COMMUNICATIONS

SPHERICAL SWELLING OF RETINAL AXONS IN THE AGED*

BY

FR. VRABEC

Department of Anatomy, Institute of Ophthalmology, London

Introduction

WALLERIAN degeneration of an interrupted or otherwise badly damaged nerve fibre has been known for more than 100 years (Waller, 1852). Its consecutive changes were definitively analysed by Ranvier, Perroncito, Tell, and others (cited by Cajal, 1928). Cajal also described minute anatomy in his work on the degeneration and regeneration of the nervous system. Nevertheless, quite recently Wohlfart (1955), Woolf (1956), and Coers and Woolf (1959) have encountered another type of change in the nerve fibres involving the axons supplying voluntary muscle. Wohlfart (1955), in his first description, thought this change to be a form of Wallerian degeneration of an interrupted fibre, but Coers and Woolf (1959) stated that it represents another kind of change. They pointed out the unusual behaviour of such nerve fibres in so far as the axon on both sides of such a spherical swelling did not show any other signs of degeneration. They were able to find different stages of spherical swelling, sometimes enclosing a dark nucleus, sometimes with many concentric layers of varying density. Many of the swellings stained metachromatically with methylene blue. They could demonstrate these changes in a number of chronic diseases of the nervous system such as vitamin B₁₂ deficiency, the hypochromic anaemias, and other chronic conditions, but only rarely in diabetic neuropathy.

In their studies of the pathology of the optic nerve fibres, Wolter and Liss (1957, 1959) followed the development of hyaline corpuscles in the human optic nerve and the retina. In the latter, hyaline bodies commonly represent the terminal stage of hyaline degeneration of the ganglion cells. In the optic nerve, the authors were able to follow the metamorphosis of the degenerating axons into hyaline corpuscles. Wolter and Liss mainly studied badly damaged axons in totally atrophic optic nerves and found that most hyaline corpuscles arise from the interrupted axons and their terminal swellings. The same authors also reported that there is evidently a special development of hyaline bodies within nerve fibres of the optic nerve and the nerve-fibre layer of the retina of normal aged eyes. Even here, such changes are not necessarily found in interrupted fibres, or on axons showing other signs of degeneration.

* Received for publication April 22, 1964.
In the course of a study of the nerve-fibre layer of the retina in several vertebrates and in man the present author has met the same phenomenon in otherwise normal human retinae of older people. Other macroscopical or microscopical changes (cotton-wool patches, cytoid bodies, etc.) were not found in the retinae studied. The ages of the patients whose retinae were studied varied between 52 and 81 years.

Materials and Methods

Flat whole mounts of the human retina in balsam were used after being impregnated by the Bielschowsky-Gros method. In such mounts it was possible—with the exception, of the papillomacular bundle where the massive accumulation of axons excludes detailed study—to follow most of the axons along their path from the periphery of the retina to the optic nerve head.

Findings

The majority of the axons in the nerve-fibre layer of all retinae examined were without pathological change. In a 74-year-old male spherical swellings were found on a small number of peripheral fibres. Examination of other retinae of aged people impregnated by a similar method revealed identical changes in their axons. The degenerative changes were to be found on both thick and thin varieties of the retinal axons.

The first stage appears as a simple dilatation of the axon most frequently in its central portion; the swelling arises first in the axoplasm and the neurofibrils are simply pushed apart. This central dilatation then develops into a spherical swelling. At this stage the neurofibrils can be seen clearly on the surface of the dilatation. Even fine axons can be involved. Within the swellings a granular substance appears in the later stages and eventually the whole formation is filled by dense material.
SWELLING OF RETINAL AXONS IN THE AGED

Fig. 2.—Spherical swelling on a medium sized axon, with more peripherally situated body. × 200.

Fig. 3.—A group of spherical swellings of different sizes and stages of development. × 266.

Fig. 4.—The central dark body of the corpuscle is shrinking; its surface is rough and it is surrounded by a clear space. × 266.

forming a black spherical mass. These changes take place either in the central portion of the axon (Fig. 1), or more eccentrically, when the axon can be seen extending uninterrupted along one side of the dark corpuscle (Fig. 2). Rarely, groups of such corpuscles can be found (Fig. 3). In the later stages further degenerative and resorptive changes occur within the corpuscle; the dark body seems to shrink centrally and a concentric clear peripheral zone appears (Fig. 4). Later,
the remainder of the central nucleus becomes absorbed (Fig. 5) and many concentric layers may develop (Fig. 6). Finally, the axon may undergo degeneration as well. Some findings seem to suggest that a hyaline corpuscle could be expelled from the fibre without interruption of the axon (Fig. 7).

This type of degeneration differs fundamentally from the normal type of degeneration in interrupted fibres, minutely described in the human retina by Wolter (1956a, 1956b, 1961; Wolter and Liss, 1957). Here, when the axon is badly damaged, the
so-called "digestive chamber" (Cajal, 1928) is formed, enclosing the swollen central axon (Fig. 8). The interrupted axon swells and both ends form terminal clubs (Cajal, 1928). The peripheral club soon disappears. The whole fibre stands out clearly from the surrounding normal axons by its size and strong argyrophilic tendency.

**Discussion**

The fundamental difference between the spherical swelling described and Wallerian degeneration is clear. The major difference appears in the relative integrity of the axon or, at least, in the length of time required for the degeneration of the whole of the axon. Since Wallerian degeneration is initiated by damage to the axon, another cause must be sought for the changes described. Relevant in this context is the finding of newly growing nerve fibres in the clinically normal human cornea in iridocyclitis and in the normal eyes of the aged (Vrabec, 1955). Here it was
evident that the newly formed fibres, growing first without Schwann's sheath, entered into close relationship with the keratocytes; they clearly showed dilatations when passing close to the nucleus, i.e., close to the central part of the body of the cell. Close connexions with the mesenchymal elements are described even by Cajal in his studies on the sprouting of nerve fibres in the first stages of neurogenesis or, in experimental conditions, when a newly formed fibre grows across scar tissue.

Nerve fibres of normal corneal epithelium which are devoid of a myelin sheath regularly show such dilatations in the nuclear region of the epithelial cell (Boeke, 1925).

In studying growing axons in the ciliary body of the human foetus from the beginning of the sixth month, the present author has found changes closely resembling the so-called "ravelling of axons" (Cajal, 1928). Even here, in a growing normal fibre, we can see the central vacuole pushing the neurofibrils apart. In a later stage, however, subsequent changes closely resemble the spherical swelling found in aged people.

Similar ravelling of the nerve fibres is to be found in almost every case of growing nerve fibres in the regeneration of sectioned nerves in normal corneal tissue (Rexed and Rexed, 1951).

In the cornea and ciliary body of aged persons nerve fibres are found to grow without any apparent cause. In the cornea numerous newly formed fibres can be recognized by their profuse and sinuous growth. In the ciliary body, even the enormous number of fibres normally present is surpassed and their regular distribution along the muscle fibres is disturbed by newly formed nerve fibres growing apparently without any order. Some fibres spiral around other fibres in a similar manner to that frequently described in spinal and other ganglia of aged people by Cajal (1928) and others.

Spherical swelling of the axons does not appear only in the special conditions of the human retina; Coërs and Woolf found it in voluntary muscle in quite different surroundings. The present writer found it frequently even in the ciliary body of aged people. Such appearances were often considered to be ganglion cells. There are many true ganglion cells in the ciliary body and the choroid, but they are quite different from the spherical swellings. They have large, mostly multipolar cell bodies, a clearly defined nucleus and, as a most salient feature, they are almost always accompanied by the capsular elements (satellite cells).

Summary

Spherical swellings on the axons of retinal ganglion cells have been studied by silver impregnation methods.

It is shown that these swellings differ from those encountered in Wallerian degeneration.
REFERENCES


Oxford University Press, London.


SPHERICAL SWELLING OF RETINAL AXONS IN THE AGED

Fr. Vrabec

doi: 10.1136/bjo.49.3.113

Updated information and services can be found at:
http://bjo.bmj.com/content/49/3/113.citation

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/