him to remedy defects both of form and of substance.

E. C. CRITTENDEN

BUREAU OF STANDARDS,
WASHINGTON, D. C.

SPECIAL ARTICLES

THE EFFECT OF ANESTHETICS UPON PERMEABILITY

THERE is much uncertainty as to the mode of action of anesthetics and particularly as to their effect upon permeability. While some writers hold that anesthetics increase permeability, others take the opposite view.[1] To clear up this confusion appears to be a necessary step toward a theory of anesthesia.

A definite solution of this problem seems to have been attained in the cases here described. This result is due to the employment of quantitative methods without which it would not have been possible.

The experiments were made by measuring the conductance of living tissues of a marine plant, *Laminaria*. Under the conditions of the experiment an increase or decrease of conductance signifies a corresponding increase or decrease of permeability.[2]

The anesthetics were mixed with sea water and sufficient concentrated sea water was then added to make the conductivity equal to that of sea water. The material was then placed in the mixture and its conductance was measured at frequent intervals.

Material having resistance of 1,000 ohms[3] was placed in a mixture of 990 c.c. sea water plus 10 c.c. ether, to which was added sufficient concentrated sea water to make its conductivity equal to that of ordinary sea water. In the course of 10 minutes the resistance rose to 1,100 ohms: in the next 10 minutes it fell to 1,070 ohms; in 20 minutes more to 1,020 ohms, and in 20 minutes more to 1,000 ohms. In the next 20 minutes it dropped to 990 ohms, at which point it remained stationary for a long time. Subsequently it decreased very slowly, but at exactly the same rate as the control which remained in sea water during the experiment. After 24 hours it had the same resistance as the control.

In order to find out approximately what part of the resistance is due to the living protoplasm the tissue was killed at the end of the experiment by adding a little formalin: after rinsing well in sea water the resistance was 320 ohms. This represents the resistance of the apparatus and dead tissue; on subtracting it from the resistance previously given we obtain approximately the resistance due to the living protoplasm. This may be called the *net resistance* while the resistance before subtraction may be called the *gross resistance*. In this experiment, therefore, the net resistance before treatment with ether was 1,000—320 = 680 ohms and the net conductance $1 \div 680 = .00147$ mho. The loss in net conductance due to ether is 13 per cent., which means a decrease of permeability amounting to 13 per cent.

It is evident that this decrease of permeability is completely reversible and involves no injury. The fact that after the resistance has fallen to a stationary point it is 10 ohms below the starting point does not indicate injury, but only an increase in the conductivity of the solution due to the evaporation of the ether.

In another series of experiments the effects of the evaporation of the anesthetic were avoided by constantly renewing the solution by means of a steady current. It was then found that the resistance, after rising rapidly to a maximum, remained stationary for a long time (often for two hours or more) at the maximum point, afterward falling slowly to the normal. This more prolonged exposure to the anesthetic seemed to produce no injurious effects.

In these experiments the amount of ether in the solution was 1 per cent. by volume. Smaller amounts of ether produced less effect:

[1] Cf. Höber, "Physikalische Chemie der Zelle und der Gewebe," Dritte Auflage, 1911, pp. 219, 223, 489; R. Lillie, *Am. Jour. Physiol.*, 29: 372, 1912; 30: 1, 1912; Lepeschkin, *Ber. d. bot. Ges.*, 29: 349, 1911.

[2] The method has been described in SCIENCE, N. S., 35: 112, 1912.

[3] All the figures in this paper refer to readings at 18° C.

below 0.2 per cent. little or no effect was observable.

Higher concentrations of ether give a very different result. With 3 per cent. by volume of ether the resistance rises very rapidly to a maximum (which is about the same as when 1 per cent. is used) and then falls very rapidly. But instead of stopping when the normal is reached the resistance continues to fall rapidly until death ensues. If the concentration of ether be increased the period during which the resistance remains above the normal becomes shorter until finally it becomes impossible to detect it even when readings begin 30 seconds after placing the tissue in the anesthetic. There is a corresponding increase in the rapidity of the fall of resistance and of the onset of death.

The decrease of permeability observed in these experiments may be easily and quickly reversed by placing the tissue in sea water. Is this also the case with the increase in permeability? This was tested in the following manner: The material was allowed to remain in the anesthetic until its resistance had fallen about 100 ohms below the normal (*i. e.*, below the resistance it had before being exposed to the anesthetic). It was then replaced in sea water and readings were taken at frequent intervals; recovery would be shown by a rise in resistance.

No such rise in resistance was observed. The experiment was varied by replacing the tissue in sea water after the resistance had fallen only 50 ohms below the normal and also by choosing a concentration of ether which caused the resistance to fall very gradually. Even then there was but rarely any sign of recovery and this was of short duration and small in amount.

Similar results were obtained with chloroform, chloral hydrate and alcohol, but not at the same concentrations: the concentrations which correspond to 1 per cent. ether are approximately as follows: chloroform 0.05 per cent., chloral hydrate 0.05 per cent., alcohol 3 per cent.

Two distinct effects are observable in these experiments. One is a toxic effect evidenced by an increase in permeability, while the other involves a decrease of permeability. A very important question is, with which of these is the anesthetic action associated? Since the distinctive mark of an anesthetic is the reversibility of its action, it is not reasonable to suppose that this action is associated with an irreversible change in permeability. Such a change is in no way peculiar to anesthetics, but is common to all toxic substances. We are, therefore, forced to the conclusion that it is the reversible change, involving a decrease of permeability, which is associated with the anesthetic action.

The fact that typical anesthetics (ether, chloroform, chloral hydrate and alcohol) decrease the permeability of the tissue to ions is profoundly significant in view of the fact that the transmission of nervous and other stimuli is believed to depend on the movement of ions within the tissues.

W. J. V. Osterhout
Laboratory of Plant Physiology,
Harvard University

Partial Sex-Linkage in the Pigeon

That certain characters in pigeons are sex-linked is shown by the work of Staples-Browne,[1] Cole[2] and Strong.[3] Both Staples-Browne and Strong, however, encountered certain exceptions which I shall try to show are explicable on the assumption that there is in the female pigeon a pair of sex-chromosomes, between which crossing-over of the factors may occur.

Staples-Browne found that a white female crossed to a dark male produced all dark offspring, showing that white is recessive to dark. The reciprocal cross, viz., white male by dark female produced dark males and white females. So far, this last cross is a typical case of "criss-cross" inheritance, in which the recessive character entered the cross from the parent homozygous for the sex-differentiating factor, viz., from the male in this case.

Staples-Browne found, however, in this F_1, in addition to the white females, one dark fe-

[1] R. Staples-Browne, *Jour. Genetics*, June, 1912.
[2] L. J. Cole, Science, August 9, 1912.
[3] R. M. Strong, *Biol. Bull.*, October, 1912.