REPORT

OF THE

COMMITTEE OF THE BRITISH MEDICAL
ASSOCIATION TO INVESTIGATE THE
ANTAGONISM OF MEDICINES.By JOHN HUGHES BENNETT, M.D., F.R.S.E.,
Chairman and Reporter.

THE series of researches which I am about to describe owes its origin to the Address on Medicine I had the honour to read to the Association in Chester, at the annual meeting of 1866. I then urged the propriety of endeavouring to solve some of the scientific or practical difficulties with which our profession had to contend. This appeal was responded to, a grant of money was made, and a subscription raised to defray the expenses of a Committee that was to determine the question whether mercury had or had not any power to stimulate the liver to an increased secretion of bile. The report on this subject I had the pleasure of reading to the annual meeting at Oxford in 1868, and I may venture to say that the two years' labour of the Committee finally settled this long disputed subject, and demonstrated beyond the possibility of reasonable objection that in this respect mercury had none of the properties that had so long been attributed to it.* At the following annual meeting, in Leeds, another grant of money was made by the Association to investigate the antagonism of medicines, and again I was entrusted to form a Committee, and, as its Convener, to report the results. The Committee that was formed for this purpose consisted of Dr. McKendrick, my assistant, Dr. James Rogers, formerly of St. Petersburg, Dr. Macadam, lecturer on chemistry, Mr. T. Smith, head of the eminent firm of Messrs. T. and H. Smith, chemists and druggists, Edinburgh (the preparation of whose alkaloids is so thoroughly appreciated, and who at once promised to furnish us with the purest drugs that could be obtained, gratuitously), and Dr. Edmund Cook, chief chemist in the employment of the Messrs. Smith. This Committee appeared to me to embrace all the essential qualities and to possess all the necessary means and appliances for prosecuting the inquiry. On the resignation of Dr. Cook, who was obliged to leave Edinburgh, Dr. Alexander Bennett was added to the Committee.

At the preliminary meetings of the Committee, it was determined to introduce the substance under examination in solution below the skin of animals, and ascertain, by careful observation—

1. The physiological actions produced.
2. The minimum fatal dose.
3. The influence of one supposed antagonistic substance, on the physiological action of the other when both were simultaneously injected.
4. The influence of the supposed antagonistic substance when introduced some time *before* the fatal one.
5. The influence of the supposed antagonistic substance when introduced some time *after* the fatal one.
6. The limits of the antagonism when such existed.
7. The performance in all cases of a crucial test consisting, when any supposed antagonistic action had saved the animal, in injecting the same dose of the active substance into the same animal a week or ten days afterwards. If death then took place, it was held that the two substances were antagonistic.

By such a method, we hoped to ascertain, beyond the possibility of doubt, whether one drug could really antagonise the fatal or injurious properties of another, choosing in the first instance, for experiment, such as exhibited the most powerful and unequivocal action. In this manner there have been investigated, during the four years over which the Committee's labours have extended, the antagonistic properties existing between—

1. Hydrate of chloral and strychnia.
2. Sulphate of atropia and Calabar bean.
3. Hydrate of chloral and Calabar bean.
4. Hydrochlorate and meconate of morphia and Calabar bean.
5. Sulphate of atropia and meconate of morphia.
6. Meconate of morphia and theine.
7. Meconate of morphia and caffeine.
8. Meconate of morphia and guaranine.
9. Meconate of morphia and infusion of tea.
10. Meconate of morphia and infusion of coffee.
11. Extract of Calabar bean and strychnia.
12. Hydrate of bromal and atropia.

Doubtless these researches would have been much more extended, had not my illness, at the commencement of 1872, and consequent absence from Edinburgh, prevented my taking any very active part in them after the first four subjects named. This also threw such an amount of teaching, systematic and practical, upon my assistant, Dr. McKendrick, as equally to prevent his paying more than occasional attention to the work of the Committee. The absence of Dr. Rogers and Dr. Cook also caused it to stand still for several months. Nevertheless, a large number of experiments have been made and carefully described; indeed, they amount to 619 in number, the labour of performing, recording, tabulating, and reporting upon which can only be appreciated by those whose time has been occupied in similar investigations.

The experiments have been numbered in the order of their performance, and the results tabulated in columns, so that all the facts are condensed in the smallest possible space, and are easily studied. I shall be satisfied if it appear that the Committee has performed the task entrusted to it, and usefully expended the funds placed at its disposal by the Association.

I.—ANTAGONISM BETWEEN STRYCHNIA AND CHLORAL HYDRATE.

The minimum fatal dose of each of these substances was first ascertained.

A. On Rabbits.

TABLE I.—Showing the Effects of a Minimum Fatal Dose of Hydrate of Chloral on Rabbits.

No.	Weight of Rabbit.	Dose in Grains.	Result.	No.	Weight of Rabbit.	Dose in Grains.	Result.
1	4 lbs. 3 oz.	18	Recovery	11	3 lbs.	22	Death
2	4 lbs. 6 oz.	19	"	12	3 lbs.	21	Recovery
3	4 lbs. 10 oz.	22	"	13	3 lbs.	19	"
4	3 lbs. 8 oz.	21	"	14	4 lbs.	24	"
5	3 lbs. 9 oz.	20	Death	15	4 lbs. 2 oz.	25	Death
6	4 lbs. 2 oz.	24	Recovery	16	4 lbs. 3 oz.	24	Recovery
7	4 lbs.	26	Death	17	4 lbs.	24	"
8	3 lbs.	23	"	18	3 lbs.	22	Death
9	4 lbs. 1 oz.	20	Recovery	19	3 lbs.	23	"
10	3 lbs. 10 oz.	18	"	20	3 lbs.	21	Recovery

This table shows that twenty-one grains of hydrate of chloral may be regarded approximately as the minimum fatal dose for a rabbit of three pounds weight. At the same time, it has been observed, both in this research and in others in which chloral hydrate was employed as a hypnotic, that not unfrequently a dose, which in the great majority of instances is not ordinarily fatal, may destroy life. This is a fact of considerable practical importance, and might be explained by the supposition that, in certain conditions of the blood or tissues, chloroform may be produced more rapidly than usual by the action, according to the theory of Liebreich, of alkaline salts in the blood on chloral hydrate. The effects produced by chloral hydrate are now so well known as not to require special description. The period of hyperæsthesia is well marked in the rabbit. Frequently a slight pinch will cause the animal to utter prolonged screams, which would not be so occasioned in the normal condition.

TABLE II.—Showing the Effects of a Minimum Fatal Dose of Strychnia on Rabbits.

No.	Weight of Rabbit.	Dose in Parts of a Grain.	Result.	No.	Weight of Rabbit.	Dose in Parts of a Grain.	Result.
21	3 lbs. 1 oz.	1-100th	Death in 20 minutes	28	2 lbs. 8 oz.	1-98th	Death in 16 minutes
22	4 lbs.	1-50th	Death in 14 minutes	29	3 lbs.	1-96th	Death in 20 minutes
23	3 lbs. 6 oz.	1-80th	Death in 12 minutes	30	3 lbs.	1-95th	Recovery
24	4 lbs. 2 oz.	1-90th	Recovery	31	3 lbs. 4 oz.	1-98th	"
25	3 lbs.	1-90th	Death in 28 minutes	32	3 lbs. 5 oz.	1-98th	"
26	3 lbs. 1 oz.	1-95th	Recovery	33	3 lbs.	1-98th	Death in 45 minutes
27	2 lbs. 10 oz.	1-95th	Death in 18 minutes	34	3 lbs.	1-96th	Death in 1 hour

The result of these fourteen experiments indicate that the minimum fatal dose for rabbits of strychnia is 1-96th of a grain for every 3 lbs. weight of animal, or 1-288th of grain for every pound. Here also it must be understood that the fatal dose is to a certain extent approximate; for in several instances animals died from a smaller dose, apparently from asphyxia produced by strong tetanic convulsions of the muscles of respiration.

Having thus determined the minimum fatal dose of the two substances, the action of both together was investigated.

Influence of Hydrate of Chloral on a Fatal Dose of Strychnia, when

* Researches into the Action of Mercury, Podophylon, and Taraxacum, on the Biliary Secretion, etc. Second edition, with appendix, 8vo. Edinburgh: 1874.

both Substances are given simultaneously.—The phenomena produced are described in the following detailed experiment.

Experiment 35.—Female rabbit, weighing $3\frac{1}{4}$ lbs. The average number of cardiac impulses was 85 in 20 seconds, and the respirations 26 in 20 seconds. One-ninetieth of a grain of strychnia dissolved in 20 minims of distilled water was injected under the skin of the left shoulder. Immediately afterwards, 15 grains of hydrate of chloral in 30 minims of distilled water were injected under the skin of the loins. The animal remained quiet for twenty minutes, apparently becoming drowsy. At the end of that time, slight twitchings of the muscles were observed. Five minutes later, the animal was prone and had a very feeble convulsion, with a tendency to slight opisthotonos, which state lasted ten seconds. The animal then lay upon its side, apparently in deep hypnotism. During the next two hours, it remained in this condition, the only phenomena observed being—first, twitching of the internal rectus muscles of the eyeballs, and, second, a convulsive start on touching one of the extremities, or on tapping smartly on the table. At the end of three hours from the time of receiving the active substances, the animal began to move about, and it apparently soon became quite well.

Experiment 36.—On the tenth day after the former experiment, one-ninetieth of a grain of strychnia was again injected into the same animal, under the skin over the left loin. The animal remained quiet for five minutes, when it became restless, and moved about with a staggering gait. In two minutes more, it leaped from the table, fell on its side, and had severe convulsions, with an extreme degree of opisthotonos. These convulsive attacks occurred three times, when death ensued, twenty-six minutes after the administration of the poison.

The dose was thus proved to be fatal; but, as it was comparatively a small one, a series of experiments was made with the view of testing the influence of hydrate of chloral on still larger doses of strychnia, when the two substances were given almost simultaneously. These experiments are registered in the following table.

TABLE III.—Showing the Results of Varying Doses of Hydrate of Chloral when injected with Fatal Doses of Strychnia.

No.	Weight of Rabbit.	Dose of Chlor. Hyd. in grains.	Dose of Strychnia in parts of a grain.	Result.	Result of crucial experiment of giving same dose of Strychnia to same animal seven days afterwards.
37	3 lbs. 1 oz.	18	1-80th	Recovery	Recovery
38	3 lbs. 3 oz.	19	1-80th	"	Recovery after severe spasms
39	3 lbs.	16	1-60th	"	Death in 20 min.
40	3 lbs.	16	1-50th	"	Death in 10 min.
41	3 lbs. 2 oz.	16	1-25th	Death	
42	2 lbs. 13 oz.	14	1-70th	Recovery	Death in 18 min.
43	2 lbs. 13 oz.	15	1-60th	"	Death in 14 min.
44	2 lbs. 10 oz.	15	1-60th	"	Death in 18 min.
45	3 lbs.	17	1-40th	"	Death in 10 min.
46	3 lbs.	16	1-40th	"	Death in 12 min.
47	3 lbs.	12	1-29th	Death in 30 min.	
48	3 lbs. 2 oz.	10	1-60th	Death in 3 hours	
49	3 lbs. 3 oz.	8	1-80th	Recovery aft. severe spasms	Death in 20 min.
50	3 lbs.	14	1-30th	Recovery aft. severe spasms	Death in 14 min.
51	3 lbs.	12	1-24th	Death in 40 min.	
52	2 lbs. 11 oz.	12	1-32nd	Death in 36 min.	
53	2 lbs. 12 oz.	18	1-40th	Recovery aft. severe spasms	Death in 12 min.
54	2 lbs. 13 oz.	17	1-42nd	Recovery	Death in 16 min.
55	3 lbs.	16	1-50th	"	Death in 12 min.
56	3 lbs.	18	1-54th	Recovery aft. severe spasms	Death in 18 min.

It will be seen from this table that in twenty cases a fatal dose of strychnia was administered simultaneously with varying doses of chloral hydrate. In five instances, death ensued, notwithstanding the action of the latter drug. But in these, with the exception of No. 48, the dose of strychnia was very large, being about four times that of the minimum fatal dose. Even in these cases, however, chloral hydrate prolonged life, and, in No. 48, in which 1-60th of a grain of strychnia was given, with a dose of only ten grains of chloral hydrate, life was much prolonged. This will be more readily seen by comparing No. 48 with the result of the crucial experiments in Nos. 39 and 44, in which the animals died after the injection of 1-60th of a grain of strychnia in twenty and eighteen minutes respectively. These experiments, therefore, show, in a very conclusive manner, that chloral hydrate antagonises fatal doses of strychnia, and modifies the symptoms to a very remarkable extent.

It was found by experience that recovery from a fatal dose of strychnia, even after the administration of an antagonistic dose of

chloral hydrate, was rendered more certain if means were taken to prevent, as far as possible, the body of the animal from being irritated. It was frequently observed, after the administration of both substances, that, although the rabbit lay tranquilly on its side, and apparently deeply under the influence of the chloral hydrate, still peripheral irritation caused muscular twitchings and even severe spasm. These phenomena indicated that the reflex excitability of the spinal cord was still increased by the action of the strychnia. The best results, therefore, were obtained, so far as the recovery of the animals was concerned, by placing the rabbit under a large bell-jar, so arranged as to insure perfect ventilation.

Influence of Hydrate of Chloral when injected some time after a Fatal Dose of Strychnia.—A minimum fatal dose of strychnia produces its first visible physiological effects from fifteen to twenty minutes after its introduction into the system. It became a matter of great practical importance to determine how far chloral hydrate could influence the physiological effects of strychnia after these had made their appearance. Twelve experiments were made, with the view of determining this point. The rabbits were as nearly as possible of equal weight and in equally good condition; the same amount of strychnia was introduced into each. The counteracting dose of chloral hydrate was introduced in the first case almost simultaneously, and in the other cases at successive intervals of two minutes. The following table shows at a glance the result.

TABLE IV.—Showing the Influence of Hydrate of Chloral given at different intervals of time after a fatal dose of Strychnia.

No.	Weight of Rabbit.	Dose of Strychnia in parts of a grain.	Dose of Chloral Hydrate in grs.	Interval between the administration of Chloral Hydrate.	Time of the first appearance of effects of Strychnia.	Results.	Remarks.
57	2 lbs. 15 oz.	1-96th	16	Simultaneously	Slight spasms 20 min. after	Recovery	
58	3 lbs.	"	"	2 minutes after	No spasms	"	
59	3 lbs.	"	"	4 minutes after	Slight spasms 18 min. after	"	Slight twitchings of muscles for 3 hrs.
60	3 lbs. 1 oz.	"	"	6 minutes after	Slight tetanic spasm 22 m. after	"	Ditto for nearly 2 hours
61	3 lbs.	"	"	8 minutes after	Tetanic convulsion 20 m. after	"	This animal had numerous tetanic spasms
62	2 lbs. 14½ oz.	"	"	10 minutes after	Tetanic convulsion 21 m. after	Death	Died 35 min. aft. strychnia
63	3 lbs.	"	"	12 minutes after	Severe tetanic convulsions 20 min. after	"	Died 32 min. aft. strychnia
64	3 lbs.	"	"	14 minutes after	Ditto	"	Died 29 min. aft. strychnia
65	3 lbs. ½ oz.	"	"	16 minutes after	Very severe convulsions	"	Died 24 min. aft. strychnia
66	3 lbs. 1½ oz.	"	"	18 minutes after	Ditto	"	Died 22 min. aft. strychnia
67	3 lbs.	"	"	20 minutes after	Ditto	"	Died 20 min. aft. strychnia
68	3 lbs.	"	"	22 minutes after	Ditto	"	Died 20 min. aft. strychnia

From these experiments, it will be seen that chloral hydrate becomes less efficient in counteracting the fatal effects of strychnia in proportion as it is administered at more distant intervals of time from that of the administration of the strychnia. If the physiological effects of strychnia showed themselves in a marked way before the animal came under the influence of the chloral hydrate, death was liable to ensue from asphyxia due to tetanic spasm of the muscles of respiration. The sooner the chloral hydrate was given after the administration of strychnia, the more certain was the animal to survive. From this, the practical conclusion follows that, in cases of accidental poisoning by strychnia, the patient should be brought as rapidly as possible under the influence of chloral hydrate, either by subcutaneous injection or even by the direct introduction of the substance into a vein.

Influence of Strychnia when simultaneously injected with a Fatal Dose of Hydrate of Chloral.—It was pointed out by Oscar Liebreich*, who first investigated and brought under the notice of the profession the hypnotic effects of hydrate of chloral, that the injection of minute doses of strychnia had the effect of rousing rab-

* Oscar Liebreich, *Comptes Rendus des Séances de l'Académie des Sciences*, 1870, vol. lxx, p. 403.

bits from under the influence of deep coma produced by chloral hydrate, and even of saving life after a lethal dose of the latter. As chloral hydrate is now much used in practical medicine, and as not a few cases are now on record of deaths from too large doses, it became of importance to reinvestigate this point. In fifteen experiments, therefore, in which fatal doses of chloral hydrate were first given, and after the animals had come deeply under the influence of the drug, minute non-fatal doses of strychnia were injected. The results are seen in the following table.

TABLE V.—Showing the Influence of Injecting Strychnia when Fatal Doses of Chloral Hydrate had been previously Administered.

No.	Weight of Rabbit.	Dose of Chloral Hydrate in grains.	Dose of Strychnia in parts of a grain.	Time between Injection of Dose of Chloral and Dose of Strychnia.	Results.	Remarks.
69	3 lbs. 2 oz.	21½	1-100	15 minutes	Recovery	Killed 4 days afterwards with same dose of chloral hydrate
70	3 lbs. 1 oz.	22	1-93	15 minutes	"	Recovered 4 days afterwards with same dose of chloral hydrate
71	2 lbs. 15 oz.	22	1-94	14 minutes	"	Killed 5 days afterwards, ditto
72	3 lbs.	23	1-110	13 minutes	Death	Died in profound coma, with but slight muscular twitchings
73	3 lbs.	24	1-150	10 minutes	"	Ditto, ditto
74	3 lbs. ½ oz.	21	1-100	12 minutes	Recovery	Recovered 4 days afterwards with same dose of chloral hydrate
75	3 lbs. 1½ oz.	22	1-80	Simultaneously	"	Killed 6 days do. do.
76	3 lbs. 1½ oz.	22	1-60	"	Death	Died in profound coma, with but slight muscular twitchings
77	3 lbs.	25	1-50	"	"	Coma, one smart tetanic spasm
78	3 lbs.	24	1-40	15 minutes	"	Coma, three spasms, opisthotonos
79	3 lbs. 2 oz.	23	1-90	12 minutes	Recovery	Killed 3 days afterwards with same dose of chloral hydrate
80	3 lbs. ¼ oz.	22	1-98	10 minutes	"	Recovered after same dose 5 days afterwards
81	2 lbs. 14 oz.	23	1-96	20 minutes	Death	Profound coma, slight twitchings
82	2 lbs. 15 oz.	21½	1-92	20 minutes	"	Ditto, ditto
83	3 lbs.	22	1-100	18 minutes	Recovery	Recovered from same dose, given 4 days afterwards

It will be apparent from a consideration of this table that the evidence in favour of the view that strychnia antagonises fatal doses of chloral hydrate is not so satisfactory as might be expected. In the fifteen experiments, eight recovered from what were supposed to be fatal doses of chloral hydrate (Nos. 69, 70, 71, 74, 75, 79, 80, and 83); but, when the same dose of chloral hydrate was given to the same animals a few days later, four died (Nos. 69, 71, 75, and 79) and four recovered (Nos. 70, 74, 80, and 83). It was also observed that, in those cases in which the animals died notwithstanding the injection of strychnia, they died in profound coma, although, from the muscular twitchings and from the ease with which reflex spasms could be excited, it was evident that the strychnia was physiologically influencing the spinal cord. It would appear, therefore, that there is little hope of saving life after fatal doses of chloral hydrate by the subsequent injection of strychnia. Chloral hydrate acts, not only on the centres of the spinal cord, but also on the brain, as is evidenced by the profound coma following a large dose, and the injected condition of the membranes of the brain found after death. Strychnia, on the other hand, exercises no known influence on the brain; and, although it may stimulate the reflex centres of the cord, depressed in vital activity by the action of chloral hydrate, it cannot relieve the condition of the encephalon, and consequently, even though there may be muscular twitchings and even tetanic convulsions, the animal dies comatose.

B. On Rats.

In this inquiry, numerous experiments were made on rats. The animals employed were common brown rats (*Mus decumanus* Lin.) caught in stables. They were from twelve to sixteen ounces in weight. The inquiry was conducted in the same manner as in the case of rabbits, and the general results were found to be the same.

1. *Minimum Fatal Dose of Hydrate of Chloral on Rats.*—This was found to be, after twelve experiments (detailed in Table VI), 1⅞ grains for an animal weighing nearly twelve ounces. In two cases, Nos. 90 and 91, the animals recovered from a dose of two grains; but they appeared to be more powerful and better fed specimens.

TABLE VI.—Showing the Effects of a Minimum Fatal Dose of Hydrate of Chloral on Rats.

No.	Weight of Rat in ounces.	Dose of Hydrate of Chloral in grains.	Result.
84	10	1½	Recovered
85	11	1½	"
86	12	1	"
87	11	1½	"
88	13	1½	"
89	11	1½	"
90	11½	2	"
91	10½	2	"
92	11	1½	Died
93	11½	1½	"
94	11½	1 8-9ths	Recovered
95	11½	2	Died

11. *Minimum Fatal Dose of Strychnia on Rats.*—After twelve experiments (detailed in Table VII), this was ascertained to be 1-60th of a grain. It is remarkable that rats required a larger dose of strychnia to destroy life than rabbits, the fatal dose for the latter being about (see Table II) 1-96th of a grain. This is still more striking, if we compare the fatal dose according to pound weight: rat, 1-60th of a grain; rabbit, 1-288th—more than four times less in the rabbit than in the rat. On the other hand, it was noted that, when the physiological effects of strychnia did manifest themselves in the rat, they were much more violent than in the case of the rabbit, and the animal usually died in the very first tetanic spasm. In many other experiments, it was observed that it was more difficult to kill rats than rabbits.

TABLE VII.—Showing the Effects of a Minimum Fatal Dose of Strychnia on Rats.

No.	Weight of Rat in ounces.	Dose of Strychnia in grains.	Result.
96	11	1-150th	Recovered
97	11½	1-140th	"
98	11½	1-130th	"
99	12	1-120th	Recovered; slight convulsion
100	11½	1-100th	"
101	11½	1-90th	Recovered; more severe convulsion
102	10	1-80th	Recovered; severe convulsion
103	9½	1-70th	Severe convulsions, frequently repeated; recovery
104	12½	1-60th	Convulsions; death
105	12	1-70th	Severe convulsions; recovery
106	12	1-60th	Convulsions; death
107	11	1-60th	"

111. *Influence of Hydrate of Chloral injected simultaneously with a Fatal Dose of Strychnia.*—This was determined in the following six experiments, which were deemed sufficient to determine the point, so far as rats were concerned.

TABLE VIII.—Showing the Antagonism between Hydrate of Chloral and Strychnia in Rats.

No.	Weight of Rat.	Dose of Chloral Hydrate in grains.	Dose of Strychnia in parts of a grain.	Result.	Result of crucial experiment of giving same dose to same animal 5 days afterwards.
108	10 oz.	1½	1-34th	Died in 16 minutes in severe convulsions	Chloral hydrate apparently had not time to act
109	11 oz.	3	1-44th	Recovered after considerable twitchings in 3 hours	Killed in 20 minutes with same dose
110	11 oz.	3	1-14th	Ditto, ditto	This animal had repeated tetanic spasms; killed with same dose in 18 minutes
111	10½ oz.	2½	1-44th	Died 10 hours after	Slight convulsions; died apparently from effects of chloral
112	11 oz.	2½	1-60th	Died 15 hours after	Ditto, ditto
113	11½ oz.	2½	1-60th	Died 14 hours after	Ditto, ditto
114	11½ oz.	3	1-50th	Died 8 hours after	Became suddenly asphyxiated; much mucus in air-passages

This table shows (1) two instances (Nos. 109 and 110) in which the animals recovered from fatal doses of strychnia; (2) that larger than

fatal doses of chloral hydrate were required to antagonise fatal doses of strychnia, and that in three instances (Nos. 111, 112, and 113) the animals died apparently from the effects of the former. The convulsions, except in No. 108, were much reduced, both in force and frequency, by the action of the chloral hydrate.

GENERAL CONCLUSIONS REGARDING THE ANTAGONISM BETWEEN CHLORAL HYDRATE AND STRYCHNIA.

It appears to be established from these experiments :

1. That, after a fatal dose of strychnia, life may be saved by bringing the animal under the influence of chloral hydrate.

2. That chloral hydrate is more likely to save life after a fatal dose of strychnia than strychnia is to save life after a fatal dose of chloral hydrate.

3. That, after a dose of strychnia producing severe tetanic convulsions, these convulsions may be much reduced, both in force and frequency, by the use of chloral hydrate, and consequently much suffering saved.

4. That the extent of physiological antagonism between the two substances is so far limited, that (1) a very large fatal dose of strychnia may kill before the chloral hydrate has had time to act ; or (2) so large must the dose of chloral hydrate be to antagonise an excessive dose of strychnia, that there is danger of death from the effects of the chloral hydrate.

5. Chloral hydrate mitigates the effects of a fatal dose of strychnia by depressing the excess of reflex activity excited by that substance, while strychnia may mitigate the effects of a fatal dose of chloral hydrate by rousing the activity of the spinal cord ; but it does not appear capable of removing the coma produced by the action of chloral hydrate on the brain.

It is scarcely necessary to point out the vast importance of these results to practical medicine and the indications they afford, not only in cases of poisoning by strychnia, but in cases of tetanus and other spasmodic diseases, reflex and central.

At a meeting of the Medico-Chirurgical Society of Edinburgh, on April 6th, 1870, and at the annual meeting of the Association at Newcastle in 1870, I demonstrated experimentally with what certainty rabbits might be saved after receiving a fatal dose of strychnia, by the injection of a solution of chloral hydrate. Take two rabbits of about 3 lbs. weight ; inject under the skin of both 1-96th of a grain of strychnia, and then in one a solution of fifteen grains of chloral : in ten minutes the first one will leap into the air and fall down tetanic and dead ; the other will go to sleep, and in about two hours will wake up as if nothing were the matter. A more certain antidote does not exist.

[To be continued.]

INTRAVENOUS INJECTIONS.—The late discussions as to the harmlessness or danger of intravenous injections of chloral appear to have been anticipated by a physician named Godefroy, who practised in Orleans in the seventeenth century, and who has left a number of very interesting manuscripts. Dr. Champignon, of the same city, laid before its Société des Sciences some extracts from these documents, in which M. Godefroy discusses transfusion of blood, which he stigmatises as murderous, whilst he strongly approves of "medicated infusions into the basilar vein". He quotes three experiments tried by Fabricius at the hospital at Dantzic. Two of these experiments were made on two women suffering from epilepsy and some other doubtful disease. They were not cured, but there were no unpleasant consequences. The substance injected is called by Godefroy, who writes in Latin, *medicamentum purgans*, and in the *Journal des Savants* (1660-1667) *liqueur purgative*.

The third incident is interesting. A soldier was affected with syphilis of old standing, with numerous exostoses. Three drachms of the *liqueur purgative* were injected into the vein of the arm. Great pain in the elbow and swelling of the arm followed ; the medicine acted at the end of four hours with five actions of the bowels ; the following days the same action went on. The exostoses diminished, and soon there were no traces of the lues venerea left. The *Journal des Savants* of January 23rd, 1668, relates these cases, but gives no details respecting this purgative liquor (*medicamentum purgans*). Might it not have been calomel, then the universal panacea recommended by Paracelsus ? Would the direct injection of calomel or any other mercurial preparation into the blood be more efficacious than ingestion by the stomach, as the partisans of hypodermic injections in syphilis have asserted ? However this may be, it is certain that surgeons in former times have made medicated injections into the veins without any untoward consequences, though with imperfect instruments ; and even seem to have obtained beneficial results from their use.

BRITISH MEDICAL ASSOCIATION : SUBSCRIPTIONS FOR 1874.

SUBSCRIPTIONS to the Association for 1874 became due on January 1st. Members of Branches are requested to pay the same to their respective Secretaries. Members of the Association not belonging to Branches, are requested to forward their remittances to Mr. FRANCIS FOWKE, General Secretary, 36, Great Queen Street, London, W.C.

BRITISH MEDICAL JOURNAL.

SATURDAY, OCTOBER 3RD, 1874.

THE MEDICAL ADDRESSES.

WE are no great admirers of Introductory Addresses. It may very much be doubted whether the toil and anguish of mind which many of them evidently cost their authors, and the suffering which some inflict upon their audience, are at all adequately repaid by the exceptional pleasure and profit to be derived from the occasionally successful orations which October 1st evokes. A dozen of these orations were produced, and several more will be called for during the next few weeks in England, Ireland, and Scotland. It is a very hard fate which compels each member of the medical staff in succession to become that for which nature has not always fitted him ; for an orator is almost as rarely born as a poet. Fortunately, however, custom allows the speakers on October 1st a considerable range of subjects ; fortunately also the audiences are thoroughly sympathetic, and well understand that the delivery of the oration is more often an accepted duty than a voluntary display ; and it must further be said that the range of medical study and the variety of culture which it encourages are such, that the medical orators accomplish their task with a higher average of success than could be fairly expected, and one which we think no other profession could well surpass. Most clergymen are, we believe, of opinion that, if fate had ordained their lot otherwise, they would have made very good doctors, and are disposed, under any circumstances, to a little poaching ; and, after reading through a series of October addresses, the idea always passes through our mind that medical orators would for the most part cut a very good figure in the pulpit.

Granting all the difficulties of the position, it must be admitted that the lecturers have, this year, acquitted themselves of their task with great ability. The address of Sir William Gull was looked forward to with much eagerness, not only by Guy's men but by the profession generally ; and—although the announcement made some weeks since that we should, by the courtesy of the orator, publish the address *in extenso*, and that we should supply proofs for abstract to our contemporaries, may have diminished the numbers who were willing to submit to the inconvenience of overcrowding, for the sake of hearing the spoken words of one who is a born orator as well as an eminent thinker and practitioner—the crowd that assembled could not be accommodated in the precincts of the hospital, and an adjournment was necessary to a more spacious hall. This spontaneous tribute paid to the school and its great physician, the hearers were gratified with an oration which, if it failed to excite their imagination or to dazzle their intelligence, must have left them impressed with some thoughts very pregnant with germs of progress. Sir William Gull, as a teacher, has long been viewed with feelings of admiration mixed with suspicion. Gifted with a fatal facility for epigram, which springs almost unbidden to his lips, and tutored by research as well perhaps as tempted by his native keenness of intellect into cultivated scepticism, he has been regarded askance by the great body of medical workers, who shrink from a negative usefulness in practice, and long to do their work as priests of a positive faith armed with formulae that have the highest sanctions.

The study which he has made fashionable, of the natural history of