These data show that at least one nutrient is required, in addition to choline and manganese, to prevent perosis in chicks. Furthermore, this substance is not identical with any of the recognized vitamins. The fuller's earth adsorbate (Group V) and a 0.2 N ammonia eluate of the fuller's earth adsorbate (Group VI) are fair sources of the nutrient.

The perosis due to a deficiency of the unidentified factor is similar to that produced by a deficiency of manganese or choline, but is usually less severe. If it were possible to supply all other essential unrecognized vitamins in a concentrated form, the chicks probably would grow faster, and presumably they would develop more severe symptoms.

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Relationship Between Anesthetic Potency and Physical Properties.*

NELLIE M. CONE, SYLVAN E. FORMAN AND JOHN C. KRANTZ, JR.

From the Department of Pharmacology, School of Medicine, University of Maryland.

A new series of cyclopropyl aliphatic ethers has been synthesized in this laboratory. The first two members of this series, cyclopropyl methyl ether (cyprome ether) and cyclopropyl ethyl ether (cypreth ether) have been shown to be useful anesthetics.[1, 2, 3] In comparative studies with these new agents it became necessary to study the physical properties of these compounds to determine their value in predicting anesthetic potency. The literature available on the oil/water coefficients of the generally used anesthetics is confusing and data are not concordant. The authors believe that this is due to: first, the technical difficulties inherent to the determination; second,

* The material contained in this paper is part of a thesis submitted by Nellie M. Cone to the Faculty of the Graduate School of the University of Maryland in partial fulfillment of the requirements for the degree of Master of Science.

The expense of this investigation was defrayed in part by a grant from the Ohio Chemical and Manufacturing Company of Cleveland, Ohio.

1 Krantz, J. C., Jr., Carr, C. J., Forman, S. E., and Evans, W. E., Jr., *J. Pharm. and Exp. Therap.*, 1940, **96**, 207.

2 Black, C., Shannon, G. E., and Krantz, J. C., Jr., *Anesthesiology*, 1940, **1**, 274.

3 Krantz, J. C., Jr., Carr, C. J., Forman, S. E., Evans, W. E., Jr., and Wollenweber, H., *J. Pharm. and Exp. Therap.*, 1941, **72**, 233.

the use of oils containing free fatty acids, and third, the employing of analytical procedures which lack precision. Accordingly, the field was restudied and more dependable comparative data obtained.

Oil/Water Coefficients. Corn oil was selected as the fat of choice as it is available with a titer of less than 0.03% fatty acids. Fifty cubic centimeters of the oil was weighed in a bottle of about 200 cc capacity. A volume of the anesthetic agent was added, calculated to make the oil volume 0.1 Molar with respect to the solute. Having stoppered the bottle with a tightly-fitting, tin-foil covered stopper, the amount of anesthetic introduced was determined by weighing. An equal volume of water was added and the bottle agitated vigorously for 1 hour in a constant temperature room at 25° ± 0.5°. Most of the oil was withdrawn by gentle suction through a pipette and exactly 1 cc of the perfectly clear aqueous layer removed in a chilled pipette for analysis. With certain minor modifications the dichromate method of Andrews, *et al.*,[4] for the quantitative determination of ether was applicable to the determination of these compounds. The results are set forth in Table I.

TABLE I.
Oil/Water Coefficients of Anesthetics.

Compound	No. of determinations	Oil/water coefficient	Probable error ±
Ethyl ether	10	4.1	.8
Cyprome ether	9	5.0	.4
Cypreth ether	7	16.3	.7
Allyl methyl ether	10	4.1	.5

Despite the precautions observed and the tediousness of the determination the probable error in a series of analyses is rather high. It occurred to the authors to attempt again, as many previous investigators have done, to correlate some definite physical property with anesthetic potency.

In the series of anesthetic agents studied we have found the simple determination of the water solubility of the compound to bear a striking relationship to the biological potency. This datum appears to be a more faithful physical index than the oil/water coefficient and the simplicity of determination bespeaks its general applicability. Our determinations were carried out in 100 cc "Cassia Flasks." One hundred cubic centimeters of water was introduced and an exact volume of the anesthetic agent in excess of its water solubility was added. The flask was agitated vigorously for 2 hours and after

4 Andrews, E., Potter, R. M., Friedmann, T. E., and Livingstone, H. M., *J. Lab. and Clin. Med.*, 1940, **25**, 966.

complete separation, the volume of the undissolved agent was measured in the graduated neck of the flask. We have expressed our data most significantly by plotting the reciprocal of the solubility (1/cc in 100 cc) against the logarithm of the number of moles per kg which we determined were required to produce respiratory arrest in the dog. Fig. 1 shows these data.

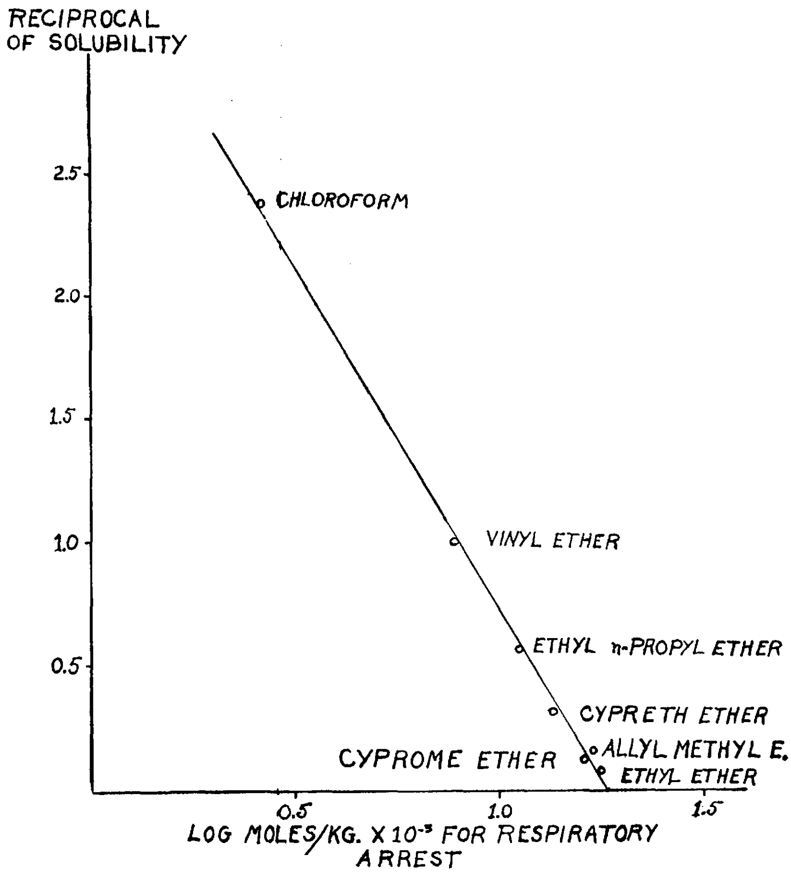

FIG. 1.

Summary. In a series of new anesthetics and also among certain of those agents widely employed today, the authors have found the insolubility of the compound in water a faithful criterion of anesthetic potency.