ON PARENCHYMATOUS SYSTEMIC DEGENERATIONS MAINLY IN THE CENTRAL NERVOUS SYSTEM.

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IN a "Demonstration of various types of changes in the giant-cells of the paracentral lobules," a report of which, with illustrations, is published in the *American Journal of Insanity*, vol. liv., pp. 221 to 226, October, 1897, a description is given of the findings, in a case of senile melancholia, of "changes somewhat similar to those found in the motor cells of the cord and the medulla from which the nerve process has been cut off at the periphery." A type of this lesion is seen in the cells of the facial nucleus in a case of facial paralysis due to infiltration of the periosteum of the internal auditory canal, published in the *Journal of Experimental Medicine*, November, 1897. The lesion of the cells consists in a focal reduction of the size of the stainable portions, or complete decay into dust-like particles, leaving in certain places (usually opposite the axone) an area of an almost homogeneous transparent character, which progresses to general swelling of that part of the cell body, and usually to dislocation of the nucleus to the surface. In the above case of melancholia both paracentral lobules showed lesions of the large pyramidal cells. In all of them the stainable portions were smaller than normal. In part of the protoplasm there is in many cells a homogeneous dissolution of the structure as if the details had been washed out; the nucleus frequently seemed distorted and flattened, as if pressed to the wall by this swollen portion. Independent of this, or sometimes along the margin of the swollen area, there

appears an accumulation of yellowish pigment. Sections of other cells show practically no "glassy" swelling, but a peculiarity in having the very slender Nissl-bodies arranged in striking whirlpools, such as I have not seen in any normal cells, in fact, in no human nerve-cell outside of this case, and which, to my knowledge are not described anywhere. The nucleus forms in many cells the centre of these vortex formations, and frequently is so covered up by them that the Nissl stain does not give an outline of its capsule. In other cells there is a combination of glassy degeneration with whirlpool formation; in some of them apparently two distinct foci of glassy decay separated by a distinct capsule of slender Nissl-bodies. An explanation of this condition is somewhat difficult. It might be intelligible from the supposition that the glassy degeneration of part of the cell body might produce certain distortion of the internal structure in the rest, as is actually seen in many of the cells, and that cells which showed these vortex formations, would be in a state of recuperation. I would not like to be understood as considering this case as the type of what occurs in senile melancholia, since other experience in this line is not favourable to this view, and since a further examination of the basal ganglia will probably reveal lesions of the projection fibres within the internal capsules. During the correction of the proof, the following foot-note was added: "This proved to be true to a limited extent only. A second case, examined later, a patient with typical senile melancholia, gave evidence of identically the same changes as those described above. Both will be published in full as soon as the basal ganglia of the second case are examined."

During a period of three years eight cases of this type have come to autopsy. They have greatly helped to clear also the clinical side of the picture. It seems opportune to publish them at the present time, especially since publications are coming forth which in part belong to the same field, and may be furthered by a communication of our findings.

The following notes are abstracts of the histories of my cases, given rather fully, in order to allow the alienist to

form an opinion of the varying mental picture, as far at least as our records furnished the data. The relatively atypical nature of most of the cases will excuse the length of some of the records, without which it would be impossible to appreciate the peculiar similarity with, and yet difference from, general paralysis. To the record of my cases I add further an unpublished case of Dr. August Hoch, and abstracts of other cases collected from the literature.

Case 1 (from Dr. Noble's service).—Psychosis beginning like an ordinary climacteric melancholia, then passing into a condition of mutism with vague nervous disorders following a slight left hemiplegia. Three weeks before death diarrhœa; finally twitching of arms. Aged 68 years.

D. S. R., born in 1829, widow, housewife. The patient's grandmother, father, two brothers and one son were insane. October, 1895, she became depressed; "she groans, wrings her hands, sways from side to side in mental anguish, worries in self-reproach for having murdered a whole family." She became sleepless, restless and noisy, refused food, and was admitted to the hospital on the eleventh day of her illness. She was fed with the tube for several days; in November she ate well; only occasionally till December, 1895, she required tube feeding; her mental condition remained about the same. She would say that she was the devil, was much depressed, rarely answered questions, and was quite inactive. March, 1896, she stayed in bed; later, during the summer of 1896, she was up during the day. She hardly ever spoke, and did not answer questions, and remained depressed and inactive, and lost flesh. October, 1896, the first entry concerning her physical condition was made. There was no evidence of dementia, but complete inactivity and mutism. The patient was always in bed. The state of nutrition was fair, but the face pale; the head large, rectangular, prominent in front; the pupils responded sluggishly to light; exaggeration of the knee-jerk is noted and ankle clonus on the left side. No reaction to prick of pin. The sleep was poor. In December, 1896, the tendon reflexes were less active; almost no knee-jerk was elicited on the right side. Bed sores began to form. January, 1897, she answered a few questions, but sometimes she did not open her eyes when spoken to, and for several days she did not swallow readily, but held the food in her mouth for a long time. This was transitory. From the answers no evidence of real deterioration was gained. There was then

dribbling of urine and consequent eczema; the left arm and leg are held rather rigid, and the knee-jerk is moderate on both sides, especially on the left, on account of the rigidity. Patient takes hold of the hand, but is slow in her motions. January 25, she is said to take nourishment better and to converse somewhat more freely; "she told me this morning that she was frightened, and that she heard noises about her." End of February and in the beginning of March occasional diarrhoea was reported. March 16, 1897, twitchings of both hands and feet were noticed, and a tendency to contraction of forearms and hands, the right pupil was wider than the left; the pulse 138, weak; the respiration 40, and the temperature 100.3°. The patient was uneasy when put on her right side, and required to be moved back to the left. No definite picture of the mental condition could be made on account of the continued mutism. Death occurred March 17, 1897.

The following is the summary of the autopsy report:—

Subcutaneous ecchymoses on the forearms and over the ensiform process. Sacral decubitus. The *heart* rather large, with atheromatous patches on the mitral valve and on the beginning of the aorta. The *kidneys* slightly granular, with a number of small cysts, and sclerosed parts in the right lower pole. Weights 84 and 87 grammes. The *lungs*, with slight adhesion of the right apex, slight bronchitis in the right lower lobe, probably with beginning broncho-pneumonia. Weight of the left lung 265 grammes, of the right lung 360 grammes. Remnants of parametritis (strings of calcareous nodules). One large gall stone. *Skull*, with vortex-like *hyperostosis* on the inner plate of the frontal bone, thick. The calvaria weighs 610 grammes, instead of about 300 grammes. *Pia* oedematous, thickened and white along the longitudinal fissure. *Basal vessels* whitish. *Convolutions* somewhat atrophic.

No macroscopic lesions in the brain, except a *small scar in the right caudate nucleus*, nearly reaching the internal capsule. The spinal cord was not removed. The microscopic examination furnishes the following additional data:—

The specimen from the lung showed a number of alveoli filled with blood and with polynuclear cells, and the kidneys typical arterio-sclerotic shrinkage, with marked sclerosis of many glomeruli and their capsules. The microscopic examination of the various parts of the cortex (right and left paracentral lobules, F., T., and cornu ammonis) showed no tissue alteration, except the very marked axonal reaction of the Betz-cell on both sides,

described in the first communication, and a small hæmorrhage in the cornu ammonis. The semilunar ganglion showed advanced pigmentation of almost all the cells; in many cells the nuclei are dark, in various stages of homogenisation, in others clear and large, and in a few eccentric. The stainable portions are very scanty. Sections through the basal ganglia showed that the internal capsule was not involved in the scar.

Case 2 (from Dr. Boynton's service).—Senile depressive hypochondriacal delirium with profound emaciation and aimless restlessness. Rapid physical decay without typical nervous phenomena. Death from broncho-pneumonia. Duration of the whole process two months. Aged 63 years.

J. W. H., born in 1834, shoemaker, married. His father died of apoplexy. The patient was a very conscientious worker. In 1888 he fell over unconscious (fainting?) when walking across a bridge, and was sick for two days; in 1894 he had a "fainting turn, a cold sweat came over his chest and he smelt like a dead person." Within the last two years mental efforts have become more difficult to him (such as speaking in his "lodge"); his son noticed forgetfulness for three or four years. Last winter (1896 to 1897) the patient had an attack of influenza from which he recovered imperfectly. In June, 1897, a "specialist" found his spleen enlarged. After three days of medication he became delirious; he said he was filled with wires. Reduction of the amount of medicine left him with the same somatic delusions. His wife found him a few days later out in the back yard, shoes and stockings off, carefully looking down into the toe of the stocking. "The whole of my insides have fallen out; I am trying to find them down there." In August a neighbour said something about a thing smelling bad, and the patient began to have ideas that *he* smelt bad, that he was all rotten; he said of the electric cars, "see how fast they go by now, they all smell me;" passers-by "held their handkerchiefs to their noses or went on the other side." Or he would get up at night saying, "my legs have rotted off and gone and I want to see if I can walk." He refused food because it went "to the top of his head," and on August 27 made several weak attempts at suicide by means of a twisted cloth, a shoe knife, and oxalic acid. "It is no use to live any longer." At the same time he became confused, had difficulty in recognising neighbours, was restless and did not sleep. When admitted, August 31, 1897, he only weighed 100 lbs. against 156 lbs. one year previous, and he had tremor of the hands and

feet, arterio-sclerosis, prominent veins, slight enlargement of the heart, exaggerated tendon reflexes, sluggish pupils and arcus senilis. He was dazed, restlessly and helplessly standing or wandering without aims, occasionally mumbling unintelligibly; he once showed marked fear of being killed, and then could apparently not answer questions or even understand them; he did not show the tongue even when shown what was wanted. He was tube-fed from the beginning. He usually stared in a vacant manner, mouth open; once answered to the question who he was, "it was H." From September 3 he was kept in bed; restless, pulling at the bed-clothes, probably utterly disoriented. September 13: his respiration was 38, the temperature 103.8°. Hypostatic pneumonia. Death at 6 p.m.

Anatomical Summary.

Arterio-sclerotic kidneys, practically no other internal arterio-sclerosis. Heart weighing 280 grammes; flabby, but few atheromatous patches at beginning of aorta. Slight old adhesion of left lung; hypostasis of both lower lobes. Skull thin; dura adherent with small endothelioma in the temporal fossa; pia slightly thickened and cedematous, slightly whitened, with arachnoid cysts; nowhere adherent. A small lipoma in the pia of the tuber cinereum. Careful inspection of the brain revealed no macroscopic lesion in any part. No granulations of ependyma.

The cortex of the *paracentral lobules* shows the typical axonal alteration in most of the largest pyramids (Betz-cells). Among fifty there is only one normal, a few have whirlpools. The large pyramids of the third layer are not affected, except that they frequently show a decided rarefaction of the stainable spindles in parts of the apex and around the perfectly normal nucleus; especially in the polymorphous layer, many nuclei are folded. In the second and third layers there are rather numerous pigmented glia cells, and a moderate number of satellites in the deeper strata. No spider-cells. The nerve-cells are moderately pigmented.

The *frontal cortex* also presents the axonal reaction in many of the largest elements. The cells are generally more pigmented and with a spongy appearance of the protoplasm; the nuclei are, however, normal. The number of satellites is a little greater than in the *paracentral lobules*.

The *cornu ammonis* and the *cerebellum* are normal; in the *Golgi specimens* the dendrites have a normal number of gemmules. The cells of the motor plate of the upper *cervical cord* are con-

siderably pigmented, and many of them small and with few lumps of stainable substance. There are two instances of axonal degeneration among the twenty cells examined; four are normal and large, two are mainly pigment bags. In several cells the lining of the nucleus is denser and its granules larger and the nuclear membrane is lost. Among the long spindle-shaped cells of the centre many have thick spindles; but one shows the axonal reaction, also one of the large cells of the dorsal horns.

The cells of the *semilunar ganglion* are of varying type; pigmentation is more moderate than in case 1, but present in most cells; the stainable substance is either present in rather large lumps uniformly throughout the cell, or much more frequently there is a marginal row of large lumps while the central part of the cell has smaller granules. In many cells the central granules are more or less hazy or even quite indistinct and the marginal lumps clotted together, and sometimes such clots of lumps form caps around the nucleus. There is probably no typical axonal reaction. The nucleus is frequently considerably eccentric; but nowhere does it break through the marginal ring of the lumps. The nucleus is normal in many cells, in others the net of granules is more dense, and all stages can be followed into the type with dark sap and absence of membrane.

In the left *lung* pneumonia with hepatisation and the diplococcus pneumoniae is established. The *kidneys* show only moderate arterio-sclerosis. The *liver* is hyperæmic and the cells moderately vacuolised.

Case 3 (from Dr. Fleming's service).—*K. H., senile deterioration, with depression, progressing in the course of three to five years to delusions of persecution and restlessness, and finally disorientation; arterio-sclerosis. Peculiar attacks of tremor, January, 1897; from October, 1897, progressive exhaustion. Death from pneumonia, December 18, 1897. Age between 62 and 71.*

Patient is a woman 61 years old (her niece says about 70). The father died of phthisis and the mother in the latter years of her life developed a mild form of insanity. The patient was born in Ireland. She was always healthy; came to America in 1867 and worked as a domestic. Nothing is known of her sexual history, nor is there any statement concerning alcoholism. She had no school education, can neither read nor write.

Five years ago she began to show loss of memory and to worry over trifles; she was depressed, cried frequently, became retrospective; she talked and cried over things that had occurred

in her early life. Two years ago she gave up work and lived alone; when her niece would visit her she would find her with but little to eat, but the patient would say that she did not want anything. Delusions developed at this time, that people were stealing and wearing her clothing. About a month before admission she boarded out, and the lady with whom she boarded was unable to keep her in the house—she would get up in the night, wander around the house, and during the day she would try to get away, saying she wanted to visit the neighbours. She became disoriented; did not realise that she was in W——, but thought she still lived in G——. (She had formerly lived there.)

She was admitted July 25, 1896, because she began to wander away from home aimlessly, and got lost. Since admission she was somewhat depressed—cried when spoken to. She removed her clothing and at times tore it, and was very restless, and her general intelligence was very defective. No delusions or hallucinations were elicited, the patient often talking to herself in an incoherent manner.

Physically she was very poorly nourished: the pupils sluggish, the knee-jerks diminished. General tremor was present at times, the grasp somewhat weakened. Dulness at the apex of right lung, without râles, but with prolonged expiration. A systolic murmur partly replaces the first sound in the mitral area. Atheroma of temporals and radials. Inguinal hernia, more marked on the right than on the left.

By August, 1896, the patient did not cry as much as formerly, answered when spoken to, but could not give a coherent account of herself. In December, 1896, she became more restless, undressing herself often, and tearing her clothing. January 19, 1897, she was unusually restless and destructive; about 11 a.m. she began to tremble all over; her mouth was drawn to the left and she was unable to speak for ten minutes; about 3 p.m. there was a similar attack, lasting only a few minutes. Nothing of the kind was observed later.

Towards May the patient became more feeble, unable to stay up long, but very restless in bed. In June, œdema of the eyelids was noticed once; but the urine was found normal on repeated examination. In July she was stronger and up; it was impossible to keep her in bed; but in October she became finally bedridden. The physical examination brought out nothing new, except that the left knee-jerk was a little more marked. In December, 1897, œdema of the feet appeared and occasional

diarrhoea; the restlessness continued, the hernias became more troublesome, and finally, December 24, 1897, the patient succumbed to a pneumonia.

The autopsy revealed general atrophy, pneumonic infiltration of the posterior part of the right lower lobe and moderate œdema of both lower lobes. The anterior surface of the right lung and both apices showed old pleuritic adhesions. The heart had very brittle and tortuous coronary arteries and there were thickened patches in the mitral and the beginning of the aorta; small, slightly cystic kidneys, partial sclerosis of the basal arteries of the brain, a few hyperostoses of the frontal bone. The brain showed nothing, except general atrophy (1,132 grammes) and œdema of the pia; no granulations of the ventricles. The other organs weighed: the spleen 40 grammes, the kidneys 70 and 75 grammes, the heart 140 grammes, the right lung 330 grammes and the left 335 grammes, and the liver 640 grammes.

Microscopically we found a pneumonia with Friedländer's bacillus, and in the cortex marked shrinkage (the œdema alteration of Hoch) and axonal alteration of the Betz-cells on both sides, also of a few of the larger cells in the first frontal gyri, but none in the temporal, third frontal, cornu ammonis or cerebellum. The sympathetic cells, however, showed much pigmentation, and almost throughout the sections a condition similar to that in case 6.

Case 4 (from Dr. Gurley's service).—Depressive hallucinosis; after a six months' course rapid decay and fatal termination within a few weeks with features not unlike those of general paralysis, but without speech disorder or other distinct nervous symptoms. Aged 50 years.

F. P. G., born in 1849, painter and agent for sewing machines. The maternal grandmother was insane after the birth of patient's mother and died insane. The patient reports of himself excessive masturbation from 10 to 12; at 15 consequent nervous debility, dizziness, inability to bear heat of the sun, two "sunstrokes" (symptoms vague); no full recovery although he was sometimes better, sometimes worse; at 20 to 25 a course of books and medicines on lost manhood, &c.; at 23 he married, and two to three months later was divorced; re-married at 25; masturbation during marriage; probably no syphilis; he was always (at least since marriage) melancholy, easily disturbed; it was hard to get him up after an illness, especially since 1894, when he had "lead poisoning" (continual

constipation, pain throughout the intestines, arms, and legs, swelling of legs); he was also subject to bronchitis, and since marriage to "liver trouble" (attacks with coated tongue, retching, vomiting, and a soreness in the hepatic region). Since 1894, a change of character became noticeable, a disposition to let things drift and to spend more than he could pay for, gradually increasing to a maximum in the spring of 1898, when he bought boats, thinking he could make plenty of money. He could not pay for them and failed; he did not worry about his work; he became interested in socialistic papers and at times excited. He grew more secret and quick to take offence, would not be dictated to by his family, his wife did not dare to ask about his business. In the spring of 1898, on return from a seven weeks' trip, his eyes looked heavier; October 10 he had abdominal pains, he was fearfully depressed, thought he could not get well; that there were people around who were going to harm him; and that the doctors were going to cut him up; he thought his wife and children were against him. He was in bed until admission. From November 5 he had hallucinations of hearing: He heard his wife tell their daughter of 17 and his physician that he had laid on her too much, whereupon the doctor said that such a mean man as that should not be allowed to live; and the daughter said she did not know that he was such a mean man. Later he heard them say such a mean man ought to be killed, and they talked about having the nurse kill him. He did not believe the improbability of such conversation; he must believe it because he heard it. He remarked it was all right, and that he ought to be killed. He produced self-accusations, mainly for trivial real deeds, as thefts at 12 and 13 of money from an aunt, and his behaviour with his wife. The voices became very numerous and distressing by their threatening or disgusting contents, as "God is a whoremaster, and all the world is a whoremaster; come to meet your doom." On November 8 the patient cut his throat to forestall others harming him; November 15 he hit himself over the head with an iron; he was very changeable, at times apathetic and listless, then suddenly alarmed, or at times in deep study and averse to conversation, at other times talkative. But orientation was never affected. November 15, 1898, on admission, he was carried into the ward. "The arrest took all the strength out of my legs." He soon rallied. From the beginning he was constantly under the influence of hallucinations. Far away voices say all kinds of abominable things like "God is a fool: Frank, come here, I want you, arise, turn

to the left and meet your doom," &c. He does not answer the voices but obeys them in all his actions (he took off his shirt several times, looked into the mirror to see whether he really was a beast, &c.), and frequently is at a loss: "I don't know what to do; one tells me to go up to the right, and when I did that was not right; others tell me to turn to the left, and when I did it that was not right. I don't know what to do; I wish somebody would tell me straight." Sometimes the voices are just ideas, then they become faintly audible and then louder, as if from the corridor.

The patient is a man slightly below medium height, weighing 120 pounds, with gray hair, anæmic mucous membranes and blue sclera, slight arcus senilis, but no atheroma. The wound from his attempt at cutting his throat is healing. Apart from muffled heart-sounds and a systolic murmur over the apex and left axilla and subclavicular fossa, disappearing in recumbent position, he shows much exaggeration of the knee-jerks, less of the elbow reflexes and the cutaneous reflexes, a slight fine tremor of the hands and fingers on rest and rotation, and some defect of coordination of fingers with eyes closed. Gait and speech were normal, sleep and appetite fair. The patient often sat by himself with a perplexed and depressed look; he gradually (during December) began to associate himself as travelling companion to any new and restless patient, walking up and down with him. His fear of execution varied. A voice told him to go out of doors with the others to have his bowels taken out. "I am ready to meet whatever is coming; the voices tell me my head will be cut off, the eyes taken out, the teeth pulled. I expect something dreadful is going to happen." Or he heard he was never married, the minister not ordained and the children not his, his wife dead, &c. When she called he thought she was a little stouter and her voice a little different and he doubted whether it was she. In January he appeared more indifferent to the voices and more and more devoid of affect. Orientation was always good and he showed no deterioration of memory; he had some sort of insight—"my mind is in a bad state; it keeps on thinking bad things; and I hear voices calling me to my doom." He often came to the physician with the question: "Did you call me? A voice told me to come to my doom." He took a scratch from an excited patient without resistance, "it is part of my doom." He is almost over willing to obey any instructions or orders, just as he does with the voices. Some of the voices he attributes to his own mind, and January 5, 1899, he remarked that the people around

him must read his thoughts, because as soon as he thought of anything he heard it said after him. The self-accusations are meagre and are overshadowed by hallucinatory incriminations against which he remonstrates, such as having killed someone: he had only let his mother-in-law's nurse go. The idea of punishment increased. January 24 he bared his buttocks and deliberately burned them against the radiator, saying he wanted to begin on his punishment. In March, he often asked for his punishment. One day he said the food tasted metallic and he was constipated: "part of my punishment." Hæmatoma of the ears developed in April (attributed to the watchman); then he attempted to gouge his own eyes, because the voice told him to and because he was mixed up (he was ashamed of his actions); when his hand had to be restrained he tried to strike his eyes on sharp corners of chairs, faucets, &c.; he often got up at night obeying the "rise and meet your doom." Under increasing emaciation the patient finally showed a few times subfebrile temperature and vomiting, and he died unexpectedly in a collapse on May 18, 1899, after having stayed in bed four days.

The *autopsy* was made twelve hours after death and established general emaciation, residuals of hæmatoma of both ears, decensus of transverse colon and stomach, a few cysts of the kidneys, moderate adhesion of the dura to the skull, œdema and slight milkiness of the pia; the lobes were easily separated. No granulations of the ventricles. No evidence of atheroma, not even in the beginning of the aorta. General atrophy of the organs; heart 170 grammes, left lung 200 grammes, right lung 210 grammes, liver 820 grammes, spleen 50 grammes, right kidney 85 grammes, left kidney 75 grammes, brain *in toto* 1,285 grammes.

The *paracentral lobules* show no tissue alteration characteristic of general paralysis, but the axonal reaction in the greater number of the cells, in various degrees and combined with rather extensive pigmentation in many of the cells. Around the smaller cells of the deeper layers there are frequently a group of satellites. The *frontal* and *cerebellar cortex* are free.

Sympathetic (semilunar) ganglion. About one-fourth of the cells are fairly normal (large peripheral lumps and small central ones of stainable substance, and a fairly central nucleus) the majority of the cells have only a peripheral crust of stainable substance, not in distinct lumps. The centre is glassy, only occasionally laden with pigment granules, and the nucleus is more or less eccentric, in some cells reaching the surface completely as in the pictures of pronounced axonal reaction. Only few nuclei show

degrees of homogenisation and slight loss of the membrane. About half the cells show pigment, but not to excess. There are no eosinophilous granules.

The *Gasserian ganglia* have large cells with fairly even and dense distribution of medium-sized and small stainable particles and rather numerous "fatigue nuclei" (condensation and beginning loss of membrane).

Case 5 (from Dr. Gurley's service).—Alcoholico-senile deterioration. For two years periods of one to three weeks of weakness and indistinct speech. June, 1898, jerking of all the muscles and acute hallucinatory delirium, followed by a partial remission; from September, 1898, depressive delirium with somatic delusions and increasing weakness. Death from broncho-pneumonia, October 28, 1898. Aged 57 years.

T. D., 57 years old, teamster, with good family history as far as known; with uneventful personal history, except for excessive alcoholism; he always was a heavy drinker, of whisky mostly, often taking as much as a pint daily, and he was frequently intoxicated. He married at 20, and had seven children; four died in infancy. He had not worked steadily for two years. In the summer of 1897, while working in the yard, he fell, not entirely unconscious, but with great weakness, so that he could not use either leg; understood what was said, but could not speak; he made a complete recovery in three weeks. However, from this time he had a monthly occurrence of attacks of the same kind, weakness and indistinct speech; he could not get upstairs without aid, and it was difficult to understand him. These attacks lasted one week. From the first attack the patient showed more irritability, he was hard to get along with, and drank much. June, 1898, he had jerking of all the muscles, so that he could not stand up; he acted strangely, and showed slight asymbolia, *e.g.*, he held his pipe in his hand and tried to cut it as if it were tobacco; then, about June 14, his speech became very thick and indistinct, yet he was jabbering all the time; by June 20 he had to go to bed, where he was unable to move without assistance (?). The following day there was a sudden appearance of hallucinations of sight and hearing—fairies and witches and people about the house; carpenters boring holes through the walls. He jumped out of bed, dressed, and went into the street, consulted lawyers about papers he imagined he had lost, imagined people were trying to get his property, &c. His gait was feeble and shuffling, his speech silly, careless and

at times unintelligible, his attitude somewhat bewildered. He was admitted July 1, 1898. The following is an abstract of the *status* of July 9:—

Very gray thin hair, grayish moustache and beard; fair nutrition, flabby muscles, eczema on chest. Slight hypertrophy of the left ventricle. Hard radials. Marked arcus sensilis, internal strabismus of right eye (from childhood), chronic conjunctivitis. Hearing very defective (watch not heard in contact); odour of oils not recognised. Tactile sense not acute. *The knee-jerks were absent*, the reflexes of the arm present. Slight tremor of hand and tongue. Bleeding hæmorrhoids. The writing tremulous and defective in spelling, not unlike that of a general paralytic, whereas the speech was merely careless. The patient was quiet and tidy in the ward, occasionally wandering restlessly, with a simple apathetic manner, and slow, somewhat unsteady gait. He was very deaf, and slow in answering, and at times rambling. Place and persons were recognised; time orientation defective—year, month, hour of the day, age, &c. Only the simplest calculations were done; but he has insight into his difficulty and in the defect of memory. Patient has a vague idea that he sometimes was pushed about—"They keep me here wrestling and I don't know what they do it for, because I am no fighting man. I have no fault to find with the folks here, only they have a good time, I suppose." His son-in-law "stole his will." He admits insight into the hallucinations at home; he hears and sees "nothing imaginary now," and "feels very silly." He ascribes his failing to drinking. No history of syphilis could be obtained.

From August 19 his appetite failed. September 15 everyone called his name at the meals. From October 4 he became restless at night, pounding the door, seeing potatoes, grass, roads, a quarry on the floor; praying. From October 11 he groaned also by day, praying, "Oh God, Oh God, Oh! I am in hell, pretty near." October 12 he jumped into a shallow pool of water on the lawn, and when his daughters visited him he prayed for their salvation, making a scene and crying bitterly. October 15, he "wanted to lick all the devils in hell, out of hell, and below hell." He became unsteady, stumbled and fell around the ward often. October 17, he was leaning over the side of his bed, coughing and retching: "The devils are into me and I am trying to get them out." After October 20, he also caused a prolapse of the rectum. "The devils have gotten down there and I try to get them out." He tore the mucous membrane, and bled. Finally, October 22,

a rise of temperature and signs of broncho-pneumonia came on, and the patient died October 28.

The *autopsy* established broncho-pneumonia and œdema of both lower lobes, the left lung weighing 555 grammes, the right 830 grammes; a milk-spot on the anterior wall of the right ventricle and hypertrophy of the left ventricle (the heart weighed 365 grammes), with a few yellow patches in the mitral valve and a very few atheromatous elevations in the beginning of the aorta; a small cyst and a small scar in the right kidney (right kidney 112, left kidney 125 grammes); slight thickening of the capsule of the liver (1,470 grammes); distension of the stomach and intestine, hyperæmia of the rectum and a healing ulcer of its mucous membrane; atrophy of testicles. The skull was normal, also the dura; the pia was moderately œdematous and very slightly hazy over the blood-vessels, perfectly translucent at the base and thin over the Sylvian fossa; the lobes were easily separated; on the right anterior cerebral artery there was an atheromatous patch; the two sixth nerves were of equal size. No granulation of the ventricles. Weight of the entire brain, 1,235 grammes. The dissection of the formaline-hardened brain into the thin laminæ gave no abnormal findings, except perhaps very slight broadening of the vessels and perivascular spaces in the external capsules.

The cortex of the first frontal and paracentral lobules were examined with methylene blue after alcohol fixation. In the paracentral lobules the tissue as a whole has a normal orientation of the cells, no marked vascularity, a rather striking abundance of pigmented spindles with poorly defined nuclei in the adventitia of some medium-sized vessels, but no characteristic infiltration of the sheaths, and a moderate increase of "free nuclei," many of which surrounded with slightly pigmented protoplasm, either free in the ground substance or as satellites, and about as numerous in the layer of the medium-sized pyramids as in the polymorphous layer, certainly not more numerous around the affected cells. The first glance at the specimen shows the axonal reaction of the Betz-cell, with almost no exception and in various degrees, and modified by various degrees of pigmentation. The larger and medium-sized pyramids are not altered in the same way, but show very marked rarefaction of the stainable substance of the apex process; and many of these cells and especially the polymorphous cells are pigmented and their nucleus is shrunken a little.

In the frontal cortex there are but few cells with axonal

reaction; many pyramids have a very slender rarefied apex and pigmentation is prevalent. The cerebellar tissue is not altered. The *Purkinje-cells* have no axonal alteration; the spindles are plain and often form caps around the frequently irregular nucleus. In the spinal cord the *motor cells* are mostly normal, though perhaps a little pale and much pigmented; the nuclei are darkened a little in a few cells, and very few show the typical axonal alteration. The cerebellar afferent cells of *Clarke's column* are all affected and show uniformly the axonal alteration, especially well on longitudinal sections. There is a moderate number of corpora amylacea throughout the cord, but no evidence of posterior sclerosis. The cells of the *spinal ganglia* are large; not over one-third of them are pigmented. The nucleus of all the cells is without membrane, more or less dark, granular, of uneven slightly irregular outline, but with a plain nucleolus. There is a halo around the nucleus. The stainable substance of the cell body is rather heavy along the periphery, and thin or absent around the nucleus. A few cells show the axonal reaction. Among the internal organs, the *liver* shows a very slight increase of connective tissue; the *lungs* a moderately extensive infiltration with rich infection, with streptococci and staphylococci, and the *testis* has unusually open canals, but a fair amount of sperma in various stages of formation. The *kidneys* have but few obliterated glomeruli with thickened capsule; they are on the whole well preserved. In one papilla of the kidney there is a small curly fibroma well limited against the other tissue. The kidney has a few septa proceeding from the capsule and rather thick vessels, but few sclerosed glomeruli. The liver has not much blood and a moderate fatty vacuolisation of the cells in the periphery of the lobules.

Case 6.—Recurrent (partly hysterical and hypochondriacal) depression, with several exacerbations and partial remissions; termination in stupor with some twitching, and death by pulmonary embolism. Aged 44 years.

T. J. H., born 1856, painter, married. Family history: mother died of brain fever; three of the patient's cousins have been insane, also his paternal aunt, and one paternal uncle is a drunkard; a sister is melancholy. They are described as a rather nervous, excitable family. The patient at the age of 9 months injured his right hip and leg, which remained short. At the age of 14 years (1870) the left knee was crushed by a

waggon. The patient went to school up to 1871, "never very bright," from childhood he was quarrelsome and cranky, and he often picked up imaginary insults. He did not get along well with his step-mother. From 1871 to 1874 he turned a wheel in a rope factory, and the next seven years he worked in a pottery. In 1878 the patient was troubled with sleeplessness and melancholia. In 1879, he was at the Carney Hospital with "symptoms of paralysis and severe 'convulsions,' and exaggerated shaking with apparent loss of consciousness and loud outcries." One night he got up from this "unconsciousness" to look in the mirror; he denied this at the time, but admitted it later. He was admitted to the *Danvers Lunatic Hospital*, September 19, 1879; he ate and slept well, was hysterical and lied a great deal, telling many foolish and impossible stories, and he had a series of convulsions relieved by an active cathartic. From February 20, 1880, he became more cheerful and contented, gained in weight, and was discharged *recovered* March 12, 1880.

The patient returned to his work, which he changed for house painting; this he continued up to April, 1898.

In 1889 he married, after an uneventful life of sexual abstinence, a woman of doubtful character. In 1892 or 1893 he acquired a urethritis from her; otherwise he knows of no sexual disorder, except that he failed to have erections from the Spring of 1898, while before he had cohabited about twice a week. He also mentions a lead colic in 1893, which kept him two weeks in bed. In 1896 the patient had an operation for rectal fistula. About that time he did not sleep well, and took sleeping medicine regularly since that time. He was afraid of getting sick and unable to make a living; finally, April 18, 1898, he quit work on account of depression, shaking of hands, and a pain in his bowels and lacking ambition. He became hypochondriacal, went from physician to physician, exaggerated his symptoms (*e.g.* his sleeplessness). After taking an overdose of cathartic pills in October, he began to feel that his bowels were ruptured. He was nervous, much excited, and on October 28 he had a marked convulsion of epileptic character. At home he was threatened of being strapped down for being so restless, whereupon he *cut his throat* with a razor, and was admitted here *November 1, 1898*, "for having complained of pain in his bowels, crying hysterically and for having attempted suicide."

Here the patient appeared physically normal, but for his traumatic deformities of both legs, and hypochondriacal exaggerations and prolix reiteration of his ailments, the too active motion of

his bowels, and the wound of the neck, &c., the circulation in his legs—"you see, doctor, my legs are rotting off," when they were slightly blue and cold. "You will see I am going to die a terrible death."

At night the patient was frequently restless, moaning, out of bed, and requiring hypnotics.

A careful physical examination established, besides his deformities and the healing wound, exhaustion, cold extremities, a numb feeling of the legs with somewhat sluggish tactile reaction, some epigastric pulsation. The knee-jerks were equal, not exaggerated; he had a fine gelatinous tremor of the tongue, and a coarse jerky tremor of the hands at rest, increased on motion. The abdomen was scaphoid; the internal organs and the urine normal. He improved somewhat physically and also mentally, when, April 24, 1899, he was taken with a febrile tonsillitis. During the night of April 25-26 he became greatly agitated and noisy, very fearful of being killed, burned, &c. In the morning he had wild, staring eyes; he clutched the doctor, begging him not to let "them" burn him up "down there," pointing to the corners of the room; reiterating this with many groans, sobs and cries; he frequently got out of bed and kept up the same agitation all day, but with complete orientation. The temperature was 104° on the evening of the 24th, continued about 103° the 25th and sank to 100° and normal on the 26th; for some time it reached 100° on several evenings (May 25 and 26, and June 11 and 14), and occasionally in the morning (May 7 and 16); with the sinking of the temperature a quieter condition returned. But up to July 15 he maintained an undercurrent of fear with slight exacerbation of his complaints and of interpretations of the following character: a patient gave H.'s wife two letters, which she mailed for him. H. then felt "pretty sure" that he was going to be put to death. "I heard people in the dining room saying I was going to be put to death with big hatchets and an attendant said this is the last meal you will ever eat with me" (May 16). The only more complicated interpretation was maintained from May 2 until October 21, when he recognised it as imagination, but was sure he heard the talk that time: Dr. G. brought "Judge Almy" from C. to the door of the patient's room and said—"Is this the man you sentenced?" The judge replied "Yes," and Dr. G. said "that is all I want to know." This episode is referred to about April 26. H. was then sure that it was a death sentence. June 13 he said: "I am sure of it. I can see it. I can see it everywhere. I am to be taken

to my room ; five men will kick me with spurs and then take me to ward 'S' and string me up on the shower baths of scalding water." He at times maintained having heard, at other times having made out, that his attendants said : " Jesus Christ, when I get hold of him, I'll stitch those things into him " ; or he heard that they were going to take him into Gage Hall, to take out his eyes, and " they are going to cut my testicles out the first thing." " Who said so ? " " The attendants and all of them ; they know all about it. They are going to chop me up to-night " (June 13). He often asked up to July—" Doctor, will you let me live another night?" or " for four days ? " and then on the second day he said : " Doctor, did you mean when you said I should live over the fourth that I should not be tortured ? " He realises that he was committed for an attempt at suicide, which was insane, but does not admit that his prognostications are ridiculous. He repudiates their being in any way as insane as those of B., who maintains that he is to be buried alive. His memory and orientation are good throughout, and there is at no time any foundation for his ailments. His complaints are usually produced with a mask-like countenance.

July 16, 1899, he displayed perfect insight—" They were all imaginations and I am going to brace up ; " he even wanted to work ; but August 20 he is again described as groaning, and weaving back and forth, slapping his hands. " My wife and furniture are all going to be lost. The probate court sits the fifth, and I am going to lose all, and everything will be swept out and my wife will be brought up here crazy." " How do you know ? " " I told myself so ; I made her so ; no one told me." After four days of noisy lamentation, he continued depressed and restless till the middle of September. From then till November 3 he was quiet, out of doors every day, hardly volunteering anything, except occasional requests for " sleeping powder," which he did not get, or need ; he, however, answered the questions promptly, was perfectly oriented as to time and place, remembered clearly all the previous conversations, called the episodes with Judge Almy " all imagination." " It was a man who looked like him, and I heard the talk about the sentence." He did not really hear the attendants say that he was to be killed ; but when he heard them talking indistinctly he imagined it was about his death, " because I felt so bad." He was calm and rational, not especially depressed or anxious, only a little scared occasionally at night when he did not sleep. But he knew that it was foolish.

November 3, 1899, there was a sudden turn for the worse. An attack of diarrhoea with incontinence confined him to bed for seven days. Saliva was constantly flowing from his mouth; he often groaned and moaned: "my God, my wife is going to starve to death. She will be turned from her home." From November 10 he was up, but required bathing every day, very often asked for something (as for milk, water, to go to the closet, &c.). He spoke of the sheriff selling his household goods, but did not express any anxiety. His face became very oily and the nose especially became crusted with a simple seborrhoea, and roughened up to the forehead. November 29, the patient made an attempt at suicide. He asked to go to the closet, filled a bowl with water and attempted to drown himself in it. From November 30 he was kept in bed on account of weakness, diarrhoea, filthiness and destructiveness. He groaned and moaned often, had his mouth full of saliva and spoke almost unintelligibly, whereas before he never had shown the slightest speech-defect; he was restless, often trying to tear the bed-clothes; on several occasions he had a number of spasmodic twitchings of the arms, but they seemed to appear only when he thought himself watched. He took his food well and showed no other symptoms beyond the peculiar pseudo-stupor. January 3, 1900, his temperature was 99° at 8.30 a.m. Two hours later a rattling in the throat was noticed; the patient's temperature was then 103°; he was lying on his back with 44 respirations per minute, fixed eyes (but reacting pupils), considerable blind agitation and occasional trembling of arms and hands, especially during the forcible expiration; once or twice he drew his face in contortions, showing the teeth and lifting the arms during the inspiration in apparent distress. The heart beats were covered up by the tumultuous breathing. The radial pulse could not be obtained on account of the agitation, and the inguinal pulse was weak and irregular. The percussion of the lungs was negative. The patient flinched when pricked; both the knee-jerks were exaggerated. Death occurred at 11.30 p.m., January 3, 1900.

The autopsy, made three hours later, showed pulmonary embolism with beginning engorgement of the left lower lobe; several old adhesions of the left lung, a few yellow patches in the mitral valve and the beginning of the aorta. The weights were: left lung 280 grammes, right lung 340 grammes, heart 265 grammes, spleen 110 grammes, right kidney 155 grammes, left kidney (?), liver 1,475 grammes. The source of the embolus was searched for in vain.

The skull had almost completely obliterated sutures with the exception of the posterior end of the sagittal, a fair amount of moderately hyperæmic diploe; a moist non-adherent dura; the pia of the convexity was very slightly whitened along the blood vessels and considerably œdematous in the depending parts; the lobes separated easily; there were no granulations of the ventricles. The basal arteries were white (not sclerosed) and contained clotted blood. The weight was 1,505 grammes.

The microscopic findings were as follows:—

The sections of the *paracentral lobules* stained in methylene blue, without embedding, present a combination of acute alteration and Hoch's alteration in most cortical elements. The large pyramids have, moreover, throughout the typical axonal reaction and are little modified by the other accidental terminal alterations. The blood-vessels are not affected and the general arrangement of the tissue is normal. In the *frontal cortex* the axonal alteration is demonstrable only in the very few large pyramids. The calcarine cortex and the cerebellum are also free, and the latter not affected by the acute alteration. In the *medulla oblongata* all the cell groups showed more or less numerous instances of cells with typical axonal reaction, far in excess of what is usually found. Not only the cerebral afferent cells but even those of the nucleus ambiguus were extensively affected.

The *Marchi specimens* give the following findings:—The *paracentral lobules* show a large number of degenerating fibres of varying course, but mostly descending with the marrow of the convolution and appearing in or beneath the deepest layer of the cortex, and only rarely in the third layer. In the *first frontal convolution* there is only here and there an isolated degenerated fibre. The *medulla* shows scattered black lumps in the pyramidal tract, in the region of the cerebellar afferent tract, throughout the nuclei of Goll and Burdach, and among the arcuate fibres and the fillet. *But the degeneration in the pyramid is much slighter than the findings in the paracentral lobule would make one expect.*

The *cervical cord* has a marked degeneration in the postero-median columns more on one side than on the other, few lumps in the postero-lateral column, more in the lateral columns and in the direct pyramidal tract and relatively few in the anterior ground bundle.

Case 7 (from Dr. Fleming's service).—*M. D.*, a woman of 33 years, of French-Canadian origin. *Melancholia* with marked perplexity, leading to a peculiar delirious agitation with twitchings

and attacks of fright during an irregular partly febrile episode of enteritis lasting nearly four weeks.

The maternal grandmother of the patient is 106 years old, and has been peculiar mentally in her old age. *The oldest child of the patient is an epileptic imbecile.* The other children are normal, also four brothers of the patient. The mother died in December, 1899, of unknown cause. The patient was born in Canada, 1867. She went to school very little, if at all, and was obliged to weave in a mill at the age of 11. She was rather weak physically (on account of the early work) but normal otherwise. At the age of 21 she married Mr. D., after two years' acquaintance; of very retiring disposition, she devoted herself to the housework and the children, and to learn to read was her only pastime. Her husband calls her an intelligent and good housekeeper, of temperate habits and cheerful, never gay and never despondent.

Two of the patient's brothers of 12 and 22 years boarded with her; two other brothers lived in the neighbourhood. In 1896 her husband became a Methodist and they began to read the gospel, and the wife and two younger brothers were also converted. The two other brothers would often come to the house and worry their sister by telling her that their grandmother, "who was a witch," had given her the imbecile boy and had changed her religion.

On December 21, 1899, the patient's mother died. From this time the patient became greatly depressed, cried often, and finally almost incessantly day and night for four or five weeks. She would say "my mother is dead and my grandmother too" (she had only heard that she was weak), and she would cry out "I am damned," because the grandmother was dead. Up to February 2 she did all her work, except three weeks' washing which she neglected. She thought she saw her mother in dreams, but she did not hear her speak, nor did she have any hallucinations when awake. During this period her brothers persisted in coming to the house during the husband's absence, and in worrying the patient about her conversion.

Anxiety began to make the patient sleepless. She would not go to bed. She heard people come in downstairs, and although she did not hear them speak she knew they wanted to kill her. "As soon as I fall asleep they will come up." Hence she sat up most of the night. During the night of February 23, 1900, her husband saw her jump from the second storey window, but succeeded in catching her arm and in pulling her in. She was very much excited, she "had married the devil, and she and her children were to be killed." In a paroxysm of anxiety she

had tried to commit suicide, and it was impossible to quiet her. She was taken to the Poor Farm the next day. She was locked up and restrained several days, wanted to go home, but became more quiet, and passed into an attitude of timid apprehensive bewilderment. She never spoke to any of the inmates, but often picked their clothing and followed them around. She would stand by the matron from five to thirty minutes without saying a word. When her relatives came she recognised them, but would only sit by them holding their hands, looking at them in a puzzled way, and would hardly say more than four or five sentences in an hour; she wanted to go home, objected to being shut up, and said that she would do better at home. She did not know clearly where she was; she was not untidy, but required dressing and undressing.

On April 4, 1900, the patient was admitted to the hospital. She was a woman of about five feet, weighing only about 87½ pounds, hair brown, rather thin and fine, eyes gray, complexion sallow. There were several ecchymoses on the left leg and arm and around the left eye. The palate shallow. The lobules small and adherent; the right lobe of the thyroid somewhat enlarged. The recti abdominis muscles were separated, and there were numerous lineæ albicanthes. No disorders of the senses were discovered; the knee-jerks were brisk, the wrist and elbow reflexes present, the plantar reflex normal; ankle clonus and abdominal reflexes were absent. There was a slight tremor of hands on rotation and a slight gelatinous tremor of the tongue. No other motor disorders. The internal organs showed nothing abnormal. The urine was reddish-yellow, somewhat clouded, acid, of specific gravity 1030, free from albumen or sugar; no casts.

On April 5 the patient was found sitting on a settee. When spoken to she looked with an expectant half-puzzled expression without fear. To repeated questions she said she was fairly well, and spelled her name; she was difficult to understand, as she spoke hesitantly and hardly above a whisper, and in very poor French. She was led into a room and she sat down with a simple inquiring expression, slightly parted lips and sleepy eyes. While this description was dictated she remarked: "They brought me in a carriage." When smiled at she smiled. "Where do you live?" "I live here." "What is this?" "I don't know; I don't know all the rooms. Doctor, have I got to go into all the rooms here?" "What kind of a house is this?" "It is here." "What do you call it?" After it was

explained she was asked what had been said. "You said the hospital." "Where?" "In Worcester." "Are you ill?" She hesitates, looks around uncertainly, and finally says after several starts: "I am not ill." "Is your head troubled?" After long hesitation and numerous repetitions of the question, she whispered "no" to the side with a slightly embarrassed negative expression. "What did I say this was?" After many repetitions of the question, she said, "The hospital of St. John, you said." When the physician left her, she also left her chair in a simple, contented, though uncertain, hesitant manner. The general picture was that of a poorly-nourished woman, who is puzzled, uncertain, not able to grasp the situation for any length of time, but evidently anxious to do something. She follows the attendants with a perplexed look. The emotional tone is rather indifferent.

April 12, she presented very much the same picture: she is hesitant, perplexed, looks around puzzled, but remembers the writer. "Yes, I think I have seen you before." "Where?" "I was in a room with the mistress of the house (pointing to Dr. F.). Is she the mistress of the house?" "What house is this?" "I don't know, they took me here." "What did I tell you it was?" "You told me" (here she paused and began to cry a little) "You told me—they took my ring." "Who?" "A woman that brought me here. They brought me here to make me live. I would like to have my shawl," pointing to her shoulders. "In what city are we?" She looks around studying, breathing deeply, and after many questions she mumbled something unintelligible. "Are you in Canada?" She brightens up a little and finally says, "Yes." "Can we do anything for you?" Here she begins to whimper and finally mumbles something. "Do you need anything?" "Make me live." "Are you ill?" No answer. "Are you dead?" She smiles and says: "I don't want to die either." "What do you want?" "I want to stay with those people (*créatures*) out there, with the people" (*monde*). "Are you afraid?" "If one does not do anything, I'm not afraid, but if one does something, I am afraid." "Why are you so sad?" She begins to breathe more rapidly, whimpers a little and says, "I want to—I want to—" Then she pulls out her handkerchief and blows her nose on the extreme corner. "Do you need anything?" "No." The *perplexity* and *hesitation* and *slight uneasiness* are plainly in evidence. The answers were difficult to elicit, but when the patient once spoke, she did so without retardation.

April 19 and 26, the picture was similar. In the meantime she ate fairly well, but lost flesh; she weighed but 78½ pounds. On April 30, she had to be helped in undressing and resisted somewhat; usually she sat quietly on a settee with an expectant half anxious face, and occasionally worry, or she followed the attendants, or was anxious to have them sit down beside her. At times she suddenly jumped up, shook her dress and assumed a frightened expression. On the 19th she was greatly perplexed and uneasy; sitting on the chair with the physicians, she leaned over to the left side while slowly peering around, then made symmetrical movements with both hands around her waist, and then down the thighs and legs. "What do you want to say?" "I am all right" (without changing her puzzled attitude). "Please go and shut the door." She turns around slowly, still leaning to the left, turning her head to the right to the door. When requested again, she gets up slowly and awkwardly, and remains standing near the door; after about a minute she puts her hand on the door knob and draws the door open; then turns puzzled to the physician, wipes her face and takes hold of the door again. "Come and sit down!" She opens the door again. "Now close the door and come and sit down!" She leaves the door open and comes sideways with slow steps and sits down. "You know this house?" "Yes," but nothing could be elicited. "Have you pains?" "Why do you look so?" Her eyes became a little flushed and the face more troubled. "Can I do anything for you?" She begins to breathe more hastily and looks as if she would begin to cry. "Well, what have you to say?" She looks puzzled, the head slightly stretched forward, makes a few starts as if to speak, but remains silent. On April 26, she had the same expression of extreme uncertainty, reached out her hands in an uncertain half ataxic way and held the hand; she said: "This is the hospital." "And what is it called?" "My name is Mathilde D." Beyond this nothing could be obtained.

On May 10 she appeared equally hesitant and perplexed. "Do you feel sick?" "I am—I am—I am—I am not sick; I don't want any medicine. They make me take medicine and it does not do me any good" (making motions with the hand over the stomach).

On May 17, she had been in bed three days with a cold. "How are you?" "I have a cold" (rhume). After this frank response she shut her eyes, would not answer, and resisted slightly.

On May 11 her temperature was 99·8°, from May 12-13 101° to 101·6°, from May 14-22 99° in the morning and 100° in the evening. The appetite was poor; food was taken on persuasion only, and the sleep began to sink from eight hours to almost nothing on the 23rd and 24th, when the temperature rose above 102° and in the evening to 104·6°, to sink to the normal again May 25-29. May 20: a blood count was made showing 4,000,000 red and 6,500 white corpuscles. Diarrhœa came on; in one of the five stools of May 22 there was some blood. The abdomen became slightly distended and occasionally a little painful to touch. May 23: the blood count was the same (4,000,000 and 6,500), with a temperature of 103. The diarrhœa was arrested until May 28, and later reappeared irregularly. Widal's test was negative (May 25).

The *mental condition* became that of a *perplexed agitation* with occasional attacks of fear and screaming. May 23, when her *husband visited her*, she first cried "eh—eh—eh," &c., stretched arm and hand against him and turned the head away, but then at once took his hand and kissed him. She knew him but asked no questions and answered none except "Are you in L. or in W.?" "In this little corner." "Do you worry about the children?" "No." She often said "T." (the name of the brother who had troubled her), and at times cried and screamed, and tossed the arms around. She called the husband back but had nothing to say. May 24: she was found with dry, cracked lips, sordes, but moist tongue, with a number of aphthæ, somewhat distended, tympanitic and gurgling *abdomen*, hardly sensitive to palpation; the skin of the chest and arms red and scratched from the restless friction and picking. She makes uncertain, unsteady movements with the hands, mostly symmetrical, often with one finger down on the body or lips, moving along tremolo-fashion or making a poorly-defined picking movement. The facial expression varies; a smile she answers with a sardonic smile. She pays prompt attention but *from time to time she gets the expression of fright*, with increased restless, partly defensive, movements of the arms, and a stare and scream. "Yes." "What do you want?" "I want Caspar." "Do you want Caspar?" "Yes." "Your brother?" "Yes." "Do you need anything?" "Oui,"—long drawn out, while she puts her fingers to the lips, and ending in a scream and a movement of the arms to cover the face. "What do you need?" "I need—I need nothing," again in a calmer, half-whispering tone. When asked to show the tongue she said "oui," answered a smile, then

began to stare, and screamed and struck at the physician, looked away crying "docteur, docteur," and was quiet again. After the tongue and throat were examined, under slight resistance, she was asked, "Are you afraid?" "Yes, oui, oui," and again she screamed, staring with a slight *nystagmus* and ending up with a "non-non-non-non-non," returning to her palpation movements. "Do you know me?" "Yes." "Who am I?" She looks and finally says "no," and "I am afraid of you," with a new attack of fear which was rapidly pacified. Later she again answered a smile. She often repeats a few words of a question or answers "oui" without always grasping the sense. To a repeated "Who came to see you yesterday?" she said "Nobody." "Your husband?" "Yes." "Are you sad?" "Yes." "Why?" "I don't know," just with the lips. Then after a long pause, with movements of the hands and lips and another screaming attack, she turned to Dr. F., saying, "bonjour, bonjour." No orientation; she does not shake hands when the physician leaves her.

From May 26, she was more quiet, slept more, and took food and medicines better; she still had from one to five movements most days. The pulse remained about 110. On May 31, although the temperature had again risen above 100° and 101°, she spoke rather more freely and was less frightened. "Good morning; how are you?" "Good morning; I am glad to see you." "Do you want to take me away?" "I have 2,000 piastres at home; my father is dead, but he left me 2,000 piastres. Won't you take me up to X. (unintelligible)? I want to get out of here." "What is this?" "A hospital." "Where?" She looks to the ceiling and answers: "I am going to give you money if you take me away." To many questions whether she is sick, she answers nothing. She shows the deep red, slightly parched tongue, but gets it hardly beyond the teeth. "Do you need anything?" "Yes, I want to eat." "What city are we in?" (repeated)—no response, nor to the question whether the husband had been here, who the physicians were, whether palpation of the abdomen hurt. She mumbled several times something like "I want to go away." "Have you pain?" "No." No speech disorder was established at any time.

The first week of June she grew more sleepless; she ate poorly, cried often, and from June 6th she began to show a peculiar twitching of arms and body, with occasional twists of the head; she picked herself almost constantly, and at times straightened out suddenly and screamed at the top of her voice,

as if in pain. She is resistive to almost all the attentions of the attendants and quite untidy. She took her food only on persuasion, from the spoon.

On June 8 she was found in great *perplexed and helpless agitation*, very much emaciated, with a facial expression reminding one of a miniature of Rameses' mummy, the angles of the mouth pulled down, the profile almost cutting, the forehead occasionally in a play of contractions in efforts to open the usually but half-open eyes, accompanied by even further downward movements of the angle of the mouth, or in vain efforts to say something with pointed lips; the eyes and mouth are red and slightly excoriated from the continual palpation with the fingers and the rubbing; the olecranon region and the wrists and the chest are scaly and almost copper-coloured from the friction in the continual movements of the hands, which go on fumbling tremulously, often with lifted elbows, digging with the index on the bedding or the face or the chest, or pulling the sheets a little. The legs are pulled up and held rather firmly, but the resistance is overcome with some effort. The plantar reflex is prompt on both sides; on the right the toes go down a little and then slightly up, and on the left they all go downward. The knee-jerks are somewhat exaggerated; no ankle clonus is elicited. The patient had been too weak to get out of bed for over a week; twice she had been seen to break down suddenly when she had walked into the hall.

The patient appears to notice the physicians and that they speak to her, since she looks up at once when spoken to. In her fumbling and grimacing she makes vain efforts to speak. "Show me the tongue." She opens the mouth and puts her finger in tremulously. Another time the request caused her to open the mouth and show the lips; but she does not protrude the tongue. She takes hold of a watch held out to her, in a very tremulous and awkward way, and mumbles "Trois heures" and "mo-mo-mo." It was 9.12 a.m.

The examination of the internal organs is very difficult owing to the unrest, the irregular and at times tumultuous breathing, and the frequent and sudden contractions of the pectoral and clavicular muscles. No dulness or râles are discovered. The respiration varies from 20 to 25 per minute when the patient is calm, the pulse between 100 and 110, the temperature 101.8°; the sleep is much reduced; food is often refused. The *diarrhœa* was not constant, as she would several times go two days without a stool, though at other times she would have from two to four

stools a day, generally during the afternoon, from 3 to 8 p.m. The tympanitic condition of the abdomen has disappeared. On June 8 she began to refuse the food, pointing to the throat, making a motion as if it hurt her or as if she could not swallow. She took the food into her mouth, but would be unable to swallow it. She shook the head when more was offered her. The sleep became more impaired, and the general condition weaker.

On June 9, at 5 p.m., the patient showed signs of collapse, the fever had risen to 104°. She stared intently at the ceiling, reached up her hands as if attempting to grasp something, mumbling continually. Death occurred at 11.45 p.m.

The treatment had been mainly palliative (against the diarrhoea) and trying to effect rest and better nutrition. The diagnosis first was anxious melancholia, although the depression gradually gave way to a more or less anxious perplexity. The diagnosis of a "central neuritis" became very probable when a typhoid infection could be excluded, and the agitated weakness gave signs of jactation. The *autopsy* was made twelve hours after death by Dr. Dunlap.

The body is that of a small *emaciated* woman. Rigor mortis complete. Hypostasis marked over posterior part of thorax and buttocks. Panniculus adiposus 1 mm., pale yellow. Intestines but moderately injected, filled with gas, moist and free. Omentum retracted, containing very little fat. Appendix normal. Liver not visible anywhere below the rib margin. In the pelvis about 10 cc. clear fluid. Diaphragm at the fourth interspace on both sides. The lungs retract considerably. No pleuritic adhesions.

Pericardium free, with 8 cc. of clear fluid. The left heart fairly firm, the right lax. The pulmonary artery contains a soft mixed clot.

Heart, 135 grammes.—The right auricle contains a small amount of non-adherent mixed clot. The right ventricle is pale, the walls from $1\frac{1}{2}$ to 3 mm. The tricuspid valves are thin and normal, also the pulmonary valves. The left auricle is free. The mitral ring admits two fingers easily. The left ventricle walls are from 8 to 13 mm. thick, pale, brownish-red; the valve curtains are normal.

Left lung, 265 grammes.—The upper lobe gray with a purplish tint. The lower lobe a little firmer and a darker purple. A few scattered pin-head sized *sub-pleural ecchymoses*. The consistency is soft throughout, a little boggy in the dependent parts.

Section: Grayish-pink in the upper, red in the lower lobe. The cut surface of both lobes is smooth and from each a *bloody fluid* and *some froth* can be expressed; much more abundantly in the lower lobe. The bronchi contain frothy pink mucus. The larger vessels are free, except for a few soft dark clots.

Right lung, 300 grammes.—The middle lobe and anterior part of the upper lobe gray and soft. Lower lobe and posterior half of the upper, purplish pink with projecting light pink lobules and on the outer surface of the *lower lobe*, *three dark red*, *almost black*, elevated resistant *nodules* about 8 by 8 mm.

Section: Upper and middle lobes in gray portion normal and dry. Lower lobe and posterior part of upper, red with smooth surface; considerable *frothy pink fluid* flows from the upper lobe, practically none from the lower, from which, however, a bloody fluid with fine froth can be expressed. Section through the dark areas shows the nodules to extend about 8 mm. below the surface.

Spleen, 110 grammes.—Flabby, with considerable pulp. Trabeculae very indistinct. Substance on section quite friable.

Left kidney, 95 grammes.—Capsule splits considerably without tearing the cortex. Surface pale and smooth. One *yellow speck* 1 mm. in diameter. Cortex 3 to 4 mm., pale, with yellowish streaks. The glomeruli appear as translucent points.

Right kidney, 115 grammes.—The capsule tears the substance considerably. External appearance, section and glomeruli similar to left kidney.

Liver, 1,080 grammes.—Smooth, reddish-purple. Section: light purple, with very indistinct lobules. One gall stone the size of a large cherry.

Intestines.—About 13 cm. from the ileo-cæcal valve, in the ileum, is found a shallow ulcer with rather indefinite edges and slightly elevated peripheral zone (about 3 mm. in width). Part of its base has a translucent, healed appearance. The whole depressed area is 16 by 4 mm., the deeper area with ragged base 8 by 1½ mm. No enlargement of Peyer's patches; the mesenteric glands average about 6 mm. in diameter.

Skull, 373 grammes.—Symmetrical, smooth; sutures indistinct. Sulci shallow. Considerable diploe throughout. Slight pachionian depressions along the sagittal suture.

Brain, 1,100 grammes.—Rather flabby. Lobes separate easily. Pia of convexity thin with but little fluid in the sulci. Cysterna clear. Vessels of base thin. No granulations of the ventricles.

Anatomical Summary.

Emaciation. Small erosive ulcer in ileum. Ecchymoses in one and slight œdema in both lungs. Dark nodules (and beginning pneumonia?) in the right lower lobe. Gall stone.

Microscopically the lower lobe of the left lung contains intra-alveolar clumps of streptococci with barely beginning reaction in the tissue. A small dark nodule shows hæmorrhagic and fibrinous infiltration of the alveoli with but few traces of cocci.

The heart muscle shows beginning fragmentation. Liver and kidney had no characteristic lesion. The intestinal erosion shows hardly any granulations.

When the *axonal reaction of all the Betz-cells* was established, the brain was subjected to an extensive study with the *osmic acid reaction*. The *right hemisphere* yielded:

(1) Sections through the radiations of the frontal lobe as far back as the foot of the central fissure (fig. 3, *a*, and fig. 4, *a*).

(2) Sections through the radiations of the upper part of the motor area and the upper parietal lobule (fig. 3, *b*, and fig. 4, *b*).

(3) Sections through the auditory radication (fig. 3, *c*).

(4) Sections transversely through the hemisphere, at the level of *d* (fig. 3 and fig. 4).

(5) Transverse sections through the occipital lobe.

The *left hemisphere* was trimmed for a series of transverse sections of the basal ganglia, and the somewhat defective results of the study of the right occipital lobe called for a study of a series of sections through the left occipital lobe. The rest of the *brain-stem* was examined in a section through the mid-brain, and several transverse sections through the hind-brain, in the trigeminal segment, the pneumogastric-hypoglossal segment, and the first cervical segment.

The result is recorded in the drawings, and is here summed up as follows:—

(I.) The segmental elements, as far as examined, were little affected. The motor cells of the hypoglossal, the spinal-accessory and vagus, and the facial nuclei, show varying degrees of irregular rarefaction of the stainable portions and in each section from two to four cells, with typical axonal alteration in each nucleus. The same holds for the first cervical segment. Only few root-fibres are affected. Among the cells of the nucleus reticularis, in the auditory-facial-abducens segment, there are many with axonal alteration, but a small number perfectly normal. Many cells of the lateral nucleus have the axonal change. The

respiration-bundle has but few large lumps of decaying myelin, and the caudal root of the fifth nerve is practically free. In the Gasserian ganglia the cells show moderate shrinkage or none. They vary in diameter between 25 and 60 μ . The free marginal border is practically absent. The preponderating cell-type is

FIG. 3.

FIG. 4.

that with a marginal zone of rather large stainable lumps, gradually decreasing in number and size until a free perinuclear zone is reached; in a relatively large number of cells the stainable portions are practically limited to the marginal ring, and in about an equal number the medium-sized lumps are rather evenly

distributed from the periphery to the nucleus. The nucleus is normally fairly central and only in very few cells broken through the marginal ring of stainable portions, so that an undoubted *axonal reaction* could be established. It has usually a plain membrane, a diameter of 11-15 μ , a nucleolus of 3.5-5 μ with frequently plain apposition bodies, whereas the sap and linin-frame remain free of other blue granules in the Unna specimens. There are but few "fatigue-nuclei." Moderate pigmentation, usually perinuclear. The sympathetic ganglia present cells of the most varying types, from the rested cell, with even distribution of the stainable substance and clear central nucleus, to those with extensive dissolution of the stainable substance, and eccentricity of the frequently darkened nucleus, even beyond the marginal ring of granules.

(II.) The fore-brain and its dependent parts :—

(1) The *fillet* is slightly affected from the nuclei of Goll and Burdach (many of whose cells show the axonal reaction) to the ventral nucleus of the thalamus, and to the posterior corpora quadrigemina. The *optic tracts* are not affected.

(2) The *thalamo-cortical connections*, as seen in sections through the basal ganglia, are intensely involved to the following extent :—

(a) The radiations *between the lateral nucleus of the thalamus and the motor cortex* are very deeply blackened (see fig. 9).

(b) The *optic radiation* appears to be free in the external geniculate bodies.

(c) The *auditory radiations* have a small number of degenerating fibres.

(3) The *medulla of the convolutions and the centrum ovale* :

(a) The *motor region* and its projection fibres are profoundly affected. A few of the blackened fibres penetrate the polymorphous layer of the cortex. The presence of degenerating fibres is not absolutely limited to the central convolutions but overwhelmingly so ; backward the degenerating fibres are sharply limited to the posterior central gyrus. Degenerating fibres to the corpus callosum are not very numerous. From the irregular course of some of the fibres one might well infer that also association-fibres are involved.

(b) The white matter underneath the *first temporal gyrus* and the transverse temporal gyrus alone have degenerating fibres, especially the former, while the second temporal gyrus is devoid of them (see fig. 7).

(c) In the *occipital lobe* the maximum degeneration involves

the forceps, and it is easy to follow into the splenium of the corpus callosum on the one hand and into the cortex on the other, especially into the lateral cortex (see figs. 15 and 16). The optic radiation is relatively free, and also the inferior longitudinal fasciculus. Whether the degenerating fibres of the subcortical layer of the calcarine cortex belong to the forceps, is not definitely settled.

(4) The *cerebral efferent elements* have suffered to the following extent :

(a) The *pyramidal tract* shows a marked decay of myelin-sheaths of some of its fibres. The relative number is smaller than the appearance of the cortex would make one suspect, though the difference is not as marked as in case 6. This discrepancy led to a study of the thalamus which shows that so many of the degenerating fibres were thalamo-cortical.

(b) The cerebro-pontile fibres are only very slightly involved, so that Türk's bundle as well as the median part of the crus appear free.

(c) The fornix is free, with the exception of one or two fibres in a section.

(d) The corpus callosum has fairly numerous degenerating fibres in the splenium and about the region belonging to the motor area, but not very clearly limited.

The *typical axonal alteration* was found to be present in the paracentral lobule in all the Betz-cells and in many of the large pyramids. In the frontal lobe the alteration was much rarer throughout the cerebral cortex, the cells are very pale, with great reduction of the stainable substance but practically no diffuse stain of the non-stainable parts. The *blood-vessels* are nowhere infiltrated or thickened, but slightly distended.

III. The *cerebellar apparatus* is involved in three points :

(1) There is a distinct degeneration of a number of fibres in the restiform body in its course around the dentate nucleus to the vermis.

(2) Many of the cells of the dentate nucleus show a beginning of axonal alteration.

(3) The cells of the roof-nucleus have pronounced axonal alteration. The Purkinje cells are free.

Case 8 (from Dr. Budd's service).—H. B. P., aged 56. Alcoholic senile deterioration with stuporous delirious episode. Collapse.

The father of the patient had a shock at 68 and was mentally feeble afterwards, and died of a second shock. The two brothers and three sisters are free of hereditary features.

The patient was born in Maine, 1844. He went to the war at 17 and left the service in a year with "black measles and dysentery." "He did not recover his health for many years." He worked on the farm two or three years, and then became lineman on telegraph-lines, a good worker with highest wages. In this work he sustained *several injuries* from falls; he also was given to alcoholics and venereal excesses (many drinks of raw whisky every day; no venereal infection known of). He married and had children; about 1890 he left wife and family on account of his drinking and abusive and hot-headed disposition, and since then he has boarded in different places.

November 10, 1898, he was run over by an express-waggon. He was admitted in the Boston City Hospital with lacerated wounds of the face, and the next day he developed a probably *alcoholic delirium* which lasted nearly a week and necessitated the use of a straight-jacket. He was discharged well November 26, but his daughter thinks that he began to fail after this. He drank more, "seemed to stay half full all the time," and it happened that when he took down a wire for repair he went away forgetting to put it up again. He had to be given the easiest work, and about February he had to give up even that, because he was unable to go to the shop on account of physical weakness, especially in his legs. He spoke of getting a pension from the government and was very impatient about it.

For the last month he wandered about the house acting like a child, but up to within a week before his commitment he talked rationally and sensibly and was neither troublesome nor violent; his memory only was very defective.

About a week before his admission to the hospital he began to produce a confused talk about Heaven; that his son was being "buncoed" out of Heaven, that there was a war going on in Heaven, &c. He began to go two to three days without eating, knew those about him, but was very restless. He would be sitting down talking and suddenly jump up and go out into some other room, look around and come back again, saying, "It's all right," then he would sit down, only to get up again in a few minutes. He slept very little at night.

No evidence of delusions of persecution, of reference, of robbery or of expansive ideas, or of hallucinations could be obtained from informants.

Lately he has been very weak but not in bed. The last day at home he was arrested at the instigation of the boarding-house keeper, because they said he grabbed one of the children by the

throat. The daughter says he was not cross and irritable, and thinks he really intended no violence. He also threatened and tried to jump out of the second storey window.

On admission, May 19, 1900, the patient required assistance to get into the ward on account of his apparent weakness. On the evening of the 19th and the morning of the 20th, he had no idea of the city or nature of the place, but refused to assent to absurdities (stable, &c.). He twice said he came from Omaha, Nebraska. He did not know the year, month or day, and when pressed for the season, said it was winter. He was told the place, but on the evening round of the 20th he did not remember being told, and he had no better orientation, except that he said that the doctor "acted like a doctor," because he felt his pulse. He did not remember seeing him before in the morning, but said he had seen him before he came here. He constantly said there was nothing the matter with his mind. On admission his pulse was very irregular, intermittent, dropping one every two or three beats.

Physical Examination (May 22).

The patient is found to be a tall, moderately slender, well developed and well nourished man with thin gray hair and beard, abundant growth of hair over the thorax and abdomen, and dark, tanned complexion. Skin somewhat flabby, warm, moist and free from eruptions. Recent abrasion on lower third of right shin, 2 by 4 inches. Over left malar-bone, a scar 2 cm. in length. No other abrasions or noticeable scars. The left *clavicle* at junction of middle and outer thirds has an old callus, the inner end overriding the outer; union is complete. *Skull* symmetrical; *adherent lobules*; palate of medium height and width; *teeth* sound but well worn. Hands well formed. Large toe of each foot is much abducted, and the *metatarso-phalangeal joint* is *very prominent*. Penis and testicles normal; no scar is found.

General condition.

He remains in bed, but now and then gets up and goes to the closet; does not complain unless asked, then saying nothing further than that he "is sick" (ill). His tongue is clean; appetite only fair; bowels regular; sleep only by aid of hypnotic.

Eyes.—Dark blue, well opened and prominent. Conjunctiva clear: *pupils slightly displaced toward inner side, but*

equal, $2\frac{1}{2}$ mm., react to light and accommodation. Movements unrestricted. Vision normal. No hemianopsia.

Smell unaffected, and *taste* unaffected.

Hearing.—Good on either side.

Cutaneous sensibilities.—Touch and localisation, prompt and accurate. Pain and temperature tests are unreliable because of resistiveness of patient; believed to be normal.

Motor functions.—Muscular power of arms, equal but poor. Power of legs equal and good. *Gait*, slow and feeble. *After standing a few minutes he begins to reel as if dizzy, and complains of weakness, and he is helped to bed. Very slight individual tremor of fingers, becoming more marked on rotation. Tongue small and median, with jelly-like tremor at sides. Marked swaying in Romberg position. No speech defect.*

Reflexes.—On plantar stimulation the smaller toes flex somewhat, the large toe remains still. No ankle clonus. Achilles reflex, equal and moderate. *Knee-jerks both exaggerated, perhaps a little more so on the right. Elbow and wrist-jerks are equal and somewhat exaggerated. Cremasterics slow and long continued. Epigastric not obtained.*

Lungs.—Expansion equal and good. On percussion at the right apex, in front and over the entire surface of the lower lobe behind as far as the angle of the scapula, there is a higher pitched resonance. The respiratory murmur is relatively somewhat harsher over this area, and the expiration slightly prolonged. No râles are heard; no increase of fremitus.

Heart.—Pulse 64, intermittent and irregular, but full and of good quality. *Radials thickened, brachials slightly thickened. Temporals not visible. Apex beat not visible, but felt weakly in the fifth interspace, inside of nipple line. Heart boundaries*.—12 cm. to the left of median line at the sixth rib, 4 cm. to right of median line; whole width 16 cm. There is a distinct systolic murmur, rather rough in quality, best heard over the sternum, opposite the attachment of the third ribs, and better over the aorta than over the pulmonary ostium. No marked accentuation of the second sounds.

Abdomen.—Stomach even with costal margin. Liver from the sixth rib to the costal margin. Spleen not palpable. Inguinal glands felt plainly.

Urine.—May 21. Dark amber colour, clear with light cloudy sediment. Acid 1030, no albumen or sugar. Calcium oxalate, amorphous urates, epithelial cells, no casts.

May 23. Asked where his home is, he hesitates a long time,

and finally says: "Have none." "Where are your people?" "Have none." "Are you married?" "No." "Where did you live before you came here?" "Don't know."

Mental Status. (May 29).

Attitude and manner: Confined to his bed, he tries to run out or to pull clock down; At times he is irritable; feeds himself and is cleanly; often calls out.

Too weak to stand more than a few minutes at a time, he had been in bed since admission. At first he seemed to be ill at ease in bed, and often tried to get out, a number of times succeeding. He would then run to the door and try the handle, but on finding it locked, he would turn away saying nothing. Once he ran and reached and tried to pull the clock down from the wall and was prevented just in time. He would give no rational answer to questions about his conduct. He usually lies flat on his back. He often called out when lying in bed, saying such words as "whoa," "Over in the ten-acre lot," "Her name is Bailey," "All right," "It looks like it," "What?" "There, there," "Yes, there, east corner, 40 rods—timber land," &c., and then relapses into silence for some time. He shows but little interest in his surroundings, and answers questions in a low tone. During the first few days he showed considerable irritability when restrained from getting out of bed, but after a few days he did not try to get up so often and only showed occasional temper. Even when angry he said very little. He has been uniformly clean, always asking for assistance to go to the closet, or even to expectorate, and he has fed himself without trouble. On occasions he will absolutely refuse to eat one or two meals, and then again will drink milk when he does not take solid food. Once in a while he pulls and picks at the bed-clothes a little.

The following gives an idea of his stream of thought under a minimum of urging:—

Conversation: Volunteers rambling remarks, but finishes sentences.—"I've heard nothing from the general report. I think it is proper and right. I haven't been to the meetings only once." "Eh!" "Yes, that's all." "What have you got to say?" "I've been telling you about going into it. I suppose it was fixed over long time ago before I had anything to do with it." "What?" "What collects the seed?" "What do you mean?" "I don't know. I suppose you belong to the government, and know the seed of the womb. I suppose it would proper, you

ought to know." "What else?" "Why, I've got to reckon everything right through. When they are full they will take no more, that is all there is to that." "What is that?" "That's so, they give birth to young." "Who?" "A hive of bees isn't it? It is made by bees. They suck the seed from different meals and far different climes and different places." "What seed?" "The seed to manufacture the substance, its a honey." "Who spoke of honey?" "I don't know. That is the way I've always heard." "What have you been talking about?" "What have I? I don't know. I've been talking but little on account of"—(stops). "What?" "I didn't say anything."

Orientation: He calls the doctor as such; says it is 1900, but does not know place, day or month; his answers show confusion.—"What place is this?" "Wakefield Junction, is it?" "No." "I don't know." "What building is it?" "I couldn't give the first guess." "Why do you think it is Wakefield?" "Well, I don't know. I surmised, that's all." "What day is it?" "You have me now." Question repeated. "I don't know. I couldn't say." "What month?" "July." "Why do you think so?" "That will have to go. I guess you can put it down or not, just as you choose. They don't interest me very much now." "What year is it?" "Well, some say it is one, some another. It is supposed to be 1900 by some." "What do you say?" "Well, I don't know." "Is this your home?" "I wasn't born here, no." Question repeated. "Well, I come here before I was married. I had children before I enlisted." "Do you know me?" "Doctor, yes. Dr. Jones," (rising inflection). "Are you sure?" "Well, I heard you called that a good many times. I don't know as I was ever introduced to you, but I know you attended me, that's all." "When?" "Well, ever since they transferred the old Grand Army out, and transferred the old pensions on to this list to be transferred right on." "What was the trouble?" "Well, disability. I've been broken down pretty bad. You've been with me and ought to know pretty well."

Memory for remote events: generally fair, specifically poor.—"Where were you born?" "New Gloucester, Maine." "When?" "About 55 years ago." "What date?" "October 16. I was born in 1844." "Did you go to school?" "I was four years old." "How long did you go?" "I didn't go but little; went summers and winters three months each." "How long?" "I had to work the farm summers, and could only go winters." "How old were you when you stopped?" "17, I think." "What did you do then?" "I worked in a cotton factory in

Lewiston." "How long?" "Pretty near a year." "What then?" "Enlisted in the army. I wasn't there very long. I was ill considerable." "In any battles?" "Yes, I was in the seven-days' battle before Richmond." "Who was your general?" "General McClellan at that time." "What regiment were you in?" "The 11th Maine." "What date were you discharged?" "I haven't just the date." "About?" "I couldn't tell." "What year?" "I don't know." "How long were you in the war?" "You can reckon that up yourself as well as I, or better." "What year was it when you quit the army?" "It was '63, I guess, I couldn't say." "When were you married?" "Tenth day of January, 18—1880." "What?" "Eh?" "When were married?" "I couldn't tell you the day and date." "When was it?" "I don't know. I knew the day and date at the time, but I don't now." "How old were you?" "I don't know. I suppose I was 17 or 19, something like that—19 I guess." "What was your wife's name?" "E. D." (Correct). "Where is she now?" "I don't know." "Is she alive?" "She was, the last I heard of her." "Where?" "M——" (Correct). "How long ago?" "Some time ago." "Ten years?" "Oh, no." "One year?" "I've seen her in a year." "Where?" "At M——" (Correct). "Any children?" "Yes, three girls and one boy." "Where?" "The girls are all married; the boy lives with the other ones. All the children live together, except the one, Edith. She is in the same place, but different, in the same town, married." "What is your business?" "I've been working at electrical work considerably, called a lineman."

Recent memory: very variable, confused answers at times; stereotyped: "I don't know."—"How long have you been here?" "I don't know." Question repeated. "I don't know as I've been here but once." Question repeated. "Not knowing, I couldn't say, otherwise, don't remember." "A month?" "I don't know." "A year?" "Couldn't say." "When did you see me last?" "I saw you when you put those—heard the remark you made to—heard it before." "When?" "You came through here and put those pamphlets on my bed to-day." "What remark did I make?" "You said: 'Oh, yes, I prefer being on this side, and you skipped over.'" "What did I mean?" "I suppose you thought it was the last day and the world was coming to an end, or an earthquake or something. A lot of foolish stuff. It sounded foolish." "Where did you come from?" "I don't know." "Why did they bring you?" "Who brought me?" "Don't you know?" "No, I don't

know, I'm sure." "Where did you work last?" "For Webb, I believe." "Where?" "I suppose it was here." "Where?" "Wakefield Junction, is it? I don't know where."

Grasp of surroundings exceedingly poor.—"What kind of a place is this?" "An armory, I suppose." "Why are you in bed?" "You said I was sick." "Are you?" "I ain't very well." "What is the trouble?" "I told you I was all broken up, and you said here was a tender spot, and you ought to know, I suppose. If you call me a healthy man, let it go at that, and I won't say anything." "Do you know anyone here?" "No." "Did you ever see them before?" "What, the people that come here to view the—? no, I don't know." "What time is it?" "I don't know" (looks out of the window), "I don't know. I should say it was considerably after noon." "What time do you have supper?" "Well, different people have supper at different times." "What time do you?" "Sometimes one and sometimes another; sometimes I don't have any." "Ordinarily what time?" "Well, split the difference between that and—and you will get it as near as I can tell you. Ordinarily I get what I want to eat." "What time do you see me in the morning?" "Eight o'clock, is it?" "How many times have you seen me to-day?" "Three times, I guess." (Right.) Asked what the attendant did, he said: "As regards the collection of the seed, he is in it all right." Reads a watch correctly. "What am I writing?" "I think you are writing a full set of—I don't know—to have the thing progress, I guess." "What purpose?" "They have it to drill with, I suppose."

General information: (Answers not reliable).—"Who is president?" "What day?" "Now." "When now?" "1900?" "Do you know?" "No." "Who was shot during the war?" "I don't know." "What president got shot?" "I know a man who got shot, but no president."

Calculation: poor for combinations.— $3 + 9$? "27." $4 + 4\frac{1}{2}$? "12." $9 + 9$? "81." 13 and 7? "19." $2 + 13$? "26." $9 + 12$? "108." $3 + 13$? "I don't know." $17 - 9$? Pause. "It would be 9."

Counting.—He counts from 1 to 20 in five seconds, keeping on up to 50 rapidly.

Hallucinations: are not elicited, although he often calls out (see above).—There has never been any direct evidence of hallucinations, and nothing of that character can be elicited by questioning the patient.

Delusions: nothing definite elicited.—"Did you have trouble

with your wife?" "Yes." "What?" "A little domestic trouble." "What was it?" "Just a little." "What?" "Her daughter had a kid to-day." "Is that the trouble?" "Yes." "Have you any property?" "No." "Do they treat you well here?" "I've been treated all right." He occasionally jumps out of bed and tries the outside door, but never gives a rational explanation.

Insight: perhaps partial; answers contradictory and lacking animation.—"Is there anything the trouble?" "I have heart trouble bad." "For how long?" "Five or six years. Had it pretty much all my life." "Has your mind ever been affected?" "Some, not much." "What caused it?" "Liquor caused it, I presume." "How did it affect you?" "When I didn't have any it affected me." "How?" "Because I wanted it." "Did it affect your mind?" "No, it didn't affect my mind any." "Is it affected now?" "It isn't any better than it ought to be." "Have you ever been crazy?" "No." "Were you ever out of your head?" "Yes." "When?" "I was up to the City Hospital awhile." "What was the trouble?" "I got injured by a team." "Are you as sound in your mind as ever?" "You are the best judge of that." "Are you confused?" "Yes." "When?" "Well, most of the time" (in a lifeless manner). "This is an insane hospital, why were you brought here?" "Because of that arm." "Have you ever been insane?" "I told you no."

Reaction to questions: monotonous, forgetful of questions, occasionally irritable; some surprisingly accurate answers.—He lies in bed, looking out in a calm, deliberate, rather sleepy way, occasionally glancing at the speaker with a little gleam of animation, answering the questions in a low, monotonous tone, but when asked to repeat always repeating the same word or phrase, and finishing his sentences. Sometimes he makes an irrelevant or confused answer. This is more noticeable where he is persuaded to talk voluntarily (see conversation). When direct questions are put, he often makes a surprisingly accurate reply, but will perhaps make an equally foolish answer to the next question. Now and then when a question has been repeated several times, he will show irritation and elevate his tone somewhat to emphasize his reply, or sometimes saying "I told you before," or "I don't know, I tell you," then readily relapsing into his easy way again, in order to keep it in his mind.

June 16. *Restless; out of bed; diarrhœa; sudden death with cyanosis.*—Patient continued to remain in bed, observing in

listless manner those about him; occasionally speaking as if to himself as already noted. He was less restless than when admitted, but would occasionally try to get out of bed, and seemed especially restless at night, so that quite often he required light restraint. He at first showed no mental change either in voluntary speech or in reaction to questions from that already recorded. About two weeks before his death he was found to have fallen from the seat in the water-closet and to have bruised his forehead. He was lying quietly on the floor, and was not unconscious or more than usually stupid. Previous to this he had been taken to the closet after he had voluntarily started, and was always able to sit alone and to walk back with assistance. After this, however, he seemed to be growing weaker. He would often try to get out of bed, and when asked if he desired to go to the closet, he would say "yes," but he was not able to walk the whole distance, and unless he was helped he would soon sink to the floor. He was thereafter carried until about one week before he died, when he was not allowed to attempt to walk. He became noticeably weaker during the last week, and slightly more restless during the day, often pulling the bed-clothes about and attempting to get up, but when prevented he would lie back and apparently sleep. On several occasions when he succeeded in getting out on the floor, he was only able to walk a short distance, and would then sink easily to the floor, apparently too weak to go farther. There was at no time any evidence of muscular twitchings or spasms, nor any drawing of the facial muscles. He gradually became less talkative and observant. When spoken to he answered in a low tone, and generally irrelevantly. When his answers were relevant, it was thought he did not understand, but that it was merely accidental. He often took no notice of questions at this time. It was observed some two or three weeks before death that he would hold saliva in his mouth for some time waiting for help from the attendant, as he would readily expectorate when given opportunity. His expression was stolid and heavy. He often spoke about "electricity" and "wires," but not in connection with anything about the wards.

About four days before death he began to have diarrhœa, and he then was so stupid that he did not appear to notice when his bed was soiled. He had to be fed by a spoon, and passed the day lying flat on his back with eyes closed, and could hardly be aroused. He would occasionally rouse up slightly, but only for a few moments. He had not attempted to get out of bed for some

time before the time of death. The condition of the reflexes did not change.

He died June 16, in the morning, about 7 o'clock. After getting out of bed and walking through the door, he sank to the floor easily, fell backward in a heap, began to gasp in a strangling way, and to roll his eyes back. He was placed on the bed, and only breathed a few times afterward. The attendant noticed that he was at first very cyanotic over the most of the body, but, shortly after, this faded away.

Autopsy, June 16, at 11 a.m. Body of a well-developed and fairly-nourished man. Body heat present. Rigor in jaw, slight in legs, little if any in arms. Hypostasis considerable in dependent parts; purplish lividities on thighs and legs, even on anterior portion. Scrotum slightly abraded on right, lower half dark purple. Panniculus, about 2 cm., rather pale yellow. Intestines moist, but slightly injected; omentum retracted. Mesenteric glands not enlarged. *In the mesentery* of the ileum, near the scrotum, are about a half-dozen *calcareous nodules*, varying from small pin-head size to that of a small bean. Some of these lie near the intestine, others at the mesenteric attachment. Appendix normal. Diaphragm, fourth rib on right, fifth interspace on left. Liver in mammary line about 4 cm. above costal margin, nowhere visible on opening the abdomen. Lungs retract considerably; at the *right apex there are two narrow bands of strong adhesions*. Elsewhere the lungs are free; very little fluid. Pericardium contains about 10 cc. clear serum; pulmonary contains soft clot; right heart flabby and full of blood, left firmly contracted.

Heart, 315 grammes. Over the anterior surface of the right ventricle is a *thin white patch* (milk-spot), 2 by 3 cm.; *coronaries are tortuous, thickened and roughened*, embedded in a small amount of fat. *Over the left ventricle are two groups of pin-point to slightly larger ecchymoses*. Right auricle contains a dark, rather soft clot mixed with lighter clot. This does not adhere to the endocardium. Appendix contains a tough clot between its trabeculae. *Tricuspid opening admits easily five fingers* (perimeter, 14 cm.). *Right ventricle enlarged*; contains a stringy, light clot; walls from about 1 to 3 mm. Colour rather pale. The tricuspid valve curtains are thin and translucent. *Pulmonary valves are large, flabby, thin and free*; the measured diameter of the posterior valve is 4 cm. Left auricle free, except for slight stringy, non-adherent clot in the auricular appendix. Mitral ring admits two finger-tips rather easily. Left ventricle walls are rather pale

brownish, from 2.5 to 20 mm. *Mitral* thin and normal, except for a *slight yellow streak*, a little elevated and a little roughened on the posterior surface. Aortic valves leak water slowly; thin and translucent in general, with but slight thickening near the attached margin of the right posterior valve. *The ring and beginning of aorta show small streaked yellow elevations, varying from pin-point to 3 mm. in diameter.*

Left lung, 235 grammes. Dark steel-gray, soft and uniform; interlobular fissure absent in its middle third, without any evidence of adhesions. On section, tissue is grayish-pink, dry and leathery. Small amount of dark blood is squeezed from the vessels. Bronchi very slightly injected.

Right lung, 290 grammes. Externally the same as left, except for a *patch of thickened pleura* about 3 by 1 cm. at apex, and a few emphysematous-looking lobules near this patch. Middle lobe faintly indicated by a depressed line near the anterior margin, and by a notch, 2 cm. in depth, at the fissure. Section similar to left, except for the upper lobe, which is of a pale gray.

Spleen, 155 grammes. Purple; little pulp can be scraped off; trabeculae fairly distinct, substance rather friable.

Kidneys, left, 155 grammes. Surrounded by a thick layer of fat; substance *deep purple*. The line of lobulation shows very plainly, and the capsule splits considerably and is very thin, it tears the substance slightly. Section very dark purple. Glomeruli give a granular appearance.

Right kidney, 160 grammes. Similar to left.

Liver, 1,645 grammes. Normal in external appearance. Section rather light reddish-brown. Lobules very indefinite.

Skull-cap. Fairly regular, rather long; sutures well preserved; sulci moderately deep, in part ragged; very little diploë; marked patch of depressions about 15 mm. outside of median line, corresponding to Pacchionian granulations, visible on the outside of the dura. Longitudinal sinus practically empty, with broad fields of Pacchionian granulations. *Dura moderately adherent* to skull in frontal region. *The falx has a great number of perforations*. The inside of the dura is free; Pacchionian patches correspond to the entrance of the largest veins into the sinus. *The pia of convexity is slightly hazy, very oedematous*. The blood-vessels of the base are thin and tender, except the entrance portion of each middle cerebral. *The cisterna is thin, with a few flaky thickenings*. The lobes are very easily separated. *Weight of the brain in toto*, 1,375 grammes. The fourth ventricle is not granular.

Anatomical Summary.

Dilatation of the right ventricle, the tricuspid, and pulmonary rings. Congestion of kidneys, spleen, and probably liver. Ecchymoses on surface of left ventricle. Œdema and slight haziness of pia of convexity; cisterna shows few flaky thickenings. Moderately adherent dura. Perforations of the falx cerebri. Arterio-sclerosis of coronaries, aortic ring and beginning aorta; slight of one mitral flap; very slight of aortic valves. Milk-spot on right ventricle. Narrow bands of adhesion and thickened pleura at right apex. Calcareous nodules in mesentery.

The *paracentral lobules* show very strikingly the pure axonal reaction of practically all Betz-cells and some of the larger pyramids without disturbance in the general appearance of the cortical tissue. Many of the large cells resemble considerably the vortex type of fig. 2. In the frontal cortex many cells show a similar alteration—rarefaction of the stainable portions of the cell-body and dendrites, and occasionally a cell with fairly typical axonal alteration (fig. 2a).

The medulla has extensive axonal alteration in almost all the cell types, except the hypoglossal cells, which differ but little from the average appearance in beginning senescence. Many of the cells of the nuclei of the posterior columns, especially those of the external nucleus of Burdach and also those of the lateral nucleus, are markedly affected. In the cerebellum the roof nucleus and the dentate nucleus have the axonal alteration in practically every cell, whereas the Purkinje cells are not affected.

The Gasserian ganglia are free; the sympathetic cells show varying types. The *examination with osmic acid* was limited to the basal ganglia of the left hemisphere, the mid-brain, and the hemispheres of the cerebellum. The number of blackened and decaying fibres is small. They are limited to:

- (1) The thalamo-cortical tract of the motor and visual areas.
- (2) There are few fibres in the red nucleus.
- (3) The pyramidal tracts are very little affected, and the same holds for the fillet.
- (4) The restiform body is considerably involved.
- (5) The corpus callosum has but few degenerating fibres, and these are limited mainly to the splenium and to the motor region.

To these cases *Dr. August Hoch* kindly allows me to add another one accidentally discovered by him. Dr. Hoch's case was admitted to Dr. Charles F. Folsom's service at the Boston City Hospital, November 16, 1898. The patient was a carpenter, according to his own statement 58 years old, born in

Maine, with negative family history. The history is difficult to obtain on account of disinclination of the relatives. Alcoholism is denied.

For about two years the patient has had considerable headache and has been slow in thinking. For a year he has been unable to keep his books, but continued to work until three months before admission. Since then he has had vertigo, swollen ankles, delirium at times (?), was more irritable in his home life, had some abdominal pains, and for two or three months looseness of the bowels, which "pulled him down." He finally began to fall on the street, and one day children had to bring him home. He looked 65 or 70 rather than 58, and was really ill two weeks before he went to the hospital. He would sit on a chair with a cap drawn down over his face, and would not say anything to anyone. He finally became restless, and could not be controlled any longer by his wife. He would pick his clothes, jump over the foot of the bed, and follow his wife. He would "holler murder." His diarrhœa became worse. His wife would no sooner get him cleaned up than he would be all "mussed up again." He could not control it, although he tried to go to the closet. It took him a long time to get down stairs on account of a tendency to fall backward, as he did on the street. He never lost consciousness, and always got up by himself. He did not want to be taken away where his wife could not go with him.

On admission it was noted that the pupils were normal; arcus senilis and irregularity of arterial walls were present, but a regular equal slow pulse. No other abnormalities. November 20.—"Since entrance the patient has had hallucinations; the temperature has been subnormal; the bowels much better. November 24.—The patient is delirious and making strange movements of the hands all the time; does not recognise his wife, and will not answer questions intelligently. November 28.—Marked rigidity of muscles for the past few days; no paralysis evident; he makes peculiar purposeless movements, flourishing the arms about and often rolling fingers and thumb together; continued stupor and delirium.

December 3.—The patient appears weaker each day. The mental condition continues the same; peculiar movements also continue. Flexion of head on chest is resisted; rotation is normal; pressure on the back of the neck and tapping on the head causes apparent pain, even hyperæsthesia. The abdominal walls and the muscles of both extremities are in intermittent tonic spasm and fibrillary twitching. No elbow reflex; knee-

jerks sluggish; no patellar clonus. Slight pressure of skin causes pain. Flexure of legs on thigh causes intense pain. The plantar reflexes are increased; the abdominal, cremasteric, and dartos absent. December 6.—The patient has continued about the same, gradually weakening. Tracheal râles developed this morning, and the patient died at 2.30 p.m. The temperature had ranged between 96° and 97°, and only once, December 3, reached 97°. The clinical diagnosis was "Tuberculosis, diarrhœa." The autopsy, made two hours after death, established the existence of lobar pneumonia, adhesive pleurisy, dilatation of the lymphatics of the pleura; the dura was firmly adherent along the longitudinal sinus; the pia normal; the basal vessels absolutely free of arterio-sclerosis. The brain weighed 1,470 grammes, and was firm and macroscopically normal. The appearance of the body was that of a man of 75.

The paracental lobule and first frontal convolution were examined by Dr. Hoch and Dr. Dunlap with methylin blue, Weigert's mitosis stain, Berkeley's Golgi reaction, Cox-Golgi, and Marchi. The result was the finding of the axonal reaction in the Betz-cells, the presence of a small number of degenerating subcortical fibres, and practical integrity of the tissue as a tissue, so that general paralysis was absolutely excluded.

Similar lesions have been reported, since the note on my first two cases, by Drs. Worcester, Maurice Faure and John Turner. To these are added my eight later cases, and the one of Dr. Hoch. A careful search in the literature of melancholia and other mental disorders brought further to my notice an article by Joseph Wigglesworth, "On the Pathology of Certain Cases of Melancholia Attonita or Acute Dementia, with a report of two cases" (1883). In order to convey a better idea of the material on which my conclusions are to be built, the cases are here reproduced in abstract:—

Dr. W. L. Worcester's case of Landry's paralysis (*Journal of Nervous and Mental Disease*, 1897):—

A widow of 40, during the middle of December, 1895, three years after the menopause, began to be troubled by the delusion that she was pregnant and poisoned from a dead fœtus; she consulted a number of physicians, and finally remained in bed. Later, she read of Gov. G. having died of Bright's disease, and concluded she had it too; indeed, about the middle of March her

urine was found to contain albumen and casts, not previously found. She also had numbness in the hands from that date, and on April 9 she became awkward in their use; two days later she appeared paralysed in all the extremities. April 14, there was slight paralysis of the left facial nerve (including the ocular branch); in the extremities the parts near the trunk were more paralysed than the fingers and toes. The knee-jerks and cutaneous reflexes were absent. Diminution of faradic irritability and abolition of the same in the thighs, upper arms, and pectoral muscles, were found. There was great loss of sensibility of the extremities; the head and neck were free; the patient was rather apathetic. The *post-mortem* findings were: axonal reaction of the large cells of the motor cortex; beginning axonal alteration of the motor cells of the cord; practically no degeneration of fibres, neither in the cord nor in the peripheral nerves.

Faure's cases (*Revue Neurologique*, December, 1899) probably do not fit altogether into our picture; they are mainly cases of alcoholic-cachectic polyneuritis or delirium, from a general hospital:—

(1) A woman of 42, with cachexia, cancer of the uterus, hydro-nephrosis, frequent convulsions, profound mental confusion and typical axonal alteration of a great proportion of the large pyramids, slight sclerosis of the vessels and a slight degree of embryonic infiltration.

(2) A woman of 38, with tuberculosis of lungs and liver; very fatty liver, and queer incoherent and childish behaviour before death. The arrangement of the elements in the cortex is normal; but a small number of the large pyramids show axonal degeneration. No other lesions elsewhere.

(3) A woman of 30, with alcoholic-tubercular polyneuritis with mental confusion (the extent of the lesion is not stated).

(4) A woman of 32, also alcoholic and tubercular, with slight polyneuritis and mental confusion (the extent of the lesion not stated).

(5) A tubercular-alcoholic man of 35, with occupation delirium and a final temperature of 41°. A few cells show axonal reaction.

(6) A woman of 50, with acute lobar pneumonia and systematised deliria. Pigmentation of the cells; in a few the axonal reaction.

Turner's cases (BRAIN, 1899) are all the more important, since they come from a clinical material similar to mine and because

they are accompanied by an excellent description of the clinical manifestations. The anatomical condition was studied by him in the cortex only; hence, probably, his conclusion, expressed by the title of the paper. The cases are:—

(1) A woman of 45, with a history of alcoholism, fits, and melancholia in the family, alcoholic herself, depressed, with violent outbreaks for eighteen minutes; delirious and extremely emaciated. Finally, parotitis and broncho-pneumonia, with jactation of limbs, exaggeration of knee-jerks, absence of plantars, coma.

(2) A widow of 52, following an influenza (in July), became irrational, with alternate periods of depression ("a lost woman") and hilarious excitement; after four months she was excited one day and quiet the next. She had no tremor, but exaggerated knee-jerks. About the eighth month of her illness she began to fall frequently; a week later she was unable to stand, became lost and silly; one day, five weeks later, when excited, she was "rushing about the ward and falling about," and after two months of this motor disorder she died with diarrhœa. The brain weighed 1,198 grammes, and was otherwise normal.

(3) A woman of 42 was admitted in 1895, with a history of eighteen years of delusional insanity (some women were plotting against her and her husband). April, 1898, she developed agitated melancholia, began to fail. In May, her knee-jerks were exaggerated; she was much agitated. In July she had occasional diarrhœa. In September she became demented, dirty, very greedy. In November she lost the use of her legs, fell often, and was restless and bedridden. In December she exhibited involuntary jerking movements of the arms and legs, and risus sardonicus, and succumbed to exhaustion. Atrophy of the internal organs.

(4) A sober woman of 37, always hysterical, was nervous and apprehensive for a year, would not leave the house, lost the use of hands and legs, shook and fell often, and was finally committed with screaming attacks, greasy skin, absence of knee-jerks and plantar reflexes, but equal pupils, and no reaction to pricking. Mostly incoherent ejaculations. Death in four days. Slight atrophy of frontal convolution; brain weight 1,137 grammes. The radial and post-tibial nerves in degeneration.

(5) A woman, born in 1830, who had a three months' attack of melancholia in 1889 and was readmitted in 1890 with deep depression and agitation, but free of motor disorders. January 24, 1899, she took to bed with diphtheria and died February 6,

1899. There was found arterio-sclerosis of the basal arteries, cedema of the pia, atrophy especially of the parietal convolutions and a brain weight of 1,283 grammes. Turner raises the question whether the axonal alteration might not be due to the asthenic type of the diphtheria.

(6) A man of 36 whose father had been insane, was taken with incoherence, violence and raving shortly before admission; was restless, resistive, incoherent, not heeding questions, filthy, and normal physically but for involuntary jerking of the limbs and finally inability to stand. Collapse five days after admission. The meninges were very opaque over the vertex, thick, not adherent; atrophy of the convolutions. Brain weight 1,412 grammes.

(7) A man of 52 whose father had been melancholic and committed suicide, was admitted in 1892 with agitated melancholia which passed into dementia; 1894, weakness of the lower limbs came on; in 1897 he became bedridden, and died in 1898 of phthisis. There was atrophy of the frontal convolutions and dilatation of the lateral ventricles. The brain weighed 1,296 grammes.

Nine further cases published by the same writer are to be found in the *Journal of Mental Science*, vol. xlv., pp. 719—720. The notes are very brief. It appears that at least case nine of Turner's series fulfils the desirable conditions for a diagnosis of general paralysis. Two cases were imbeciles, at least case 14 one of chronic alcoholism with delirium, and cases 8, 10, 12 and 13 probably some form of melancholia.

Wiglesworth's report contains two cases, one of "melancholia attonita," and one of "acute dementia."

(1) A woman of 48, addicted to gin, developed delusions of persecution eight months before admission, and two months later delusions of poisoning, but appeared normal to friends; one week before admission she took to bed, became weak, mute, shaky when walking; in the second week she was a little brighter but still confused, the third week she did some needlework once or twice, wandered restlessly, asked for the bill. She was feeble, had tremor of the hands, and could not protrude the tongue well. The fourth week she was restless and excited one evening. She was sad at heart, nobody cared for her, she had a child at the top of her head. She rolled on the floor and had much tremor. The sixth week she was alternately dull and talked nervously. The seventh an attack of diarrhoea came on and twitchings of tendons

and sub-febrile temperature; the eighth week the diarrhoea was arrested. The patient had a fixed expression; the arms were kept rigid, and there was occasionally a slight jerking of the tendons. Temperature normal. Death. Typical alteration of many pyramidal cells. Tuberculosis of the left suprarenal capsule.

(2) A woman of 30, married ten years, sterile and of poor health. One week after an attempt of her husband to commit suicide she became much excited, was in a panic, clutching hold of everybody, muttering words like "judgment," &c. She showed occasional tremor and in a week more or less rythmical jerks of the right arm, self-absorption, resistance, and the picture of acute dementia. Death on the nineteenth day from mere exhaustion. Wigglesworth remarks that the cell changes (inflations of nerve cells with dislocation of the nucleus) are probably analogous to those described by Charcot as occurring in the large cell of the anterior cornua of the spinal cord in so-called "infantile paralysis."

To this we add that Spiller and Hirsch have found similar changes, Spiller in the cortex of an imbecile who died with meningeal hæmorrhage (the description only shows the axonal alteration of the Betz cells; there are no Marchi specimens of the cortex, and the material was preserved several days after death), and Hirsch throughout the nervous system of an imbecile, also without Marchi impregnation.

ANALYSIS OF THE AVAILABLE CLINICAL AND ANATOMICAL DATA.

On looking over this material, its heterogeneous clinical character can hardly escape attention. Taking for granted that we have good reasons, owing to the uniform findings at the autopsy, to subject all these cases to an analysis with some expectation of finding common clinical features, we meet with some disappointment at first sight. The point in which we should naturally expect most uniformity would be the physical condition, since the lesion involves mainly cells which have generally acknowledged functional attributes in the motor mechanism. In this direction as well as with regard to the mental condition and the etiological

constellation there is, however, a considerable divergence of the data.

The cases of Turner, Worcester and Wigglesworth and my own were all patients committed to hospitals for insane. Those of Ballet and Hoch died in general hospitals. Those of Ballet were cases of cachectic or alcoholic-tubercular delirium, some of them with more or less evidence of polyneuritic disorders. The case of Folsom and Hoch was one of a protracted apathetic depressive state—a more accurate picture of the general condition cannot be obtained beyond what is contained in the summary. Worcester's patient with "Landry's paralysis" began with a hypochondriacal paranoic condition, and three months later she developed the symptoms of polyneuritis, which terminated fatally in four weeks. Turner's, case 4 was one of polyneuritis accompanied by a nervous apprehensive state of one year's duration.

Turner's case 6 was one of "acute delirium" of very rapid course, and not unlike certain cases of peracute general paralysis.

My case 4 was one of alcoholico-senile deterioration of a very uneven course, also my case 8.

The great number of the cases 1, 2, 3, 5, 6 and 7 of mine, and 1, 3, 5, 7, and perhaps also 2 of Turner's, were at the outset depressive psychoses of the period of involution. In Turner's cases 3, 5 and 7, and in my cases 1 and 3, the diagnosis of agitated melancholia was made; Turner's case 1 and probably also 2 are atypical depressions, my case 2 a depressive delirium, case 5 an unusual depressive hallucinatory paranoic condition with a final deterioration resembling general paralysis, and case 6 a case of recurrent hypochondriacal depression with many features of agitation in the second attack.

After having seen the first two cases (1897) I was inclined to think that the condition present was one liable to occur on the ground of senile or pre-senile melancholia (see my foot note in the first communication), and in my differential diagnosis I depended greatly on the existence of this condition, especially when it presented somatic

deliria and rapid physical deterioration under neurological and general symptoms not unlike those seen in certain cases of general paralysis with a rapid decay, but without the typical speech defect and less definite neurological alterations. On this ground the diagnosis was made before death in the cases 4 and 5, while in case 6 even the possibility of a lesion was but vaguely entertained, since it was a second attack of a psychosis rather unlike the others. In several cases in which the general picture of the psychosis and the general condition was very suggestive shortly before death, although the motor disorders were quite vague, a diagnosis of probability was ventured upon, but with negative result, so that to-day I should put the chief emphasis on the physical findings and consider the psychosis merely as the expression of a favourable ground. It would lead too far to present here the material of negative cases, although it would prove decidedly instructive. I also omit the cases in which the histological alteration was present only in isolated cells, since these cases require more careful investigation than we have been able to give so far.

Our present knowledge can be summed up as follows. Under conditions which are not as yet clearly understood, usually in the course of certain forms of melancholia or in asthenic conditions, such as alcoholic-senile or alcoholic-phthisical deliria (and perhaps also in the course of true general paralysis?), a peculiar symptom-complex has been found to occur. With a delirious or stuporous mental condition a progressive weakness develops, usually shown first by occasional falls and a stumbling gait. This, of course, fails to be noticed in patients who are already bedridden owing to general reduction of strength or owing to stupor, or asthenic deliria, and it is in no way characteristic since it is also found in certain alcoholic deliria and in states of ordinary weakness. In most cases it is probably not correct to say that there is a paresis in the sense of well localised paralysis. The patients often present a very striking power of resistance, especially in the arms, when they do not display much strength otherwise, on account of the absence of attempts at well-

directed spontaneous motility. This condition of weakness, as Turner has pointed out admirably, is frequently, but not always, accompanied by a peculiar motor restlessness, which may vary from a blind general excitement (see Turner's case 6) to a more occasional twitching of the arms, or a subsultus tendinum. It really resembles the physical symptoms of a protracted delirium tremens, rather than the convulsive episodes of general paralysis. These symptoms are frequently very vague and, I suspect, not infrequently overlooked by attendants and physicians or merely described as weakness, or "nervous" or "hysterical" manifestations, such as tremor, peculiar motions, &c. In my sixth case, the attendant reported that the patient had occasional peculiar spasmodic twitchings in his arms, but only when he thought himself watched. The rigidity, too, which occurred at times is hardly characteristic enough. It is very difficult to distinguish it from negativistic resistance of ordinary deliria, and the pain evidenced in Hoch's case on attempts to overcome it is by no means sufficiently characteristic for any special rigidity. The description of the final episode in our case 6, and that of the more lasting condition in our case 7 and in another form in Dr. Hoch's case; and, on the other hand, the total absence of these symptoms of irritation in our case 8, show some of the extremes observed. In a few cases only (Turner, Ballet, and Worcester) polyneuritic symptoms were present. In case 7 there was difficulty in swallowing, and a partial ptosis during the last two days. There were, however, in all cases certain derangements of the *reflex-mechanisms*, either in exaggeration of the tendon-reflexes (most commonly) or absence of the knee-jerk (as in my case 5, without plain polyneuritic symptoms, and Turner's case 4 with polyneuritis). The cutaneous reflexes vary. The plantar reflex is by no means always absent. It is of interest to note that an unequivocal Babinski reflex has not been observed so far. Tests of sensibility are very fallacious, owing to the mental condition. Turner mentions the occurrence of diarrhoea during the later period of the disorder, also observed in several of our patients; our case 7 also showed irregular fluctuations of the tem-

perature without leucocytosis and without Widal-reaction; the others were not continually enough observed, so that we have only a final fever curve associated with the very common terminal broncho-pneumonia.

The vagueness of the symptoms makes it difficult to say anything concerning the *duration*. It seems to be an acute or sub-acute disorder of from two to four or more weeks, usually implanted on a more chronic deterioration. Cases like my third and fifth would almost suggest the possibility of partial remissions.

The anatomical findings. *Macroscopically* nothing characteristic could be noted in the nervous system. The findings are the same as those met with in cases of the same age and general condition, without the characteristic microscopic alterations. The brain weights, too, vary greatly. The membranes show various degrees of a very moderate thickening of the pia, but no adhesions, and the vessels at times varying degrees of beginning arterio-sclerosis. The first case had a scar of softening in the right caudate nucleus; no other macroscopic lesion of the brain substance was noted. In the same case there was also marked thickening of the skull with hyperostosis of the inside of the frontal bone.

Microscopical findings. The nervous system as a tissue is not markedly altered. Even the thickening of the vessels described by Turner was not present in all cases, and only few small hæmorrhages were found (as in case 1, in the cornu ammonis).

A small-celled infiltration of the blood-vessel sheaths, such as is so extensively present in those cases of general paralysis which show an anatomical lesion, was not seen in any of the cases. The neuroglia was not more abundant than in other brains of the same ages, and certainly not as it is found in general paralysis. We deal with a disorder which does not involve the tissue as a whole, but is mainly a *parenchymatous alteration of certain nerve elements* with remarkably little general reaction of the tissue. The alteration became first obvious on account of the appearance of the cell bodies, and the examination with the

Marchi-reaction showed that many fibres were in a condition of decay of the myelin sheath.

The first description quoted in the introduction mentions my first suspicion that the whole picture of the change in the cell bodies pointed to a lesion of the projection fibres, since it was typical for the "axonal alteration." It became next evident that a lesion of the brain stem was found only in the right caudate nucleus of the first case, that it was accidental and did not account for the bilateral disorder in the Betz-cells. The later cases showed no such coarse lesions, and it became further evident that the typical axonal alteration was found also in cells outside of the cortex. Similar cell changes of the character of axonal reaction had, in the meantime, been published repeatedly concerning the segmental motor neurones in nerve lesions and cases of polyneuritis and in Clarke's columns of cases of tabes and meningitis, and I had drawn attention to the same change in these and several other cell types under less characteristic conditions in my "Critical Review," &c. The examination with the Marchi method yielded positive results in the hands of Turner and Hoch. But when it was applied to our case 6, it showed a marked discrepancy between the number of fibres which have the reaction of degeneration in the pyramidal tracts, and the number of cells with axonal alteration, and this led to a more extensive examination of my cases 7 and 8.

The result shows conclusively that it would be wrong to see in it only a disorder of the cerebral cortex alone. It is a diffuse affection, mainly of elements within the neural tube, but undoubtedly also present in some of the neurones constituting the "peripheral nerves." In several cases (Turner, Worcester, Ballet) the polyneuritic features were indeed quite prominent.

The general histological character of the lesion is the same as what is described in parenchymatous peripheral neuritis or degeneration. From the standpoint of general pathology, we see in this a degenerative process, analogous, but of course not necessarily homologous, with degenerative processess of other cell types, but considerably modified, owing to the

peculiar structure of the tissue elements of the nervous system, and especially of the elements most directly under consideration, the nerve-elements or neurones, with their highly differentiated cell bodies and processes and medullary sheaths, &c.

There is, unfortunately, no general term available for this condition. The most common distinctions are those according to localisation. From the "preneuronic" period, we have a very crude way of dividing the nervous system into brain, spinal cord and peripheral nerves. In the peripheral nervous system, we speak of peripheral neuritis, a vague term which includes the reaction to traumatic and infectious and toxic results. Like the type under discussion above, the *parenchymatous peripheral neuritis* does not involve so much the coarse anatomical structure "nerve," as the individual nerve fibres; and when we speak of parenchymatous neuritis of certain sets of nerves, we imply by it a degenerative affection of more or less of the nerve fibres which help constitute the "nerve."

In the central nervous system this condition has attracted attention, mainly in connection with a few chronic diseases of the spinal cord. There it is spoken of as systemic and non-systemic degenerations, involving a more or less great number, either of fibres of a recognised set, or of several sets, or diffusely scattered without any regard for a limitation to such sets. The systemic and polysystemic degenerations in the cord have received their special terminology, usually derived from the clinical picture, and as long as only few "systems" were usually considered, the tracts with degenerations were easily enumerated. For the diffuse degenerations found, for instance, in pernicious anæmia, a more definite description was not attempted, beyond a general localisation of areas in the cord section.

The difficulty makes itself much more felt in those who work on the brain, in which system diseases have been relatively little described outside of the typical secondary degenerations; and those who work with some forms of the neuron concept have additional reason to be dissatisfied with the existing terminology because we cannot stop

at the study of bundles of fibres; we must take into consideration that the fibres are parts of cells, and that the correlation of cells and fibres is a prominent postulate of neurological accuracy. The conditions which occurred in our cases illustrate this well. At first we discovered a change in the cell bodies, and now we know, moreover, that there are special sets of corresponding fibres in degeneration. In polyneuritis the degeneration of the myelin sheaths was the first finding; and the cell changes became known later. As we shall presently see the change in the cell is quite characteristic; but its nature, and the nature of its correlation with the alterations of the fibre is hardly explained, not even with the most high-sounding theory.

In a discussion on Landry's paralysis, the writer has already pointed out in 1896, how vague the terms "polyneuritis, myelitis, and encephalitis" are when we deal not with the local disease of the entire tissue of a locality and its remote consequences, but with more general toxic, infectious or asthenic parenchymatous degenerations in the nervous system. The present experience shows that the traditional nomenclature based on coarse anatomical localisation is inadequate for description and didactic purposes. Many cases of peripheral neuritis of a not local origin are probably peripheral only because the other parts of the nervous system are not examined with equally adequate methods as the peripheral nerves. To judge from a rather large material treated with the Marchi method, the extent of decay of medullary sheaths throughout the nervous system is far greater than the old hæmatoxylin methods made one suspect. Unfortunately it is difficult to find a term which would apply indifferently to all degenerated conditions with decay of myelin sheaths of any nerve unit. I propose to adhere to the shortest word, "neuritis." It should not meet many objections, because the concept "inflammation" is more and more dissolved, and one would hardly see anything "inflammatory" behind the syllable "itis." But the terms might seem to refer especially to nerves, and their next analogues, nerve fibres. The very

persistence with which the attribute "peripheral" reappears with the word neuritis shows, however, that the use of the term is not as fixed that we should not be allowed to speak of "central neuritis," or in more general conditions of "general neuritis," instead of a long descriptive expression, "diffuse degenerative affection of nerve elements with myelin decay and axonal reaction." It seems probable that the rising generation, with the increased knowledge of the life of nerve elements or neurones acquired since Forel's inspiring paper of 1887, will think more in terms of nerve elements than the generation from which we received our training, and also some of our prejudices. They will get accustomed to think more of the histologically important correlations of parts than of coarse anatomy whenever they are not especially anxious to refer to topographical conditions, such as encephalitis, myelitis, and neuritis of local origin.

There is another feature which we usually think of in connection with the terms neuritis or polyneuritis. We can safely say that no diffuse parenchymatous neuritis is truly general. There are—clinical experience shows this—fairly definite types of distribution more or less characteristic for the origin, so that even in the great diffusions there is usually a certain system. On the other hand, the more accurate methods have shown that system diseases are rarely strictly monosystemic. Tabes does not limit itself absolutely to the intraspinal course of the afferent segmental neurones; amyotrophic lateral sclerosis is not merely a degeneration of the pyramidal fibres, &c. The cases under consideration are classed under the name of *central neuritis* with the understanding that we deal with a parenchymatous degeneration of nerve elements, *mainly* of the *central* nervous system, and that this type is one belonging to the general group of "diffuse neuritis" with a certain degree of systematisation.

Concerning the extent of the central neuritis, I refer to the cases 7 and 8, which show that there are various degrees of the disorder and perhaps also various distributions.

We cannot omit the discussion of a rather difficult point

in the problem, namely, the peculiar distribution of the changes within the same nerve elements. This, unfortunately, is a question in which we ought to have at our command a larger material and working force than our State hospital furnishes to-day. Many of the conflicting statements one meets in a digest of the pertinent literature come from the looseness partly of the nomenclature of the writers, partly of the descriptive evidence furnished, so that perhaps the problem is not quite as hopeless as it appears. In my "Critical Review" I pointed out how small our chances are under the best opportunities to really get a sufficiently definite idea of the condition of any entire nerve element, and this makes it especially desirable that results should not pass into the literature without a careful analysis of the validity of the facts as well as the descriptive terms and the definitions adhered to.

As an instance, I quote the very article in which Faure communicates his six cases of cell changes in the cortex in toxic infectious mental disorders quoted above (p. 95). He discusses the question whether the cell alteration is always secondary. Several of his cases had plain polyneuritis, but he used only alcohol methods in the cortex and not Marchi's method, and he remains wisely reserved. He merely adduces one argument against the necessarily secondary character of the cell alterations, which might well be criticised in a few words. Together with Ballet, he sectioned the projection fibres underneath the motor cortex in seven dogs and killed them eight, eleven, eighteen and twenty-one days after the operation. "Comparison of the sections of cortex from the operated and normal side demonstrated plainly the disappearance of the large pyramidal cells." In three cases they also examined with Marchi's method without finding any alteration in the fibres—hence there is a discrepancy with "the complete disappearance of the large pyramids"—or have the fibres too completely disappeared in three weeks? Only one case of the seven (and that one was complicated by infection) did present the axonal alteration (instead of the "disappearance"?). These contradictions invalidate the weight of the communication

very seriously and relieve our feeling of standing before another great puzzle. His statements are so flatly at variance with what Bregmann and others have shown and also our own experience concerning the cortex in subcortical lesions, that we are forced to suspect a serious error of observation, and that we regret to see the article quoted without criticism of this glaring contradiction.

A further complication lies in the indiscriminate use of the term "chromatolysis." The expression came into vogue when the stainable portion of the cell body and of the dendrites were newcomers in neurological descriptions, and, perhaps, absorbed undue attention. Since then it has again become evident that in the physiological and pathological life of nerve-cells it is wrong to classify all the changes according to the condition of only one part of the cell. While we cannot claim to be anywhere near a final recognition of the possible changes and their classifications, we are able to-day to speak at least of a few *types* with a possibility of being understood by those who take the trouble to acquaint themselves with well-described distinctions. The most striking types are those of pyrexia (commonly called acute alteration), the axonal reaction present in our cases, Hoch's shrinkage-alteration, the mere rarification of the stainable substance, &c. To classify these as varieties of chromatolysis promotes the existing confusion. The term "central chromatolysis" is utterly misleading, since there are at least two such types, the pigmentary and the axonal reaction, and because it suggests a change *around* the nucleus. By *axonal reaction*, we understand that cell alteration which we can produce experimentally by the section of the axone. It is as it were a focal disorder within the pericaryon; splitting up and dissolution of the stainable bodies usually between the place of origin of the axone and the nucleus (not *around* the nucleus), swelling of this region with involvement of the greater part of the cell-interior and dislocation of the nucleus towards the surface and even beyond the normal contour; persistence of a peripheral ring of lumps, and of the spindles in the dendrites. Decay, or at least fatty alteration of the medullary sheath of the axone is

a frequent accompaniment. When this alteration is combined with acute alteration (see p. 108) the stainable bodies of the periphery and dendrites are also dissolved, and the dendrites showed the characteristics of the acute alteration. When we speak of "axonal alteration," we imply that this is the *type* identical with that always observed where section of the axone occurred near enough the cell body to produce any reaction at all; and this *type* we have now found to exist where the nerve fibre was merely diseased as it was already found in polyneuritis, and also under conditions in which disease of all the nerve fibres in question has not been demonstrated, but where at least some fibres show the presence of the general conditions for degeneration of fibres (my case 8 and the instances mentioned in p. 94). It would seem from our cases that the cell body may show the alteration before the fibre is visibly affected, unless we should assume the other possible alternative that many of the *débris* of fibres were already resorbed; and Warrington, Goldschieder and Marinesco claim that the same change may occur if a set of superimposed neurones is affected which is normally the source of stimulation of these cells. It is obvious that the question is still complicated; but this should be a special reason to make the distinction of the type which is already recognised, instead of throwing it together into the hazy "chromatolysis." The axonal reaction to us is an, as yet, unexplained complex of manifestations, which as far as we know now, seems closely related to the constellations under which we recognise also myelin decay. Not all the cell types react equally, and the assumption of a "central neuritis" is probably justified only where entire sets of cells show the reaction without there being any disease of the *tissue* which would account for the occurrence of degeneration after the type of secondary and retrograde degeneration. The frequent occurrence in Clarke's columns and in other cell types requires further studies, and we must admit that we are still far from knowing all the possible histological steps in the process.

The *nosological position* of this condition is as little within the reach of definite decision as the mental disorders

which formed the beginning, or as little as other not directly toxic forms of polyneuritis; and this is not the place to rehearse the reasons why we prefer a statement of ignorance to a discourse on auto-intoxications at this stage of "mental pathology." We propose to wait or work for more tangible data, and commit ourselves to the following remarks.

In order to obtain the necessary amount of data concerning frequency of the central parenchymatous nerve decay, we need a larger number of thorough examinations also of the *supraspinal* nervous system in many types and conditions of nervous diseases. I refer here to such possibilities as studies of cortex in polyneuritis or more or less diffuse spinal affections, such as were described by Russell, Batten, and Collier, under the name of subacute combined degeneration of the spinal cord, and to such lines of work as the studies of Zappert on the root and cell changes in the central nervous system of the child, the studies of Kirchgässer on the nervous system in cancer, cachexia, &c., and the publications of Luce. My own experience in the study of the nervous tissues, with modern methods for the observation of the cells as well as the fibres, cautions me against hasty statements. I merely venture to make the remark that our ideas of the normal nervous system, on the one hand, and of what might be called fatal true degenerations on the other, represent extremes, and that our present delicate methods show us stages to which the standards of text-book correlations obtained from less discriminating methods—viz., the law that degeneration implies abolition of function and, probably, irreparability, if found in the central nervous system—should not be applied without much care. There are most probably various degenerative conditions in the central nervous system, not all of clearly-known clinical significance, and some of them may be functionally trivial, and it is quite probable that the Marchi method does not merely show old facts in a more precise garb, but certainly also conditions of less striking importance than the serious degenerations of the more primitive neuro-pathology, which saw degeneration only when it was

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Fig. 1a.

Fig. 1.

Miss F. Byrnes del.

macroscopically visible. It is especially deplorable that studies of the axones are so difficult in the central nervous system, since the recognition of a disorder of the axone should be furnished in addition to the one of its myelin sheath, before the relation between function and lesion should be discussed. My studies in this direction are hardly mature for publication.

Findings similar to ours have lately been established by Bonhoeffer and by Starlinger. Starlinger describes, in his "Beitrag zur pathologischen Anatomie der progressiven Paralyse" (Monatsschrift of Wernicke and Ziehen, vol. vii., p. 1-13), the presence of fairly-localised degenerations which do not differ much in their general distribution from what we found in our case 7, were it not for their more unilateral occurrence and the difference in the clinical history of the cases and in the condition of the cortex, which Dr. Starlinger kindly demonstrated to me. The latter shows the correctness of his diagnosis with just as much certainty as we should exclude the typical lesion of general paralysis in our own cases. The distinction is probably in the main as follows:—The predominant character of general paralysis is that of a tissue alteration, whereas our findings are strikingly devoid of this feature. According to Starlinger, the distribution of the degenerations in general paralysis is dependent on the extent and localisation of tissue alterations, and it is, therefore, less systemic and less symmetrical. Besides this process, there *may* exist in general paralysis one allied to the type of central neuritis, as case 9 of John Turner's series might suggest. Personally, I have not met a case of true "central neuritis" in clinically and anatomically plainly established general paralysis.

The findings of Bonhoeffer refer to alcoholic delirium (Wernicke's Psychiatrie) and to "Seitenstrangerscheinungen bei acuten Psychosen" (Psychiatrische Abhandlungen, Heft 2, Breslau, 1896). The latter, although observed clinically only, suggest strongly a more frequent occurrence of central alterations than has been commonly surmised, and form a reason why we prefer to be rather conservative as to conclusions. The alcoholic degenerations found by Bon-

hoeffer are most likely akin to those in our own cases, and we can confirm the observation from a case of plain alcoholic delirium in which, however, the lesion was in no way as extensive as in those of "central neuritis" of non-alcoholic origin described above and in which the cell alteration was far from general.

Turner, in his first description, calls our cases a "form of dementia associated with a definite change in appearance of the pyramidal and giant cells of the brain." Since the above was written he has even ventured to base on these cases his theory "concerning the physical conditions of the nervous system which are necessary for the production of states of melancholia, mania, &c." While we have seen that most of our cases have arisen on a basis characterised by depressive states, we have met at least two cases of alcoholic-senile deterioration in which depression was absent or trifling; and in a sufficient number of cases we have failed to establish all the findings in undoubted instances of profound depression. Neither the expression "dementia" nor the inferences as to melancholia and mania appear to me warranted at this stage of our observation. Hypotheses have a value only if they stimulate to further research, but not if they give premature satisfaction. For this reason I prefer to call the general condition of our patients by the terms "delirium," "stupor," and "coma"—not by the term "dementia," simply because I consider it impossible to establish what deserves the name "dementia" in any of these states, as they prove fatal before an examination for dementia is quite conclusive. We might as well call a more or less profound delirious and stuporous condition of the fever-alterations and of certain intoxications a "dementia." Another question is the relation of these mental states to the preceding melancholia or alcoholic or senile delirium. Here, too, reserve is advisable. As long as we do not know the conditions from the point of view of entities fulfilling the requirement for an admission into true causal chains, we do best to treat them merely as empirical chains of facts.

That the modern views even on "general paralysis of the insane" to-day appear to be in a harbour of dogmatic

FIG. 2.

FIG. 2a.

FIG. 5.

FIG. 6.

security, is chiefly due to their plausibility and their value in practice and teaching; yet even they would hardly be able to stand a moderately severe criticism unless we modestly admit their empirical character. The discussion has merely been stopped owing to the difficulty of getting at more accurate facts. For this reason we avoid a long discussion of the question whether our group of cases should be called a type of general paralysis.

Summary.—(1) Eight times in 200 autopsies in which a microscopic inspection of the cortex took place a condition of bilateral changes of the nature of the axonal reaction in practically all the Betz-cells was observed, accompanied by the same changes in other cell types and, where this was looked for, by decay of the medullary sheaths of some of the corresponding sets of fibres, whereas the characteristic disease of the tissue of general paralysis (gliosis, vascular infiltration, &c.) was absent. An extensive examination of large areas of the brain in three cases shows the existence of a partially systemic but widely distributed and strikingly symmetrical parenchymatous alteration of numerous nerve elements, chiefly of the cortico-thalamic connections of the motor area, the auditory radiation, the forceps, the pyramids, the fillet, the restiform body and, to a lesser degree, the posterior columns of the cord, the intersegmental elements, and the segmental efferent motor elements. The change is that of axonal reaction in many of the large cell types and decay of the myelin sheaths. Instead of the long descriptive term, "Partially systemic parenchymatous degeneration principally of the central nervous system," we propose the expression, "central neuritis" in the sense of an equivalent of parenchymatous neuritis, but mainly of central distribution.

(2) This alteration has been found to occur in peculiar forms or end-stages of depressive disorders, near or after the climacteric period, alcoholico-senile and alcoholico-phthisical cachectic states, idiocy, and perhaps also general paralysis (Turner's case). Ordinary infectious and cachectic states do not, however, appear to form an important link in the causes.

(3) Clinically, the symptoms are rather vague: after a

course in which there is no suspicion of organic disorder, there appears, more or less suddenly, difficulty of locomotion, increasing weakness for coordinated movements, at times jactations of the limbs and rigidity and disorders of the reflexes, often together with diarrhoea and occasional febrile fluctuations; the mental condition in this terminal episode is either that of anxious perplexed agitation, delirium, or stupor, similar to a protracted delirium tremens. The nature of the disorder appears to be an equivalent of the general type of parenchymatous nerve-cell alterations, but, in distinction from the well-known infectious and toxic types of "polyneuritis," of pre-eminently central distribution.

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EXPLANATION OF THE FIGURES.

FIG. 1.—Betz-cell from *Case 1*. Axonal reaction. $\frac{1}{12}$ oil immersion, Leitz.

FIG. 1a.—Betz-cell from the same case. Vortex conditions of the chromophilic portions. $\frac{1}{12}$ oil immersion.

FIG. 2.—Betz-cell with vortex formation, *Case 8*.

FIG. 2a.—Large pyramid of the frontal cortex (*Case 8*), with axonal alterations. $\frac{1}{12}$ oil immersion.

FIGS. 3 and 4 (in text).—Right hemisphere of *Case 7*, with the levels of the slices for Marchi specimens: (a) through the foot of the frontal lobe;

brach. corp. quadr. sup.

FIG. 11.

FIG. 12.

Pyramid
FIG. 13.

FIG. 14.

FIG. 15.

FIG. 16.

FIG. 17.

FIG. 18.

(b) underneath the paracentral lobe; (c) through the temporal lobe; (d) frontal section through the motor area and in front of the anterior commissure.

FIG. 5.—Section from fig. 3a. Degenerating fibres limited to the motor area and its part of the centrum ovale, and of the corpus callosum.

FIG. 6.—Section from fig. 3b. Degenerating fibres limited to the projection system of the motor area. Only few fibres from the parietal lobe.

FIG. 7.—Section from fig. 3c. Degenerating fibres limited to T₁.

FIG. 8.—Section from fig. 3d. Degenerating fibres from the motor cortex to the dorsal part of the internal capsule and the corpus callosum.

FIG. 9.—Section from the anterior part of the thalamus (only the left side drawn; the whole being symmetrical). Degeneration of fibres of the internal capsule and its radiation into the lateral thalamic nucleus only.

FIG. 10.—Section from a posterior level. Division of the degenerating fibres into a radiation of the ventro-lateral nucleus of the thalamus and pyramidal fibres.

FIG. 11.—Mid-brain, with degeneration of pyramidal fibres only in the crus, few fibres in the fillet, and few fibres in the arm of the superior corpus quadrigeminum.

FIG. 12.—Section through the posterior corpus quadrigeminum. Degenerating fibres in the pyramid and fillet.

FIG. 13.—Section through the trigeminal segment. Degenerating fibres in the pyramid, the corpus restiforme, and few in the fillet.

FIG. 14.—Section through the pneumogastric segment. Degenerating fibres in the pyramid, the corpus restiforme, and few in the fillet.

FIG. 15.—Section from the left occipital lobe. Degeneration practically limited to the forceps and its radiation.

FIG. 16.—The same on the right side, with evidence of degeneration in the splenium of the corpus callosum.

FIG. 17.—Horizontal section through the left thalamus of *Case 8*. Degeneration limited to the internal capsule and the radiation of the anterior half of the lateral thalamic nucleus; scanty degeneration in the radiation of Gratiolet.

FIG. 18.—Section parallel with the last one. Very scanty degeneration, limited to the pyramidal tract.