Treponema pallidum in nerve fibres

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In our previous reports (1972a, b) we have demonstrated the distribution of *Treponema pallidum* in blood vessels and adjacent cells. We proved that treponemes may reside in periendothelial areas and interstitial spaces, as well as migrating freely into and out of the blood vessels. The phagocytosis of treponemes by perivascular and other cells has also been described.

In this report we present electron micrographs showing *T. pallidum* in various parts of nerve fibres. In reviewing the literature, we found no reference to such findings in electron microscopic studies, probably because it is difficult to detect treponemes in peripheral nervous tissue. Grigoryev (1938), using light microscopy, found spirochaetes in the endoneurium and perineurium of nerve fibres within a primary syphiloma.

Material and methods

We studied a fragment of a chancre from rabbit No. 8944 inoculated with lymph node material from another rabbit, which had been infected 6 weeks before and treated with 800,000 units of benzathine penicillin. The lymph nodes were removed at a time when the Wassermann reaction was negative and the FTA 200 test showed + + + +.

Within a month after infection, rabbit No. 8944 developed pea-sized nodules, which grew steadily and in a week became very large, densely infiltrated, and covered with a firm dry sanguineous crust. Numerous treponemes were present. The rabbit was exsanguinated and the chancre was removed for electron microscopic study.

The material was processed by the methods described in our previous publications.

Findings and discussion

Figs 1 and 1A show in cross-section fibres of a peripheral nerve within the rabbit syphiloma. The structures seen include the cytoplasm of a Schwann cell with axons (A) and their associated mesaxons (mes), cytoplasmic filaments, synaptic vesicles (sv), the basal lamina (bl), and the endoneurium (en), with treponemes (T) distributed among collagen

fibres (cl). Around a treponeme the collagen fibres are destroyed (Details A and B). This phenomenon is observed also in other areas where treponemes lie in endoneurial collagen. The treponemes themselves are almost unaltered, their fibrils and the outer body wall being distinctly visible. The perineurium (pn) consists of elongated cells encircling the endoneurium. A small amount of endoplasmic reticulum (er) and numerous pinocytotic vesicles are also displayed. The perineurium is enveloped by the basal lamina; the epineurium (ep) is filled with transversely-cut collagen fibres and contains treponemes.

A similar appearance is shown in Figs 2 and 2A, but here many treponemes are present in the endo-, peri-, and epineurium. The organisms are well preserved, and the adjacent collagen is destroyed. Myelin bodies (mb) and lipofuscin (lf) are also visible.

Fig. 3 demonstrates the same structures, but the peripheral parts of the endoneurium and the epineurium contain more treponemes. The collagen around them is destroyed. There are many pinocytotic vesicles in the perineurium.

Along with the above structures, Fig. 4 clearly shows Schwann cells with neurofilaments, axons and mesaxons, the axolemma (al), synaptic vesicles (sv), and the axoplasm with transversely-cut axoplasmic filaments. The treponemes residing in the endoneurium have undergone no significant morphological alterations, but the neighbouring collagen fibres are destroyed.

The nerve fibres were surrounded by the usual cellular elements, some of which contained phagocytosed treponemes.

Thus we may conclude that the nerve is involved in the specific pathological process, but the significance of the presence of treponemes in the nerve fibre requires further study.

Firstly, in our opinion, this indicates that as well as passing along the blood stream infection may be transmitted directly along the nerves to the spinal canal, meninges, and cerebrospinal fluid. The changes in the CSF found in some cases of primary syphilis may arise in this way.

FIG. 1 Cross-section of nerve fibre from rabbit syphiloma. Treponemes are present in endo- and epineurium. $\times 30,000$

FIG. 1A T. pallidum in cross section. Fibrils (f) and outer wall (me) are clearly visible. $\times 70,000$

FIG. 1B (overleaf)

FIG. 1B Axons (A), mesaxon (mes), Schwann cell cytoplasm (csch) with filaments (fsch) and vesicles, and the basal lamina (bl) are distinctly outlined. The endoneurium contains a well-preserved treponeme. $\times 70,000$

FIG. 2 Cross-section of nerve fibre from rabbit syphiloma. $\times 10,000$

FIG. 2A (overleaf)

FIG. 2A Treponemes are present in the endo-, peri-, and epineurium. Collagen (cl) around them has disappeared. Along with the structures displayed in Fig. 1, this micrograph shows myelin bodies (mb), lipofuscin (lf), and mitochondria, which are somewhat damaged. Numerous pinocytotic vesicles (pv) are seen in the perineurium. $\times 30,000$

FIG. 3 Cross-section of nerve fibre from rabbit syphiloma. $\times 20,000$

FIG. 3A (overleaf)

FIG 3A *T. pallidum* in the endo- and epineurium. $\times 35,000$

FIG. 4 Cross-section of nerve fibre from rabbit syphiloma. Schwann cells (csch) surrounded by basal lamina (bl). Axons (A) with axoplasmic vesicles, filaments, axolemma (al), as well as mesaxons (mes) are well displayed. The Schwann cell cytoplasm has numerous filaments. $\times 35,000$

Secondly, these observations suggest an additional mechanism for the meningeal symptoms which sometimes occur in the early stage of the disease. As well as being induced directly by the invading infection they could represent a reflex mediated by nerve impulses arising in the lesion.

Thirdly, the presence of *T. pallidum* in the nerve may explain the absence of pain, since the organisms may injure the sensory fibres innervating the syphiloma.

Summary

Ultrathin sections of a rabbit scrotal syphiloma were examined by electron microscopy. Treponemes were observed in the endo-, peri-, and epineurium of the nerve fibre. The significance of these findings, in that infection may be transmitted *via* the nerve fibres and pain reduced by damage to the afferent fibres, are discussed.

References

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KEY TO FIGURES

- A—axon
 af—axoplasmic filament

- al—axolemma
 av—axoplasmic vesicles
 bl, bm—basal lamina
 ch—chromatin
 cl—collagen
 csch—Schwann cell cytoplasm
 en—endoneurium
 ep—epineurium
 er—endoplasmic reticulum
 f—fibrils
 fsch—Schwann cell filaments
 lf—lipofuscin
 mb—myelin bodies
 me—outer wall
 mes—mesaxon
 mN—nuclear membrane
 N—nucleus
 pn—perineurium
 pv—pinocytotic vesicles
 sv—synaptic vesicles
 T—treponeme

Présence de *Treponema pallidum* dans les fibres nerveuses

SOMMAIRE

Des coupes ultra-fines d'un syphilome scrotal de lapin furent examinées au microscope électronique. On observa des tréponèmes dans l'endo- la péri- et l'épinèvre d'une fibre nerveuse. On discute de la signification de ces constatations et on pose la question de savoir si l'infection peut se transmettre par l'intermédiaire des fibres nerveuses et si une altération des nerfs afférents ne peut pas réduire les phénomènes douloureux.