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Transformation of Adult Schwann Cells Into Macrophages.*

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As was shown previously by one of us,[1] embryonic Schwann cells in tissue culture can transform into macrophages. The following experiments prove the same faculty for the Schwann cell of adult nerve.

In a total of 574 tissue cultures, over 1,000 fragments of peripheral nerves of white rats were cultured for 2 to 9 days in fowl blood plasma with traces of chick embryo extract. Both freshly transected and predegenerated (2 to 100 days) nerves were used. Growth was excellent and no harmful effect of the heterologous medium was noticed. Schwann cells and "fibroblasts" migrate from the explanted fragment in the known manner.[2,3,4] These two cell types are sharply distinguished by size, nuclear properties, staining reaction, etc.

During cultivation, the culture medium undergoes certain changes (Fig. 1). A protein-rich exudate spreads from the explant (E) along the mica cover slip (M), and a liquid layer (L) separates the central portion of the plasma clot (P) from its support (M). Thus 6 different zones become evident: (1) interface mica-liquid; (2) interior of liquid; (3) interface liquid-plasma clot; (4) interior of clot; (5) outer surface of clot; (6) interface clot-mica. Each one of these zones has its peculiar physicochemical properties and ultrastructural pattern, and the behavior

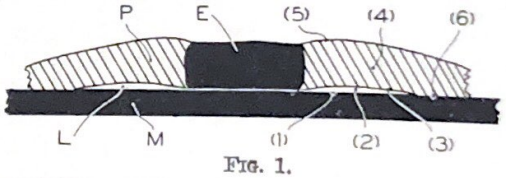

FIG. 1.

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1 Weiss, P., *Anat. Rec.*, 1944, **88**, 205.

2 Ingebrigtsen, R., *J. Exp. Med.*, 1916, **23**, 251.

3 Murray, M. R., and Stout, A. P., *Am. J. Path.*, 1940, **16**, 41; *Anat. Rec.*, 1942, **84**, 275.

4 Abercrombie, M., and Johnson, M. L., *J. Exp. Biol.*, 1942, **19**, 266.

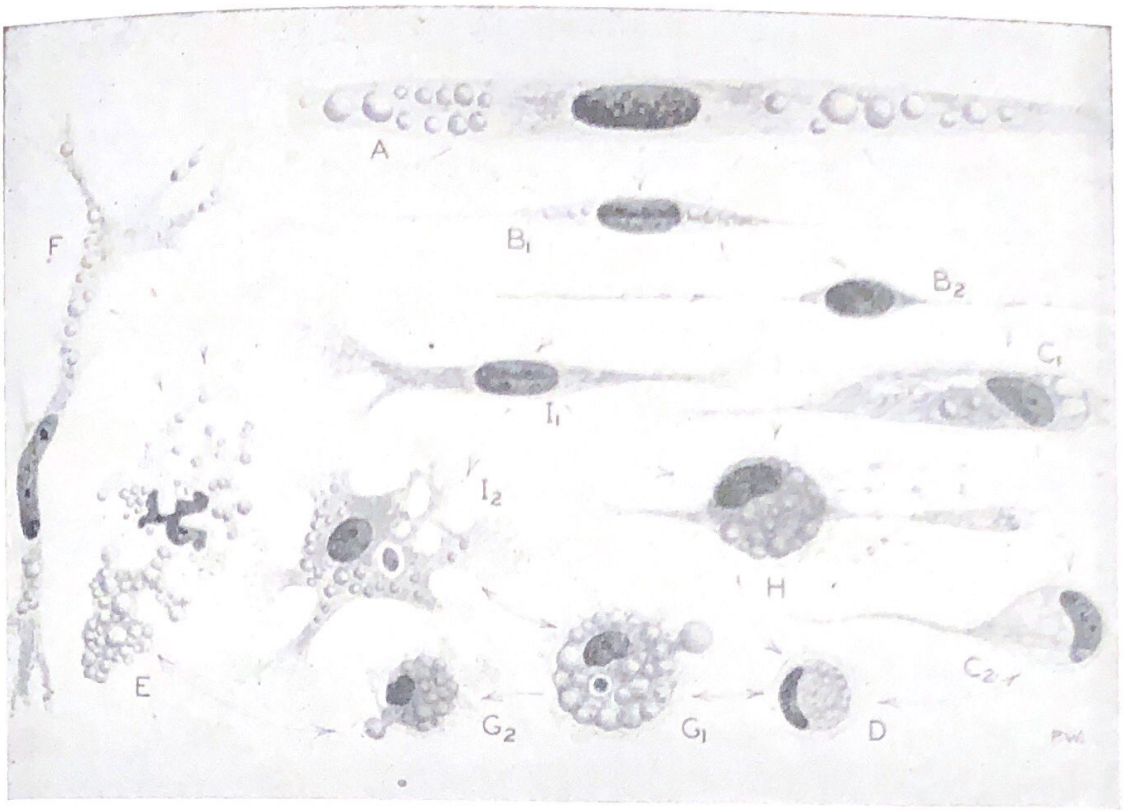

FIG. 2.

and shape of the cells entering it vary accordingly, as is more fully explained in the following summary based on observations of both living and fixed cultures.

The Schwann cells emerge from the neurilemmal tubes in tandem file, either singly or in bands (Büngner's cords). Depending on the conditions which they encounter, they may then assume any of the shapes and characters illustrated in Fig. 2. All cells are reproduced in correct proportions. Size differences are partly real (*e.g.*, B_1-B_2; G_1-G_2), partly simulated by extreme flattening (*e.g.*, I_1-I_2). All cells leave the nerve in forms A, B_1 or F. Transformations observed regularly are indicated by arrows; reciprocal arrows indicate reversible changes. Linear spindle cells (B_1, B_2) are filaments less than 1 μ wide (except near the nucleus) and up to 0.5 mm long; their ends taper to 0.2 μ and below. They prevail in layers 4 and 5. Cells in surface 1 expand by means of terminal pseudopodia and transform into macrophages ($B_1 \rightarrow I_1 \rightarrow I_2$) in the same manner as described for embryonic Schwann cells.[1] In surfaces 3 and 5, transformation to a monocyte-like round cell occurs by retraction of the cell processes ($B_1 \rightarrow H \rightarrow D$), sometimes by way of a monopolar phase ($A \rightarrow C_1 \rightarrow C_2 \rightarrow D$). In area 6, the cells assume the highly ramified form E with polymorphic nucleus, a form also assumed by Schwann cells emerging from the nerve in the form F. All forms may round up into forms G_1 and G_2, which are highly phagocytic and in active amoeboid motion.

These transformations are accompanied by changes in staining properties, nuclear shape and size, hydration, fat content, and mode of locomotion. They were so abundant in most cultures that they could be studied in great detail in many thousands of specimens. High motility, mitotic activity and phagocytosis distinguish these transforming cells from the moribund types often seen in old tissue cultures. Mitoses were repeatedly observed in A, B_1, F, H, D and G. Phagocytosis of ink particles was intense in I_2 and G. Fat

was being actively extruded from E and G. Myelin fragments (from early nerve degeneration stages) are actively ingested by forms I and G, and their subsequent intracellular digestion has been followed under the microscope.

Transformation of Schwann cells to macrophages can also be seen inside the explanted nerve fiber tubes themselves. Removal of blood from the nerves prior to explantation (Ringer's perfusion of the donor) and Trypan Blue injections indicate that the contribution of hematogenous and preformed histiocytes to the macrophage population of our cultures was negligible. Most of the macrophages present were transformed Schwann cells, and all cultures exhibited some transformation. Fibroblasts (endoneurial cells) also turned into macrophages, but less readily; moreover, phagocytes from Schwann cells and those from fibroblasts each retain distinguishing features of their strain. The observed conversions thus belong clearly in the class of cell "modulations".[5,6]

Conclusions. (1) The adult Schwann cell is capable of a wide range of modulation in the course of which it can assume numerous shapes and characters often associated in neuropathology with distinct cell types. (2) Schwann cells presumably are a major source of macrophages during Wallerian nerve degeneration, and their control becomes a prime consideration in nerve regeneration.[7] (3) The active role of the Schwann cell in removing myelin by phagocytosis and digestion has been experimentally verified. (4) The filamentous shape of the spindle-type Schwann cell makes it a superb guide for axons.[8] Its dimensions and staining properties are very close to those of axon sprouts, which suggests one source of error in past unfounded claims of "autogenous" nerve regeneration. (5) The results place increased emphasis on the great versatility of even the adult cell, within the limited potentialities of its strain, in response to the composition and microstructural organization of its environment.[5]

5 Weiss, P., *Principles of Development*, 1939, Henry Holt & Co., New York.

6 Bloom, W., *Physiol. Rev.*, 1937, **17**, 589.

7 Weiss, P., *J. Neurosurg.*, 1944, **1**, 400.

8 Weiss, P., and Taylor, A. C., *Arch. Surg.*, 1943, **47**, 419.