

Contributed and Selected

THE RAPIDITY OF ELIMINATION OR DESTRUCTION OF STROPH- ANTHUS AND DIGITALIS GLUCOSIDES BY GUINEA PIGS.

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In the summer of 1911, experiments were performed in our laboratory to determine whether ouabain showed any tendency to manifest the so-called "cumulative" action on guinea pigs. With this end in view, the minimum lethal dose of ouabain in 25 percent alcohol was determined and four pigs were given barely sub-lethal doses. These same animals were injected with varying amount of ouabain on subsequent days, after the lapse of about 24 to 48 hours. The following protocol illustrates the results secured in all instances.

Experiment I. M. L. D. Ouabain 0.00000028—0.00000030 gm. per gm. weight.

9/9/11—Black male pig, wt. 260 gm.: 0.00000029 gm. ouabain at 10:57 a. m. Almost died.
 9/12/11—Wt. 264 gm.: 0.0000002 gm. ouabain at 3:24 p. m.
 9/13/11—Wt. 242 gm.: 0.0000002 gm. ouabain at 10:57 a. m.
 9/14/11—Wt. 246 gm.: 0.0000002 gm. ouabain at 4:20 p. m.
 9/15/11—Wt. 250 gm.: 0.0000002 gm. ouabain at 4:20 p. m.
 9/16/11—Wt. 247 gm.: 0.00000027 gm. ouabain at 11:27 a. m.
 9/18/11—Wt. 256 gm.: 0.00000028 gm. ouabain at 3:58 p. m.
 9/19/11—Wt. 258 gm.: 0.00000028 gm. ouabain at 5:02 p. m.

Experiment discontinued.

It is apparent from these results that ouabain is rapidly destroyed or excreted by the guinea pig and that when twenty-four hours have elapsed a guinea pig that has previously received a large dose of ouabain is no more susceptible than is an animal that has previously received none. If, however, the second injection is made in considerable less than 24 hours after the first, the animal succumbs. This may be seen from the following experiments:

EXPERIMENT II.

Male pig. Wt. 416 gm.
 9/9/11—2:33 p. m.: 0.00000028 gm. ouabain.
 5:03 p. m.: 0.00000010 gm. ouabain.
 Died during night.

EXPERIMENT III.

Male pig. Wt. 613 gm.
 9/9/11—2:37 p. m.: 0.00000015 gm. ouabain.
 5:07 p. m.: 0.00000026 gm. ouabain.
 Died during night.

The question then arose, do the animals acquire a greater degree of resistance as a result of these sub-lethal doses? That this is not the case is shown by the following protocol:

EXPERIMENT IV.

Male pig. Wt. 439 gm.
 9/11/11—10:34 a. m.: 0.00000028 gm. ouabain.
 9/12/11— 3:23 p. m.: 0.00000020 gm. ouabain.
 9/13/11—10:59 a. m.: 0.00000028 gm. ouabain.
 4:20 p. m.: Found dead.

These results are in full accordance with the experience of Vanderkleed and Pittenger.

In June, 1912, Hatcher read his excellent and comprehensive paper on "The Persistence of Action of the Digitalins," and reported that the action of ouabain showed little tendency to persist when tested on cats, but that digitalis did show such persistence. He found that some cats, after a larger, sub-lethal dose of digitalis, showed diminished resistance for as long as a month. Experiments upon rabbits showed that these animals are not rendered more susceptible to digitalis by sub-lethal doses when several hours elapse before the second injection.

In view of these results of Hatcher's, it seemed advisable to determine the behavior of guinea pigs toward digitalis; consequently, experiments similar to those already carried out with ouabain have been performed, digitalis preparations being used for the first injection, while ouabain or digitalis was used for the second injection. The results may be tabulated as follows:

Interval between Injections.	Percent of First Inj.	Aver. M. L. D. Second Inj.	Results.
1 day.....	36	80	Survived
1 day.....	55	80	Survived
2 days.....	74	74	Survived
2 days.....	92	37	Survived
3 days.....	57	86	Survived, almost died
3 days.....	86	57	Survived, very sick
1 day.....	86	74	Died (two hours)
3 days.....	84	89	Died (33 minutes)
3 days.....	84	50	Survived
4 days.....	75	75	Died (two hours and 24 minutes)
4 days.....	45	75	Died (lived more than six hours)
4 days.....	50	75	Died (lived more than two hours)
7 days.....	90	75	Died (lived more than two hours)
7 days.....	91	75	Died (2½ hours)
10 days.....	60	67	Died (45 minutes)
11 days.....	90	89*	Died (40 minutes)
11 days.....	75	89*	Died (45 minutes)
15 days.....	95	75	Survived

*Three fresh pigs injected with this same dose all survived.

No guinea pig was used for a second injection until its general condition seemed normal. In a number of instances, the weight showed a decided increase between injections, but the site of the former injection was always marked by induration or an open slough.

In a recent paper, Vanderkleed and Pittenger call attention to the fact that erroneous statements have been made concerning the cost of guinea pigs for an assay of a heart tonic by Reed's method. They state that the cost should be based, not upon the total number of animals employed, but upon the number that succumb, for it is possible to use an animal time after time until it finally succumbs.

From the results secured in our experiments, it seems that digitalis glucosides are comparatively rapidly eliminated or destroyed by guinea pigs in some instances, while in others a state of increased susceptibility is induced by large sub-lethal doses of digitalis which persists for at least eleven days and has no connection with the animal's general condition.

Therefore, the conclusion seems justified that as test animals, the use of guinea pigs which have already received an injection of digitalis is unsafe until the length of time required for complete recovery can be definitely decided. It has been my own impression (unsupported by any experimental evidence) that even after a month has elapsed, unsatisfactory results may be secured, and it has been our invariable custom to use fresh animals in the final assay of any preparation.

If uniformly satisfactory results may be obtained after a month has elapsed, it is obvious that the second use of such animals as recovered will be nearly as costly as purchasing fresh pigs, because the food and care, added to loss from natural causes, will amount to a considerable sum.

REFERENCES.

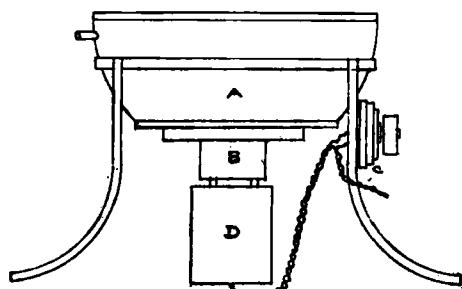
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 CONVENIENT ELECTRICAL WATER BATH.

JOHN W. FORBING, CREIGHTON UNIVERSITY.

An electrical steam bath filling the demand for convenience and safety, in laboratories lacking live steam and employing inflammable liquids, may be easily constructed:



A, Water bath.
B, Electric unit.

D, Attachment plug.
C, Snap switch.

A 500 ampere General Electric heating unit, round and flat, is soldered into the bottom of the ordinary copper constant level water bath. The unit is connected with an attachment plug screwed into one of the legs of a tripod which may be used to support the bath. Cord and hubble attachment plug enables the user to move the bath to suit convenience. As used by the author on a 110 volt, 60 cycle alternating current, 475 watts are consumed. But three

minutes are required to bring contents of bath to ebullition.

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PROFESSOR EUGENE CHARABOT, SC. D., PARIS, FRANCE.

Professor E. Charabot, Sc. D., of the Sorbonne of Paris, was presented to the large audience by Professor Samuel P. Sadtler, who in his introduction stated that the speaker by virtue of his numerous and monumental labors and contribu-

*Report of a lecture delivered before the Philadelphia College of Pharmacy, Oct. 17, 1913, and reported in English by Prof. I. V. S. Stanislaus.