A

C O N T R I B U T I O N

to the

STUDY of PARALYSIS AGITANS

and

TWO ASSOCIATED CONDITIONS

by

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I hereby declared
this thesis to be my own
work. done at the
National Hospital Queen Square
London W.C.1., where I
have been resident physician
for the last two years.

Henry J. Macbride.

C O N T E N T S

close similarity

Pathological findings (1) Substantia nigra

(2) Globus pallidus

(b) BENEDIKT'S SYNDROME

Description of a Case

Situation of lesion.

Kinnier Wilson's cases of Argyll Robertson pupil with a paralysis agitans tremor.

CONCLUSIONS

The relation between rigidity and tremor.

The relation of the pallidal to the autonomic system.

CONCLUSIONS of THESIS

THOUGH Paralysis agitans is not an uncommon disease and though it has been recognised as a definite syndrome for many years, yet its causation is not known. Likewise its Pathology is still not clearly understood, though much work has been done in recent years which has enabled us to attribute it to a lesion of the so called extra-pyramidal system, and to associate it with the syndromes of Wilson and Vogt, in both of which there are lesions in the basal ganglia. Trétiakoff and Souques[13] have recently drawn attention to changes in the midbrain, in the substantia nigra.

AFTER considering Paralysis agitans from a clinical point of view, I shall endeavour, by a consideration of the associated conditions, to weigh the relative importance of lesions in the basal ganglia and lesions in the substantia nigra.

I propose to divide the paper into three Sections

1. Clinical.
2. Pathological.
3. Discussion.

I. CLINICAL

I. CLINICAL

THE onset of Paralysis agitans is about middle age. In a series of 50 cases selected at random, the average age was 44 years.

BETWEEN	the	ages	of	20	and 30	- 2 Cases
"	"	"	"	30	and 40	- 12 Cases
"	"	"	"	40	and 50	- 20 Cases
"	"	"	"	50	and 60	- 14 Cases
"	"	"	"	60	and 70	- 2 Cases.

JUVENILE forms of the disease occur, but they are comparatively rare. During the last two years, I have only seen two such cases, one commencing at the age of 15 years, and the other at the age of 19 years. These cases were not included in the group of 50.

BOTH Sexes are affected about equally. 26 were males and 24 females in my series.

THE hereditary and familial occurrence of this disease has been observed by some writers, especially in the juvenile form. In none of my cases was any other Member of the Family affected, as far as was known to the Patients. Therefore, on account of the rarity of its occurrence, one can place hereditary and familial occurrence as no more than a coincidence.

FROM the previous history of my Patients no infection could be of any help, so far as the causation of the disease was concerned. Syphilis has certainly no relation to this disease, though writers have found tabes and paralysis agitans in the same Patient. In no case of Paralysis agitans was the wassermann reaction positive over a number of 17 Cases. Many Cases gave in their history shock as the factor which brought on their illness. Since the Air raids quite a large percentage of the Paralysis agitans cases now coming into hospital date the commencement of their trouble from that time. In one or two cases the trembling began immediately after the raid and continued after it. It is well known that any excitement increases the tremor in Paralysis agitans, so that any violent shock could quite well bring into prominence a hitherto unnoticed tremor. Constant worry was put forward in a few cases as the cause. One cannot accept shock or any emotional factor as giving a satisfactory explanation of the cause of Paralysis agitans.

Trauma was given as the cause in a few cases and

in two cases the tremor began in the limb affected. But in the cases, where Trauma had to be considered as a cause, I have come to the conclusion that it no more than hastened on a condition which had already started.

SINCE the discovery in recent years of a Paralysis agitans syndrome following Encephalitis Lethargica, one has gone carefully into the history of all cases of Paralysis agitans and one has found no evidence that the "ideopathic" Paralysis agitans which is under discussion is due to the causal factor which produces Encephalitis lethargica.

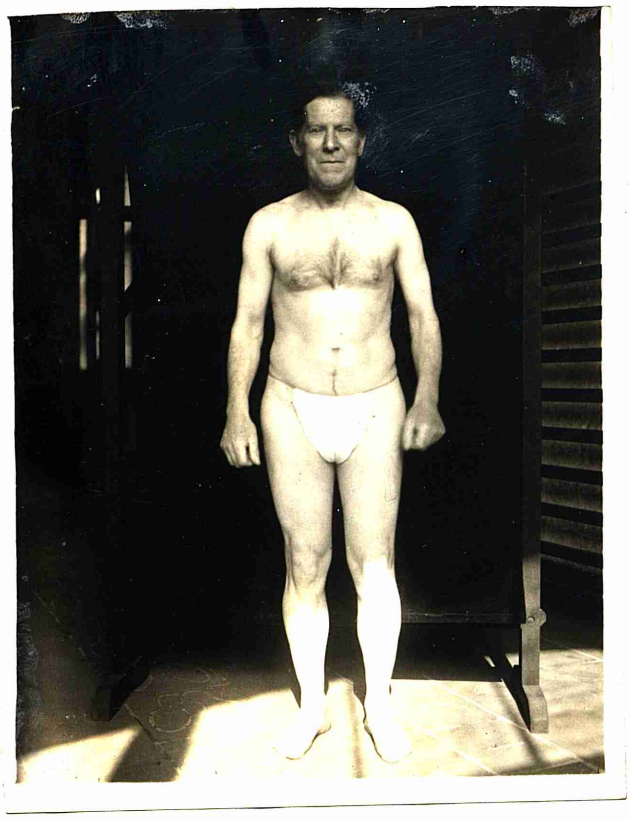
FOR this Section of the paper the writer is drawing from observations on close on a 100 cases of Paralysis agitans seen at the National Hospital.

THE earliest symptom observed by many patients was weakness especially felt at the lower part of the back and which was brought into prominence when the Patient attempted to turn in bed or sit up. In some cases the weakness was confined to the arm which later developed the tremor. Stiffness of a limb was the first thing noticed in some cases, while other patients first became aware of

their illness with the onset of the tremor, their previous condition having been normal.

IN one or two cases severe pains in the limbs of the side first affected were among their early symptoms and in two cases swelling of the limbs was the earliest sign. In several very early cases of Paralysis agitans which have been under my observation, loss of associated movements seemed to be the first of the cardinal signs of this disease to appear. It was well brought out when the Patient was asked to walk down the Ward. His arms would remain by his side and not swing as in the normal person. In one Patient where the disease was, up till the time of observation confined to one side, the other arm hung motionless by the side when he walked.

THE next sign in order of appearance was rigidity and lastly tremor. The time interval between these last two varied. In some cases according to the Patient's history they appeared together and in others several months intervened before the onset of the tremor. In one case the complete picture of Paralysis agitans was present except for the tremor and had been so for well



Photograph of a case of left unilateral paralysis agitans without rigidity. Note the typical attitude of the left arm.

over a year. In another case on the other hand in which the trouble was confined to one side, there was practically no rigidity though the tremor was well marked, The term "practically no rigidity" must be explained. The forearm could be taken and whip like movements made with the hand; the hand flopped about freely,yet,when the hand was passively moved,there was a very occasional interruptiom of the movement as if one were overcoming rigidity which was less than momentary. This case will be referred to later.

TAKING the tremor as the most reliable guide for the onset of symptoms, (as many Patients often notice nothing wrong till the appearance of the tremor) one found that with a few exceptions an upper limb was the first affected, the right more frequently than the left. After an interval, usually a few months, the homolateral leg was affected then the contra lateral arm and lastly the contralateral leg. In a few cases one arm was affected then the contralateral arm and in two cases the contralateral leg was the second limb affected. This more or less

constant march of the disease might be explained by the fact that as the arms execute finer movements, the tremor would manifest itself sooner there than in the leg; also a tremor in the arms would be noticed much more readily than one in the legs, because the hands are always under observation. As there is evidence of some form of localisation in the extrapyramidal, as well as the pyramidal system, the poorer blood supply to the anterior superior portion of the basal ganglia, which probably controls arm movements, may be the factor which determines the mode of onset of this disease.

THE Patient gradually assumes the typical picture of Paralysis agitans which will now be described. Not very much can be added to the splendid descriptions already given by many able writers (49) and therefore the well known signs will be described as briefly as possible.

THE full description of a typical case will now be given. In the next Section the pathological findings in this case will be added.

Miss C------ Dressmaker. Aged 59 years. Spinster.

Admitted 25th July 1921.

Died - 16th November 1921.

Complaint

Gradual loss of power in the left arm and leg for the past three years with a somewhat rapid loss in the right arm and leg during the past few weeks; also severe pain in the back.

Past health

Bronchitis and asthma nearly all her life. 12 years ago was said to have had a left sided pneumothorax. In 1914 her sputum was examined for tubercle bacilli but none were found. Since the beginning of the War Patient has been unable to work on account of general weakness, trembling in the hands and pain in the back of the neck.

Family history

Her Father died of bronchitis and asthma, her Mother of "creeping Paralysis" otherwise "nil ad rem"

Present Illness

In 1914 Patient noticed that her left hand trembled. About three years ago Patient began to have a pain in the palm of this hand, of an aching character and intermittent lasting about ten minutes at a time th

trembling then spread to both legs. She had to give up dressmaking owing to the increasing weakness in the left arm and leg. Gradually she began to feel that she had lost all spring in her movements and felt she was going to fall forwards.

A few months before admission pain began in the back and groins and continued. About the same time weakness and tremor began in the right arm and leg. Patient has felt herself getting gradually helpless.

Present Condition.

A woman of 59, somewhat thin with pale and mask like features. The arms were slightly abducted from the sides flexed at the elbow and wrist, with adduction of the forefinger and thumb and flexion of the other fingers. A fine rhythmical tremor was present in the hands and arms at rest. There was no trmor of the fingers face or legs.

Intelligence and memory were normal.

Cardio vascular system Apex beat inside the nipple line Heart sounds were slow and of poor quality.

Alimentary system showed nothing abnormal.

Genito Urinary System

Menstruation ceased twelve years ago, and there was nothing abnormal.

Some difficulty was experienced in holding urine

Respiratory System

There was dulness on the left side anteriorly merging into the heart dulness. Breath sounds were moist, and metallic râles with rhonchi were present on inspiration and expiration. The breath sounds were faint and signs of pleural thickening were present at the apex;the breathing had an amphoric quality.

The right side had harsh inspiration and prolonged expiration,rhonchi on expiration with occasional medium moist râles just below the clavicle.

Cranial nerves

I. Smell somewhat blunted.

II. Visual Acuity R. and L. $\frac{6}{24}$

Fields a little reduced to rough test.

Fundi normal.

III, IV. and VI. Pupils equal,central,regular reacted to light direct and consensual and to accommoda-

tion. Movements free in all directions. Convergence normal. Slight fine horizontal nystagmus at rest and on extreme lateral deviation.

Tremor was present in both eyelids and was fairly rhythmical. This Tremor was also present when the eyes were closed. The left lid drooped slightly.

V. Temporals and masseters were weak but equal on both sides. Corneal reflexes were present. Taste was normal. Jaw jerk was present.

VII. With the mask like expression the smile had a transverse appearance. Some weakness of the face muscles was present, more noticeable on the right side. The orbicularis oris muscles were weak.

VIII. Weber's test: Sound was referred to left ear.

Rinne: Air conduction was better than bone conduction on the right side,while bone was better than air on the left.

Deafness was present in the left ear. The left ear had a discharge and polypi were removed from it many years ago.

IX.& X. Palate moved well in the middle line,no dysphagia.

XI. Sterno mastoids and trapezii moved equally and well,though some rigidity was present in the neck

muscles and was of a "cog wheel" character.

XII. The tongue was well protruded in the middle line and was slightly tremulous, no atrophy was present.

Sensory System Subjective

Pain of an aching character was present in the back of the neck, left arm and lower part of the back.

Tingling was often present in both arms.

Objective

All forms of sensation appeared normal.

Motor System Arms { Movements full but slow: Power was weak especially in the left arm and hand.

Trunk There was no excursion of the umbilieus, when trunk was raised, but musculature generally was weak.

Breathing was abdominal and thoracic.

Legs Movements were difficult owing to the rigidity; practically no movement could be performed by the left lower limb.

Tone All muscles showed rigidity except the abdominals.

No wasting was present.

Co-ordination

Could not be tested for in the legs because

of the feebleness of voluntary movements, nor well tested in the left arm for a similar reason. The finger nose test was performed accurately and without tremor with the right hand.'

Dysdiadochokinesia could not be tested on account of the general rigidity.

Reflexes.	R.		L.
Supinator	+	=	+
Biceps	+	=	+
Triceps	+	=	+
Knee	+	=	+
Ankle	+	=	+
Abdominal	+	=	+
Plantar	flexor		flexor
Clonus	0		0

+ = Present 0 = Absent

Sphincters Nil abnormal.

Spine and skull Nil abnormal, except a slight rounding of the upper dorsal spine associated with the Paralysis agitans attitude of flexion.

Vasomotor System Frequent flushings occurred in the arms followed by profuse perspiration.

Gait Patient walked with small steps though she was very weak. The whole attitude was one of flexion. Propulsion and retropulsions were present.

The three cardinal signs of the disease are :-

1. Tremor
2. Rigidity
3. Loss of associated and automatic movements.

Tremor of the upper limb, in all my cases, was most marked peripherally in the hand and fingers. In the fingers, the movements were chiefly at the metacarpophalangeal joints and usually the digits all moved synchronously. In some cases there was a want of this synchronicity, one finger occasionally getting out of the rhythm. In most cases the "pill rolling" movement was observed in the thumb and forefinger. The wrist movements were sometimes distinctly flexor-extensor, sometimes lateral and sometimes pronator-supinator. Often the tremor consisted of a combination of these. Frequently flexor-extensor tremor was present at the elbow. No movements of the shoulder were observed except those conveyed from the periphery of the limb.

In a small number of cases tremor was noticed in the neck muscles, giving nodding and lateral movements of the head. In some cases the tremor from the arm was conveyed to the head. The commonest tremor in the face was that in the lower lip and chin muscles, giving rise

to the "litany" tremor. With the expressionless face and the muttering movements made by the lower lip the Patient has the appearance of saying a prayer. In one case a tremor was observed in the frontalis muscle. Tremor was often present in the tongue. The tremor of the lower limb was usually confined to movements of the foot. In some cases the tremor was so marked that, when the Patient was sitting in a chair, the heel would tap the ground loudly and rhythmically. Tremor has been observed at the knee and hip.

I have not seen any cases with tremor of the trunk muscles apart from tremor of the pectorals.

The tremor was rhythmical and its average rate was about five oscillations per second. The amplitude varied, in some cases it was fine, in others coarse and often in the same Patient it varied.

The characteristics of the tremor are that it is present when the limb is at rest; volitional movement such as touching an object it usually ceases to recommence on reaching the objective; to a certain extent the Patient can control the tremor for a few seconds occasionally for a few minutes; any excitement

or emotion greatly increases it.

The tremor is always best elicited when the limb is at rest. In some cases the Patient was asked to outstretch the arms and let the hands hang loosely at the wrist, so that a group of muscles was stretched against gravity. The hands remained often some time without visible tremor, but immediately the arms were allowed to rest on the bed the tremor re-commenced. In one case of postencephalitic paralysis agitans which is, as I shall describe later, essentially the same as the classical disease, the tremor could be stopped indefinitely by deviating the hand to the ulnar side. This led to my having a small splint made which could hold the hand ulnar deviated. The application of this splint stopped the tremor (so long as the radial group of muscles was sufficiently stretched) but it gave rise, unfortunately, to considerable discomfort, so that the splint could only be worn for an hour or so at a time.

The tremor always stopped during sleep, so far as one could observe.

Although the tremor is essentially one of the resting limb, yet in some cases it may abate when the limb is at rest and recommence when any voluntary movement is made. Even in these cases, however, there is no relation to the intention type of tremor found in Disseminated Sclerosis.

The rigidity usually followed the same course as the tremor, beginning in one limb and gradually spreading to the others, the trunk neck and head not being exempt in the later stages. This rigidity usually predominates in the flexors and when once established it gives rise to the typical attitude of this disease. In the typical picture of the disease the head is bent forward on the chest, the back slightly rounded, the arms abducted slightly from the side and a little flexed at the elbow, the hands usually extended at the wrist, the fingers flexed at the metacarpo-phalangeal joints, the phalanges extended and the thumb adducted to the forefinger; the legs are slightly flexed at the knees. This description applies to a Patient who is able to stand. Those Patients whose weakness and rigidity confines them to bed have slight variations from it

and some little additions. The arms are usually flexed across the abdomen or chest. The legs may be flexed at the hips and knees and slightly adducted. In some cases the feet were slightly inverted and the toes slightly flexed. The face is expressionless and has a starched appearance. The eyes are staring and the Patient blinks less frequently than the normal individual. Some writers in their descriptions have divided the face into upper and lower parts and have claimed that the upper, which is the forehead, gives rise to an expression which varies with the direction of the wrinkles, transverse surprise and vertical concentration; they allow that the lower, the part of the face below the forehead, is expressionless. To a certain extent the wrinkles can be accounted for by the flexed attitude of the head and the difficulty in seeing to the front, unless the eyebrows are slightly elevated. Still this does not account for all cases, as I have one case where only one side was wrinkled. I cannot agree

with Souques who says that the wrinkles are not any more marked than in a normal person of the same age, as I have found the forehead wrinkled in a Patient of 35 years whose head was only slightly flexed on the chest.

There is a distinct difference between the rigidity of Paralysis agitans and that of hemiplegia for example. In hemiplegia the rigidity is of a "lead pipe" type, i.e. when passively flexing the limb one gets the impression of bending a lead pipe. In Paralysis agitans the rigidity is of a "cog wheel" type. The broken movement when a limb is passively flexed or extended is best elicited when the hand is moved at the wrist.

With the rigidity is weakness, but never complete Paralysis. Most movements can be performed, but they are performed slowly. The greatest slowness was found to be in commencing the movement.

Loss of associated and automatic movements. is most noticeable, as already mentioned, in the arms. One can bring it out by placing the Patient sitting on a stool and suddenly pushing his trunk backwards;

the automatic movement of extension of the legs , to bring the centre of gravity forward, is wanting.

Here one can consider the gait. The Patient seems to move 'en bloc'. He walks with very small steps throwing his weight more on the fore part of the foot, and has a tendency to increase his pace till he is running forward; then he cannot stop himself - "propulsion". A similar thing happens when he is asked to walk backwards - "retropulsion". "Lateropulsion" can also be observed in many cases,if the Patient is gently pushed sideways .

Trousseau believed that this festination of the gait was accounted for by gravity,saying that the Patient ran after his centre of gravity. This was easily disproved in a Patient who had no propulsion only retropulsion. Even when her body was well bent forward,thus lowering and throwing forward her centre of gravity, still there was no propulsion, only retropulsion. Merely turning the eyes upward is sufficient to start retropulsion in some Patients, though it does not alter the position of the centre of gravity. One can only think that the loss of associated movements is an important factor in the causation of this festination.

If a Patient, who shows retropulsion and who holds his arms in the typical attitude of flexion, is set into retropulsion there is no associated movement whatsoever to recover the balance. A normal person would throw the arms forward and try to take a long step back to recover his balance. Likewise in lateropulsion the Patient makes no movement to recover his balance. A normal person would raise the arm further away from the side to which he was falling and try to take a long side step in that direction in an attempt to recover his balance. These associated movements are entirely lacking in Paralysis agitans.

Another point of interest which was noticed was the inability of the Patient to make a sharp turn when asked to change his direction while walking. When asked to walk up the Ward and return he does not turn in his own ground, but walks in a small semicircle to come back: the more advanced the disease, the wider this semicircle becomes. This again can be closely related to the loss of associated movements.

Mention will only be made here of the monotonous voice and often broken type of speech.

In a few cases difficulty was found in beginning to speak, but when once a beginning had been made the words came out freely. During speech the upper lip tends to remain motionless while the lower jaw makes small excursion movements.

The writing is characteristic of this disease It is usually small and gets smaller the more Patient writes till it is not more than an irregular line.

Pains in the limbs have been mentioned. These are often associated with the rigidity, but rigidity is not sufficient to account for all of them and some must be of central origin.

The vasomotor changes have been carefully noted in several cases. These consisted of attacks usually nocturnal in which the Patient experienced a feeling of great heat all over and asked to have most of the bedclothes removed. Accompanying this was a great increase in the tremor and profuse general sweating. The temperature was elevated to 102.2^{o} in one case and to 101^{o} in another, the temperature having been taken in the mouth. No elevation of temperature has been observed by most

of the writers who have described such attacks. On the other hand, some Patients complained of periodic attacks of extreme cold. Osdema has already been mentioned as occurring in two cases. Another sign, showing the disturbance in the vasomotor system which is very common in this disease, is sialorrhoea. In six cases of my series the accommodation convergence movement of the eyes was defective.

The tendon reflexes were reduced (though sometimes brisk) and depended on the amount of rigidity for this reduction. The abdominal reflexes were usually active and the plantar reflexes flexor except in one case in which occasionally an extensor plantar reflex was obtained on the side most affected.

I do not propose to enter into a discussion of the mental state of this disease. Sufficient be it to say that the vacant expression belies the intelligence and that the cerebration is quite quick as a general rule.

SECTION II

PATHOLOGY.

SECTION II

PATHOLOGY

TWO Cases have been examined pathologically.

CASE I.

Miss C---. A Clinical Account of this case was given in the preceding Section.

The autopsy was performed by Dr. Greenfield in my presence 20 hours after death.

Slight flexion contracture of the knees and hips was present.

The Brain and Spinal Cord were removed and appeared externally to be normal.

The Skull, Spine and Bones appeared normal.

Chest The right lung was enlarged and considerably overlapped the heart and aorta. The left lung was shrunken and collapsed and was slightly adherent to the chest wall and diaphragm . It was scarcely seen when the chest was first opened. The adhesions stripped fairly readily from the parietes except at the apex, where the pleura was about a quarter of an inch thick and could only be taken away from the chest wall with difficulty.

There was one small area of adhesion over the right lung anteriorly, but elsewhere this lung was free in the chest cavity.

On section the right lung showed some early broncho pneumonia at the base, with general congestion and some compensatory emphysema.

The left lung was generally collapsed, though not completely. At the apex were several areas of consolidation with slight cavity formation; there was one very solid calcareous area about the size of a haricot bean. Elsewhere in the lung there was a suggestion of miliary tuberculosis, but no definite tubercles could be found.

Heart

This was much enlarged. The right auricle and ventricle were dilated and hypertrophied. The left auricle and ventricle were hypertrophied and dilated, but to a lesser degree. All the valves were healthy. Patches of atheroma were seen at the origin of the aorta and the point where the vessels left the arch.

Stomach and Intestines

These were healthy.

Liver

There was considerable enlargement. On the surface the organ was pale and mottled; the consistence was soft. On section, the lobules were pale with the central veins large and darkly coloured.

Spleen

This was large and soft with the capsule thickened. The Malpighian bodies were prominent on section

Kidneys

The right was represented by a fairly small hydronephrotic sac, while the left was large and congested.

Suprarenal Glands.

They were both healthy.

Uterus

With the exception of a small firm subcapsular fibroid, this organ appeared healthy.

The Brain and spinal cord were immersed in 10 per cent formalin saline. After hardening, the brain was cut in the following manner. Horizontal slices were cut approximately 5 millimetres thick. The first cut passed just under the highest part of the corpus callosum and the last passed through the middle of the midbrain at the level of the inferior corpora quadrigemina.

1st. slice included:-

The lowest part of the corpus callosum and

body of the fornix and the uppermost parts of the head and the body of the candate nucleus and the uppermost region of the thalamus.

2nd. slice included:-

The head of the candate nucleus, upper part of the thalamus and uppermost parts of the putamen and claustrum.

3rd. slice included:-

The head of the Candate nucleus, the whole width of the lenticular nucleus, the lower part of the thalamus and the uppermost part of the superior corpora quadrigemina.

4th. slice included :-

The lower part of the head of the caudate nucleus and of the lenticular nucleus, the uppermost part of the midbrain, containing the nucleus of Luys and the upper end of the nucleus ruber.

5th slice contained practically no part of the basal ganglia except the amygdaloid nucleus. It included the middle section of the midbrain with the substantia nigra, the lower part of the nucleus ruber

and the inferior corpora quadrigemina.

The basal ganglia appeared to be of normal size and no abnormality could be made out by the naked eye.

The pieces from the left side of the basal ganglia in slices 2, 3 and 4 and the whole of the midbrain from slices 4 and 5 were treated by the Marchi Busch method and embedded in celloidin. No tract degeneration was demonstrated by this method.

Pieces including the basal ganglia from slabs 2, 3 and 4 and pieces of the motor cortex, island of Reil, cerebellar cortex and dentate nucleus, midbrain, pons, medulla and spinal cord were embedded in celloidin, cut and stained by Nissl's method and by haematoxylin with Van Gieson's counter-stain.

Microscopical Examination

The cerebral cortex appeared normal in every respect. The layers were intact and the Betz cells stained well. The cerebellar cortex was normal, the Purkinje cells showing up well. There was no abnor-

mality in the dentate nucleus.

The pons and medulla appeared normal. The various nuclei stained normally and no tract degeneration could be found when stained by Marchi's method. The spinal cord presented no tract degeneration by Marchi's method nor any abnormality in the anterior horn cells when stained by Nissl's method.

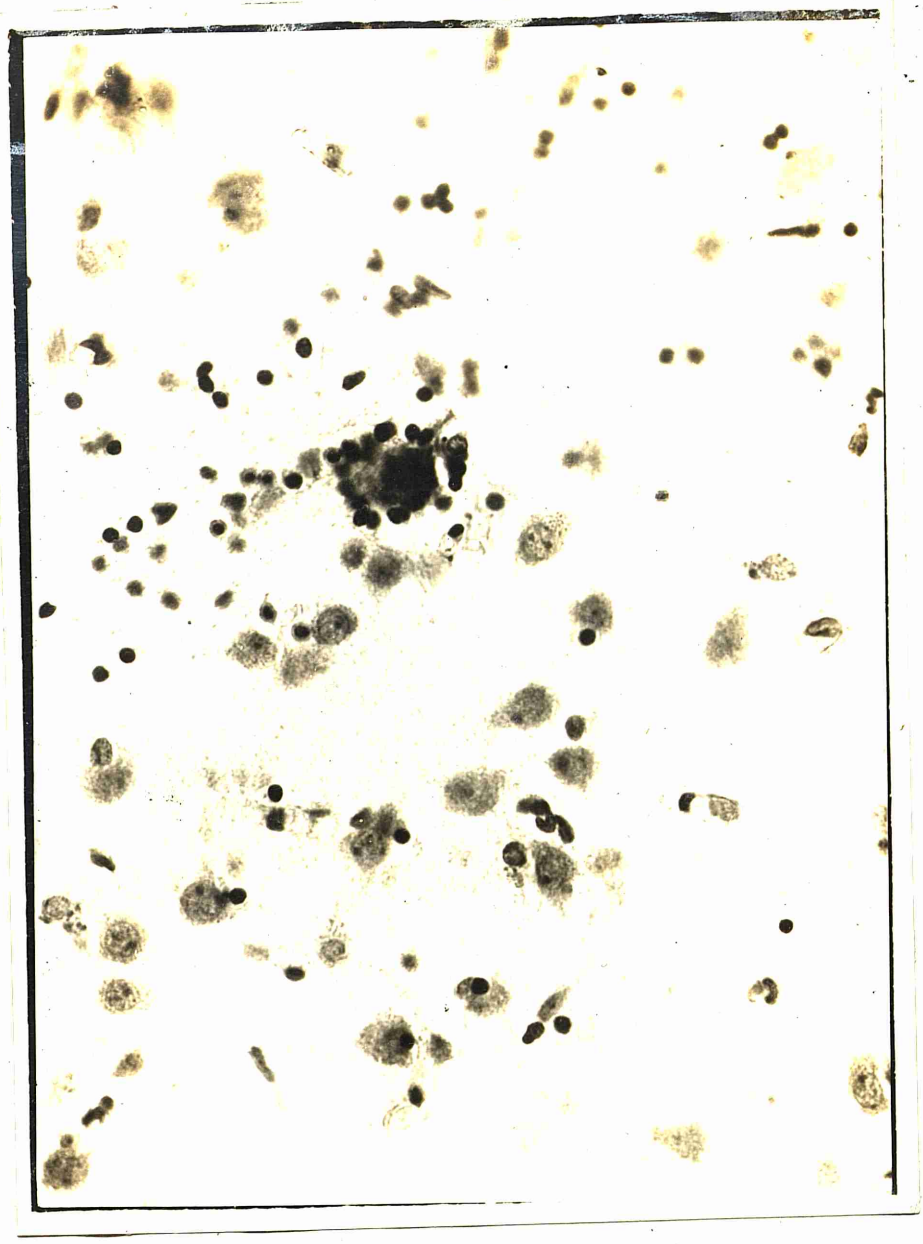
The Basal Ganglia

[Histologically the globus pallidus differs from the Putamen and caudate nucleus. The cells of the globus pallidus are large, fusiform or multipolar, with a well marked axis cylinder. The putamen and caudate have a few cells of the globus pallidus type but more numerous are smaller star or polygonal shaped cells].

Caudate

No atrophy of any cells could be made out. The large cells appeared as numerous as in the normal and there was no disturbance of the smaller polygonal cells.

Glial cells were fairly numerous and appeared in clumps. As shown in the accompanying photograph, there



Photograph of part of the caudate nucleus from Case I showing the satellite glial cells.

was marked satellitosis. The satellites were glial cells of small size. The satellite glial cells seemed to surround the large cells along the lines of entering fibres, but many of the large cells were free from them. The Blood vessels appeared normal.

Putamen

Here again no atrophy of any cells could be made out. The large cells appeared as numerous as in the normal and stained normally. Their processes did not appear to be in any way fragmented. The polygonal cells also appeared normal.

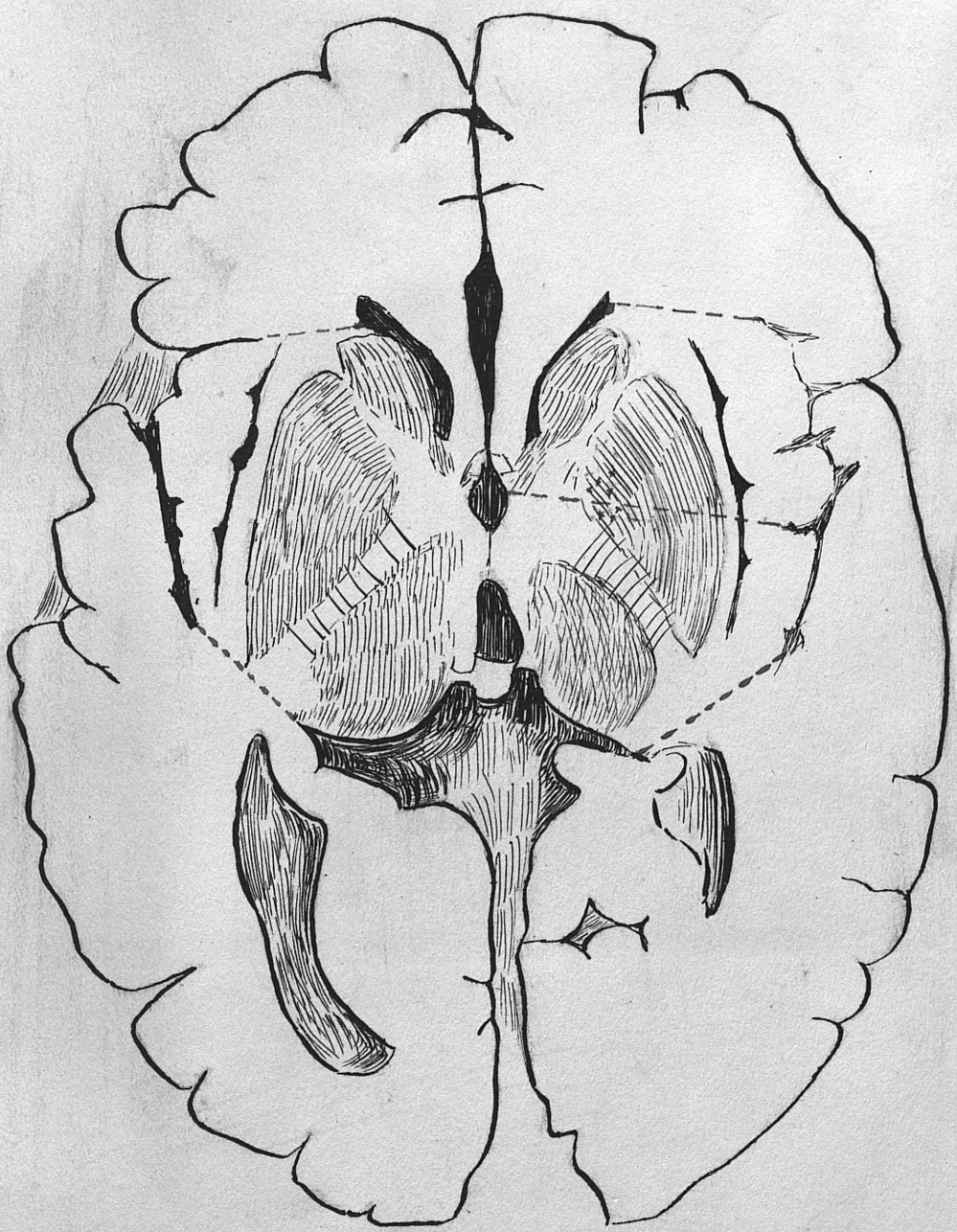
Glial cells were again numerous, but not so much so as in the candate. Here and there a large cell showed a few satellite glial cells. The blood vessels were normal.

Optic Thalamus

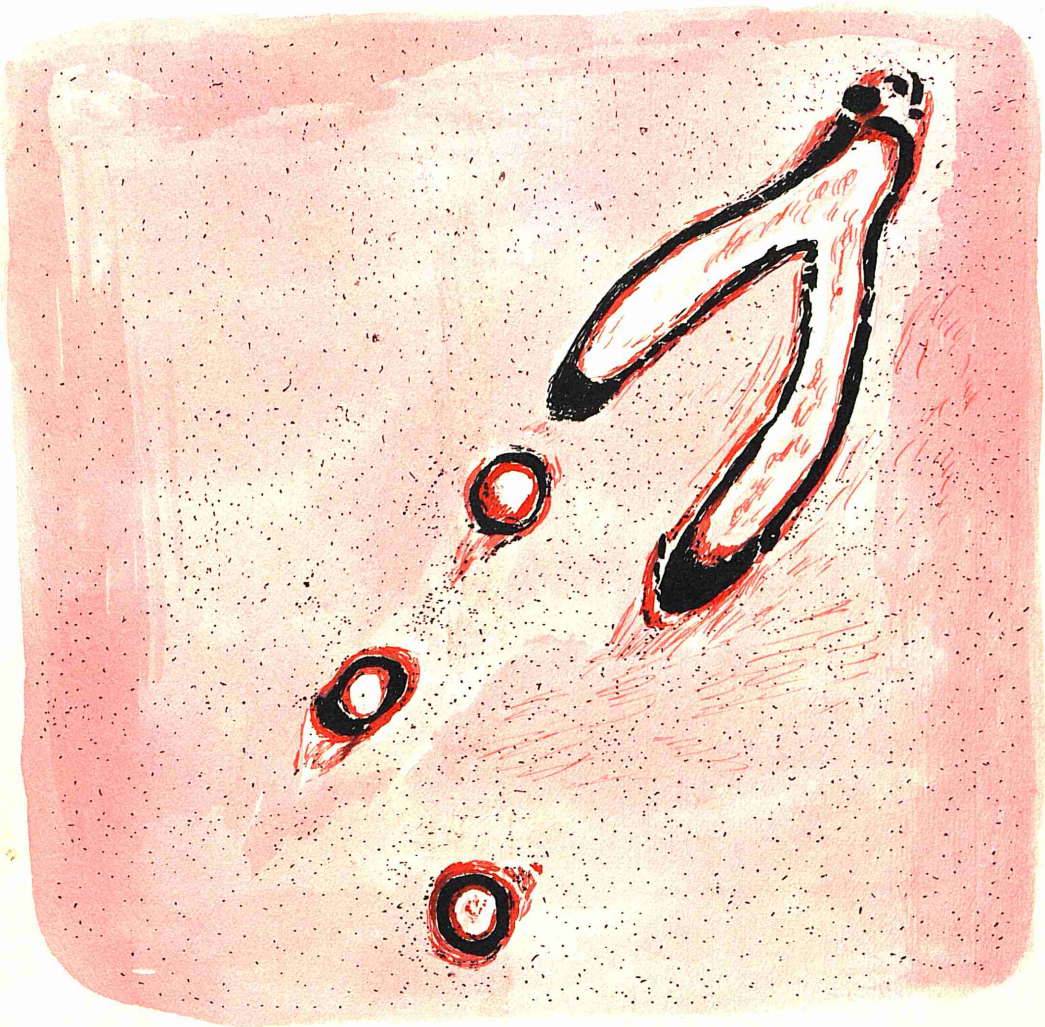
The cell groupings were well preserved and no abnormality of cells could be made out. The glial cells were again fairly numerous. The blood vessels appeared normal.

Globus Pallidus

The large cells of this region appeared as numerous as in the normal. They stained well, the



A tracing of Slab 3 from Case II shewing where the calcified vessels were found. The red crosses correspond to the calcified vessels. The dotted red lines indicate where the pieces were cut out for embedding in celloidin. In Case II the calcified vessels were in exactly the same area.



Painting of some of the vessels of the anterior part of the globus pallidus from Case I shewing the calcification of the media.

granules showing up well by Nissl's method. The nuclei were normal and no fragmentation of the cell processes could be discerned. Glial cells were again fairly numerous.

The outstanding feature of this region in the haematoxylin and Van Gieson sections was well marked calcification of the blood vessels confined to the anterior part of the globus pallidus. The calcified vessels could be made out with the naked eye.

The accompanying painting I have done in the colours seen under the low power of the microscope. The calcified middle coat of the vessel wall stained almost black. The Virchow Robin space was slightly widened. There was also a small space between the periadventitial sheath and the glial tissue. The intima and adventitia were practically normal.

Some calcified material was found scattered about in the neighbourhood of the calcified vessels.

The internal capsulse showed no diminution in size, nor any other abnormality.

Photograph of part of the substantia nigra from Case I shewing the free melanin pigment.

Midbrain

The nucleus ruber showed normally staining cells which were not diminished in number.

The Substantia nigra was examined in 12 sections taken at intervals from one end of the mid brain to the other. The cells appeared to be of normal number but considerable dropping out of pigment was observed. This pigment could be seen along the sides of the vessels. None of the cells showed any sign of atrophy.

CASE II

Mrs. L -

The brain of this case was obtained from an infirmary. No detailed clinical material was obtained with it, but I am assured, on the authority of the visiting neurologist, that clinically it was a typical case of paralysis agitans.

It was hardened in 10 per cent formalin saline and cut in slabs in the same way as Brain I.

In this case owing to the long standing nature of the disease the Weigert Pal (Kultschitsky Pal)

method was used for demonstrating tract degeneration instead of the Marchi Busch method used in Case I.

Pieces including the left basal ganglia from Slabs 2 and 3, the right basal ganglia from 4 as well as pieces from the pons and medulla were stained by the Kultschitsky Pal method.

Pieces from the opposite basal ganglia and almost the whole of the midbrain along with pieces of the Rolandic area of the cortex island of Reil, cerebellar cortex, pons and medulla were embedded in celloidin cut and stained by Nissl's method and by haematoxylin with Van Gieson's counterstain.

Microscopical examination.

Cerebral Cortex.

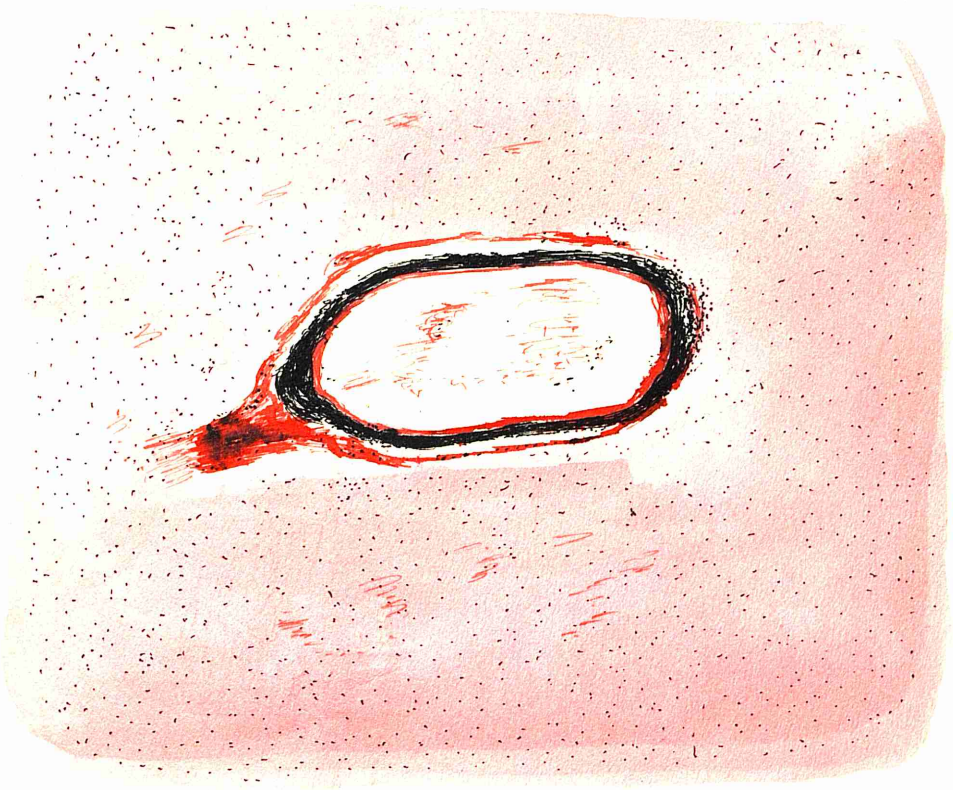
No abnormality could be made out. All the Betz Cells stained well.

Cerebellar Cortex.

The Purkinje cells stained well and no abnormality could be found. This section included the dentate nucleus which appeared to be normal.

Pons and Medulla

No evidence of any degeneration in the tract fibres could be found. The pyramidal tract appeared normal as also did the fillet. The nuclei had a normal appearance. The glial elements were not increased. No vascular disturbance was noticed.



Painting of a vessel in the anterior part of the globus pallidus in Case II shewing the calcification of the media.

could be detected. The nuclei and granules showed up well in the Nissl sections. No fragmentation of the cell processes was present. Glial cells were not numerous.

The blood vessels showed calcification. This calcification was not so intense as in the first case A painting of one of the vessels has been included here. The calcification was confined almost entirely to the media; which was of normal thickness. As in Case I, there was some dilatation of the Virchow Robin space and the periadventitial sheath was slightly separated from the surrounding glial tissue.

Calcified material was also found scattered about in the same region of the globus pallidus.

Midbrain

The cells of the nucleus ruber appeared in every way normal. No tract degeneration could be made out. The cells of the substantia nigra showed no sign of atrophy and their numbers did not appear to be diminished Some collections of melanin pigment were again found and some of it was accumulated along the lines of the vessels.

Serial sections of a midbrain believed to be normal - from a young man who died of a cerebellar tumour - were cut and every second section was stained with haematoxylin and Van Gieson's counter-stain The remaining sections were kept for staining by Nissl's method, but unfortunately this was not completed Two sections in every twenty were stained however and these were sufficient for a comparison to be made with the serial sections taken in the case of paralysis agitans.

In none of these sections could I find any dropping out of pigment from the cells of the substantia nigra.

The sections of the basal ganglia were compared with sections from a brain which was believed to be normal and also with the diagrams given by the Vogts.

The results of the findings in my two cases are

1. A pathological condition of the blood vessels confined to the anterior portion of the globus pallidus. This consisted in a calcification of the media. There was no atrophy of cells.

2. Minor changes in the substantia nigra consisting of collections of free melanin pigment.

With regard to the increase in the glial cells and the satellitosis, one cannot say how far it is abnormal, as supposedly normal sections vary so much in the numbers of these glial cells present.

Ramsay Hunt[11] found in a case of juvenile paralysis agitans degeneration of the large "pallidal" cells throughout the globus pallidus, putamen and caudate The substantia nigra he found to be normal.

Trétiakoff and Sougues[13] found in two cases of paralysis agitans no disturbance of the corpus striatum while the substantia nigra showed marked degeneration.

The Vogts[15] found in seven cases of paralysis agitans definite pathological changes in the putamen and caudate nucleus and to a lesser extent in the globus pallidus. These changes consisted of a diffuse atrophy of the large cells and of the fibres, and of small lacunae caused by softening or haemorrhage. In one case of paralysis agitans sine agitatione the changes were principally in the globus pallidus.

III.

DISCUSSION

In the previous two sections have been given the symptoms and pathology. Now it is desirable to see how far they correspond to each other. For this purpose two conditions giving symptoms similar to paralysis agitans will be described. The first is the after effects of Encephalitis Lethargica. The second is Benedikt's Syndrome.

During the last two years 55 cases of Parkinsonism, the name given by the French School to the after effects of Encephalitis Lethargica, have been seen by me at the National Hospital.

The aetiology was the factor which distinguished Parkinsonism from the classical Parkinson's disease.

Considering the differences between the two from a general point of view, Parkinsonism was either patchy, less in degree, or more than what one found in Paralysis Agitans. The tremor was a less prominent sign, while in cases of moderate severity, the rigidity was more or less constant. Sialorrhoea seemed worse when present. One point of difference which I have noted to be fairly constant was the tendency to walk on

Photograph of a boy suffering from Parkinsonism showing the tendency to stand on the toes.

the toes. I have been unable to find this in any of my cases of paralysis agitans. Some writers mention it as having been observed but nevertheless considering the large number of cases of Paralysis agitans and Parkinsonism that have been seen this point of difference is noteworthy. The accommodation convergence movement of the eyes was lost in the post-encephalitic cases, with but few exceptions, while in Paralysis Agitans there were only a few cases with the loss of this synergic action. Lack of the power of concentration was found in several cases of Parkinsonism, otherwise the patients were mentally quite bright. Some cases tended to be enphoric, others depressed and in many cases the emotional reaction was a little above normal. Extensor plantar reflexes were obtained in several cases, showing the liability of the pyramidal system to be involved.

A resumé of 4 cases will now be given bringing out various points of interest.

Photographs of Case I Section III

again pulled down.

On examination in March of this year, patient's face was asymmetrical, the right lower lid had more wrinkles beneath it and appeared slightly pulled down. The upper lip was drawn very slightly towards the right and the right nasolabial fold was more definite than the left. There were numerous sudden twitches of the right corner of the mouth unconscious to the patient.

Voluntary movements - The right forehead wrinkled up better than the left.

The right eye could only be feebly held closed.

The right side of the mouth was weak in shewing the teeth, and in whistling the right half of the mouth was not pursed up.

Normal winking of the eyes was present.

In laughing, the left side of the face moved normally. The right would do so in a stiff fashion and not so fully as the left. In smiling both sides started to move synchronously.

When asked to close the eyes firmly or lightly,

the right could not be fully closed,while the right corner of the mouth moved out and up.

The pupils were unequal,the left being larger than the right.

The cranial nerves were otherwise normal.

The sensory system showed nothing abnormal.

The motor system showed a slight diminution in favour of the right arm and leg compared with the left. The tremor of the right arm was coarse and slightly irregular. At the wrists and fingers it was mostly flexor extensor in type with a slight addition of lateral deviation. Voluntary effort and excitement increased the tremor. When the arms were at rest the tremor was diminished. The right leg occasionally gave a few twitches but no definite tremor.

Muscle tone was normal throughout the limbs

The reflexes were:

	Right	Left
Supinator	++	+
Biceps	++	+
Triceps	++	+
Knee	+	+

	Right	Left
Ankle	+	+
Abdominal	+	++
Plantar	flexor	flexor

Sphincters were normal

Gait. Feet were placed accurately and the length of step was normal. The head was held over to the right. The right arm was held immobile by the side.

The Blood Wassermann reaction was negative.

Respiratory, Cardiovascular, Genito-urinary and Alimentary systems showed nothing abnormal.

Resumé.

Here was a case showing the recrudescence of the encephalitis. The right side of the face was paralysed and on examination showed the hyperactivity associated with partial recovery. The right arm had a tremor which was more of the paralysis agitans type though it had some slight resemblance to the intention type. Associated and automatic movements were lost in the right arm.

This case shows the patchy nature of Parkinsonism

in comparison with paralysis agitans. The loss of associated movements in the right arm and to a certain extent the tremor were the points of similarity to the classical disease. The condition of the face had no resemblance whatsoever.

CASE 2.

A woman of 32 years of age who complained of a bent attitude, shaking of the arms, falling in all directions and of diplopia. The duration was five years. Past history and family history revealed nothing bearing on her condition.

In February 1918 patient fainted one day and the doctor thought she had strained her heart. About one week later, she saw double followed by great drowsiness. She became unconscious on the 28th February and remained so for 17 to 18 days. When consciousness was recovered she felt dull and had difficulty in concentrating her mind on anything. Her neck was bent forward. After she had been up out of bed for a few days, she noticed that her arms and legs trembled and she was quite unable to stop them. This trembling she stated continued during sleep.

Photographs of Case 2 Section III

About April 1918 patient was sent to bed again and given medicine which stopped the shaking. She was in bed a fortnight and during that time was practically unconscious. When she got out of bed, she found that her feet had dropped and her heels would not go to the ground. When she tried to put the heels on the ground, she fell backwards. She also felt stiff all over.

On the 2nd May she became an inpatient of Great Northern Hospital. While there she was semi-conscious and could not take any interest in things. She had some retention of urine and some dysphagia. The latter she said was due to the stiffness of her neck muscles.

In August she improved slightly and her periods which had been absent since February returned. During her stay in hospital she had difficulty with her speech.

In November she was discharged. By that time she had a bent attitude and double vision. Her condition remained about the same till June 1921, when she had an attack of influenza and an abscess on the left ankle.

The abseess was lanced and patient was then taken into the Metropolitan Hospital,where her ankle was put in plaster of Paris.

The right arm began to shake in July 1921 and has got gradually worse. Recently there has been a tendency to a tremor of the right leg, but there had been as yet no tremor of the left arm and leg except during the early part of her illness.

Patient states that at the onset of her illness when her arm was held above her head by the doctor she had not the energy to lower it though it was uncomfortable.

On examination in February of this year patient was found to be exceedingly intelligent. She gave a good history and was a good witness. During the examination she laughed too readily and unnecessarily, as it was not the expression of her real feelings at the moment. The face was masklike and the whole attitude that of a paralysis agitans patient,with the exception that she walked on her toes. Propulsion, lateropulsion and retropulsion were well marked.

Cranial Nerves.

I. Sense of smell normal right and left.

II. Visual Acuity R. difficulty in fixing the eyes on the card. L.$\frac{6}{10}$.

The visual fields were full to the rough test.

The Discs healthy.

III, IV, & V. Pupils were equal, very small, quite regular and central. Reaction to direct light sluggish and of small excursion. No consensual reaction could be made out. On accommodation, no reaction occurred and the eyes failed to converge.

External ocular movements.

At times the patient exhibited an external strabismus, the left eye moving laterally with a series of quick side to side movements. This strabismus patient could correct, but after a short interval the left eye again diverged.

The movements of the eyes were full in all directions, but the eyes did not always act synchronously and sometimes were distinctly jerky. There was difficulty in fixing the right eye on an object, when the left was covered.

V. No sensory disturbance found Masseters and temporals acted well and equally. Corneal reflexes present.

VII. No hyperacusis, no less of taste.

Face expressionless. The eyelids when lowered were very tremulous - the tremor being quite rhythmical When she shewed her teeth, her lips, especially the upper, showed a regular fine tremor. The cheeks could be blown out quite well. Movements were full, strong and quickly done, yet her face lacked expression. When she was asked to smile, a smile slowly passed across her face and quickly passed into laughter.

VIII. No discharge from the ears, no timitus.

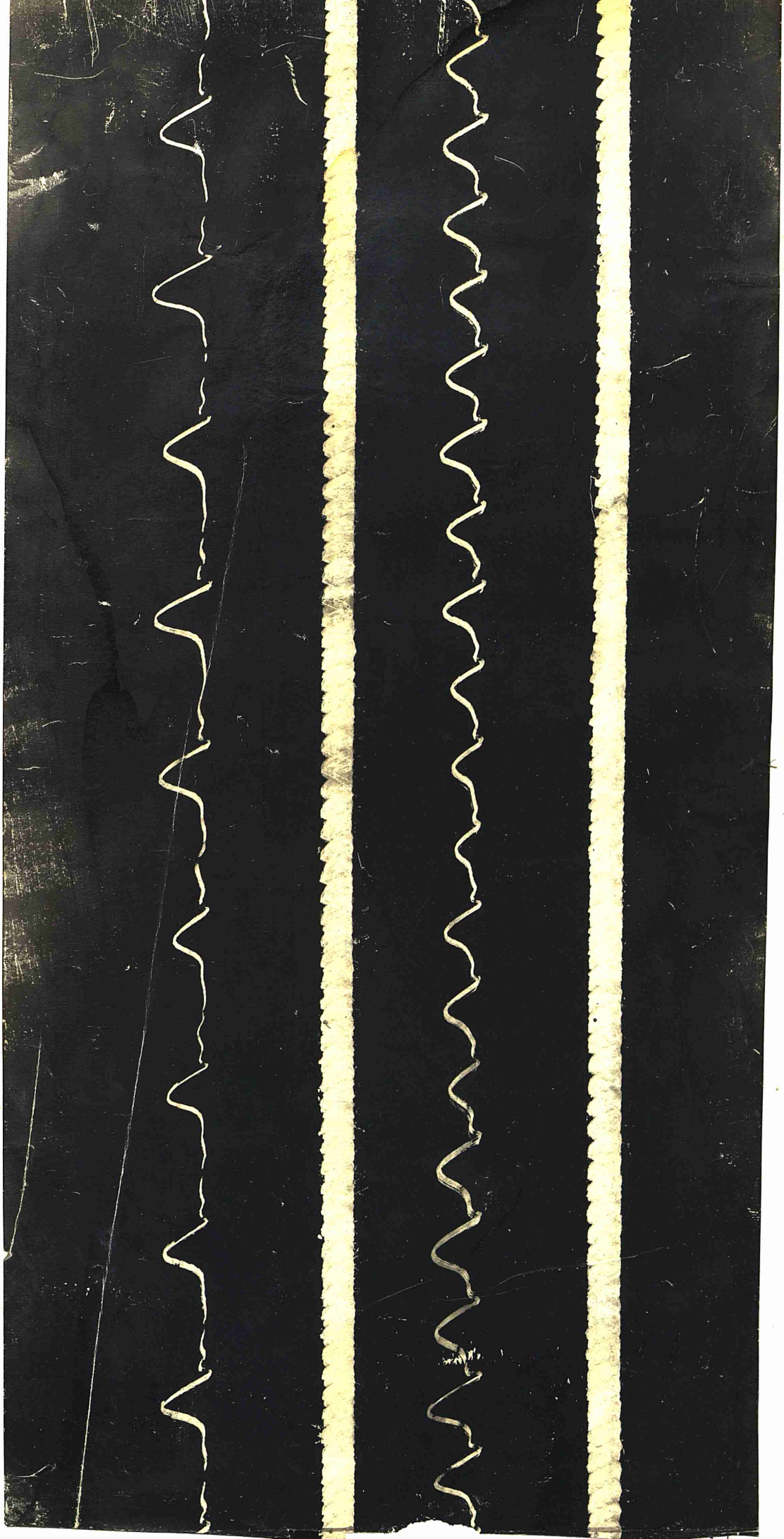
Watch heard well with both ears.

Weber and Rinne tests normal.

IX and X Now and again she had difficulty in swallowing, especially if the bolus was large. There was no nasal regurgitation.

The palate moved well in the mid-line.

XI. Sterno-mastoids and trapezii acted well and equally.



Both tracings are taken from the movements of the right wrist joint. Lower tracing shows movements twice as rapid as the upper, the upper showing 10 and the lower 20 complete movements in 3 seconds.

Case 2 Section III.

Tracing from the right wrist movements in a typical case of paralysis agitans.

Time marker $\frac{1}{25}$th of a second.

XII. The tongue was protruded straight shewing a fine regular tremor. No atrophy was present.

Sensory system.

No loss or diminution to any form of sensation was found.

Motor system.

The upper extremities showed no limitation of movements in any direction, but movements were carried out with deliberation and slowness. She stated that she was unable to play the piano as well as before, as her fingers would not move so quickly. The outstretched hands and fingers were held quite steadily, but, during the examination, there was occasionally for a few minutes a well marked rhythmical tremor of the right arm and hand of the paralysis agitans type. I succeeded in obtaining a tracing of this tremor which is adjoined for comparison with a tracing made by a patient suffering with Parkinson's disease. It, will be seen that the tracings were in every way similar.

There was a slight suggestion of rigidity in both arms.

Trunk.

No weakness was found.

Lower Extremities.

There was no limitation of any movement, though movements were slow. The right foot, while resting in bed was slightly inverted and plantar-flexed with extension of the toes. There was no weakness though the right leg was slightly stronger than the left. Slight rigidity was present in both legs.

Co-ordination

The finger nose tests were performed accurately and steadily as were the heel knee tests.

Associated movements were wanting in all four limbs, trunk and neck muscles as in paralysis agitans.

Reflexes	R.		L.
Supinator	+	>	+
Biceps	+	>	+
Triceps	+	>	+
Knee	+	>	+
Ankle	+	>	+
Abdominal	+	=	+
Plantar	flexor		flexor

All the tendon reflexes exhibited some briskness.

Resumé.

This case exhibits the typical attitude and facies of paralysis agitans and in addition the tendency to stand on the toes. The tremor is not a marked feature and comes on in spaams - an uncommon condition in paralysis agitans.

Rigidity is not marked, while in paralysis agitans, with the same degree of alteration of posture, the stiffness is usually well marked.

The affection of the eyes, which is common in Parkinsonism, as opposed to the classical Parkinson's disease, is shown in this case.

The spasmodic laughing of this patient is in contrast to the usual emotional reaction in paralysis agitans.

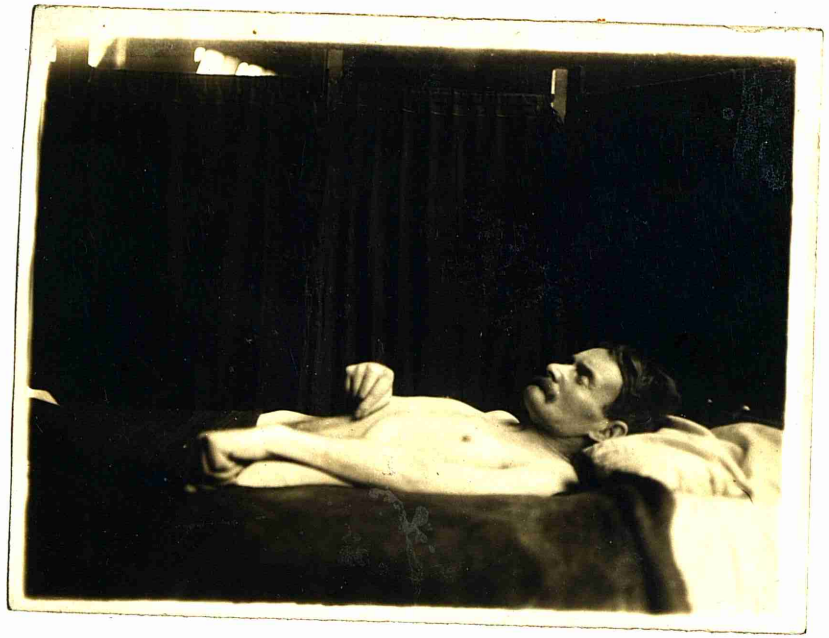
Case 3.

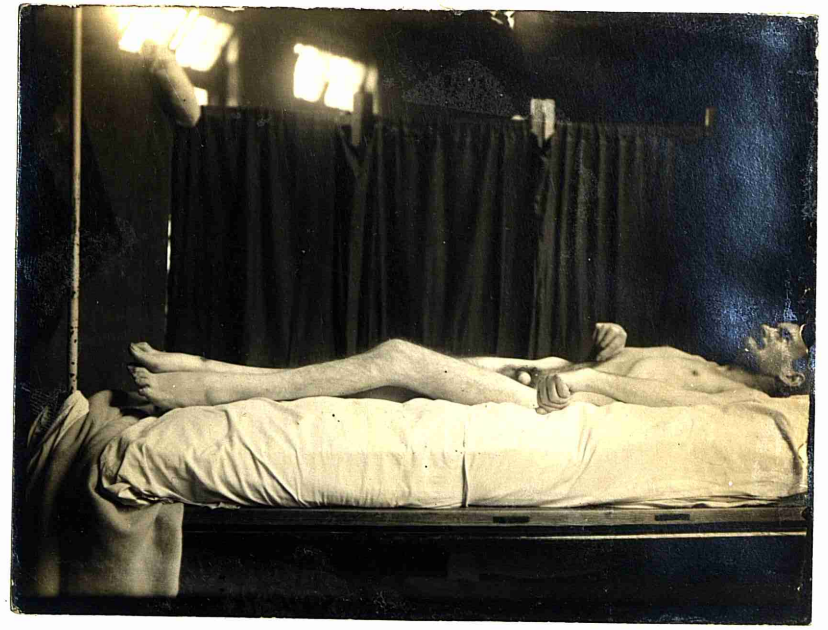
A man of 36 years of age whose complaint was of general stiffness and inability to do anything for himself as a result of it.

Patient had an attack of encephalitis lethargica in January 1921. The history from his relatives was

in-definite, but I gathered that there had been a gradual onset of stiffness. This stiffness was first noticed in the jaw muscles in chewing. It spread to other muscles and progressed till he was in the condition in which I saw him in December 1922

The patient lay motionless in bed like a wax figure. As he lay on his back, the Sterno-mastoids and scalene muscles stood out rigidly. The left arm was extended by his side and internally rotated, while the right was flexed at the elbow, internally rotated and with the forearm resting on the chest. Both hands had the forefinger and thumb in a "pincer" position, while the other fingers were flexed into the palm. The legs were semiflexed at the knees while the feet were plantar flexed. The face was expressionless and the eyes staring. His jaws were clenched firmly together, with the lower lip tucked under the upper. There was a constant tremor round the lower lip and chin. There was also an irregular tremor of the eyelids. The eyes could not be closed and opened voluntarily, except with great difficulty, the opening was especially difficult. They could be opened





Photographs of Case III Section III

passively without any difficulty. Ocular movements were fairly well performed,except the internal movements of either eye. Accommodation convergence movement was absent. The pupils were equal, central and regular, but their reaction to light was very slow, though well sustained. An external strabismus was present in the left eye. No ptosis or nystagmus was present. The fundi were normal. The jaw jerk was much exaggerated and accompanied by a blinking movement of the eyes. This blinking of the eyes was not elicited when a pretence was made to tap the chin. Tapping over the anterior border of the masseter caused a brisk reflex movement of the jaw to that side. The tongue could not be protruded and was tremulous in the floor of the mouth. A gag had to be used to obtain a view of it. Swallowing was possible when fluids were introduced between the cheek and jaws.

Patient was as if devoid of joints. When the trunk was raised forwards and then allowed to fall back again, it would do so very slowly and as it

reached the bed the legs were raised. There were limited movements of the arms, but these were extremely slow, just like a slowed down cinematograph film movement. Limited movements were possible in the legs, but again were extremely slow. Before commencing any movement, there was an interval of a few seconds. The rigidity was obvious on any attempt at passive movement of the limbs and the muscles gave a brisk contraction when tapped - the arm and leg muscles and also the pectorals.

No tremor could be made out in the limbs when the patient was observed at rest, but when the hands and arms were passively moved a very fine paralysis agitans tremor could be elicited.

Tendon reflexes wereall present and equal with the exception of the ankle jerks, the rigidity in the muscles governing the ankle jerks was very marked. The abdominal reflexes were brisk and equal and both plantar reflexes were flexor.

Resumé.

This case had a typical facies of paralysis

agitans and the attitude of flexion except for the left arm.

The rigidity was a gross exaggeration of what is usually found in the classical Parkinson's disease. The tremor was present though clamped down by the rigidity - a condition which is found to a certain extent in the late stages of paralysis agitans.

To sum up the case is something more than paralysis agitans.

Case 4.

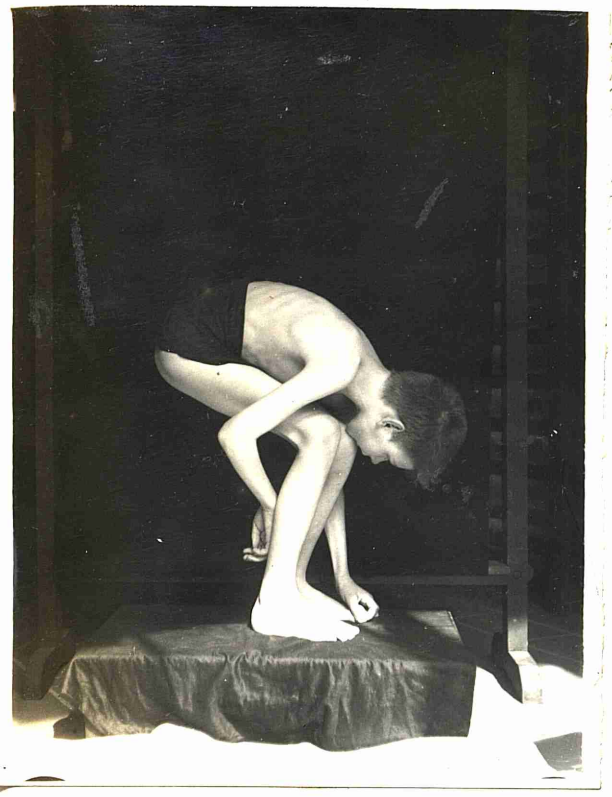
A boy of 14 years of age who complained of difficulty in walking.

History of illness.

In December 1920 patient complained of a headache one evening. He then became delirious for 14 days and when he recovered his senses on the 16th day, he was very restless and sleepless. The right arm and leg became gradually weaker till in 4 months he could not use them. About December 1921 he began to shake all over: admitted to the National Hospital July 1922.

His facial expression was moderately masklike The eyes winked very infrequently and gave him a staring expression. Occasionally he had bouts of blinking both eyes for a few seconds. There was slight overaction of the frontalis muscles when the head was bent forward. Frequently he broke into a wide foolish grin or a fit of giggling which was unprovoked and difficult to suppress. He stated that he could not help laughing. When he spoke the right side of the face moved more than the left while in smiling both sides moved equally well. Sialorrhoea was very marked. The head was held forwards stiffly and both shoulders were carried forwards. When made to sit up in bed he slowly sank back on to the pillows behind him.

The right arm was held slightly adducted at the shoulder, arm fully pronated, fingers almost fully extended with the thumb partially adducted to the index finger. The elbow was slightly flexed. The left arm had a more natural position, though flexed across the chest while patient was lying in bed.



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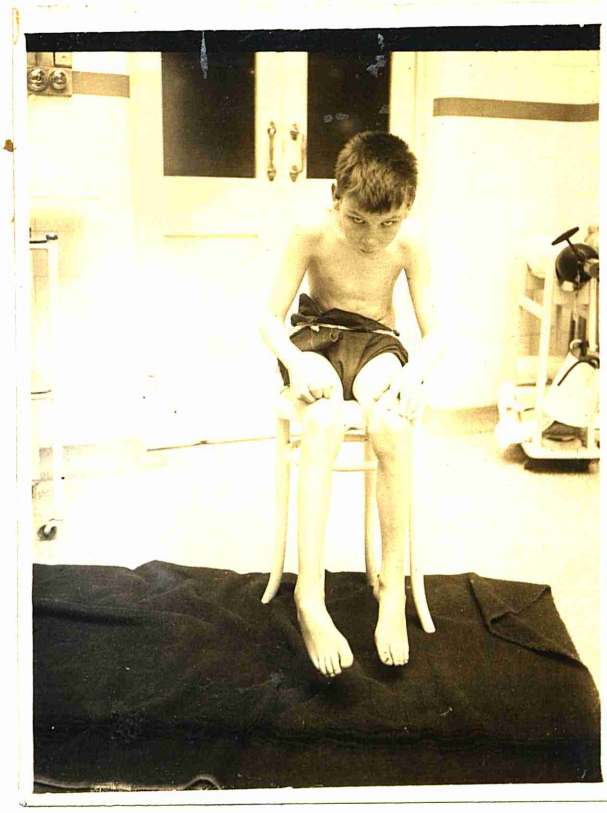


II

Photographs of Case IV Section III.

In I the patient was supported by a hand from behind the screen or otherwise he would have fallen down. The tendency of the patient to sink to the floor is well brought out.

The legs were extended and plantar-flexed at the ankles. The halluces tended to be upturned. The left foot was rotated inwards.

The tremor was confined to the right upper limb and head. The whole right arm was slightly tremulous. There was a rapid, fairly regular tremor of the fingers, best seen in the index as a lateral movement. When he lay back against the pillow the head was unsteady and tremulous.

He walked with the shoulders forward, the back slightly bent and with the gaze on the floor. His steps were short and with increasing speed he ran forward on his toes till some object stopped his course. If he tried to stand still, he sometimes put one foot back and immediately he would show retropulsion, till he came against some object. When my hand was placed on his head lightly, he seemed to double up slowly like a pair of bellows and sink to the floor.

Cranial Nerves I. Sense of smell normal.

II. Visual Acuity R. & L. $\frac{6}{6}$

Fields and Fundi normal

III, IV, & VI. The left pupil was greater than the right, and they reacted normally to light.

Accommodation convergence movement almost fully active. Ocular movements were full.

V. Normal.

VII. There was slight weakness of the right side of the mouth.

VIII to XII showed nothing abnormal.

Motor system.

Movements of the arms were full, though there was some disinclination to use the right, as he said it ached. Power was fairly good in both though the left was stronger thanthe right. The trunk muscles were fairly powerful. Ankle and toe movements were poor, otherwise the movements and power in the lower limbs were almost normal; the left leg was a little stronger than the right.

Hypertonicity was slightly marked all over and more pronounced in the right side than in the left Associated and automatic movements were defective generally.

There was no sensory loss.

Reflexes	R.	L.
Supinator	+	+
Biceps	+	+
Triceps	+	+
Knee	++	+
Ankle	+	+
Abdominal	+	+
Plantar	extensor	extensor

c/ No sphincter trouble was present.

Resumé

This case is again something more than paralysis agitans. The patient walks on his toes and his festination is more marked than I have seen in any case of the classical disease. The rigidity is much less than one finds in paralysis agitans and the tremor is very localised considering the general condition of the patient.

Then there is the fact that both plantar reflexes are extensor in type, showing bilateral involvement of the pyramidal system. Such an involvement is very rare in Parkinson's disease.

The pathological findings in these cases of Parkinsonism are either

1. In the Globus Pallidus or

2. In the Substantia Nigra.

One case at this Laboratory showed marked disturbance of the Substantia nigra and Goldstein(*) describes similar findings in his case.

I had an opportunity of seeing the sections of a case of Parkinsonism of Dr. Martin in this laboratory. This was a case of almost fully developed paralysis agitans associated with subacute encephalitis lethargica. In this case the substantia nigra was normal, while the globus pallidus was affected, having calcification of the vessels very similar to my cases.

(2)

CASE of BENEDIKTS SYNDROME.

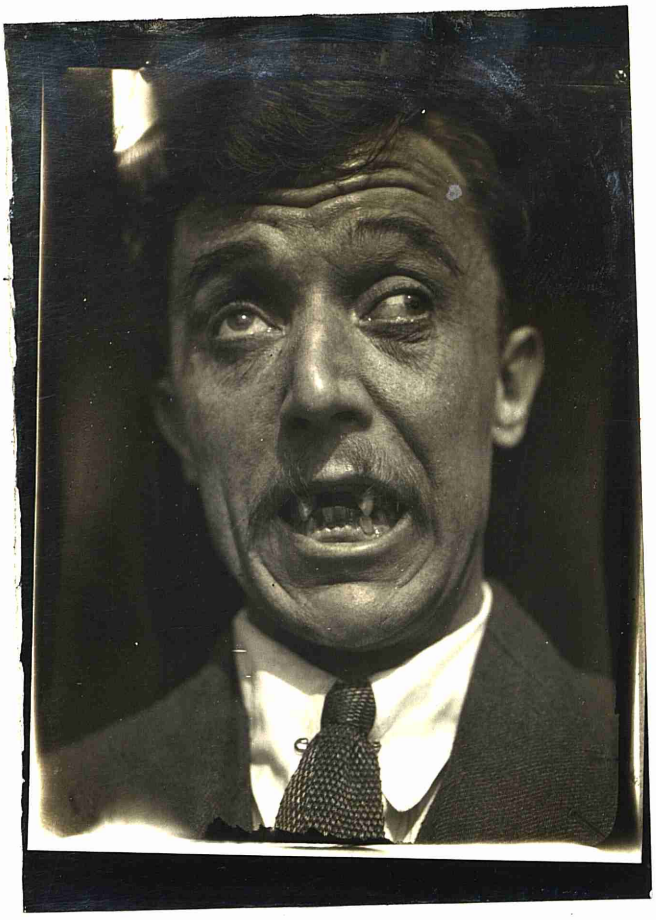
A man of 37 years who complained of weakness in the right arm and shaking in the right arm, leg and sometimes the head.

The duration was three years&seven months from the onset of his illness.

His past and family history revealed nothing bearing on his illness.

About three years&seven months before admission, patient was working as a stoker in an electric power station. One morning,when he got out of bed,he found that his left eye was turned out and downwards. He continued at his work with this condition of the left eye, but otherwise he felt well. Two or three weeks after the eye condition started he felt unsteady on his feet one day and fell down. There was no loss of consciousness and he felt all right after this attack. For six months he attended the eye hospital and by the end of that time the eye was normal again.

A few months from the onset of his trouble,the right hand began to shake. Accompanying this tremor was unsteadiness on his feet. Gradually the whole arm began



Photograph of the case of Benedikt's syndrome shewing the paralysis of the left third nerve and the weakness of the right side of the face

to shake and a few months later the right leg also shook.

A year from the onset the eye again began to squint and has continued to do so till admission.

Five or six months before admission he began to experience slight weakness in the right arm.

Condition on admission.

Patient was a well nourished man of 37 with rather a pale complexion. He gave a fair account of his illness though his memory was not very good for details. He had no hallucinations or delusions. Emotional reaction was a little above normal. During examination he cried for no special reason. Speech was indistinct and of a stammering nature. This speech difficulty, he stated, was present before his present illness.

Alimentary, Respiratory, Genito Urinary and Cardiovascular systems all appeared normal.

Nervous system

Cranial Nerves I. Sense of smell normal

II. Visual Acuity R. $\frac{6}{9}$
L. $\frac{6}{18}$

The visual fields were full to the rough test.

The fundi were normal.

III. IV. & VI. The pupils were unequal, the left larger than the right. They were central, but very slightly irregular. The left had no reaction to light or accommodation. The right reacted to light and accommodation. Movements of the right eye were full: the left had complete paralysis of the third nerve with over-action of the VI nerve, giving a well marked external strabismus.

Nystagmus horizontal, fairly regular and of medium rate was present in the right eye on right lateral deviation.

There was slight ptosis of the left eyelid with over-reaction of the frontalis.

Diplopia was present in the right field of vision.

V. Showed no abnormality.

VII. The right side of the mouth was weaker than the left and occasionally had a slight tremor.

VIII. Showed nothing abnormal.

IX. & X. The palate moved in the midline and no dysphagia was present

XI. The Sterno mastoids and Trapezii were normal and equal on both sides.

XII. The tongue was well protruded, deviating slightly to the right. No atrophy or tremor was present.

Sensory System

Subjective. Patient had constant pain on the top of the headas if being hit with a bar of iron.

Objective. Appreciation of light touch (cotton wool)

Vibration sense

Sense of passive movement

Position in space

Localisation of touch

were all normal.

Appreciation of pain (Pinprick) was slightly diminished in the right arm, but was elsewhere normal. There was no astereognosis.

Motor System

Arms. The movements were full and of fair power on both sides though the left arm was more powerful than the right

Trunk. No weakness could be found.

Legs. All movements were full and powerful, the left very slightly more powerful than the right

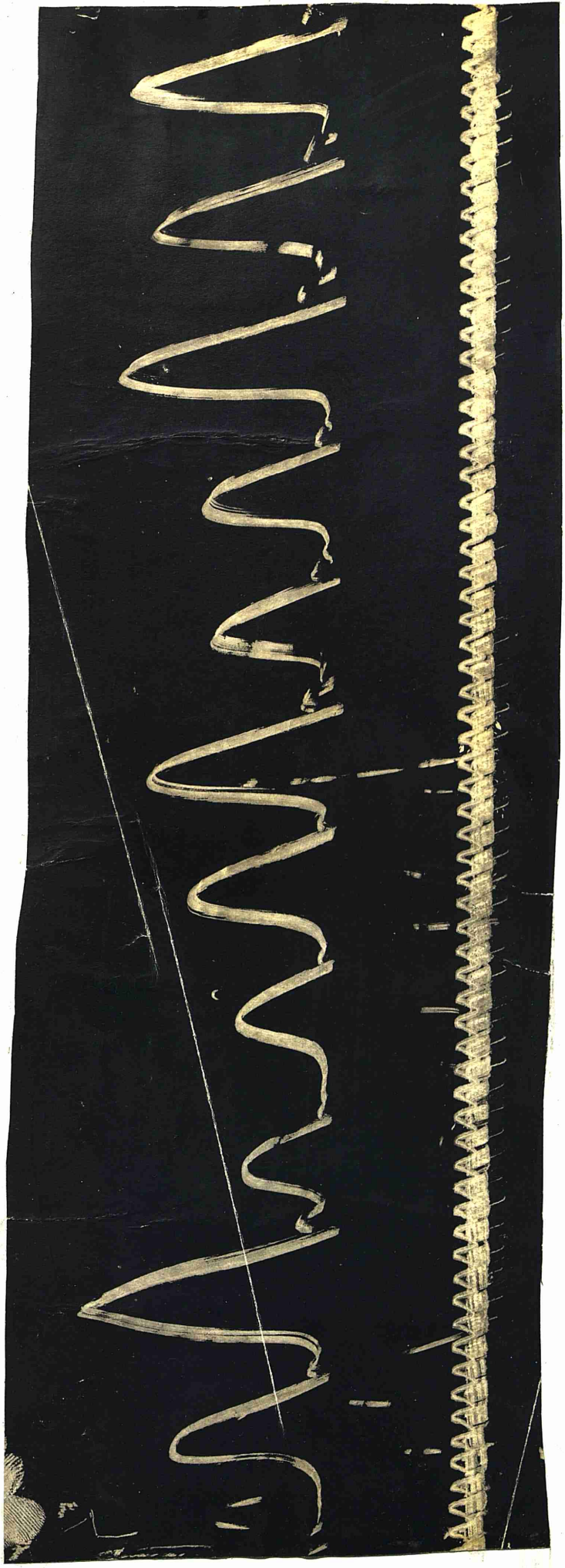
Muscle Tone. This was normal all over.

Co-ordination.

There was a constant undulating tremor of the right hand and arm at rest and when the arms were outstretched. The movements were a combination of flexion and extension at the wrist with pronation and supination. The fingers had a few lateral movements occasionally. The tremor was regular and of fair excursion. It did not increase in the finger nose test. The patient could control it for several seconds During sleep, as far, as was observed, the tremor stopped.

Finger-nose and finger tests were performed accurately.

The heel-knee test was well done with the left leg but was accompanied by a slight tremor in the right leg. This tremor of the right leg was present occasionally at rest and consisted of flexion and extension movements at the knee and ankle.
This tremor in no way resembled the intention type, because voluntary movements occasionally stopped it and was in every way comparable to that of paralysis



Tracing from the right wrist movements in the case of Benedikt's syndrome.

Time marker $\frac{1}{25}$th of a second.

agitans.

I took a tracing on a moving drum of the tremor of the right hand and it will be seen by comparing this tracing with that made by a patient suffering from true Parkinson's disease that the tremors in the two conditions are almost identical.

Reflexes

	R.		L.
Supinator	+	<	+
Biceps	+	<	+
Triceps	+	<	+
Knee	+	=	+
Ankle	+	=	+
Abdominal	+	<	+
Plantar	flexor		flexor
Conus	0		0

+ = present 0 = absent

Sphincters. These were normal.

Gait. The Patient walked erect; he swung the left arm normally, while the right was held extended by the side without any swing. There was just the slightest clumsiness in the movements of the right leg and he appeared to dwell longer on the left foot than the right.

The Wassermann Reaction was negative in the blood and cerebrospinal fluid.

The lesion in this case must be in the left side of the midbrain involving the third nerve and the fillet slightly. The nucleus ruber and Substantia nigra will in all probability be involved. There is no reason to assume any lesion in the basal ganglia.

Dr. Kinnier Wilson[16] mentions four cases with Argyll-Robertson pupils and a tremor similar to that of paralysis agitans. He believes that the lesion in these cases is in the midbrain, because there is strong evidence to suggest that the Argyll Robertson phenomenon is due to a lesion in that situation.

From the foregoing conditions of this section, it is apparent that tremor of the paralysis agitans type may be associated either with a lesion in the corpus striatum or with one in the midbrain.

At first this might seem to suggest that such a tremor is not due to injury of any specific structure in the brain, but when we remember that the corpus striatum and midbrain are anatomically connected, the whole picture becomes much clearer. Wilson[16] has shown in his experiments on the corpus striatum that centrifugal fibres from it reach the nucleus ruber and substantia nigra.

Not only are they anatomically connected, but according to Mirto[8] the substantia nigra is phylogenetically connected to the corpus striatum and is therefore part of the pallidal system.

By taking account of this connection between the basal ganglia and the midbrain, we are enabled to reconcile the differing pathological findings in paralysis agitans. It would seem that a lesion of the pallidal system, whether in the midbrain or in the corpus striatum, can give rise to the syndrome; it is probable that a lesion almost anywhere in the pallidal system, if of sufficient extent, is capable of producing the same symptoms.

The relationship of tremor to rigidity has been one of the difficult problems which paralysis agitans has offered us for solution.

Cases of paralysis agitans exist in which there is no rigidity though a well marked tremor is present. In the first section mention was made of one such case. Also I have seen a case where rigidity was present and no tremor. In this case the rigidity was not more than in a moderately severe case of paralysis agitans with tremor, so that the amount of rigidity could not acoount for the damping down of the tremor. In this Section III a case of Benedikt's syndrome was described where the tremor existed without rigidity.

Some writers state that rigidity is a further stage of tremor and that it afises when stimuli reach the muscles with sufficient frequency to produce tetanus. If this were so, rigidity and tremor could not be present in the same limb at the same time, as is nearly always the case. Furthermore rigidity does not replace tremor. Though in the late stages of paralysis agitans the rigidity damps down the tremor, one cannot say that it replaces it.

For these reasons and because they may be separated clinically, I believe that rigidity and tremor must be different entities with different morbid anatomical bases.

Attention has been drawn in Section I to the almost constant involvement of the autonomic system in paralysis agitans. It is evidenced by flushing, sweating, sialorrhoea and occasionally inequality of the pupils.

If, as I have tried to show, paralysis agitans is due to a lesion in the pallidal system, then it is reasonable to infer that there must be some close association between the pallidal and autonomic systems.

Conclusions

(a) A lesion in the pallidal system, either in the basal ganglia or in the midbrain, can give rise to the paralysis agitans syndrome.

It is probable that a lesion anywhere in the pallidal system can give rise to this syndrome.

(b) Rigidity and tremor are to be regarded as separate symptoms.

(c) There is some close association between the pallidal and autonomic systems.

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