the experiment. Elimination of these variables seems highly desirable.

Determinations of osmotic pressures of 11 apparently normal medical students give values ranging from 321 to 380 mm. of water. The serum albumin and serum globulin were determined by analysis using the method of Wu and Ling[5] and give values of 6.32 to 6.81 gm. of protein per 100 cc. of serum. In calculating osmotic pressures from these protein values the data of Govaerts were used (75.4 mm. of water pressure per gm. of albumin and 19.5 mm. of water pressure per gm. of globulin) and the osmotic pressures were found to be 361 to 394 mm. of water, values which are consistently higher than those obtained by direct measurement.

Our results indicate a fair degree of accuracy and it is hoped that with the accumulation of more extensive data a better correlation between observed and calculated osmotic pressures may be obtained.

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A Note on the Minimal Fatal Dose of Nicotin for Unanesthetized Dogs.

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The following observations were made as part of a study of the cause of death in nicotin poisoning in dogs. Sollmann[1] mentions that 2 drops of nicotin placed on the gums of a dog may rapidly cause death. Blake[2] injected 2 drops of nicotin into the jugular vein of a dog, death occurring about one minute and a half after the administration of the poison.

At the time we carried out our experiments we were not aware of any reports in the literature dealing with the minimal fatal dose of nicotin for dogs. von Anrep[3] reports that 1.5 drops of nicotin

[5] Wu and Ling, *Chinese J. Physiol.*, 1927, **1**, 161.

[1] Sollmann, Manual of Pharmacology, 1922, Saunders, Philadelphia.

[2] Blake, *Edinb. Med. and Surg. J.*, 1840, **53**, 35.

[3] von Anrep, *Arch. f. Physiol.*, Leipz, 1879, Suppl. Bd., 167-191.

is a dangerous dose and 3.5 drops is fatal in a few minutes, for dogs weighing from 10 to 17 kg. Expressed in mg. of nicotin per kg. of dog's weight, the dangerous dose would be approximately 5.7 to 9.75 mg. per kg. and a dose of 13.4 to 22.75 mg. per kg. would be fatal in a few minutes. Kobert[4] places the minimal fatal dose at 0.5 to 2 drops of nicotin.

Nicotin was administered to 48 dogs. In a majority of the experiments no drug other than nicotin was given. In a few cases a small amount of novocain was used to produce local anesthesia for the exposure of a vein or artery. In some the blood pressure was recorded, but without the use of any anticoagulant. Neither the minor operative procedures nor the local anesthetic had any observable influence on the results.

Three methods of administering the drug were used:

1. By mouth. Nicotin was dropped on the tongue or between the lips and gums in the form of the undiluted alkaloid.

2. By injection into the circulating blood. The alkaloid in 10% solution in Locke's fluid was injected into a vein (with or without surgical exposure) or directly into the cavity of the left ventricle.

3. Subcutaneously or intramuscularly, in 10% solution of the hydrochloride.

The results are summarized in Table I. The smallest dose of nicotin which proved fatal in a high percentage of dogs was, when given by mouth, 10 mg. per kg., and when injected into the circulation, 3 mg. per kg. Doses larger than 12 mg. per kg. by mouth and 5 mg. per kg. injected into the circulating blood were uniformly fatal. The fatal dose when given subcutaneously was not ascertained but 23 mg. per kg. failed to cause death. In one dog, 7.7 mg. per kg. intramuscularly proved fatal. The nicotin for intramuscular and subcutaneous administration was measured as the alkaloid but administered as the hydrochloride.

There was considerable individual variation in susceptibility. Two dogs recovered after receiving 5 mg. per kg. into the circulation, and one animal died after receiving only 2 mg. per kg. It happened also that all of the animals in this group that received 3 or 4 mg. per kg. died.

The last column of the table gives the time elapsing after giving the nicotin until the palpable pulse and respiration ceased. Most of the animals died in 4 minutes or less. Those given the drug intravenously died in about 2 minutes. It is remarkable that in these animals there is no appreciable difference in the time till death corresponding to the

[4] Kobert, R., *Lehrbuch der Intoxikationem*, 1906, Bd. 2.

TABLE I.

Administration	Dose	No. of experiments	No. fatal	No. non-fatal	% fatal	Average time till death
	(mg. per kilo)					minutes
By mouth	20	2	2	0	100	2.5 (1 exp.)
" "	12	1	1	0	100	3.5
" "	9.2 to 10.3	14	8	6	57.1	3.77
" "	4.6 to 5.0	2	0	2	0	
Intracardiac	5.7 to 6.0	3	3	0	100	2.5
"	5	1	0	1	0	
Intravenous	10	5	5	0	100	1.93 (4 exps.)
"	5	7	6	1	85	1.96 (5 exps.)
"	4	1	1	0	100	2.00
"	3	3	3	0	100	1.88
"	2	4	1	3	25	2.3
Subcutaneous	23	1	0	1	0	
"	15	1	0	1	0	
"	9	1	0	1	0	
"	8.8	1	0	1	0	
Intramuscular	7.7	1	1	0	100	4.0

difference in dosage. Ten, 5, and 3 mg. per kg. caused death in an average time of 1.93, 1.96, and 1.88 minutes, respectively.

A study of the minimal fatal dose of nicotin when given intravenously to etherized dogs was previously reported.[5] Comparison of those results with experiments reported here indicates that small doses of nicotin (2 to 4 mg. per kg.) are more likely to prove fatal in normal than in anesthetized animals. For example, 4 animals out of 5 in the etherized series recovered following administration of 3 mg. per kg., whereas that dose was uniformly fatal (3 animals) in this series, and one animal out of 4 that received but 2 mg. per kg. died. Furthermore, the unetherized animals died much more quickly than the etherized animals. The average time till death after giving the drug in 12 etherized animals was 7.8 minutes. In the 24 animals of the present (unetherized) series that received the drug in the same way (into the circulating blood), the average time until death was 2 minutes.

[5] Thomas, J. Earl, and Franke, F. E., *J. Pharmacol. and Exp. Therap.*, 1928, **34**, 111.