A COMPARATIVE STUDY OF THE ABSORPTION OF DIGITALIS WHEN GIVEN ORALLY AND RECTALLY TO CATS.*,[1]

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INTRODUCTION.

The effect of digitalis on the heart when given intravenously to cats is known to be rapid and certain, as this means of administering the drug has been used for some years as an assay method.

An investigation of the absorption by rectum (1) revealed that digitalis is absorbed very slowly and that the absorption is irregular in that it varies greatly in different animals. Nausea and emesis followed the rectal administration in approximately half of the experiments. This information would at first appear to be contradictory to the available clinical reports on the rectal administration in humans, but the fact must not be overlooked that toxic quantities of the drug were given in the laboratory while therapeutic doses were employed in the clinic. The conclusion was therefore drawn that the above findings would not become quantitatively significant regarding relative absorption rate until the absorption rate following oral administration had been determined in the same manner. This prompted the work which follows.

EXPERIMENTAL WORK.

Three series of experiments were conducted, two in which digitalis was given orally, and one series of controls. The technique employed throughout this work was essentially the same in all cases with the exception that no digitalis was given orally in the series of control experiments. The cats were anesthetized by means of intraperitoneal injections of an alcoholic solution of chloretone in quantities sufficient to maintan anesthesia until the end of the experiments. In a few cases, however, ether was given as a supplement to the chloretone. A quantity of fluidextract of digitalis diluted with a convenient amount of water was then introduced into the stomachs of the cats of series Nos. 1 and 2. A rubber catheter attaced to a hypodermic syringe was used to effect administration of the solution. About five hours later, sufficient digitalis was given intravenously to cause death in from 30 to 45 minutes. The intravenous digitalis solution was made by diluting 1 volume of the fluidextract (the same product in all cases) with 99 volumes of normal saline solution. The cats of series No. 3 (control series) were merely allowed to remain anesthetized for about five hours and then were given the intravenous digitalis solution. The results of the experiments are tabulated below.

SERIES NO. 1.

The quantity of fluidextract given orally in the following experiments corresponded to 7.7 M. L. D.[2] per cat as computed from the quantity of fluidextract required to kill the cats used in the series of controls.

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[1] From the laboratory of Marvin R. Thompson, Professor of Pharmacology, School of Pharmacy of the University of Maryland.

[2] One M. L. D. is the amount of digitalis necessary to kill a cat when given intravenously in accordance with the technique which has been followed.

TABLE I.

Cat No.	Weight of Cat in Kilos.	Time Allowed for Absorption. Hrs.	Mins.	Cc. of 1:100 F. E. Digitalis Solution Administered Intravenously.	Cc. of F. E. Digitalis Absorbed.*	No. of M. L. D. Absorbed.
1	1.87	4	53	4.6	0.20	0.81
2	2.12	5	16	6.2	0.11	0.41
3	1.89	5	8	5.0	0.20	0.80
4	1.50	3	25	...	0.21	1.00

* Obtained by subtracting the amount given intravenously from the amount calculated to cause death.

Cat No. 4 died approximately three and one-half hours after administration of the digitalis and the others showed rather marked absorption so the quantity of digitalis was decreased by one-half in the series which follows.

SERIES NO. 2.

Fluidextract of digitalis, corresponding to 3.85 M. L. D., was given by stomach tube to each cat of this series.

TABLE II.

Cat No.	Weight of Cat in Kilos.	Time Allowed for Absorption. Hrs.	Mins.	Cc. of 1:100 F. E. Digitalis Solution Administered Intravenously.	Cc. of F. E. Digitalis Absorbed.*	No. of M. L. D. Absorbed.
5	2.35	4	26	26.4	0.04	0.13
6	1.64	4	39	10.0	0.11	0.53
7	2.00	5	22	24.3	0.02	0.07
8	1.90	5	5	8.3	0.16	0.66
9	2.07	5	24	11.2	0.16	0.58
10	2.00	5	5	13.9	0.12	0.47
11	2.30	5	19	7.7	0.22	0.74
12	2.40	5	3	17.7	0.14	0.43
13	2.65	5	21	6.5	0.28	0.81
14	1.95	5	6	6.0	0.19	0.76
15	1.40	5	39	15.1	0.03	0.17
16	2.45	5	32	30.4	0.01	0.05
17	2.42	6	2	38.2	..	..
18	2.65	5	14	25.9	0.09	0.25

SERIES NO. 3.

In this, the control series, no digitalis was administered orally. As previously stated, the cats were anesthetized and allowed to so remain for about five hours. Sufficient digitalis was then given intravenously to cause death.

TABLE III.

Cat No.	Weight of Cat in Kilos.	Cc. of 1:100 F. E. Digitalis Solution Administered Intravenously.	
19	1.70	26.5	15.6 cc. per Kg.
20	2.40	32.6	13.6 cc. per Kg.
21	1.65	19.5	10.8 cc. per Kg.
22	1.85	22.7	12.3 cc. per Kg.
23	2.25	26.5	11.8 cc. per Kg.
24	1.90	26.5	14.0 cc. per Kg.

25	1.57	22.7	14.4 cc. per Kg.
26	1.60	18.0	11.2 cc. per Kg.
27	2.55	36.3	14.2 cc. per Kg.
28	2.70	31.6	11.7 cc. per Kg.
29	2.85	36.5	12.8 cc. per Kg.
30	2.70	35.2	13.0 cc. per Kg.
			12.95 cc. per Kg.-Av.

DISCUSSION.

The 12 cats employed in series No. 3 required an average of 13 cc. of the 1:100 intravenous digitalis solution per kilo body weight of cat to cause death. In series No. 1, the animals required an average of 2.1 cc. per kilo showing that an average of 0.84 M. L. D. had been absorbed from the 7.7 M. L. D. which had been given orally. Likewise, in series No. 2, in which the cats received 3.85 M. L. D. orally, they consumed, on the average, 8 cc. per kilo intravenously revealing that 0.38 M. L. D. had been absorbed. From these figures it may be seen that, from the quantity of digitalis given by mouth, only about ten per cent had been absorbed in approximately five hours.

When digitalis was given rectally in the form of the dealcoholized tincture, the form from which it was most readily absorbed, an average of 4.8 M. L. D. was administered. Of this, 0.36 M. L. D. was absorbed in the five-hour period allowed, corresponding to 7.5% absorption of the amount of drug given.

These results indicate that the absorption of the drug from the stomach is slightly better than that from the rectum but there is not a great enough difference in the absorption from the above two avenues of administration to draw any definite conclusions, except that the drug is absorbed at a not greatly differing rate by both routes of administration.

Several clinicians, whose work on rectal digitalis therapy was reviewed, state that nausea is rare after digitalis has been given rectally. When the unpleasant gastric disorders which often accompany oral therapy set in and even minute doses cause vomiting, the rectal mode for giving the drug is favored. With the experiments on cats, rather the contrary is at first apparent, but it should be emphasized that in clinical use, nausea, etc., may result from definitely sub-toxic dosage, whereas in these experiments, the nausea, etc., appeared along with other symptoms of toxicity.

CONCLUSIONS.

1. Digitalis is absorbed when given either orally or rectally to cats.
2. The absorption, when given either rectally or by mouth, is slow and the rapidity of absorption varies greatly in different cats.
3. The evidence obtained did not reveal a definitely significant difference in absorption rate in the two modes of administration.

REFERENCE.

(1) Purdum, W. A., "The Rectal Absorption of Digitalis in Cats," JOUR. A. PH. A., 24, 374 (1935).