Differential Nerve Block by Local Anesthetics

In this issue of *Anesthesiology*, Gissen and colleagues challenge the traditional concept of sequential nerve blocking action by local anesthetics. It has long been held that the larger the diameter of an axon, the more resistant it is to local anesthetic blockade. These beliefs may have to be modified, for Gissen et al. now present data suggesting that the larger the diameter of an axon, the more susceptible it may be to conduction block.

The classic concept of differential nerve block evolved from the work of Gasser and Erlanger, who, in the 1920s, explored the electrical properties of nerves with the just-discovered cathode ray oscilloscope. The new technology enabled researchers to examine noninvasively the fiber representation of intact nerve by scanning the compound action potential for blips from axons conducting impulses at different speeds. It also proved to be an excellent tool to study blockade of nerve impulses by local anesthetics. Gasser and Erlanger categorized nerves into three main classes. They called myelinated somatic axons A fibers, myelinated autonomic axons B fibers, and nonmyelinated axons C fibers. While the small-diameter B and C fibers are quite homogeneous anatomically as well as physiologically, the A fibers encompass a wide range of sizes in man (from about 2 to 20 μm in diameter) and a wide range of electrical properties (conduction velocities from about 10 to 120 m/s). For that reason, the A group was further divided into four bands—labeled A alpha through A delta—according to decreasing diameter and impulse conduction velocity.

Though that classification was based on electro-physiologic characteristics, many other neural properties such as physical (response to cooling or pressure) and pharmacologic (response to local anesthetics) also showed inter-class differences. For instance, conduction in nonmyelinated C fibers was blocked by a lower concentration of cocaine than was conduction in A fibers. Further, large-diameter A alpha fibers proved more resistant to cocaine blockade than small-diameter A delta fibers.
From this seminal work the general teaching developed that the larger the diameter of a nerve fiber, the more resistant it is to local anesthetic blockade. However, it soon became evident from clinical experience (as with spinal anesthesia) that block of sympathetic preganglionic fibers consistently was more extensive than block of cutaneous sensory fibers. This property was used to advantage in differential spinal block, for instance, to relieve pain of autonomic origin without affecting cutaneous sensation or skeletal muscle function. Clearly, the B fibers had to be more sensitive to local anesthetics than pain-conducting C or delta fibers. Later, this clinical observation was confirmed experimentally by Heavner and de Jong.3

Nevertheless, it was still held that B fibers were an exception, and that large-diameter A fibers were more resistant to local anesthetics than were nonmyelinated C fibers. But even that rule was weakened when Nathan and Sears4 demonstrated that certain small A fibers in spinal roots were a trifle more susceptible to procaine block than were the much smaller C fibers. Gissen and associates now go one step further in toppling old teachings and propose that the larger the diameter of an axon, the more susceptible it may be to conduction block by local anesthetics.

Does this mean that previously held concepts are out of step? Perhaps, but not necessarily. There are some controversial aspects relating to the methodology used by Gissen et al. that will require further examination before we can accept fully so sweeping a conclusion. For one, the experiments on nerve from a warm-blooded animal (38°C) were done at room temperature (22°C). For another, A-fibers were lumped into a single group (30–60 m/s), rather than split into bands of axons with dissimilar characteristics.

Mammalian myelinated axons conduct at optimal speed around 38°C. In the range of 27–37°C, conduction velocity decreases by about 5 percent for every degree drop in temperature.5 And at about 8°C, A fibers cease conducting impulses altogether. Unmyelinated mammalian axons are less affected by cooling and conduct down to about 4°C. Also to be considered is that depression of membrane excitability to perhaps one-third of normal by cooling could have lowered the safety factor to such an extent that even minimal additional depression by local anesthetic rendered A fibers totally inexcitable to stimulation. Altogether, a measure of inadvertent differential block may have been introduced by doing the experiments at room rather than at body temperature.

As discussed, the A family of myelinated axons is made up of four distinct velocity bands, comprising four groups of axons of different diameters and different modalities. Though we can accept the observation that under the conditions of this experiment fast-conducting fibers are blocked at the lowest anesthetic concentration, we cannot tell from this study whether large rapidly conducting (80–120 m/s at 38°C) alpha motor fibers are more sensitive again than slower (20–40 m/s at 38°C) small-diameter sensory delta fibers. Certainly, clinical observation of peridural block intimates that large motor fibers are more resistant to local anesthetics than are thin fibers conducting cutaneous sensation (though etidocaine provides a puzzling and challenging exception).

These remarks in no way are meant to detract from the important observations made by Gissen et al.; they merely intend to lend perspective and to point the way towards further fruitful research. As is so often the case, we see one question answered and several new ones raised. There remains plenty to be done yet before the book on differential nerve block can be closed. The best one can say at present is that, under the conditions of their experiment, the authors’ conclusions are valid. Extending them beyond that scope, however, will require additional experimentation.

RUDOLPH H. DE JONG, M.D.
Tufts University School of Medicine
Boston, Massachusetts 02111

References
2. Gissner HS, Erlanger J: The role played by the size of the constituent fibres of a nerve trunk in determining the form of its action potential wave. Am J Physiol 80:522–547, 1927