Neuroglia and the myelin-bearing cell: a symposium

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DYNAMIC ASPECTS OF THE MYELIN-GLIAL RELATIONSHIPS IN DEVELOPMENT AND REPAIR

RICHARD P. BUNGE (New York) An understanding of the mechanism of myelin breakdown required a detailed analysis of the structural and metabolic relationship between myelin and the myelin related cell—that is, the peripheral Schwann cell and the central oligodendrocyte. The present discussion emphasized the following aspects of this relationship.

The oligodendrocyte formed the central myelin sheath by the spiral disposition and compaction of its plasma membrane around the axon (often simultaneously myelinating a number of axons). After a period of active myelin formation the oligodendrocyte apparently retained continuity with the cytoplasmic constituents which had been demonstrated on the internal and external aspects of the mature sheath and at the region of the termination of the myelin lamellae near the node of Ranvier. The special junctions established between terminating myelin loops and the axolemma in the perinodal region might be significant for normal saltatory conduction; observations on pathological changes in these contacts during demyelination would be of interest.

The cytoplasmic constituent of myelin contained a prominent microtubule component. This component might provide a mechanism by which materials were conveyed from the perikaryon of the oligodendrocyte to the more distal parts of the myelin-glial complex. The ongoing activities of the mature myelin-related oligodendrocyte were emphasized by its active incorporation of RNA precursors and by evidence that certain molecular components of myelin might be in equilibrium with component pools, presumably within the oligodendrocyte perikaryon. Recent evidence that the demyelinating agent, diptherial toxin, was a potent inhibitor of protein synthesis suggested that this ongoing metabolism might apply to protein as well as to lipid myelin components.

Dramatic changes in myelin structure (with apparent fluid accumulation between myelin lamellae) occurring in response to triethyl tin administration, in certain forms of spongy degeneration, and in a number of experimental situations (as well as the proclivity of the oligodendrocyte to swell acutely in a variety of disease conditions) suggested that the myelin related cell might be unusually active in ion (and secondarily water) transport. This process might be expected to require energy and had been little explored in myelin related cells.

Additional dynamic aspects of the myelin-glial cell system were evident in the variety of cytological reactions observed in glial responses to disease. A number of workers now believed that small glial cells were capable of proliferation and provided a reserve supply of glial cells for the disposal of debris, for repair, or for scarring. The responses for repair included the potential for remyelination of demyelinated axons within the central nervous system. This had been observed in a number of situations and had involved either oligodendrocytes or apparent Schwann cells (the latter perhaps derived from contiguous peripheral nerve).

SOME ASPECTS OF THE KINETICS OF THE NEUROGLIA

J. B. CAYANAGH (London) A comparison was made between the rates of the responses of neuroglial cells and microglia after a brain wound and after chemical denervation of a spinal tract. A quantitative approach to cell proliferation around a brain wound showed that from the second day onwards there was an increase in cells which was greatest at the wound edge but extended for several hundred micra into the brain parenchyma. At the wound edge the mitotic cells might be, as Konigsmark and Sidman (1964) have shown in the mouse, largely haematogenous in origin. Beyond the first 200 μ it was principally endogenous cells that divide. Results of this quantitative approach to cell proliferation disclosed the importance of rapid perfusion-fixation to show the true mitotic rates, and also showed that colchicine did not penetrate into the brain. This useful mitotic inhibitor could not, therefore, be used for the study of cell proliferation in the brain. As might be expected, proliferation rates fell off logarithmically with distance from the wound edge.

Contrary to previous views, neuroglia were quite susceptible to X-irradiation provided that their mitotic function was being studied. Doses of more than 500 r profoundly affected the capacity of astrocytes and microglia to respond to injury. After 2,000 r the mitotic rates of these cells were significantly lowered. After 1,000 r the astrocytes showed an anomalous enhanced activity that might be due to failure of the vascular bed to reconstitute after injury (Cavanagh, 1968). The finding of Hopewell and Wright (1967) that the suppression of proliferation was as marked one year after irradiation as after one week suggested a use for this type of injury to determine the replacement rates of these cells.

Ultrastructural studies showed that the chief feature of this type of lesion was leakage of protein into brain (Blakemore, 1969). Astrocytes, as well as microglia, were active in taking this up and re-establishing the normal low protein condition of the brain extracellular space.