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Editorial

Sensory Ganglion Cell Culture for the Study of Diabetic Polyneuropathy

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The commonest form of diabetic neuropathy is a distal symmetric sensory polyneuropathy. Its pathological basis has been disputed. One view has been that it is the result of multifocal hypoxic lesions in nerve that summate to produce symmetric distal axonal loss, although there are substantial indications that this is only a partial explanation. The autopsied cases reported by Sugimura and Dyck,[1] which showed multiple focal proximal lesions in nerve trunks, were both elderly with advanced peripheral vascular disease and this may well have complicated the situation. Dyck *et al* [2] found that the fibre loss in sural nerve biopsies was non-uniform which suggested to them an ischaemic basis. On the other hand, Llewelyn *et al*[3] observed a similar patchy loss in non-ischaemic neuropathy. Although abnormalities in endoneurial micro vessels are prominent in diabetic neuropathy,[4] they are not consistently present.[5]

The alternative view is that diabetic polyneuropathy is distal axonopathy of dying-back type. This has been demonstrated in teased fibre studies which have additionally shown secondary demyelination proximal to the site of axonal interruption.[6] A postmortem study on a case of severe chronic diabetic distal sensory and autonomic polyneuropathy[7] suggested that the pathology was a central-peripheral distal axonopathy with degeneration involving not only the distal parts of the axons of dorsal root ganglion cells in the peripheral nerves but also the rostral part of their centrally-directed axons in the dorsal columns of the spinal cord. In neuropathy of this type, the cell bodies have difficulty in maintaining the structural integrity of the extremities of their axons. All synthetic activity in neurons occurs in cell bodies and structural proteins, enzymes, neurotransmitter substances, etc., are then translocated down the axons in the anterograde transport system. Growth factors are also taken up from the target organs by axon terminals and taken back to cell bodies in the retrograde transport system where they influence the metabolic activity of the neuron. One or more aspects of these processes therefore fail in diabetic polyneuropathy.

In diabetic polyneuropathy, regeneration is initially vigorous [8,9] but later declines. The reasons for this are so far uncertain. Regenerating axons extend by the advance of growth cones at their tips which attach to receptors on the surfaces of Schwann cells or on

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components of the extracellular matrix (ECM). There is evidence of marked changes in the ECM in diabetic neuropathy, affecting both the Schwann cell basal laminae and endoneurial collagen.[10] The basal laminal changes are possibly the result of abnormal cross-linking of collagen 1V related to nonenzymatic glycation. The consequences may be that the microenvironment in nerve becomes inimical to axonal regeneration.

An opportunity for making observations on the effect of nonenzymatic glycation on neurite extension has been provided by tissue culture studies on sensory ganglion cells. Encouraging results have recently been reported by Luo *et al*.[11] When rat dorsal root ganglion cells grown on glycated substrates were compared with those grown on nonglycated substrate, there was found a reduction in the proportions of cells attached to the substrate and in the proportion of neurite- bearing cells. There were also considerable morphological abnormalities in the growth cones with appearances that suggested extension and retraction of neurites. These features suggest that sensory ganglion cell culture could provide a surrogate system of studying diabetic distal axonopathy and the opportunity for experimental manipulation to examine the mechanism of the abnormal neurite behaviour.

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