

past year, throughout all our researches on pituitary substances, and are thoroughly convinced that the uterine method is by far the better of the two. We will not go into a detailed description of the advantages of the uterine method, as our results agree in every instance with the claims made for it by Dale and Laidlaw.

In our experimental work on pituitary extract, we have succeeded in preparing colorless extracts of the *whole gland*, possessing all of the characteristic physiologic properties of the posterior lobe. Such a solution, in sterile ampul form, is here shown, together with tracings, showing the characteristic blood-pressure-raising power, and also the uterus-contracting power, peculiar to the posterior lobe, to a marked degree.

This solution has been prepared as follows: First a watery extract is made of the whole gland. This is then purified by a series of precipitations which deprive the extract of practically all inert proteid substances. This purified extract is then treated with metallic salts of aluminum (or other suitable metals), after which it is neutralized, thus precipitating the metallic derivative. This precipitate is then filtered off, washed, and dried. An aqueous solution of this dried material forms the solution exhibited in the ampoules. The product, therefore, is in reality a solution of a metallic derivative or derivatives of the active principles, in the purification of which, the presence of the relatively inert anterior lobe seems not to interfere, thus permitting of a great saving in the labor and resultant expense of separating the lobes.

We have not yet been able to determine exactly the nature of these metallic derivatives, but are continuing our researches and will give more detailed accounts of further experiments in subsequent papers.

RESEARCH LABORATORY OF H. K. MULFORD COMPANY, August 13, 1913.

VARIATION IN SUSCEPTIBILITY OF THE GUINEA PIG.

(Continuation of a previously reported study.)*

CHAS. E. VANDERKLEED, PHAR. D., AND PAUL S. PITTENGER, PHAR. D.

In a paper read at the 1912 meeting of the American Pharmaceutical Association in Denver, the results of a series of experiments covering one year were given, in which it was shown that the average minimum lethal dose of crystallized strophanthin, Thoms, (ouabain) for 250 gm. guinea pigs, varied during the course of the year from 0.0000511 gm. in September, 1911, to 0.0000844 gm. in May, 1912, the average for the year being 0.0000661, and the extreme variation ranging from 22.7 percent below to 27.7 percent above this average. These experiments having conclusively shown that sex and weight may be dismissed as unimportant, this conclusion having been fully concurred in by other investi-

* Variation in the Susceptibility of the Guinea Pig to the Heart Tonic Group, (Second Paper), by Chas. E. Vanderkleed, Phar. D., and Paul S. Pittenger, Phar. D., Journal of the American Pharmaceutical Association, II, May, 1913, p. 558.

gators,** these factors were eliminated in extending our observations over a number of months during the past year, the results of which are given in the following tables. The doses are in all cases those given per 250 gm. weight.

AUGUST, 1912.

Temperature of Laboratory, 29 to 30° C. Aver., 29.5° C.
Temperature of Guinea Pig Quarters, 28 to 29° C. Aver., 28.5° C.
Pigs varied in weight from 220 to 430 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000045.....	— Recovered	0.000060.....	+ Died
0.000050.....	— Recovered	0.000065.....	+ Died
0.000055.....	— Recovered	0.000075.....	+ Died
0.000055.....	— Recovered	0.000070.....	+ Died
x0.000060.....	+ Died		

M. L. D. = 0.000060

OCTOBER, 1912.

Temperature of Laboratory, 21 to 27° C. Aver., 24° C.
Temperature of Guinea Pig Quarters, 10 to 16° C. Aver., 13° C.
Pigs varied in weight from 240 to 655 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000050.....	— Recovered	0.0000575.....	— Recovered
0.000050.....	+ Died*	0.0000575.....	— Recovered
0.0000525.....	+ Died*	x0.000060.....	+ Died
0.0000525.....	— Recovered	0.000060.....	+ Died
0.000055.....	— Recovered	0.000060.....	+ Died
0.000055.....	— Recovered	0.0000625.....	+ Died
0.000055.....	+ Died*		

M. L. D. = 0.000060

* Died "out of order."

NOVEMBER, 1912.

Temperature of Laboratory, 16 to 22° C. Aver., 19° C.
Temperature of Guinea Pig Quarters, 12 to 18° C. Aver., 15° C.
Pigs Varied in weight from 250 to 505 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000050.....	— Recovered	0.0000725.....	— Recovered
0.000060.....	— Recovered	x0.0000725.....	+ Died
0.000065.....	— Recovered	0.0000725.....	+ Died
0.000065.....	— Recovered	0.000075.....	+ Died
0.000070.....	+ Died*	0.000075.....	— Recovered*
0.000070.....	— Recovered	0.000080.....	+ Died
0.000070.....	— Recovered	0.0000825.....	+ Died

M. L. D. = 0.0000725

* Died or recovered "out of order."

DECEMBER, 1912.

Temperature of Laboratory, 18 to 20° C. Aver., 19° C.
Temperature of Guinea Pig Quarters, 12 to 17° C. Aver., 14.5° C.
Pigs varied in weight from 230 to 410 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000050.....	— Recovered	0.0000725.....	— Recovered
0.000060.....	— Recovered	x0.0000725.....	+ Died
0.000065.....	— Recovered	0.0000725.....	+ Died
0.000065.....	— Recovered	0.000075.....	+ Died
0.000070.....	— Recovered	0.000075.....	+ Died
0.000070.....	— Recovered	0.000075.....	+ Died

M. L. D. = 0.0000725

** Seasonal Variations in the Resistance of Guinea Pigs to Poisoning, by C. C. Haskell, A. B., M. D., American Journal of Pharmacy, June, 1912, p. 241-246.

JANUARY, 1913.

Temperature of Laboratory, 19 to 21° C. Aver., 20° C.
 Temperature of Guinea Pig Quarters, 17 to 19° C. Aver., 18° C.
 Pigs varied in weight from 375 to 575 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000060.....	— Recovered	x0.000065.....	+ Died
0.000060.....	— Recovered	0.000065.....	+ Died
0.0000625.....	— Recovered	0.000070.....	+ Died
0.0000625.....	— Recovered	0.000075.....	+ Died
0.0000625.....	+ Died		

M. L. D. = 0.000065

FEBRUARY, 1913.

Temperature of Laboratory, 18 to 21° C. Aver., 19.5° C.
 Temperature of Guinea Pig Quarters, 9 to 18° C. Aver., 13.5° C.
 Pigs varied in weight from 200 to 290 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000030.....	— Recovered	0.000060.....	+ Died*
0.000040.....	— Recovered	0.000065.....	— Recovered
0.000040.....	— Recovered	0.000065.....	— Recovered
0.000045.....	— Recovered	0.000065.....	— Recovered
0.000050.....	— Recovered	0.0000675.....	— Recovered
0.000050.....	— Recovered	x0.000070.....	+ Died
0.000050.....	— Recovered	0.000070.....	+ Died
0.000050.....	+ Died*	0.000070.....	+ Died
0.000060.....	— Recovered	0.000080.....	+ Died
0.000060.....	— Recovered	0.000085.....	+ Died
0.000060.....	— Recovered		

M. L. D. = 0.000070

* Died "out of order."

MAY, 1913.

Temperature of Laboratory, 22 to 30° C. Aver., 26° C.
 Temperature of Guinea Pig Quarters, 22 to 28° C. Aver., 25° C.
 Pigs varied in weight from 305 to 520 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000050.....	— Recovered	0.000065.....	— Recovered
0.000055.....	— Recovered	0.000070.....	— Recovered
0.000055.....	— Recovered	0.000070.....	— Recovered
0.000060.....	— Recovered	0.000070.....	— Recovered
0.000060.....	— Recovered	x0.0000725.....	+ Died
0.000060.....	+ Died*	0.0000725.....	+ Died
0.000065.....	— Recovered	0.000075.....	+ Died
0.000065.....	+ Died*		

M. L. D. = 0.0000725

* Died "out of order."

JULY, 1913.

Temperature of Laboratory, 28 to 31° C. Aver., 29.5° C.
 Temperature of Guinea Pig Quarters, 29 to 32° C. Aver., 30.5° C.
 Pigs varied in weight from 275 to 520 gms.

<i>Dose.</i>	<i>Results.</i>	<i>Dose.</i>	<i>Results.</i>
0.000050.....	— Recovered	0.000065.....	+ Died
0.000055.....	— Recovered	0.000070.....	+ Died
0.000060.....	— Recovered	0.0000725.....	+ Died
0.000060.....	— Recovered	0.000075.....	+ Died
0.000060.....	+ Died	0.000080.....	+ Died
x0.000065.....	+ Died		

M. L. D. = 0.000065

In order that these results may be considered in conjunction with those obtained during the previous year, the following tabulated summary includes the results reported in the previous paper:

MINIMUM LETHAL DOSE BY MONTHS.

<i>Date.</i>	<i>Lab.</i>	<i>Pens.</i>	<i>M. L. D.</i>	
July, 1911.....	27°C.	0.0000519	
August, 1911.....	27°C.	0.0000519	
September, 1911.....	23.5°C.	0.0000511	
October, 1911.....	21.2°C.	0.0000544	
November, 1911.....	22°C.	0.0000577	
December, 1911.....	18.5°C.	0.0000700	
January, 1912.....	20°C.	12°C.	0.0000658	
February, 1912.....	18.5°C.	12°C.	0.0000737	
March, 1912.....	20°C.	12.5°C.	0.0000825	Old
April, 1912.....	24°C.	17°C.	0.0000800	series
May-June, 1912.....	25.7°C.	25.5°C.	0.0000844	Aver.
July, 1912.....	28°C.	25.5°C.	0.0000700	0.0000661
August, 1912.....	29.5°C.	28.5°C.	0.0000600	
October, 1912.....	24°C.	13°C.	0.0000600	
November, 1912.....	19°C.	15°C.	0.0000725	
December, 1912.....	19°C.	14.5°C.	0.0000725	
January, 1913.....	20°C.	18°C.	0.0000650	New
February, 1913.....	19.5°C.	13.5°C.	0.0000700	series
May, 1913.....	26°C.	25°C.	0.0000725	Aver.
July, 1913.....	29.5°C.	30.5°C.	0.0000650	0.0000672
Average for two years.....			0.0000665	

A study of this table shows that it is not necessary for us to make any changes in our conclusions of last year's paper. The average M. L. D. for 1911-1912 was 0.0000661 gm.; that for the new series of 1912-1913 was 0.0000672 gm.; while the average for the whole two years was 0.0000665 gm. On the other hand the extreme variations during the new series have been much smaller than those observed during the first twelve months, varying from only 9.8 percent below to 9 percent above, instead of from 22.7 percent below to 27.7 percent above. With less than a 10 percent variation in susceptibility above or below the average, with less than 10 percent of pigs dying or recovering "out of order," we contend that for all practical purposes, the guinea-pig method affords the simplest and most satisfactory means of standardizing the heart tonic group of drugs, at a very reasonably economical cost, without the necessity for standardizing the test animals, and without need for considering seasonal variations. As for the opinion which has been occasionally advanced, that experiments on ouabain really prove nothing as to the possible variation in susceptibility to digitalis or other members of the heart tonic group, we can only say that it would be very difficult to carry out a series of experiments such as we have done, with digitalis, strophanthus or any other drug as a whole. Any variation that might be noted would always cause the question to arise as to possible change in the test material. We can say, however, that in our long experience with this method as a routine one for testing all of the heart tonic drugs, we have found no evidence of any appreciable variation. Moreover, as the physiologic action

of the various heart tonic drugs is very much the same, it is not likely that much variation in susceptibility will be noted. As our opportunities to observe possible variations in the case of vacuum-preserved preparations of digitalis and strophanthus accumulate, we should be able within a year or two more to throw some direct light on this question.

PHYSIOLOGIC LABORATORY OF H. K. MULFORD COMPANY, July 27, 1913.

THE YEAR BOOK OF THE ASSOCIATION.*

Fresh from the hands of the printers comes the first year book of the Association, and, with all modesty, it must be said that it reflects the greatest credit upon the Association and upon all of those by whose painstaking efforts the publication makes such a creditable showing; particularly upon its Editor-in-Chief, our esteemed fellow-member, C. Lewis Diehl, Ph. M. and the General Secretary, Dr. James H. Beal, under whose capable direction the publication has been compiled and printed.

The volume is a distinct addition to pharmaceutical literature, not alone of this country, but of the entire world. Nowhere else can be found so completely and so well, within the limits of a single volume, such an infinite amount of valuable material to the profession, as is comprised in this volume of 621 pages. No pharmacist, who has the true interest of his guild at heart, and who desires to keep "in touch" as to its scientific and its practical progress, can fail to find in this "Year Book," matter not only of the greatest interest, but also much valuable information of distinct and immediate profit. Its value to every pharmacist cannot be stated, except in the most general way;—that there is no druggist but will find in its pages something that he can coin into profit, which will many, many times far exceed the trifling cost of the publication to him, personally. It stands as a conspicuous instance of one of the great advantages of the co-operative work which the American Pharmaceutical Association has done and is still doing for every member of the profession. It is a complete and a perfect answer to the criticism, often expressed by the uninformed, that the A. Ph. A. is ultra-scientific, not practical, etc. In the hands of every pharmacist who reads it and who takes advantage of the information packed into its pages, it will be a most useful,—a most valuable,—aid to him in the conduct of his daily affairs, and studied diligently it will make of him a wiser, better and a higher-class pharmacist and man.

In its typography and general make-up it shows the admirable workmanship, care and capacity of the Stoneman Press of Columbus, with which the readers of the JOURNAL are already so familiar.

E. C. M.

*THE YEAR BOOK OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1912, containing the Fifty-fifth Annual Report on the Progress of Pharmacy, and the Constitution, By-Laws and Roll of Members; corresponding to Volume 60 of the former Proceedings of the American Pharmaceutical Association. Published by the American Pharmaceutical Association, 1914, Scio, Ohio.