govern the origin and diffusion of epidemic and other forms of disease; and, as your experience will be gathered in all quarters of the globe, your opportunities of studying the influences of climate will necessarily exceed those of all others, and will enable you to solve problems that are yet unexplained. Nor will your duties be limited to those of a purely military or naval character; for, though I am not sufficiently acquainted with all the details of your services to describe them, I know that there are many special appointments open to those who will aspire to them. In short, to whichever branch of the service you belong, you have before you an useful and honourable career, which will be useful and honourable just in proportion to your own application of the capabilities you possess. In no case, I fear, may you expect to acquire wealth. Were this your object, you should have chosen another profession; but competency, and the means of doing justice to your families, and of supporting the position you attain, you may realise; and if so, and you feel that you have served your country well, and to the best of your ability advanced the knowledge of your profession and the bounds of science, you may be content, for you will have gained that which will bring you the truest happiness and the best reward.

And now I must not detain you longer. I have already trespassed too much on the patience of all, and I will conclude by wishing you all prosperity and success in your present and future career.

ON THE ACTIONS OF PICROTOXINE, AND THE ANTAGONISM BETWEEN PICROTOXINE AND CHLORAL HYDRATE.

By J. CRICHTON BROWNE, M.D., F.R.S.E.,
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(Continued from page 478.)

HAVING clearly established the existence of a remarkable antagonism between picrotoxine and chloral-hydrate, I next performed a few experiments with the purpose of supplying an answer to the important practical question, how long after the administration of a fatal dose of the one, may the other be administered with any hope of saving life.

TABLE VI.—Showing the Influence of Hydrate of Chloral Injected at Different Intervals of Time after Picrotoxine.

No.	Weight of Guinea-Pig.	Dose of Picrotoxine in parts of a grain.	Dose of Chloral in grain.	Interval between the administration of Picrotoxine & Chloral Hydrate.	Effect.	Result.
47	1 lb. 9 oz.	1-20th	6	10 min.	Deep sleep, twitchings	Recovery
48	1 lb. 8 oz.	1-20th	7	15 "	Restlessness, staggering, startings, convulsions, deep sleep	"
49	1 lb. 10 oz.	1-20th	7	30 "	Restlessness, twitchings, convulsions, sleep	"
50	1 lb. 9 oz.	1-20th	7	33 "	Restlessness, violent convulsions, coma	Death in 5 hrs.
51	1 lb. 6 oz.	1-20th	6	40 "	Restlessness, convulsions long continued	Death in 2 hrs.

It thus became evident that chloral-hydrate as an antidote to picrotoxine may be effectually employed for half-an-hour after the reception of that poison into the system, and even after several severe convulsive seizures. The certainty and celerity with which alleviation followed the introduction of the chloral into the system in the experiments above tabulated, as well as in a rabbit, to which twenty grains were given twenty minutes after a sixteenth of a grain of picrotoxine, which had induced four violent fits, was most striking and satisfactory. It may be safely asserted that if, after a poisonous dose of picrotoxine, chloral can be given in proportionate amount before the occurrence of clonic spasms, life will certainly be saved; and that, if it be given even after several convulsive seizures, but before the spasms have become continuous, there is still a good prospect of a favourable issue.

The next point which it was thought requisite to determine was, whether the antagonism between chloral-hydrate and picrotoxine was interchangeable. Could the lethal action of chloral be as certainly arrested and modified by picrotoxine as that of picrotoxine had been shown to be by chloral-hydrate? In proceeding to solve this problem, advantage was taken of the researches of the Edinburgh Committee to avoid a tedious preparatory inquiry. The report of that Committee

had approximately fixed the minimum fatal dose of chloral as twenty-one grains for a rabbit of three pounds weight, or seven grains for each pound of body-weight. That result being accepted as accurate, the following experiments were instituted.

TABLE VII.—Showing the Effects of Picrotoxine when injected with Fatal Doses of Chloral-Hydrate.

No.	Weight of Rabbit.	Dose of Chloral-Hydrate in grains.	Dose of Picrotoxine in parts of a grain.	Effects.	Result.
52	3 lbs. 4 oz.	23	1-40th	Prostration, sleep slightly disturbed	Recovery
53	3 lbs. 9 oz.	25	1-20th	Deep sleep, from which readily roused	"
54	3 lbs. 7½ oz.	30	1-25th	Restlessness, sleep much disturbed	"
55	3 lbs. 4 oz.	30	1-20th	Lethargy, loss of power in hind legs, deep sleep	Death in 1 hrs.
56	2 lbs. 14½ oz.	35	1-25th	Restlessness, deep sleep, great prostration	Recovery
57	3 lbs. 5 oz.	35	1-20th	Deep sleep	"
58	2 lbs. 9 oz.	40	1-25th	"	"
59	3 lbs. 5 oz.	40	1-12th	Deep sleep for nine hours, slight movements of mouth and paws	"
60	3 lbs. 6 oz.	42	1-25th	Deep sleep, occasional spontaneous movements	Death in 3 hrs.
61	3 lbs. 2½ oz.	45	1-16th	Restlessness, deep sleep, slight twitchings	Death in 1 hour and 40 min.

The conclusion to be drawn from these experiments was obvious. Picrotoxine impeded and arrested the fatal effects of chloral-hydrate to a remarkable extent when they were injected together. How long after the administration of chloral-hydrate could picrotoxine be administered so as still to exert an antagonistic action? That was the next question that suggested itself, and to it the answer was sought in a few additional experiments.

TABLE VIII.—Showing the Effects of Picrotoxine when Injected at Different Intervals after a Fatal Dose of Chloral-Hydrate.

No.	Weight of Rabbit.	Dose of Chloral Hydrate in grains.	Dose of Picrotoxine in parts of a grain.	Interval between Chloral Hydrate & Picrotoxine.	Effect.	Result.
62	3 lbs. 13 oz.	26	1-16th	30 min.	Sleep, restlessness	Recovery
63	3 lbs. 14 oz.	26	1-20th	60 "	Deep sleep	"
64	3 lbs. 4½ oz.	30	1-20th	60 "	" "	"
65	2 lbs. 14 oz.	40	1-25th	15 "	" "	Death in 2 hrs. 15m.

It thus appeared, that picrotoxine might be resorted to as an antidote to a fatal dose of chloral-hydrate, with a good prospect of a favourable issue, for about an hour after the reception of that fatal dose. This discovery seemed a very momentous one, as the wide use of chloral-hydrate at the present day makes it peculiarly desirable that an effectual and practically available antidote against its poisonous effects should be possessed. And an antidote, which can counteract double the amount of a minimum fatal dose, and overtake a poison which has had one hour's start of it, must be said to be both effectual and practically available. But the hopes which were thus not unreasonably formed, were doomed to be speedily in great measure disappointed. In ten days after the experiments which have just been enumerated, it became necessary to perform what Professor Bennett calls the crucial test, of repeating the same dose of the poison without the supposed antidote. To the rabbit which had received twenty-three grains of chloral-hydrate, and one-fortieth of a grain of picrotoxine, the same dose of the former alone was administered. It recovered just as rapidly as on the previous occasion. To the rabbit that had received twenty-five grains of chloral-hydrate, and one-twentieth of a grain of picrotoxine, twenty-five grains of chloral-hydrate were again given, and it also recovered as completely and rapidly as when the picrotoxine was conjoined with the chloral-hydrate: and so on, up to a dose of thirty-five grains of chloral-hydrate. All the rabbits that had recovered from the effects of chloral-hydrate with picrotoxine, recovered nearly as well without the picrotoxine after a sounder and less agitated sleep. The conclusion was, therefore, forced upon me, that the minimum fatal dose of chloral for rabbits had been underestimated. Whether it was that Yorkshire rabbits have more robust constitutions than

Scotch ones, or that my experiments were conducted under circumstances materially different from those under which the experiments of the Edinburgh Committee were carried on, I could not decide; but it was indubitable that our results differed to a very serious degree. A new set of experiments which was at once undertaken gave perfect distinctness to the divergence of our results.

TABLE IX.—Showing the Minimum Fatal Dose of Chloral-Hydrate in Rabbits.

No.	Weight of Rabbit.	Dose of Chloral-Hydrate in grs.	Result.
66	3 lbs. 2 oz.	30	Recovery
67	3 lbs. 11 oz.	30	"
68	4 lbs. 2 oz.	35	"
69	3 lbs. 1½ oz.	35	Death in four hours
70	3 lbs. 3 oz.	36	Recovery
71	3 lbs. 10 oz.	40	Recovery
72	2 lbs. 1½ oz.	40	Death in two hours
73	2 lbs. 12½ oz.	40	Death in two hours and twenty minutes
74	3 lbs. 1 oz.	42	Death in three hours and ten minutes
75	3 lbs. 2 oz.	46	Death in one hour and twenty-five min.
76	2 lbs. 14 oz.	46	Death in one hour and fifty-four minutes

Instead of finding, as the Edinburgh Committee did, that seven grains of chloral hydrate per pound of body weight was fatal in rabbits, I satisfied myself that nothing less than twelve grains per pound of body weight can be regarded as a fatal proportion of that drug in these animals. The only explanation of this discrepancy which I can offer is, that perhaps temperature had something to do with it. The room in which I worked had usually a temperature of about 56 degs. Fahrenheit's scale, and the rabbits, after having had chloral given to them, were always placed near a warm fire, and on cotton-wool. If the Edinburgh Committee maintained the heat of the rabbits upon which they experimented less carefully, it is conceivable that a smaller dose of chloral-hydrate would suffice to extinguish life; for Dr. Lauder Brunton has shown that warmth is most potent in hastening recovery from the effects of chloral hydrate, and in preventing death after an overdose. The chloral-hydrate used in my experiments was supplied by Messrs. Harvey and Reynolds of Leeds, and Messrs. Davy, Yates, and Routledge of London, and the solutions were prepared with scrupulous care.

To determine whether picrotoxine was really antagonistic to chloral-hydrate, and, if so, to what extent that antagonism extended, another set of experiments was clearly necessary, and these were forthwith undertaken; the minimum fatal dose of chloral-hydrate being now taken as twelve grains to each pound of body-weight.

TABLE X.—Showing the Effects of Small Doses of Picrotoxine injected with Fatal Doses of Chloral-Hydrate.

No.	Weight of Rabbit.	Dose of Chloral-Hydrate in grains.	Dose of Picrotoxine in parts of a grain.	Effects.	Result.
77	3 lbs. 3 oz.	36	1-30th	Deep sleep	Recovery
78	3 lbs. 3½ oz.	37	1-20th	Restlessness, sleep	"
79	3 lbs. 2 oz.	38	1-40th	Deep sleep	"
80	3 lbs. 3 oz.	38	1-20th	Disturbed sleep	Death
81	2 lbs. 14 oz.	39	1-40th	Deep sleep	Recovery
82	3 lbs. 1 oz.	40	1-30th	Disturbed sleep	Death
83	3 lbs.	40	1-40th	Deep sleep	"
84	2 lbs. 13 oz.	41	1-30th	"	"
85	3 lbs. 1 oz.	41	1-40th	"	"
86	3 lbs. 4 oz.	42	1-20th	"	"

These experiments made it apparent that the antagonism of picrotoxine to chloral-hydrate in rabbits is by no means so great as it was at first thought to be. Whenever the dose of the latter exceeded by four grains the minimum fatal amount, picrotoxine failed to avert death. Given in large amount, the chloral seemed to take possession of the nervous system so completely that it could not be dislodged by moderate doses of picrotoxine. And the issue of one experiment, in which a highly poisonous dose of picrotoxine, one-fourth of a grain, was given, after a fatal dose of chloral-hydrate—forty grains, did not encourage the hope that picrotoxine, in any quantity, could be employed to counteract large doses of chloral. The rabbit died, without having suffered from convulsions, much more rapidly than it would have done if left to sink under chloral poisoning. And yet, that there is a certain degree of antagonism exerted by picrotoxine against the toxic effects of chloral hydrate, is unmistakable. It does secure recovery in some cases, in which, but for its influence, death would almost inevitably ensue; and even, when it is powerless to save life, it notably controls symptoms. It rouses the cerebral centres from time to time, from that state of

torpor which chloral spreads over them. It limits the depth of the chloral narcosis, and breaks in upon it occasionally by intervals of semi-wakefulness, in which there are various spontaneous movements. It diminishes the hyperæsthesia which chloral sets up; and it prevents, to a considerable degree, that gradual production of slowness of the respiration, and that fall of temperature, which chloral constantly induces. The following table exhibits its action in keeping up the respiratory movements and the animal heat, in contrast with the unmodified effect of chloral upon these.

TABLE XI.—Showing the Effects of Chloral-Hydrate in reducing Temperature, and the Number of Respirations and the Effects of Picrotoxine in partially preventing that reduction.

No. of min. at injection.	No. 87. Rabbit weighing 3 lbs. 1½ oz., injected with 35 grs. of Chloral-Hydrate alone.		No. 88. Rabbit weighing 2 lbs. 1½ oz., injected with 35 grs. of Chloral-Hydrate and 1-25th of a gr. of Picrotoxine.	
	Temperature.	Respirations.	Temperature.	Respirations.
5	100.4	60	100.0	72
10	99.6	57	99.1	72
20	98.6	50	98.4	68
50	97.4	43	98.2	68
60	96.8	40	98.4	65
90	95.5	33	98.4	65
120	94.9	27	97.6	61
150	94.3	27	96.6	61
180	92.0	21	95.0	54
190	90.8	21	95.4	52
210	89.5	20	95.0	66
230	85.8	16	94.5	60
240	Died.	—	93.0	60
250	—	—	90.8	60
270	—	—	92.2	60
300	—	—	94.3	60
320	—	—	Ultimately quite recovered.	

[To be continued.]

CROUP AND DIPHTHERIA.

By WILLIAM CUMMING, M.D., Edinburgh.

THE question as to the identity of membranous croup and diphtheria is worthy of the attention it has recently received; but, I confess, I have some difficulty in understanding how the two diseases *can* be ranged under the same category. Many years ago, I saw a large number of cases of membranous croup, and its characters were of the most pronounced kind.

1. The type was sthenic. 2. The exciting cause was atmospheric, *i. e.*, cold and damp. 3. The treatment most successful in my hands, was antiphlogistic, *viz.*, tartar emetic in frequent and nauseating doses. 4. It was non-contagious. I never saw two cases in one family either occurring simultaneously or in immediate succession. 5. It was never followed by paralysis or other consequences affecting the nervous system. 6. It was limited to a certain age; never in my experience occurring after twelve years of age. 7. The membrane, as ascertained by *post mortem* examinations (which were sufficiently frequent), was firm, tough, tense, and of a light kid colour, and was strictly limited to the laryngo tracheal tract, at least in its upper part, though it not unfrequently passed downwards into the bronchi in the form of plastic bronchitis. The disease never invaded the pharynx, fauces, or nose.

All who have seen much of diphtheria cannot fail to remark how totally different pronounced cases of it are. 1. The type is asthenic.

2. The exciting cause is septic. 3. The treatment is antiseptic, nourishing, and stimulating. 4. It is markedly contagious, and, unless the most stringent precautions are taken, attacks, and proves fatal to other members of the family, or those in direct contact with it. 5. Nervous symptoms, and especially paralysis, are not unfrequent consequences, and are always to be feared. 6. It has no respect for age. 7. The membrane is ash grey, friable, in many cases almost pultaceous, and generally soft. It is seldom limited to the laryngo tracheal tract, but as frequently as not extends to the pharynx, fauces, and nose, and often begins there, passing downwards, which membranous croup never does.

Typhus and typhoid fever are recognised now by sufficiently distinctive characters, but they are, in my opinion, not more, or indeed so distinct, as are membranous croup and diphtheria.

A COTTAGE INFIRMARY is to be built at Mold. The Duke of Westminster, Mr. P. B. D. Cooke, and Mr. W. B. Buddicom, have each subscribed £100, and others smaller amounts, making in the aggregate about £500.