

ROBBINS, B. H.: *Preliminary Studies of the Anesthetic Activity of Fluorinated Hydrocarbons*. *J. Pharmacol. & Exper. Therap.* **86**: 197-204 (Feb.) 1946.

"Numerous reports relative to the anesthetic activity of chlorine, bromine and iodine derivatives of the lower members of the methane and ethylene series of hydrocarbons have been made. . . . Fluorine derivatives of the lower hydrocarbons have, however, received no such extensive study. . . . We have had the opportunity during the past two years of testing some forty-six fluorine compounds for their anesthetic activity. . . . Although most of these substances contain other halogens in addition to fluorine, there have been sufficient fluorine compounds in this series to show that these are not as inert physiologically as previously thought. . . . The anesthetic activity of forty-six hydrocarbons . . . has been determined in mice. Eighteen of these forty-six compounds have been used on dogs to study their effect upon the blood pressure and changes in the cardiac rhythm as shown by electrocardiographic examination. Data obtained with four of these compounds are such that further study of them as anesthetic agents is indicated." [The four compounds are $CF_3CHBrCH_3$, CF_3CHBr_2 , $CF_2CHClCH_2Cl$ and $CHF_2CHClCH_2$.] 6 references.

J. C. M. C.

KRANTZ, J. C., JR.; EVANS, W. E., JR.; CARR, C. J., AND KIBLER, DOROTHY V.: *Anesthesia XIX. The Anesthetic Action of n-Propyl Methyl Ether*. *J. Pharmacol. & Exper. Therap.* **86**: 138-144 (Feb.) 1946.

"The two ethers which are generally employed as inhalation anesthetics are symmetrical ethers, namely diethyl and divinyl ethers. Our previous studies with mixed ethers such as cyclopropyl methyl, cyclopropyl vinyl and

isopropenyl vinyl ethers, prompted us to study the simple isomer of ethyl ether, i.e., n-propyl methyl ether. . . . n-Propyl methyl ether is a volatile, colorless liquid with a characteristic ethereal odor: the boiling point is 39 C. and the specific gravity 0.726 at 16 C. . . . The potency of n-propyl methyl ether is approximately 25 per cent greater than that of ethyl ether. In the dog, n-propyl methyl ether anesthesia produces no functional liver damage as shown by the bromsulfalein test. In these experiments in the rat, dog and monkey anesthetics with n-propyl methyl ether produced no histopathological changes in the liver and kidneys. Neither the monkey's nor the dog's heart showed any significant electrocardiographic changes under anesthesia with n-propyl methyl ether. The blood pressure of the dog remains essentially unaltered under anesthesia with n-propyl methyl ether. This isomer of ethyl ether compares very favorably with ether as an inhalation anesthetic in several species of animals. This first approximation of the anesthetic properties of n-propyl methyl ether, in our opinion, warrants its careful and judicious trial in man by skilled anesthetists. Extensive and intensive studies alone in human anesthesia will reveal whether or not this mixed ether will warrant a place in the armamentarium of the anesthetist." 9 references.

J. C. M. C.

GRUBER, C. M., AND KEYSER, GOLDIE A.: *A Study of the Development of Tolerance and Cross Tolerance to Barbiturates in Experimental Animals*. *J. Pharmacol. & Exper. Therap.* **86**: 186-196 (Feb.) 1946.

"Tolerance for many drugs can be acquired by human beings as well as by experimental animals. When this occurs the dose of the drug has to be progressively increased in order to

maintain a given level of pharmacological effect. In dealing with the question of the possible formation of a tolerance to the barbiturates there has been much confusion and contradiction among various investigators. . . . Because of the differences in the method of experimentation employed in the various studies to determine whether or not experimental animals can acquire a tolerance to barbiturates and because conclusions were based on results from too few animals in most cases this work was undertaken in an effort to correlate and clarify conflicting data. Some experiments were also performed in which, after the animals showed a definite decrease in the period of sleep produced by a barbiturate, the LD_{50} of that drug was given. Additional experiments were performed to determine if an animal tolerant to one barbiturate was also tolerant to others. The sodium salts of the following barbituric acid derivatives were investigated: 1) Sec-butyl ethyl (butisol); 2) Isoamyl ethyl (amytal); 3) cyclopentemylallyl (cyclopal); 4) ethyl (1-methyl butyl) (pentobarbital); 5) N-hexylethyl (ortal); 6) Propylmethyl-carbinyl allyl (seconal); 7) N-methyl-cyclohexenyl-methyl (evipal). Dogs, rabbits and albino rats were used in this investigation. . . . If a reduction in sleeping time can be taken as a criterion of acquired tolerance to barbiturates in experimental animals then we have demonstrated (a) that dogs can acquire tolerance to butisol sodium and pentobarbital sodium (b) rats can acquire a tolerance to butisol sodium, pentobarbital sodium, cyclopal, ortal sodium and seconal sodium and (c) rabbits can acquire a tolerance to amytal sodium, butisol sodium, pentobarbital sodium, seconal sodium, cyclopal and evipal sodium. A tolerance to the barbiturate, as judged by the shortened sleeping time, is no protection against the LD_{50} . A dog, rabbit or rat made

tolerant to one barbiturate will very likely show some tolerance to all other barbiturates. Cross tolerance was shown in rabbits for butisol sodium, pentobarbital sodium and amytal sodium, in dogs and rats for butisol sodium and pentobarbital sodium. In developing tolerance in rabbits the time interval can be longer between administrations when long acting barbiturates are used than when short acting barbiturates are studied. To develop tolerance in rabbits to evipal sodium the drug must be administered twice each day. Tolerance to the barbiturate is rapidly lost in experimental animals following cessation of administration." 25 references.

J. C. M. C.

LUNDY, J. S.: *An Improved Ring Pinch Clamp*. Proc. Staff Meet., Mayo Clin. 21: 76-77 (Feb. 20) 1946.

"An improved pinch clamp . . . has been found useful in intravenous therapy. The clamp is made of stainless steel so that it has a much longer life than the ordinary clamp. On the stem forty-eight threads are used to the inch instead of the standard twenty-four. This permits fine adjustment of the drip through a tube, which is sometimes difficult to achieve with the ordinary clamp. The knob that is grasped to turn the stem has been made large so that it can be used easily. The opening in the clamp also is large so that it may be used on many sizes of tubing. The ring on the bottom of the clamp rotates freely and thus it can be adjusted by one hand of a right-handed or left-handed person. The inside of the ring has a narrow edge which facilitates withdrawal of the finger from the ring. . . . The long life of this clamp makes it particularly dependable. It appears to have several uses."

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