A CLINICAL AND PATHOLOGICAL STUDY OF THREE CASES OF EPIDEMIC ENCEPHALITIS.

By

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THESIS. "That the explanation of the main features of the symptom-complex known as postencephalitic Parkinsonism is the removal of cerebral inhibition controlling the prespinal sympathetic reflex arc."

It is now about ten years since von Economo gave an accurate clinical description of the disease which has come to be known as epidemic encephalitis. As far as the historical record of disease was concerned, this malady was something new, mysterious in its onset, and appalling in its devastation. Its etiology was a matter of conjecture, its pathology merely guessed at and its sequelæ undreamt of. During the intervening years there has been much clinical material for concentrated study of the disease and yet we must confess that the etiology is still obscure, the causative agent still unknown, the pathological riddle still unsolved and of necessity therefore treatment is practically non-existent. Harvey has told us that "Nature is nowhere accustomed to display more openly her secret mysteries than in cases where she shews her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the laws of nature by the careful investigation of the rarer forms of disease." Osler has also reminded us of "the salutary influence of the dead-house"—the place where our clinical acumen is either confirmed or rudely shattered.

In the following study we have sought to practise these guiding rules of conduct. This investigation constitutes a clinical and pathological study of three cases of epidemic encephalitis in an endeavour to correlate the symptoms, signs and histopathology in order to arrive at a working hypothesis of the distinctive clinical picture and phenomena encountered.

CLINICAL DESCRIPTIONS.

1. The first case is that of a male, C. H., aged 28, who was under observation for two years. There was no history of any acute illness prior to admission but the relatives stated that one year previously the patient had complained of transient diplopia and slight headache, since when he had been a little 'queer.'

The mental and general condition of the patient when first admitted were such as to lead to a tentative immediate diagnosis of dementia præcox, and he was thus labelled for about nine months until unmistakable signs of postencephalitic Parkinsonism made their appearance. Mentally he was dull and stupid, excessively emotional, and frequently noisy. There was inverted sleep rhythm, and on occasion he voiced auditory hallucinations. He was constantly complaining of headache and was occasionally guilty of impulsive action.

His general appearance was untidy, the face being expressionless and mask-like. Dribbling of saliva was pronounced and continuous. The posture was that of generalised flexion with festinant gait and slowing of all voluntary movements. There were tremors of the tongue, lips and eyelids and sustained frequency of the pulse rate. The reflex reactions were as follows: Pupils: equal and reacted normally to light and accommodation. Knee and ankle jerks: brisk and equal. Plantar: ambiguous; ? extensor.

2. The second case is that of a male, M. McC., aged 42, also under observation for a little over two years, in whom no previous history of any acute febrile attack could be obtained.

For about three to six months prior to admission he had become gradually depressed and apathetic: easily fatigued, slow in movement—which fact had led to his loss of employment—and finally becoming an excessive burden on his relatives because of inability to attend to his daily toilet, etc.

On his admission to hospital the mental condition was such as to lead to a diagnosis of melancholia, the more prominent features being excessive apathy and depression, complete lack of external interests and social qualities. He complained of headache, dull and continuous. As in the other case it was not until he had been resident in the hospital for some time that the diagnosis of postencephalitic Parkinsonism was made, based on the appearance of the general posture, facies, slowing of all voluntary movements and the continuous dribbling of saliva. In addition there was a coarse tremor of the tongue and a fine tremor of the eyelids. The reflex reactions were as follows: Pupils: equal: sluggish reaction to light and complete absence of response to accommodation. Knee and ankle jerks: brisk and equal. Plantar: bilateral flexor response.

3. The third case is that of a female, L. L., aged 40, under observation from 1925 to 1929. There was a history of an acute attack of encephalitis in 1924, the main symptoms being inverted sleep rhythm, diplopia and permanent strabismus. Almost immediately following the acute attack the patient became very depressed and attempted suicide by jumping from a bedroom window, this fact determining her certification and admission. She was diagnosed as a case of acute melancholia and during her residence she made two further attempts at suicide—by strangling and precipitation. It was not until she had been in the hospital for two years that the unmistakable signs of Parkinsonism made themselves evident. She rapidly developed the complete clinical picture and in addition presented the rather uncommon symptom of palilalia. If asked 'How are you?' she would reply 'My heart's bad,' 'my heart's bad,' 'my heart's bad' *ad lib.* (as many as fifteen repetitions have been noted), the voice gradually diminishing in intensity.

During her residence in hospital she had fairly frequent seizures, i.e., attacks characterised by sudden onset of coma and clonic movements affecting various parts of the body. In November, 1927 the coma associated with one of these attacks was more prolonged than usual, calling for further investigation which took the form of an estimation of the sugar content of the blood and spinal fluid, together with routine examination of the urine. A definite hyperglycæmia and glycosuria were established, with increased sugar content of the fluid. In one of these attacks the patient died suddenly, in February 1929.

The reflex reactions were as follows:—

Date.	Pupils.	Knee and ankle jerks.	Plantar.
1925	Sluggish to light. Normal to accommodation.	Brisk and equal.	Bilateral flexor.
1928	Inactive to both light and accommodation.	Brisk and equal.	Not elicited.

PATHOLOGICAL FINDINGS.

For purposes of brevity and facility of reading we shall consider the three cases together, merely noting points of difference.

In all three no part of the nervous system examined can be said to be completely normal but whereas the first two cases show the chief lesions in basal ganglia, crura, pons and cerebral cortex, the third shows the main incidence of the disease in basal ganglia, lower medulla, and upper cervical cord.

Cerebral Cortex.—In cases 1 and 2 the feature of note is the marked change in the Betz-cells (Fig. 1). None seen are normal. Most cells are swollen and stain very poorly, though some are irregularly shrunken. Nissl bodies have for the most part completely disintegrated and the nuclei are generally

FIG. 1 —Betz cells showing change simulating 'central neuritis'.

excentric. The underlying white matter shows patchy nerve-fibre atrophy. The level of the cortex chiefly affected and the almost complete absence of inflammatory reaction recall the condition to which the term 'central neuritis' has been given (Fig. 2).

Other cortical areas show a similar change in the cells of Meynert and the larger pyramids but of not so severe degree.

In case 3 the Betz-cells are perfectly normal contrasting greatly with the two previous cases. The only demonstrable cortical lesion is found in sections from Broca's area, where within the substance of the white matter

FIG. 2.—Betz-cells from a case of pellagra showing typical 'central neuritis'.

FIG. 3.—Showing one of the subcortical zones of round-celled infiltration in Broca's area of the frontal cortex.

immediately beneath the cortex small zones of round-celled proliferation with accompanying early thickening of the vascular endothelium are encountered (Fig. 3).

Basal Ganglia.—The ependymal lining of the third ventricle and upper part of the aqueduct in cases 1 and 2 shows here and there curious local ‘streaks’ of proliferating cells penetrating long distances into the subjacent nerve-tissue, and appearing as though they have taken on locally malignant properties. In addition there are numerous subependymal inflammatory streaks. In case 3 the ependyma was completely intact.

Lenticular and Caudate Nuclei.—Cases 1 and 2 show gross degeneration of all types of nerve-cells; the larger are mostly reduced to mere fragments of ragged-looking cytoplasm, while the smaller ones are in an even worse state.

FIG. 4.—Cells from the optic thalamus showing extensive vacuolation.

There is considerable excess of small round cells, perivascular gliosis and endothelial proliferation. In case 3 all neuronic elements are normal but there is definite evidence of vascular upset and round-cell increase.

Optic Thalami.—In the first two cases there is considerable degeneration of many cells and some are vacuolated (Fig. 4), but others are quite normal; i.e., the change here is much less marked than in the adjacent corpora striata. In the third case most cells are normal but a few reveal signs of degeneration. There is pronounced round-celled increase and proliferation of the vascular endothelium.

Crura Cerebri and Hypothalami.—In this area cases 1 and 2 show very severe and extensive damage to the neuronic elements (Fig. 5). Case 3 shows similar changes, but they are less severe and more limited in distribution.

FIG. 5.—Extensive nerve-fibre degeneration in left crus.

In the red nucleus most cells show chronic degeneration, but occasional individual cells appear fairly normal. For the most part the stainable substance of the cells is diffuse and the dendrites appear swollen with ragged fragmented edges. The number of small round cells is extraordinary (often eight, ten or more in satellite relation to one nerve cell) (Fig. 6).

FIG. 6.—Red nucleus. Small round cells in satellite formation to the neurones,

In the substantia nigra the cells are markedly diminished in number, very few cells approaching normality being seen, and even these show chromatolysis and deficiency of processes. Most of the cells seem to have entirely disappeared, their former stations being represented merely by irregular masses of dark pigment. Proliferation of round cells is obvious and the vessels show endothelial changes.

The tegmental areas exhibit similar neuronie, vascular and glial changes but much less pronounced. In all three cases the cells of the third nerve nucleus reveal degeneration of individual neurones. The second case shows the most marked change; in it we were fortunate enough to have the root of the third nerve, as it emerges from the sulcus oculomotorius, in the section, and very definite atrophy of some of the nerve-fibres was seen.

FIG. 7.—Upper pons. Ependymal proliferation, penetrating subjacent brain tissue.

All the cases show numerous circumscribed areas of nerve-fibre atrophy in the crusta, chiefly located among the pyramidal fibres (Fig. 5).

Pons.—In all cases there is pronounced proliferation of the endymal cells with local invasion of the brain substance (Fig. 7). There is widespread round-celled infiltration and vascular thickening. In addition, cases 1 and 2 show degeneration of many of the cells of the motor nuclei while others are perfectly normal.

Medulla.—Generally there is excess of small round cells, patchy nerve-fibre atrophy in the region of the pyramidal and rubrospinal groups of fibres and degenerative changes in some of the nerve-cells of the motor nuclei. In addition, case 2 shows widespread degenerative changes among the cells of the olivary nucleus.

Cerebellum.—There is no evidence of any inflammatory upset here, but some of the cells of Purkinje are in various stages of degeneration and in case 2 many have completely disappeared (Fig. 8). The fibres of the superior cerebellar peduncle (connecting the cerebellum with the red nucleus) show patchy demyelination.

Spinal Cord.—Cases 1 and 2 merely exhibit very slight atrophy of the fibres in the pyramidal and rubrospinal tracts. Owing to the gradual narrowing of these tracts the atrophy is only apparent in the cervical region of the cord. In case 3 the lower end of the medulla and the upper cervical cord show a most conspicuous lesion, consisting of marked proliferation of the ependyma with surrounding inflammatory exudate and round-celled infiltration.

FIG. 8.—Cerebellar cortex. Lower power view of a loop of cerebellar cortex. Normally such a loop would contain about 14-18 Purkinje cells. In this section only 4 Purkinje cells can be recognised. There is no evidence of any inflammation. The lesion is purely degenerative.

In view of the fact that in case 3 clinical investigation revealed a glycosuria and hyperglycæmia it was thought advisable to examine the pancreas. Nothing abnormal was detected.

CORRELATION OF CLINICAL FEATURES AND PATHOLOGICAL FINDINGS.

A consideration of the foregoing pathological findings indicates how widespread is the degenerative and destructive process in the neuraxis involving as it does all parts of the nervous system, from the cortex cerebri above to the

central canal of the spinal cord below, although the main incidence falls on the basal ganglia and hypothalamic regions.

This generalised histopathology releases us from the awkward situation of having to interpret all the symptoms as manifestations of striatal disease alone—a position of precarious tenancy when we reflect on the diversity of the symptoms (hypertonus, tremor, sialorrhœa, glycosuria, palilalia, etc.) encountered.

From the photomicrographs it is seen that all the pathological lesions are of a partially or completely destructive nature and it thus follows that the positive symptoms which make up the syndrome of Parkinsonism must be characteristic of release-phenomena, remembering also that the products of degeneration themselves, before they are finally removed by leucocytic activity, may act as irritants to contiguous nervous tissue and thus produce some of the symptoms.

All observers are agreed, and the present investigation confirms, that the main incidence of the pathology centres around the midbrain and basal ganglia and therefore we will deal with this region first. At the outset we find ourselves confronted by a part of the brain in which the anatomical connections are of a most intricate character and even yet by no means fully elucidated. In order to facilitate the further development of our argument we have made a composite diagram of the known connections of tracts and nuclei in this region (Fig. 9). It is purely schematic and is based on diagrams from Quain's *Anatomy* (vol. 3, part I, p. 96) and Berry's *Brain and Mind* (p. 132). The diagrammatic analysis is as follows.

On the affector side, proprioceptive impulses from joint, muscle, and tendon ascend in the spinocerebellar tracts and pass via the peduncles to the cerebellar cortex, whence through the medium of the Purkinje cells and probably other internuncial neurones they are transmitted to the dentate nucleus (from which they are freshly relayed to the red nucleus) and also to the cerebral cortex (either directly or via the optic thalamus). On the effector side we recognise cortical control of the anteroventral thalamic nuclei, which give off neurones passing to the globus pallidus of the corpus striatum, which in turn is connected with the red nucleus. Here this indirect cortical control fuses with cerebellar impulses and thus joint cerebello-striatal control, via the rubrospinal tract, is exercised over the lower somatic and sympathetic reflex arcs.

In the previous section we have noted that the main pathological incidence—of a destructive nature—has fallen on the red nucleus and substantia nigra, with secondary descending degeneration of the fibres of the rubrospinal tract, thus removing the inhibition normally exercised over the lower reflex arcs.

In destructive lesions of the pyramidal system we recognise a distinct clinical picture, the positive signs of which (i.e., everything exclusive of the paralysis) are determined by the release of impulses mediated through the lower somatic reflex arc. Now in destructive lesions of the striorubral system we

have a clinical picture quite distinct from that of pyramidal disease and yet the phenomena encountered, as far as the muscular system is concerned, are mediated by the same lower reflex arc (or more correctly, the same final common effector pathway). Seeing that both conditions—pyramidal and Parkinsonian disease—are release-phenomena, it follows that something ‘different’ or ‘extra’ is released in one or other of these disease processes. Is there any evidence of this something ‘extra’ being released? We believe that there is.

The terminal filaments of the rubrospinal tract are known to arborise around the dendrites of the neurones forming the intermediolateral cell column and also around the dorsal cells of the anterior horn. The cells of the intermediolateral column are those which furnish the preganglionic sympathetic fibres, which passing out via the ventral roots of the spinal nerves connect through the white ramus communicans with the sympathetic ganglia (connections and course of the sympathetic fibres are featured in the diagram). From which it is deduced that the something ‘extra’ which is released by destructive lesions of the rubrospinal tract is this ‘sympathetic element.’ In support of this contention, i.e., “that sympathetic overaction is explanatory of the main features of Parkinsonism” we submit the following argument.

Hypertonus of a generalised nature (though it affects some muscle groups more than others—thus determining the flexion attitude typical of Parkinsonism) is at once the most outstanding feature requiring elucidation and explanation.

First of all let us remark that a well-established clinical condition in which muscular *hypotonus* is a pronounced feature—Addison’s disease—has been definitely shown to be due to diminution or absence of the secretion of the suprarenal glands, the substance which in an intact nervous system stimulates the sympathetic nerve endings. Again it has been shown that the physical accompaniments of the emotion of fear are determined by transient hyperadrenalinæmia, and anyone who has carefully observed a cat frightened by a dog will have noted the immediate assumption of a generalised attitude of flexion under the influence of sympathetic overaction. Furthermore, Walshe has shown by intramuscular injection of novocain, with resultant temporary abolition of the excess of tone, that the causation of the hypertonus is located in the lower reflex arc; and Royle in a series of experiments on goats claims to have diminished hypertonus by section of the sympathetic—grey rami—fibres to the affected limbs.

This theory of sympathetic overaction as the basis of hypertonus in Parkinsonism has been elaborated by Hunter into a ‘dualistic theory’ of muscular tonus, and further he has made several dogmatic deductions (e.g., that the sympathetically innervated fibres of voluntary muscle are non-contractile and subserve ‘plastic’ tone; also “that the posture assumed in Parkinsonian rigidity is due to plastic tone only, exhibited in agonists and antagonists”) which have been called in question and shown to be untenable by Kinnier

Wilson, and which have brought the conception of sympathetic overaction into disrepute and called for the numerous denials thereof. While not subscribing to the determined dogmatism of Hunter in support of his dualistic theory of muscular tone, nor on the other hand accepting the denouncement of Adrian ("there is no doubt that the skeletal muscles are connected to the sympathetic system, but the sympathetic fibres are not concerned with tone"), I submit that on anatomical, histopathological, experimental, and clinical grounds there is good reason for suspecting a sympathetic factor in the control of muscular tonus.

Myoclonus and Tremor.—None of the three cases above described showed myoclonus of limb segments, but both the males demonstrated fine tremor of the tongue, lips and eyelids unaccompanied by any wasting of muscles detectable clinically. The tremor became more pronounced when the muscles concerned were put into action and was thus of the 'intention' variety. The nerve supply of these affected parts is derived from the seventh and twelfth cranial nerves; and the only pathological counterpart for these clinical phenomena which we could identify was degeneration of some of the cells of the seventh and twelfth nuclei with the presence of much intercellular debris which may conceivably have acted in the role of irritant to the remaining healthy neurones.

Glycosuria and Hyperglycorrhacia.—Much work has been undertaken and a great deal written about the sugar content of the spinal fluid and blood in encephalitis lethargica. Observations by numerous investigators employing seemingly identical methods of estimation have produced diverse results, and while some have claimed that the sugar content of the fluid shows an increase others have just as stoutly denied it. Shrewsbury and Williamson making an extensive study of the subject come to the conclusion that "a constant hyperglycorrhacia has not been observed in encephalitis lethargica and the finding of an increased spinal fluid sugar is not believed to be significant of that condition." On the other hand McCowan, Harris and Mann investigated the blood-sugar content of a series of cases of encephalitis lethargica and report thirteen Parkinsonian cases all of which showed a slight hyperglycæmia after the ingestion of 50 gms. of glucose, while out of seven cases of postencephalitis of non-Parkinsonian type only two showed a mild hyperglycæmia. The writer, having had under observation for the past two and a half years some thirty cases of postencephalitis in which sugar investigations have been carried out at varying intervals, can state that some of these cases show persistent hyperglycorrhacia and hyperglycæmia following a carbohydrate meal (i.e., when the liver is full of glycogen) while other cases, more common in the non-Parkinsonian types, show no such upset of sugar metabolism. What is the explanation of these apparently anomalous cases? All are similar in that they have been infected with the virus of encephalitis, but all do not show upset of sugar metabolism. Therefore the cause cannot reside in the original infection itself but rather in the differing results the infection produces in the nervous

systems of different individuals. In the experience of the writer it is more common to find an increase of the sugar content of the blood and fluid in the Parkinsonian type of case but by no means all of the cases of this type show the change. Is there a feasible explanation of this? We believe there is.

It will be recalled that one of the pioneers in the elucidation of the problem of glycosuria and hyperglycæmia was Claude Bernard, whose production of experimental glycosuria by puncture of the floor of the fourth ventricle has become a classic of physiology. Subsequent experimenters showed that this effect was only possible when the sympathetic nerve supply to the adrenal glands (splanchnic nerves) and from them the glycogenetic sympathetic nerve-fibres to the liver, were intact and functioning. Langdon Brown, commenting on this experimental glycosuria says, "We know that the main glycosuric effect of Bernard's puncture of the floor of the fourth ventricle is due to the irritation thereby of the splanchnic nerve-supply to the suprarenal glands". But needle puncture of the nervous system is a destructive lesion, and how can this irritate the splanchnic nerves, which take their origin in the intermedio-lateral cell column of the fifth to the twelfth dorsal segments of the spinal cord—far removed from the medulla?

We submit that the explanation is that of a release-phenomenon; destruction of certain fibres of the rubrospinal tract by puncture of the floor of the fourth ventricle releases the corresponding spinal sympathetic fibres from cerebral control, resulting in overaction of the adrenal glands and thus excess-stimulation of the glycogenetic sympathetic nerve-fibres to the liver.

In cases of encephalitis only those which show degeneration of the fibres of the rubrospinal tract will exhibit upset of sugar metabolism (i.e., Parkinsonian cases) and then only those in which the particular fibres, governing the sympathetic nerve-cells connected with adrenal and hepatic control, are affected. We submit that this explanation is tenable on experimental, pathological and clinical grounds above enumerated and also smoothes out the apparent discrepancies in sugar estimations which have been noted by different investigators.

Sialorrhœa.—This is a common symptom in cases of postencephalitic Parkinsonism and occurred in two of those here described. In the experience of the writer, in most cases, though not in all, the passage of time tends to produce a diminution in the degree of salivary dysfunction and cases have been encountered where the symptom has completely cleared up. Can we discover a pathological and anatomical basis for these phenomena?

The salivary glands derive their dual nerve supply from the cervical sympathetic cord and from the cells of the salivary nucleus (situate in the medulla close to the nucleus of origin of the glossopharyngeal nerve), the fibres passing to the glands via the chorda tympani and branches of the fifth cranial nerve. Physiological experiment shows that the fibres in the chorda tympani are secretomotor and those of the sympathetic are inhibitory.

The two cases in this series which showed this phenomenon disclosed destruction of some of the cells of the medullary nuclei, including the salivary

and glossopharyngeal nuclei, together with a generalised round-celled infiltration. It is conceivable that these products of degeneration act as irritants to the remaining functioning neurones, thus producing hyperactivity—i.e., sialorrhœa. Gradually reparative processes will tend to remove (via the blood stream) the products of degeneration and therefore the irritative factor will slowly be removed with a corresponding gradual improvement of the correlated symptom. That this symptom is an irritative one and not a release-phenomenon is supported by the fact that in the third case showing no sialorrhœa we could find no lesion of the cells of the various medullary nuclei.

Tachycardia.—Sustained frequency of the pulse rate, of moderate degree, has been noted by numerous observers. One of the above three cases showed this symptom. Hall found it in a number of his cases but did not proffer any explanation thereof. Now we know that the heart has a dual nerve supply, the vagus being inhibitory while the sympathetic is both accelerator and augmentor. If we accept the theory that in Parkinsonism the release-phenomena are manifestations of sympathetic overactivity then we have an obvious explanation of the moderate tachycardia encountered in some of these cases. But why not in all? The cardiac sympathetic fibres come from the cells of the intermediolateral column situate in the upper dorsal cord (segments 1—4). It is a feasible explanation that only those cases in which the corresponding controlling fibres in the rubrospinal tract are out of action will show the sympathetic release-phenomenon of tachycardia.

Palilalia.—The writer has only encountered this symptom in one case, that at present described in this series. It is constituted by a defect (or better a dysfunction) of motor speech. Written speech is apparently unaffected and the sensory side of the speech mechanism is quite normal. The muscular elements concerned in the act of speech (lips, tongue, vocal cords, etc.) have their neural correlates located in the third left frontal convolution, or Broca's area. In our case of palilalia the only lesion of the cerebral cortex we could discover (sections were cut from frontal, central, parietal and occipital areas) was located in Broca's area and consisted of perivascular round-celled infiltration within the substance of the white matter immediately subjacent to the cortex.

Reflex reactions.—In case 1 the plantar response was recorded as ? extensor. In view of the profound degeneration of some of the Betz-cells this observation was very likely correct. In fact considering the case from a pathological standpoint it is remarkable that the pyramidal signs were not more pronounced clinically, but doubtless they were overshadowed by the more definite picture of Parkinsonism.

In case 2 the pupillary reflexes yielded defective response to light and complete absence of response to accommodation. In this case there was pronounced degeneration of the cells of the third nerve nuclei with secondary degeneration of the fibres of the third nerve as it emerged from the sulcus oculomotorius. Similar neuronie changes but of slighter degree were found in case 3, which showed upset of the pupillary responses.

SUMMARY.

The clinical history and histopathology of three cases of Parkinsonian encephalitis are recorded.

The corresponding clinical features and symptoms are related to their possible pathological basis.

It is suggested that the only adequate explanation of the outstanding symptoms which constitute Parkinsonism is that of sympathetic decontrol due to interference with fibres of the rubrospinal tracts.

The symptoms of palilalia and sialorrhœa are probably the result of irritative phenomena due to degenerative products.

Finally, the type of inflammatory cell encountered suggests that the disease is a manifestation of a chronic progressive encephalitis rather than the sequel to an acute infection.

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REFERENCES.

- WALSHE, F. M. R., *Brain*, 1924, xlvii, 159.
ROYLE, N. D., *Brain*, 1924, xlvii, 275.
HUNTER, J. I., *Brit. Med. Jour.*, 1925, i, 197.
WILSON, KINNIER, *Modern Problems in Neurology*, 1928, (chap. ix).
ADRIAN, E. D., *Brain*, 1926, xlix, 135.
SHREWSBURY, J. F. D., and WILLIAMSON, G. F., *Jour. Neurol. and Psychopathol.*, 1928, ix, 11.
McCOWAN, HARRIS and MOON, *Brit. Med. Jour.*, 1926, i.
BROWN, W. LANGDON, *The Sympathetic Nervous System in Disease*, 1923, 73.
HALL, A., *Brit. Med. Jour.*, 1926, i.
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