

ically was bubbled through the solution in such a way as to bring it in equilibrium with the gaseous mixture as quickly as possible.

Thirty segments from 6 rabbits were tested for reactivity with acetylcholine and epinephrine in appropriate concentrations and washed carefully before applying the cyclopropane. In each case after bubbling into the bath concentrations of 10% to 25% cyclopropane in oxygen there was an increase in tone of the intestinal muscle with a decrease in amplitude of contraction (Figs. 1 and 2). Upon washing the cyclopropane from the bath there was a gradual return of the segment to its normal activity. The degree of gut stimulation was found to be roughly proportional to the concentration of cyclopropane up to 25% in oxygen at which maximum effect seemed to be obtained. In concentrations higher than this there was progressively less increase in tone. These observations indicate that less post-operative intestinal stasis and resulting distension should occur after the clinical use of cyclopropane than after ether.

8342 C

Cumulative Toxicity of Emetine Hydrochloride in Guinea Pigs.

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The minimum lethal dose of emetine hydrochloride on subcutaneous injection of repeated small doses is practically the same as on single injection. Anderson and Leake¹ concluded from their own experiments and other observations reported in the literature that excretion of emetine after either oral or parenteral administration must be slow and also that little or no detoxication takes place in the tissues. Fischl and Schlossberger² summarize work indicating that the cumulative toxic effect of emetine hydrochloride may occur in many species. Nevertheless, there is some question as to the cumulative toxicity in the guinea pig in view of the single observation of Young and Tudhope³ in which the total of divided doses of

¹ Anderson, H. H., and Leake, C. D., *Am. J. Trop. Med.*, 1930, **10**, 249.

² Fischl, V., and Schlossberger, H., *Handbook of Chemotherapy*, Baltimore, 1933.

³ Young, W. A., and Tudhope, G. R., *Trans. Roy. Soc. Trop. Med.*, 1927, **20**, 93.

emetine hydrochloride was equivalent to about 80 mg. per kg. before death occurred. Since little data is available on the cumulative toxicity of emetine when given in a series of graded doses, or on the toxicity in guinea pigs, the present work was designed to study both these points.

Seven groups of 10 guinea pigs each, ranging in weight from 150 to 250 gm. were used. Since it has been demonstrated that the LD_{50} is approximately the same for many laboratory animals, Lake's⁴ finding of a LD_{50} of 20 mg. per kg. for white rats was arbitrarily chosen as a basis for the present work. Two groups of 10 guinea pigs each were given a single subcutaneous injection of this dose of emetine hydrochloride. The same dose of 20 mg. per kg. was administered to 4 similar groups of guinea pigs in divided doses of 1.0, 2.0, 4.0 and 10.0 mg. per kg., respectively, injected subcutaneously at intervals of 2 days until the full dose was given. As controls, 10 guinea pigs were given 20 subcutaneous injections of physiological saline.

The animals were weighed at frequent intervals during the 40-day period of observation. The usual picture of emetine intoxication was encountered, with marked lethargy, loss of weight and decreased appetite. Autopsy of animals dying revealed marked distension of the gut and general congestion of the viscera.

TABLE I.
Cumulative Toxicity of Emetine Hydrochloride in Guinea Pigs.

| No. of Doses | Mg./Kg. per Dose | Mortality Ratio No. Dying/No. Used | Av. Time of Death, Days from 1st Injection |
|--------------|------------------|---------------------------------------|---|
| 1 | 20 | 6/20 | 6.7 |
| 2 | 10 | 5/10 | 22.4 |
| 5 | 4 | 5/10 | 20.4 |
| 10 | 2 | 4/10 | 17.8 |
| 20 | 1 | 5/10 | 32.4 |
| 20 | saline | 0/10 | — |

From Table I it may seem that emetine hydrochloride shows a definite cumulative toxicity even when given in doses as small as one-twentieth of the MLD. While the small number of animals used impairs the significance of the results found, it is of interest to note that the cumulative toxicity of small divided doses was apparently greater than the acute toxicity when a single dose was administered.

Summary. The toxicity of emetine hydrochloride administered subcutaneously to guinea pigs is approximately the same whether the

⁴ Lake, G. C., *U. S. P. H. S., Hyg. Lab. Bull.*, 1918, **113**, 2.

alkaloid is given in a single large dose or in repeated doses of 1/20 the acute MLD over a period of 40 days. Caution is indicated in the use of repeated doses in humans.

8343 P

Different Potentialities of Male and Female Skin in Reeves Pheasants.*

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The extraordinary similarity of feathers produced by male and female fowls after gonadectomy has led to the idea that the skin in the 2 sexes is potentially the same. This inference seems to be supported by the effects of endocrine injections and the results of skin transplantation. It is further strengthened by the fact that, although between different races there is much variation in response to endocrines, the 2 sexes of any one race react rather consistently. Nevertheless, there are frequently detectable, though generally slight, differences between feathers produced by birds that were originally male and those that were originally female. This suggests that the genotype of the male and that of the female may condition slightly different responses when all other factors are held constant.

A search for some form in which this problem could be approached more satisfactorily than in the common fowl revealed that the Reeves pheasant (*Syrnaticus reevesi*) is very satisfactory for the purpose. It is a species which breeds true to a standard type and has a plumage that is distinctive and varied, with none of the feathers of one sex duplicated by those of the other. The birds are rather expensive when purchased from dealers, but may be raised from eggs with relative ease.

Homoplastic skin transplantation immediately after hatching was chosen as the method affording the most delicate and dependable test. The procedure has the disadvantage of requiring a wait of several months between the beginning of an experiment and attainment of the final result. It also involves certain losses due to incompatibility of tissues of donor and host. But in many cases no incompatibility is revealed and the grafted skin appears to behave

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