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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.

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*MILLARY NECROSES WITH DRUSE-LIKE PROLIFERATIONS OF THE NEUROFIBRILS, A REGULAR
ALTERATION OF THE CEREBRAL CORTEX IN SENILE DEMENTIA.[1]*

Fischer's Notes

Translator's Note

This is a complete new English translation of Oskar Fischer's *Miliare Nekrosen mit drusigen Wucherungen der Neurofibrillen, eine regelmässige Veränderung der Hirnrinde bei seniler Demenz*, published in 1907 in the *Monatsschrift für Psychiatrie und Neurologie*, vol. XXII, no. 4, pages 361–372, with eight figures in the text. It is subtitled *Vorläufige Mitteilung* — preliminary communication — and Fischer's own footnote records that it was delivered as a lecture to the Scientific Society of German Physicians in Prague on 19 June 1907.

This is the paper in which the senile plaque is first described as a staged, developing object rather than as a single lesion, and in which the abnormal swollen nerve endings around it are first identified as neuronal and first explicitly separated from the deposit itself. It is also the paper in which Fischer coins *drusige Nekrose*.

The translation is complete. Nothing is abridged or summarised. Fischer's paragraphing is preserved. The pagination of the original is marked in the margin of the text as [361], [362] and so on, placed at the point where the original page turns. Fischer's own footnotes are gathered at the end under *Fischer's Notes*, and are given as he gave them. Figure captions are translated in place, set off as he set them. Anything supplied by the translator appears in square brackets and is marked *Tr*.

Three classes of decision are worth stating plainly.

Terminology. The policy is the one adopted for the 1912 translation: keep Fischer's term, do not modernise it. Two points are specific to 1907 and matter.

The first is that in 1907 Fischer calls the lesion **Plaques**, in the French spelling, throughout — the word *Drusen*, which becomes his standard term in 1910 and 1912, appears here only inside the compound *drusige Nekrose* and in the comparison to an actinomycotic *Druse*. He is writing within Redlich's vocabulary and has not yet replaced it. The shift from *Plaques* to *Drusen* between this paper and the 1910 monograph is his own, and is visible only if the 1907 word is left standing. It has been left standing.

The second is *Keulen* and *Kolben*. Both are rendered **clubs**, which is what they are; where Fischer distinguishes the swollen terminal from the structure as a whole, *Kolben* is rendered **bulb** and *kolbig* **bulbous**. These are the structures the modern literature calls dystrophic neurites, and the reader should be clear that Fischer's claim about them is a claim about *neighbouring* fibres, not about the deposit.

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

Fischer's term	Rendered here as	Modern equivalent
<i>Plaques</i>	plaques	senile (neuritic) plaques
<i>drusige Nekrose</i>	druse-like necrosis	the senile plaque, as a staged deposit
<i>Druse</i>	druse	a geode; a crystal-lined cavity
<i>Herd, Herdchen</i>	focus, little focus	plaque focus
<i>Keulen</i>	clubs	dystrophic neurites
<i>Kolben, kolbig</i>	bulb, bulbous	the swollen terminal of a dystrophic neurite
<i>Achsenzylinder</i>	axis cylinders	axons
<i>Fibrillen, Fäserchen</i>	fibrils, threadlets	neurofibrils; the fibrillar material
<i>spindelförmige Auftreibungen</i>	spindle-shaped swellings	fusiform axonal swellings
<i>Hof</i>	halo	plaque corona
<i>Wucherung</i>	proliferation	—
<i>Spinnenzellen</i>	spider cells	fibrous astrocytes
<i>Presbyophrenie</i>	presbyophrenia	amnesic-confabulatory dementia
<i>Merkfähigkeit</i>	capacity to register	anterograde/registration memory
<i>Streptotricheen</i>	streptothrices	filamentous bacteria of the actinomycete group

Clinical language. Fischer's psychiatric vocabulary is that of 1907. *Senile Geistesstörung* is rendered "senile mental disturbance"; *Geisteskrankheiten* "mental illnesses"; *geistes-gesunde Senile* "mentally healthy senile persons." These have not been softened.

Four 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 **363**: "*Eine Veränderung an den Zellen der Umgebung, besonders aber irgend eine Gliawucherung in der Umgebung der Plaques ist nicht zu konstatieren*" — no alteration in the cells of the surroundings, and in particular no glial proliferation whatever around the plaques, can be established. This is the observation with which Fischer destroys Redlich's glial theory, and it is the first statement in the literature that the deposit precedes any glial response.

The second is on page **368**, and it is the decisive one for any argument about what Fischer's earliest form actually is. The smallest plaques, he writes, are the initial stages, and one finds them "*unvermittelt, ohne Anschluss an irgend einen Gewebsbestandteil bzw. ein Gefäß*" — abruptly, without connection to any tissue component or vessel. On the same page: in the smallest foci there were **no**

nuclei at all, and a perishing of nervous elements, cells or fibres, "*wenigstens in den kleinsten der Herde nicht sicher nachweisbar war*" — was not demonstrable with certainty, at least in the smallest of the foci. Fischer's initial form is a free-lying deposit in undamaged tissue. It is not a damaged nerve ending, and he is explicit that the damaged nerve endings belong to the *neighbouring* fibres and appear as the plaque grows.

The third is the single sentence on page **369** in which he states the whole structure of the lesion: "*Es ist also der ganze Plaque nichts anderes als eine, nicht präzise zu definierende, am ehesten an Nekrose erinnernde, fremde Einlagerung mit proliferativen Veränderungen an den benachbarten Nervenfibrillen.*" The plaque is a foreign inclusion **plus** proliferative changes in the neighbouring nerve fibrils. Two objects, not one.

The fourth is on pages **369–371**, and it is the one most easily misread, including by us. Fischer places the clubs in Nageotte's scheme as central *orthophytes* and *paraphytes* — the terminal and collateral sprouts of **regeneration** — and reaches them by explicit analogy to what the same silver methods show after a peripheral nerve is cut. He then declines to call them regenerations outright, on the ground that it would be strange to read as regeneration something found in masses precisely in senile-atrophic brains. What he settles on, in a single sentence on page 371, is both terms at once: "*ein Wucherungsvorgang der Neurofibrillen, der bedingt ist durch eine Schädigung der Fasern durch die benachbarten Nekroseherdchen*" — **a process of proliferation of the neurofibrils, conditioned by a damaging of the fibres** by the neighbouring little necrotic foci. An injury that provokes a growth. Not a degeneration, and not a regeneration; a reactive outgrowth caused by damage.

The modern word **dystrophic**, which this translation uses in the glossary above because it is what the structures are now called, carries none of that and imports the opposite. It is worth saying plainly that the current literature has come back to Fischer's reading: these are described as "reactive, degenerative and sprouting-related" structures whose earliest form resembles the reactive change following structural injury to an axon, followed by "an attempt at regenerative sprouting" (Woodhouse et al., 2005); and long-term two-photon imaging in living mice finds them to be **highly plastic** — growing, re-growing new axonal segments, disappearing, and re-forming at the same site (Blazquez-Llorca et al., 2017). The club is not an end-state. Fischer declined to call it one, from morphology alone, in 1907.

Woodhouse A, West AK, Chuckowree JA, Vickers JC, Dickson TC. Does beta-amyloid plaque formation cause structural injury to neuronal processes? *Neurotox Res.* 2005;7(1–2):5–15. DOI: 10.1007/BF03033772

Blazquez-Llorca L, Valero-Freitag S, Rodrigues EF, Merchán-Pérez Á, Rodríguez JR, Dorostkar MM, DeFelipe J, Herms J. High plasticity of axonal pathology in Alzheimer's disease mouse models. *Acta Neuropathol Commun.* 2017;5(1):14. DOI: 10.1186/s40478-017-0415-y

The Translation

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(From the German Psychiatric Clinic [Prof. Dr. A. Pick] in Prague.)

MILIARY NECROSES WITH DRUSE-LIKE PROLIFERATIONS OF THE NEUROFIBRILS, A REGULAR ALTERATION OF THE CEREBRAL CORTEX IN SENILE DEMENTIA.[1]

Preliminary communication by Priv.-Doz. Dr. OSKAR FISCHER, II. Assistant of the Clinic.

In the 17th volume of the *Jahrbücher für Psychiatrie und Neurologie*, Redlich described in the cerebral cortex of 2 cases of senile dementia a peculiar alteration which he called miliary sclerosis. The cerebral cortex was strewn over with plaques staining intensely with carmine, of the size of a ganglion cell up to four to six times that, which were indeed diffusely scattered, but sat most abundantly in the layer of the small pyramids. At the centre they showed a homogeneous, slightly granular texture, "while at the periphery a fine felt of fibres was still demonstrable, which formed a gradual transition to the surrounding glial substance"; at the centre there was then also frequently the remnant of a nucleus, a little clump of protoplasm or pigment. Redlich holds these plaques to be peculiarly proliferated glia, and the last-mentioned nuclear or protoplasmic remnants to be remnants of the original glial cell; as primary for the cause of the glial proliferation Redlich holds atrophy and disappearance of individual ganglion cells, and believes he has also seen such perishing ganglion cells in some foci of this kind.

I have examined a larger number of brains in senile dementia and found the same plaques in most of them; in some brains the cortex was quite strewn over with them as in Redlich's cases. Thereby I came into the position of being able to study this peculiar alteration more exactly, which led me to a different conception of its pathogenesis, especially because in doing so the glia and the nerve fibrils were stained and investigated with specific methods.

The plaques showed the same arrangement as was described by Redlich; they lay diffusely, in part also in small groups, in the cerebral cortex, and most densely in the layer of the small pyramidal cells; to a lesser part they were also to be found in the immediate neighbourhood of the smallest vessels, chiefly the capillaries.

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With the customary nuclear and plasma stains, best with haematoxylin-eosin or after van Gieson, they show a peculiar structure which also differs with the size of the plaques.

The smallest of the foci are of roundish-spherical shape, 10–20 μ in diameter. At the usual stronger magnification (Zeiss DD) they have a homogeneous appearance recalling necrosis, with an indication of granulation, and are quite sharply demarcated from the surrounding tissue. Examined with immersion, the little body shows itself to consist for the most part of opaque clumps; to a lesser part it appears as an exceedingly dense, radially threaded texture; in the latter case the margin too is not quite circular but finely toothed and jagged, yet nevertheless quite sharply demarcated from the surroundings (Fig. 1). The next larger plaques consist of a central part similarly built to that in the previous plaques, to which is attached a ring-shaped halo 15–25 μ broad. The central portion is likewise mostly of granular-lumpy constitution and stains with haematoxylin-eosin an opaque bluish; in places, however, there also shows itself between the clumps a bluish-stained, thread-like mass, which is frequently arranged radially and sometimes projects in the form of quite fine little spines visible only with immersion. The surrounding halo has the same structure as the rest of the ground tissue of the cortex, only with the difference that it is somewhat more densely arranged. The next larger plaques, whose size usually amounts to 60–80 μ , more rarely 100–120 μ , have for the most part an appearance which most readily recalls an actinomycotic druse.

Fig. 1. Smallest necrosis with a halo already beginning at the lower circumference. Two degenerating nuclei enclosed in the latter. Magnification 900 $\times$; staining with polychrome methylene blue, section thickness 5 μ .

The centre consists of a clump staining with haematoxylin an opaque bluish in various shades, in which immersion frequently reveals a tangled net of rigid, more darkly stained threadlets having a certain resemblance to fibrin or to streptothrices. All around, the tissue stains more lightly, shows a thread-like structure and a distinctly radial arrangement. Frequently one encounters at the margin faintly greyish-blue stained, club-like formations in radial arrangement. The margin is set off fairly sharply against the surroundings, but sometimes a gradual transition is also visible. In many of the plaques the radiate construction is only indicated; many have the appearance

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of a lumpy disintegration and most closely resemble the central, cell-free portion of a tubercle.

The smallest of the plaques are always cell-free, and of the larger ones the majority; here and there one sees shrunken nuclei surrounded by a remnant of plasma, which have the appearance of being partly of glial, partly of nervous provenance, and appear to be undergoing a gradual disappearance. **These cell remnants are never in the centre, but always only in the peripheral sections of the little foci. An alteration in the cells of the surroundings, but especially any glial proliferation whatever in the surroundings of the plaques, is**

not to be established; it makes only the impression as if the surrounding tissue were somewhat pushed apart by the plaques.

In myelin-sheath preparations after Weigert the plaques appear mostly completely free of myelin as yellow globules, of which especially the larger ones distinctly push the nerve fibres apart; one sees both the vertical and the horizontal fibres running around the plaques in a slight arc.

On account of the striking granular-necrotic, frequently thread-like structure and of the club-like formations, whereby the whole greatly resembled an actinomycotic druse, the most various bacterial stains were applied in the examination of the brains, among them also those after Gram and Ziehl-Neelsen, but with a completely negative result: the little foci remained unstained. They behaved likewise with the tannin-methylene blue method, whereas they stained quite well simply with methylene blue, somewhat darker than with haematoxylin. Yet a certain bacterial structure was not to be found in them. Glial stains were further attempted, namely Weigert's specific one, then the method of Scarpatetti[2] and the staining procedure given by me[3] for the staining of pathological glial formations. In this all the glial fibres stained very beautifully, in the manner usual for the individual methods; the plaques, by contrast, remained completely unstained.

By far the most interesting and probably also the most important results, however, were yielded by preparations prepared after Bielschowsky's fibril method. I will mention that I applied throughout the freezing method, and that the preparations yielded completely faultless results, in that the fibrils were stained quite uniformly throughout the preparation. The smallest plaques thereby showed the same appearance as with haematoxylin-eosin: a round spot 10–20 μ in size with a sharp, slightly toothed margin, of reddish-brown colour and granular, to a large part also thread-like structure; in the latter case the threadlets are quite densely and radially arranged, project in part

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beyond the margin, and account for the fine tothing visible only at the strongest magnification. The neighbouring fibrils have a quite normal appearance, and appear at first glance to be interrupted; a closer following of them shows, however, that at least a large part of them is not interrupted, but only deviates. The larger plaques show a more or less uniform construction; they are of reddish-brown colour, of granular texture, at the centre mostly lumpy, sometimes also at the centre of a radially thread-like structure; at the marginal portions peculiar formations surprise us. These are radially placed, intensely black-stained clubs, whose thread-like beginning is directed inwards and whose gently rounded bulbous end is directed outwards and frequently oversteps the area of the plaque (Figs. 2–8). The bulbs are of the most various size,

Fig. 2. Little focus with fibril staining, with marginal radial clubs, and arcuately deviating fibrils with spindle-shaped thickenings. Magnification 700 $\times$.

Fig. 3. Abundant marginal clubs; the fibril drawn in the middle strongly thickened in the lower part, above ending with multiple clubs.

$\frac{1}{2}$ –2 μ in thickness and about 6 μ in length; but there are also found not a few specimens of 4–5 μ thickness and a length of up to 20 μ . A more exact following of these clubs shows that centralwards they always pass over into a mostly repeatedly wound fibril, which one can follow as far as its end, determined by the section. Since the fibrils run in the most various directions, they are always very soon cut off, and

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only on the fibrils running in the direction of the section can the course also be followed over longer stretches. For this purpose somewhat thicker sections (about 20 μ) are always better than quite thin ones, since they let far more fibrils appear in their entirety at their repeated bendings. The behaviour of the fibrils is shown by Fig. 4: fibril *c* winds, after multiple vertical bendings not representable in the drawing, and after it had at one place undergone a slight thickening, into the focus, bends off in a sharp arc in order to pass over into a club and therewith to end. Fibril *b* likewise runs after multiple windings to the margin of the little focus and ends here in a cloverleaf-like tripartition with 3 clubs. It further shows itself that the clubs, where one can follow them and their fibrils over longer stretches, very frequently do not sit

Fig. 4. Strong spindle-shaped thickening of fibril *a*; fibril *c* with multiple windings and a terminal club; *b*, *d*, *e*, termination with multiple clubs.

Fig. 5. Individual forms of the clubs; the other fibrils not drawn in.

as terminal clubs of a fibril, but present themselves as a **lateral outgrowth**. Such a fibril has either only one such lateral outgrowth or several (Figs. 6 and 7); the stalk is always thicker than the fibril, is triangularly broadened at the point of attachment, and ends either with a single club (Fig. 7) or else it also divides repeatedly,

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in order to pass over into several clubs of different size and frequently also of somewhat tortuous shape. Thereby mistletoe-like formations frequently come about (Figs. 3, 5, 6). Particularly instructive and beyond objection is the relation of the clubs to the fibril in Fig. 6, which represents a tangential section of a plaque; therein a fibril which runs lengthwise over the plaque and comes to lie precisely in its marginal portion is

Fig. 6. Deviation of the fibrils; the middle fibril also passing in an arc over (not through) the plaque, with lateral club formations. The other fibrils not drawn in.

Fig. 7. Deviation of the fibrils of the surroundings; abundant fibril net at the margin of the little focus with the wreath of clubs; lateral outgrowth of the clubs from the fibril running in the middle.

struck in its whole length and shows here several outgrowths. Fig. 8 shows the club in a relation to the fibril such as, say, a spinal ganglion cell to the sensory fibre. The clubs, especially the smaller ones, are in many plaques quite densely and radially placed at the margin and form a wreath-like closure of the plaques (Figs. 3, 4). A part of these clubs is quite intensely and opaquely blackened in the silver preparations; a smaller part, especially in the somewhat more weakly stained preparations, shows a lighter staining which, examined with immersion, presents itself as conditioned by a dense, inextricable, black-stained network. This network is of varying density, is in the smaller clubs frequently somewhat looser; sometimes there is found in the clubs only a marginal net, whereas the

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centre appears diffusely grey-stained (Figs. 5, 7); many of the clubs, especially the smaller ones, show only a black-stained line as margin, whereas the centre is only grey-stained; similarly stained is also for the most part the stalk going off from the fibril. Only rarely does one see a behaviour such as Fig. 8a shows, in that the clubs consist of wavyly arranged, finest fibrils which towards the end run somewhat irregularly, so that one cannot say exactly in what manner they terminate or whether they perhaps pass over into one another.

The fibrils running in the immediate surroundings of the plaques are throughout pushed aside arcuately, which behaviour is most distinctly to be seen on the radial fibres running in bundles (Figs. 2, 3, 4, 6, 7); the irregularly and transversely running fibres of the cortex apparently terminate at the margin of the plaque, but in reality they wind back and forth repeatedly and then finally form a marginal club; in consequence the peripheral zone of the little focus contains a fairly dense net of fibrils which stands in connection with the surroundings; **the centre of the plaque is always free of fibrils**; and there where in the drawings fibrils also run through the centre, these are always only such as are indeed within the section but run above or below the centre.

Fig. 8. Spinal-ganglion-cell-like apposition of the club. At *a* a club at 1200× magnification.

Further one sees on a large number of the fibrils running past a peculiar alteration; for the most part these are quite fine spindle-shaped swellings which, like the fibre, are stained quite black (Figs. 2, 4); in places they are somewhat thicker and longer and show a finely netted texture, like the clubs, especially there where they are more strongly swollen, as in Fig. 4 at fibre *a* and in Fig. 3.

When we pass over to the assessment of these peculiar plaques, we must in the first place call a halt at Redlich's conception. Redlich conceives the plaques described by him, and completely identical with those depicted here, as glial proliferations, and indeed in such a way that such a plaque corresponds to a peculiarly proliferated, then nucleus-less glial cell which had assumed the place of a perished ganglion

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cell. Against this conception a whole series of considerations speaks.

Redlich's conception is based in the first place on the appearance of the little foci in ordinary eosin and van Gieson preparations, in which they impress one as a simple condensation of the ground tissue of the cerebral cortex, with a frequent indication of a fine radial striation; yet already with these stains the whole appearance — the dense, finely threaded constitution, very aptly compared by Redlich with the appearance of cotton wool — is so different from the appearance of the neuroglia that Redlich himself concedes that a transition to ordinary spider cells can be established "not without difficulties." Redlich's glial staining failed; **in my well-succeeded glial preparations neither in the plaques nor around them could any glial fibres or proliferated glial cells be demonstrated.** Redlich's statement too, that at the centre of the foci a nucleus or nuclear remnants were frequently found, is not correct in general, and especially not in the direction that these nuclei could be made responsible for the origin of these plaques; **for precisely in the smallest foci, and those by all appearances to be designated as initial stages, no nuclei were found**, but only in the larger ones, and there too mostly at the periphery; these are best explained as nervous tissue gradually enclosed by the growth.

I come rather to a quite different interpretation in the question of the origin and the significance of these peculiar formations. **The smallest plaques are, by all indications, the initial stages. One finds there, abruptly, without connection to any tissue component or to a vessel, a small granule staining bluish with haematoxylin and reddish after Bielschowsky, which frequently shows a distinctly thread-like construction recalling a bacterial colony.** The whole appearance permits the conclusion of a foreign inclusion, whose nature, however, remains enigmatic. Plasma it is not, just as little anything nervous; it contains neither calcium nor iron (many of the preparations were specially examined for this too); nor is it fibrin; bacterial stains also led to negative results; most readily one could conceive it as a peculiar necrosis, whereby, however, it is in any case to be remarked that **a perishing of nervous elements — cells or fibres — was not demonstrable with certainty, at least in the smallest of the foci.** Nevertheless the designation necrosis would probably be the most apt, since the rest of the appearance still most readily recalls necrotic portions.

As the plaque grows larger the fibrils deviate more and more, and those which find themselves in the immediate vicinity exhibit peculiar phenomena of proliferation, in the form of spindle-shaped thickenings and of bulbous and club-shaped, repeatedly

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branched sprouts, which set themselves up by preference at the margin of the plaques radially and with the thickened end outwards, so that the whole greatly resembles an actinomycotic druse.

The whole plaque is therefore nothing other than a foreign inclusion, not precisely definable, most readily recalling necrosis, with proliferative alterations in the neighbouring nerve fibrils.

The behaviour of the latter is in any case the most salient and in principle most important peculiarity of the plaques described. The club-like formations are without doubt of nervous kind; their staining, their fibrillar structure permit no other interpretation; artefacts in the form of precipitates with the silver method they are not — apart from a series of other morphological considerations — for the reason that they are already to be seen with the ordinary nuclear stain; further, the connection with the fibrils is beyond doubt, an accidental agglutination being excluded by the regularity of the connection.

These formations show great resemblance to phenomena already known on growing nerve fibres; after transection of peripheral nerves the silver methods of Cajal or Bielschowsky showed multiple divisions of the axis cylinders and club-like swellings of the ends, of fibrillar-reticular structure [Cajal,[4] Marinesco,[5] Perroncito[6]]. Also there come about, especially shortly after the transection, abundant club-like outgrowths of the central stumps and within the sheaths of Schwann. In the spinal ganglia similar formations were described by Marinesco[7] in tabes and by Nageotte[8] in transplantations. The latter described, alongside the generally known terminal clubs, also lateral bulbous and branched outgrowths of the axis cylinders, and designated the former by the name "orthophytes," the latter by that of "paraphytes," and designated the regeneration by means of orthophytes as "régénération terminale," that by means of paraphytes as "régénération collatérale."

Somewhat sparser are the reports of such club-shaped buddings of the axis cylinders in the spinal cord.

Cajal[9] describes club-shaped terminations of the fibrils in

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older embryos, Marinesco[10] after transections of the spinal cord and of the posterior roots, Bielschowsky[11] in the surroundings of a compression myelitis in the monkey. In the brain, similar formations have been described only by Bielschowsky[12] in the neighbourhood of 2 gliomas, as at any rate sparse and small, knob- and bulb-shaped terminations of fibres which by all appearances had to be addressed as newly formed.

For the peripheral nerves it is subject to no doubt that these fibrillar swellings of the axis cylinders are an accompanying phenomenon of regenerative proliferation, for they are found only there where it comes to new formation of nerve fibres. The same appearance of the club at the margin of sites of destruction in the spinal cord and brain induced Bielschowsky to address these formations likewise as regenerative endeavours of central fibres. Such abundant fibril outgrowths, however, as in our cases, are still quite unknown in the brain; **according to their whole nature**

they align themselves completely with the growth-clubs named above. They are for the greatest part terminal, in part, however, laterally attached to the axis cylinders — thus central ortho- and paraphytes in Nageotte's sense.

To a generally important circumstance I should like to draw attention on this occasion, which bears on the question of the formative material of regenerated or proliferated axis cylinders and its derivatives. The one party lets the new formation of nerve fibres proceed only by the outgrowth of the central axis cylinders (His, Waldeyer, Cajal); the others, with Bethe at their head, regard as formative material only the proliferated cells of the sheaths of Schwann. The growth-clubs are now described in part as naked formations standing in connection with no cells whatever (Cajal), in part, however, they lay themselves closely against cellular elements (Perroncito); and precisely this latter occurrence could, were it regularly to be encountered, be applied as a proof for the cellular formation of the fibrils and against pure outgrowth.

For these reasons I have in my cases searched for any accompanying cells of the clubs, but found them always quite naked and without support against cells, which could for this reason easily be excluded, since the plaques, with the exception of the few degenerating cell remnants, were quite cell-free.

As what, then, are these clubs to be interpreted? The cited authors had throughout regarded the clubs seen by them as the expression of a regeneration. It would in any case be somewhat strange if one were to conceive these formations, which according to our

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hitherto knowledge occur in the brain only sporadically and according to the above are found directly in masses precisely in senile-atrophic brains, simply as regenerations. Before one arrives at the solution of this problem, one will in any case have to examine the most various lesions of the central nervous system for nerve fibrils with the modern silver methods.

For the time being it would still be premature to designate these formations as anything other than a process of proliferation of the neurofibrils, conditioned by a damaging of the fibres by the neighbouring little necrotic foci.

After we have discussed the question concerning the histogenesis of the individual elements of the plaques, a further question comes to the foreground: "What significance have these peculiar formations for the pathology of the brain at all?" For the answering of this question a short survey of the frequency of the described plaques is required.

Redlich's investigations relate only to 2 cases of senile dementia. I have examined brains from 16 cases of senile mental disturbance and found the plaques in 3 cases in about the abundance as Redlich described, in which the cortex was quite permeated by the little foci; in 9 the plaques were

represented in such a way that one could always find some in every section; and only in 4 cases were they completely absent at the most various sites of the brain. In general the little foci, whether now numerous or only sparsely represented, were of fundamentally the same construction, only that in general the more sparsely represented foci were somewhat smaller; the fibrillar proliferations were also to be found everywhere, yet they were in the brains permeated by more abundant plaques much more abundant, and the individual clubs also more massive and larger.

Given so great a frequency of the plaques in senile dementia, one had to look about to see whether similar or identical alterations might not also be discoverable in other brains. For that purpose I searched through 45 cases of progressive paralysis, 10 normal brains and 10 cases of the most various "non-organic" psychoses, on a large number of sections from the most various cortical regions, and nowhere were similar alterations found; only among 7 cases of brain atrophy following foci of softening were there found, in one case, quite isolated little foci identical with those described in senile dementia.

We can therefore say that these **druse-like necroses**, as I should like to call them for short, are as good as absent in other diseases and in normal brains; for the occurrence of them in the one case of dementia with arteriosclerotic brain atrophy, which after all has so many points of contact with senile dementia, should not surprise at all.

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If now the druse-like necroses occur only in senile dementia and in this high percentage, then the question comes to the foreground whether and how the cases with the necroses are also clinically distinguished from the others. A compilation of the clinical symptoms of all cases led to the surprising result **that the cases without necroses were simple senile dementias with a simple decline of all mental faculties, whereas the others were more or less pronounced presbyophrenias with confabulations and coarser disturbances of the capacity to register.** Indeed, precisely those cases which exhibited the druse-like necroses in quite enormously abundant number were distinguished clinically by a stormier course, and especially by manifold hallucinations.

Since we as yet know no specific alteration of the senile cerebral cortex, the druse-like necrosis is accordingly to be regarded as the essential pathological-anatomical substrate for presbyophrenia. If this is the case, alterations of this kind would have to be absent not only in other mental illnesses but also in mentally healthy senile persons. I have not yet had the opportunity to examine such brains, but I can in a certain respect call upon the work of Miyake,[13] who recently examined 25 senile brains, of which 21 came from mentally healthy and only 4 from senile-demented old people. In 2 of the latter he found the described plaques, which, following Redlich, he conceives as miliary scleroses and did not investigate more closely, whereas they were absent in the other brains.

For further conclusions, as regards both the clinical side of this question and the cause of origin of the druse-like necrosis, my hitherto and not yet concluded investigations are not suited; I wanted here only briefly to draw attention to the fact that:

1. *in senile dementia there are quite peculiar club-shaped phenomena of proliferation on the neurofibrils, which in this form are hitherto unknown in the brain,* and
2. *that in the "druse-like necroses" we have the most important anatomical substrate of presbyophrenia.*

Fischer's Notes

1. After a lecture delivered on 19 June 1907 in the Scientific Society of German Physicians in Prague.
2. *Encyklopädie der mikrosk. Technik* (Ehrlich-Weigert), p. 97.
3. *Verhandlungen der deutschen pathol. Gesellschaft* 1902.
4. *Die histogenetischen Beweise der Neuronentheorie von His und Forel*. *Anatom. Anzeiger*. Vol. XXX. No. 5.
5. *Etude sur le mécanisme de la régénérescence des fibres nerveuses des nerfs périphériques*. *Journ. f. Psych. u. Neurol.* Vol. VI.
6. *La rigenerazione delle fibre nervose*. *Boll. de la Soc. med. chir. di Pavia* 1905.
7. *Contribution à l'étude de l'histologie et de la pathogénie du tabes*. *La Semaine méd.* 1906. No. 16.
8. *Notes sur l'apparition précoce d'arborisations périglomérulaires, formées aux dépens de collatérales des glomérules dans les ganglions rachidiens greffés*. *Revue neurolog.* 1907.
9. *l. c.*
10. *l. c.*
11. *Das Verhalten der Achsenzylinder in Geschwülsten des Nervensystems und im Kompressionsgebiete des Rückenmarkes*. *Journ. f. Psych. u. Neurol.* Vol. VII.
12. *l. c.* [Fischer's note 11 serves both references — *Tr.*]
13. *Beitrag zur Kenntnis der Altersveränderungen der menschlichen Hirnrinde*. *Obersteiners Arbeiten*. Vol. XIII. 1906.