NOTE ON A FORM OF DEMENTIA ASSOCIATED WITH A DEFINITE CHANGE IN THE APPEARANCE OF THE PYRAMIDAL AND GIANT-CELLS OF THE BRAIN.

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I wish to draw attention to certain cases of mental disease which present a definite pathological anatomy and of which I have not been able to find any previous description.

The lesion shows itself chiefly in the nerve-cells and appears to be of widespread distribution, attacking the great majority of the pyramidal nerve-cells in all parts of the cerebral cortex (frontal, ascending-frontal, occipital being the regions examined).

It is especially well marked in the giant nerve-cells of the ascending convolutions, and for this reason I have chosen cells from this part for my description and photographs.

It is not a common change in insanity, as in considerably over a hundred brains of lunatics examined by Nissl's method or modifications I have besides the cases here noted only seen one or two individual cells so affected.

In the case of a man whose leg had been long amputated, no cells of this description were found in the opposite leg centre of the cortex.

The lesion appears to be identical with that described by Nissl and others after section of the axon of a motor nerve-cell, and by Barker in the forehorn-cells in cases of epidemic cerebro-spinal meningitis (see British Medical Journal, December 26, 1897); but it is questionable how far this similarity extends; at any rate, with osmic acid, very
definite alterations of structure are shown both in nerve-cell and its axis-cylinder continuation, which point to a probably degenerating state of the neuron. Although in one of the seven cases there was no mention made of a condition of dementia, but only prolonged and profound melancholia, I am inclined to think that the lesion is the anatomical groundwork of the dementia, which is often rapid in its course and probably always fatal.

Cases Nos. 1 and 2 are of interest, as with a clinical history resembling to a certain extent general paralysis in its acuter forms, the autopsy revealed naked-eye appearances quite distinct from general paralysis, neither did the microscopical investigation show any features in common with this latter disease.

As regards the melancholia case (No. 5), it is to be noted that she contracted a malignant form of diphtheria affecting the whole of her oesophagus and to which she succumbed after an illness of a fortnight.

In case No. 4 I was able from the symptoms to foresee the nature of the changes in the nerve-cells.

Certain symptoms were present in most of the cases, and of these the most obvious was paresis. The patient, for no obvious reason, occasionally fell down whilst walking, and ultimately there was complete inability to walk. Possibly the weakness of the arms was as great, but was not so obviously developed.

When the notes of the cases do not mention incapability of walking, there is mention of involuntary jerkings of the limbs. The demented condition of the patient prevented any greater precision in testing their movements, and the same cause interfered largely in endeavouring to determine sensory defects. The sensibility to pricking (painful impressions), in the cases where any reliance could be placed on the results, was greatly blunted, or entirely absent, but generally more marked in the lower extremities.

The pupils reacted to light and for accommodation to the end. The knee-jerks were exaggerated; plantar reflexes absent; tongue free from tremor; articulation not generally interfered with.
The arterial tension of three cases was high (= 150 to 210 mm. Hg.). This is interesting in view of the fact that a thickening of the arterioles of the cortex and minute cerebral haemorrhages were found in all the cases.

Diarrhoea was very commonly noted towards the end.

The whole case may run a fairly rapid course, varying from a few to eighteen months, or, after prolonged mental disorder (melancholia so far only noted), dementia sets in and death as a rule rapidly ensues.

Pathological Anatomy.

A reference to the cases will show the leading naked-eye changes noted in the head and viscera. The brain may present a fairly healthy appearance, or there may be merely evidence of atrophy in the frontal convolutions. In others the meninges are opaque and thick over the vertex, but not adherent, and, microscopically, this thickening is seen to be an increase in the connective tissue of the arachnoid, and quite unattended with any round-cell infiltration of the pia.

A general feature noted microscopically in all the sections examined was a thickening of the arterioles and capillaries of the cortex. Sometimes the lumen was nearly obliterated. In the arterioles this thickening appears to be due to increase of the muscularis and adventitia; in the capillaries, to a fibroid thickening. Probably, in both cases, this latter predominates, for when stained in picro-fuchsin, the thickened vessels stand out as prominent red rings or lines. Tortuosity was also noted to a very considerable extent. Minute haemorrhages into the cortex (microscopical) were seen in all the cases, sometimes five or six in one section.

The larger vessels of the white matter often had a copious collection of colloid bodies lying in their immediate neighbourhood. They showed a blue centre fading into a red circumference when stained with acid fuchsin and toluidin blue.

There was never any appearance of spider-cells or proliferation of neuroglial fibrils.

Nerve cells.—As noted before, the change in these is
widespread, and appears to affect the majority of all the pyramidal cells, and is especially well seen in the giant-cells.

Fresh squeezed-out portions of cortex, coloured in methyl blue or toluidin blue, show the change with the greatest clearness, and my experience, contrary to that of Drs. Robertson and Orr, is that most pathological changes are better seen by this method, when properly carried out, than in sections.

The cell is probably smaller than in its normal state, except when distended with pigment, and often somewhat globular; it has generally an irregular border staining deeply, and which often fails to show definite chromophile elements. The whole centre of the cell consists of a pale, homogeneous mass, having a blurred or washed-out appearance.

The nucleus, which is small and shrunken, stains a pale blue, and is situated at the periphery of the cell, or it may be up in its apex, or in the junction of a dendrite with the cell. It contains a dark, round or oval, and probably shrunken, nucleolus.

Generally a large part of the cell is occupied by a highly refractive bright yellow pigment, and this may distend the cell enormously in one direction. This substance stains either a dark brown or jet black with osmic acid, but that it is not wholly of a fatty nature is rendered probable by the fact that it is still seen in the cells in sections which have been subjected to chloroform and xylol. Generally a fair number of dendrites are given off from the cell, but they are, as a rule, unduly thin, and stain of a pale uniform blue, or else show a few attenuated chromophile threads.

The apex, at its junction with the cell-body, generally shows a few fine chromophile threads, but further along it does not stain at all, and is barely visible. Very often there is an abrupt line of demarcation separating the pale apex from the densely-stained cell-body border (see fig. 1).

In sections, fixed in sublimate and stained in toluidin blue, the appearance of the cell-body is much the same as in

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1 This refers to cells which have been hardened in osmic acid; in the case of films the pigment merely becomes slightly darker and takes on a dull greenish tint.
films; the pigment appears of a greenish colour, owing, probably, to the blending of its yellow with the blue stain. The nucleus is almost always shrunken, and, with a distorted outline, contains only a few loose granules and a dark nucleolus, and is almost always eccentrically placed—often, indeed, bulging from the cell-body. The pale, almost colourless, hyaline-looking body of the cell, which generally has a somewhat circular contour, gives these cells a most characteristic appearance; the pigment is often almost imperceptibly blended with it at its outer part. Even with a one-twelfth oil immersion, it appears homogeneous. In other respects, the description given of the whole cells applies to those seen in optical section.

Case No. 6, which was examined after fixing in osmic acid, gave very interesting results.

The tangential fibres of the first layer were present in fairly large numbers, and showed a normal appearance in the motor region, but in the frontal regions they were practically absent.

In the motor region the great majority of the medullated nerve-fibres in the lower strata of the cortex and the adjacent white matter showed very marked changes; the staining, in general, was not so dark, owing to the fact of disappearance of some of the myelin, and that which remained was in the form of little separate black drops on either side of the nerve-fibre, which could be seen in its place more darkly stained than usual; and often in advanced cases of degeneration, when no myeline remained, it was nearly black. Fig. 4 shows a degenerated medullated fibre.

In certain parts of the section medullated nerve-fibres were seen, which gave a normal reaction with osmic acid,

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1 I find that a mixture of carbolic acid, 5 per cent., osmic acid 2 per cent., in equal parts, gives excellent results; it penetrates with great rapidity, fixes the smallest particles of degenerated myelin or fat, and also preserves the nerve-cells well. The pieces are left in it for twelve to twenty-four hours, then placed in 10 per cent. formaline for two days, passed into alcohol for one or two days, and then through chloroform and into paraffin. The section is fixed to the slide by capillarity, and then decolourised in permanganate of potash, followed by sulphurous acid. These sections counterstain very well with Ehrlich's acid haematoxylin, which is only allowed to act for a second on the section, and then washed off.
and some of these are shown in fig. 4, to contrast with the former figure.

SYNOPSIS OF CASES.

No. 1.—I. B., a female, admitted June 29, 1898, aged 45, married. Her father was a drunkard and died about 50 of apoplexy. Her mother is stated to have had several "fits," in one of which she died. Mother's sister melancholic. This is her first attack, of eighteen months' duration, and stated to be due to menopause and alcohol; it began with depression and occasional violent fits. She has been addicted to alcohol for years.

The facts certifying to her insanity were incoherent shouting and raving. On admission she was in feeble condition and weighed only 88 lbs. Temperature normal; complexion turgid; knee- jerks exaggerated; pulse (sitting), 158. Has conjunctivitis. Was restless and noisy; obstinate, paying no heed to questions. Dirty in habits; bad appetite. Parotitis of right side developed five days after admission. Teeth covered with sordes and mouth full of muco-purulent slime. Was in a delirious state, muttering, but occasionally replying relevantly. Her speech thick and indistinct. Plantar reflexes abolished. Was very restless, occasionally screaming, and had frequent attacks of involuntary jerking of the limbs. Became worse; comatose. Left pupil the larger. they both react slightly to light. Face covered with a greasy sweat; mouth open; eyes closed. On July 7 she died. Autopsy seventeen hours later. Body fairly nourished. Blood vessels at base normal. Meninges fairly clear and stript readily; they were heavily waterlogged over the anterior two-thirds. Lateral ventricles dilated and filled with blood-tinted serum. Atrophy of convolutions of anterior two-thirds. Consistency of brain was normal. No granulations in any of the ventricles. Pons and cerebellum appeared normal. Small patch of consolidation in left lung; old adhesions of right side. The cardiac muscle was rather soft; valves normal. Liver congested; spleen firm; kidneys slightly granular.

Weights in grammes.—Cerebrum (stript), 988; meninges, 20; cerebellum, 133; stem, 27; total, 1,168. Heart, 208; liver, 1,208; spleen, 128; right kidney, 143; left kidney, 165.

The idea was present that this was an acute case of general paralysis, but the entire absence of any of the pathological appearances, macroscopical and microscopical, showed conclusively that it was not.

No. 2.—J. W., a female, admitted October 15, 1897, widow.
This is her first attack, and is said to be of only ten weeks duration, following influenza. Has been a hard-working, sober woman. Aged 52.

The facts certifying to her insanity were: irrational conversation; at times morose, and says she is a lost woman; at others hilarious, laughing and singing immoderately. On admission she is thin, and weighs 93 lbs. Temperature normal. Dark sallow complexion, coarse skin. Pupils equal, and react normally to light and on accommodation. Knee-jerks exaggerated. Tongue free from tremor, furred. Slight cough. Nocturnal urine, acid, 1016; no albumen. Is excited, spits on the floor, and answers rudely when remonstrated with; sings when her chest is being examined; replies in a flippant, careless way, “don’t know,” to most questions. In December it is noted that, as a rule, she is excited one day and quiet the next. The left pupil is slightly the larger; they both react well to light and on accommodation.

March 24, 1898.—The day before yesterday she fell forwards on her face whilst walking round the farm; was not convulsed, and did not lose consciousness. This has happened several times recently. Is now in bed, talking to herself. Tongue clean, pulse 75, arterial tension = 150 mm. Hg.

April 2.—Up yesterday, but had to be put to bed again, as she could not stand. Clean in habits. Pulse 78, temperature normal, urine free from albumen, 1010.

April 20.—Up, walks unsteadily, and leans over to the right. Is now very lost and silly.

April 30.—Was yesterday very excited, rushing about the ward and falling about. To-day she keeps chattering a lot of nonsense in a chanting tone. Diarrhoea set in on May 16, and on the 26th she died.

*Autopsy* (twenty-five and a half hours later).—Poorly nourished. Basal vessels healthy. Meninges not opaque, stript readily, rather thick. No marked wasting of the convolutions; brain of normal consistency. Lateral ventricles dilated. No granulations on them or on fourth ventricle. Both lungs bound down by old adhesions. Heart normal, no atheroma. Liver pale and soft. Spleen firm. Kidneys small, soft, pale; cortex not thin; capsules stript readily.

*Weights in grammes.*—Cerebrum (stript), 1031; meninges, 20; cerebellum, 120; stem, 27; total, 1,198. Heart, 204; liver, 1,040; spleen, 132; right kidney, 92; left kidney, 76.

No. 3.—E. E. W., female, admitted November 6, 1895, baker’s wife. First attack of eighteen years' duration. Her
father died of Bright's disease. She has a daughter insane. On admission she weighs 112 lbs., and is in fair health and condition. Knee-jerks exaggerated. Right pupil the larger; they react normally to light and on accommodation. Tongue slightly tremulous, protruded markedly to the right. Urine: specific gravity 1021, a faint trace of albumen. Her mental condition was one of delusional insanity; she imagined that some women were plotting against her and her husband, and conspiring to blow her up with dynamite. She was neat, quiet, and industrious, and gave no trouble, and remained thus till April, 1898, when she made an attempt on her life, and became acutely melancholic, restless, agitated, refusing food, and not able to sleep. Her bodily condition deteriorated greatly, she picked her face, looked miserably ill, and had to be held in bed to prevent her from jumping out and roaming in the ward.

May 17, 1898.—Pulse 102, regular; arterial pressure = 150 Mg. Hg. Knee-jerks exaggerated. Tongue clean. Temperature normal. Is very agitated and looks haggard.

During July she suffered off and on from diarrhoea, and had dermatitis of face and back of hands (probably from the sun). Mentally more composed.

In September she rapidly became demented, dirty in her habits, and very greedy. By November she was bed-ridden, and had lost the use of her legs, was filthy in her habits, very restless, and often falling about.

December 8.—Lies on her right side, and exhibits involuntary jerking movements of arms and legs, and risus sardonius. The attendant states that she has to be held when seated on the night stool, or she would jerk herself off on to the floor. She died on December 11.

Autopsy (twenty-nine hours later).—Body poorly nourished; rigor mortis present. Skull neither thick or dense: basal vessels healthy. Meninges very thin and transparent, stript readily. Brain very large and pale, with no atrophy or dilatation of lateral ventricles. Lungs small, pale, crepitant; no pleural adhesions. Left side of heart slightly hypertrophied, and mitral orifice small. Slight calcareous deposit at base of aortic valves. No atheroma of aorta beyond. Liver soft and pale. Spleen small and firm. Kidneys small, dark purple colour; cortex tough; capsules slightly adherent.

Weights in grammes.—Cerebrum (stript), 1,132; meninges, 18; cerebellum, 139; stem, 30; total, 1,321. Heart, 215; liver, 885; right kidney, 101; left, 107; spleen, 59.
No. 4.—M. E. B., female, admitted December 20, 1897, aged 37, single. First attack; has always been considered hysterical, but for the last year has been nervous, apprehensive, and could not be induced to leave the house. Gradually lost use of her legs and hands, and the latter shook so much that she could not hold a cup. At times would fall down. Took to her bed several weeks before admission, and a few days ago developed screaming attacks. Said to have been a sober woman.

On admission ill and unable to walk; slightly bedsore. Temperature, 99-6°. Complexion coarse, skin greasy and blotchy. Knee-jerks absent, plantar reflexes absent, pupils equal. Has bronchitis. Her sensitiveness to pricking is nil in face, neck, chest, arms, legs, and there is no local reaction. Is very apprehensive, and shrinks away when one goes near her. Keeps ejaculating little phrases a propos of nothing, e.g., "Who speaks English?" "Isn't Mr. Archer?" "For grief I shall read," "Do help me." Shouts occasionally. Is dirty in habits. To most questions she pays no heed, but when asked her name replied, "Why, Brass."

Remained in much the same state till she died on December 24, 1897.

Autopsy (three-and-a-half-hours later).—Fairly nourished. Skull heavy and dense; vessels healthy. Meninges congested, but not thick or adherent; they were clear. Some atrophy of the frontal convolutions. Lateral ventricles not dilated. Brain of normal consistency. Evidence of emphysema and bronchitis. Heart muscles soft, apex fatty, valves fairly healthy. Liver soft and dark coloured. Spleen soft. Kidneys fairly healthy.

Weights in grammes.—Cerebrum (stript), 950; meninges, 13; cerebellum, 143; stem, 31; total, 1,137. Heart, 239; liver, 1,629; spleen, 152; right kidney, 145; left kidney, 170.

Sections of the popliteal, post-tibial, radial, and median nerves were examined, after fixing in osmic acid. The peripheral nerves showed very marked changes, some bundles being nearly devoid of all myelin rings (radial and post-tibial). The more central nerves were affected, but to a much less extent.

No. 5.—A. E. C. This woman was first admitted on June 25, 1889, suffering from melancholia, and was discharged, recovered, August 21, 1889, and re-admitted May 13, 1890. Profoundly depressed, restless, and agitated, constantly ejaculating, "Oh, whatever shall I do!" in an agonised tone. She remained in this state of deep depression till her death, but up to her last illness she was clean in habits and capable of doing ward work,
and never showed any motor troubles. In February, 1898, her arterial tension was 210 mm. Hg. On January 24, 1899, she went to bed with a sore throat, which proved to be diphtheria, and she died February 6 following. Her temperature during this period was always subnormal (taken in the rectum). She was 69 years old.

**Autopsy** (five hours after death).—She had a thick, ash-grey membrane lining the whole of her oesophagus, but stopping at the cardiac orifice of the stomach; small infarct in spleen. Thoracic viscera fairly healthy. Kidneys granular. Liver soft and dark. Head: basal arteries atheromatous. Large collection of fluid under the meninges, which showed here and there small opaque patches, but were elsewhere thin and translucent, and not adherent. Atrophy of convolutions most marked in parietal regions. No marked dilatation of ventricles.

**Weights in grammes.**—Cerebrum (stript), 1,084; meninges, 15; cerebellum, 147; stem, 35; total, 1,283. Heart, 238; liver, 1,102; spleen, 129; right kidney, 94; left, 111.

This case is out of harmony with the others, inasmuch as she was not demented in the ordinary sense of the word, and did not exhibit any of the motor troubles seen in all the other cases; but it has to be taken into consideration that she was confined to bed for nearly a fortnight prior to death with a malignant form of diphtheria, and the question arises whether the poison of the diphtheria was the cause of the changes found in the nerve-cells, or whether these changes were associated with her prolonged and profound melancholia.

I cannot help thinking that having regard to the unanimity with which motor disturbances were noted in all the other cases with similarly affected cells, the changes noted in her case were the result in part at least of the diphtheria, although in another case examined shortly before I was unable to discover any notable alteration in the nerve-cells of similar regions.

In the case under discussion, however, the form of disease was asthenic with a persistent low temperature, and in the latter it was rapidly fatal with a considerable pyrexia (104·6).

**No. 6.**—Male, aged 36. Admitted August 17, 1899. Father insane. First attack of recent origin. The facts certifying to his insanity were incoherence, violence, raving. On admission he weighed 138 lbs., and was in fair condition. Temperature normal. Knee-jerks present. Tongue furred. Pupils equal. He was very restless and incoherent, and paid no heed to questions. Threw himself into peculiar attitudes owing to involuntary jerking of
Fig. 1. (45 oil, No. 2 eye-piece, Beck.)—Cell with nucleus distorted and bulging from the side of cell body. A darkly stained cell body border. Some yellow pigment at right edge. A darkly stained irregular border separates the pale apex from the cell body. In the former are a few very fine short chromophile threads.

Fig. 2. (45 oil, No. 2 eye-piece, Beck.)—In this cell the whole of the centre is occupied by a pale washed-out hyaline looking mass. No nucleus is seen, but in serial sections one is seen to be present, situated at the upper right hand side of cell, about where the darker area is shown in the photograph. A mass of rather coarsely grained pigment is seen at the lower left hand border of cell.
Fig. 3. (4, No. 2, Beck.)—A degenerated myelin nerve fibre seen in centre of figure, others to the right. The axis-cylinder can be seen in places.

Fig. 4. (Same magnification.)—Normal myelin nerve fibres from other parts of same section.
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the limbs, and had to be put in the padded room to prevent him from injuring himself, as he could not stand. Refused food. Rapidly got weaker, but still kept restless and very resistive; laughed causelessly, was dirty in habits. His temperature was subnormal on the two occasions it was taken. Became collapsed on the 21st, and died August 22, 1899.

Autopsy (a few hours later).—Beyond acute congestion of lungs the thoracic and abdominal viscera appeared healthy. Head: skull thick, basal vessels healthy. Meninges very opaque over the vertex, thick, not adherent. Excess of subarachnoidal fluid. Atrophy of convolutions over vertex. Slight dilatation of lateral ventricles. Brain of normal consistency. Cerebellum large. The meninges over the superior worm were opaque and thickened.

Weights in grammes.—Cerebrum (stript), 1,169; meninges, 28; cerebellum, 179; stem, 36; total, 1,412. Heart, 329; liver, 1,650; spleen, 85; right kidney, 111; left, 121.

No. 7.—W. A., male. Admitted July 2, 1892. Aged 52. Father melancholic and committed suicide. This was his first attack. He was acutely melancholic—the picture of misery—and gradually passed from this state into dementia. Picked his hands and head. Paresis of lower limbs was noted about two years after admission. He was bedridden for over a year, and died in March, 1898, of phthisis.

Autopsy (sixteen-and-a-half hours after death).—The lungs showed extensive tubercular changes. There was some atheroma of the aorta. Liver soft and pale. Kidneys pale and tough. Capsules stript well. Head: the basal vessels were atheromatous. The meninges were thick and opaque, but stript readily. Some atrophy of frontal convolutions. Lateral ventricles much dilated. Brain pale and firm. Cerebellum firm.

Weights in grammes.—Cerebrum (stript), 1,084; meninges, 24; cerebellum, 154; stem, 34; total, 1,296. Heart, 214; liver, 1,028; spleen, 109; right kidney, 110; left, 105.