requires a much greater quantity of oxygen in the former case than the latter, and a simple combustion method should not be difficult to devise.

The resorcin test, however, is capable of giving results of practical value and it need not consume much time. Standard solutions may be prepared containing respectively 20, 40, 60 and 80 per cent. by volume of methyl alcohol, the remainder consisting of 95% ethyl alcohol. Five cc of each of these solutions is to be diluted with water to make, after cooling, 25 cc.

To 1 cc of each of these dilutions is added 5 cc of water, 1 cc of "dilute" phosphoric acid, and 2 cc of potassium permanganate solution (3%). The further routine given already in detail for producing an "oxidized" solution is to be carried out, and thus standard color solutions obtained with which to compare similar solutions prepared from the sample under examination.

PRACTICAL CONCLUSIONS.

The resorcin test for methyl alcohol in spirituous liquors is easily made. The reactions involved are strikingly characteristic and not more subject to misinterpretation than other similar tests depending upon the oxidation of methyl alcohol to formaldehyde.

Ethyl alcohol influences the result of the test, but rarely so as to invalidate the conclusions drawn therefrom.

In case of mixtures pure and simple of methyl and ethyl alcohols it is practicable to determine approximately the proportions of each. This is true even when water also is present.

LABORATORY NELSON, BAKER & CO.,
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THE ANTIDOTAL EFFICACY OF FERRI HYDROXIDUM CUM MAGNESII OXIDO, U. S. P. IN ARSENICAL POISONING.

BY HUGH McGUIGAN, H. V. ATKINSON AND G. A. BROUGH.

INTRODUCTION.

This investigation was undertaken at the request of the U. S. Pharmacopœial Revision Committee, through Dr. Torald Sollmann. The Committee is interested in the antidotal efficacy of Ferri Hydroxidum cum Magnesii Oxido, U. S. P. in arsenical poisoning.

Bunsen and Berthold,[1] in 1834, recommended the use of freshly precipitated ferric hydroxide in the treatment of acute arsenical poisoning. This work has been the basis for treatment ever since. De Busscher,[2] in 1902, after an investigation of the problem, claimed the antidote was without beneficial effect.

In some cases his animals, even without antidote, survived for several months and therefore can hardly be called acute cases. In addition, laboratory animals may die from other causes when they are kept in cages this length of time. Before giving the arsenic, he did not attempt to have their stomachs practically free from food. All of these factors might be raised to render the interpretation of his results uncertain. Therefore, we have thought it advisable to reinvestigate the essential parts of his work before rejecting this standard treatment. It is not necessary to determine the smallest lethal dose; this has already been adequately done by de Busscher,[2] Morishima,[3] and also by Schwartze.[4] However, to test a treatment, we should know that a dose of arsenic sufficient to cause death has been given. Then, if the antidote is useful, we can evaluate it. We have, therefore,

used a dose of arsenic which in the majority of cases, if untreated, would be fatal. This, in practice, is the only kind of case that requires an antidote. Schwartze[4] has shown that the finer the particles of As_2O_3 the greater the toxicity, and he comments on the great variability of the results of a given dose. Since in our work the same preparation of arsenic trioxide was used throughout, it was thought unnecessary to measure the fineness of the particles. In the administration of the same sample however, owing to agglomeration, it is difficult to get exactly uniform conditions when the solid preparation is used.

Rabbits were used in the first series of experiments. These animals were used in order to check previous workers and also because they, like other rodents, cannot vomit the drug or antidote; hence this complicating factor is avoided. There are some objections, however, to the use of rabbits. Food remains in the stomachs of rabbits for a long time and it is difficult to introduce either drug or antidote unless they are fasted for several days. The food itself has some protective value; but if they are starved until the stomach is empty, the starvation itself may be a contributory factor in the causation of death. The quantity of food in the stomach should be materially reduced before giving either arsenic or antidote, and for this reason the rabbits were fasted for three days and the dogs for two days before being used. Careful post mortems were performed in each case to exclude deaths from faulty technique.

Vomiting always occurs in the dog after arsenic if not prevented. De Busscher found, and we corroborate his conclusion, that vomiting is the most effective mechanism. Apparently more of the poison was removed in this way than by washing out the stomach. Vomiting can be delayed, and in some cases prevented, by depressing the vomiting center with morphine.

For many reasons dogs are the most satisfactory animals for this work, therefore, many of them were used.

Liquor Potassii Arsenitis, U. S. P. (Fowler's Solution), made from Merck's Arsenic Trioxide, U. S. P., and the solid arsenic trioxide were the preparations of arsenic used. It was found necessary to use a dose of Fowler's Solution equivalent to at least 20 mg. of As_2O_3 per kilogram of body weight, and 100 mg. of the solid As_2O_3, in order to cause death in a reasonable length of time. Owing to the small dose required for rabbits, Fowler's Solution was diluted four times in these experiments. This was introduced through a stomach tube into the rabbits and the residue washed in with a small additional volume of water. The arsenic solution was used undiluted in the dog experiments.

The proper dose of solid arsenic trioxide was weighed into small beakers in advance and when all doses were ready the dogs were given a hypodermic injection of one-fourth grain of morphine sulphate. The vomiting mechanism was sufficiently depressed in about one-half hour. A total of about 50 cc of water was then added to the beaker in several successive portions, the material stirred and the suspended particles poured through a stomach tube. The antidote, Ferri Hydroxidum cum Magnesii Oxido, U. S. P., when used, was administered immediately through the same stomach tube and the animals placed in cages for observation.

EXPERIMENTAL DATA.

Table I gives the duration of life of rabbits poisoned with a volume of Fowler's Solution equivalent to 20 mg. of As_2O_3 per kilogram of body weight. No antidote was used in this series.

Table II gives the duration of life of rabbits treated as in Table I and then given 50 cc of antidote.

Tables III and IV give the effect of the antidote alone on rabbits and dogs. These animals were not given arsenic.

Table V gives the duration of life of dogs which were first given one-fourth grain of morphine sulphate to prevent vomiting and then Fowler's Solution equivalent to 25 milligrams of AS_2O_3 per kilogram of body weight. No antidote was given to these dogs.

Table VI gives the results on dogs treated as in Table V and then given antidote.

Table VII gives the results on dogs treated as in Table V except the dose of Fowler's Solution was reduced to 20 mg. As_2O_3 per kilogram of body weight. No antidote was given.

Table VIII gives the results on dogs treated as in Table VII except 100 cc of antidote was administered immediately after the Fowler's Solution.

Table IX gives the results obtained by administering 100 mg. of solid As_2O_3 per kilogram of body weight to dogs after they had been depressed with morphine sulphate.

Table X gives the results obtained under identical conditions as in Table IX, except 100 cc of antidote was administered immediately after the arsenic trioxide.

Table XI gives the results obtained after the administration of 100 mg. of solid As_2O_3 per Kg. of body weight when a larger volume of antidote was used. In this series, to reduce the volume, the arsenic was washed into the stomach by the antidote.

TABLE I.

DURATION OF LIFE OF RABBITS POISONED WITH FOWLER'S SOLUTION.

Number of rabbit.	Weight, Kg.	Dose of As_2O_3, Mg.	Hours until death.
1	0.84	21	60
2	1.16	29	18
3	1.31	33	29
4	1.16	29	38
5	1.30	32	18
6	1.58	39	38
7	2.46	61	17
8	2.53	63	15
9	2.29	57	26
10	2.37	59	16
11	2.17	54	10
12	2.69	67	27
			Average 26.1

TABLE II.

DURATION OF LIFE OF RABBITS POISONED WITH FOWLER'S SOLUTION FOLLOWED IMMEDIATELY WITH 50 CC OF ANTIDOTE.

Number of rabbit.	Weight, Kg.	Dose of As_2O_3, Mg.	Hours until death.
13	1.62	40	31
14	1.64	41	30
15	1.00	25	39
16	2.73	68	15
17	1.52	38	63
18	1.79	45	18
19	1.62	40	18
20	1.35	34	100+
21	1.49	37	30
22	1.14	28	63
23	1.80	45	18
24	1.76	44	49
25	1.81	45	48
26	1.82	45	46
27	1.69	42	45
28	2.69	67	16
29	2.37	59	10
30	1.72	43	49
			Average 34.6

TABLE III.

EFFECT OF ANTIDOTE ALONE ON RABBITS.

Number of rabbit.	Weight, Kg.	Antidote cc.	Hours until death.
31	1.70	100	Survived
32	1.40	100	Survived
33	1.69	50	Survived
34	1.24	50	Survived
35	1.37	50	Survived
36	1.46	50	Survived
37	3.45	50	Survived

TABLE IV.

EFFECT OF ANTIDOTE ALONE ON DOGS.

Number of dog.	Weight, Kg.	Antidote cc.	Hours until death.
1	7.5	100	Survived
2	5.5	75	Survived
3	6.5	75	Survived
4	20.0	100	Survived
5	17.5	100	Survived
6	12.8	100	Survived

TABLE V.

DURATION OF LIFE OF DOGS POISONED WITH FOWLER'S SOLUTION.

Number of dog.	Weight, Kg.	Dose cc.	Hours until death.
7	6.4	16.0	14
8	5.6	13.5	6
9	20.0	50.0	4
10	6.4	16.0	4
11	6.4	16.0	9
		Average,	7.4

TABLE VI.

DURATION OF LIFE OF DOGS POISONED WITH FOWLER'S SOLUTION AND GIVEN ANTIDOTE IMMEDIATELY.

Number of dog.	Weight, Kg.	Dose cc.	Antidote cc.	Hours until death.
12	7.6	19.0	100	33
13	8.4	21.0	100	18
14	15.2	38.0	75	10
15	3.2	8.0	75	12
16	6.0	15.0	75	10
			Average,	16.6

TABLE VII.

DURATION OF LIFE OF DOGS POISONED WITH FOWLER'S SOLUTION.

Number of dog.	Weight, Kg.	Dose cc.	Hours until death
17	11.0	22.0	11
18	14.4	28.8	10
19	11.3	22.6	7
		Average,	9.3

TABLE VIII.

DURATION OF LIFE OF DOGS POISONED WITH FOWLER'S SOLUTION AND GIVEN ANTIDOTE IMMEDIATELY.

Number of dog.	Weight, Kg.	Dose cc.	Hours until death.
20	9.0	18.0	384*
21	15.7	31.4	Survived
22	14.4	28.8	20
23	15.8	31.6	12
24	7.7	15.4	10
		Average,	14

* This dog was not in good physical condition at the start, but showed marked improvement after receiving the antidote.

TABLE IX.

EFFECT OF SOLID As_2O_3 ON THE DURATION OF THE LIFE OF DOGS.

Number of dog.	Weight, Kg.	Dose of As_2O_3, Gm.	Hours until death.
25	4.5	0.45	Survived
26	6.4	0.64	14
27	9.1	0.91	15
28	9.3	0.93	13
29	8.2	0.82	16
30	5.9	0.59	23
31	16.4	1.64	Survived
32	6.4	0.64	19
33	11.8	1.18	16
34	10.0	1.00	18
35	6.9	0.69	Survived
36	7.0	0.70	18
37	5.7	0.57	25
38	9.8	0.98	17
39	7.4	0.74	16
40	8.6	0.86	Survived
41	6.6	0.66	17
42	5.0	0.50	34
43	10.0	1.00	66
44	5.7	0.57	Survived
45	12.3	1.23	34
46	11.1	1.11	37
47	9.1	0.91	33
			Average, 24.0

TABLE X.

EFFECT OF SOLID As_2O_3 FOLLOWED BY 100 CC. ANTIDOTE ON THE DURATION OF LIFE OF DOGS.

Number of dog.	Weight, Kg.	Dose of As_2O_3, Gm.	Hours until death.
48	8.4	0.84	40
49	14.5	1.45	40
50	11.3	1.13	Survived
51	6.4	0.64	25
52	8.6	0.86	Survived
53	5.9	0.59	31

Number of dog.	Weight, Kg.	Dose of As_2O_3, Gm.	Hours until death.	Number of dog.	Weight, Kg.	Dose of As_2O_3, Gm.	Hours until death
54	5.9	0.59	Survived	59	4.1	0.41	17
55	14.1	1.41	23	60	4.8	0.48	30
56	9.9	0.99	16	61	8.4	0.84	12
57	11.4	1.14	Survived	62	7.7	0.77	24
58	6.4	0.64	13				Average, 24.4

TABLE XI.

EFFECT OF SOLID As_2O_3 FOLLOWED BY ANTIDOTE ON THE DURATION OF LIFE OF DOGS.

Number of dog.	Weight, Kg.	Dose of As_2O_3, Gm.	Volume of antidote cc.	Hours until death.
71	7.7	.770	300	Survived
72	3.9	.390	200	17 days
73	10.5	1.050	375	214
74	5.0	.500	375	23
75	5.0	.500	250	197
76	9.5	.950	375	Survived
77	5.5	.550	375	71
78	6.8	.680	250	Survived
79	15.5	1.550	400	Survived
80	8.2	.820	250	23
81	12.3	1.230	350	17 days
82	5.9	.590	No antidote	17 days
83	5.9	.590	No antidote	119
84	4.9	.490	250	Survived
85	9.0	.900	250	74
86	5.9	.590	No antidote	23
87	5.0	.500	200	142
88	10.0	1.000	250	118
89	8.6	.860	No antidote	23

TABLE XII.

RECAPITULATION OF DATA.

	As_2O_3 per kilo mg.	Duration of life without antidote hours.	Duration of life with antidote hours.	Prolongation of life. Per cent.
Tables I and II. Rabbits....	20 (as Fowler's Solution)	26.1	34.6	32.6
Tables III and IV. Rabbits and dogs.....	0 (as Fowler's Solution)	Survived	..	..
Tables V and VI. Dogs.....	25 (as Fowler's Solution)	7.4	16.6	124.0
Tables VII and VIII. Dogs..	20 (as Fowler's Solution)	9.3	14.0	50.5
Tables IX and X. Dogs.....	100 (Powdered As_2O_3)	24.0	24.4	1.7
Table XI. Dogs.....	100 (Powdered As_2O_3)	55.0	95.7	74.0

DISCUSSION—RESULTS AND CONCLUSIONS.

The work of Bunsen and Berthold was not available, hence we cannot evaluate in detail their experiments. This however, and other literature was quoted in the work of de Busscher. De Busscher's conclusions were, that the arsenic antidote is harmful in the case of poisoning by arsenic trioxide and its efficacy is temporary only with Fowler's Solution. Our work in the main is confirmatory of that of de Busscher, that is, we found the antidote of no practical value. However, we have not found as de Busscher did, that the antidote hastens death when the solid As_2O_3 is used, neither do we find it of temporary value in case of poisoning by Fowler's Solution, but rather that the antidote is without a significant influence in

either case. We feel that the average of de Busscher's work and our own would probably be more nearly correct, that is, that the antidote is without influence on the end result of the action of the arsenic. The delay of death in some cases could be attributed to the colloidal nature of the antidote and not to any specificity of the substance.

In the case of animals which we have marked "survived" we mean that they were alive at the end of two weeks. This time was an arbitrary period taken because of the great variability in the toxicity of the arsenic as pointed out by de Busscher, Schwartze and others who have investigated the subject. The same dose may kill in a few hours, or only after months. This is especially true of the solid As_2O_3. We have found that those animals which survive two weeks may survive much longer, and by taking two weeks as a limit of observation we do not think there would be any definite change in conclusions had we carried the observations over a longer period. This is especially true since the ratio of treated to untreated animals remains about the same at this time. This is obvious from the prolonged and careful observation of de Busscher.

The objection may be raised that we did not use a sufficient quantity of the antidote. The amount we did use did not modify the course of the action or the end result. Also the volume of the official preparation is too great to permit the use of much greater quantities. In the last experiment quantities as high as 375 cc were used and again we found that the individual results were of such variance that there was but little difference between the number of deaths of those given antidote and of those without it. In both cases there were marked discrepancies in the results. Again the antidote of the Belgian Pharmacopoeia is much stronger in iron than our own, and de Busscher's work answers this part of the objection. Our own work therefore, is, in general corroborative of that of de Busscher. The only change produced by the antidote is an unimportant delay in the average time of death, due, we think, to the nature of the antidote which delays absorption rather than to chemical neutralization of the arsenious trioxide.

CONCLUSIONS.

(1) Ferri Hydroxidum cum Magnesii Oxido is of no practical value in the treatment of arsenical poisoning. It has no influence in the course of poisoning by Fowler's solution.

(2) There is a slight delay in the time of death, when powdered As_2O_3 is used. This delay seems due to the colloidal nature of the antidote, and the effect on absorption, rather than to chemical neutralization.

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LABORATORY OF PHARMACOLOGY AND THERAPEUTICS,
UNIVERSITY OF ILLINOIS,
COLLEGE OF MEDICINE, CHICAGO.