hypertension and arteriolosclerotic nephritis. We are attempting to determine whether generalized hyaline arteriosclerosis can be produced by repeated injections of trypsin, and whether the proteolytic enzymes of bacteria are able to cause this lesion.

7174 C

Spinal Anesthesia in Winter Frogs.*

RAYMOND N. BIETER AND JAMES W. BROWN.

From the Department of Pharmacology, University of Minnesota Medical School.

In a previous communication[1] a simple method for producing spinal anesthesia in the frog was described. In addition, a series of 10 local anesthetics were studied in summer frogs, kept at temperatures of from 26° to 29°C. The data obtained on each drug included the determination of the minimal anesthetic dose, minimal lethal dose, duration of anesthesia produced by a sublethal dose, and the calculation of a therapeutic coefficient from the fraction M.L.D./M.A.D. Comparatively, this coefficient gives evidence of the usable therapeutic range for each local anesthetic.

In this paper similar results are described in which 7 local anesthetics were injected intraspinally into winter frogs kept before, during and after the experiments at 10° to 12°C. This series includes those local anesthetics showing, experimentally, the best possibilities for use in human spinal anesthesia. Five of these drugs had been studied previously in summer frogs, but because of the relatively high temperature prevailing at that time, it was thought advisable to repeat the work at a lower temperature and perhaps a more satisfactory one for frogs. Because of great variations noted in frogs, which are ascribed to seasonal and temperature changes, a further check on uniformity was attempted by carrying out the complete series during two winters. Consequently the first series was carried out between October 10, 1931, and February 20, 1932, and the second, between the same periods of 1932-33. As can be seen from the table no great variations are to be observed between the 2 series. It might also be added that the results obtained on winter frogs

* This work was aided by a grant from the Graduate School Research Fund of the University of Minnesota.

1 Bieter, R. N., Harvey, A. M., and Burgess, W. W., *J. Pharm. and Exp. Therap.*, 1932, **45**, 291.

show a close parallel to similar data obtained on the rabbit. These will be reported later.

The method of experimentation used was identical with that described previously. The % solutions used were as follows:

For determining	M.A.D.	M.L.D.
Nupercaine	.3	.6
Pantocaine	.15	1.
Metycaine†	.5	2.
Larocaine	.5	10.
Panthesine	.5	10.
Tutocaine	.5	10.
Procaine	2.	10.

† Metycaine was formerly called neothesine.

These variations were necessary in order to meet the requirements of a small uniform volume for all injections. The criterion for determining the M.A.D. was the same as before, that for the M.L.D. differed in one respect, namely, that the time interval for determining death had to be lengthened from 3 hours, as used in summer frogs, to 24 hours. A total of 850 male frogs was used, obtained fresh every week and contained in a running water tank for 2 to 3 days before use.

TABLE I.

Minimal Anesthetic and Minimal Lethal Doses, and Therapeutic Coefficients; intraspinal anesthetics in winter frogs

Drug	M.A.D. in mg. per gm. wt.	Aver. of 2 series	M.L.D. in mg. per gm. wt.	Aver. of 2 series	Ratio: M.L.D./M.A.D. (Therapeutic Coef.)
Nupercaine	.006*	.006	.008	.008	1.3
	.006		.008		
Procaine	.045	.045	.28	.29	6.4
	.045		.30		
Metycaine	.01	.01	.075	.075	7.5
	.01		.075		
Pantocaine	.004	.0035	.035	.0325	9.2
	.003		.03		
Larocaine	.0125	.0125	.155	.155	12.4
	.0125		.155		
Panthesine	.0075	.007	.15	.147	21.0
	.0065		.145		
Tutocaine	.015	.015	.35	.35	23.3
	.015		.35		

* Upper figure, 1931-32 series, lower, 1932-33.

Table I shows the M.A.D., M.L.D., and therapeutic coefficient for each of the 7 anesthetics. The 5 drugs used in summer frogs showed a marked drop in toxicity at the lower winter temperature. These diminutions in toxicity in per cent of the summer M.L.D.'s were as follows: Nupercaine 100%, procaine 31%, metycaine 50%, pantocaine 62%, and tutocaine 75%. On the other hand the M.A.D.'s were practically the same with the exception of nupercaine which was almost 50% less active at the lower temperature.

Summary. The three local anesthetics, larocaine, panthesine and tutocaine, which chemically are of the procaine type, but with branched side chains, gave the highest therapeutic coefficients. In a decreasing order of sensitivity (based on the M.A.D.) the anesthetics can be arranged as follows: pantocaine > nupercaine > panthesine > metycaine > larocaine > tutocaine > procaine. In an increasing order of toxicity (based on the M.L.D.) the anesthetics can be arranged as follows: tutocaine < procaine < larocaine < panthesine < metycaine < pantocaine < nupercaine.

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7175 P

Life History of Manson's Blood Fluke (Schistosoma mansoni). I. Extramammalian Phase of the Cycle.*

ERNEST CARROLL FAUST AND WILLIAM A. HOFFMAN.

From the Department of Tropical Medicine, Tulane University, and the School of Tropical Medicine, San Juan, P. R.

The work of which this contribution forms a part was carried on in Puerto Rico, where Manson's blood fluke infection is an important and extensive clinical entity. The lateral-spined eggs of the parasite were obtained from the feces of human and experimental animals. The stools were washed and concentrated either by centrifugation or by sedimentation. The numbers of these eggs obtained from a 24-hour specimen varied not only with the age of

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