Neurophysiological Studies on the Mechanism of Anesthesia

The problem of discovering the mechanisms of general anesthesia is going to be exceptionally tough. The detailed mechanism of how most drugs work is unknown but, in the case of general anesthetics, the target organs are also unknown. Neurophysiology is in a primitive and very exciting phase where the language of the central nervous system is just beginning to be unraveled and, therefore, meaningful quantitative questions about the functioning of most systems cannot yet be asked. Understanding anesthesia must depend on understanding normal systems. There was a time when it was thought that peripheral nerve tissue provided an adequate sample of all nerve tissue, and it remains true, if surprising, that no detailed class of events has yet been observed in the central nervous system which has not also been seen in the periphery. This might suggest that the central action of anesthetics could be understood by searching the more easily analyzed peripheral structures for an analogue of central mechanisms. This valuable work is going on. Barbiturate, for example, will block conduction in peripheral axons, but one wonders about the relevance of this observation when it is realized that the dose required to block peripheral axon conduction is the equivalent of giving a normal man a kilogram of pentobarbital. It may be that certain central axons are extraordinarily sensitive to blockage by barbiturate by the same mechanism as that seen in the periphery, or it may be that barbiturate has some entirely different central effect not yet observed on peripheral tissue. The assessment of the significance of the peripheral phenomenon must depend on experiments on the central nervous system.

Just as any peripheral effect of anesthetic agents is worth investigating but not necessarily relevant to the central action of anesthetics, similarly any central effect which can be analyzed should be examined for clues even though it may not explain the whole complex of central changes called general anesthesia. For example, cells in the dorsal horn which receive cutaneous afferents are depressed by normal anesthetic doses of barbiturates. These cells' connections are known and the cause of their firing can be analyzed in some detail. It is probably now possible to locate the site of action of barbiturate on the excitability of this group of cells, and it would be very important to do so. However, it should not be forgotten that their depression may well be an epiphenomenon to the phenomenon of general anesthesia. The demonstration that gross evoked potentials in the reticular formation are more sensitive to anesthetics than similar explosions evoked on the cortex does not prove that the explanation of general anesthesia has been found since no one has the foggiest idea of what these potentials mean to a behaving animal. It will be necessary for each of us to develop a concept of what would constitute
an adequate description of the location and mode of action of anesthetics. In the mean

time, it would seem tactically wise to advance step by step into the central nervous system

collecting data to locate and describe all the effects, both excitatory and depressant, of

therapeutic doses of the various compounds in the class of general anesthetics.

The paper by de Jong and Nace in this issue of the Journal shows that if anesthetic
doses of ether, methoxyflurane, halothane or nitrous oxide are given to cats already anes-

thetized with pentobarbital, there is little sig-
nificant change in the threshold of peripheral
pressure receptors or in the conduction prop-
erties of peripheral axons. These results set
the stage for asking more penetrating ques-
tions about the mechanisms of sensation and
anesthesia. An immediate question raised by
this paper relates to the possible existence of
efferent nerve fibers to skin which might con-
trol the sensitivity of cutaneous nerve endings.

Efferent control of peripheral sensitivity has
been shown to exist by way of the olivo-
cochlear bundle to the organ of Corti and by
gamma efferents to muscle spindles. There is
good evidence that efferents run to the retina
in amphibia and birds, and some believe that
they are also present in mammals. No clear
physiological or anatomical evidence exists that
efferent systems run to mammalian skin and
control sensitivity, although frog skin sensitiv-
ty does seem to be affected. However,
clinical evidence in causalgia and Raynaud’s
disease does suggest very strongly that the
autonomic nervous system is involved in patho-
logical peripheral sensitivity either by deliver-
ing efferent nerve impulses to the periphery
or by providing a pathway for especially im-
portant afferent impulses. The work of de
Jong and Nace provides the control base from
which to test the possible effect of autonomic
efferents on normal peripheral sensitivity. In
their preparation, the presence of barbiturate
would decrease the various autonomic reac-
tions to be expected from the anesthetics ad-
ministered. Furthermore, the gallamine used
to block neuromuscular transmission would
also block transmission at sympathetic ganglia
and therefore abolish whatever peripheral ef-
ficts might have occurred from alterations of
autonomic outflow. Now that it has been
shown that the anesthetics used have no direct
effect, it will be extremely interesting to see in
the decerebrate unanesthetized and unpara-
alyzed cat if they have an indirect effect by way
of the sympathetic outflow. Once these ex-
periments have been completed, it will be pos-
sible to begin an analysis of changes in first
central cells.

P A T R I C K  D. W A L L, M. D.
Professor, Department of Biology
Massachusetts Institute of
Technology
Cambridge, Massachusetts

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**On the Measurement of Myocardial Contractility**

Within the last few years, the cardiovascular
literature has been infused with a substantial
volume of terminology that, while not new,
was formerly restricted almost wholly to pa-
ers on muscle mechanics. Many of those
who are not directly involved must have won-
dered just how much the appearance of
expressions like “sliding filament model,”
“force-velocity curve,” and “active state”
should be influencing their understanding of
myocardial function. While it is true that
the terms are sometimes brought into cardio-
vascular writing as little more than fashionable
window-dressing, it is equally true that the
basic concepts behind them can be very useful
in clarifying one’s thinking about the perfor-
amce of the heart.

Consider the problems of defining precisely
what constitutes a change in myocardial con-
tractility, and of choosing the most meaningful
index of contractility for a given experimental
situation:

The term “myocardial contractility” is used
so often that few of us are bothered by the