THE STANDARDIZATION AND ACTION OF LOCAL ANESTHETICS.*

BY H. A. McGUIGAN.

How shall we evaluate an unknown anesthetic in terms of cocaine?

This necessitates a résumé of the biological methods of determining the value of an anesthetic. Before such methods are applicable the drug must be known to be available as a local anesthetic, *i. e.*, it must be devoid of certain properties: it must be non-corrosive and relatively non-toxic. Phenol, ammonia, and many other drugs, when injected hypodermically, produce anesthesia; but the preliminary pain and corrosive action is sufficient to eliminate them from consideration. Such drugs have been called anesthetica dolorosa.

The methods used by pharmacologists to determine the value of local anesthetics are:

I. The anesthetization of the conjunctiva of the rabbit's eye. This is carried out by dropping a solution of the drug into the conjunctival sac and determining the time of onset, and the duration of the anesthesia produced. The condition of anesthesia is determined by touching the cornea with a bristle or other suitable instrument. When anesthetized, no winking results, and no pain is elicited when the conjunctiva is irritated.

II. Anesthetization by dipping the foot of a frog into a solution of the anesthetic, and determining when it is anesthetized by dipping it in an acid solution. When anesthesia is induced the foot is not withdrawn from the acid solution. If it is withdrawn, the acid is washed off by dipping the foot in water and again immersing in the anesthetic solution until anesthesia is produced. Such a condition is determined by the absence of reflex when again immersed in acid. The well-known Türck method is used in this procedure.

III. Anesthesia is also determined by applying the drug to the sciatic nerve of a frog, and noting when the impulse or after-stimulation fails to elicit a contraction of the muscle. This is a motor nerve, but its use in the study of anesthesia is sanctioned by the accepted physiological law that every nerve impulse is similar to every other nerve impulse. The motor impulse is harder to block than the sensory, but in comparative work when the same nerve is used, this makes no difference.

IV. The quaddel or wheal method by injection intradermally in the skin of man, stimulating the area with a pin, hot iron or the like, and noting when the sensation disappears and returns.

V. A modification of this has been used on dogs by Pittenger. He shaves an area of the skin about one inch square, and injects one cubic centimeter of a solution of the drug into this area, and determines the minimum weight of the drug which is necessary to be dissolved in 1 cc. to cause anesthesia in five minutes. With procaine he found this method sufficiently delicate to detect differences of seven per cent. of the required amount, which was 0.07 gram per cc.

VI. Another method which has been used by Drs. Burnett and Jenkins, working under Dr. Adams at the University of Illinois, is the Gold Fish Method. They find that by putting gold fish into a solution of an anesthetic, they turn over when anesthetized in a manner resembling death. However, since they rapidly

* Read before the Unofficial Conference of U. S. P. and N. F. Revision workers at Chicago, January 12, 1924.

recover when replaced in water, they consider the condition as one of anesthesia. By plotting the effects of various concentrations on X axis, and the reciprocal of the time on the Y axis, they get the formula:

$$A = \sqrt{\frac{\tan.\theta}{\alpha}}$$

which corresponds to the strength of the anesthetic.

A = anesthetic effect.

α = the subliminal concentrations of the drug.

θ = the angle formed with the axis X by protecting to the X axis the straight line formed by the points of different concentrations.

We were interested in comparing the results of the various methods, and in comparing procaine and some other related synthetic preparations with cocaine. The results are interesting:

FOR PROCAINE IN TERMS OF COCAINE.

Rabbit's eye.	Frog's sciatic.	Pittenger's method.	Türck method.
$^3/_{16}$	$^1/_6$	$^1/_{11}$	0

The results show that when, as the result of a biological method, we state that a drug is equivalent to a certain concentration of cocaine, it is important to state the method used. The cocaine equivalent differs apparently for both method and location.

DISCUSSION.

E. L. NEWCOMB inquired if the work had been done entirely with 100% pure anesthetic or if any comparative work had been done with crude drugs containing these anesthetics.

DR. MCGUIGAN replied that the work had been entirely with the pure anesthetic.

THE EFFECT OF INJECTION, INTO RATS, OF IMPROPERLY ALKALINIZED SOLUTIONS OF SALVARSAN.*

BY H. B. CORBITT AND C. N. MYERS.

The object of this demonstration was to show the effect of adding sufficient and insufficient amounts of alkali in the alkalinization of a solution of salvarsan or other arsphenamines. Three rats were injected with 200 mg. per Kg. of salvarsan, according to the official procedure, as follows, with the results indicated.

Rat No. 1 received the unalkalinized salvarsan solution (salvarsan hydrochloride in 2 per cent. dilution). This animal died on the board.

Rat No. 2 received a partially alkalinized salvarsan solution (sufficient alkali to form, theoretically, the mono-sodium salt in solution). This animal died within fifteen minutes.

Rat No. 3 received a completely alkalinized salvarsan solution (sufficient alkali to form, theoretically, the di-sodium salt in solution). This animal lived to be chloroformed at the end of the demonstration.

* Demonstration at the "Stunt Show" of the Scientific Section, A. PH. A., Asheville meeting, 1923.