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.*

GENERAL CONCLUSIONS.

The general results obtained from the investigations detailed in the preceding report are the following.

I. *As to the Antagonism between Strychnia and Chloral Hydrate.*

In this investigation, one hundred and fourteen experiments were performed.

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

2. 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. After a dose of strychnia has produced severe tetanic convulsions, these convulsions may be much reduced both in force and in frequency by the use of chloral hydrate, and consequently much suffering saved.

4. 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) the dose of chloral hydrate must be so large in such a case to antagonise the fatal 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 to be capable of removing the coma produced by the action of chloral hydrate on the brain.

II. *As to the Antagonism between Sulphate of Atropia and Calabar Bean.*

In this investigation, one hundred and fourteen experiments were performed.

1. Sulphate of atropia antagonises to a slight extent the fatal action of extract of Calabar bean.

2. The area of antagonism is more limited than even Dr. Fraser has indicated in his paper on the subject.

III. *As to the Antagonism between Hydrate of Chloral and Calabar Bean.*

In this investigation, thirty-one experiments were performed.

1. Hydrate of chloral modifies to a great extent the action of a fatal dose of extract of Calabar bean, mitigating symptoms and prolonging life.

2. Hydrate of chloral in some cases saves life from a fatal dose of extract of Calabar bean.

3. If hydrate of chloral be given before extract of Calabar bean, so that the animal is deeply under the influence of hydrate of chloral before it receives the extract of Calabar bean, the symptoms produced by the latter are much modified, and life is saved from the effects of what would otherwise be a fatal dose.

4. Chloral hydrate is of little service as an antagonist to extract of Calabar bean, if given some time after the latter. If the symptoms of the action of Calabar bean be in full operation, it will not save life, however it may modify symptoms.

5. The antagonism is limited—

a. *By the amount of dose of the extract of Calabar bean*—more than a minimum fatal dose of extract of Calabar bean destroying life, notwithstanding the administration of chloral hydrate.

b. *By the interval of time between the administration of the two substances.* There is a great probability of saving life in those instances in which the animal is under the influence of chloral hydrate before the subcutaneous injection of the extract of Calabar bean; there is less probability when both substances are given simultaneously; there is still less if the chloral hydrate be given from five to eight minutes after

the extract of Calabar bean; and no chance at all if the chloral hydrate be given eight minutes after a fatal dose of extract of Calabar bean.

6. Even in cases in which a fatal result follows the action of the two substances, the physiological effects of extract of Calabar bean are considerably modified by those of hydrate of chloral.

IV. *As to the Antagonism between Hydrochlorate and Meconate of Morphia and Calabar Bean.*

In this investigation, forty experiments were performed.

Hydrochlorate and meconate of morphia in no way antagonise extract of Calabar bean.

V. *As to the Antagonism between Sulphate of Atropia and Meconate of Morphia.*

In this investigation, eighty-one experiments were performed on rabbits and dogs.

A. *In Rabbits:*

1. Sulphate of atropia is physiologically antagonistic to meconate of morphia within a limited area.

2. Meconate of morphia does not act beneficially after a large dose of sulphate of atropia, for in these cases the tendency to death is greater than if a larger dose of either substance had been given alone.

3. Meconate of morphia is not specifically antagonistic to the action of sulphate of atropia on the vaso-inhibitory nerves of the heart.

4. The beneficial action of sulphate of atropia in cases of poisoning by meconate of morphia is probably attributable to the action which the former substance possesses of contracting the blood-vessels, and thus diminishing the tendency to cerebral and spinal congestion produced by salts of morphia.

B. *In Dogs:*

Sulphate of atropia modifies the physiological action of meconate of morphia, and may even save life after a fatal dose of the latter. The limit, however, is so narrow as to be of no practical service.

VI. *As to the Antagonism between Tea, Coffee, Theine, Caffeine, Guaranine, on the one hand, and Meconate of Morphia on the other.*

In this investigation, one hundred and seventeen experiments were performed.

1. Theine is antagonistic to meconate of morphia, inasmuch as the action of the one substance modifies that of the other, and may even save life from a fatal dose of either substance.

2. Meconate of morphia delayed the appearance of the convulsions characteristic of the action of theine; but, on the other hand, theine, if given in large doses, did not affect in a marked degree the action of meconate of morphia, because symptoms of poisoning by theine were soon manifested.

3. Further experiments on cats showed that, (a) while a cat may recover from the effects of a dose of $1\frac{3}{4}$ grains of meconate of morphia given alone, it will not recover from the effects of a dose of 2 grains, even although the effects of the latter dose are modified by those following the introduction of 4 or 5 grains of theine; (b) that in three cases the animals recovered from the effects of $1\frac{1}{2}$ grains of meconate of morphia and 4 to 5 grains of theine, while they died when the same dose of meconate of morphia was administered eight days afterwards; (c) that, when the dose of theine was increased beyond five grains, the animals invariably died, apparently from the effects of theine.

4. Experiments on rabbits, as to the antagonism between meconate of morphia and theine, were found to be unsatisfactory as regards the purposes of this inquiry, because both drugs produce epileptiform convulsions in these animals.

5. The results obtained in investigating the action of caffeine and guaranine as antagonists to meconate of morphia were similar to those observed with reference to theine.

6. Experiments were made on dogs to ascertain the effects of strong infusions of tea and decoctions of coffee as antagonists to meconate of morphia. These were unsatisfactory, chiefly because the tea or coffee was usually vomited so soon as to prevent the possibility of the exercise of any physiological antagonism. At the same time, it was observed in several instances that the administration of tea or coffee so excited the animals as to prevent them from falling into stupor or coma after a dose of meconate of morphia, which would have produced this effect had the tea or coffee not been given.

VII. *As to the Antagonism between Extract of Calabar Bean and Strychnine.*

In this investigation, thirty experiments were performed.

Although the symptoms produced by either substance were modified considerably by the action of the other, there was no instance of recovery from a fatal dose.

* Concluded from p. 806 of the JOURNAL for December 26th.

VIII. *As to the Antagonism between Bromal Hydrate and Atropia.*

In this investigation, thirty-six experiments were performed.

1. There is a distinct physiological antagonism between bromal hydrate and atropine.

2. After a fatal dose of bromal hydrate, the introduction of atropia arrests excessive secretion from the salivary glands and mucous surfaces of the lungs, and thus obviates the tendency to death from asphyxia caused by the accumulation of fluids in the air-passages. Atropia also causes contraction of the blood-vessels, and thus antagonises the action of bromal hydrate, which causes dilatation of these vessels by paralysis of the sympathetic nerve.

3. While atropia may save life after a fatal dose of bromal hydrate, the converse apparently does not hold good, as we have never succeeded in saving life after a fatal dose of atropia by the subsequent injection of bromal hydrate.

In concluding this report, I feel it to be necessary to allude especially to the labours of two members of the Committee—viz., first, Dr. Alexander Bennett, who completely worked out the physiological actions of cocaine, theine, caffeine, and their allied compounds; and, secondly, Dr. McKendrick, on whom the bulk of these researches ultimately devolved, and by whom the lengthened investigation on the antagonism between the sulphate of atropia and meconate of morphia was carried out. To him also we are indebted for the remarkable discovery of the antagonism between bromal hydrate and atropia. The long survey into which I have entered can convey no adequate idea of the many hours spent in laborious toil; of the skilful manipulation, sustained power of observation, judgment in inventing and comparing the results of experiments, and, I may add, patience under failures, which have characterised the efforts of these gentlemen. Even the account of the investigations themselves, with the tabulated results of the experiments, can give only a feeble conception of the laboratory work accomplished. The preparation of the report and its careful revision was in itself a work demanding no small time and labour.

I venture, however, to say that such are the toils and sacrifices required by modern medicine, if it be sincerely desired to solve existing difficulties, and prosecute those new inquiries which are so necessary for maintaining its position as a science and as an art. I sincerely trust that no parsimony nor error in administration will restrain the British Medical Association from continuing the noble efforts it has commenced, and rewarding by liberal grants the arduous labours of men who will dedicate themselves to these pursuits. It is gratifying to know that the present and, it is to be hoped, the future flourishing state of its finances, will enable it to take a lead in this patronage of scientific and practical endeavour for the benefit of humanity. I shall always esteem it a proud distinction for myself that I first indicated at least one method in which this could be accomplished,* and have demonstrated, in the two reports I have had the honour of laying before the Association, on the one hand, how error may be corrected,† and, on the other, how new fields may be acquired for the therapist in neutralising poisons and extending our means for the cure of disease.

CASE OF IDIOSYNCRASY.

THE following curious case of idiosyncrasy came under my notice lately. Mrs. R., aged 35, widow, a person of somewhat spare habit and active disposition, informs me that, since her early childhood, she has had a very strong aversion for *potatoes*. She knows no reason for this aversion; certainly it is not due to any fanciful notion. It is the result, apparently, of a peculiar idiosyncrasy. When she was quite a little creature, her uncle was very fond of playing a trick on her by concealing a small morsel of potato in a bit of butter, and inducing her to take it. The result always was *very severe vomiting*. She remembers her mother being very angry with her uncle on the occasion when he indulged in this practical joke. If she happened to be present where potatoes were being cooked, she became quite faint; and, until within a few years back, she could not even handle the tubers. At present, she would rather take the vilest medicines than taste a potato; indeed, she could not bring herself to do the latter. It is rather singular, that throughout life Mrs. R. has displayed an extraordinary susceptibility to febrile and "catching" diseases. Thus she states that, in her early childhood, she had hooping-cough, measles, scarlet fever, and since then small-pox, typhus fever, rheumatic fever, enteric fever, and lastly relapsing fever. Since suffering from relapsing fever, she has experienced some dyspnoea after exertion, and recently she had hæmoptysis.

JAMES W. ALLAN, M.B., Belford Hospital, Fort William, N.B.

* *Researches into the Action of Mercury, Podophyllin and Taraxacum on the Biliary Secretion.* Second edition. Edinburgh: Edmonston and Douglas, 8vo, 1874.
† See Address in Medicine for the year 1866, delivered at Chester.

DESCRIPTION

OF A

NEW PORTABLE THERMO-ELECTRIC APPARATUS
FOR MEDICAL AND PHYSIOLOGICAL
INVESTIGATIONS.*

By J. S. LOMBARD, M.D.,

Formerly Assistant Professor of Physiology in Harvard University, U.S.

ALTHOUGH many important facts regarding the general temperature of the body in disease have been ascertained of late years by the application of thermometers to clinical purposes, yet little or nothing has been done in the study of the temperature of different portions of the surface of the body as affected by morbid conditions of the internal organs. The reason of this is, undoubtedly, that it is only with thermo-electric apparatus that investigations of this kind can be properly made, and up to the present time all such apparatus has been of a nature to preclude its general employment by medical men. The writer has endeavoured, in the instrument to be described (see fig. 1), to combine portability and compactness with sufficient delicacy for all clinical and many physiological investigations. He believes that a very little practice will enable any one to use the apparatus with ease and accuracy. Portions of the apparatus are not new, having been devised by the writer in 1866, and described by him in *Archives de Physiologie*, July 1868.

The instrument may be divided into five parts—the galvanometer; the rheostat; the two thermo-piles; a tin kerosine lamp; and a brass stand, with a horizontal arm having a clamp at its end. Added to these are a compass and a magnifying glass. A board, three-tenths of an inch in thickness, and exactly fitting the interior of the box in which the apparatus is contained, with just sufficient allowance to permit of its being slid out at a door in one end, forms a second or false bottom to the box. The galvanometer, rheostat, lamp, and stand, are all on this board. The levelling screws of the galvanometer rest in holes in the board, and the rheostat also is secured to it. Calling the end of the box in which the door is the *front*, we have (fig. 12) from before backwards, on the left, first, the ebonite base of the rheostat, four and two-tenths inches from left to right, and three inches from front to back; second, the galvanometer, four and four-tenths inches in diameter at its base. On the right, we have, first, the tin kerosine lamp; and, second, the brass stand. This completes the description of the arrangement of that portion of the apparatus which is on the board.

Both the galvanometer and the rheostat can be removed from the board; but it is not intended that they should be, except in case the mercury cups of the rheostat are to be emptied. In experimenting, the board, bearing on it the galvanometer, rheostat, lamp, and stand, is simply slid out at the door of the box; and the lamp and stand having been removed, the galvanometer and rheostat remain on the board as permanent fixtures.

The Galvanometer is constructed as follows. It has a circular wooden base, the levelling screws of which rest (as before mentioned) in holes, or rather depressions, in the false bottom of the box. On this wooden base is screwed a square plate of ebonite, with rounded corners, so as to clear the groove in the wooden base in which the glass shade rests. On the plate of ebonite is fastened the frame on which the wire of the galvanometer is wound. The frame is one and nine-tenths inches long, one inch wide, and one and one-twentieth inches high. It does not stand in the centre of the ebonite plate, but at one side. Placing the board (fig. 2) so that the rheostat is to the front, facing us, and, therefore, the galvanometer to the rear, the frame stands on the left hand edge of the plate (the observer's left hand), its length being from before backwards: the wire of the coil runs, therefore, in the same direction.

From each side of the frame two flat brass stanchions rise, converging towards a point over the centre of the slit in the coil, until at a height of two and one-tenth inches they are united by a brass platform, three-tenths of an inch square. On this platform is a brass cylinder, three-tenths of an inch high, covering the platform, with the exception of its four corners; and again on the cylinder, in the centre, is a split tube two-tenths of an inch long. Both cylinder and platform are pierced by a hole of the diameter of this split tube. In the split tube, and through the cylinder and platform, there slides a second tube with a milled head, and to the milled head inside this second tube is fastened one end of the fibre of unspun silk, which forms the suspension of the

* The instrument is made by William Ladd and Co., 11 and 12, Beak Street, Regent Street, London.