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A Further Contribution

To the clinic and pathology of presbyophrenic dementia — the paper in which Oskar Fischer answered his critics, counted forty ordinary brains, and found the threadlets to be protein

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Oskar Fischer

German Psychiatric University Clinic, Prague · 1912

Zeitschrift für die gesamte Neurologie und Psychiatrie, Originalien XII, 99–134, with one plate

A new English translation

Benjamin Aaron Gustafsson

AdultCognitiveDisease.com · September 2026

Two cases out of two hundred and seventy-five did not fit. Fischer kept them, and reasoned from them that a lesion must exist for a time before symptoms appear, that a certain degree of it is required, and — in a parenthesis — that the degree required probably varies between individuals. Then he went to the general hospital, took forty brains of the ordinary old, and counted.

The translation is complete and unabridged; the pagination of the original is marked throughout.

Contents

Translator's Note

The Translation

I. Seniles with Sphaerotrichia cerebri

II. Psychic illness in advanced age (from 50 years upward) without Sphaerotrichia cerebri (with the exception of the paralyses)

Supplement at the Correction

Explanation of Plate IV

Fischer's Notes

Translator's Note

This is a complete new English translation of Oskar Fischer's *Ein weiterer Beitrag zur Klinik und Pathologie der presbyophrenen Demenz*, published in 1912 in the *Zeitschrift für die gesamte Neurologie und Psychiatrie* (Originalien, vol. XII), pages 99–134, with one plate. The paper carries the line (*Eingegangen am 31. Juni 1912*) — received 31 June 1912 — a date that does not exist; Fischer's own footnote records that the work was presented in abstract at the annual meeting of the German Association for Psychiatry in Kiel on 31 May 1912, and the received-date is presumably a compositor's error for May, or for 30 June.

The 1912 paper is the sequel to the 1910 monograph *Die presbyophrene Demenz, deren anatomische Grundlage und klinische Abgrenzung*. It is the paper in which Fischer answers his critics — Alzheimer and Simchowicz principally, and in passing Obersteiner, Ziehen, Wada, Spielmeyer, Bielschowsky and Marinesco — reports a second series of cases, adds a control series of forty brains from a general hospital rather than an asylum, and sets out the solvent and staining experiments from which he concludes that the material of the plaque threadlets is a protein.

The translation is complete. Nothing is abridged or summarised. Fischer's paragraphing is preserved. His emphasis — set in the original by letter-spacing — is rendered here in bold. The pagination of the original is marked in the margin of the text as [99], [100] and so on, placed at the point where the original page turns, so that a reader working from the German can find any passage. Fischer's own footnotes are gathered at the end under *Fischer's Notes*; they are almost all bare citations, and are given as he gave them. Two bracket conventions run through the text and do not overlap: a **bold** bracketed number is the page of the original, and runs from [99] to [134]; a plain bracketed number is one of Fischer's twenty footnote markers, and runs from [1] to [20]. Anything else supplied by the translator appears in square brackets and is marked *Tr.*

Two classes of decision are worth stating plainly.

Terminology. Fischer's vocabulary is his own, and several of his terms have no modern English equivalent because the things he named were later renamed by other people. The policy here has been to keep his term, not to modernise it: to translate *Drusen* as **drusen** rather than as "plaques," and to leave *Sphaerotrachia* standing as he coined it. The reader who wants the modern name will find it in the table below; the reader who wants to know what Fischer thought he was looking at is better served by his own word. Where he uses a term that is simply older German for a thing we still have — *Achsencylinder* for the axon — the modern sense is given at first occurrence and his word kept thereafter.

Clinical language. Fischer's psychiatric vocabulary is that of 1912 and some of it is now offensive. *Verblödung*, literally a becoming-stupid, is rendered as "deterioration" or "dementing deterioration" according to context; *Irrenanstalt* is rendered "insane asylum," which is what it says. These have not been softened, because the register of the original is part of the evidence. One case history contains a coarse Czech expletive, transcribed by Fischer as a specimen of preserved speech in a patient who had lost ordinary language; it is translated as he translated it, and for the same reason.

Table 1 — Fischer's terms and their modern equivalents.

Fischer's term	Rendered here as	Modern equivalent
<i>Drusen</i>	drusen	neuritic (senile) plaques
<i>Sphaerotrichia multiplex / cerebri</i>	Sphaerotrichia	the plaque process as a whole
<i>Fädchen</i>	threadlets	the fibrillar material of the plaque
<i>Herdchen</i>	little foci	plaque foci
<i>Sterndrusen, Sternchen</i>	star-drusen, little stars	earliest plaque forms
<i>Keulen, kolbige Wucherungen</i>	clubs, club-shaped proliferations	dystrophic neurites
<i>Achsenzylinder</i>	axis cylinders	axons
<i>grobfaserige Fibrillenwucherung</i>	coarse-fibred fibrillary proliferation	neurofibrillary tangles
<i>Infiltrate, Infiltratstadium</i>	infiltrates, infiltrative stage	diffuse/infiltrative deposits
<i>Zipfje</i>	plaits	radiating fibrils of the corona
<i>Hof</i>	halo	plaque corona
<i>Morgensternform</i>	morning-star form	spiked-mace form of the core
<i>Merkfähigkeit</i>	capacity to register	anterograde/registration memory
<i>Merkfähigkeitsstörung</i>	disturbance of the capacity to register	amnesic syndrome
<i>Presbyophrenie</i>	presbyophrenia	amnesic-confabulatory dementia
<i>Aussaat</i>	seeding	dissemination of deposits
<i>marantisch</i>	marasmic	cachectic, wasted
<i>Anstalt</i>	institution, asylum	—

Three passages deserve to be found rather than stumbled upon, and are noted here because the modern literature does not quote them.

The first is on original page **102**: the argument that an organ lesion must exist for a period before symptoms appear, that a certain degree of the lesion is necessary, and — in a parenthesis — that the degree required is probably subject to individual variation. That is the latent period, the threshold, and individual reserve, derived in 1912 from the two cases out of two hundred and seventy-five that broke Fischer's own scheme, and published rather than discarded.

The second is on pages **105–106**: the reading of Case 12 alongside Case 33 of the 1910 series, in which Fischer proposes that an acute fresh crop of threadlet formation produces a delirium which can resolve, that the drusen persist and mature, and that a second crop produces a second delirium — a staged, episodic account of deposition, with a remission in which the brain is nonetheless diseased.

The third is the solvent series on pages **117–119**, in which Fischer establishes by exclusion — not dissolved by acids, not by alkalis, not by fat solvents, still demonstrable by aniline after xylol, ether, acetone — that the threadlets consist of a protein-like substance. He is arguing against Marinesco, who held the material to be lipoid, and against Alzheimer, who held that the structure was an artefact of the silver method.

The Translation

A further contribution to the clinic and pathology of presbyophrenic dementia.[1]

By **Oskar Fischer**.

(From the German Psychiatric University Clinic in Prague.)

With 1 plate.

(Received 31 June 1912.) [sic — Tr.]

[99] In the publication that appeared in 1910 in volume III of this journal, "Presbyophrenic dementia, its anatomical basis and clinical delimitation," I attempted, on the basis of a larger anatomically and clinically investigated material, to delimit a particular group of senile psychoses in which the brain change designated by me as *Sphaerotrichia multiplex* could regularly be demonstrated, and which could also be distinguished quite sharply in many respects, clinically as well, from the other forms of illness of the senium. It will be expedient if I now at once briefly adduce all the grounds that led to this classification.

It emerged that the peculiar little foci which had previously been seen only sporadically in senile brains (Redlich, Bloq-Marinesco, Alzheimer) are very frequently to be encountered in the senium, and that the Bielschowsky method permits, so to speak, a specific demonstration of them, whereas with most other staining procedures customarily practised they remain invisible. On the basis of the Bielschowsky method I was able to demonstrate that the little foci consist of finest threadlets, and a large series of formations could be observed which had to be construed as different developmental stages of these structures. In the surroundings of these peculiar little foci, which in part displaced the nervous tissue, the axis cylinders [axons — Tr.] were proliferated, often in large masses, in club form, and in addition there were found, particularly around the larger and older foci, proliferated and enlarged glial cells. About the origin of these little foci nothing definite could be said; it could only be established that the druse-like arranged formations stood in no kind of direct connection with ganglion or glial cells, and that the smallest formations — those [100] to be regarded as initial forms — were found lying quite free in the tissue, without any other alteration of the directly adjoining tissue portions. I have pointed out that we are so far not in a position to form a definite conception of the nature of these formations, but drew attention to the fact that they recall in many respects colonies of streptothrices (though — and this I should like to emphasise again — without my ever having presented them as actual bacteria), and declared that we have before us a pathological formation for which neither pathology nor biology can point to an analogue.

We thus had before us a particularly sharply characterised and very frequently occurring histological alteration of the brain; and the question, whether this particular brain change might not also go together with certain more or less independent clinical symptoms, followed as a self-evident consequence. A review of the clinical side of our material, carried out from this point of view, did in fact lead to results which permitted such a conclusion.

110 brains of persons over 50 years of age were examined (progressive paralysis not included). In 56 of them the process designated as Sphaerotrichia was found; of these, in 42 cases the typical picture of Wernicke's presbyophrenia came to observation: high-grade disturbance of the capacity to register with confabulations, in the greater part of them combined with delirious states. In the remaining 14 cases the clinical picture was: paranoid, manic and melancholic state-pictures, and finally symptoms of incoherence which in some respects recalled dementia praecox. Yet most of these cases had in addition more or less pronounced symptoms of Wernicke's presbyophrenia, so that these cases too could without difficulty be attached to the first group; the view that the paranoid, manic and melancholic state-pictures represent symptoms of a secondary kind appeared plausible already on the basis of these relations, presupposing that the results of the investigation of the remaining material agreed with it.

The counter-test with the remaining material yielded the following. Of the senile brains which contained no Sphaerotrichia, one part showed a simple, more or less pronounced atrophy; in the others, arteriosclerotic softening foci could be demonstrated. Clinically, no case of simple brain atrophy actually showed symptoms of presbyophrenia; as basic symptom in this group, to which 27 cases were reckoned, only a simple dementia could be demonstrated, to which in a smaller part of the cases **[101]** melancholic, manic and catatonic features had attached themselves. (For simplicity's sake a case of dementia praecox which had lived into the senium was also included in this group.) The group of pure encephalomalacias (without Sphaerotrichia) related to 32 cases; most of them showed clinically, with the exception of the direct focal deficit phenomena, only a simple dementing deterioration; 6 cases, however, showed quite distinctly symptoms of presbyophrenia, namely a severely disturbed capacity to register with confabulations, several times also combined with delirious states; usually, however, these symptoms were much more weakly pronounced than in the cases of the first group, and came to observation, interestingly enough, only when either very large cerebral deficits were found, or else multiple foci were present, particularly in the basal ganglia.

Finally, in 2 further cases the disease picture of presbyophrenia was found whose brain contained neither softenings nor Sphaerotrichia, but in which a quite excessive brain atrophy had developed, so that the convolutions presented themselves shrunk to a comb-like form. In one, a very severe arteriosclerosis was found as cause; in the other, a widely extended spongy cortical loss.

In a control material of 15 normal brains, and in 110 paralyses (among which were also several senile paralyses), no Sphaerotrichia could be demonstrated.

We accordingly had 3 groups of illnesses before us:

I. Cases with Sphaerotrichia and clinical symptoms which could without difficulty be combined into a particular clinical group.

II. Senile psychoses without Sphaerotrichia and without the clinical symptoms of group 1.

III. Cases which had symptoms similar to group 1, and in whose brain extensive and mostly multiple encephalomalacias were found, to which the 2 cases with the severe diffuse cortical atrophy attached themselves.

On the basis of this material I came to the following conclusion. Since in so large a number of cases the formation of Sphaerotrichia goes together with definite, clinically fairly uniform symptoms, we can hardly form any other conception than that of a causal connection of this anatomical brain change with the psychosis described; since most cases were pronounced cases of presbyophrenia, though some deviated from the type of this clinical form, I proposed the name **presbyophrenic dementia**. The name arteriosclerotic pseudopresbyophrenia I then proposed for that small group of encephalomalacias which had shown presbyophrenic symptoms.

[102] My material amounted at that time to 275 cases. This proposed classification now held for all cases save 2, which during life showed only a simple dementia without presbyophrenic symptoms and nevertheless had drusen in the brain; I should like to emphasise, however, that the seeding of the drusen in these 2 brains was very sparse in comparison with the other cases.

If a larger number of such cases had occurred, one could not have spoken at all of a clinical significance of Sphaerotrichia; but since these 2 cases represented only a quite minimal percentage, and the drusen were moreover rather sparsely developed, there emerged the view that a kind of latent brain change had here developed, which would have led to clinical signs only if it had come to a stronger development.

For it is surely self-evident that when some definite organic disease underlies a clinical symptom-picture, that disease must first, for a period of time, already exist before the clinical symptoms develop; and secondly, that a definite **degree** of the anatomical lesion is necessary; for the organ lesion always unconditionally precedes the clinical symptom-picture.

It is therefore surely plausible that cases will be found in which an organ disease is encountered without the expected clinical symptom-picture, particularly when the organ disease has attained only a slight intensity (which may well also be subject to individual variations). Something of this kind is generally known for somatic diseases, and the same has been demonstrated also for progressive paralysis (Alzheimer).

It could further be established as an interesting fact that a correspondence showed itself between the duration of the illness and the kind of the drusen. Already from the appearance of the drusen I had concluded that the different forms of them are likely to correspond to different stage-ages; in agreement with this, the clinical compilation then yielded the finding that the cases with short duration of illness also predominantly showed the younger stages, and those with longer duration of illness the older stages of the drusen. It further emerged that in the delirious cases, which must indeed be conceived as the most acute form, the severest degree of brain damage by the drusen occurs, in the form of the infiltrative proliferation of the threadlet masses. This circumstance must surely be conceived as a very important proof of the close connection between brain change and psychosis, and cannot be passed over so lightly as has hitherto happened in all discussions of this subject.

In the following period there appeared already a quite considerable number of works which occupied themselves with these changes; some [103] of my statements were confirmed; my view of the great clinical significance of Sphaerotrichia was, on the other hand, almost unanimously rejected as incorrect, at least in the version proposed by me. Before I enter upon a further discussion of this question, however, I should like to report on my further experiences, which I have had occasion to gather since the publication mentioned; for I have deliberately avoided intervening in this discussion earlier, before I could carry out, on the basis of a new material, a re-examination of my earlier statements, namely with regard to the reservations raised in the literature. Precisely with the questions which bear on the clinical significance of certain pathological changes, an exact clinical-anatomical statistics — if I may so call it — has the first and most important word; the regular coincidence of a definite pathological organ change with definite clinical symptoms yields with compelling necessity the conception of a causal connection; the more material stands at disposal, the smaller are the sources of error; only in the second place comes the consideration of how we can explain this causal connection to ourselves, and in this it always depends only on our previous knowledge whether we must accept such a connection resulting from the statistics merely as a simple fact, or can already understand it.

My newer material relates to the following cases.

I. Seniles with Sphaerotrichia cerebri

12 cases of typical presbyophrenia, that is, of amnesic symptom-complex with pronounced delirium, came to observation.

Case 1. Piša, Wenzel. 64-year-old . Onset: ? Observation: 9 June to 15 September 1911. Amnesic symptom-complex. Dementia. Delirious since July. On 24 August an epileptic seizure. *Macroscopic*: No brain atrophy. *Microscopic*: Not very abundant drusen of the older stages, but abundant infiltrates. No coarse-fibred fibrillary proliferation.

Case 2. Jirousek, Wenzel. 68-year-old . Onset: demented for 1 year. Observation: 8 August to 15 September 1911. Typical Korsakoff with delirium. *Macroscopic:* Brain strongly atrophic. *Microscopic:* Abundant drusen of the younger stages, in addition infiltrates. Sparse clubs. No coarse-fibred fibrillary proliferation.

Case 3. Scheffl, Marie. 70-year-old . Onset: ? [104] Observation: 21 March to 4 April 1911. Korsakoff with delirium. *Macroscopic:* Brain atrophy. *Microscopic:* Abundant drusen of all stages, among them also infiltrative stage. No coarse-fibred fibrillary proliferation.

Case 4. Tesar, Josefine. 71-year-old . Onset: half a year ago. Observation: 31 July 1910 to 19 February 1911. Manic state-picture; disoriented; confabulating and delirious. *Macroscopic:* High-grade brain atrophy. *Microscopic:* Abundant drusen, mostly in the frontal region, and infiltrates as well. Abundant coarse-fibred fibrillary proliferation.

Case 5. Hala, Ludmila. 71-year-old . Onset: demented and forgetful for 2½ years. Observation: 29 November 1910 to 12 January 1912. Dementia, confabulating and delirious, at first only at night, later also by day. *Macroscopic:* Distinct brain atrophy. *Microscopic:* Abundant drusen of various ages; infiltrates in the frontal region; no coarse-fibred fibrillary proliferation; sparse clubs.

Case 6. Voitl, Anna. 73-year-old . Onset: only a few weeks. Observation: 17 February to 3 March 1912. Paraphasia of sensory kind, amnesic symptom-complex, delirious. *Macroscopic:* Distinct atrophy, especially of the left temporal lobe. *Microscopic:* Abundant drusen mostly of older date, no infiltrates, sparse clubs, coarse-fibred fibrillary proliferation.

Case 7. Kurel, Therese. 76-year-old . Onset: for 2 years increasing dementia, at times epileptic seizures, confabulations. Observation: 31 March 1910 to 7 October 1911. Typical Korsakoff with delirium. *Macroscopic:* Distinct brain atrophy. *Microscopic:* Abundant drusen of all stages; infiltrates; no coarse-fibred fibrillary proliferation.

Case 8. Kadlecek, Marie. 79-year-old . Onset: ? Observation: 19 June to 15 September 1911. Typically amnesic symptom-complex with delirium. *Macroscopic:* Distinct brain atrophy. *Microscopic:* Abundant drusen of the younger stages, and abundant infiltrates as well. Sparse clubs. No coarse-fibred fibrillary proliferation.

Case 9. Bohatý, Marie. 84 years old . Onset: for 2 years increasing dementia. Observation: 15 January 1910 to 1 January 1911. Amnesic symptom-complex. Delirious since March 1910. *Macroscopic:* Distinct brain atrophy. *Microscopic:* Abundant drusen of all stages with the exception of the oldest; among them also smallest little stars and infiltrates. Coarse-fibred fibrillary proliferation.

Case 10. Rajtoral, Wenzel. 81-year-old . Onset: ill for 1 year; after an anxious affect at first anxious and then gradually demented. [105] Observation: 14 May 1910 to 24 February 1911.

Demented, disoriented, confabulating and delirious. *Macroscopic*: No noticeable atrophy of the brain. *Microscopic*: Abundant drusen mostly of older stage; no infiltrates, no coarse-fibred fibrillary proliferation.

Case 11. Krajic, Anna. 66-year-old . Onset: for about 1 year increasing dementia. For 4 weeks anxious, especially in the evenings, hallucinates figures which threaten her; sleepless. Observation: 25 April to 5 May 1912. Strongly senile individual. Severe disturbance of the capacity to register. Disoriented. Anxious; at night optical and acoustic hallucinations of persecutory content. In the last 4 days pronounced delirium at night, with anxious searching about in the bedclothes. Confabulations. *Macroscopic*: Distinct brain atrophy. *Microscopic*: Moderately abundant drusen, mostly of the older stages. No distinct infiltration stages.

In these 11 cases we have throughout the picture of the typical senile Korsakoff, the presbyophrenia of Wernicke, before us; in all cases the amnesic symptom-complex is associated with a delirious state. In Case 11 a kind of persecutory hallucinosis preceded the delirium, a circumstance which speaks for the close connection of the senile hallucinations with the Korsakoff.

Case 12. Kosař, Jakob. 68-year-old . Onset: acutely, some days ago, as delirium. Observation: 19 January to 20 January 1911. Shows the picture of a delirium tremens, with massive hallucinations and occupational delirium. *Macroscopic*: Distinct brain atrophy; an old hazelnut-sized softening in the lingual lobule. *Microscopic*: Abundant seeding of smallest star-drusen and massive infiltrates. No older forms. No coarse-fibred fibrillary proliferation; very severe cell change.

The case described last is in many respects important and interesting. In my earlier publication I have already pointed out that in most cases which ended with a delirium, abundant infiltrative seeding of the smallest threadlet formations, and of those already morphologically imposing as the youngest stage, was found. Since other druse stages occurred alongside them, it was obvious, and generally pathologically easily understandable, to bring the infiltrative formation of young *Sphaerotrichiae* into causal connection with the delirium. In this case, which began as a quite acute delirium and had previously shown no psychic symptoms, only the acute threadlet seeding was found, no older druse formations, which surely speaks for a close connection. To this attaches itself, as an important counterpart, Case 33 of my first investigation series; this was a senile woman who had likewise fallen ill with an acute delirium, and in whose brain a fresh seeding of *Sphaerotrichia* was likewise found alongside older drusen. It is now remarkable that [106] this patient had gone through a quite identical delirium a year earlier and remained healthy the whole year through, until the fatal second delirium overtook her. The peculiar findings in these 2 cases hardly permit any other conception than this: that **a quite acute fresh *Sphaerotrichia* seeding leads to an acute delirium which can pass over into recovery; the drusen persist in the brain, gradually assume the more mature forms, and when it then comes again to a thrust of threadlet formation, there arises anew a delirious state.** In this behaviour too we

would have a far-reaching analogue with progressive paralysis, in that **we have here a kind of remission before us, while anatomical proofs are present that the brain was diseased also in the remission.**

Case 13. Janouskovec, Anna. 56-year-old . Onset: for 2 years right-sided hemiplegia; in the last period become demented. Observation: 17 December 1910 to 31 July 1911. Severe dementia, forgetfulness, with a hint of confabulations; at night she is sometimes restless in a manner similar to delirious patients. *Macroscopic:* Old cystic softenings in the pons and basal ganglia. *Microscopic:* Sparse Sphaerotrichia of older stage.

Case 14. Abeles, Berta. 63-year-old . Onset: 12 and 3 years ago a depressive state which passed off after some months. Now depressive for 3 months after an affect. Observation: 2 January to 8 December 1910. At first hallucinatory-paranoid state with massive acoustic hallucinations of persecutory content, and since June increasing dullness and dementia. *Macroscopic:* Only hinted brain atrophy. *Microscopic:* Sparse drusen in various regions.

Case 15. Mastalka, Marie. 58-year-old . Onset: ? Observation: 3 December 1907 to 23 January 1912. At first anxiously confused, with hints of insight into the illness, then for a longer time depressive, and at the close complete dulling; in the process sometimes negativistic. *Macroscopic:* Sphaerotrichia of older date only in both frontal lobes. Sparse clubs. [The original heads this finding *Makroskopisch*, evidently for *Mikroskopisch* — Tr.]

Case 16. Indra, Anna. 63-year-old . Onset: depressive for some weeks. Observation: 24 September 1909 to 10 November 1911. At first anxious-depressive, then paranoid features emerged, finally the patient became stuporous with catatonic-negativistic features. At the close hints of hallucinations. Death from typhus. *Macroscopic:* No brain atrophy. *Microscopic:* Sparse drusen mostly in the frontal region.

Case 17. Dusatko, Johann. 73-year-old . Onset: ? Observation: 8 October 1909 to 30 January 1912. Patient is demented and slightly manic, occupies himself with all sorts of nonsensical building projects, in the process locally [107] not properly oriented; likewise he never knows how long he has been in the institution. An epileptiform seizure. Somatically old tabes, with arthropathy of the knee. *Macroscopic:* No brain atrophy, quite slight clouding of the meninges, grey degeneration of the posterior columns. *Microscopic:* Old tabes dorsalis. In the cerebral cortex fairly abundant Sphaerotrichia mostly of older date. Nothing of paralysis.

The last 5 cases show no clear clinical picture, and can accordingly not be reckoned among the typical psychoses without further ado; common to all is the high age and the dementia; nevertheless certain symptoms allow themselves to be picked out which make a clinical classification possible. Thus we see in Case 13, besides the dementia, a strong forgetfulness and a hint of confabulations and of a delirious nature; one can therefore see in it, even without artificiality, a disease picture

which, though not quite pronounced, leans upon the preceding cases.

Cases 14, 15 and 16 have in common that after an anxious-depressive beginning they fell, under paranoid symptoms, into very severe dementia. All these cases allow themselves to be ranged easily in the paranoid group of presbyophrenic dementia distinguished by me.

Case 17 is now the least pronounced; as far as the symptoms are concerned, it approaches most nearly to a progressive paralysis, since it is a matter of a tabetic with demented euphoria and manic notions in the sense of grandiose ideas; if we wish to range him in the system given in the previous work, we can without difficulty reckon him to the manic form, which besides the dementia exhibits manic features.

We see accordingly, from this material of 17 cases, that all the cases in no way step out of the framework of the earlier system.

II. Psychic illness in advanced age (from 50 years upward) without *Sphaerotrichia cerebri* (with the exception of the paralyses)

Case 18. Hais, Franziska. 60-year-old . Onset: for a longer time increasing dementia. Observation: 4 July 1906 to 19 April 1911; simple progredient dementia which had gradually heightened to the severest and deepest deterioration. *Macroscopic*: High-grade hydrocephalus with strong cortical atrophy.

Case 19. Havlik, Marie. 73-year-old . Onset: ? Observation: 21 March 1906 to 31 January 1911. From the beginning of the observation the patient shows nothing other than a dull dementia with catatonic features. *Macroscopic*: Strong cortical atrophy. *Microscopic*: Far-advanced spongy cortical loss of both frontal lobes.

[108] Case 20. Hlaváček, Josef. 55-year-old . Onset: ? Observation: 5 September to 27 September 1910. Showed only a very strong anxious stupor. *Macroscopic*: Slight haemorrhage of the meninges, slight atrophy.

Case 21. Kušta, Franziska. 81-year-old . Observation: The patient has already been depressive for 4 years, and during the observation too showed only an anxious depression. *Macroscopic*: Strong brain atrophy.

Case 22. Duben, Katharina. 70-year-old . Onset: The patient is ill for the 3rd time, first 3 years ago, then half a year ago, each time a short depressive state, and now for some weeks. Observation: 30 May 1905 to 30 November 1911; anxious-depressive, became at the close completely dull. *Macroscopic*: Slight atrophy of the brain.

Case 23. Konopác, Josef. 64-year-old . Observation: Severe anxiety state in a patient suffering for many years from tabes. *Macroscopic*: Old tabes. No brain atrophy; multiple small

meningeal haemorrhages of several weeks' duration.

Case 24. Hirschl, Johann. 64-year-old . Observation: 20–29 September 1910. After an affect an acutely arisen manic state-picture, with flight of ideas. *Macroscopic*: Only quite slight brain atrophy.

Case 25. Engländer, Markus. 83-year-old . Observation: 12–20 February 1911. Patient, who has been very forgetful for 1½ years, became in the last period dull and very demented, severely immobile. *Macroscopic*: Multiple softenings of the basal ganglia, distinct atrophy.

Case 26. Kocourek, Anton. 61-year-old . Observation: 8–15 October 1911. Onset acutely delirious, delirious for some days, then he got hemi-epileptic seizures which accumulated into a status epilepticus, and in which the patient perished. *Macroscopic*: No atrophy. The meninges thickened around some small vesicles; microscopically this proves to be a plastic meningitis which had formed around several cysticercus vesicles.

Cases 27–32 are throughout cases of sensory aphasia on the basis of softening processes in the temporal lobe. These are: 66-year-old ; 80-year-old ; 59-year-old ; 61-year-old ; 66-year-old ; 70-year-old . Since they otherwise offered nothing particular, they shall not be further described.

In these last 15 cases of various illnesses of the senium without Sphaerotrichia of the brain there were likewise found no symptoms of the kind which I formerly adduced as characteristic of presbyophrenic dementia. Only in Case 26 did we find a delirious state, which however is completely cleared up by the cysticercus epilepsy.

There shall further be adduced some cases which, in their anatomical and clinical behaviour, attach themselves entirely to the disease [109] picture for which I have proposed the name arteriosclerotic pseudopresbyophrenia.

Case 33. Feigl, Moriz. 67-year-old . Onset: 1½ years ago with forgetfulness and progressive dementia; repeatedly small apoplectiform attacks. Observation: 20 June to 19 November 1910. High-grade disturbance of the capacity to register with disorientation and confabulations; at times insight into the illness, hint of delirium. *Macroscopic*: Multiple softening foci in the basal ganglia. High-grade brain atrophy. *Microscopic*: Very slight change of the ganglion cells.

Case 34. Stein, Anna. 71-year-old . Onset: 3 years ago a stroke; increasing dementia. Observation: 12 April to 17 June 1911. Amnesic and optical aphasia. Disturbance of the capacity to register with confabulations and disorientation. *Macroscopic*: Far-reaching old encephalomalacia of the left occipital lobe.

Case 35. Merhaut, Franz. 74-year-old . Onset: ? Observation: 18 February to 9 April 1911. Disorientation and delirious state. *Macroscopic:* Several small softenings of the basal ganglia and haemorrhagic infarction of the cerebral cortex after repeated thrombosis of veins. *Microscopic:* Fairly severe cell changes.

Case 36. Klusáček, Katharina. 68-year-old . Onset: for half a year increasing forgetfulness and dementia. Observation: Manic euphoria; amnesic symptom-complex; delirious states at night. *Macroscopic:* High-grade atrophy, in which especially the frontal convolutions show comb-like shrinkages. *Microscopic:* Shows an atrophy of the cerebral cortex heightened to the highest degree, without spongy cortical loss and without arteriosclerosis.

These 3 cases too allow themselves to be ranged without difficulties among the cases of my first work; the first 4 are cases of extensive or multiple encephalomalacia (basal ganglia!), and the last case is almost quite identical with cases 108 and 109 of my previous publication.

Case 37. Krajíček, Johann. 57-year-old . Onset: blind for many years; psychosis arose quite acutely. Observation: 25 May to 3 June 1910. Was brought in delirious; apart from the blindness nothing somatic was to be noticed in him; after some days a croupous pneumonia showed itself, of which he perished. *Macroscopic:* Old softening of the right temporal lobe. *Microscopic:* Strong change of the ganglion cells.

In this case the delirium may well be traced back to the pneumonia, which in the first days is likely to have existed latently and without fever.

[110] Case 38. Stěrba, Marie. 65-year-old . Onset: for many years blind on the basis of a trachoma. For 4 weeks forgetful; delirious. Observation: 19 June to 10 October 1911. Forgetful, hintingly confabulating and delirious. *Macroscopic:* Very strong atrophy of the cerebellum. *Microscopic:* Quite strong disease of the ganglion cells.

This case is likely to be difficult to range; I believe that here the blindness is to be regarded as the most important moment, in the sense that, as is known, blind persons incline more easily to delirious states. A very severe cell change was present without a cause for it being somatically discoverable.

Very weighty, indeed perhaps even annihilating for my view of the significance of Sphaerotrichia, is the objection that in mentally healthy old people the same druse formations have been found (Constantini,[2] Oppenheim,[3] Hübner[4]).

But I have already emphasised at the time that the communication of such individual cases can have no significance, because from it no conclusion is to be drawn as to the relative frequency of such cases; for with this question everything depends only on whether such contradictory cases occur relatively frequently, or whether they are found so rarely that they must then be construed as

exceptions, respectively as anatomical latent forms, as I have already set out on page 102.

Therefore I have laid great weight on investigating a greater number of brains of normal old people. For obvious reasons the material was so chosen that brains of individuals over 60 years of age were investigated which originated from the local general hospital (thus not from the insane asylum) and which came to autopsy in the pathological-anatomical institute.[5] So far these have been 40 brains of persons whose age moved between 60 and 93 years.

These are the following cases:

I. 20 Sept 1911 · 78-year-old	IX. 28 Oct 1911 · 73-year-old	XVII. 7 Feb 1912 · 67-year-old	XXIX. 14 Mar 1912 · 83-year-old
II. 18 Sept 1911 · 63-year-old	X. 6 Nov 1911 · 64-year-old	XVIII. 14 Feb 1912 · 73-year-old	XXX. 14 Apr 1912 · 67-year-old
III. 21 Sept 1911 · 60-year-old	XI. 8 Nov 1911 · 78-year-old	XIX. 15 Feb 1912 · 83-year-old	XXXI. 11 Apr 1912 · 64-year-old
IV. 17 Oct 1911 · 81-year-old	XII. 15 Jan 1912 · 72-year-old	XX. 17 Feb 1912 · 79-year-old	XXXII. 14 Apr 1912 · 62-year-old
V. 15 Oct 1911 · 68-year-old	XIII. 23 Jan 1912 · 66-year-old	XXI. 19 Feb 1912 · 71-year-old	XXXIII. 23 Apr 1912 · 65-year-old
VI. 23 Oct 1911 · 81-year-old	XIV. 22 Jan 1912 · 60-year-old	XXII. 19 Feb 1912 · 63-year-old	XXXIV. 23 Apr 1912 · 66-year-old
VII. 21 Oct 1911 · 80-year-old	XV. 25 Jan 1912 · 66-year-old	XXIII. 20 Feb 1912 · 93-year-old	XXXV. 24 Apr 1912 · 76-year-old
VIII. 20 Oct 1911 · 78-year-old	XVI. 6 Feb 1912 · 67-year-old	XXIV. 20 Feb 1912 · 67-year-old	XXXVI. 24 Apr 1912 · 79-year-old
		XXV. 27 Feb 1912 · 76-year-old	XXXVII. 7 May 1912 · 73-year-old
		XXVI. 1 Mar 1912 · 64-year-old	XXXVIII. 6 May 1912 · 86-year-old
		XXVII. 2 Mar 1912 · 64-year-old	XXXIX. 14 May 1912 · 85-year-old
		XXVIII. 13 Mar 1912 · 68-year-old	XL. 15 May 1912 · 85-year-old

[111] Among these 40 cases the brain was found free of drusen 33 times; in the remaining 7 cases (VI, XI, XV, XVII, XXVI, XXXV, XXXVII) variously abundant Sphaerotrichia drusen allowed themselves to be demonstrated. It was now a matter of whether these Sphaerotrichia patients had

also actually appeared mentally healthy, for which purpose exact anamneses were taken about the behaviour of the patients in the hospital and with their relatives. The following emerged.

Case VI. 81-year-old ; marasmic for 1 year; several months before death forgetful, disoriented, confabulating, at night distinctly delirious, but so that she could just still be kept in the hospital (with a side-board on the bed). *Microscopic:* Abundant Sphaerotrichia drusen of various ages.

Case XV. 66-year-old . Was in the hospital only one day, was completely disoriented and delirious. *Microscopic:* Sparse drusen mostly in the frontal region.

Case XXXV. 76-year-old . Was in hospital because of a severe bronchitis for 4 weeks. According to the statement of the nursing personnel and of the physicians, he is said to have been quite quiet and "good," not disoriented, senilely dull, somatically very frail. According to the statements of the relatives the patient was mentally ill at home; disoriented, anxious, sleepless at night, always wanted to run away, and in the process always tied his bedclothes together into a bundle. Sometimes he hid himself under the bed and slept there. *Microscopic:* Abundant drusen of various ages.

All these 3 cases are typically presbyophrenic and must therefore drop out of the list of the mentally healthy aged.

Case XVII. 67-year-old . Was only half an hour in the hospital, brought in moribund. No anamnesis obtainable. *Microscopic:* Abundant drusen.

Case XXVI. 64-year-old . Died of a purulent meningitis which had attached itself to a phlegmon. Was correspondingly delirious with the meningitis. *Microscopic:* Sparse drusen and initial purulent meningitis of the convexity.

These 2 cases too must — as surely appears self-evident — drop out of the list of the mentally healthy aged.

Not quite clear appears

[112] Case XXXVII. 73-year-old . Was on an internal ward with left-sided hemiplegia, was quite dull, very marasmic; in the hospital itself nothing psychopathic could be observed. On the other hand we learned from the relatives that the patient had been struck by the stroke 14 days before his admission to hospital, recognised nobody any more, always wanted to climb out of bed at night, and because of this restlessness he was brought to the hospital. *Macroscopic:* A walnut-sized haemorrhage in the right-sided basal ganglia. *Microscopic:* Moderately abundant drusen of middle age in all brain parts.

Thus one cannot regard this case as mentally healthy, although the psychosis actually emerged only through the cerebral haemorrhage, so that the latter could be conceived as the immediate

cause. For it is indeed easily possible that if the patient had not suffered a haemorrhage and had died at the same time from another cause, he might perhaps have exhibited no striking psychotic features up to death.

Only in one single case of *Sphaerotrichia cerebri* could absolutely nothing of psychic disturbance be ascertained even on exact anamnesis.

Case XI. 78-year-old . Lay severely prostrate for 3 months because of marasmus and myocarditis, was also sometimes unclean, but showed nothing psychotic. *Microscopic:* Sparse older drusen only in both frontal lobes.

Cases VI, XV, XXXV, XVII and XXVI must completely drop out. Although Case XXXVII is not quite pure, I will nevertheless carry it as not psychotic; then we get, among 35 cases of clinically mentally healthy (non-presbyophrenic) aged, only 2 with *Sphaerotrichia*, which corresponds accordingly to a percentage of about 6%.

The ascertainment of such a low percentage naturally proves much more than the general statement that the said cortical disease is found also in mentally healthy aged. For if one sees on the one hand that patients with the symptoms of presbyophrenic dementia suffer almost without exception from *Sphaerotrichia cerebri*, and on the other hand can demonstrate that **only in 6% of mentally healthy aged (between 60–93 years) does the *Sphaerotrichia* appear, and there too only in weak intensity**, then one can assume nothing else than that the *Sphaerotrichia* can remain latent for a time, and that when its bearers die relatively soon, they also remain mentally healthy up to death; it is surely plausible that the intensity of the disease may in this be subject to individual variations.

A compilation of my entire material (from my earlier publication together with the cases now investigated and mentioned) yields the following relations.

[113] I. 59 cases of typical presbyophrenia with or without delirium.

II. 7 cases in which a paranoid state-picture stood in the foreground, but to which in almost all cases a more or less pronounced confabulatory amnesia, respectively delirious states, had been added.

Upon the closer clinical connection between delirium, disturbance of the capacity to register and paranoid states I have indeed already pointed earlier, and, as I have only later come to see, Heilbronner[6] has expressed himself similarly in a very interesting discussion of the traumatic and alcoholic psychoses.

III. 11 cases in which either manic, or melancholic or catatonic states showed themselves, and of which some also exhibited the other symptoms of presbyophrenia, though individual ones were

nevertheless to be missed.

We have accordingly 72 cases before us which I reckon to presbyophrenic dementia.

By contrast we see in 42 cases of psychic disturbance of the senium (in part only simple deterioration), in which no *Sphaerotrichia cerebri* was demonstrable, nothing of the characteristic symptoms of presbyophrenia.

Over against this, only in 2 senile dementias (one with and one without encephalomalacia), in which no presbyophrenic features whatever were demonstrable, were *Sphaerotrichia* drusen found — though, and this I should like to emphasise, in quite sparse seeding. We have therefore 112 senile psychoses which in every respect speak for the clinical significance of the *Sphaerotrichia*, and only 2 cases which nevertheless had drusen in the brain (albeit few, which I do not wish to take into account for the time being, although this too could weigh in the balance) and were clinically in no way to be diagnosed as presbyophrenic dementia. If we then see that among 35 apparently normal aged only 2 with drusen are to be found, then this quite low proportional relation of such exceptional cases must surely give food for thought. But even this so significant disproportion between *Sphaerotrichia* cases with and without mental disturbance could be used only with difficulty for the clinic if we were to find all possible psychopathic states in wild confusion in individuals who exhibit *Sphaerotrichia cerebri*; then it would be impossible to construct a new clinical entity. But if we see that the symptoms — disturbance of the capacity to register, confabulations, deliria, hallucinations and paranoid states — occur in 85%, and in such a way that one can nevertheless find a kind of transition of the individual sub-forms into one another,

[114] when then only 15% of the cases present manic, melancholic and catatonic states, and even among the latter repeated echoes of the symptoms of the first group are found: then we can easily unite all these states into one disease group, especially when it allows itself to be demonstrated that with all these states the same alteration (one can then hardly speak of a *circulus vitiosus*) is found in the brain.

I have already earlier pointed out that we represent a quite similar standpoint with progressive paralysis, where there are also cases which step quite out of the clinical framework of paralysis and attach themselves clinically rather to all other psychoses than to paralysis. Here, however, the clinical diagnosis is nowadays much easier, since both the so frequent somatic alterations and the serology and cytology show us the right way. With presbyophrenic dementia this is not yet the case; there we have for the time being no other aids than the psychotic symptoms. Thereby the diagnosis is under certain circumstances made very difficult, because the purely clinical symptomatology often fails with many diseases. Thus it will surely occur to nobody to base the diagnosis of a carcinoma, a tuberculosis, a typhus and so on **only** on the purely clinical symptoms, or to exclude such a diagnosis where these symptoms are lacking; precisely for therapy there are for example very important initial states in which clinical symptoms are still lacking and only serology, bacteriology,

radiology and so on must furnish the under certain circumstances probative points of reference for the diagnosis. And this can also hold for a time in which such diseased individuals still feel themselves quite healthy and in general still appear relatively little or hardly ill; with this kind of disease the concept of disease has indeed crystallised out of the experiences of the clinic and of pathological anatomy, but in such a way that the anatomical experiences were the decisive ones; also the experience that now and then some one of the indicated diseases shows another course or other symptoms than the bulk could alter nothing in this conception; in such a case we speak of atypical or **latent** disease, whereby in the latter case we form the conception, again resulting from experience, that when the process shall progress further, corresponding typical symptoms will still come to appearance; and finally it is again experience which teaches us that these symptoms come to appearance in different individuals very differently, even with quite far-advanced anatomical alterations.

To the material adduced hitherto there then come in addition the cases of arteriosclerotic brain destruction, of which I in total

[115] (material of both publications) was able to observe and investigate 44 cases. Of these, 10, thus 23%, had presbyophrenic symptoms without the Sphaerotrichia allowing itself to be demonstrated in the brain. These cases are thus the only positive exception, but can in my view not overturn the system set up, since under certain circumstances 2 different processes can also call forth similar disease pictures. Therefore I have already earlier summarised these cases as arteriosclerotic pseudopresbyophrenia, namely for the reason that one can also distinguish them clinically from the other cases. (Progression in thrusts, repeated apoplectiform attacks, focal symptoms, and mostly only slightly pronounced presbyophrenic symptoms.)

In supplement to the material adduced I will further mention that I have in the last period also investigated a greater number of other psychoses under 50 years, and paralyses, and could find Sphaerotrichia in the brain in none of the cases; these were so far in total 45 psychoses under 50 years and 136 paralyses of all age levels, among which 6 were over 60 years old.

I will now turn to the objections which have been raised by the individual authors against my expositions, whereby I shall naturally not enter further upon the works which already came up for discussion in my earlier publication.

There, in the first place, the work of Simchowicz is to be mentioned, which appeared almost at the same time as my earlier publication, so that the author could take account only of my first preliminary publication. Simchowicz,[7] who had worked up a large number of senile brains in the laboratory of the Munich clinic, comes to the result that the drusen, which he calls senile plaques, are only a consequence of the senile involution process in the cortex, and that they are regularly to be found in greater number in the cortex of the senile demented; a preference of presbyophrenia over simple senile dementia was not to be found. By contrast the drusen are found in mentally

healthy aged in sparser number, as a sign that a gradual transition from the normal senium to senile dementia exists. Simchowicz concedes the great significance of the Sphaerotrichia for senile dementia, indeed holds it to be characteristic, so that he regards the cases in which the plaques are completely lacking as belonging to other disease forms.

If we compare the results of Simchowicz with mine, we find hardly any fundamental contradictions; for Simchowicz too holds the "senile plaques" to be characteristic of a

[116] definite psychosis, only he calls this not presbyophrenic dementia but senile dementia; Simchowicz too finds in mentally normal aged now and then drusen, but always only in sparse number. It is now a disadvantage **that Simchowicz brings no case histories of the cases with Sphaerotrichia, so that one does not rightly know what he understands by simple senile dementia.** For according to my experiences there is found, in the cases of really deep simple senile deterioration without other disturbances (such as confabulations, deliria, paranoid and other states), a very far-reaching severe brain-cortical atrophy **but without drusen.** Precisely because these cases are relatively quite frequent, I have delimited them as simple senile dementias from the Sphaerotrichia group, for which I have proposed the name presbyophrenic dementia. Simchowicz would regard these cases as "belonging to other disease forms than senile dementia"; one sees, the difference lies chiefly in the designation and conception of senile deterioration without Sphaerotrichia cerebri.

Simchowicz has besides also a somewhat differing view about the structure of the Sphaerotrichia drusen, but I should like to settle this part of the discussion at the same time with the now following discussion of Alzheimer's work.

Alzheimer[8] raises against me the objection that it is not justified to attach significance to the appearance alone, as some Bielschowsky preparations show it; for, just as Hübner does, Alzheimer too sees the threadlet structures only relatively rarely; mostly one sees amorphous granular structures, a picture which the Mann-Alzheimer stain also shows. Upon the result of this stain Alzheimer lays — as it appears to me — the chief weight; with this stain one sees in the drusen a central core which is mostly homogeneous, and around this a halo, about whose formation Alzheimer does not express himself clearly, and in whose formation he in any case assigns a role also to the neuroglia. To this I should now like to reply that I find the threadlet structures not exceptionally but quite regularly, that no case has yet come before me in which one could not have demonstrated to anybody the composition out of finest threadlets, but that in most cases the structures are visible in just as distinct a manner as in my illustrations. The further objection too, that I had judged the appearance of the histological formations in question only after the staining results of a single method, the silver stain, I cannot accept as justified. For I have already in the first preliminary communication, but especially in the later presentation, expressly emphasised that the

[117] central core is quite distinctly stainable both with basic aniline dyes and with ordinary haematoxylin, and that with these simple methods too the threadlike structure of the same allows itself to be demonstrated almost equally distinctly; the plait-like radiations too can be made visible with these stains, whereas the threadlike structure of the halo does not come clearly to expression. I have in the last period endeavoured to perfect these simple stains somewhat, and, after formol or alcohol fixation, paraffin or celloidin embedding, using a dye mixture of methylene blue and methyl violet, obtained a demonstration of the Sphaerotrichia drusen which is in no way inferior to the Bielschowsky preparations, indeed in some respects even surpasses them; unfortunately the staining does not always succeed, but where it succeeds it shows pictures as in Plate IV; one sees, in the otherwise beautifully blue-stained cortical preparation, the drusen tinged luminously red-violet upon the blue ground, the central core has the accustomed morning-star form, and the plaits proceeding from it, as well as the little fibres forming the ring, are likewise coloured in a red tone and stand out sharply from the other tissue of the cortex. The arrangement is thus exactly the same as in the Bielschowsky preparation, only that the threadlets here appear somewhat thinner, which is easily understandable since the Bielschowsky staining has precipitate formation as its basis.

I have naturally also prepared preparations after the Mann-Alzheimer method. In these preparations one sees only rarely, and there too rather indistinctly, a differentiation into threadlets; most frequently only a bluish-opaque, slightly granular mass comes to demonstration. Under these circumstances the question, to which staining result one should give preference in the judgement of the structure of the drusen, will have to be answered somewhat differently; for in general one will always rather have to take into consideration the method which shows more details than that which can bring the structure in question to demonstration only blurred — all the more so when one can, as has also happened here, demonstrate **that with quite differently acting dyes and with different fixation and embedding always the same structures allow themselves to be demonstrated.**

Alzheimer stands upon the standpoint that the drusen arise in such a way that first the druse core forms by deposition of some as yet unknown metabolic product, and that this amorphous substance is only altered in various ways by the chemical reagents of our staining procedures. The possibility of such an origin is from the outset to be conceded; one must only

[118] consider whether certain experiences do not contradict this conception. My experiences actually hardly permit such an explanation.

A substance which is chemically and namely also physically altered in various ways by our staining procedures would surely also have to be attackable by the chemicals used in the staining procedure, or soluble therein. Already the circumstance that in a brain piece fixed in formol or alcohol and, after passage through ether, embedded in celloidin, the drusen allow themselves to be stained, as Plate IV shows, proves **that the substance of which the threadlets consist is not**

soluble in ether and alcohol. With the ordinary Cajal method the drusen indeed remain unstained, but they are not disappeared, since one can demonstrate them on after-staining with aniline dyes, as I have already communicated earlier. Also the small alteration of the method after Levaditi (Hauptmann,[9] Marinesco[10]), whose difference from Cajal's impregnation actually consists only in this, that the formol-fixed pieces are placed in alcohol before the silver mordanting, makes the Sphaerotrichia appear very beautifully stained out — a proof that the alcohol, applied also in this manner, does not dissolve the threadlets. Upon treatment of formol frozen sections with various solvents the following results: If formol frozen sections are placed in acids, alkalis or strongly concentrated salt solutions, or subjected to an oxidation with potassium permanganate with subsequent reduction by sulphurous acid, then upon subsequent treatment after Bielschowsky the Sphaerotrichia drusen allow themselves to be demonstrated exactly as without this pretreatment. If on the other hand one places such sections before the silvering in ether-alcohol, xylol or acetone, then the drusen sometimes remain completely unstained; **they are however not dissolved**, for they allow themselves in such sections still to be after-stained quite distinctly with aniline dyes (methyl violet, methylene violet, cresyl violet, carbol fuchsin) in the earlier threadlet structure.

The threadlet structure has thus not disappeared through the fat-dissolving agents; only the stainability with the Bielschowsky method has mostly (but not always) been lost. If on the other hand one places a quite thin little piece of such a cerebral cortex in xylol for a day (until it becomes transparent), then drives out the xylol with alcohol, places it for a day in formol and stains after Levaditi, then the drusen appear exactly as stained as without xylol treatment; the xylol has thus not dissolved the threadlet masses, which I should like to emphasise especially over against Marinesco.

The threadlets thus consist of a substance which

[119] is dissolved neither by alkalis nor by acids nor by fat-dissolving agents; it can accordingly hardly be a question of anything other than a protein-like substance.

Can we now assume that such a substance is not pre-formed, but arises only through the action of our reagents? I do not believe so. If we thereby see that the threadlets in question allow themselves to be demonstrated in identical formation after formol fixation as after alcohol fixation, then we can assume nothing else than that the threadlets are already pre-formed in the ordinary formol section (regardless whether with or without embedding); if we then further learn that in such a section the Mann-Alzheimer stain leaves the threadlets unstained, then we can explain the circumstance that in the Mann-Alzheimer preparations the threadlets are not visible not thereby, that they are lacking here, but only thereby, that the method does not bring the details of the Sphaerotrichia formation distinctly enough to demonstration.

I must therefore, despite Alzheimer's objections, remain with the assertion that the threadlets are pre-formed. (I reckon in this always with Nissl's equivalent-picture, since in the last instance almost all structures which we see histologically represent artefacts.) Whence, to be sure, the

threadlets, the basic element of the drusen, originate, and in what way the drusen enlarge themselves, remains in my view still unclear.

The circumstance that the drusen mostly arise in atrophic brains naturally permits the thought that it is a question of a metabolic product, and indeed most probably of a metabolic product which originates from the brain itself and is also deposited there; but this alone can hardly be regarded as proof; just so could one — *sit venia verbo* — regard a carcinoma as the direct consequence of senile breakdown, as consequence of a deposition of metabolic production. Incidentally I should like to point out that I have already earlier, exactly as later Fuller,[11] emphasised that the Sphaerotrichia (especially in the case where only initial forms were found) also affects brains which macroscopically allow no atrophy to be recognised and in which only a sparse glial proliferation allows itself to be demonstrated; and yet such brains are sometimes strewn over with threadlet formations.

Also with the view that the Sphaerotrichia represents the basis of a definite, clinically characterised disease picture, Alzheimer is not in agreement. He says about it: "The further question is now whether the drusen, or as Fischer expresses himself, the Sphaerotrichia, is to be regarded as cause of a quite definite classifiable and also clinically diagnosable psychosis.

[120] There are cases of undoubted *dementia senilis* in which the drusen are not very numerous; besides, the drusen, as Fischer himself emphasises, displace the nervous structures more than they destroy them. Thus in these cases the damage of the cortical tissue by the drusen can be no very considerable one. Further we also meet, in places where we found no drusen in the cerebral cortex, the known widespread senile alterations: sclerotic-fatty-pigmentous and granular degeneration of the ganglion cells, alteration of their fibrils, as Brodmann and Bielschowsky have described in detail, fibre formation of the glia, pigment accumulations in the glia, degenerative phenomena on the vessel walls, which we cannot possibly regard as caused by the drusen. We found alterations in the basal ganglia, the medulla, the cerebellum and the spinal cord, although there no drusen at all, or only quite isolated ones, are to be found. Thus we must surely come to the conclusion that the drusen are not the cause of senile dementia, but only an accompanying phenomenon of the senile involution of the central nervous system.

"Since however they seem to occur regularly in greater number with presbyophrenic dementia, while in high age without severe dementia they are found only isolated, they may have an essential significance for the histological diagnosis of senile dementia, just as we regard the diffuse infiltration of the lymph sheaths with plasma cells not as cause, but yet as important differential-diagnostic aid for the disease of the paralytic disease process."

First of all I should like to clear up a small misunderstanding which has here crept in; I have in my publication never asserted that the Sphaerotrichia causes senile dementia; according to the system of the senile psychoses which I set up there, the (simple) **senile dementia** is for me nothing other than a decrease of all mental functions **as consequence of a simple atrophy of the**

brain going beyond the normal limit, for in no case of simple deterioration of the senium of my material at that time did I find the Sphaerotrichia. For this reason I should like everywhere, where Alzheimer in the cited section has used the word *dementia senilis*, to insert the expression presbyophrenic dementia; for **for me the presbyophrenic dementia and senile dementia were (and still are) 2 completely different illnesses**, which perhaps stand in a similar relation as senile marasmus and carcinomatosis.

According to Alzheimer the Sphaerotrichia is nothing other than an accompanying phenomenon of the senile involution of the central nervous system, especially for the ground adduced by him, because in the

[121] cases concerned the drusen are not to be found in the whole nervous system, and yet the nervous elements of all sections of the central nervous system exhibited severe damage. This objection is however likely to be refuted by the clinical-anatomical statistics, which teaches us that the bearers of Sphaerotrichia cerebri also present common clinical features.

Into Alzheimer's work a second misunderstanding has crept, which concerns my utterance: "the Sphaerotrichia is to be regarded as cause of a definite psychosis." Upon the grounds cited above Alzheimer rejects this view as incorrect, since Alzheimer understands my exposition, after everything, to mean that I had the conception that the drusen quasi mechanically call forth the corresponding damage of the tissue. That I have formed no such conception is clear from the following: when I said on p. 449, "that the Sphaerotrichia is accordingly a disease diffusely affecting the cortex and damaging the brain in its total function," then in the sentence, "that in the Sphaerotrichia we have before us not only a peculiar and particular alteration of the brain, but a brain disease in the clinical and pathological-anatomical sense, and that we must regard it as cause of a quite definite classifiable and also clinically diagnosable psychosis," I did not have exactly the individual drusen before my eyes, but the sum of the alterations found in the brain in these cases, thus the **pathological process** that had thereby come about.

If I understand Alzheimer rightly, his argumentation goes in the direction that he assumes that the drusen are a quite particular and peculiar deposited metabolic product which is only an accompanying phenomenon of the senile brain involution. Now, supposing the case that the conception that the drusen are a metabolic product were correct, then there still results the following consideration. If the nervous system on the basis of the senium enters into an involution, then it comes to a material breakdown of the ordinary kind; if then in a percentage of the cases quite particular metabolic products show themselves which in every respect differ morphologically and chemically from the others, then we must surely form the conception **that the metabolism and material breakdown in the two groups will be quite different**; if then further the clinic shows us that these 2 groups of brain breakdown also run clinically differently, **then we have again nothing else before us than 2 different processes, 2 different diseases**; the one is

the presbyophrenic dementia, the other comprises the remaining senile psychoses, and this I should like for the time being (so long as no other differentiating moments allow themselves to be found) to designate as senile dementia

[122] *s. str.* or simple senile dementia, and thus have I also conceived it in my earlier work. It is therefore indifferent whether we regard the drusen as metabolic product or not; **always the disease process in a brain which exhibits drusen is quite another than in the simply atrophic brain.** In this I should like again to emphasise that the drusen can hardly be a metabolic product originating from the decay of nerve material; for apart from several other cases already mentioned in my earlier work, Case 12 of this work again proves the improbability of such an origin; for in this brain, which originated from an acute delirium, no atrophy was to be seen, the glia was only minimally proliferated, other alterations of the nervous parenchyma were also not present, and yet the brain was strewn over with large masses of the threadlet drusen, which for the greater part infiltratively pervaded the tissue.

As regards the other authors who have expressed themselves in this question, I should like to emphasise that hardly one of the authors has declared himself in agreement with my conception of the clinical significance of the Sphaerotrichia. Upon this question I need not enter more closely after what has already been discussed, since I stand upon the standpoint that the experiences on my already quite considerable material permit no other conclusions. A further discussion about the clinical side of this question will thus be possible only when elsewhere too a material collected under equal cautions and studied under corresponding points of view will be at disposal.

About the drusen themselves the various authors have expressed themselves quite differently. Obersteiner[12] and Ziehen[13] stand in their newly appeared textbooks upon the standpoint that the drusen consist of neuroglia. In a certain respect this holds indeed for the quite large Sphaerotrichia plaques with the strong reactive glial proliferation, but to designate the entire substance as glia will not do, because it is after all chemically and morphologically quite different from what we have hitherto conceived as glia.

Wada[14] conceives the drusen as necrosis, without however troubling himself about the whole developmental process of the drusen, which I have already given in my very first publication. This author appears not to believe my histological findings (not to speak at all of the interpretation), and without discussing the question any more exactly

[123] he explains the formation simply as necrosis; in any case the shortest conduct of proceedings.

As a curiosity I should like further to mention that some French authors have misread the original designation "*drusige Nekrose*" and imputed to me the concept of a "*nécrose glandulaire*." What one may imagine by that?

Spielmeyer[15] has in general the same view as Alzheimer; for him the druse is a deposition of a metabolic product and only a sign of a more abrupt breakdown of the nervous system in the senium. Bielschowsky[16] is of the view that the beginning of the drusen is a condensation of the glial reticulum (just as this had also been conceived earlier by Perusini), and that only into this plasma mass are the threadlets embedded. Bielschowsky supports himself upon preparations which are stained with cresyl violet, and I must hold against him the same as I did at the time also to Perusini: that one can see the very smallest druse formations only with the silver method, and that one can also then, when paraffin sections of piece-stainings after Bielschowsky or Levaditi have been very intensively after-stained, see nothing of condensation in the smallest star-drusen. Finally I should like to emphasise that no fundamental significance attaches to this question; for even if one had to regard this conception as proved, the nature of the threadlets would in no way be clear; in this one must also always keep before one's eyes that any such alteration of the glial framework around the drusen need not be primary, but can also be secondary. Marinesco,[17] who was in general able to demonstrate similar formations as I have described them, holds the substance of the druse to be lipoid — a conception which I, on the basis of the circumstances discussed on p. 118, cannot share.

In the discussion of the clinic and the histopathology of the senile psychoses one must also take into consideration the peculiar form of the senile psychoses for which Kraepelin[18] has proposed the name **Alzheimer's disease**.

The disease form develops, according to Kraepelin, first in the form of increasing dementia; then the patients become confused, disoriented; later a restlessness develops, such that the patients chatter, sing, laugh, run about, fiddle, rub, pluck, become also unclean; they show hints of asymbolic and apractic disturbances, do not understand demands, carry out no ordered actions; in this the speech is very severely disturbed; the patients are able

[124] to bring out perhaps still single words and sentences comprehensibly, but usually fall into a quite senseless babble which is similar to the logoclonia of the paralytics, and which Kraepelin conceives as a form of perseveration. Gradually this babble dissolves into a completely incomprehensible sequence of mostly senseless syllables. The close is complete dulling and deterioration.

As anatomical basis Alzheimer found in these cases a severe brain atrophy with massive druse formations, and the disease of the ganglion cells later designated by me as coarse-fibred fibrillary proliferation.

Alzheimer has in his already repeatedly cited work by contrast pronounced against conceiving this disease form as a particular disease, but regards it as an atypical form of senile dementia. The most peculiar thing about these cases is the strange speech disturbance, which lifts them completely out of the framework of the other illnesses of the senile psychoses. I have already had occasion to investigate 4 such cases clinically and anatomically; 2 of the cases are already contained in my first

work, which was already in print when the relevant edition of Kraepelin's textbook appeared; these are Cases 55 and 56, whose case histories shall now be adduced *in extenso*.

Case 55. Novák, Johann, 66-year-old . Observation: 10 June to 3 August 1907. *Anamnesis*: Nothing of heredity; for 5 years an increasing dementia shows itself; for 4 years in the poorhouse, since which time he spoke quite senselessly. Admitted because of nocturnal restlessness.

In bed the patient is constantly occupied in a delirious manner with his bedclothes, and in the process mutters something continually to himself, which at first sounds like a completely incomprehensible stammer, since it is uttered quite blurred, but which on attentive listening allows itself to be recognised as a mixture of quite senseless, ever-repeating syllables, thus: *je — je — je, ta — ta, ta, ca — ca — ca, ma — tscha — tscha, tscha — tscha, de — de — de ...*

If one draws him into a conversation, he stops at every question and then promptly sets in again afterwards with his jargon, almost as if he had wanted to give an immediate answer; this procedure is the most frequent; sometimes, however, he repeats the last words of the question echolalically, then usually repeats them a few times and comes again into the stammer. Sometimes, however, he reacts to questions with quite correct linguistic reaction; these correct linguistic reactions do not relate to definite times, but are found suddenly in the examination, whereupon then at once the jargon sets in again.

At night he is mostly delirious, speaks more comprehensible words; mostly he apostrophises (to all appearance) hallucinated persons.

The state remained on the whole unaltered, and the patient perished of a phlegmon. [Fischer here gives a specimen of the patient's speech, partly in Czech; the exchange includes a coarse expletive, delivered fluently and correctly at a moment of irritation while ordinary language was lost. Fischer supplies a German translation and notes that a rendering was in places quite impossible because the utterances turn on sound-permutations. — *Tr.*]

Case 56. Zamrazil, Katharina. 65-year-old . Observation: 16 November 1907 to 13 July 1908. *Anamnesis*: Since the death of her husband (8 years ago) she gradually became demented; 3 years ago the dementia was already so deep that she no longer recognised her relatives; 3 months ago the patient had an epileptic seizure, and since that time she speaks and cries in a constant sing-song quite incomprehensible stuff together.

[125] Left to herself, she sits crouched in bed and sings softly to herself; there are various little songs which, as far as the melody goes, she mostly sings to the end, frequently repeating them again and again, but also often beginning again at once after the ending; as text it is in part the correct text, but in part she interweaves fragments of the Lord's Prayer, whose individual words she at first pronounces correctly, then permutes single ones out of them, whereupon finally a quite senseless jingle of syllables results, which she substitutes as text for her little songs; this frequently breaks off

abruptly, whereupon then eventually the correct text comes to appearance again. In this she rubs continually, in quite even rhythmic tempo, her hands one against the other, on the thighs, on cheeks and chin. In addition she fiddles, likewise in constantly repeating uniform manner, at her bedclothes.

[A sung specimen follows in Czech, in which fragments of the Ave Maria and the Lord's Prayer alternate with senseless syllable-strings; Fischer gives a German rendering and marks the passages he found untranslatable. — *Tr.*]

[126] When one addresses the patient, she mostly stops with her chatter; now and then she takes up one of the last words of the questioner, permutes it, and then perseverates the individual syllables. It nevertheless happens quite frequently that she understands the questions put and reacts to them. Thus, when a question is put to her and she does not answer, and one repeats the question several times, she becomes visibly angry and says: "Now wait, stop it." Some samples of correct answers: to the greeting "Good morning" she says promptly: "Good morning, I wish."

Where she comes from? Yes, just wait.

How old she is? An incomprehensible murmur comes.

Why she does not answer? Says angrily: "But I have already said that several times."

How old she is? Looks dully before her.

After repetition of the question she says, as if angry: "I understand it well enough, when I cannot, cannot."

Whether she can pray? Prays everything.

To objects presented she pays no attention, does not heed them at all; if they are pressed into her hand, she at once lays them away.

Very frequently it makes the impression as if the patient saw nothing at all; she stares constantly dully before her, does not heed what happens around her, reacts only to acoustic stimuli; even when one shines a light into her eyes she does not blink once, only when a light was shone directly into her eyes with a Nernst lamp does she say, turning away: "Sun."

The ocular fundus is however completely normal. Somatically also nothing particular.

She must be fed, since she throws the food about and smears it; she is completely unclean. She does not recognise her daughter, does not heed her at all. At night she is mostly restless, speaks much, wants to get up; the stereotyped rubbing movements are in this somewhat livelier.

On 21 December 1907 a general epileptic seizure, without the patient's condition being thereby altered. Later the patient becomes quite marasmic, completely dull, speaks already almost nothing more, and perishes of a collapse.

The clinical registration of these 2 cases was not easy. The leading thing for me at that time was in the first line the anatomical substrate, the Sphaerotrichia in the brain, especially for the reason that certain symptoms did allow themselves to be picked out whereby these 2 cases recalled the others in many respects. Especially was this, in the 1st case, the quite pronounced delirious restlessness and the constant fiddling about, which latter the 2nd case also showed. Also the circumstance that the illness exhibited severe progression, so that in Case 2 there finally resulted complete dull apathy and deterioration, spoke for it; for even individual quite typical cases have finally ended with fullest dulling and deterioration. (As Cases 34–41 in the earlier publication.) Very difficult, however, proved the question how the speech disturbance is to be conceived, respectively to be explained.

As organic disturbance of the kind of one of the known aphasia forms this speech disturbance was not properly to be understood; at first sight the patients did indeed make the impression as if they suffered from severest sensory aphasia with quite senseless paraphasic jargon; it had the appearance that they neither understood the words uttered before [127] them nor were able to answer them in any way; but a more thorough occupation with the patients showed that they nevertheless repeatedly heard and correctly apprehended demands and questions, only one had to stimulate them constantly by name through repeated questioning; in this one had precisely the impression that it was not the speech which was essentially disturbed, but that the patients are so inattentive and indifferent towards everything that happens around them, and that only then does a stimulation of the attention lead to correct understanding and answering. The whole behaviour of the patients awakened the impression that it is in the first line a matter of a disturbance of the attention. Besides, the whole form of the speech disturbance recalled most nearly individual ones of the rare severe forms of speech disturbance of dementia praecox, where with severe speech confusion a quite senseless word- and syllable-salad is produced; there too we see alliterations, permutations and perseverations of the most various kinds, very frequently leaning upon certain heard or correctly uttered words. Since moreover, especially in Case 56, certain features of motor stereotypies came to observation, and in some of the other cases other features of dementia praecox were also found (namely in Case 5), I have also conceived the 2 cases with the described speech disturbance as a catatonic sub-form. In this, naturally, the "catatonic" should for the time being mean nothing other than the reference to a superficial similarity with certain features of dementia praecox.

I should like now to communicate two further typical cases of this disease form, which I have had occasion to investigate since that time.

Kriesch, Barbara. 73-year-old . Observation: 3 June to 31 August 1910. *Anamnesis*: No heredity. For about 4 years a gradual dementia developed; for about 3 years abscess-like states appeared, and also about since that time she no longer recognised her son, spoke "senseless stuff" together, was unclean.

Left to herself in the sickroom, she lies in bed, is continually occupied with the blanket or with the shift, crumples it together or plucks at it, pulls at it in a uniformly repeating manner to and fro; at times she likewise makes uniformly recurring rubbing movements on various parts of the body. As one approaches her, she begins to chatter: in very rapid tempo she speaks then before herself — sometimes so as if she wanted to tell the person standing by her something — a completely incomprehensible something, which consists in part of quite senseless syllables, which either change rapidly one after another or again are uniformly perseverated; at times the speech is so rapid that it comes to no proper articulation, but everything flows into one another in the most rapid tempo; here and there, however, one understands one or the other correct word, upon whose syllables sometimes the next syllables of the word-salad lean themselves. The conversation has at first the tone of a correct narration; later it becomes ever more monotonous and degenerates finally into a quite monotonous sing-song. When she is addressed, she always stops, but attaches herself to the question mostly so promptly that one would believe she wished to [128] answer; in this it mostly makes the impression that she does not understand the question; sometimes she repeats the last words of the question echolalically, but then attaches her jargon at once. An example of such an examination (the patient spoke German):

What is your name? "Yes I am called call," and now it passes into a quite incomprehensible syllable-murmur, into a "*taratarata*."

What her husband was? "Yes it was later always *tararara tamtarara*, he has said *tamtarara* it will be quite good *tamtarara*" (these last words are repeated several times), "that is false, must be also cooked again so, I shall bite such people" — and thereupon she becomes quite incomprehensible.

Meanwhile her son is spoken of, and there appears in her incomprehensible jargon the word "Karl," and then after a quite senseless syllable-salad a further fragment, and again something incomprehensible.

Who Karl is? "The Karl, the Karl — the Karl is the Karl, is indeed with us, no, that is the Karl and the uncle."

What time is it? "I believe 9 five-ers is he in this."

To objects:

Bread! "That is the good, the good, the goodest, fresh, that is delicious."

Roll! "That is more edible, light."

Flat-iron! "Yes yes that is indeed so beautiful, beautiful, I am not so old any more, I am old, I am old flesh."

Little basket! "That is a little basket."

A very large roll! With laughter: "Those are perhaps specially made."

A cross! "Yes that is Christ."

Crown! "That is 10."

Candle! "Yes that is 20."

Matches! "That, that is drift-wood, you are indeed the friend."

As the attendant enters, she says: "Kiss the hand, Miss!" Single numerals she reads correctly, likewise also single words; to writing she is not to be brought, as indeed to no action at all.

She is altogether very inattentive, reacts to most questions not at all, so that one mostly has the impression that the patient does not understand the question at all; suddenly, however, she reacts to several questions one after another, sometimes even isolatedly so, that one unconditionally gets the impression that she understands the questions and attempts to answer them; after each of the answers, however, she comes, as already repeatedly mentioned, into the hardly comprehensible jargon.

That she was not sensorially aphasic is proved among other things by the following: In an examination she was told quite softly, as something everyday, without emphasis, that her son was dead; she at once fell thereupon promptly into affect, which heightened itself still further when one says to her that she is to be hanged; there she begins to weep and brings out in her gibberish quite distinctly: "she has done nothing, one should believe her, she has after all done nothing to anybody," and lets herself thereupon be calmed only with great difficulty. When behind her a cap-pistol is fired, she starts and says: "Jesus Maria, what are you doing there."

On 18 June she had a general epileptic seizure, without her condition being otherwise altered thereby.

[129] On 30 August seizures appeared again; afterwards she is comatose and perishes on the following day.

Richter, Anna. 53-year-old . Observation: 11 October 1909 to 21 June 1911. *Anamnesis:* No heredity. 2 years before admission (thus in her 49th year of life) a gradual dementia was noticed, until she became unclean and constantly wanted to run away. For some weeks epileptic seizures

showed themselves.

Somatically the patient is senile-marasmic, for her age very aged, otherwise nothing particular.

The patient shows a speech disturbance similar to that of the preceding cases. She is attentive, listens to questions put to her, answers however most of them with a completely incomprehensible jargon which consists of quite senseless, in the process hardly comprehensibly uttered syllables and of mutilated paraphasic words. Here and there a correct word appears therein. To single questions, however, the patient reacts with quite correct answers; sometimes it comes to such an answer that at first a correct beginning with quite correct and correctly placed words is taken, upon which however very soon the jargon attaches itself, which does not end earlier than when the patient is interrupted.

Objects shown she recognises correctly, designates them in part correctly, in part paraphasically, in part however she also gives quite senseless answers there.

The same goes on with reading; to writing she is not to be brought.

Pronounced ideatory apraxia, whereby one gains the impression that the patient forgets the individual parts of the action and therefore acts apractically.

Left to herself the patient lies scarcely quiet; she creeps constantly out of the bed, tugs at her bedclothes, wants always to undress herself and then again to dress herself, crumples everything she can reach into bundles, or wants again to throw it away; in short, she is always busily occupied; in this she murmurs before herself in her incomprehensible jargon. At night she is always livelier, whereby the occupation makes the impression of an occupational delirium; at times she also speaks a great deal at night, and indeed she then speaks much better than otherwise, so that in this delirium one hears only rarely jargon-words or paraphasias; mostly she speaks then to delirious persons, whom she treats with all manner of terms of abuse.

In April 1910 her speech becomes striking in that she very frequently repeats single, quite senseless syllables in the paraphasic word-flood, and in the process sometimes also permutes them.

She has repeatedly epileptic seizures, thus on 8 July, 9 July, 6 November and 7 November.

In January the speech disturbance becomes such that she brings out always only single comprehensible words; then comes a quite incomprehensible gibberish arisen through permutation and perseveration; in part however the origin of this syllable-salad is quite incomprehensible.

[130] Objects shown she names only when one puts before her a plate with food; she says then promptly: "That I like!"

Then suddenly everything is thrown from the table onto the ground before her, and in the process a great disorder is made; she remains standing before it smiling, claps her hands together

and says finally something quite incomprehensible ("that is that, that is terrible").

Then with a great crash a chair is thrown onto the ground; astonished, she looks at the physician and says as if deliberating something incomprehensible ("what — what — what — what lies there, that").

What her name is? Something incomprehensible ("but you know, know, know").

On 12 February, 28 February and 17 March a general epileptic seizure. Gradually the patient becomes somewhat duller, but otherwise unaltered in speech; and perishes under increasing marasmus on 21 June.

In all the 4 cases we recognise the picture which Kraepelin has so aptly drawn for us in his textbook. Of all the symptoms which we encounter, the speech disturbance stands out most, which to my knowledge scarcely occurs in like manner with any other disease. It develops in such a way that the patients at first persevere single words, then they persevere only single syllables, always in connection with spoken or heard words; further it comes to transformations of the syllables in permutatory manner, in that the individual sounds out of which the syllables are formed are exchanged, whereby senseless syllables arise which are constantly repeated, and finally there results an incomprehensible jargon which is sometimes spoken so hastily that one can no longer understand the individual syllables either. **Characteristic, however, is that the patients, right into the time of the severest speech disturbance, can often unmediatedly, often upon stimulation, bring out quite correct and correctly placed words.** Quite similar is it with the understanding; there are times when one can in no way come into contact with the patients, they appear to understand speech, writing and gestures not at all, respectively they heed nothing — indeed it very often makes the impression as if the patients were quite blind (Case Zamrazil on p. 125); then again it happens that they understand, see, observe. Something of this kind shows in general none of the known aphasia forms, so that it would be quite difficult to trace this speech disturbance, as would appear plausible at first glance, back to a temporal lobe disease. Also the anatomical finding does not speak for this conception; for a quite especially prominent disease of the temporal lobe is not present; in all the cases the entire brain is affected in exceedingly strong measure by the Sphaerotrichia and by the coarse-fibred fibrillary proliferation of the ganglion cells; also in most cases the frontal and the temporal lobes are somewhat more strongly diseased, but one of the

[131] named cases shows precisely in the temporal lobes comparatively much lighter alterations; the experience that a whole number of the other presbyophrenic dementias also have such strong alterations in the temporal lobes then speaks in a certain respect against the conception that the speech disturbance is of focal nature. The diffuse disease (perhaps of the whole temporal lobe) is likely to be the decisive moment.

The motility stands, similarly as the speech disturbance, quite under the sign of perseveration, in that the patients repeat single gestures in ever-recurring monotony, which recalls most nearly the ever-recurring stereotyped movements of some dementia-praecox patients; in this the patients often have a manner of expression which one could most nearly compare with a catatonic mannerism, as when for example the patient Kriesch says on being shown a roll: "That is more edible."

Analogous to the speech disturbance are surely also the apractic disturbances; for these too come to appearance only at times and call forth the impression that they are for the greater part conditioned by a very far-reaching inattention. Quite characteristic for this form is that the patients lie there quite dull, are at most occupied with only some gestures and linguistic stereotypies, and take no notice at all of the surroundings, appear to understand nothing at all; but as soon as something quite particular happens in their surroundings — such as the mentioned throwing down of the plates, or when one said to the one patient she was to be hanged — one does see a quite corresponding reaction; in any case a sign **that the disturbance is for the greater part based upon a very far-reaching impairment of the attention**;^[19] it is clear that still other moments play a part, but of what kind these are is likely for the time being still not to be quite clear.

Only this disturbance of speech and of action is what distinguishes these 4 cases from the other cases of presbyophrenic dementia; in the other symptoms they come very close to one another, and indeed: repeatedly delirious states occur; the fiddling about at the bed-linen I should like also to conceive as an echo of the delirious restlessness, because this remains behind in many presbyophrenic dementias that have become demented, after they have gone through a delirious state; the progression, which then, when the patients live to see it, leads to severest deterioration — all these are circumstances which allow these forms to appear to me, namely also on account of the

[132] common anatomical basis, as a sub-group of the presbyophrenic dementia.

As Alzheimer already mentions, these patients are relatively young; Alzheimer's first case fell ill in her 40s; of our 4 cases, 3 fell ill in their 50s, whereas one case fell ill only at 70 years; the circumstance that also individuals standing in high senium can fall ill with this form was also one of the grounds why Alzheimer will not conceive this form as an independent illness, but as an atypical form of senile dementia, the latter also because, as he emphasises, also the severely demented end-state offers nothing characteristic for this form, but occurs also with other forms of senile dementia; this is shown also by Cases 34–41 of my first series, whose course was typically presbyophrenic and which ended with an almost equally far-reaching deterioration and dulling. Because I should like to reserve the name senile dementia, as I have already emphasised above, only for the simple senile deterioration, these cases belong, also on all the other clinical and anatomical grounds already mentioned, to presbyophrenic dementia, in which they form a particular sub-group; one can then call them, in attachment to Alzheimer, atypical. Incidentally I should like

still to remark that three of my four cases had, interestingly enough, epileptic seizures; this occurs indeed also with the other forms of presbyophrenic dementia, but there much more rarely.

Also from the anatomical standpoint these cases have something particular about them: the brain atrophy is, as Alzheimer has emphasised, mostly more strongly pronounced; the Sphaerotrichia has occupied the entire brain in enormous masses; the nervous parenchyma, especially the ganglion cells, are severely altered, namely in the form of the coarse-fibred fibrillary proliferation, which appears to be missing in no case; it does indeed occur also in the other cases, but yet much more rarely; thus according to my earlier material only in 17%, according to the present in 21%. The clubby proliferations of the axis cylinders are however not so regularly present in this. Precisely the coarse-fibred fibrillary proliferation signifies a quite especially severe disease of the ganglion cells, which is surely to be regarded as a process leading to the destruction of the cells. Alzheimer is not in favour of the expression "coarse-fibred fibrillary proliferation" proposed by me, for in his view one cannot speak in this of a fibrillary proliferation. Now, I believe, according to the appearance of these curiously twisted thread-like formations in the ganglion cells, it is quite excluded that they arise for us from the nerve fibrils of the ganglion cells, since these are indeed arranged in quite another manner; and one sees, in the study of such altered ganglion cells, again and again pictures which speak in favour

[133] of the view that these twisted thread-like formations first form when no neurofibrils are any longer demonstrable in the cells; especially beautifully has Bielschowsky demonstrated this, who depicts ganglion cells in one part of which the nerve fibrils are missing, and precisely there the known twisted threadlets have developed.

We have accordingly a new formation of thread-like structures which, though as I too was able to show very fine, mostly present themselves stuck together and thereby become coarse fibres; they wind themselves into bizarre formations, fill the whole cell — they are thus not only newly formed, but have also a certain tendency to proliferate, and under certain circumstances also outlive the cells; therefore I believe the expression coarse-fibred fibrillary proliferation is developmentally-historically not incorrect; thereby it is naturally not said that the newly proliferated fibrils are to be conceived as nerve fibrils; whether this is only a particularly constituted destructive process, or whether to these formations a regenerative tendency should be ascribed, as some authors assume of the clubby proliferations of the axis cylinders arising in the same process, remains to us still quite unclear.

In any case it is interesting that this cell alteration is, so to speak, only to be found in brains in which the Sphaerotrichia had developed. I have with my quite large material never been able to raise this finding without Sphaerotrichia; in the literature, however, a case of Schnitzler[20] is described; it was a matter of a 34-year-old patient who in the course of 3 years deteriorated in the severest manner in the form of a simple progressive dulling; the brain was highly atrophic, and

microscopically numerous cells were found affected by the coarse-fibred fibrillary proliferation. Sphaerotrichia drusen were lacking. The case has surely, as Schnitzler too emphasises, hitherto a special position, and one must await further such observations until a classification will be practicable.

Supplement at the Correction

In the meantime Spielmeyer's treatment of the psychoses of involution and senescence has appeared in Aschaffenburg's Handbook of Psychiatry. Therein this author places himself upon a similar standpoint as Simchowicz, in that he declares that the "alteration of the brain" made recognisable by the Sphaerotrichia "belongs only to definite disease forms, and that from these ascertainments one can gradually go over to a delimitation of the pertinent disease picture." This, however, is "senile dementia," and Sp. does not see why I have proposed another name for this disease form, which appears to him somewhat forced. Sp.

[134] goes in this, out of the way of the question not to be solved for the time being of what the Sphaerotrichia actually is, with right, but appears nevertheless to imagine that the drusen are consequential states of the ordinary senile brain breakdown, namely for this reason, because he emphasises that one has found this alteration also in quite normal old people. Therefore he also concludes that the Sphaerotrichia disease — *sit venia verbo* — corresponds to senile dementia, and that all dementia processes which run in the senium without Sphaerotrichia formation belong to other disease forms.

Thereupon I should like to object that, so far as I can survey the state of affairs, Spielmeyer's conclusions are the result of an inverted formulation of the question. Within the framework of this work I believe I have proved that the objection, the Sphaerotrichia is found also in normal old people, can no longer be regarded as tenable. If this is so, then one must leave the normal senium out of consideration; for in the normal aged brain drusen are also not found even when it has come to quite considerable breakdown. Therefore the drusen are not the consequence of the ordinary — even if possibly assumed to be stronger — senile brain breakdown, but something quite different. And if this is so, then one cannot support oneself upon the setting up of the senile psychoses from earlier, because at that time as principle of classification only the gross senile involution came into consideration. If, however, we now make the experience that

1. in normal aged no drusen come to development,
2. that senile deteriorated states occur which are nothing other than a loss of the total psychic capacities, which distinguishes itself from that of the normal senium only by the pathological heightening,
3. that in patients in whose brain the Sphaerotrichia is demonstrable a much more complicated, but yet quite uniform symptom-complex can be observed —

then it is surely more justified to designate the processes adduced under 2 as simple senile dementia, and to introduce a new term for group 3, than to persist, in this case actually only historical, in the name of senile dementia. As is plainly evident, my classification does not differ very much from that of Spielmeyer, yet I believe that my nomenclature approaches more nearly to the natural system of the age-psychoses.

Explanation of Plate IV

Sphaerotrichia formations stained with carbol-methylene-blue-methyl-violet.

Fig. 1. Alcohol fixation and celloidin embedding.

Fig. 2. Formol fixation and paraffin embedding.

Fischer's Notes

1. Presented in abstract at the annual meeting of the German Association for Psychiatry in Kiel on 31 May 1912.
2. *Riv. speriment. di freniatr.* **37**.
3. *Neurol. Centralbl.* 1909.
4. *Archiv f. Psych.* **46**.
5. For the kind provision of the material I express my best thanks also at this place to the Director of the Pathological-Anatomical Institute, Professor Dr. Ghon.
6. *Senium, Alkohol und Trauma. Betrachtungen zur Frage der Ätiologie der Psychosen.* Psychiatr. en Neurol. Bladen, 1905.
7. Nissl-Alzheimer, *Arbeiten über Pathol. u. Histopath. der Grosshirnrinde.*
8. *Zeitschr. f. d. ges. Neur. u. Psych.* **4**.
9. *Zeitschr. f. d. ges. Neurol. u. Psych.* **9**.
10. *L'Encéphale*, 1912, Févr.
11. *Amer. Journ. of Insanity*, 1911.
12. *Anleitung beim Studium des Baues der nervösen Zentralorgane.* 5th ed., 1912.
13. *Lehrbuch der Psychiatrie.* 4th ed., 1912.
14. *Obersteiners Arbeiten* **18**.
15. Wanderversammlung der südwestdeutschen Neurologen und Irrenärzte, Baden-Baden, 1911.
16. *Journ. f. Psych. u. Neur.*, 1911.
17. *l. c.*
18. *Lehrbuch der Psychiatrie.* 8th ed., vol. II, p. 624.
19. In this I should like only briefly to remark that in many respects similar states of far-reaching inattention (namely for acoustic stimuli) have been observed with some aphasia forms resting upon temporal lobe lesion.

20. *Zeitschr. f. d. ges. Neur. u. Psych.* **7.**