ALZHEIMER'S DISEASE.*

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In 1906 Alzheimer reported the case of a woman, æt. 51, who, in addition to the expression of ideas of suspicion and jealousy, failed mentally to such an extent that she was unable to find her way about her own home. During her hospital residence she was perplexed, disoriented for time and place, and had difficulty in understanding and in expressing her thoughts. There were delirious phases, during which she was hallucinated. Her power of retention was greatly impaired. She showed paraphasia and perseveration. The illness persisted for a period of four and a half years, and at the time of her death she suffered from contractures. The *post-mortem* examination showed a striking alteration of the neurofibrils: "In an otherwise normal cell there appear at first one or more fibrils, which on account of increased thickness and increased stainability stand out prominently. In the further course of the alteration many neighbouring fibrils are similarly affected. These then form thick bundles, which gradually come to the surface of the cell. Finally the nucleus and cell disintegrate, and only a tangled bundle of fibrils remains to indicate the site of a former ganglion cell." In addition, throughout the entire cortex, especially in the outer layers, there were many miliary foci or plaques.

The clinical and histopathological picture described above subsequently became known as "Alzheimer's disease."

Previous to Alzheimer's description, Blocq and Marinesco and Redlich had described the occurrence of plaques which were considered as a form of miliary sclerosis, and as being an indication of a severe clinical process. Since then plaques have been described

* A paper read at the Annual Meeting, Oxford, July 3, 1930.

as occurring not only in the cortex of psychotic senile patients, but as an accompaniment of normal senility. Thus it was recognized that cases showing, in addition to plaques, the neurofibrillary changes peculiar to Alzheimer's disease, occurred at an earlier period—the pre-senile stage—and were differentiated from senile cases in which plaques alone were the outstanding feature. Naturally, the question arose of the relationship between cases showing the changes peculiar to Alzheimer's disease, and those designated as presbyophrenia. Presbyophrenia has been described as a presenile state showing a retention defect with confabulation—a mental picture similar to that seen in Korsakov's psychosis, but differentiated from it by the absence of any polyneuritic changes. As our clinical experience has increased, it has seemed clear that presbyophrenia and Alzheimer's disease cannot be differentiated. They are part and parcel of the same disease process, presbyophrenia being merely a stage in the development of Alzheimer's disease.

We have not thought it necessary to make an extensive review of the literature, because that has already been done by others. We would, however, take this opportunity of acknowledging our indebtedness to the papers published by Fuller, Tiffany, Lambert, Barrett, Grünthal, Malamud and Lowenberg. Grünthal's report covers a group of 14 cases, most of whom were diagnosed by Kraepelin. In 13 of these cases senile plaques were present as well as the fibrillary changes of Alzheimer. The plaques and fibrillary changes occurred throughout the cortex, but neither the cerebellum nor the basal ganglia were involved. The majority of Grünthal's cases were between fifty-two and sixty-three years of age, and Grünthal described the clinical course as being divided into three stages:

(1) A stage of gradual loss of memory and disturbance in perception, carelessness in work and appearance, place disorientation, weakness or epileptiform attacks, with some loss of words and slurring speech.

(2) Complete disorientation for time, place and person, dulling of comprehension, restlessness at night, inability to read, write, or do simple arithmetical sums.

(3) A stage of extreme irritability, with paraphasia, uncleanliness, stereotyped movements.

Grünthal takes exception to the cases published by Schnitzler, Schaffer, Weimann and Barrett. He believes that all such cases occurring under the age of forty years, and characterized by a

complicated neurological picture, should be kept apart from those known as Alzheimer's disease.

More recently Malamud and Lowenberg have reported the case of a youth, æt. 15, who at the age of 7 had suffered from scarlet fever, and had shown a consequent lack of mental and physical development. The occurrence of this case, interrupted by a remission of approximately four years' duration, was very atypical, and eventually death occurred from tuberculosis. The histopathological examination revealed miliary plaques and the nerve-cell changes described by Alzheimer, but in addition there was extensive degeneration of the vessels of the villi of the choroid plexus. All such cases, occurring in comparatively young people, are of extreme interest, but we agree with Grünthal that, for the present, it would be much better to keep all cases under the age of 40 years distinct from the more typical group.

While considerable attention has been paid to Alzheimer's disease in German, Italian, French and American literature, British psychiatry has taken little notice of it. It is with the idea of directing more attention to this interesting group of cases that we have thought it of value to publish two cases which have been confirmed by autopsy, and two other cases which clinically seem characteristic.

CASE I.—*A case of profound mental disorder occurring in a middle-aged woman, æt. 57, characterized by a defect of memory, with disorientation and total lack of insight. The progressive course, the serious defects both in the emissive and receptive functions, the dyspraxia and the terminal state of spastic contracture and extreme helplessness are typical of the clinical picture of Alzheimer's disease. This diagnosis was confirmed by the histopathological examination.*

Miss I. C—, æt 57, forewoman in a factory, was admitted to the Glasgow Royal Mental Hospital, Gartnavel, on March 26, 1921.

Her *family history* was negative for nervous or mental disease. She was described as having been a strong, healthy woman, who rose to a position of considerable responsibility as a forewoman in a calico-printing works.

Two years previous to her admission she gave up work owing to incapacity and forgetfulness. It was noticed that her memory and temper were failing, and, in addition, she showed peculiarities of conduct. She insisted that she had made statements when she had not done so. This loss of memory and forgetfulness became increasingly conspicuous. She understood what was said to her, but her power of attention and retention was so defective that in a few minutes she had forgotten what she had been told. Her memory for remote events was better preserved. She made mistakes while dressing, sometimes putting on her underskirt above her dress. Gradually she became duller, lacking in interest, and so unfit to care for herself that mental hospital treatment was necessary.

The medical certificates described her as demented in her conduct and appearance. She did not know the use of common objects, and behaved in a peculiar

way. Her memory for things that happened from day to day was much impaired; for instance, a few minutes after being told a name she had no idea what it was. Her memory for places and dates was also very defective and incomplete. She was unable to carry out the simplest arithmetical calculations, offering five farthings for a penny. She could not give her own address or spell her name.

On admission to hospital she was pleasant and cooperative and seemed to understand the purpose of the examination. She gave her name correctly, but the wrong address. Simple questions were answered correctly, but principally in monosyllables. Her mood was one of contentment, with lack of appreciation of her seriously disordered state. The most striking defect was in the intellectual field. This defect was characterized by diffuse memory disturbance, affecting both recent and remote events, but especially the former. There was considerable disorientation for time and place. She remembered having come to the hospital in a motor car, but was unable to give the names of those who had accompanied her. Her memory was so poor that she could not give an adequate account of herself. She remembered that she was born in Belfast, but was unable to give the year of her birth—said she was about fifty (57). She was unable to recall the various places where she had been employed. She made foolish mistakes in simple calculations. When talking, she stumbled over words, and at other times showed word amnesia. There was also a degree of paraphasia. She had no insight into her condition.

Physically, she was a well-nourished, middle-aged woman, who was in good general health. Her tendon reflexes were equally exaggerated on both sides, but otherwise there were no special neurological signs.

She cooperated in an aphasia examination, but tired easily. She made mistakes in saying the alphabet, and was unable to repeat the days of the week, the months, the Lord's Prayer, etc. While repeating words spoken to her she made mistakes, for instance, in saying "Go, gone gold," she could not proceed further than "Go." Simple orders were correctly performed, but as soon as the orders became more complicated she failed, *e. g.*, the "three paper" test. She made mistakes in naming objects, even such familiar things as coins. Reading showed numerous errors, *e. g.* "Keniloff" instead of Kenilworth, and this difficulty was constantly repeated. In picking out objects she also made errors, selecting a comb instead of a brush and so on.

In August, 1922, this patient was transferred to the Glasgow District Mental Hospital, Woodilee, and we are greatly indebted to Dr. Carre, the Medical Superintendent, not only for his subsequent notes, but also for preserving the brain, and sending it for examination.

While at Woodilee, she is described as being simple and facile, and as taking no interest in her surroundings. She was easily managed, and for a period of two years was "boarded out." Latterly she became so untidy and dirty in her habits, and was so resistive to all care and attention, that she was returned to the mental hospital at Woodilee.

In the terminal stages she had no realization of her condition, or of where she was, and until the time of her death there was a steady and gradual deterioration. Her habits became degraded; she chattered, muttered and laughed to herself. A number of days before her death on January 7, 1929, she was in a state of extreme dementia, exhibiting spastic contractures.

Post-mortem Summary.

The head only was examined in this case. The dura was very much thickened, presenting the appearance of a chronic pachymeningitis. No gross abnormality of the pia-arachnoid was observed. The blood-vessels at the base of the brain showed patchy atheroma. On removal of the leptomeninges, atrophy was noted in various regions. This was most pronounced in the frontal lobes, and more particularly on the left side. The convolutions in the region of the Sylvian fissure appeared to be smaller

than normal. This feature also was present in the occipital lobes, and again especially on the left side.

Histological Examination.

Pia mater.—Slight pial thickening was present. In some situations the pia was adherent to the brain. The pial vessels showed thickening of their walls, especially of the middle coat, but no total obliteration of a vessel was seen.

Cortex.—A noteworthy feature in sections stained with hæmalum and eosin was the presence of a band of vacuolation in the region above the layer of large pyramidal cells (layers 2 and 3). This band seemed to be peculiar to the frontal areas. In the occipital and other regions, areas of vacuolation, less localized, and encroaching sometimes on the white matter, were present. The band in the frontal area, however, was so well delimited that it presented a very striking appearance. The blood-vessels did not show any marked alteration in their walls. The choroid plexus appeared to be normal. Abundant corpora amylacea were present, especially in the hippocampal region, where they were seen in great numbers at the margin of the cortex.

With Victoria blue stain there appeared to be no attempt at repair in the vacuolated areas. There had occurred, however, a degree of fibrous neuroglia reaction, most intense in the occipital area, and to a lesser degree in the hippocampal gyri. In the frontal areas the reaction was extremely small. Some degree of subpial felting was present, and in both the fourth and the lateral ventricles a mild degree of ependymitis granularis was observed.

In sections stained with Scharlach R an abnormal amount of fat could be seen in the ganglion cells, and round some of the blood-vessels a perivascular infiltration with fat-granule cells had taken place. With Nissl's stain there appeared to be a great "falling out" of cells in the upper layers of the cortex, although the architecture did not show any great disturbance. The ganglion-cells presented some non-specific alteration of the Nissl bodies, but the Betz-cells were very well preserved.

No notable rarefactions of the myelo-architecture could be observed in the sections stained by Weigert's method.

The most important histological changes were revealed with Bielchowsky's staining method. Abundant typical senile plaques were seen scattered throughout all the cortical areas examined—frontal, pre- and post-Rolandic, parietal, temporal, occipital and hippocampal. These plaques were most abundant in the hippocampal

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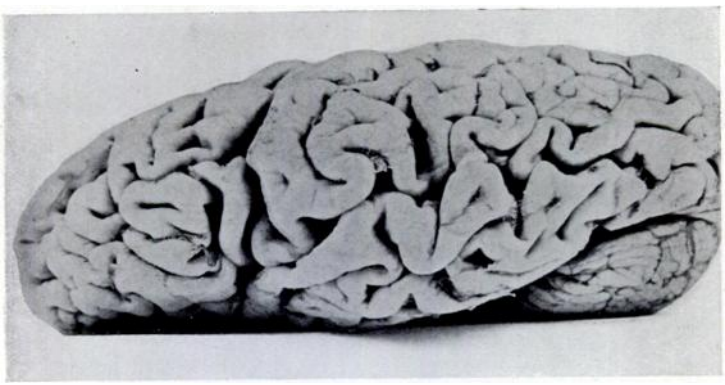
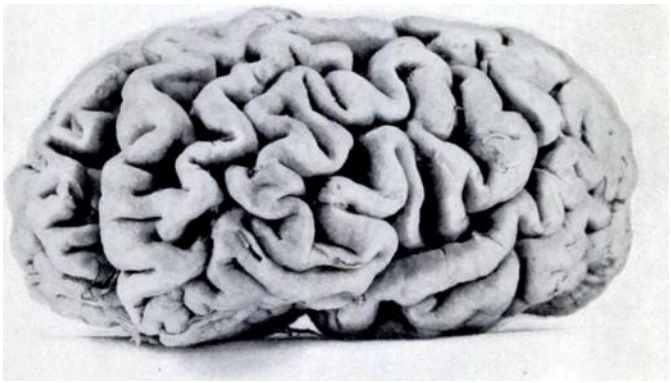
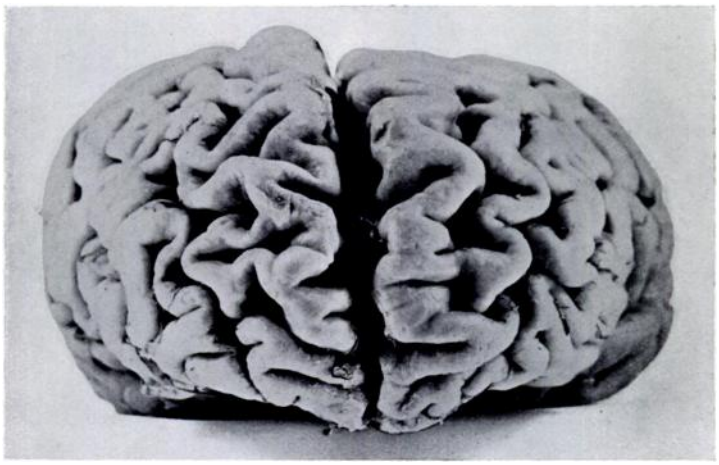


CASE 1.—Showing some atrophy of the gyri and widening of the sulci in the region of the Sylvian fissure.



CASE 2.—Showing atrophy of gyri and widening of the sulci.



CASE 2.—Showing atrophy of gyri and widening of sulci in the frontal regions.

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region, and they appeared to have a preference for the second and third layers of the cortex.

The nerve-cells had undergone profound changes. For the most part these changes took the form of the fibrillary degeneration of Alzheimer. All forms were present, including basket-cells, figures of eight, and the thickened agglutinated fibrillary forms with the shape of a flame, comma, crescent or triangle. All parts of the cortex were affected. In the hippocampal region the greater proportion of the nerve-cells were affected by this degeneration, and most striking was the appearance of the groups of cells in the plexiform layer, where the cells showed exceedingly thick fibrils. In the other regions of the cortex the Alzheimer change seemed to affect the small and medium-sized pyramidal cells. The large pyramidal cells showed a more or less normal appearance.

Other ganglion-cells showed another form of degenerative change of the neuro-fibrils, which conformed to the description of the "granulo-vacuolar" degeneration of Simchowicz, where "the cell protoplasm shows one or more confluent vacuoles of varying shape containing granules of various size often isolated. Often the nucleus is pushed to the periphery.

These cell changes had occurred in the neighbourhood of senile plaques, and were present also independently of plaques.

Basal ganglia.—No plaques were noted. The cells of the globus pallidus showed a "granular" change. In the caudate nucleus scanty small plaques could be distinguished. Some cells had undergone Alzheimer's fibrillary change, others presented a granular condition of the neurofibrils. The cells of the red nucleus also participated in these degenerations. The cerebellum showed no abnormality.

CASE 2.—*A married woman, æt.* 54, *who for several years had suffered from memory defect, on the basis of which delusions of persecution developed. Later she showed emotional instability, complete disorientation, word amnesia and paraphasia. An aphasia examination revealed defects in all fields. The course, extending over a period of six years, was one of progressive mental and physical deterioration, resulting in complete incapacity. The terminal state was characterized by generalized muscular twitchings. The case was confirmed by autopsy.*

Mrs. M. G. B—, æt. 54, nurse, was admitted to the Glasgow Royal Mental Hospital, Gartnavel, on August 30, 1921.

The *family history* was negative for nervous or mental disease.

Personal history.—The patient was described as a bright, sociable woman, but quick tempered and irritable. She was determined and obstinate. She married when 25 years old, but before the birth of her only child was divorced from her husband because of his drunkenness and infidelity. After her divorce she became an efficient and successful maternity nurse.

Onset of illness.—Several years previous to her admission, her memory began to fail, and during the last two years this failure had become accentuated. She forgot where she placed things, accused people of stealing her property, and reported supposed thefts to the police. She hoarded her belongings in dressing-cases and drawers. She became suspicious of those with whom she was closely associated, and finally she was so impossible to deal with that care and treatment in a mental hospital was imperative.

The medical certificates stated that the patient accused people of stealing her handkerchiefs and said that they were returned to her through the wall of her bedroom. The police inspector at P— stated that the patient called repeatedly at the police station and said that everyone was stealing from her. She constantly repeated her statements.

On admission the patient was a healthy-looking woman, who seemed much younger than her years. Her blood-pressure was 90. Her tendon reflexes were unequal, the left knee-jerk being increased and the right diminished. Apart from this there were no neurological signs.

Mentally, she was not able to cooperate satisfactorily in an examination. She recognized the institution as a hospital, but did not know where it was situated, and wondered if it might be a maternity hospital. She did not know the day, month or year, and while being asked these questions showed perseveration: for instance, when asked what month it was, she replied "September," and when asked the year, said, "No, it is September; no, it is August"; usually she repeated the question before replying. Her loss of memory was distressing to her, and she became perturbed and irritable when questioned. She said, "I don't understand why people are worrying about me. I have some difficulty in finding my words; sometimes the word comes to me just at once, sometimes I cannot get it." She could not tell how long she had been troubled in this way, but took refuge in vague statements, such as "A good long while." She said she understood everything that was said to her, but her difficulty was in getting a phrase to reply. Her memory for remote events was also seriously involved. She did not know how old she was, when born, how old when married, etc. When asked whether she had any children, she replied, "Oh, no, its Mr. R— has the children. Yes, my own daughter—I remember now. Just for the moment I did not know." She could not tell her daughter's age. When asked her own name, she gave her maiden name. She could not state whether she had become a nurse before her marriage or afterwards. She complained of being depressed, and wept at times; at other times she was taciturn. No delusions or hallucinations could be elicited. Her grasp of school and general knowledge was greatly impaired. She could not say the alphabet correctly. She made mistakes in counting backwards from 20 to 1, and while doing this test she showed considerable perseveration. She could not mention the days of the week, the months of the year, rivers in Scotland, or when the Great War began. In reading short stories she made numerous mistakes, and she was unable to give the gist of the story afterwards.

An aphasia examination was made. Her hearing was unimpaired, her vision was satisfactory. The patient was right-handed. She showed a striking word-amnesia. The defect was not constant, but varied from moment to moment; a word "coming through" at one time would be forgotten a moment afterwards. There was marked echolalia, perseveration and paraphasia. The writing test revealed defects parallel to those obtained with the tests for speech defects. When asked to say the Lord's Prayer, she started by saying, "The Lord's my Shepherd," and when the question was repeated, she said, "Oh, that's not it." She then started correctly, but could not complete it. Her spelling was defective; ordinary words of two syllables were spelt correctly, but compound words like "threepence" had to be given in two parts. Long words she could not spell at all. Her repetition of words and sentences was fairly accurate: words like "Third Riding Artillery Brigade," and short phrases, were usually correctly repeated. She could not compose words spelt to her beyond two syllables. The reaction to words heard was normal. She picked up objects correctly from a

selection placed before her. She was able to recognize things heard, the jingling of keys, the tick of a watch, and so on. She showed a certain defect in the recognition of things smelled, but named things tasted. Symbols and signs were not understood.

Writing from dictation showed an inability to write certain letters. Perseveration was present in this. She often left out letters and syllables, and sometimes showed a paragraphia. There was considerable dyspraxia, but she was able to copy actions shown her.

During the course of her residence she came to recognize that she was in a mental hospital. She complained bitterly about this, but at the same time she was able to accommodate herself, and for a short period was employed in the laundry.

In 1924 she is noted as having deteriorated considerably. She had become untidy in her habits, was extremely incoherent in her speech and completely disoriented for time and place and person. The irritable state mentioned previously had been replaced by one of contentment and happiness. A gradual progressive decline continued, and her general appearance and conduct were more suggestive of an old lady than of a person sixty years old. In 1927 she was muttering nothing but a mass of incoherent phrases, and all attempts at an examination were futile. In the latter part of 1927 she became bedridden. In February, 1928, twitching of the muscles of both sides of the face, the right leg and both arms was noticed. The right leg and both arms were held stiff, and pain was elicited on movement. The hands were held tightly clenched, the elbows were bent at an acute angle, and the right knee was also bent. The twitching affected all the muscles at different times in the parts mentioned. The right hand was clenched tighter than the left, and was cyanosed. There was incontinence of bladder and bowels, and on the 11th of May, 1928, she died. Her hospital residence had extended over a period of 6 years and 9 months.

Post-Mortem Summary.

The body was that of an emaciated woman, whose appearance was that of at least 70 years. The ribs were somewhat fragile. The heart was small, the valves normal, and the coronary arteries healthy. There was pneumonic consolidation of the right upper lobe, with commencing consolidation of the left lower lobe. The left pleura was adherent to the diaphragm, and to the chest-wall at the level of the sixth rib. The aorta showed slight atheromatous changes. The spleen was soft, otherwise the abdominal organs showed no abnormality

The dura was adherent to the skull. The meninges were normal, except for some congestion of the blood-vessels. Œdema of the brain was present. No marked atheroma of the arteries was noted,

The brain showed intense atrophy of the convolutions, especially of the frontal lobes, where the sulci were markedly widened. The pre- and post-Rolandic areas were well developed. The occipital convolutions were relatively small, but showed no atrophy. On removal of the pia-arachnoid, the convolutions, especially in the frontal areas, had a moth-eaten appearance. On section some degree of vessel congestion was observed, and a moderate degree of internal hydrocephalus was present.

Histological Examination.

The pia-arachnoid showed some proliferation, which varied in different areas, that of the frontal region being marked, while that of the occipital area was slight. The walls of the pial vessels had undergone degenerative changes, the middle coat being much thickened. This was most pronounced in the frontal area.

Cortex.—The band of vacuolation noted in the frontal gyri of Case 1 was also present in this case, and equally well marked. Other areas of vacuolation were present throughout the cortex, and in Ammon's horn the vacuolation had again taken the form of a band in this area running along the plexiform layer of the gyrus. The blood-vessels in these areas showed proliferation of their walls, and were very congested.

The choroid plexus was normal. Abundant corpora amylacea were present, but were not so numerous as in Case 1.

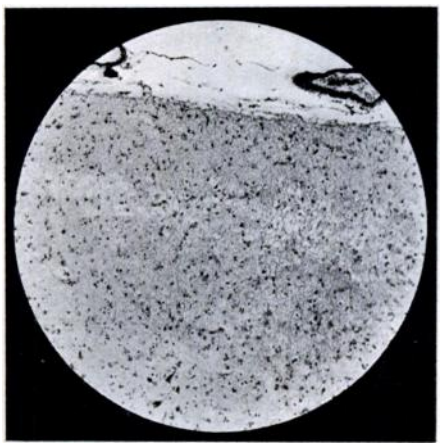
With toluidin blue there appeared to be a diminution in the number of cells of the cortex, especially in the frontal regions, where the architecture was to some extent deranged. Here the large pyramidal cells stood out well-stained in comparison with the other more poorly-staining layers. The Betz-cells appeared to be normal.

With Victoria blue no increase of fibrous glia was noted, although an increase in the number of small glia-cells was present. A degree of subpial felting and some granular ependymitis were also present in this case.

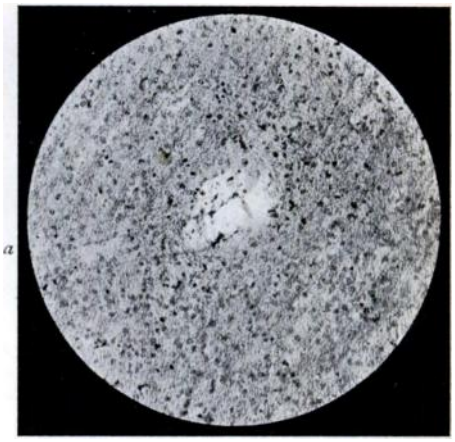
The increase of fat in the ganglion-cells noted in Case 1 in sections stained by Scharlach R was much more prominent in Case 2, and perivascular infiltration of the vessels of the cortex with "fat-granule cells" was a noteworthy feature. There appeared to be some rarefaction of the myelo-architecture in sections stained by Weigert's method.

Sections stained by Bielchowsky's method showed senile plaques in great numbers. These were abundant in the frontal, occipital and hippocampal gyri, and few in the Rolandic areas. The Betz cells were well preserved. Alzheimer's cells in all their forms could be seen in all parts of the cortex, but a large proportion showed the granulo-vacuolar appearance of their protoplasm described in Case 1. These could be seen interspersed with Alzheimer's cells. In the pre- and post-central and occipital gyri few Alzheimer or "granular" cells could be seen.

It is to be noted also that in the cortical regions the plaques were most abundant in the upper layers, and that the various

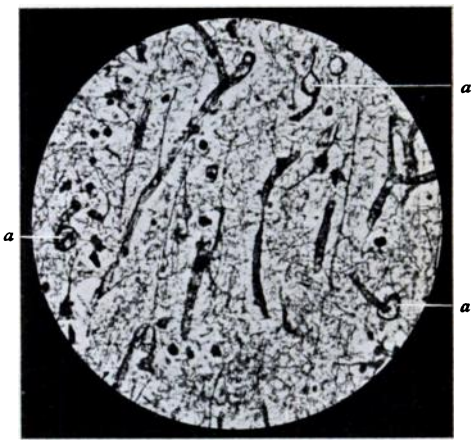


CASE 2.—Band of vacuolation in frontal cortex. (Hæmaulum and eosin.)



CASE 2.—Perivascular infiltration with (*a*) "fat-granule" cells in frontal cortex. (Sharlach R and acid hæmatoxylin.)

CASE 2.—Cells in plexiform layer of Ammon's horn. (Bielchowsky stain.)



CASE 1.—Parietal cortex. (*a*) Showing Alzheimer cell degeneration.

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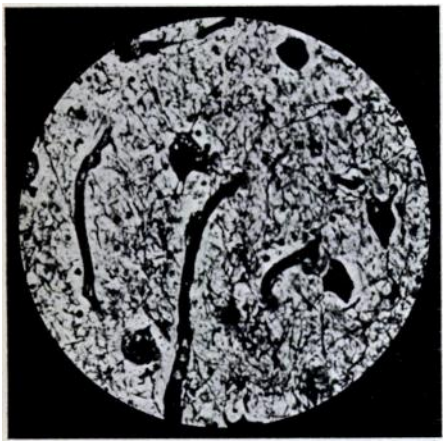
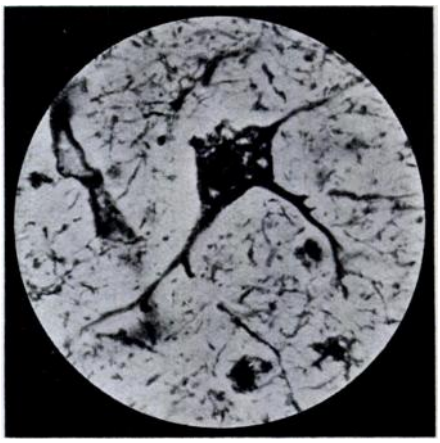
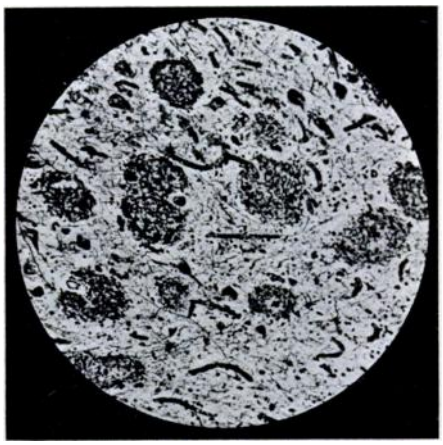


CASE 2.—Cells in right optic thalamus.



CASE 2.—High-power view of a cell in right optic thalamus.



CASE 1.—Senile plaques in Ammon's horn.

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degenerative changes occurred for the most part in the small and medium-sized pyramidal cells.

The cornu ammonis showed typical and abundant Alzheimer's cells—the most prominent form being that of thickened agglutinated fibrils, like bundles of wire. Senile plaques were very numerous in this area.

The basal ganglia showed noteworthy changes. The cells in the caudate nucleus, lenticular nucleus, globus pallidus and optic thalamus had undergone degenerative changes of varying degree and of the granulo-vacuolar type. The cells of the optic thalamus, because of their size and distance between each other, lent themselves admirably for detailed study. The greater proportion of the cells showed change similar to that described by Simchowicz. The fibrils appeared firstly to have become thickened, then so arranged as to give a honey-comb appearance of the cell. Later the fibrillary network beçame broken up into granules, the cell still retaining its processes and outline. At a later stage there was seen a darkly staining nucleus surrounded by a granular protoplasm, the processes being lost. Still later the nucleus dropped out, and all that remained of the cell was a collection of granules, distinguishable from their background by their deeply staining quality. This change, which conforms to Simchowicz's description, occurred in practically all areas of the brain examined, and in the spinal cord it was present in a marked degree. Simchowicz states that this change is closely allied to the cell-lesion of Alzheimer, but says that true granulo-vacuolar degeneration is only present in the pyramidal cells of Ammon's horn. Alzheimer's cells could be seen in these areas, but were few in number.

The cerebellum showed no plaques, and the ganglion-cells had undergone only slight changes.

In the cortex especially, the blood-vessels had a very hyperchromatic quality in sections stained by the silver impregnation method.

CASE 3.—*A married woman, æt.* 56, *who for a period of three years had been becoming forgetful, disoriented in all fields, and incapable of carrying out her ordinary duties. Later there was a phase resembling a delirium, which never completely resolved. There has been gradual physical and mental deterioration, along with paraphasia, perseveration, word-amnesia and dyspraxia.*

Mrs. K. K— or R—, æt. 56, was admitted to the Glasgow Royal Mental Hospital on March 19, 1930.

Family history was negative for nervous or mental disease.

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Personal history.—She was described as a healthy child, who had been exceptionally clever. She had worked as a clerk in a law office until the time of her marriage in 1900. She lived a quiet, happy life. The only incident of note in her history is to the effect that about eighteen years previous to her admission a neighbour had some kind of seizure while she was in the patient's garden, and this acted as a tremendous shock, so much so that the patient was for a few weeks in a nursing home. She made an excellent recovery, was active, interested and healthy.

Her *personality* was that of a methodical, conscientious wife and mother, who interested herself very much in everything pertaining to the happiness of her family.

Present illness.—In September, 1927, the patient had a great deal of anxiety in nursing her husband, who was ill with pleurisy, and it was noticed that she became forgetful, and had little appreciation of time. A gradual, progressive change took place. She did not know what day it was, talked of the members of her family as if they were still children, and it seemed as if she did not recognize them accurately. Her methodical habits had undergone a complete change, she was forgetful and confused, so much so that she would turn on the gas and not light it. She was restless at night time. Her former efficiency disappeared, *e.g.*, she was unable to do her shopping as she forgot her messages; she seemed unable to get the words she wanted to say, but there never was any indication of a stroke, nor complaints of giddiness. Later on she complained of headache, as if there was a band round her head. On December 17, 1928, her daughter was called home from her work, and on arriving found a smell of gas in the house. The patient was found going about with a lit lamp, and had been unable to find her way back to her room. She insisted that there were strange people in the house, and could not be convinced otherwise. She failed to recognize her husband, saying "Which of my uncles are you?" and asked him if he were going to Liverpool. She was apprehensive, as if she were hearing voices; she was suspicious, accused the family of being against her, and in addition her mental confusion was so pronounced that she was unable to dress herself correctly.

On January 30, 1929, one of us saw her in consultation in a private nursing home. She had little appreciation of time or place, and greeted me as an old friend, saying that she had known me quite well, whereas we were complete strangers. Her power of retention was so poor that in a minute or two she had forgotten what had been told her. She confabulated, described visual hallucinations, but said that she did not feel frightened.

Her tongue and skin were dry, her tendon reflexes were greatly exaggerated, amounting to a clonus when her knee-jerks were elicited. There was no evidence of any focal symptoms, but the condition seemed to be a delirious state, probably due to some toxic focus.

Later she was admitted to another nursing home, where the significance of her illness became more apparent. She was under observation for a period of approximately three months, and during that time no appreciable change took place in her condition. She never gained an accurate appreciation of time or place, had difficulty in naming things, used words in a peculiar way, had difficulty in finding the right words, and showed paraphasia and perseveration. The clinical state was typical of Alzheimer's disease.

Gradually the patient's condition became more aggravated, and when seen again on March 19, 1930, a further change had taken place. She still had no idea of time or place, or those around her; she called her daughter by a wrong name and referred to her son as "Daddy." She had become childlike, expressed vague suspicions, seemed depressed and frightened, saw reflections in mirrors, and talked constantly as if there were people about when no one was present. She complained of headache and backache, but there was no complaint of giddiness. She had been becoming more stiff and feeble in her movements, but there had been no indication of a stroke. At meal-times she frequently mixed up the articles which she wished to use, using a spoon when she should be using a fork. In every way she was much more enfeebled; she used peculiar words, and she was so obviously unable to care for herself that she was admitted to the Glasgow Royal Mental Hospital.

Physically she was a slightly built, rather frail lady of 56 years. Her pupils reacted briskly to light and accommodation, her visual acuity was good, her

hearing was good. There was a tremor of her facial muscles and tongue. The limbs showed a slight degree of spasticity, with a general exaggeration of all her tendon reflexes. Her blood-pressure was 160/120. Her pulse was 80.

Mental examination.—On admission she sat quietly in the reception-room. When spoken to she answered at once, with a slight smile, but her reply bore no relation to the question. She did as she was told. The following questions and answers give a good idea of her condition:

What is your full name? "No, that is the wrong way, and it always moves a bit. He was here when I was going to school at Calder Street."

When did you come here? "That's the bit I can't get just, but it will come. K— K— G—yes, yes. But it was cleaner in those old days than it is now. If you could give me a big bit to put together quick. I have never thought of having anything done."

Are you married? "Not again."

Question repeated. "Yes,—R—."

How long married? "This one here" (touching her ribbon).

The above sample shows the disjointed character of her conversation. There were times when she was quite unintelligible; there were other times when she had great difficulty in getting the word she wanted to say. She showed a certain amount of perseveration, *e.g.*, shown a pencil, and asked what it was, she replied, "A pencil"; when shown a handkerchief she called it a pencil. She could not say the days of the week or the months of the year, or count up to twenty. She could repeat single words, and groups of words like "It is a good day," but anything more complicated she was unable to repeat. Attempts were made to get her to read, but she complained that she was unable to do so. She was unable to read even the simplest commands, and made no attempt to execute written demands. Her attempts at writing were illegible—she merely scrawled on the paper and could not complete a word.

A further examination was made on May 17, 1930. She was unable to tell her name, but said, "Katherine is my middle name, but I think you could get as much out of it as R—'s tea tables a bit." Her face was noted as lacking expression; she spoke with a good deal of over-action of the muscles of the lower part of the face. She was very emotional and tearful, seeming to realize her condition. Further attempts were made to get her to understand written commands, but to no purpose; even when her name was written out fully in front of her she did not understand that this was her name.

A further physical examination showed marked tremor of the lower facial muscles. Her reflexes were noted as being greatly exaggerated, and the plantar response on both sides was equivocal.

A cerebro-spinal fluid examination showed no increase of cells, and Pandy, Ross-Jones, Wassermann and gold-sol tests were all negative.

CASE 4.—*A married woman, æt. 60, who for two years had shown a failure of memory, followed by a state of placidity and lack of interest, then a suspicious hallucinatory phase, akin to delirium. Her condition is now characterized by a variable, emotional state, accompanied by paraphasia, word-amnesia, and difficulty in understanding spoken speech.*

Mrs. E. S— or S—, æt. 60, was admitted to Glasgow Royal Mental Hospital on November 15, 1929.

Family history.—One brother had died from a cerebral seizure when he was sixty years old. An older sister died in a mental hospital in South Africa.

Personal history.—The patient is described as an ordinary child who developed normally. She trained as a nurse. She was very fond of her work, and had been matron of a small hospital for five years when she married. Her married life was happy. She had three children, all of whom are alive and well. She is described as a shy, retiring woman, but capable and industrious, a good wife and mother. She was well-balanced, even-tempered, ready to lend a helping hand where she

could; she took an interest in public affairs and her husband's work, and in every way she seemed a thoroughly well-balanced, sensible woman.

So far as her previous health had been concerned, she had been operated on ten years previously for a squint of her right eye, and for several years she had been treated for stomach trouble.

Present illness.—About two years previous to admission her memory began to fail, and her industry and efficiency to decline. She commented on her failure of memory and concentration and was distressed about it, but latterly came to accept it. She lost interest, and got out of touch with her former social activities, even with her own children.

In October, 1929, when her husband was from home on business, she suddenly developed the idea that he was in prison. She insisted on going to his office, where she created a disturbance, and stated that some of the office girls were away with him. Gradually her condition became more aggravated. She heard voices talking to her, and replied to them. She misidentified people and misinterpreted ordinary, everyday happenngs. When taken to an entertainment she was liable to get up in the middle and leave, saying that such and such a thing was indecent when there was no suggestion of indecency. This type of conduct was quite unlike her former self. Afterwards she appeared to have no recollection of such incidents. She became incoherent in her talk and was facile, foolish, and perpetually happy.

Medical certificates described her as being restless, noisy and excited; confused and delusive in her ideas, taking no active interest in her surroundings, unable to answer simple questions in a sensible manner, and peculiar in her actions.

Physically, she was a healthy-looking, well-nourished woman, who showed no gross disorder. There was a certain amount of slurring in her speech, but there was no disordered response, either of pupils or reflexes. Her blood-pressure was 160/120.

Mentally, she was quiet, and cooperated as well as she could. She did as she was told, and appeared contented, but failed to recognize that she was a patient in a mental hospital. When spoken to she had a difficulty in understanding, and often misinterpreted what was said; sometimes her replies would be to the point; usually they were irrelevant, and often she tended to ramble on in a disconnected, unintelligible way:

What is your full name? "Eh—what is it? as always—full age, name—I couldn't give you—I didn't notice you coming in here at all. You won't be able to see them."

Can you tell me what day it is? "Will it be Wednesday?" (Saturday).

What is the date? "The old date. We were going off for the day, but something came in the way."

What place is this? "I am in this place. It is Dr. Wilson's place."

What town is it? "I don't want any more of that."

She was unable to give any satisfactory account of herself. She admitted hearing voices, but very little reliance could be placed on her answers. The simplest questions she was unable to answer.

How many sixpences in a shilling? "No, I don't think so."

How many pennies in a shilling? "I don't know."

What are 2×2? She gave no answer, but spoke in a disconnected way.

At a staff meeting which was held on November 29, 1929, she gave her name correctly; recognized the place as one of the fever hospitals. She repeated test words, but with considerable difficulty and some confusion. It was noticed that she had a fine tremor of her tongue, facial muscles and fingers. She was able to carry out one or two simple orders correctly, but when the order became in the least complicated she was unable to do it.

Her Wassermann reaction was negative. In April, 1930, an aphasia examination was done.

She was able to understand and carry out simple commands, but with more complicated instructions she was not so successful; for instance, she was quite unable to do the "three paper" test. Her spontaneous speech was slow, but distinct. She recognized common objects and named them. She repeated the days of the week correctly. When asked to repeat the months of the year she said, "I am not very good at keeping it up." On being encouraged, she replied, "I am awfully dense at that part." She then got up from her seat and walked

away, but came back in a short time. She was again encouraged to say the months of the year, and was even given a start, but it was impossible to get her to continue. She was unable to count numbers from 1 to 20. When encouraged to do this, she said, " No, I have not the time ; it is too near the New Year time. You should give me something I have time to do." She could repeat simple phrases. She was able to read large print fairly well, but she failed to carry out instructions, even such simple orders as "Close your eyes," " Put out your tongue," etc. She was able to write her name, but made many mistakes when asked to write from dictation. She became perturbed and distressed by her failure. When asked to copy the printed word " cat," she looked at it and said, " It is a 'p' you put down first, isn't it ? " Then said, " Isn't it a 'v' next ? I forget how to make a 'v.'" Eventually she put "V" down, followed it up with the letter "F" and seemed quite pleased with her effort.

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