurely old person, and held it very rigid as she walked, with the arms to her sides and not swinging with each step. In none of these cases was there any reeling or staggering. It was frequently remarked how closely the gait in each of these cases resembled that of cases of paralysis agitans. The gait of Cases 3, 4, 5 and 8 was, on the other hand, very irregular and ataxic, the patients staggered from side to side, always more to the side of the affected limbs, and reeled in the drunken way characteristic of cerebellar disease. The gait of Case 7 was only affected by the weakness of the left lower extremity, and in Case 8 it was normal when he came under observation, though he stated that for some time after the onset of his illness he reeled like a drunken man.

The hemianæsthesia, permanent or temporary, observed in six of the nine cases, was always slight in degree. In no case was there absolute loss of even light touches (with cotton-wool), but the localisation of the touches was defective, and the patient was unable to feel them so distinctly as on the normal side. The diminution of pain and temperature senses was relatively equal to the tactile loss, and as it was more pronounced on the distal portion of the extremities than proximally or on the trunk, the sense of position of the affected limbs and the recognition of the shape and form of objects placed in contact with them, were only slightly defective. Despite this relatively slight degree of sensory loss, many of the patients complained of a numbness or loss of feeling in the affected limbs, that is, of subjective loss without a corresponding degree of objective change. The

condition of the reflexes in the various cases depended on whether the pyramidal system was involved in the lesion, or remained intact. In the latter case they were normal, or only a slight relative increase of the knee-jerks could be made out.

Special attention must be directed to the ocular symptoms, as they form the chief aid to the localisation of the lesions. From the notes on the cases it is seen that all excepting No. 6 presented some defect of the ocular movements. Six of the other remaining eight cases exhibited weakness or loss of the vertical movements of the eyes—bilateral in Cases 1 and 4, unilateral in Cases 2, 5, 8 and 9. In each instance the upward movements were more affected than the downward, and the weakness was, where any difference between the two sides existed, greater in degree on the side opposite to that of the limbs affected. In Cases 1, 2 and 9 the lateral movements of the eye-balls remained intact. In Case 1 the complete loss of vertical movements while the lateral were perfect was remarkable, and in this respect was the complement of the condition met with in lower pontine destructive lesions. As in Case 8, the history of diplopia with vertical separation of the images was the only indication of a previous ocular palsy, it cannot be more fully discussed. In Cases 4 and 5 there was some weakness of the external rectus of the same side. In Case 3 palsy of both external recti was present when the patient first came under observation, and he later developed complete bilateral ophthalmoplegia. In Case 1 there was persistent absence of the pupillary reaction, and in Case 4 the reflex contraction both to light and on accommodation disappeared. In Case 1, too, there was defect in the power of accommodation of both eyes, and in Case 2 on the side opposite to the limb affection.

In Case 7 no definite ocular palsy could be made out, but there was persistent violent nystagmus on fixing as well as with lateral and vertical movements.

Homonymous hemianopia to the side of the affected limbs, with absence of the hemianopia pupillary reaction (Wernicke's test) was present in Cases 5 and 7.

From this discussion of the symptomatology of the cases

described it is necessary to turn to the consideration of the site and nature of the pathological lesions on which the symptoms are dependent. From the general similarity of these cases and the presence of a more or less identical but exceptional symptom in all, it may be assumed that the site of the disease may be practically the same in all, and, further, it may be seen that the symptoms of each case can most naturally be explained from disease of a common region in the whole series. It is proposed to argue to the site of the disease from the symptoms independently of the *post-mortem* findings in two of the cases, and only use these latter as confirmatory of the conclusions from clinical facts.

In the first place, there is in the presence of ocular palsies in a large proportion of the cases a definite indication of the site of the lesions. This palsy most frequently took the form of loss or defect of the vertical movements of the eyeballs, certainly due to disturbance or loss of the function of part of the oculo-motor nuclei or of fibres which spring from them. The fact that there was generally only paresis of the certain muscles and not indiscriminate ophthalmoplegia, points to the affection being nuclear and not a lesion of the oculo-motor nerve trunk. That there is a segmentation of the oculo-motor nuclei and probably representation of the separate ocular muscles in its various parts, has been for long recognised, but despite the work of Hensen and Völkers, Kahler and Pick, Starr, Bernheimer, Perlia, Edinger, and others, our knowledge of this representation is far from being final or complete. The view which has been hitherto most generally accepted as being at least probably approximate to the truth is that of Starr, according to whom each oculo-motor nucleus is subdivisible into segments, arranged in a lateral and medial group, in which the ocular muscles are represented from before backwards in the following order:—

Medial.	*Lateral.*
Ciliary muscle.	Sphincter iridis.
Rectus inferior.	Levator palpebræ.
Rectus internus.	Rectus superior.
	Obliquus inferior.

This result was obtained chiefly by the compilation of clinical observations. The conclusions of other authors, chiefly from experimental work, are very divergent, probably as their results were obtained from experiments on various classes of animals. Schwabe, for instance, by Nissl's method of retrograde tigrolysis, has in the rabbit localised the two elevators of the eyes, the rectus superior and obliquus inferior, in the most caudal part of the nucleus; while Bernheimer, employing the same method in the ape, came to the conclusion that the arrangement of the central representation of the muscles from before backwards is levator palpebræ, rectus superior, obliquus inferior, rectus inferior and trochlearis, with the rectus internus and the intrinsic muscles of the globes supplied by the medial group of cells. The divergence of these views is so great that none can be applied to man without further evidence and confirmation than we now have. Bernheimer's results, as obtained in the ape, would, *a priori*, be the most probably correct, and clinical observations, chiefly personal, tend to support the representation of the elevators of the eye-balls, rectus superior and obliquus inferior, most anteriorly, and the fact that isolated lesions may paralyse the depressors together, and they alone, points to the representation of the rectus inferior in the caudal end of the oculo-motor nucleus in the proximity of the trochlear nucleus. But, as in my Case 1, the vertical movements were at one time quite lost, though the lateral were unaffected, it is difficult to accept Bernheimer's localisation of the cells of the rectus internus, intermediate between those of the elevators and depressors, especially as the lesion must have been bilateral. Clinical observations make it probable that the centre of the elevators lies close to that of the pupillary reflex arc in man, as paralysis of the upward movements was frequently associated with inactive pupils.

In this discussion it is of course assumed that there is no lower co-ordinating centre for the vertical movements of the eyes as there is for the lateral. Of this there is, as far as my knowledge extends, no direct evidence, though from analogy the existence of such seems probable.

From this consideration of the question, it must be

concluded that we are not yet in a position to deduce from paresis of any one ocular muscle a lesion in any definite position of the oculo-motor nucleus, owing to the incompleteness of our knowledge.

The affection of accommodation and the pupillary reflexes is explicable, whatever be the level of representation of the vertical movements, as it seems probable that the intrinsic ocular muscles are supplied from the medial group of cells of the oculo-motor nuclei, though perhaps indirectly through the ciliary ganglia (Bernheimer, Bach, Marina and others).

It is unsafe to assume a destructive lesion of the abduceus nucleus or nerve from slight palsy of the external rectus in cases of tumour, as from its long course the nerve is very liable to suffer from indirect pressure effects, as in Case 5, but the bilateral external rectus palsy in Case 3 was evidently a direct result of the lesion, the tumour extending into the fourth ventricle and compressing its floor. With the defect of the conjugate lateral movements, as in Cases 4 and 5, it is different. This, it is known, may result from a lesion of the lower co-ordinating centre of the movement—Deiter's nucleus, or of the fibres which leave it, dorsal longitudinal bundle, or, secondly, of the system of cortical origin which bears the volitional impulses for the movement. Monakow represents this tract as passing through the anterior part of the mid-brain in the formatio reticularis ventro-lateral to the aqueduct, lateral to the oculo-motor nucleus and at about the same level as it. In Case 4 it was evidently, from the autopsy, to affection of this system above its decussation that the defect was due, and the same is probably true in Case 5, as there was no clinical indication of a lower pontine lesion.

The hemianopia present in Cases 5 and 6 allows an accurate localisation of the lesion, as the presence of Wernicke's sign, inactivity of the pupil to rays of light thrown in from the blind portions of the visual field, makes it necessary to postulate a lesion of the one optic tract on the base of the brain, or at its termination in the quadrigeminal region in the primary optic centres. In each case, however, the associated symptoms pointed to the latter site, and

makes it very probable that the tumour was situated in the anterior tectal portion of the mid-brain.

Another symptom in some of the cases, the localisation of whose cause is of interest, was the defect of expressional or emotional movement of one or both sides of the face without a corresponding degree of volitional paresis. It is a symptom first described by Nothnagel and since extensively studied of Bechterew, Bruns and others, and has been by all ascribed to disease of the optic thalamus, probably in its caudal end, or of an efferent tract from it to the facial nucleus. The course of this thalamo-facial connection has not yet been described, but it seems probable that it passes through the mid-brain near the raphe, as the tract of each side must lie close together to be affected by such presumably small lesions, as in Cases 1, 2 and 7. Borst, on the other hand, thinks it probable that this psycho-reflex facial tract passes through the lateral part of the tegmentum, but he does not offer any definite positive evidence in support of his view. The bilaterality in these three cases makes it probable, apart from the other symptoms, that the disease does not lie in the thalamus, but interrupts the connection of the latter with the facial nucleus, and in Cases 4 and 5, where the phenomenon was unilateral, the associated symptoms pointed to the same localisation; in Case 4 this was verified *post mortem*. The psychical state of Cases 1, 2 and 7, associated with this defect of emotional display, where there was no evidence of cortical or subcortical affection, is of interest from the psychological standpoint.

The slight degree of hemiplegia present in some of the cases could not be used as a sign in the localisation of the lesions, but its association with sensory loss, evidently not of the cortical type, points to the disease being situated below the basal ganglia, where motor and sensory tracts run in close proximity.

From these symptoms the conclusion may be drawn that the site of the lesion in each case, in some with as absolute certainty as we can attain in clinical medicine, in others less definitely indicated, is in the mid-brain, possibly in some cases extending into the posterior part of the optic thalamus.

Further, the relative escape of the cortico-spinal system indicates that the disease is limited more or less sharply, in several of the cases, to the dorsal or tegmental portion of the mid-brain.

In some of the cases (1, 2, 8 and 9) the ocular palsies indicated that it was evidently of small extent and lay close beneath the aqueduct of Sylvius, at a level corresponding to a circumscribed part of the oculo-motor nuclei. When hemiplegia of any degree and ocular palsies were together present they comprised Weber's syndrome or hemiplegia alternans superior, the cranial nerve symptom being on the side opposite to the hemiplegia. In other cases instead of ocular palsies there was homonymous hemianopia, indicating involvement of the anterior end of the mid-brain and a more lateral position of the lesion. The autopsies in Cases 3 and 4 confirmed this diagnosis and localisation, as in the latter case the tumour was limited to the region indicated, and in the former its chief mechanical and destructive effect was exerted at the same level. In Case 7 there is less definite evidence of the site of the disease, but the persistent nystagmus and the history of diplopia make it at least probable that the same region was affected as in the other cases.

In studying the pathogenesis of the tremor, the symptom common to the series of cases in which our interest is at present centred, it is necessary to determine as far as possible the essential and constant factor in the lesions concerned. This may offer considerable difficulty, for the mid-brain, besides being as it were a bridge between the fore-brain and the lower receptive and effective centres and the structure through which the impulses afferent and efferent which functionate in our ordinary existence pass, contains certain structures of its own, and sends efferent tracts to the cord, while some of its nuclei are links in the systems connecting the higher and lower centres.

But if this tremor is regarded as a symptom peculiar to or dependent on a lesion of this region, as seems probable from its association in the above series of cases and in several others which have been collected from literature, it is necessary to connect or correlate it with affection of some

one portion of this part of the brain. The conclusion has already been drawn that in each of the series of cases here presented a focus of disease occupied or involved the dorsal or tegmental portion of the mid-brain. Of the structures contained in it to whose involvement the tremor may be ascribed, it is natural to first come to the consideration of the large nucleus which occupies its ventral and mesial part, and the ascending and descending systems in connection with it. This is the nucleus ruber, whose structure and anatomical relations and connections have become fairly accurately known of recent years. Developmentally it is a portion of the thalamencephalon, and its anterior end projects within the usual anatomical limits of the thalamus, while caudally it extends so far into the mid-brain that the roots of the oculo-motor nerves pass through or in close relation to it. As it thus lies ventral to the oculo-motor nuclei, and in close relation to the roots of the nerve, it seems probable, from the frequency of ocular palsies in the series of cases, that it must have suffered in the lesions, and that its damage may be the essential factor in the causation of the tremor. As is known the greater bulk of the superior peduncles of the cerebellum end in or around it, their fibres being in great part a system efferent from the cerebellum, and as they decussate before they reach it its relation to the lateral lobes of the cerebellum is crossed.

Any direct connection of the superior cerebellar peduncles with the fore-brain cortex may, with considerable certainty, be excluded, though Monakow believes that there is an indirect relation through the gray matter of the tegmentum, and possibly, too, through that of the basal ganglia. The nucleus ruber, according to the same author and others, has, in relation to its size and in comparison with the other nuclei of the thalamencephalon, but little connection with the cortex. Secondary change could be found in it only after lesions of the opercular region in man, and then in the form of slight atrophy of the ground substance while its cells remained normal, so the connection must be efferent from the cortex. On the other hand, each nucleus ruber sends fibres caudalwards to the cord—tractus rubro-spina-

lis (Monakow's bundle), and as these decussate almost immediately after their origin, each nucleus is in connection with the contra-lateral half of the cord. From these facts each nucleus ruber stands in relation to the opposite lobe of the cerebellum, the opposite side of the cord and to the homolateral optic thalamus, and possibly to the other basal fore-brain ganglia, and through them indirectly to the pallium of the same side. In this way quite apart from its cerebral connections it forms a limb in a system which connects each lateral lobe of the cerebellum with the same side of the spinal cord. This may be known as the cerebello-rubro-spinal system. From phylogenetic grounds it is presumably of considerable importance, and from its anatomical relations it cannot but be of physiological significance, as it comprises the chief efferent cerebellar system and is one of the most definite and direct routes by which the cerebellum may influence the lower motor centres as well as the fore-brain. It seems from anatomical and other considerations that it is to some involvement of this system that the tremor above described is to be attributed. The arguments in favour of this view may be stated as :—

Firstly.—The clinical symptoms of my cases make probable, and the cases which came to autopsy confirmed, an involvement of either the superior cerebellar peduncle, or of the red nucleus. Further, in a large number of cases collected from the literature, in which the localisation of the disease was confirmed by microscopical examination, either of these structures was involved. In some of these cases the lesions were more or less accurately limited to the involvement of these parts.

Then, too, in cases of destruction of the portions of the mid-brain other than that containing the cerebello-rubral system, no such tremor has been observed. This statement can easily be fully substantiated from personal observation as well as from cases published.

Secondly.—The character of the tremor and the conditions of its existence seem to be identical or closely similar to the tremor described by Ferrier and Turner, as resulting from section of the superior cerebellar peduncle of the same

side in apes (Macacus.) The descriptions of the authors are, "except when quite at rest, a constant tremor was observed in the homolateral arm and leg, which passed into larger oscillations on volitional effort"; "the limbs were the subjects of fine tremors which became greatly amplified on exertion."

Strongly in favour of this view that this tremor was directly the result of lesions of the first link of the cerebello-rubral system is the fact that they were homolateral to the injury, while, when the nucleus ruber was involved, *i.e.*, above the decussation of the peduncles, as in the clinical cases cited, it was contralateral to the lesion.

Thirdly.—It seems to me probable that such tremor may result from interruption of the final link of this system, that is, of the tractus rubro-spinalis. In a brain which I had the opportunity of examining anatomically, a small tubercular focus destroyed this tract in about the middle of the pons, and it alone. No definite clinical history of this case was obtainable, as the patient, I believe, only came under observation when moribund from hæmoptysis; but he was said to have had for some time tremor of the limbs of the same side. Such an indefinite fact, however, cannot be used as serious argument in support of the view expressed, especially as nothing is known of the character of the tremor.

Of greater importance is a case which has been under the care of Dr. Ormerod in the National Hospital. He was a boy of 17 years of age, who presented unmistakable signs of a tumour in the right half of the lower part of the pons varoli, *i.e.*, left hemiplegia and hemianæsthesia, paralysis of the right external rectus, later of the left in addition, and finally of the lateral conjugate movements of the eyes; complete flaccid palsy of the right half of the face and progressive deafness on the same side. The power of the right limbs remained good, but a few days before death they presented slow rhythmical tremor similar to that in the cases above described. The autopsy verified the diagnosis, and the appearance of the tremor was explained by recent degeneration of the right rubro-spinal tract, visible by Marchi's method. Here it may be observed that as both the superior cerebellar peduncles and Monakow's bundles decussate in the neighbourhood of the red nucleus, the one before entering it, the other after leaving it,

the tremor, if due to an affection of the cerebello-rubro-spinal system must be homolateral to the lesion if this be situated caudal to the decussations, as was so in the case just mentioned.

Fourthly.—If the tremor be due to a lesion of the cerebello-rubro-spinal system in any part of it, it should be associated with a homolateral lesion of the superior cerebellar peduncle or of the origin of this in the nucleus dentatus of the cerebellum, as Ferrier and Turner described it in the ape. As no such case has come under personal observation it may be permissible to cite one from the literature to complete the study. Sander has published a case in which the right limbs were constantly the seat during voluntary rest of a "coarse oscillatory movement and of intention tremor, quite unlike cerebellar inco-ordination, or voluntary action." Further, there was weakness of the left limbs, and the gait was reeling. In the autopsy a tumour was found in the right lobe of the cerebellum, compressing the same side of the pons and destroying the nucleus dentatus and superior cerebellar peduncle. Touche and others have published similar cases.

This case, then, is consistent with the hypothesis raised in this paper, and illustrates the association of tremor and disorder of co-ordination of the limbs of the one side with motor weakness of the opposite limbs.

If it be then admitted that the tremor as described is or may be due to an involvement of the nucleus ruber, or if some part of the rubro-spinal system, it next becomes necessary to consider its pathogenesis, the mode of its causation. In this attempt it is first essential to decide whether the lesions are to be regarded as negative or as positive, whether the symptom is the result of the merely destructive lesion of the part or of an irritative effect the lesion may have.

Either of these alternatives may be considered possible when the affection is the result of a tumour or growth, either progressive or for the time being latent, but in several of the cases where the pathological condition was in all probability due to a vascular lesion and the symptom persisted for long after its onset, it is extremely improbable that this continued to act as an irritative focus giving rise to positive symptoms. This being so in several of the cases it must be assumed

from the similarity of the symptom in all, that it is to a destructive effect on the parts concerned that the tremor is to be attributed.

But as negative lesions cannot directly produce positive symptoms, other centres or parts of the central nervous system must be concerned in the genesis of the tremor, and a full consideration of the symptom leads us to the determination of these centres to whose abnormal activity the symptom may be directly due.

As in man the fore-brain cortex and the efferent tracts which leave it to pass to lower centres are so directly concerned in the maintenance of the normal condition of the peripheral motor system, and as this is affected by each slight modification, either structural or functional, of the cortex and its connections, it is justifiable first to consider if the latter may be, or may contain, the mechanism to whose over-activity or to the perversion of whose function the super-positive symptom of tremor is directly due.

The same argument has been accepted by various authors who have contributed to the discussion of this or of similar symptoms, and has been supported by a considerable array of facts. It has been especially emphasised by Massalongo. The probability that it is to such over-action that the physiology of the tremor is to be attributed is strengthened by certain deductions, apparently natural and logical, from the symptomatology of the cases described.

Thus in the *first place* the tremor was in every case observed to cease during relative cortical inactivity, as in sleep and during perfect rest of the part involved by it. If not to be regarded a necessary result, it is at least a natural corollary to the association of the involuntary movements with the over-action of any centre, that they should vary in degree or even bear a definite relation to the normal activity of the latter. For, in considering disease, it is necessary to assume that unnatural activity or function of any organ varies only in quantity or quality from the natural, and is not different in kind.

Secondly, the converse of this was present in each case, *i.e.*, the tremor increased with cortical activity, in psychical,

as with any excitement or agitation of the patient, and in volitional, as in discharge of motor impulses. In the latter case the increase or accentuation of the symptom coincided not only with volitional discharge from the areas of central representation of the limbs affected, but also with movement of the opposite limbs, provided that it was sufficiently forcible, which may be interpreted in the result of the overflow or diffusion of normal discharges.

Thirdly, the tremor could in no case be controlled by volition, and frequently only increased with the attempt. On the other hand, were it the result of the over-action of a lower centre, it seems probable that the dominant system of our nervous organisation should have at least some power to inhibit it.

Finally, it was indicated in each case that there was no direct involvement or only relatively slight affection of the cortico-spinal tracts, and, further, as in Case 4, the tremor ceased as the hemiplegia increased. This fact in conjunction with the absence of such tremor in cases in which there has been any extensive destruction of the pyramidal system, even though the site of the lesion be the same as in the cases above recorded, makes it probable that for its appearance it is necessary that the cortico-spinal system should be relatively intact.

If it be then admitted that these tremors are due to cortical over-action, secondary to a lesion of the cerebello-rubral system, it must be assumed that, under natural conditions, the latter structure exerts an inhibitory influence in the former. Thus the final question arises as to whether this inhibitory function is normally exerted on the higher or on the lower motor centres, on the cortex or on the spinal cord; whether the cortical influence is regulated or modified at its point of origin, or inhibited and co-ordinated as it acts upon the spinal centres? There is not sufficient evidence available to definitely decide this question, but the two cases above cited, in which the rubro-spinal tract was interrupted below its origin, point to the probability of the latter alternative; but neither case is free from objection, as in the one the lesion was extensive, and in the other the clinical character of the symptom was not definitely ascertained.

If the other alternative is accepted, that is, that the inhibitory action of the cerebello-rubral system is exerted on the cortex, possibly through intermediary of the optic thalamus or other basal ganglia, the tremor should also result from a lesion of these parts or of the cerebralward continuation or connection of the superior cerebellar peduncle or nucleus ruber. As my clinical material does not include any such case, the question must be considered from any evidence to be obtained from the literature.

Apart from this, it may be finally concluded from the cases personally observed and above described, that tremor of the character found in these cases is the result of disturbance of the functional equilibrium of cerebellum and cerebrum, which is normally maintained by efferent impulses from the cerebellum, leaving it by its superior peduncle. It seems probable, too, that when its character is recognised it may be used as a clinical sign in the diagnosis and localisation of cerebral lesions. Too much importance must not, however, be attached to its absence or to variations in its character, for if it be, as it is assumed to be, due to a disturbance of a physiological equilibrium, there is much room for the play of other factors, according to the extent and nature of the lesion.

The close resemblance the symptoms of some of these cases bear to the classical symptomatology of paralysis agitans is at once evident. There is the same tremor during rest, regular or irregular in the time and space of its oscillations, slow in rate, and, as in many cases of paralysis agitans, it is intensified on the voluntary movement of the limb affected. A certain degree of paresis and marked rigidity, neither, however, due, in all probability, to disease of the cortico-spinal system, also formed part of the symptom-complex. In some of the cases there was the same mask-like expression, due to fixity rather than to obliteration of the facial lines, a similar rigidity of the whole body in progression, and a gait of short, shuffling steps, without, however, a tendency to propulsion or retrogression.

Other authors have drawn attention to this resemblance in publishing their cases. Raymond, for instance, remarks

on "Un aspect général de raideur, de soudure, d'immobilité dans l'attitude qui rapelle un peu le facies de la paralysie agitante." This resemblance was so pronounced in a few of my cases that it leads to consideration of the question whether there can be any relation between the origin of the two conditions. As hitherto little has been discovered of the pathology of paralysis agitans, it is rash to go to hypotheses, even though there be so strong a similarity in their component symptoms, but it seems permissible to suggest the possibility of the pathology of paralysis agitans being some disease of the cerebello-rubral system. I would venture to suggest the possibility of its site being in the red nucleus, and that it consists in a slow and chronic sclerosis secondary to a vascular condition. In the first place, paralysis agitans appears as a rule in older patients, in whom there is often some degree of arterio-sclerotic disease, and experience in our *post-mortem* rooms teaches that is impossible to exclude such change in the cerebral vessels from absence of any evidence of it elsewhere. The larger arteries at the base of the brain, and especially the basilar, from which the blood supply of this region comes, are known to be particularly liable to it and to suffer often the most severely when it is general. Nor is it needful to postulate a local arterio-sclerosis, for, as the nucleus ruber is one of the most vascular portions of the central nervous system, it can be assumed that for its function a liberal supply of blood is necessary, and that consequently it would suffer the most in any general reduction of the same. Should this suggestion prove correct, the sudden onset and exacerbations of the symptoms in many cases would be intelligible, and their occasional association with shocks, moral or physical, or other conditions which may modify or act on the cerebral circulation.

A full review of the literature on such conditions as the above or of closely-allied states, is at the same time very difficult and more or less unpromising of profitable results. This is chiefly by reason of the fact that there has hitherto been but little attempt to distinguish between or classify the various forms of disorders of movement which have been recognised and described, and it is scarcely possible now, as

in a large proportion of the published cases there is no accurate description of the clinical observations, many of the authors being contented with describing what they observed merely by a conventional term, or even in unconventional nomenclature. This is more or less pardonable, as there is admittedly nothing more difficult than to accurately convey by description movements observed, but the result is that this absence of accurate and systematic description makes it almost impossible to utilise in a scientific study the large material which has accumulated during the last thirty years As an instance of this may be mentioned the evident variety of conditions to which the name athetosis has been attached, and undoubtedly as large and dissimilar a series of cases has been included under the term chorea. The earlier authors included various forms of involuntary movement under some generic title, and subsequent observers have frequently been content to make some such title the diagnosis of their condition, without devoting themselves to a full clinical and anatomical study of their cases, and a scientific correlation of their results.

Post-hemiplegic chorea has been a favourite generic name for the several varieties of the symptom, but more preferable, as less binding, is the term post-hemiplegic disorders of movements, suggested by Gowers. Yet this term, too, as that proposed by Wier-Mitchell—post-paralytic chorea—is inexact and unsuitable in a certain proportion of the cases, as the involuntary movements may precede any paralysis, or may never be associated with such, nor does it express the spontaneous nature of the movements.

Yet there is such evident difference between choreoid, athetotic, tremulous and other varieties of involuntary movements when they are analysed, that it seems warranted to rigidly separate them in clinical study, and to assume that they must be due to, or constantly associated with, lesions different in nature or site. It will be seen that the definition of tremor I have adopted excludes the voluntary movements which characterise chorea, myoclonus, the classical athetosis of Hammond, and spasmodic movements due to cortical discharge (Jacksonian fits), as in none of these is there a close

succession of alternate contractions of one group of muscles and its antagonists.

Physiologically, too, the class of involuntary movements under consideration seems to differ from these others in there being at least a low degree of co-ordination or regulation of the muscle contractions, which is not to be observed in choreic, myoclonic, or Jacksonian spasms. The mobile spasms of true athetosis may, perhaps, be regarded as to some extent co-ordinated movements, but it needs little argument to show that even if related in causation or origin, they differ so much in effect that the one form must be considered at least an essential modification of the other.

There has been much speculation as to the nature of their pathogenesis. Almost the earliest attempts were to associate their appearance with some affection of the cortico-spinal system—either positive, *i.e.*, irritative, as Kahler and Pick, or negative, as Charcot, Bidon, Kolish, and the majority of the subsequent French observers. This view was also put forward by Sharkey in the Gulstonian lectures of 1886. According to Kahler and Pick, the lesion, or some part of it, lies near the pyramidal system and directly irritates it. On the other hand, those who have regarded a destructive lesion of the pyramidal system the essential condition, the involuntary movements may be either an early expression of a progressive lesion (Sharkey) ; or may be the permanent result of fully-developed or retrogressive disease, which, however, has been only partial (Bidon, Charcot) ; or may be the direct result of the consequent lateral sclerosis, as Charcot at one time held. On the hypothesis of Rendu and Gombault, involuntary movements occur when the tracts are incompletely destroyed, or compressed in such a way as to hinder the regular and continuous transmission of motor impulses, without completely interrupting them. Owing to this resistance there is an accumulation of energy central to it which can only from time to time break through it, so that the voluntary impulses reach the lower motor centres intermittently, and not, as under normal conditions, continuously.

Similarly Eulenberg and others, and especially Massa-

longs, regard the involuntary movements as of purely cortical origin, and Demange has published a case which has seemingly supported this view. The later authors have recognised that neither of these theories are compatible with facts in a certain proportion of the cases, and the greater knowledge of to-day, attained by the very large number of cases which have been published, allow an emphatic refutation of them.

In the first place, in many of the cases which have been examined anatomically the lesion has not lain in the proximity of, or involved any part of, the cortico-spinal system; then lesions which fulfil these conditions are frequent, while post-paralytic disorders of movement are relatively rare. Such symptoms, too, have been found practically only in disease of the region extending from the internal capsule to the upper margin of the pons, while, as the pyramidal tracts are identical in constitution throughout their whole length, an injury to them in the bulb or spinal cord should produce the same symptoms as elsewhere. Then in a considerable proportion of the cases there has been at no time such definite voluntary paralysis as accompanies lesions of the pyramidal system. These spontaneous movements are also unlike those which result from affection of the cortico-spinal system, and in certain cases (where the disease has been in the mid-brain or cerebellum) this symptom has been homolateral with the lesion.

One of the first attempts to connect the symptom with any circumscribed region was made by Charcot, who assumed that there is in the posterior limb of the internal capsule, in front of the sensory system, a layer of fibres with peculiar motor functions, whose disease leads to hemichorea. This view was later adopted by Raymond and Brissaud. The fact, however, that in a majority of the cases no disease has been found in this region has made Charcot's assumption of a system with such specific functions untenable. Soon after, Gowers, drawing attention to the constant absence of such involuntary movements in completely paralysed limbs, attributed their occurrence to "damage to the gray matter of the brain, to local perverted nutrition of the nerve cells, in

consequence of which they overact, either spontaneously or on the stimulus of a volitional impulse, which is by their over-action perverted or irregularly distributed;" and he assumes that this gray matter must be in connection with the volitional centres. From the result of the anatomical examination of one of his cases he further asserts that this gray matter is that of the optic thalamus. In a later publication Gowers suggests that the symptoms may be due in many cases rather to the quality of the lesion than to its site. Monakow closely follows Gowers in regarding "irritative disease of the optic thalamus, in the form of multiple small foci," as the direct cause, assuming that from these abnormal impulses ascend to the motor cortex. Since then this localisation of the lesion has been widely accepted, and it has in many cases been verified by autopsy. In every case the disease has been limited to the posterior end of the thalamus, with the doubtful exception of one recorded by Lauenstein, in which hemiathetosis resulted from an affection of the anterior end. That in the majority of the cases the lesion has been unprogressive, of long duration, and often only the remains of vascular disease, as well as the permanency of the symptoms, are, however, strong arguments against the view of the pathogenesis of the symptom accepted by these authors. Benedict had still earlier assumed that the essential condition was an affection of some accessory motor organ which has a regulating influence on the primary motor system, and pointed out its association with disease of the mid-brain.

The accumulation of published cases with a number of autopsies showing very various sites of the disease, has caused the later authors to take a more comprehensive view of the subject. Muratow, for instance, regards the symptom as due to a disturbance of the equilibrium between the inhibitory action of the cerebellum and the tonic influence of the thalamus, on the spinal cord. Anton, in his earlier work, assumed a disturbance of the equilibrium between the centres for automatic and those for voluntary movement. Theoretically this might occur anywhere that the connections of the centres are relaid in gray matter, but it most

frequently results from disease of the basal ganglia, and especially of the lenticular nucleus. It would thus be due to loss of the inhibition which the basal ganglia normally exert on the cortex. In a later publication he assumed the direct cause to be the destruction of a centrifugal tract of cortical origin, which passes to the cord through the cerebellum.

Bonhoeffer, on the other hand, regards the condition as the result of the interruption of a cerebro-petal tract which carries co-ordinating impulses to the cortex, probably from the cerebellum, and asserts that the relative integrity of the cortex and pyramidal system are necessary for its appearance. Only part of these co-ordinating impulses reach the cortex, the rest becomes disseminated in the basal and mid-brain ganglia, and from there passes to the cord through centrifugal tracts. In this way he explains the existence of automatic movements.

Nothnagel and others have expressed the opinion that, though it may result from disease of fibres in relation to the optic thalamus, the symptom has no localising value, and may be due to the central irradiative of volitional impulses.

I have been able to collect sixty cases, with autopsies, from the literature which during life presented the symptoms of spontaneous involuntary movements. Only those were taken for statistics of which there was a definite description of the nature of the involuntary movements, though in many cases, for the reasons above mentioned, it can scarcely be hoped that the description was either true or accurate; yet they serve at least to give an indication of the site of the disease associated with each variety. On the other hand, cases have not been included in which the lesion was either multiple or too extensive to warrant conclusions.

For the purpose of tabulation the involuntary movements have been divided into three classes, namely, athetosis, chorea, and tremor. The published records of fifteen cases of the first form were investigated. In four cases the lesion was accurately limited to the optic thalamus, in six it was chiefly situated in the basal ganglia, frequently involving the thalamus too; in two cases the internal capsule was the chief site of the disease; in one case the corona radiate, and in another the mid-brain was involved.

Movements described as hemi-chorea resulted in two cases from affection of the optic thalamus; in five cases of the other basal ganglia, but especially of the nucleus lenticularis; in ten cases from mid-brain lesions; in two from tumour of the pons and bulb, and in one from disease of the cerebellum.

Twenty-five cases were found in which, from the description, the involuntary movements seem to fall within the definition of tremor above given. In three of these cases the lesions were situated in the thalamus and basal ganglia; in twenty cases in the mid-brain; in two cases in the cerebellum; and in one in anterior part of the pons, extending dorsalwards, to compress or directly involve the cerebellum.

No trustworthy case has been published in which the lesion was limited to the cortex. In that of Demange almost one-half of the hemisphere was involved in the softening, and the deep portions of the brain were not carefully enough examined to exclude disease in them.

As regards the variety of the symptom found associated with disease of the different regions, we see that in twenty-one cases the disease was limited to the optic thalamus, basal ganglia, and internal capsule; and in eleven of these cases athetosis resulted; in seven choreiform movements; and in three tremor. In thirty-one cases the disease was in the mid-brain, and in these the relative frequency of the various forms are reversed, athetosis only appearing once, choreiform movements ten times, and tremor twenty times. In three cases the cerebellum was involved, in the one producing choreic symptoms, and tremor in the other two cases. In three cases, too, the pons varolii and medulla were affected, producing in two of the cases choreiform, and in one tremor-like movements. And, finally, in one case, in which the movements took the form of athetosis, there was some destruction of the corona radiata.

Although these figures may not accurately represent the relative frequency of the different varieties of involuntary movements, or of the sites of the lesions associated with them, it may safely be assumed that athetosis almost always results from disease of the basal ganglia, but especially of

the optic thalamus, that choreiform movements occur with about equal frequency in lesions of the basal ganglia and of the mid-brain, while in the large majority of the cases of tremor the lesion involves the mid-brain.

Finally, it remains necessary to point out that these facts are entirely consistent with the conclusions arrived at from the study of the cases above recorded, viz., that tremor, associated with focal cerebral disease, may depend on a negative lesion of the mid-brain, or rather of the cerebello-rubral system. It must be remembered that the nucleus ruber is phylogenetically, as well as developmentally, a portion of the thalamencephalon, and though it is generally regarded as a mid-brain structure, it projects so far into the 'tween-brain that direct injury of it must frequently result from disease which is described as limited to the thalamus.

References.

Anton. *Jahrb. f. Psychiatr. und Neurologie*, Bd. xiv., 1895. Bd. xix., 1900.
Archambault. *Progrès med.*, 1877.
D'astros et Hawthorn. *Revue neurologique*, 1902.
Bach. *Archiv. f. Ophthalmol.*, xlvii., 1898.
Bechterew. *Archiv. f. Psychiatrie*, xix.
Bechterew und Ostankow. *St. Petersburger Klinik. cit. Neurol. Centralbl.*, 1900.
Béchet. Thèse de Paris, 1892.
Benedikt. *Nervenpathologie und Elektrotherapie*, 1874. *Bulletin médical*, 1889.
Bernhardt. *Berliner klinische Wochenschrift*, 1875. *Archiv. f. Psychiatrie*, xxvii., 1895.
Bernheimer. *Archiv. f. Ophthalmol.*, xlvii., 1898; lii., 1901. *Handb. d. Augenheilk.*, 1899.
Bidon. *Revue de médicine*, 1885.
Bonhoeffer. *Monatschrift f. Psychiatrie und Neurologie*, Bd. i., iii., x.
Borst. *Neurologisches Centralblatt*, 1901.
Broadbent. *British Medical Journal*, 1871.
Bruns. *Archiv. f. Psychiatrie*, Bd. xxvi., 1894.
Canfield and Putnam. *Boston Medical and Surgical Journal*, 111, 1884.
Ceni. *Rivista sperim. di Freniatria*, 1899. *Neurolog. Centralb.*, 1900.
Charcot. "Lectures."
Collier and Buzzard. Brain, 1902.
Combe. *Rev. mens. des Maladies de l'enfance*, t. xxii., 1904.
Cook. *Lancet*, 1892.
Dejerine. *Semeiologie du Système nerveux.*
Demange. *Revue de Médicine*, 1883.
Edinger. *Vorlesungen*, Aufl. 7, 1904.

EISENLOHR. *Jahrb. der Hamburg. Staatskrankenanstalten*, 1889.
EULENBERG. *Handbuch der Krankheiten des Nervensystems*, 1875. *Wiener Med. Presse*, 1887.
FERRIER AND TURNER. *Phil. Trans. Royal Society*, vol. clxxxv., 1894.
FRAENKEL. *Deutsche Med. Wochenschrift*, 1898.
GILLES DE LA TOURETTE ET CHARCOT. *La Semaine médicale*, 1900.
GORDINIER. *Journal of Mental and Nervous Diseases*, 1901.
GOWERS. *Medico-chirurgical Transactions*, vol. lix., 1876. BRAIN, vol. i., 1878. "Manual," 1888.
GREIFF. *Archiv. f. Psychiatrie*, Bd. xiv., 1883.
HAENEL. *Deutsche Zeitschrift f. Nervenheilkunde*, Bd. xvii. and xxi., 1900.
HENOCH UND GRAVITZ. *Deutsche Med. Wochenschrift*, 1883.
HALBAN AND INFELD. *Arb. aus. d. Neurolg. Institute a. d. Wiener Univ.*, H. ix., 1902.
HENSEN UND VÖLKERS. *Archiv. f. Ophthalmologie*, xxiv.
HODSON. BRAIN, 1882.
INFELD. *Wiener Klinische Wochenschrift*, 1900.
KAHLER UND PICK. *Prag. Vierteljahrschrift*, 1879. *Bietrage zur Pathologie und Pathologischen Anatomie des Centralnervensystems.*
KOLISH. *Deutsche Zeitschrift f. Nervenheilkunde*, Bd. iv., 1892.
LEYDEN. *Virchow's Archives*, xxix., 1864.
MARIE ET GUILLAN. *Nouvelle Iconograph. de la Salpêtriere*, 1903. *Soc. de Biologie*, 1903.
MARINA. *Deutsche Zeitschrift f. Nervenheilkunde*, xiv., 1899.
MASSALONGO. *Revue Neurologique*, 1903.
MENDEL. *Berliner Klinische Wochenschrift*, 1885.
WEIR MITCHELL. *American Journal of Medical Science*, 1874.
MIURA. *Mitth. aus der Universität. Tokio*, Bd. iv., 1898. *Neurolog. Centralb.*, 1899.
MONAKOW. "Gehirnpathologie," 1897.
MUNZ. *Wiener Klinische Wochenschrift*, 1892.
MURATOW. *Monatschr. f. Psychiatrie und Neurologie*, Bd. v.
NOTHNAGEL. *Topische Diagnostik d. Gehirnkrankheiten*, 1879.
VAN OORDT. *Deutsche Zeitschrift f. Nervenheilkunde*, xviii., 1900.
RAYMOND. *Revue Neurologique*, 1900.
RAYMOND ET CESTAN. *Revue Neurologique*, 1902. *Gaz. des Höpitaux*, 1902.
RENDU ET GOMBAULT. *Rev. de Science Medicale*, vii.
SANDER. *Deutsche Zeitschrift f. Nervenheilkunde*, xii., 1898.
SEPELLI E LEVI. *Riv. sperm. di Freniatria*, xxiv. *Neurolog. Centralb.*, 1899.
SHARKEY. "Gulstonian Lectures," 1886. *Lancet*, 1886.
SORGO. *Neurologisches Centralblatt*, 1902.
SOUQUES. *Nouv. Iconograph. de la Salpêtriere*, 1900.
STARR. *Journal of Mental and Nervous Diseases*, 1888.
STEPHAN. *Archiv. f. Psychiatrie*, Bd. xviii., xix.
TOUCHE. *Archiv. gén. de Med.*, 1900. *Revue Neurologique*, 1900.
VIGOUROUX ET LAIGNET-LAVASTINE. *Revue Neurologique*, 1901.
WALLENBERG. *Archiv. f. Psychiatrie*, xix.