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ON CHARACTERISTIC MODES OF FATAL TERMINATION IN MULTIPLE NEURITIS, WITH CLINICAL AND PATHOLOGICAL INVESTIGATION OF AN ILLUSTRATIVE CASE.

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On Characteristic Modes of Fatal Termination in Multiple Neuritis, with Clinical and Pathological Investigation of an Illustrative Case.

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Many patients who have suffered from multiple neuritis recover completely, as was pointed out by Sir Thomas Grainger Stewart in the earliest contribution on this subject in our language,[1] but in a considerable proportion of those who have been attacked by this disease, the event is not so satisfactory. In one class of cases, although the termination is favourable in regard to the life of the individual, various lesions are left behind by the effects of the toxic agents which have caused the nervous symptoms. The peripheral nerves may remain permanently damaged; but a more common observation is that, while they regain their functions and become restored in structure, some part of the central nervous system undergoes degenerative changes. It may be that a system lesion is developed in the spinal cord. In our own experience, for instance, spastic phenomena have not infrequently followed upon severe attacks of multiple neuritis, and must be due to some alteration of structure in the lateral tracts. More common, perhaps, has been the evolution of ataxic symptoms, very completely simulating the great features of tabes dorsalis; but much more frequent even than this has been the insidious growth of the multifarious phenomena of disseminated sclerosis.

But in another group of cases recovery does not in any way take place, and the patient dies while neuritis is present. In the vast proportion of patients belonging to this class, death occurs through failure of the organic centres or their

[1] *Edin. Med. Journ.*, 1881, vol. xxvi. p. 865.

connections, and more especially of those subserving the respiratory functions. One of the most striking points presented by patients cut off in this way, is that, in spite of the peripheral lesions, there is no appearance of trophic changes —no destructive processes in the skin or any of the viscera, simply a failure of the organic functions of some vital structure.

One of the most instructive cases belonging to the group just referred to was under observation in Ward 25 last year, and as the symptoms and lesions form a most striking clinical picture, we propose in this contribution to describe and analyse them.

For notes of the case we are indebted to Mr. W. A. Garbutt, who, at the time of the admission of the patient, was acting as Resident Physician.

Clinical Report.

Mrs. H., æt. 38, housewife, was admitted to Ward 25 of the Royal Infirmary, on the recommendation of Dr. Veitch, on 2nd April 1894, complaining of general debility, great weakness of the hands, and almost complete loss of power in the feet and legs, with numbness, and a sensation of "pins and needles" in the legs and arms.

The weakness in the legs had lasted a fortnight, and the numbness and loss of power in the upper limbs had been present for four days.

Her family history was good; her parents dying of old age.

She herself had a family of six healthy children. She had been married twelve years, and had been pregnant six times. All her labours were easy, but she suffered from swollen legs during all her pregnancies. Her last labour occurred three months before the commencement of the illness for which she was admitted. Two days after her confinement she got up for a short time, and on the next day she got up altogether. She suckled the baby.

Before her latest illness she had always been very healthy, and had only suffered from scarlet fever when a child.

Her *present illness* began about a fortnight previous to her admission, when she had a "shivering" attack, and other

slight febrile symptoms. She took to her bed for a day, and then resumed her household duties with difficulty for nearly a week, when she was compelled to take to her bed again. She remained in bed for four days, and then, on attempting to walk, she staggered like a drunken person, and had to be assisted to bed again. All this time, that is, during these four days, she complained of severe pains in her back, which were relieved by sitting up. She sent for Dr. Veitch on 30th March. He noticed the weakness in her hands, legs, and feet, and as she had not slept for six nights, he gave her a powder to make her sleep, but without effect. For her weakness he ordered her a tablespoonful of whisky four times daily.

On Sunday, 1st April, she got up, but fell to the floor, and, being unable to rise, was lifted into bed. During the night following she suffered much from numbness of the hands, and on the following day (2nd April) she was admitted to the Royal Infirmary. According to Dr. Veitch, who saw her for the first time on 30th March, the symptoms seem to have come on in the following order:—

1. Weakness, amounting to staggering—about a fortnight's duration.
2. Sleeplessness (due probably to the nocturnal pains which began simultaneously) about a week before admission.
3. Numbness in the hands—the day before admission.

It may be mentioned here that most careful inquiry was made with regard to the question of infection, and though a neighbour's child had recently died of diphtheria, there was no history of sore throat in any member of the patient's family.

Habits.—Her food does not seem to have been plentiful or of good quality. Her friends assert that she was not given to drink; but close inquiry has been made by Dr. Veitch, who has learned that she was frequently in the habit of locking herself in a room with no good reason for doing so; and he further states that she told a neighbour that they had gone through nine large bottles of whisky during New Year's week. They had no visitors to help them. She had a liking

for whisky, and had borrowed money to get it. She suffered frequently from morning sickness and headaches.

State on admission.—Height, 5 ft. 6 in.; weight, 9½ st. Her development and muscularity very fairly good. She wore an anxious expression, and seemed greatly depressed. She stared in a vacant manner when spoken to, but was quite reasonable and perfectly intelligent.

Her appetite was good; pulse and respiration perfectly normal; temperature about 98° Fahr. on admission. The nervous system was the only one affected.

Sensory functions.—Patient complained of pain in the "small of her back." This was so great that she had continually to change her position, and, when touched in any part of her back, the pain was excessive. It was relieved by sitting up, as a rule. There was no history of pain anywhere else.

Numbness was present in the hands, feet, and legs; in the hands she also experienced "pins and needles" sensation.

Her *sensibility to touch* was unimpaired in all regions—localisation and rate of conduction being perfect.

Sensibility to pain was normal except over the right external malleolus, where the prick of a pin was referred to as a "touch."

Temperature sense was impaired, in that delay of conduction was manifested, but she could correctly distinguish between heat and cold.

Muscular sense was markedly impaired—the usual tests being applied. She said that her right lower limb did not feel as if it rested on the bed at all.

Pupils equally and moderately dilated.

Motor functions.—Organic reflexes unimpaired.

Skin reflexes.—The plantar reflex on each side was abolished; the other superficial reflexes were present.

Tendon reflexes.—The patellar reflex was absent on both sides; no ankle clonus was present.

Voluntary movements.—There was distinct pointing of the toes on both sides, due to a condition of talipes equinus of long standing (since birth).

The patient could not draw up her knees, but if put up

for her she could extend them. The inability to use her flexors was more marked on the right side.

The grasp was feeble, and the flexors and extensors of the forearm weak; the muscles of the upper arm were a little stronger.

The muscles of the lower extremity did not react to faradism, but reaction was obtained in the upper extremities, although feeble, especially so on the right side.

Vasomotor symptoms were absent, except a slight cyanosis of the feet, and distentions of the superficial veins.

Visceral functions.—There were no symptoms of disturbance of the functions connected with the viscera.

The patient was extremely feeble and irritable, and altogether incapable of undergoing a minute investigation, and the clerk had not completed his examination when she became so ill that no further clinical observations were possible. The provisional diagnosis was peripheral neuritis.

The treatment adopted was a careful regulation of diet, the subcutaneous administration of strychnine, and the employment of mild faradism and gentle massage.

From the time of her admission the patient was extremely restless, and constantly desired change of position. She slept very little at night, notwithstanding the administration of potassium bromide and chloral hydrate. So great was her discomfort, that the nurse's attention was constantly taken up with her. She took her food well, but was extremely irritable, and complained of intense pain in the lumbar region when moved.

She was seen at 2.30 A.M. on Thursday, 5th April, by the Resident Physician, who had occasion to sit up with another patient till that hour, and looked at Mrs. H. before retiring. The nurse had put screens round her, as she thought the patient felt more inclined to sleep when shut out from all her surroundings. At this time she was sleeping, and seemed to be no worse than on the previous day.

At about 9.5 A.M. on Thursday, the Resident Physician was summoned, and, on going to the ward, was surprised to find the patient quite unconscious, and exhibiting marked cyanosis about the face and lips. The nurse reported that

she had complained of shortness of breath at about 6.30 A.M., but took her breakfast well shortly after. At 9 A.M. she called for the bed-pan, and when it was removed she exhibited intense dyspnœa, and became cyanosed, whereupon ether was injected and brandy given till the arrival of the Resident Physician. She was, as already mentioned, unconscious and cyanosed; her respirations were 24 per minute, very feeble, and carried on solely by the extraordinary muscles of respiration with the upper two, perhaps three, intercostal muscles on each side. There was no movement whatever of the diaphragm or lower intercostal muscles; the pulse was very frequent, small, and irregular. Her eyes were almost closed, and her eyeballs turned upwards. The conjunctival reflex was absent; Sylvester's method of artificial respiration was commenced at 9.15 A.M., in the hope of keeping her alive till her friends, who had been sent for, arrived.

No change of note took place during the first five minutes, but by the end of about ten minutes her face began to assume a more favourable colour; the cyanosis disappeared almost completely. At this point she opened her eyes, and spoke for the first time in answer to questions put to her.

Artificial respiration was kept up for five minutes longer, and then stopped to test her own respiratory powers, but in less than a minute her face assumed its former condition of cyanosis, and the artificial respiration had to be continued. She had already received ether subcutaneously and brandy internally, on account of the extreme feebleness of her pulse. Her pulse several times showed signs of failure, and required similar treatment.

About 11 A.M. several students undertook the respiration, and an examination was made as far as possible. Her breathing became stertorous, due to the presence of mucus in her bronchi. She had not power to expectorate, and various devices were tried without effect.

The vocal chords moved extensively with each breath; her speech, understanding, and memory at this time were quite as good as when admitted.

Conjunctival reflex absent in both eyes; pupils equal and

moderately dilated, and reacted to light and for accommodation; the movements of the eyeballs were normal. The patient complained at this point of double vision. The sense of smell and of taste on each side was confused, but more so on the left; the hearing was good.

The deglutition was apparently unimpaired; and her micturition and defæcation had been quite normal up to this stage.

She complained greatly at this point of pains in her legs and back, and of numbness in her arms and legs, but of no other subjective phenomenon.

Her sensibility to touch, pain, temperature, etc., as well as her muscular sense, were as on first examination.

The plantar and patellar reflexes were lost, as when first examined.

Her lower extremities were now (mid-day of Thursday, 5th April) quite paralysed, as were also her trunk muscles, intercostals, and diaphragm, as well as those of her upper arm on both sides. The muscles of the forearm and hand on each side were considerably weakened, but retained a little power up till the time of her death.

No reaction to faradism could be got in the lower extremities, nor in the intercostal muscles. It was slight in the upper extremities.

With one pole over the spine in the region of the third, fourth, and fifth cervical nerves, and the other on the sternum or abdomen, no reaction could be got.

Artificial respiration was kept up, without intermission for even a minute, altogether for sixty-eight hours, at the end of which time the patient died from exhaustion. It was carried out by relays of students, and although other methods were tried, Sylvester's seemed to be most effective. Occasionally her respiratory power was tested, but in no instance did she breathe longer than half a minute without artificial aid. In addition to the employment of artificial respiration, brandy, ether, and strychnine were repeatedly given—the two latter often subcutaneously. The nourishment consisted entirely of milk, beef-tea, and meat extract. Oxygen was given at various times, but without effect.

In this case there was no difficulty in regard to the diagnosis. The one fact that there was paralysis of the diaphragm, while there was retention of power in the upper extremities—innervated from a lower group of spinal cells—pointed strongly to the probability of peripheral lesions; and on reviewing the entire complex of symptoms—pain, numbness, tingling, loss of plantar reflex and of knee jerk, selective paralysis of groups of skeletal muscles, absence of any vesical or rectal disturbances, and loss of reaction to faradism—the conclusion was obvious that the patient suffered from multiple neuritis of alcoholic origin.

Pathological Report.

The following are the notes of the post-mortem examination performed by Dr. Leith :—

Peripheral Neuritis.—Ward 25. E. H., æt. 36; died 8th April 1894; post-mortem, 9th April 1894.

External appearances.—The body was fairly well nourished. Rigidity well marked throughout. Marks of slight diffuse bruises on the shoulders and upper part of the thorax (the result of long-continued artificial respiration).

Head.—The superior longitudinal sinus was filled with imperfectly clotted blood.

Brain.—Weighed 3 lbs. 4 oz. The convolutions were very slightly flattened. Vascularity of surface was normal. The membranes and vessels at the base showed nothing abnormal.

The pons and medulla showed nothing abnormal beyond general congestion of the grey matter.

Spinal cord.—The membranes were normal.

For about 1½ in. in the lower dorsal region the cord felt somewhat soft, but the structures could be quite distinctly seen on section. The rest of the cord was firm, and appeared quite healthy, with the exception of congestion of the grey matter. No distinct softening.

The peripheral nerves showed nothing abnormal on naked-eye examination.

Thorax.—There were some fibrous adhesions on the

anterior part of the right lung. The left pleura and pericardium were normal.

Heart.—Its external appearance was normal. Both ventricles contained ante-mortem coagula, extending along the arterial trunks. The arterial valves were competent.

Cone Diameters.

Aortic	0·95 in.
Pulmonary	1·0 „
Mitral	1·5 „
Tricuspid	1·8 „

The valves were normal.

The left ventricle was slightly hypertrophied. The other cavities were normal; the heart muscles appeared healthy. Heart weighed 13 oz.

Lungs.—Left lung weighed 1 lb. 3 oz. Posteriorly it was congested and very œdematous, and the bronchi contained abundant frothy and blood stained mucus. Right lung weighed 1 lb. 4 oz., and was in a similar condition. No consolidation in either of the lungs.

Abdomen.—The peritoneum was normal.

Liver.—Weighed 4 lbs. It was congested—otherwise normal.

Kidneys.—Right weighed 6 oz. The capsule was very slightly adherent in parts, but there was nothing else abnormal. Left kidney weighed 6½ oz., and showed nothing abnormal.

Spleen.—Weighed 6 oz., and was perfectly normal.

None of the other organs showed anything abnormal.

There were no tumours or evidence of anything pressing on cord or nerves. No gross lesions discoverable on naked-eye examination to cause the paralysis.

For these details we are indebted to the courtesy of Dr. Leith.

Microscopic Examination.

The portions of the nervous system specially examined were—the brain and cord, the brachial plexuses, the right ulnar, the sciatic, posterior tibial, and the right anterior

crural nerves, the nerve to the left gastrocnemius muscle with a portion of the muscle attached, the fourth right intercostal nerve, and the phrenic nerves with portions of the diaphragm, the vagi nerves and the sympathetic on the right side, with the superior cervical ganglion. Unfortunately the external popliteal nerves were not obtained, nor any of the ganglia on the posterior nerve roots.

The specimens were preserved in Müller's fluid in the usual way.

The methods of staining mostly used were osmic acid; Pal's modification of Weigert's hæmatoxylin stain for medullary sheaths;[1] hæmatoxylin and eosin; and Ranvier's picro-carmine; to a less extent Rehm's congo-red method, for the axis cylinders.[2]

Pal's modification of Weigert's method was selected in place of Marchi's method, because in our hands, at least, it gave better results for photographic purposes.

It should be stated here that medullated fibres which are in an early stage of degeneration, stain by this method so deeply *all through the fibre* that the uniform depth of colour alone is a fairly reliable guide; whereas, properly treated normal fibres show a much deeper stained peripheral portion of the myelin, with a clear, almost transparent, central part round the axis cylinder.

The results are of special interest, because the whole duration of the disease was only twenty days from the very commencement, and the intercostals were only seriously affected for seventy to eighty hours. There are extremely few cases on record which are similar in respect of rapidity.

The brain and medulla showed nothing abnormal. In the cord the postero-internal columns stained much more deeply than the rest of the white matter; this change was marked all along the cord, from the lumbar enlargement upwards. On naked-eye examination these areas appeared slightly whiter, although the alteration was not very apparent. In sections in both lumbar and cervical enlargements the postero-external

[1] *Ztschr. f. wissensch. Mikr.*, Brnschwg., 1888, s. 88.
[2] *München. med. Wchnschr.*, 1892, No. 13.

tracts were seen to have suffered in the same way, although only for a short distance. These tracts stained more deeply with eosin, and showed slight increase of connective tissue, but little proliferation of nucleated cells.

Close to the medulla, and in the dorsal region of the cord, the central portions of the postero-internal tracts appeared normal.

In one section, taken from the region of the cervical enlargement, a small hæmorrhage was seen in the grey matter at the root of the posterior cornu, on the right side. The capillary from which the hæmorrhage had occurred showed very slight, apparently hyaline degeneration of its wall. No other hæmorrhage was observed.

The anterior and posterior cornua otherwise appeared normal, but the posterior nerve-roots between the ganglia and their entrances into the cord, and to a much less extent the anterior, showed increase of nucleated cells, to be presently described, especially near the vessels in the septa of the endoneurium. A few of the fibres, especially those peripherally placed, or next the septa, showed slight granular degeneration of their medullary sheaths, but the majority were normal.

The following changes—some of which are of the greatest interest—were observed in the nerves:—

I. *Interstitial.*

1. *Vascular changes.*—These are best marked in the arterioles and capillaries, and much less marked in the veins. We take an arteriole for the purpose of description, because in these vessels the appearances are best marked. This change shows itself first in the intima. Roundish or oval cells, with a single large rounded nucleus, generally showing karyokinetic figures, and with a very small amount of protoplasm, appear next the lumen of the vessel, and project into it. These gradually increase in number till there is an almost complete regularly arranged circle of these cells; greatly diminishing the lumen of moderately sized arterioles, and almost blocking the smaller ones. In fact, in some of the minute arterioles and capillaries, the lumen is completely obstructed

by one or two of these large cells, so that a red blood corpuscle could hardly squeeze past. In the outer layers of the intima, in the media, and in the adventitia, similar cells appear, but are compressed, and look more like connective tissue cells, with greatly enlarged nuclei and a minimum of protoplasm. The karyokinetic figures, which stained very indistinctly in specimens preserved in Müller's fluid, are not so well marked in the media and adventitia. Coincident with these cell changes there is thickening of the arteriole

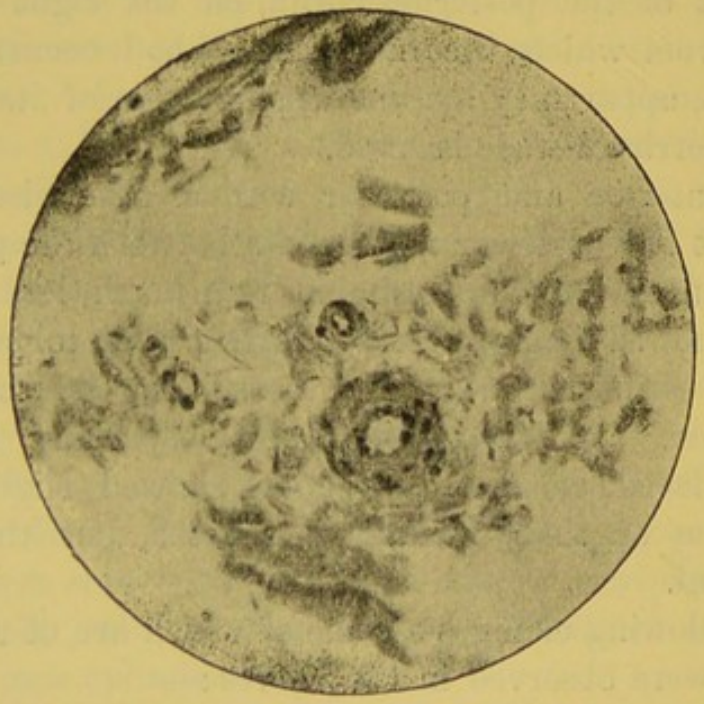

Fig. 1.—Hæmatoxylin and eosin (× 650). Arterioles in connective tissue between funiculi of right posterior tibial nerve, showing the nucleated cells in all three coats of the larger vessel, though mostly confined to the intima of the smaller. Note also narrowing of lumen.

coats, especially the media and intima, and the whole vessel has in some cases a peculiarly translucent appearance. The veins only show in their smaller branches a few of these cells next the lumen, and they are neither so large nor so regularly arranged (Fig. 1).

These changes are seen in the vessels of the connective tissue between funiculi, in the perineurium,—especially the inner layers,—and in the septa of the endoneurium. These phenomena have been described previously in 1893 by Dr. Sigmund Fuchs, in a case of multiple neuritis, but in his case the patient lived for five months after the commencement of

the disease.[1] The first observer was Minskowski, who noted similar changes in 1888.[2]

Some of the nerves show very early stages of capillary formation, especially in the endoneurium and the inner lamellæ of the perineurium.

2. *Connective tissue changes.*—In the perineurium in some nerves there is marked thickening of the inner lamellæ, with proliferation of connective tissue cells, and in many cases the same kind of cell, seen in the arterioles, appears between the lamellæ; these are mostly in groups, though they also appear singly. These lymphoid-like cells show here, too, karyokinetic figures, and they may be easily distinguished from the normal connective tissue cells by the great size of their nuclei, and by the examination of sections of the nerves cut longitudinally.

In the endoneurium the septa are thickened to a greater or less extent, and the lymphoid cells—if we may so call them—are seen in and between the connective tissue strands, generally more numerous in the neighbourhood of vessels, but also free between the nerve fibres. They are found in great numbers towards the periphery of the funiculi. Many show karyokinetic figures, some are seen in process of division, and two cells may be seen which have evidently just divided.

Leucocytes are also present, but the cells almost invariably present in all the nerves, though in very varying numbers, are the lymphoid cells, which so closely resemble in appearance the cells in the capillaries. The apparently free lymphoid cells between the nerve fibres are generally, however, considerably larger than the cells in the vessels.

These free lymphoid cells are in greatest numbers, and are best seen in spaces which have evidently been occupied by exudation. This exudation leaves a few fibrinous shreds behind as evidence of its previous existence, and in addition these lymphoid cells.

In nearly all the nerves affected there is evidence of more or less of this exudation separating the nerve fibres or squeez-

[1] "Deutsche Ztschr. f. Nervenheilk.," 1893, bd. iv. p. 38.

[2] "Mitth. aus d. med. Klinik zu Königsberg," Leipzig, 1888, s. 59.

ing them together, and this is always best marked next the perineurium.

II. *Parenchymatous.*

1. *Myelin sheath.*—The medullary sheaths are greatly altered, often granular, or the myelin is collected into droplets, or may be absent altogether, leaving the primitive sheath empty.

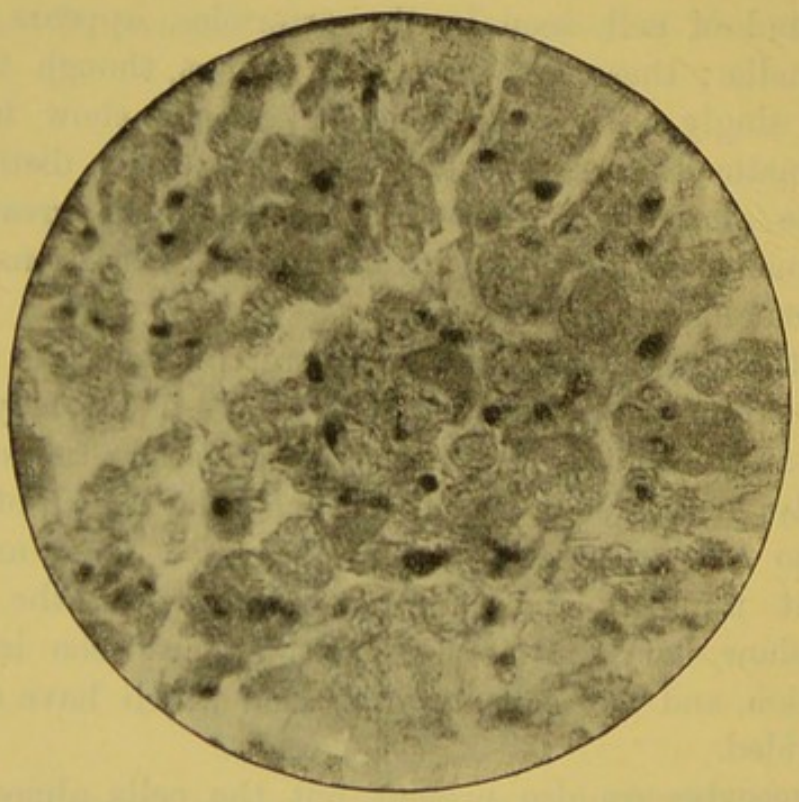

FIG. 2.—Hæmatoxylin and eosin (× 1100). Fourth right intercostal nerve. Transverse section. Shows changes in nerve fibres and especially mass of homogeneous myelin filling half of sheath (seen in centre of field), nuclei are mostly segmental.

Sometimes, however, the myelin collects into one-half of the primitive sheath, or possibly the myelin from several fibres collects and forms one homogeneous-looking mass, practically a corpus amylaceum (Fig. 2).

2. *Primitive sheath.*—The nuclei, which might be called for brevity "segmental," are found to be greatly swollen here and there throughout the sections of many of the nerves, often twice or thrice their original size, and are generally surrounded by a small amount of clear protoplasm. In some of the nerves these cells have proliferated, and they

can be readily differentiated from the lymphoid cells by their relationship to the nerve fibres, and by their spindle-shaped appearance on longitudinal section. From a very careful study of a large number of sections of all the nerves, we may confidently assert that where these changes in the segmental nuclei exist, the myelin of the fibre is inevitably degenerated.

3. *Axis cylinders.*—These are seen in certain nerves to be much distended, in others swollen up and vacuolated, and in many fibres of the most affected nerves they have disappeared altogether.

The parenchymatous changes will be referred to at greater length where requisite.

It should be stated that different portions of each nerve were examined so as to compare changes at different levels, so far as the specimens permitted; and we can assert that in these nerves, though there were marked differences in detail, the chief characteristics remained the same; generally, however, the nearer the termination the more marked the degenerative changes were.

Taking the nerves in order:—

Right sciatic.—The changes in the arterioles, etc., are well marked, though not to the same extent as in the right posterior tibial nerve. They are well seen in the connective tissue between the funiculi, but specially within the funiculi themselves. The cells are most numerous in the intima, and there is less thickening of arteriole walls than in the right posterior tibial. The perineurium is little changed, only here and there aggregations of lymphoid cells.

There are few lymphoid cells in the interior of the funiculi, and only a small proportion of these show karyokinetic figures.

Of the nerve fibres, many are normal, but more are granular; here and there, nearest the periphery of the funiculi, a few fibres have apparently run together, but these are not numerous. Some of the axis cylinders show swelling, and some have totally disappeared, especially in those fibres showing most advanced degenerative changes.

Right posterior tibial nerve.—In this nerve the most marked

changes in the vessels are seen; in fact, all the appearances already described are met with here. In the arterioles outside and inside the funiculi, the intima, media, and adventitia are all affected, all show numbers of these typical cells, and here, as in Fig. 1, the cells are found lining in more or less regular order the lumen of the vessel. They may be to some extent altered existing cells, but many of them show karyokinetic figures, and appear to be actively proliferating. Between the lamellæ of the perineurium the lymphoid cells are well marked and mostly in groups, and there are great numbers of these cells inside the funiculi. These cells all show karyokinetic figures with extreme distinctness, better perhaps than in any other nerve.

There is some connective tissue increase in the septa within the funiculi, and also evidence of commencing formation of new vessels.

The nerve fibres are, comparatively speaking, less affected than might be expected. Many are finely granular, and in some peripherally placed fibres there are only myelin droplets left, or nothing at all. The granular appearance of the fibres is remarkably well seen in some dissociated fibres stained with osmic acid.

The segmental nuclei show here and there enlargement and proliferation, and in some fibres they are seen deeply indenting the myelin.

The axis cylinders show the appearances already described, but are comparatively little affected.

It is extremely interesting to find in this nerve such marked interstitial changes associated with an early stage of degeneration in the nerve fibres themselves, especially when we remember that the limb was so completely paralysed, suggesting far more marked degeneration in myelin and axis cylinders.

Right anterior crural nerve.—Some vessel changes are seen as described in the last nerve, but much less advanced.

There is less change in perineurium, only some groups of lymphoid cells between inner lamellæ, but these are very infrequent.

There are considerable numbers of lymphoid cells inside

the perineurium among the nerve fibres, many showing karyokinetic figures, and mostly grouped near the periphery of the funiculus.

There is slight increase of connective tissue of the septa inside the funiculi. The fibres are apparently, to a great extent, normal towards the centre of the funiculi, those degenerated are mostly peripherally placed, although they are met with scattered here and there among healthy fibres throughout the funiculi. The axis cylinders show to a less

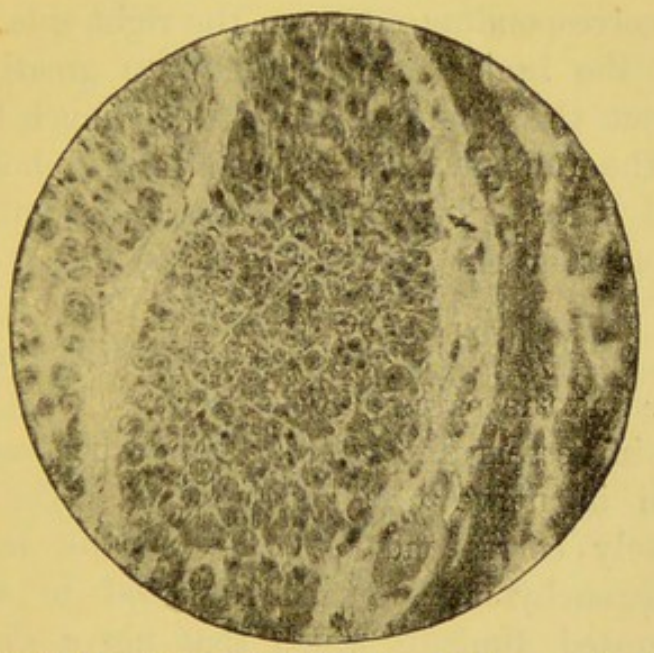

FIG. 3.—Hæmatoxylin and eosin (× 350). Right posterior tibial nerve. Transverse section. Shows lymphoid cells and also greatly enlarged axis cylinders.

extent the changes described in the right posterior tibial nerve.

Left sciatic nerve.—The changes here closely resemble those met with in the right sciatic, but in certain funiculi the lymphoid cells are in much greater numbers, and show better marked mitotic figures.

There is also much greater proliferation of segmental nuclei, especially in certain funiculi, and in these the medullary sheaths appear much more degenerated, and more universally so.

Some of the axis cylinders show great bulging or ballooning out. One in particular was observed fully twelve times

its normal size, very faintly stained with eosin and very highly refractile. Curiously enough, this ballooning is not necessarily associated with degenerative changes in the myelin, at least at the same level, for a narrow, perfectly clear rim of apparently normal myelin surrounds the axis cylinder in the fibre referred to, and the segmental nucleus which chanced to be cut at the same level was normal also. Such ballooning of the axis cylinder was, however, always noticed to be associated with degeneration in the myelin at a lower level.

Left posterior tibial nerve.—Changes are much less marked than in the corresponding nerve on the right side.

Between the funiculi the vessels are greatly distended with blood, but the arteriole changes are much less marked, and inside the funiculi there are fewer lymphoid cells and more normal fibres. The degenerative phenomena are not further advanced in this nerve than in the parent trunk—the sciatic.

Nerve to the left gastrocnemius.—Interstitial changes are not so marked as the parenchymatous.

Changes in vessels and perineurium much more slightly marked than in nerve fibres themselves. The interstitial changes closely correspond to those of the left posterior tibial, the parenchymatous greatly exceed in severity the most degenerated funiculi which that nerve showed. The lymphoid cells were gathered in groups within the funiculi, and were mostly peripheral or near septa, and were not very numerous. In many of the nerve fibres the myelin is only represented by droplets; in some cases the outer sheath is empty altogether, and many of these fibres have lost their axis cylinders.

Gastrocnemius muscle.—Transverse striation is to a considerable extent lost. Many fibres are granular, and some show clear droplets, which blacken with osmic acid.

The nerve fibres running to the muscle fibres show even more advanced degeneration than in the trunk of the nerve, but there seem to be even here some almost unaffected nerve fibres.

Right and left brachial plexuses.—The right shows more marked changes than the left, and these are more interstitial

than parenchymatous. Very early changes in the arterioles are evident; but, curiously enough, the perineurium round many of the funiculi is thickened in the right plexus, and there are more nuclei on that side within the funiculi, the excess being apparently due mainly to lymphoid cells.

The nerve fibres are very slightly affected in both; certainly more are degenerated on the right side than the left.

FIG. 4.—Weigert-Pal (× 55). Fourth right intercostal nerve. Transverse longitudinal section, shows the indefinite outline of the fibres.

Right ulnar nerve.—Changes in vessels are much less marked than in nerves of right leg. The coats of the arterioles are slightly thickened; those in the connective tissue between the funiculi show better than in any other nerve that the intima and media have a distinctly hyaline appearance.

The nerve fibres have suffered to some extent, though many are normal. As usual, the peripheral fibres show the most advanced changes.

Fourth right intercostal nerve.—This is perhaps one of the most interesting nerves of those examined. It shows practically little interstitial change, only a few large nucleated cells appear in the intima of the arterioles; comparatively little change in the peri- or endoneurium, and a few lymphoid cells here and there, especially peripherically, constituting the principal alterations. The nerve fibres stain better than might be expected, by Weigert's method, but as the whole process in this nerve was so rapid, this is not after all so remarkable. Note, however, how blurred and thick the fibres seem to be in Fig. 4. On examining sections cut in paraffin and stained with hæmatoxylin and eosin, the condition was at once clearly made out.

There are practically no normal fibres at all. Many have run together, apparently due to rupture of the primitive sheath, and form masses of myelin, which are to all intents and purposes small miliary scleroses.

Many fibres have their myelin collected into one-half of the primitive sheath, as in Fig. 2.

The myelin is sometimes homogeneous, sometimes extremely granular. No fibre retains the normal concentric ring arrangement of the myelin. Some sheaths of the fibres are almost empty, save for the axis cylinder, and some have lost even that. The axis cylinders show very marked bulging, and in not a few of these bulgings vacuoles are present. The segmental nuclei are markedly altered, many being swollen, and many have proliferated to a considerable extent.

The phrenic nerves.—Here the changes are much slighter than we should anticipate from the clinical history.

The arterioles, especially in the endoneurium, show early but quite distinct cell proliferation affecting the intima mainly. There is little change in the perineurium, and the number of lymphoid cells present varies considerably in different parts and at different levels of the same nerve bundles.

Many of the nerve fibres are normal, those much degenerated being only found peripherally. Both nerves closely correspond, the left being perhaps, if anything, more affected than the right.

The diaphragm.—Portions near to and at the entrance of the phrenic nerves were examined.

There is no great change in the transverse striation, except in a small proportion of the fibres, where it appears very faintly marked. Far better marked is the proliferation of the nuclei of the sarcolemma. This is well seen in the left half of the diaphragm close to the entrance of the nerve, and is better marked than in the right half. The sections of

FIG. 5.—Weigert-Pal (× 60). Right phrenic nerve. Transverse section (slightly slanting).

diaphragm, including smaller branches of the phrenic, show more marked degeneration in the myelin of the nerve fibres than in the nerve trunks themselves.

Fig. 5 is a nearly transverse section of the right phrenic; many of the fibres are normal.

Fig. 6 is taken from a longitudinal section of a branch of the right phrenic in the diaphragm.

Some surprise may be felt that, where the diaphragm was so markedly paralysed, so little change, comparatively speaking, should be found in the nerve fibres themselves. It must, however, be remembered that women breathe far more with

their intercostals than men, and that the advanced changes seen in the fourth right intercostal, and no doubt also present in the other intercostal nerves, would be quite sufficient to bring on marked dyspnœa. Then, when we find that the vagi are affected, interfering to some extent at least with the connecting link between lung and medulla, and that the phrenics have not entirely escaped, we do have an almost sufficiently satisfactory explanation of the clinical phenomena.

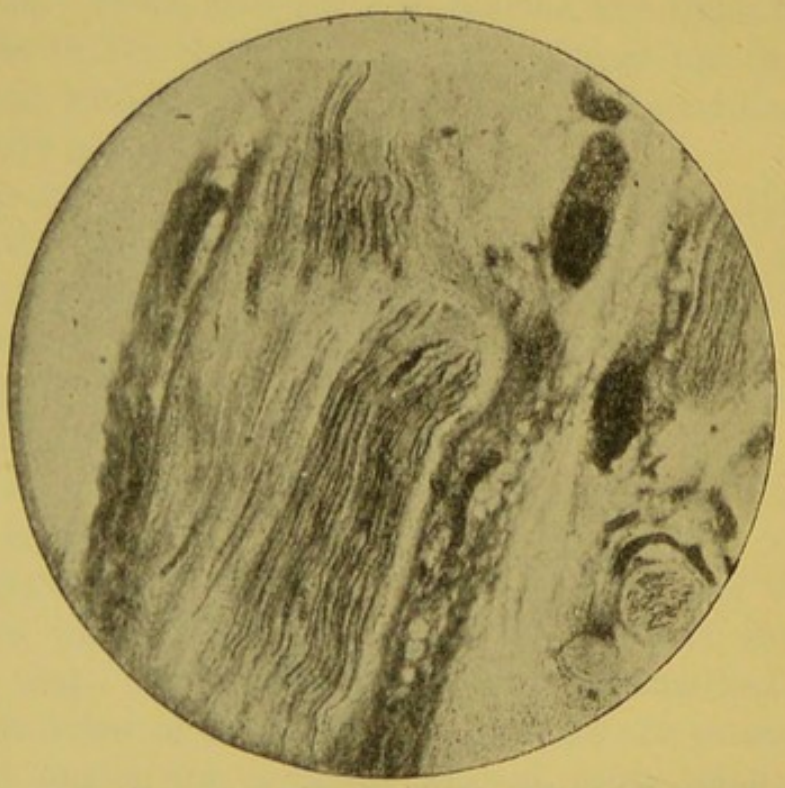

FIG. 6.—Weigert-Pal (× 70). Right phrenic nerve, intramuscular branch, longitudinal section.

The vagi.—These nerves, which are always more difficult to examine, show early changes in the arterioles, and most marked within the funiculi. There are a limited number of free lymphoid cells, and a very few of the medullated nerve fibres show an early stage of granular degeneration. This change, slight though it is, may possibly account for the rapidity of the pulse.

Right sympathetic on the neck.—The ganglia were examined. The cells show an abnormal amount of yellowish-brown pigment, the granules being very highly refractile.

The arterioles show proliferation of cells in the intima,

and to a less extent in the media. Many larger nuclei are seen, especially surrounding the ganglion cells, and these are evidently undergoing proliferation.

The changes seen in the nerves are so interesting, that a somewhat lengthy description has been given of the most important appearances; yet many interesting details are of necessity omitted, which, however, may be published later.