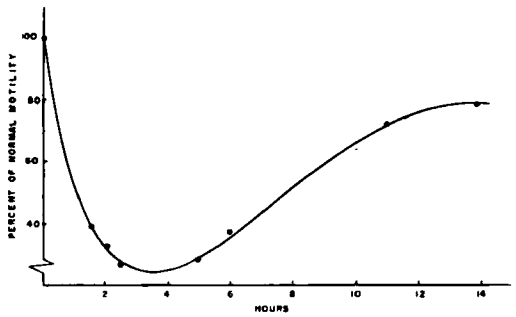

Fig. 1.—Pattern of surgically induced gastrointestinal atony and restoration in cecectomized mice as determined by the 30-minute passage of orally administered charcoal. Normal motility = 100%.

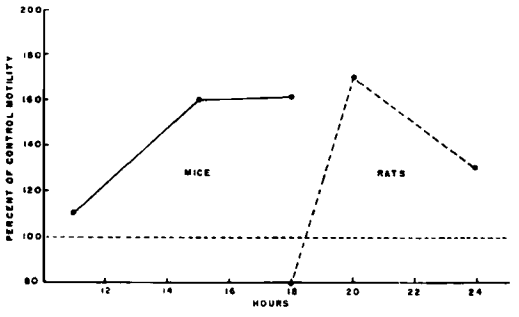

Fig. 2.—Pantothenyl alcohol (10 mg./Kg.) effect in the response phase of surgically induced atony as determined by the 45-minute passage of charcoal. Control motility in cecectomized animals = 100%.

upper gastrointestinal motility in regard to surgical cecectomy and pantothenyl alcohol effect appears to be: (*a*) an atony phase, (*b*) a restoration phase, and (*c*) a pantothenyl alcohol-effect phase.

The results suggest that upper gastrointestinal motility as measured by 30 or 45 minutes charcoal passage rates at 14 to 24 hours postoperatively in mice and rats is optimal for evaluating pantothenyl alcohol or similarly acting compounds.

The data presented tend to confirm in part the work of Unna and Greslin (9) in that pantothenic acid does not exert a direct pharmacologic effect in normal animals, and substantiates the report of Polacek, *et al.* (10), in which pantothenyl alcohol hastened the return of normal gastrointestinal motility. The difference in response of normal and post-surgical animals suggests that surgically induced atony may be related to a depression in function of the pantothenate-coenzyme A-acetylcholine biochemical pathway. Pantothenyl alcohol may act by accelerating this function in the post-surgical animal.

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Quantitative Evaluation of Surface Anesthetics in Albino Mice

By W. R. JONES and L. C. WEAVER

The corneal reflex of the albino mouse is satisfactory for the quantitative determination of relative potency of local anesthetics. It was found that dyclonine was more active, benzonatate equally active, and procaine less active than cocaine.

THE CORNEAL reflex of cats (1), dogs (2), rabbits, and guinea pigs (3) has been used for the detection of local anesthetic activity. Pittenger (1) suggested the use of the cornea of cats for the qualitative detection of local anesthetic action. However, Munch (2) concluded that cats are not as suitable as rabbits because of greater individual differences in activity and because of greater reluctance on the part of the test animal to permit the touching of the cornea at frequent intervals. He also concluded that qualitative tests made upon the cornea of dogs offer no particular advantage. The corneal reflex in the rabbit has not been successfully standardized and has not withstood statistical examination (3). Although Chance and Lobstein (3) report that guinea pigs show a more regular reflex response, both normally and when anesthetized, than do rabbits, Bulbring and Wajda (4) found that guinea pigs frequently fail to blink even if the cornea is not anesthetized. Regardless of the relative advantages of guinea pigs *vs.* rabbits, however, Chance and Lobstein (3) introduced a method which made possible a quantitative comparison of local anesthetics.

When preliminary tests indicated that the albino mouse might be a satisfactory animal for the bioassay of local anesthetics, an experiment was carried out to determine a dose-response curve for cocaine, procaine, dyclonine, and benzonatate. The ac-

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TABLE I.—POTENCY OF SEVERAL SURFACE ANESTHETICS IN ALBINO MICE

	Dyclonine	Benzonatate	Procaine	Cocaine
ED_{50} (mg./ml.)	0.27	2.45	34.5	2.45
Fiducial limits P — 0.95	0.16–0.47	1.64–3.68	23.0–51.8	1.23–4.90
Slope	2.72	2.03	2.11	2.08
Fiducial limits P — 0.95	1.13–6.53	1.08–3.82	0.75–5.91	1.16–3.74

tivity of these compounds relative to cocaine was then calculated.

EXPERIMENTAL

Male Swiss-Webster albino mice were used. After trimming the eyelashes, one drop of the solution to be tested was placed on the surface of each eye. (Grasping the skin near the back of the head caused the eyes to protrude so that the drop readily adhered to the surface.) Approximately 25–30 seconds later, the remaining solution was removed by touching the eyes with a piece of absorbent tissue (Kleenex). One minute from the time the solution was applied, the surface of the cornea was touched with a small glass probe[1] and the presence or absence of the corneal reflex was recorded. Corneal stimulation was repeated at one-minute intervals until the animal failed to show anesthesia on three successive occasions. In testing for the corneal reflex, the animal was placed on a piece of wire mesh and held by the tail with one hand while the other hand was braced on the table top and used to manipulate the glass probe so that the surface of the eye could be gently touched without touching the eyelids. For purposes of calculation, only the first 10-minute interval was used. Thus, each animal contributed 20 responses to the total. The number of times the animal failed to blink was divided by the number of times the eyes were stimulated and the percentage response for each group was plotted against the dose (in mg./ml.). Six to nine mice were used to locate each point on the dose response curve, which was calculated by the method of Litchfield and Wilcoxon (5).

Relative potency was determined by comparing the dose-response curves of each drug to that of cocaine (Table I) and the following results obtained: (*a*) Dyclonine was significantly more active than cocaine. The potency ratio and 19/20 confidence limits were 9.07 and 3.73–21.94. (*b*) Benzonatate did not differ significantly from cocaine. The potency ratio and 19/20 confidence limits were 1.00 and 0.45–2.24. (*c*) Procaine was significantly less active than cocaine. The potency ratio and 19/20 confidence limits were 0.07 and 0.03–0.16.

[1] A piece of glass tubing (0.5 cm. i.d.) was heated and drawn out so that the tip, when sealed, was approximately 1 mm. in diameter. To facilitate the application of this tip to the cornea, the final 2 mm. were bent at a 60° angle and a 30° angle was made 2 cm. above this point. The overall length was about 13 cm.

DISCUSSION AND CONCLUSIONS

These data suggest that the procedure presented may be used for quantitative evaluation of surface anesthetics in mice. Accurate dose-response curves were economically and easily obtained. A further advantage was the fact that stimulation of the unanesthetized cornea of the albino mouse never failed to elicit a blink in our studies to date.

This test, as most tests, is not entirely objective. At the time the drug effect begins to wane, some difficulty may arise in scoring corneal responses. The response which occurs when the unanesthetized eye is touched is clean, clear-cut, and distinct. The total lack of response of the fully anesthetized eye likewise presents no difficulty to the observer. However, at some point between these extremes, the animal squints or blinks in response to corneal stimulation in a manner very different from the normal rapid response. Any movement of the eyelid was taken as lack of anesthetic effect. This was actually a minor problem in the experiment and should not be unduly emphasized.

Since it is common practice to modify procedures, the following variables might well be investigated to improve on the procedure presented. These include: (*a*) Choice of different time intervals. (*b*) Alterations of the time of drug contact with the eye. (*c*) Examination to determine whether there is less variability between the right eye and the left eye than there is between different animals. If so, a more valid comparison of relative potency could be obtained by treating one eye with a standard drug and the other eye with the drug whose relative potency is to be determined. In this manner, both drugs could be compared in the same animal at the same time.

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