

sible for the growth of head furnishings and rudimentary Wolffian ducts while the female hormone liberated by the stimulated cortical tissue is responsible for development of the oviduct.

Preliminary experiments in collaboration with Dr. H. B. Van Dyke using a purified gonad-stimulating hormone prepared from sheep pituitary glands yield even more pronounced effects in some respects.

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Influence of (H⁺) Concentration on the Anesthetic Value of a Series of General and Local Anesthetics and Hypnotics.

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The purpose of this investigation was to determine whether any differences were to be observed in the relative anesthetic effects over widely different pH ranges, comparing a series of general anesthetics with a series of local anesthetics and a series of hypnotics. Alcohols such as allyl and isoamyl, and also general anesthetics such as chloroform, ether, chloretone, etc., do not form salts and consequently their distribution between oil and water is not markedly changed by a change in the (H⁺) concentration of the water phase.

Local anesthetics like neothessin, cocaine and butyn are lipo-soluble organic bases with relatively low solubility as free bases in water, but in the presence of acids they form water-soluble salts. Consequently the oil-water distribution coefficient shifts from a high oil-solubility and low water solubility on the basic side, to a low oil-solubility and high water solubility on the acid side.

In the case of the barbituric acid hypnotics exactly the reverse relation is found. The barbituric acids are lipo-soluble organic acids possessing very low water-solubility but on addition of alkali to the water phase water-soluble salts of the barbituric acids are formed. Consequently the distribution coefficient shifts from a high oil-low water solubility on the acid side, to a low oil-high water solubility on the basic side.

It follows from the above that if the induction of anesthesia is in any measure dependent upon the lipoid-water distribution coefficient of the anesthetic a shift from the acid or neutral to the basic side should exert little or no effect on the alcohols and general anesthetics, should increase the effect of bases like cocaine and decrease the effect of pseudo acids of the barbituric acid type.

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The experiments to be reported in this experiment were conducted on arenicola larvae. The gelatinous strings containing arenicola eggs were cut into small pieces and kept under sea water in the laboratory. The larvae hatched in 24 to 48 hours and being heliotropic accumulated near the surface at the point most exposed to light. The mass of larvae was collected and added in 0.2 cc. amounts to dishes containing a given concentration of anesthetic in 10 cc. of sea water adjusted to the desired pH. This semi-quantitative procedure has given consistent results during 3 seasons at Woods Hole.

TABLE I.
Anesthetic Down Doses for Arenicola Larvae.

	pH 7.0	cc. per 100 cc.	
		8.0	9.0
Iso-Propyl Alcohol	2.5	2.5	2.5
Propyl Alcohol	0.5	0.5	0.5
Allyl Alcohol	0.25	0.25	0.25
Iso-Amyl Alcohol	0.1	0.1	0.1
Chloroform	0.012	0.012	0.025
Chloretone	0.025	0.025	0.025
<i>Local Anesthetics</i>			
		gm. per 100 cc.	
Cocaine	0.01	0.005	0.0025
Procaine	0.002	0.001	0.0005
Neothessin	0.001	0.0005	0.0005
Butyn	0.001	0.00025	0.00025
<i>Hypnotics</i>			
		gm. per 100 cc.	
<i>Barbituric Acids</i>			
Iso-Amyl Ethyl	0.006	0.025	0.05
Di-ethyl Carbonyl Ethyl	0.006	0.012	0.05
Normal Amyl Ethyl	0.006	0.012	0.05
Propyl Methyl Carbonyl Ethyl	0.003	0.006	0.012

Table I gives the minimum concentration of anesthetic expressed in the first group in cc., in the second and third groups in grams per hundred cubic centimeters required to render the larvae immobile within a period of 5 minutes. Even after exposure to the solutions in question for a period of an hour the larvae recover their full motility when transferred to a large excess of sea water. Variations in (H⁺) concentration cause no variation in the anesthetic effect exerted by the first group of alcohols and general anesthetics. A shift toward the alkaline side from pH 7 to pH 9 causes an increase ranging from 2 to 1 to 4 to 1 in the anesthetic effect exerted by a series of local anesthetics. The same shift from pH 7 to pH 9 causes a diminution ranging from 4 to 1 to 8 to 1 in the anesthetic effect exerted by a series of barbituric acids.

The above data harmonize with the conception that the induction of anesthesia is in some measure dependent upon the lipid water distribution coefficient of the anesthetic in the cell and its immediate environment.