

tension develops after subtotal nephrectomy. Therefore, if the hypertension is due in some way to a relatively narrow renal vascular bed, its degree is exquisitely adjusted to maintain a normal rate of renal blood flow.

Conclusion. Rats which become hypertensive several months after subtotal nephrectomy do not have renal ischemia; the flow per gram of renal tissue is 19% less than in rats a few days after subtotal nephrectomy, but the same as that in rats with unilateral nephrectomy and without hypertension.

9169

Experimental and Quantitative Analysis of Local Anesthesia of the Frog's Isolated Sciatic Nerve.

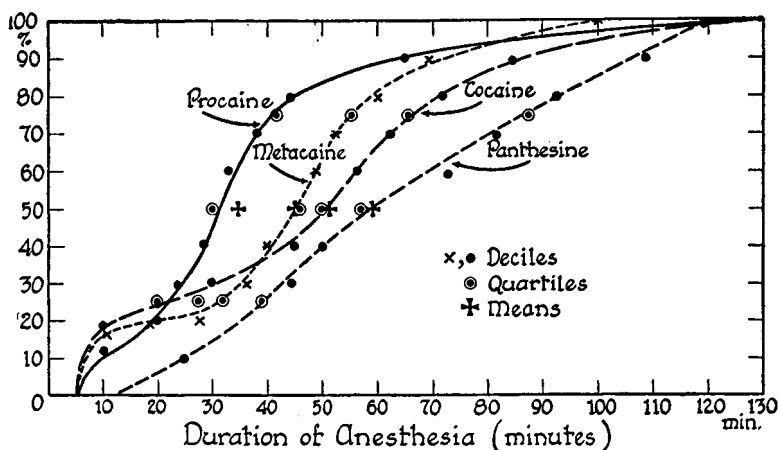
RAYMOND N. BIETER AND RICHARD E. SCAMMON.

From the Department of Pharmacology and the Graduate School, University of Minnesota, Minneapolis.

It is a commonly known fact that the characteristic action produced by certain local anesthetic drugs is a somewhat variable function. The extent and behavior of this variation are not well known. In an attempt to describe this variation, quantitative data on the duration of sensory anesthesia in frogs are herein presented. The data were obtained from class experiments of medical students over a period of several years.

The following experimental technique was used. The frogs were single pithed and one sciatic nerve in each frog was exposed in the thigh. The other leg served as a control. The normal reaction of the frog was determined by immersing the toes of one foot in 1% HCl. This causes a rapid withdrawal of this leg from the acid solution. Then the local anesthetic was applied to the isolated sciatic nerve by carefully placing a whisp of absorbent cotton about 3 mm. wide, thoroughly moistened with the local anesthetic solution but not dripping, under and around the nerve. This was allowed to remain in place for exactly 5 minutes. The whisp of cotton was then removed and the toes of the leg so treated were tested in the acid solution every 15 to 30 seconds until sensory anesthesia was produced (that is, when the leg is no longer drawn out of the acid solution during a period of application of 30 seconds). The duration of anesthesia was determined from this time forward by testing

the leg every few minutes. It was terminated when the leg was again pulled out of the acid solution as a result of an exposure to



| Substance (1/4% conc.) | n | Measures of duration of anesthesia (minutes) | | | | | Skewness |
|---------------------------|----|--|------------------|-------------------------------|----------------|------------------|----------|
| | | Mean & S.E. | Median & S.E. | Semi-inter- quartile range | S.D. & S.E. | C.V. & S.E. % | |
| Procaine HCl | 73 | 34.4 ± 2.2 | 30 ± 1.9 | 11 | 18.9 ± 1.6 | 54.9 ± 5.8 | +0.14 |
| Cocaine HCl | 76 | 51.9 ± 3.0 | 50 ± 2.5 | 18 | 26.0 ± 2.1 | 50.4 ± 5.1 | -0.22 |
| Metacaine | 78 | 45.1 ± 2.3 | 44 ± 1.9 | 12 | 20.3 ± 1.6 | 45.0 ± 4.3 | -0.13 |
| Panthesine | 72 | 63.3 ± 3.4 | 59 ± 2.9 | 24 | 28.3 ± 2.4 | 44.7 ± 4.4 | +0.18 |

| Substance (1/4% conc.) | Deciles & quartiles of duration of anesthesia (min.) | | | | | | | | | | | | |
|---------------------------|--|----|----|------------------------|----|----|------------------------|----|----|------------------------|----|-----|-------------------------|
| | (0) | 10 | 20 | Q ₁ (25) | 30 | 40 | Q ₂ (50) | 60 | 70 | Q ₃ (75) | 80 | 90 | Q ₄ (100) |
| Procaine HCl | 6 | 12 | 20 | 21 | 24 | 28 | 30 | 33 | 38 | 42 | 44 | 59 | 120 |
| Cocaine HCl | 6 | 19 | 25 | 28 | 30 | 45 | 50 | 56 | 62 | 64 | 73 | 85 | 130 |
| Metacaine | 6 | 19 | 25 | 31 | 36 | 40 | 44 | 49 | 52 | 54 | 60 | 69 | 95 |
| Panthesine | 11 | 25 | 35 | 39 | 43 | 50 | 59 | 73 | 81 | 88 | 92 | 102 | 120 |

| Differences between means of duration of anesthesia of pairs of substances | | | | |
|--|------------|---------------|------|--------------|
| Substances compared (a-b) | Difference | S.E. of diff. | R | P |
| Cocaine HCl. (a) ~ Procaine HCl. (b) | 17.2 | ± 3.7 | 4.65 | 0.000,006 |
| Metacaine (a) ~ Cocaine HCl. (b) | 10.7 | ± 3.2 | 3.34 | 0.000,9 |
| Procaine HCl. (a) ~ Panthesine (b) | 28.9 | ± 4.0 | 7.20 | 0.000,000,-- |
| Cocaine HCl. (a) ~ Metacaine (b) | 6.5 | ± 3.8 | 1.71 | 0.087 |
| Panthesine (a) ~ Cocaine HCl. (b) | 11.7 | ± 4.5 | 2.60 | 0.0093 |
| Panthesine (a) ~ Metacaine (b) | 18.2 | ± 4.1 | 4.44 | 0.000,15 |

FIG. 1.

Ogive graphs and tables showing the measures of central tendency, scatter and comparison of a series of anesthetics applied to the frog's isolated sciatic nerve.

the acid of no longer than 30 seconds. Four local anesthetics were studied, namely, Procaine HCl, Cocaine HCl, Metycaine and Panthesine (each in 0.25% concentration in 0.75% NaCl). From 72 to 78 determinations were obtained on each solution. A separate frog was used for each determination.*

Figure 1 presents our findings in graphic and tabular form. The first panel shows a series of ogives of the distribution of duration, in minutes, of anesthesia by the several substances. In this panel the percentage of observations forms the ordinate and the duration of anesthesia the abscissa. Deciles, quartiles, means and medians are indicated. The curves are drawn by inspection without smoothing.

The second panel gives various measures of central tendency and scatter of duration of anesthesia of the several drugs. All of the measures are the generally accepted ones with the exception of that for skewness. Here we have chosen from the several measures of the quantity the expression suggested by Rietz:¹

$$\text{Skewness} = \frac{Q_3 + Q_1 - 2Q_2}{Q_3 - Q_1}$$

The third panel gives the quartile, decile and minimum values for each of the drugs studied.

The fourth panel presents tests of the significance of differences of the means of duration of anesthesia of the several drugs. According to commonly accepted conventions, these differences are highly significant for Cocaine HCl—Procaine HCl, Metacaine—Cocaine HCl, Procaine HCl—Panthesine, and Panthesine—Metacaine. The significance of the difference for Panthesine—Cocaine HCl is probably significant and that for Cocaine HCl—Metacaine is very questionable.

Summary. Sensory anesthesia produced by 0.25% concentration in normal salt solution on the frog's sciatic nerve has been tested on a considerable series by immersion of the toes in 1% HCl. The results obtained were: 1. The mean and median durations of anesthesia fall in the following ascending order: Procaine HCl, Metacaine, Cocaine HCl, Panthesine. 2. A high degree of range is found for the 4 drugs studied. 3. The absolute variability in dura-

* Grateful appreciation is accorded to the following firms: The Winthrop Chemical Company, Inc., Eli Lilly and Company, and Sandoz Chemical Works, Inc., for generously supplying the Procaine (Novocain), Metacaine, and Panthesine, respectively, used in these experiments.

¹ *Handbook of Mathematical Statistics* (H. L. Rietz, Editor-in-Chief), Chap. II, p. 31 (Rietz), Boston, 1924.

tion of anesthesia falls in the following ascending order: Procaine HCl, Metacaine, Cocaine HCl, Panthesine. 4. The relative variability in duration falls in the following order: Panthesine, Metacaine, Cocaine HCl, Procaine HCl. 5. All distributions of duration of anesthesia show a distinct measure of skewness, those for Procaine HCl and Panthesine being positive and those for Cocaine HCl and Metacaine being negative. 6. The differences in mean duration of anesthesia between the several drugs is highly significant in 4 pairings, probably significant in one, and doubtful in another.

9170 P

Effects of a Divalent Cation on Sodium Removal from Intestinal Loops.

R. C. INGRAHAM AND M. B. VISSCHER.

From the Departments of Physiology, University of Illinois, Chicago, and University of Minnesota, Minneapolis.

It has previously been found that in the presence of any polyvalent anion, the univalent anions such as chloride¹ or bromide² move from the intestinal loop into the blood against great concentration differences. The univalent anion may fall to a concentration in the intestine less than 1% of its blood concentration.

The comparable situation has now been tested with respect to cations. A solution containing sodium chloride and magnesium chloride, each in half isotonic quantities, was placed in a washed loop of the lower ileum of the amytal anesthetized dog as previously described.¹ Samples were taken at intervals and sodium determined by the Barber-Kolthoff³ method, chloride by the Van Slyke⁴ technique, and ammonia by the Nash-Benedict⁵ procedure.

Figure 1 shows the results of a typical experiment. It is to be noted that the sodium content decreased over a period of 1½ hours, from an initial level which is approximately one-half of the blood plasma level, to 8 mM., which is approximately 5% of the blood plasma level. Meanwhile the chloride content fell to approximately its blood concentration. These results have been obtained uniformly in 10 trials. Other experiments, not reported in full in

¹ Ingraham, R. C., and Visscher, M. B., *Am. J. Physiol.*, 1936, **114**.

² Ingraham, R. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 453.

³ Barber, H. H., and Kolthoff, I. M., *J. Am. Chem. Soc.*, 1928, **50**, 1625.

⁴ Van Slyke, D. D., *J. Biol. Chem.*, 1923, **58**, 523.

⁵ Nash, T. P., and Benedict, S. R., *J. Biol. Chem.*, 1921, **48**, 463.