Researches into the action of mercury, podophylline, and taraxacum on the biliary secretion : being the report of the Edinburgh Committee of the British Medical Association / by John Hughes Bennett.

RESEARCHES

INTO THE ACTION OF

MERCURY, PODOPHYLLINE, AND TARAXACUM

ON THE

BILIARY SECRETION;

BEING

THE REPORT OF THE EDINBURGH COMMITTEE OF THE BRITISH MEDICAL ASSOCIATION.

BY

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REPORT

OF THE

EDINBURGH COMMITTEE

ON THE ACTION OF

MERCURY, PODOPHYLLINE, AND TARAXACUM

ON THE

BILIARY SECRETION.

At the Meeting of the Association in Dundee (1867), I read as a communication some of the results arrived at by a Committee which had been investigating the action of mercury as a cholagogue. The inquiry originated in a suggestion made by myself, in the annual address in medicine I delivered to the British Medical Association at Chester in 1866. The physiological department of Section D considered the results so interesting and important that a grant of money was voted in aid of the Committee's researches, with the understanding that a full report was to be made on the whole inquiry at the next Meeting of the Association to be held in Norwich. The Committee consisted of Dr. Hughes Bennett, Professor of the Institutes of Medicine or Physiology in the University of Edinburgh, the Chairman and Reporter, Dr. Christison, Professor of Materia Medica, Dr. Maclagan, Professor of Medical Jurisprudence, Dr. James Rogers, formerly of St. Petersburg, Dr. W. Rutherford, assistant to the Professor of Physiology, Dr. Gamgee, assistant to the Professor of Medical Jurisprudence, and Dr. Fraser, assistant to the Professor of Materia Medica, Edinburgh.

The first meeting of the Committee was held November 16th, 1866. On proceeding to consider by what method the action of mercury on the biliary secretion was to be accurately ascertained, the conclusion was arrived at that no kind of examination of the fæces could yield trustworthy results. Supposing that the chief and characteristic constituents of the bile found their way into the alvine evacuations unchanged, imperfection in the analytical methods at our disposal render their quantitative analysis impossible. The plan of ascertaining bile-acids indirectly by means of nitrogen and sulphur determinations of the alcoholic extract, while most unsatisfactory in the case of pure bile, is still more so when applied to the alcoholic extract of fæces. The method of Professor Hoppe-Seyler of Tübingen, who calculated the amount of bile-acids from the effect which their solutions exert upon the ray of polarized light, presents such complexity and difficulty as to render its

systematic employment in any series of analyses altogether inapplicable. As to the colouring-matters of bile, there is no direct method known by which they can be estimated. But it was further argued that, did we even possess proper means of estimating the bile-products, it is only a small portion of such as are secreted by the liver which can be found in the alvine discharges. Bidder and Schmidt ascertained that the amount of unoxidized sulphur in them only represented one-eighth part of the total sulphur which the liver secretes, and that of the other constituents of the bile the larger proportion are absorbed. Indeed the utter impossibility of detecting the constituents of bile in the fæces is admitted by one of the most reliable physiological chemists of Europe, viz. Professor Hoppe-Seyler. That under the influence of purgatives unchanged bile is occasionally discharged from the bowel is true; but this furnishes no proof of any increase of that secretion; for under ordinary circumstances it is decomposed and absorbed in the alimentary canal, and any cause which increases the rapidity of its passage there, must render absorption and decomposition less complete.

As it was evident that no accurate information concerning the amount of bile secreted by the liver was to be obtained by an examination of the fæces, the Committee arrived at the conclusion that the formation of biliary fistulæ in living animals, and collecting the bile directly through such fistulæ from the gall-bladder, was the only means open to them of determining how far mercury influenced that secretion.

History.

It next became necessary to ascertain what had been made out by previous observers as to the amount of bile secreted by the liver, under varied circumstances, through biliary fistulæ. For literary researches into this matter, the Committee are greatly indebted to Dr. Rogers. He informs the Committee, in his report on this branch of the inquiry, that efforts to establish biliary fistulæ and to collect the bile have been attended with extreme difficulty in the hands of all experimenters, and have led to a large mortality among the animals operated on. In the few cases which have succeeded, however, it is important to remember that an amount of valuable information regarding the bile has been obtained that never would have been arrived at without them.

The operations performed by physiologists on animals in order to establish biliary fistulæ have, with a few modifications, been essentially the same, and will be subsequently referred to when detailing the experiments of the Committee.

The results arrived at may be divided into:—1, the amount of the biliary secretion in health, and the circumstances which influence it; 2, the special effect of mercury on the secretion of bile.

1. *Previous Researches to determine the amount of Bile Secreted in Dogs, and the Circumstances which influence it.*

Haller*.—In Haller's 'Physiology,' reference is given to several cases in which attempts had been made to ascertain the quantity of bile secreted in a given time by experiments on living dogs. The description of them, however, is so very vague and general that they possess little interest for the physiologists of the present day. Van Reverhord found the quantity of bile secreted by a dog in twenty-four hours to be 6 oz.; and Haller, estimating the secretion in the human subject at four times that in the dog, suggested 24 oz.

* Physiologia, tom. vi. page 605.

to be the quantity secreted daily in the healthy human adult. He likewise alludes to an interesting case of a man in whom a biliary fistula was formed in consequence of a wound of the gall-bladder. Tacconus, who saw the case, estimated the amount of bile discharged by the fistula at 4 oz.; but whether the expression "eodem tempore" refers to six or twenty-four hours, it is impossible to say—probably to the former.

Schwann*.—It was not till 1844 that any serious attempts were made to investigate this subject by Professor Schwann of Louvain. He made several interesting experiments, by means of biliary fistulæ, to ascertain the utility of bile in the animal economy. Unfortunately he does not appear to have carried out his intention of ascertaining accurately its amount.

Blondlot†.—In 1846 Blondlot succeeded in establishing a biliary fistula in a dog of middle size, in which he gives approximately 40 to 50 grammes as the amount of bile secreted in twenty-four hours. His estimate, however, was not made with great precision; for he only collected the fluid for short periods at a time, and could not therefore ascertain its exact amount in twenty-four hours.

H. Nasse‡.—Heinrich Nasse of Marburg published in 1851 an interesting memoir giving an account of a series of experiments performed on one dog in which a biliary fistula had been established, and which lived afterwards five months and a half. His object was to ascertain the influence of the quantity and quality of the food on the biliary secretion. As we have not succeeded in obtaining the original work, the result of his researches will be subsequently tabulated as obtained from the abstract given of them in Canstatt§.

Bidder and Schmidt‖.—In 1852, Bidder and Schmidt, in their work on the Digestive Fluids, gave an account of the most elaborate experiments yet made to determine the amount of the biliary secretion. They succeeded in establishing biliary fistulæ in four dogs. In one dog the daily observations extended from Feb. 17th to April 15th, when he was killed. The bile was collected by holding a balloon-shaped glass over the fistulous opening for fifteen minutes at a time; and this was repeated daily from six to ten times successively. The varying amount of biliary secretion obtained at one period was corrected by the results obtained at other periods, and the average amount calculated from a large number of observations. This method, though excellent for determining the amount of the secretion at different periods of the digestive process, is, as regards the daily quantity, evidently unsatisfactory. Besides, as the dog did not consume the same amount of food under these varied circumstances, that might vitiate the result. To simplify the Tables, and render calculation easier, they estimated the amount of bile secreted at so much per kilogramme weight of dog. Thus, if a dog weighing 5 kilogrammes secreted 100 grammes of bile in twenty-four hours, it would be said that 20 grammes of bile were secreted for each kilogramme of dog in twenty-four hours. They estimate the average amount of bile per kilogramme in twenty-four hours at 19·999.

The following Table gives the average amount of biliary secretion in the four dogs, with the average amount of food per kilogramme taken hourly and daily. One kilogramme weight of dog gives 6 grammes.

* Müller's 'Archiv,' 1844, page 127.
† Essai sur les Functions du Foie, 1846.
‡ Commentatio de bilis quotidie a cane secretæ copia et indole. Marburg, 1851.
§ Canstatt's Jahresbericht, 1856, 1st Heft, p. 87.
‖ Verdauungs-Säfte und der Stoffwechsel, 1852.

	1.	2.	3.	4.	5.	6.
In 1 Hour.						
Fresh bile	0·539	0·663	0·696	1·023	1·198	0·824
Dry residue	0·040	0·035	0·029	0·049	0·057	0·042
In 24 Hours.						
Fresh bile	12·936	15·912	16·704	24·550	28·750	19·99
Dry residue	0·960	0·840	0·696	1·176	1·268	0·988
Daily amount of food per kilogramme weight of dog.		32·49 flesh; 1·74 bacon and butter.	17·85 flesh; 7·87 milk.	79·51 flesh; 8·32 bread.	66·42 flesh; 8·59 bread (rye).	

The first column gives the quantity of bile obtained from recently formed biliary fistulæ, the four following ones the quantity obtained in cases of fistulæ of some standing, and the sixth gives the average amount of the different observations.

Bidder and Schmidt found that the amount of bile secreted in a given period varies much in different species of animals. Thus for every kilogramme of animal there is produced on an average—

In 1 Hour.					
Cat.	Dog.	Sheep.	Rabbit.	Goose.	Crow.
0·608	0·824	1·059	5·702	0·491	3·004 Fluid.
0·034	0·042	0·056	0·103	0·034	0·219 Solids.
In 24 Hours.					
14·50	19·990	25·416	136·84	11·784	72·096 Fluid.
0·816	0·988	1·344	2·47	0·816	5·256 Solids.

It appears remarkable that the rabbit should secrete five times as much bile as the other larger animals do, and that the crow should secrete so much more than the goose; but from the manner in which the bile-collections were made, little confidence can be placed in these results. They found that the amount of the biliary secretion was much influenced by the quantity and quality of the food and drink. Taking from six ounces to ten ounces of water produces a rapid increase of the secretion, attaining its greatest measure in from forty-five to sixty-one minutes after it had been taken, and diminishing as rapidly. They found that, when the food of cats consisted almost exclusively of fat, the secretion of bile was reduced to about the quantity furnished by fasting animals. Blondlot (p. 62) says that the use of fat increases the amount of bile; and Ritter and Nasse say that the addition of fat to the food increases the secretion—at least when the supply of flesh at the same time is not great. Bidder and Schmidt also ascertained that the quantity of the biliary secretion varies at different periods of the digestive process, and that it attained its maximum thirteen to fifteen hours after a meal. On this point it may be here observed that Arnold supposed it to reach its maximum two to four hours after solid food was taken, Kölliker and Müller generally from five to eight hours, and Dr. Flint from two to eight hours. Dr. Dalton, from observations made on a case of duodenal fistula, thinks biliary secretion is at its maximum an hour after feeding. Ritter and Nasse, like Arnold, remarked two maxima in the course of the day—the first occurring during the

first or second hour after feeding, the other so much the earlier the more scanty the supply of food.

In Bidder and Schmidt's tabulated observations on the first dog, it will be seen that the greatest amount of fresh bile was secreted between six and seven hours after a meal. It is true that the greater amount of dry biliary residue was found in one of the collections made from fourteen and a half to fifteen and a half hours after feeding; but in another quantity collected at the same period after feeding the amount both of fresh bile and dry residue was much less than that collected between six and seven hours after a meal. Again, of two quantities collected respectively on the 2nd and 6th of November, from fourteen to fifteen and a half hours after feeding, the amount of fresh bile in the first collection was only about the half of what was secreted from three to four hours after a meal; and in the second collection it was about half of that secreted from four and a half to five and a half hours after a meal. The tabulated observations on the third dog seem to give more support to Bidder and Schmidt's opinion; but quantities of biliary secretion given for different periods after feeding are too fluctuating to permit the amount of bile secreted at any given stage of digestion to be accurately estimated. The observations of Bidder and Schmidt themselves, therefore, do not support their own conclusion; and as this is opposed to those of other experimenters, it must be concluded that the amount of bile secreted varies considerably in the same animal, and at the same period of digestion, even independently of food and drink.

Arnold*.—In 1854 Dr. Arnold published a work on the 'Physiology of the Bile,' and afterwards made some additional experiments on the subject in 1857. The apparatus he employed consisted of a canula 4½ centimetres long and 4 centimetres wide, attached by a screw to an elastic caoutchouc bag 10 centimetres long and 1 centimetre broad. Fifteen millimetres above this attachment, and at right angles with the canula, was a metallic plate, 12 millimetres in diameter. This plate was placed between the skin and the muscles; and the wound healed perfectly over it, preventing all escape of bile between the soft parts and the canula. The distal extremity of the bag had a cork stopper, by taking out which the bile collected in it could be removed. The operation was performed in the usual manner on a healthy dog of middle size, weighing 9·250 kilogrammes, on the 18th of June, 1853. The common duct was first tied close to the duodenum, and again half an inch from the gut. The portion between the two ligatures was then excised. Although after the operation the dog was exhausted, and vomited its food more than once, on the following day he appeared to be quite well. The bile flowed freely through the canula until July 1st, when it ceased. Another and wider canula, with a broader border, was then inserted. This also, subsequently, was so forced forwards by the contraction of the wound that no bile could flow, and the canula was withdrawn. The apparatus first inserted was then employed, and answered perfectly, as the canula was firmly fixed in its place by the wound healing over it; so that not a drop of bile escaped at its edges. From the 18th of June until the 6th of July, the dog was fed on bread, milk, flesh, and potatoes. It lost 375 grammes in weight during this period, without any perceptible derangement of digestion. The fæces were pultaceous, without any trace of bile-pigment, had a putrid odour, and contained a considerable quantity of fat, but no trace of muscular fibre. To prevent him from licking the bile he was muzzled. From July 6th to August 2nd he was fed entirely on flesh. From the 6th to the 9th

* Zur Physiologie der Galle, 4to, Mainz, 1854.

of July he ate daily 500 grammes of fat flesh. During this period the fæces were like clay, soft, and contained a quantity of fat. The weight of the body diminished rapidly, so that on the 8th it was 8·203 kilogrammes, and on the 9th 7·750 kilogrammes. He was then lean, but lively, and had 750 grammes of flesh, pretty free from fat, divided into three portions, which he ate morning, midday, and evening. During the period he lived on flesh his hair fell out largely, and could easily be pulled out in tufts without causing pain. There was also a large development of gas in the intestines, with borborygmi and liquid fæces. About the 20th of July they assumed their natural consistence, and were brown externally, though of an ash-colour internally. Each time the fistulous opening was interfered with or irritated, the fæces became softer and more liquid, and their odour more cadaverous; while, when consistent, it was less penetratingly putrid. From August 3rd to September 1st, the food consisted of old rye-bread, of which there was consumed, on an average, daily 470 grammes, and was commenced because the dog refused all animal food. During this period its weight increased to 8 kilogrammes, the emaciation disappeared, and the falling off of the hair diminished. Indeed the hair in a few months grew abundantly, so that it presented a black shining coat, as before the operation. The appetite returned, and he ate greedily. The digestion was good; the fæces of firm consistence, of a yellowish-grey colour, like that of the bread, and less offensive than when he was fed on flesh. Their quantity also was increased as three to two. Their average daily weight was 320 grammes; whereas, when fed on flesh, it was 210 grammes. He also drank more. When the diet was bread, he drank daily the average quantity of 450 cubic centimetres; when fed on flesh, only 340 cubic centimetres.

The quantity of bile secreted on the average, when fed upon 750 grammes of flesh and upon 470 grammes of rye-bread, is shown in the following Table:—

Daily food.	Weight of dog.	Bile secreted daily.	Bile solids daily.	Bile secreted daily per kilo.	Bile secreted hourly p. kil.
750grms.flesh.	7·750 kilogs.	90·295 grms.	2·892 grms. to 3·056 grms.	11·65 grms.	0·486 grm.
470 grms. rye-bread.	7·812 kilogs.	63·024 grms.	1·662 grm. to 2·634 grms.	8·067 grms.	0·336 grm.

From hourly observations it appears that the largest quantities of bile were secreted during the first hours after getting food; drinking water also increased the secretion. The dog caught cold September 1st, and died September 3rd, from peritonitis. On September 4th the body of the animal weighed 7·512 kilogrammes. On dissection, it was found that where the ductus communis choledochus had been cut out, a new one three lines long was formed, having on one side of it a small collection of pus containing the ligatures. It was therefore believed that in a short time the common duct would have been reestablished. Round the plate of the canula a newly formed mucous membrane was discovered, continuous with the gall-bladder.

The following are the more important conclusions drawn by Arnold from the whole inquiry (p. 19):—1. Cutting off the bile from the intestines, if a sufficiently increased quantity of food can be digested, is not injurious to an animal. For two dogs of the same weight, one with and the other without fistula, the first will require five-eighths more flesh or three-fifths more bread than the second. 2. The quantity of bile secreted is influenced by the quantity and quality of the food. A dish of bread gives rise to a less secretion of bile than one of flesh. 3. From experiments on dogs with biliary

fistulæ, in consequence of the increased diet they require, no conclusion can be drawn as to the quantity of bile likely to be secreted in healthy dogs in proportion to the amount of food they take. 4. The quantity of bile secreted in proportion to the weight of the animal is estimated too highly by Bidder and Schmidt, and also by Nasse; because all animals with biliary fistulæ require much more than their ordinary food to keep up their usual weight, while the quantity of diet influences the amount of bile secreted. 5. Besides food, the drinking of water considerably increases the secretion of bile. 6. The nature of the food does not much influence the solid constituents of bile. Arnold admits, however, that in this respect Nasse's observations may be more accurate than his own. 7. The secretion of bile, apart from the influence that it exerts on the absorption of fat, plays an important part in the process of nutrition. 8. In Arnold's dog the biliary secretion was most copious during the first hours after taking food. After the fourth hour it began to diminish until the twenty-fourth hour, when it was least, but the diminution was not regular. His manner of collecting it, however, like that of Bidder and Schmidt, is objectionable, viz. at varying periods of fifteen minutes, half an hour, and an hour. Instead, therefore, of determining how much bile flowed in twenty-four hours, this was made to appear by multiplying so many times the half-hour or hour collections.

Kölliker and Müller* made some experiments on the bile during the years 1853 and 1854, of which they published an account in the Wurzburg Abhandlungen for 1855. They succeeded in establishing biliary fistulæ in three dogs. For one kilogramme of dog, they found in twenty-four hours—

Hours after food.	Fresh bile.	Dry residue.	No. of observations.
1 to 2	1·450	0·051	8
3 to 5	1·407	0·047	5
6 to 8	1·514	0·048	8
16 to 22	1·320	0·051	7

Another dog gave the largest quantity four to five hours after feeding, and least after nineteen to twenty-one hours. A third dog gave the maximum five to six hours after a meal, and not much less after sixteen or seventeen hours. They found, as other observers had done, that the quantity of food consumed has a decided influence on the quantity of the biliary secretion. When, for example, a dog ate 18½ ounces of flesh in twenty-four hours, the bile collected amounted from 5·3 to 6·6 grammes in an hour, but when it ate 33½ ounces of flesh, it was increased from 7·5 to 7·8 grammes. It is important to observe that the calculations of Kölliker and Müller, like those of Bidder and Schmidt, were derived from collections of bile made during a quarter of an hour, half an hour, and occasionally one hour, and the amount per day was estimated from the averages of these. In no case was it collected continuously for twenty-four hours.

Scott †.—Dr. Scott appears to have been the first who collected all the bile secreted by a dog during twenty-four consecutive hours. We must refer to his paper for a description of the method he adopted for collecting it, and for the account he gives of his interesting and carefully conducted experiments and analyses. He avoided the error liable to occur in calculating the amount of bile secreted in twenty-four hours from quantities obtained during a part only of that period. He estimated the amount of fresh bile given off in twenty-four hours at about 23·15 grammes; of dried residue at 1·13 per kilogramme.

* Würzburg Abhandlungen für 1855, Band V. † Beale's 'Archives,' vol. i. 1868.

Dalton*.—Dr. Dalton of New York attempted to ascertain the amount of bile which passed into the duodenum from the choledic duct by means of a duodenal fistula. But as in this manner it is obviously impossible to determine the amount of the entire quantity given off by the liver, no account of his researches need be given.

Flint†.—The last experimenter we need cite is Dr. Flint of New York. As his object, however, was rather to ascertain the amount of cholesterine secreted by the liver, than to determine the quantity of biliary secretion, he does not give us much information on this point. In one dog the bile was collected for thirty minutes at a time during various periods of the day, and was found to be secreted at its maximum four hours, and at its minimum twenty hours, after feeding. The dog weighed 10 pounds; and there were collected, in the twenty-four hours, 243·233 grains—an amount which gives an index of the quantity secreted during that period. He further says that, disregarding slight variations, which might be accidental, it may be stated in general terms that the maximum flow of bile from the liver is from the second to the eighth hour after feeding, during which period of time it is about stationary.

We here subjoin a Table containing the results of the experiments of different physiologists who have investigated the subject of the biliary secretion. With the exception of the results of those of Dr. Flint and Dr. Scott, the Table, of which the arrangement is slightly changed, is taken from Canstatt's Jahresbericht for the year 1863, No. 1. p. 141. The weight is given in grammes.

Names of observers.	Amount of bile secreted in 24 hours per kilogramme weight of dog.		Food taken in 24 hours per kilogramme weight of dog.	Quantity of bile secreted in 24 hours for 100 grammes of food.	
	Fresh bile.	Dry residue.		Fresh bile.	Dry residue.
Nasse, 1851	19·2	0·685	155 flesh	12·3	0·440
	22·8	0·700	208 „	11·1	0·337
	23·1	0·784	260 „	8·9	0·300
	24·0	0·765	At will	...	...
	28·4	0·760	„	...	...
	17·7	0·446	100 flesh and 100 br.	...	...
	17·9	0·400	130 „ 100 „	...	...
	12·2	0·500	87 bread	13·9	0·575
Bidder and Schmidt, 1852.	15·9	0·840	32·4 flesh, 1·7 fat	49·3	2·608
	16·7	0·696	17·8 „ 7·8 milk	83·5	3·48
	24·5	1·176	79·5 „ 8·3 bread	25·7	1·23
	28·7	1·268	66·4 „ 8·5 „	35·1	1·54
Arnold, 1854–57 ...	11·6	0·373	96 flesh	12·0	0·385
	8·1	0·215	60 bread	13·4	0·357
Kölliker and Müller, 1853.	32·7	1·034	...	...	...
	32·6	1·290	98 flesh	...	...
	26·1	1·013	92 „	28·56	1·694
	21·5	0·748	94 „	22·85	0·792
	36·1	1·162	64 „	56·50	1·816
	53·6	1·683	94 „	56·7	1·79
	32·1	...	37·9 bread, 90 cubic centimetres of milk	...	...
				...	...
Scott, 1858	23·11	1·128	58·7 flesh, 10·3 milk	35·0	1·6
Flint, 1862	11·98	0·440	...	...	...

* Physiology, p. 190, 3rd edit.

† American Journal of Medical Sciences, vol. xliv. p. 306.

2. *Previous Researches to determine the Influence exercised by Mercury on the Biliary Secretion.*

Nasse*.—Professor H. Nasse was the first who attempted to ascertain, by experiment on the dog with biliary fistula, the influence of mercury on the secretion of bile. It is stated in Canstatt that the result of his experiments was that calomel increased the absolute quantity of the bile, but diminished its solid constituents.

Kölliker and Müller administered to one of their dogs, which had biliary fistula, 4 grains of calomel at ten o'clock on the morning of the 28th. Five half-hour observations made after midday gave an average of 3·823 grammes of bile excreted, an amount a little above that of previous averages. On the following day, however, four half-hour observations gave on an average 3·267 grammes,—that is, rather less than the usual average.

On the 21st and 29th days the dog took again 4 grains of calomel, but the biliary secretion, instead of increasing, diminished. Seven observations of half an hour each, from the 28th to the 31st day, gave an average of only 2·183 grammes, and the bile at the same time was of a brownish colour, and so thick that at last it scarcely dropped from the canula. This circumstance was undoubtedly owing to the dog's health, which was bad. It had lost weight, had diarrhœa, greyish-coloured and even later bloody stools. For several days at this period the animal took only a little bread and milk.

Dr. Mosler†, in his investigations, proposed to himself the question, "What substances introduced into the blood appear in the bile?" In some of the experiments a solution of the substance to be tried was injected into the blood, in others the medicine was given by the mouth, and the bile afterwards tested, to ascertain if it contained any trace of the substance administered. With regard to mercury, he tells us that on the 23rd of May, at seven o'clock A.M., 5 grains of calomel in a little bread and milk were given to a dog, who had a completely healed biliary fistula. All the bile secreted till three o'clock P.M. was collected by means of a sponge and tested for mercury, but not the slightest trace of it could be discovered. At four o'clock P.M. 10 grains of calomel were administered to the same animal, and for greater accuracy a small tube with a caoutchouc bag attached was introduced into the fistula, and kept there till next morning. No trace of mercury was found in the collected bile, and no striking increase of the biliary secretion was remarked. After this experiment the animal was dull, ate less than usual, and had thin very offensive stools. To make a trial of the drug in smaller doses, Dr. Mosler gave the same animal one grain of calomel every hour from the 25th to the 26th of May, so that altogether 25 grains of calomel were given; no trace of mercury could be found in the collected bile. To another powerful dog with biliary fistula he gave, on the 19th of August, at nine o'clock, three pills, each containing 3 grains of calomel. Next morning at six o'clock A.M., three similar pills were given, and at nine o'clock two more—so that the dog had 30 grains of calomel in eighteen hours. The bile discharged from the fistula was carefully collected by a sponge, from three o'clock on August 11th till the same hour on August 12th. Compared with the quantity collected during twenty-four hours on the day previous to that of the experiment, there was no striking increase of bile, nor did it contain any trace of mercury. He repeated this experiment with 24 grains of calomel with the same negative result. Dr. Mosler concludes

* Cantsatt's Jahresbericht, 1852, Heft. i. p. 156.
† Virchow's 'Archiv,' Band xiii. S. 29 (1858).

from these experiments that, when mercury is administered in the form of calomel, either in small or large doses, it does not pass so rapidly into the bile, nor produce the marked increase of the biliary secretion that medical men imagine. It is much to be regretted that Dr. Mosler did not measure the bile passed during these experiments, which would have given far more value and precision to his observations.

Scott.—The only other experiments made to determine the influence of mercurial preparations or, rather, of calomel on the biliary secretion with which we are acquainted are those of Dr. Scott, who deserves great credit for the careful and scientific manner in which he has carried them out. We shall have occasion, however, to indicate some circumstances which seem clearly to show that they must be regarded rather as valuable contributions to aid us in determining the influence of calomel on the biliary secretion than as data which, of themselves, warrant any definite conclusion; indeed Dr. Scott himself has fully admitted the truth of this remark. Dr. Scott made four trials with calomel, in which he estimated the amount of increase of the biliary secretion by taking the average of two days previous and of two days subsequent to its administration.

In the first trial 3 grains of calomel were given to the dog at three o'clock P.M. on the 13th of June*. The daily average amount of bile secreted on the 11th and 13th of June was 1960 grains, and that of bile secreted on the 14th and 15th, 1358 grains, showing an average diminution of 602 grains for each of the two days subsequent to the administration of the calomel.

In the second trial 6 grains of calomel were administered at eleven o'clock A.M. on the 16th of June†. The amount of bile secreted during twenty-four hours, and collected on the morning of the 16th, was 1639 grains, and of that secreted during the subsequent twenty-four hours, and collected on the 17th of June, was 518 grains, indicating a diminution of 1121 grains in the biliary secretion during twenty-four hours after the administration of the calomel.

In the third trial 12 grains of calomel were given at 4.30 P.M. on the 3rd of July, the average daily secretion of bile for two previous days (2nd and 3rd of July) amounting to 3044 grains, and that for the two subsequent days (4th and 5th of July) to 2720 grains, showing a diminution of 324 grains on the average daily quantity of bile secreted after the administration of the calomel.

In the last trial 12 grains of calomel were given at 5.45 P.M. on July 7th; the daily average amount of biliary secretion on the two preceding days (the 6th and 7th) being 2658 grains, and on the 8th and 9th July being 1724 grains, showing a diminution of 934 grains in the daily average quantity of bile secreted after the administration of the calomel.

We subjoin a Table of the daily amount of fresh bile collected for several days, in order that our subsequent remarks may be intelligible to the reader. The "†" before the dates indicates the days on which calomel was administered.

* The bile secreted during twenty-four hours was always collected on the morning of the day indicated. The amount obtained on June 12th was not used in calculating an average, as a considerable quantity was lost in collecting it.

† The amount of bile collected on the 15th was not used in making an average, probably because Dr. Scott supposed the secretion of the previous twenty-four hours was still under the influence of the calomel.

Amount of Bile secreted in Twenty-four Hours, in Grains.

June	11	1628·00	July	1	2168·051
„	12	1767·700	„	2	2941·239
†„	13	2293·527	†„	3	3148·400
„	14	1819·636	„	4	2560·300
„	15	896·680	„	5	2881·500
†„	16	1639·968	„	6	2644·300
„	17	518·701	†„	7	2673·900
„	18	1810·450	„	8	1963·500
„	19	817·717			

Dr. Scott concluded that all the trials gave but one result, viz. "a diminution in the amount of bile and bile solids secreted after the administration of large doses of calomel." We are of opinion, however, that the diminution is not nearly so great as he has made it appear; thus, for example, if in the first trial we set aside the results of June 12th (as Dr. Scott has done), and only take the amount of bile secreted during the twenty-four hours previous and subsequent to the administration of calomel (as Dr. Scott has done in the second trial), the amount of decrease will be considerably less than he has calculated it to be.

Again, if we take the average amount of bile collected during two days previous and two days subsequent to the administration of the second dose of calomel, the result will be very different from what Dr. Scott's calculations make it. Instead of a diminution of 1121 grains, it will amount only to 104 grains; and we must not overlook the fact that on the day when the calomel was administered the dog did not get any food.

Dr. Scott does not mention at what hour of the morning the bile was collected. If we suppose it was collected at 10 o'clock A.M., twenty-three hours would thus be left for the action of the calomel, which was administered at 11 o'clock A.M. on the preceding day. It might be said that the action of the calomel would not be exhausted in that time, and that we ought not, therefore, to admit the collection of bile of the 15th into the calculation for obtaining a daily average amount on the two days previous to the administration of the calomel. On June 18th, however, the second day after the second administration of calomel, the amount of biliary secretion increased from 518 grains on the 17th to 1810 grains on the 18th, 171 grains more than the quantity secreted on the 16th, a day on which calomel could not have had any influence on the amount. Consequently we must conclude that the influence of the calomel did not extend, in this case, to the second day after its administration; or, if it did, it was not to diminish, but to increase very largely the secretion. Up to the present time we know little or nothing of the duration of the action of a dose of calomel on the biliary secretion; so that we have no reason to assign a period of two days, rather than of one or of three, as the duration of its action. . It would be to ascribe in the one case an increase and in the other a diminution to the same cause; that is, the action of the mercury on the second day after its administration. In short, the number of Dr. Scott's observations are far too few, and not sufficiently long continued, to allow us to draw any definite conclusions from them.

It must, I think, be evident, from this notice of all that has been previously accomplished, that no exact information has yet been obtained as to the influence of mercury on the secretion of bile, or as to any other action it may exercise on the liver.

Description of the Mode of operating for Biliary Fistulæ and of collecting the Bile practised by the Committee.

All the operations were performed by Dr. W. Rutherford, who ultimately succeeded in overcoming the great difficulties which presented themselves. The propriety of collecting the bile for a period of at least twenty-four hours at a time was considered incumbent to avoid error, a proceeding which caused great trouble and constant failures; it was considered necessary, however, in order to avoid the obvious fallacies into which all previous experimenters, with the exception of Dr. Scott, had fallen. In now giving a detailed description of the method followed, the Committee are of opinion that they will save future experimenters much of that trouble and mortification which, from want of experience, they themselves encountered. It will be regarded as more valuable in consequence of the modifications which have been introduced having led to a far greater amount of success than has attended the efforts of other physiologists.

1. *Operation for establishing Biliary Fistulæ.*

1. Place the animal under the influence of chloroform, taking care to administer it slowly with an abundant admixture of air.

2. Open the peritoneal cavity by an incision extending from the xiphoid cartilage to the umbilicus. Before opening the peritoneum, all bleeding should be stopped.

3. Make an incision through a non-vascular part of the omentum, to the same extent as the external wound.

4. Find the gall-bladder and seize the most prominent part of its fundus with artery forceps. See if the fundus can be brought to the linea alba without subjecting it to any tension. If it can, proceed with the operation. If it cannot, judging from the experience of the Committee, it is better to abandon the operation altogether, as the dragging of the gall-bladder will almost certainly give rise to peritonitis, or such irritation as will prevent adhesion of the fundus to the cut edges of the linea alba.

5. Find the common bile-duct; draw the duodenum gently downwards and towards the left side of the animal, and the liver upwards and to the right, so as to stretch the duct.

6. With a blunt-pointed bistoury make an incision about one-eighth of an inch in length along the duct about its middle; gently isolate it with the point of an aneurism needle, pass the aneurism needle with a double strong silk ligature round the duct, and tie it in two places, at a sufficient distance from each other to allow of the duct being *simply divided* between them. After division of the duct cut the ligatures close.

7. Observe at what part of the linea alba the fundus can be most easily retained. Pass a curved needle with a silk ligature through the skin, linea alba, and gall-bladder on either side of the fundus, so as to stitch the gall-bladder to the linea alba, and retain it there.

8. Make a slit by means of a sharp-pointed bistoury in the most prominent part of the fundus, and allow the bile to flow out, taking care to hold a sponge at the side of the opening to prevent, as much as possible, the entrance of bile into the peritoneal cavity. With the same view, the animal should be turned on its side before the opening is made in the gall-bladder. This opening should be just large enough to admit easily a piece of india-rubber tubing about two lines in diameter.

9. Introduce a portion of india-rubber tubing of the above calibre into the aperture in the gall-bladder, put a silk suture through it, and fasten it to the ligatures holding the fundus to the linea alba, in order that the tube may be kept from coming out.

10. Close the wound in the abdomen by interrupted sutures, placed deeply in the linea alba, and then connect the edges of the skin in the same way. The skin should not be closed completely around the tube, but should be left open for an inch or so, in order that blood may be prevented from accumulating.

11. The projecting extremity of the tube should be cut within a quarter of an inch from the abdominal wall, in order that when the dog lies on its face there may be less danger of closing the tube by its being bent upon itself.

12. The tube should be removed at the end of forty-eight hours or so, for then adhesions will in most cases have taken place between the gall-bladder and linea alba, which the continued pressure of the tube would only tend to break up. The dogs operated upon by the Committee were never kept muzzled after the operation, and no dog ever interfered with the elastic tube.

13. The operation should always be performed when the stomach is empty, for if distended it is a most serious impediment to the operator. Very soft sponges, perfectly freed from all sandy particles, should be used, and the greatest care should be taken to prevent hairs from getting inside the peritoneum.

14. In male dogs the urine is apt to be discharged into the wound during the operation, and against this the operator must carefully be on his guard.

15. Great care should be taken to prevent bleeding into the peritoneal cavity. Any accumulation of blood inside the abdomen gives rise almost certainly to peritonitis. In all cases a little bile escaped into the peritoneum, but it seemed to produce no injurious effect.

16. The ligatures around the common bile-duct usually become encysted. The wound almost always heals by first intention; this union is very rarely permanent in the cutaneous wound, however; commonly pus is formed between the skin and the wound in the linea alba. When such is the case, sutures must be removed from the cutaneous wound to give free exit to the purulent matter. No lotions or other dressings are necessary for the wound. The bile as it flows over it forms an excellent dressing, under which healthy granulation proceeds, in most cases with rapidity.

17. For two days after the operation the animal should be fed on milk, given in small quantities at a time, so that the abdomen may not be distended.

The above mode of performing the operation differs from those described by other operators in two particulars:—1. The mode of fixing the fundus of the gall-bladder to the abdominal wall. Bernard recommends a clamp to fix the fundus to the edges of the wound, and act as a canula also. 2. In the non-removal of any portion of the common bile-duct. Other operators recommend that two ligatures be applied to the common duct, one close to the duodenum, the other close to the junction of the cystic with the hepatic duct, and that the intervening portion should be excised. The object is to prevent as much as possible the reestablishment of the duct, a contingency which appears to have been very liable to occur in the experience of other observers. The shock produced by cleaning and removing the whole duct is very great, owing to the extensive injury of the sympathetic nerves; and the danger from hæmorrhage is most serious.

Since the removal of any portion of the common bile-duct has been abandoned, the success attending the operations of the Committee has been unprecedented. In only two out of the thirty-three dogs operated on has the

common bile-duct become reestablished; in one of these nearly the whole duct had been excised, in the other the duct had simply been divided between the two ligatures.

The experience of the Committee has shown that young dogs are not suitable for the operation, only *full-grown strong* good-tempered dogs of any breed should be selected. Had the Committee been aware of this precaution, their success as regards the number of useful fistulæ might have been greater even than it has been.

2. *Method of collecting the Bile.*

The collection of the bile may be begun usually within a fortnight after the operation, as soon indeed as the fistula can bear the daily pressure of a silver canula. Before its insertion into the fistula, it is well to wait until the whole of the wound except the fistulous opening is completely healed. During the healing process, the fistula must be kept patent by the daily passage of a glass rod, which serves admirably the purpose of a bougie; for notwithstanding the flow of the bile, the canal has a great tendency to close.

The great difficulty which the Committee have had to overcome, has been the daily collection of bile for a period of twenty-four hours. The following apparatus, devised by Drs. Rutherford and Gamgee, has been found to accomplish the end perfectly.

The canula used was that of Scott (Beale's Archives, vol. i. p. 210), with the cup removed, and the holes in the tube filled up. The Committee found that in the very first case in which they used Scott's canula, the cup failed to fit the skin accurately, and soon produced ulceration by its pressure. They have found that there is no need for providing for an escape of bile along the side of the canula, provided a *perfectly free* exit be allowed *through* it. The canula was retained in the fistula by elastic bands attached to it, and passed round the body of the dog. These bands were fastened to each other by hooks and eyes, which permit of their easy removal and adjustment. Scott collected the bile in a bottle. It appeared to the Committee that an elastic bag tied on the free end of the canula would be less apt to be damaged by the movements of the animal. They found, however, that a much more satisfactory method is to collect the bile flowing from the canula by means of a large sponge. In this way *no resistance* is offered to the flow of bile through the canula—such as is apt to occur when the bag is used, by its folding over the free end of the tube. This acted as a valve, which resisted the feeble pressure with which the bile flowed through the fistula.

The sponge was placed in a tin box, fixed round an oval opening on the abdominal aspect of a thick gutta-percha shield, which extended from the fore legs to a little behind the umbilicus. The shield was made to fit accurately the body, so that it might have no tendency to turn round when the animal lay down. It embraced three-fourths of the circumference of the body, and the one side of it was connected with the other over the animal's back by means of leather straps with buckles. Between the back and these, a soft leather saddle was placed to prevent ulceration by their pressure. With the same view a flat bag filled with air was placed between the shield and the sternum, and a piece of thick-walled india-rubber tubing an inch or so in diameter, was placed between the skin and the posterior part of the shield. To this the bag and tube were both immoveably fixed.

The shield tends to slip backwards, owing to the pyramidal shape of the body of the animal. To prevent this, a leather collar must be placed loosely round the neck, and the anterior edge of the shield fixed to it by thick twine

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TABLE I.—SHOWING THE CONSTITUTIONAL EFFECTS OF MERCURY ON SIX DOGS.

Dogs without Biliary Fistulæ.

Dog A—Retriever, 12 months old, weight 30½ lbs.

Days.	Amount of corrosive sublimate given.	Effects.
		Animal in excellent health; fæces of a light-brown colour, semisolid.
1st day.	·05 grain.	No change.
2d ,,	·10 ,,	,, ,,
3d ,,	·10 ,,	,, ,,
4th ,,	·10 ,,	,, ,,
5th ,,	0·2 ,,	,, ,,
6th ,,	·30 ,,	,, ,,
7th ,,	·40 ,,	,, ,,
8th ,,	·40 ,,	Colour of fæces changed to a very dark brown. Animal in good health.
9th ,,	·50 ,,	,, ,, ,,
10th ,,	·55 ,,	,, ,, ,,
11th ,,	·70 ,,	,, ,, ,,
12th ,,	·80 ,,	,, ,, ,,
13th ,,	·80 ,,	,, ,, ,,
14th ,,	1·60 ,,	,, ,, ,,
15th ,,	1·60 ,,	Nasal discharge of mucus. No apparent salivation. Fæces as on the 8th day. Appetite unimpaired.
16th ,,	1·60 ,, 20 mins. tinct. opii.	Nasal discharge unaltered. Slight diarrhœa; fæces brownish yellow.
17th ,,	1·60 grain. 30 mins. tinct. opii.	Nasal discharge less marked. Diarrhœa more decided. Fæces greenish-brown, contain a little blood. Appetite impaired.
18th ,,	·80 grain.	Salivation; not profuse, however. Fœtid breath. Slight ulceration under margin of tongue. Tongue pale and œdematous. No sponginess of gums. Profuse lachrymation. Nasal discharge, muco-purulent, profuse. Fæces fluid, bloody. Animal refuses all food.
19th ,,	...	Dog found lying dead, with a stream of colourless fluid on the floor of the cage, which had evidently flowed from its mouth. Animal much emaciated. Weight 22 lbs.
Total amount of corrosive sublimate given.	12¼ grains, given during a period of 18 days.	

Dog B—Collie, 5 months old, weight 18½ lbs.

Days.	Amount of corrosive sublimate given.	Effects.
		Animal in excellent health; fæces solid, brown.
1st day.	·10 grain.	No change.
2d ,,	·40 ,,	,, ,,
3d ,,	·40 ,,	,, ,,
4th ,,	·50 ,,	,, ,,
5th ,,	·55 ,,	,, ,,
6th ,,	·70 ,,	,, ,,
7th ,,	·80 ,,	,, ,,
8th ,,	·80 ,,	Colour of fæces changed from brown to greenish brown, appetite impaired.
9th ,,	No mercury. ¼th grain morph. mur. given.	Diarrhœa; fæces greenish yellow.
10th ,,	No mercury. 30 mins. tinct. opii given.	Diarrhœa profuse; fæces contain blood. Slight nasal discharge.
11th ,,	No mercury. 30 mins. tinct. opii given.	Diarrhœa profuse; fæces of a slate-brown colour. Nasal discharge more abundant. Decided salivation. Gums unchanged.
12th ,,	No medicine given.	Nasal discharge; muco-purulent, very profuse. Salivation less marked than on previous day. Breath fœtid. Diarrhœa has nearly ceased. Animal is constantly trembling; takes almost no food.
13th ,,	...	Found dead. Weight 14½ lbs.
Total amount of corrosive sublimate given.	4¼ grains, given during a period of 8 days.	

Dog C—Skye Terrier, 15 months old, weight 24½ lbs.

Days.	Amount of corrosive sublimate given.	Effects.
		Animal in excellent health; fæces solid, light brown.
1st day.	·30 grain.	No change.
2d ,,	·70 ,,	,, ,,
3d ,,	·80 ,,	,, ,,
4th ,,	·80 ,,	,, ,,
5th ,,	·80 ,,	Appetite impaired.
6th ,,	1·60 ,,	No change.
7th ,,	1·60 ,, 30 mins. tinct. opii given.	Slight diarrhœa; fæces brown.
8th ,,	No medicine given.	Profuse salivation. Breath very fœtid. Slight nasal discharge. Slight diarrhœa; fæces brown.
9th ,,	·80 grain.	No change.
10th ,,	...	Dog found lying in the morning with a stream of saliva flowing from its mouth. Breath very fœtid. Ulcers on the gums, on the side of the tongue, and on the inside of the lips. The ulcers have a dark-grey surface. Slight diarrhœa; fæces contain blood. Dog died in the afternoon with slight convulsions. Weight 21¼ lbs.
Total amount of corrosive sublimate given.	7½ grains, given during a period of 9 days.	

Dogs with Biliary Fistulæ.

Dog D—Young Retriever, 6 months old, weight 11¼ lbs.

Days.	Amount of corrosive sublimate given.	Effects.
1st day.	1·6 grain given in two doses, with 20 hours' interval between them.	Twenty hours after the first dose of ·8 of a grain were given, a nasal discharge of mucus was observed. Two hours after the second dose it was observed to be exceedingly weak; it was in a state of constant tremor, and staggered in attempting to walk. Liquid fæces of a clay-colour mixed with blood were passed. Nasal discharge became more decided. No apparent salivation. No fœtor of breath.
2d ,,	...	Dog found dead thirty-six hours after the first dose was given. Weight 11 lbs. (See Dog 5, Table IX.)
Total amount of corrosive sublimate given.	1⅗ grain, given during 1 day.	

Dog E—Bull-dog 2 years old, weight 38½ lbs.

Days.	Amount of corrosive sublimate given.	Effects.
		Animal is in excellent health; fæces clay-coloured.
1st day.	·4 grain.	No change.
2d ,,	·8 ,,	,, ,,
3d ,,	·8 ,,	,, ,,
4th ,,	·8 ,,	,, ,,
5th ,,	·8 ,,	,, ,,
6th ,,	·8 ,,	,, ,,
7th ,,	·8 ,,	,, ,,
8th ,,	1·2 ,,	,, ,,
9th ,,	1·6 ,,	,, ,,
10th ,,	2 grains.	,, ,,
11th ,,	3 ,,	,, ,,
12th ,,	2 ,,	,, ,,
13th ,,	4·5 ,,	Appetite impaired. Breath fœtid.
14th ,,	No mercury given.	Slight nasal discharge. Profuse salivation. Stream of saliva flowing from the mouth. No purging. No blood in fæces, which are of a clay-colour.
15th ,,	...	Died during the night. Weight 31½ lbs.
Total amount of corrosive sublimate given.	19½ grains, given during a period of 13 days.	

Dog F—Collie, 18 months old, weight 37 lbs.

Days.	Amount of corrosive sublimate given.	Effects.
		Animal is in excellent health. Fæces semisolid, clay-coloured.
1st day.	·4 grain.	No change.
2d ,,	1·6 ,,	,, ,,
3d ,,	1·6 ,,	,, ,,
4th ,,	3 grains.	,, ,,
5th ,,	2 ,,	,, ,,
6th ,,	4·5 ,,	Appetite much impaired.
7th ,,	6 ,,	Fæces slate-coloured, semisolid.
8th ,,	No mercury given.	Slight nasal discharge. Fœtid breath. Salivation. Saliva dropping from mouth. Ulcers have formed in the skin where the injections were made; the ulcers are circular, and about the size of half-a-crown. Fæces slate-coloured.
9th ,,	...	Nasal discharge and salivation more decided. Dog vomits everything it takes. Blood in fæces, which are semisolid and of a slate-colour.
11th ,,	...	Died during the night. Weight 30 lbs.
Total amount of corrosive sublimate given.	19$\frac{1}{10}$ grains, given during a period of 7 days.	

Appearances found on Dissection

	Dog A.	Dog B.	Dog C.	Dog D.	Dog E.	Dog F.
Mouth and Salivary Glands.	Tongue pale, slight ulceration under its right margin. Vascularity of salivary glands not increased.	Tongue pale, œdematous. No ulceration. Vascularity of salivary glands not increased.	Tongue covered with a white fur. Ulcers inside lips on gums and below margin of tongue. Vascularity of salivary glands not increased.	Nothing abnormal in the appearance of the mouth or salivary glands.	Tongue pale. Gums ulcerated.	Tongue pale and œdematous. No ulceration.
Stomach.	Distended by clear fluid tinged with bile. Mucous membrane healthy.	Contained a quantity of partially digested food. Mucous membrane healthy.	Empty. Mucous membrane healthy.	Contained partially digested food. Mucous membrane healthy.	Contained a large quantity of colourless watery fluid. Mucous membrane healthy.	Contained a large quantity of colourless watery fluid. Mucous membrane healthy.
Intestine.	Marked redness of mucous membrane of duodenum, jejunum, ileum, and large intestine. Small intestine contained fluid similar to that in the stomach.	The mucous membrane of the small intestine was marked with bright red lines and patches from the pyloric orifice of the stomach to the ileo-colic valve. There are patches of lymph on the mucous membrane of the ileum. Large intestine is quite pallid. Duodenum contained some chyme of an orange-yellow colour.	Marked redness of mucous membrane of duodenum. Slight redness of jejunum and ileum. Mucous membrane of large intestine marked with bright red striæ running longitudinally. Duodenum contained a little bile; the large intestine contained some bloody fæcal matter.	Marked redness of mucous membrane in the jejunum. Slight redness of that of the large intestine. The latter contained fæces mixed with blood.	Bright red patches on the duodenal and jejunal mucous membrane. Most marked in the former. Mucous membrane of large intestine marked with bright red striæ.	Mucous membrane of small intestine covered with bright red patches from the pyloric orifice of the stomach to the ileo-colic valve; they were most marked in the jejunum. Large intestine marked with longitudinal bright red striæ.
Liver and Gall-Bladder.	Engorgement of hepatic vein. Gall-bladder filled with greenish-yellow bile. Hepatic cells apparently normal.	Engorgement of hepatic vein. Gall-bladder filled with orange-yellow bile. Hepatic cells apparently normal.	Same as the preceding.	Engorgement of hepatic venous system. Hepatic cells apparently normal.	Same as the preceding.	Same as the preceding.
Other Organs.	Pancreas very vascular. Hypodermic tissue œdematous where the injections had been made. Other organs normal.	Pancreas very vascular. Congestion of lower lobe of right lung. A layer of lymph on the visceral pleura of this lobe. Other organs normal.	Pancreas very vascular. Hypodermic tissue œdematous where the injections had been made. Other organs normal.	Other organs normal.	Pancreas very vascular. Small abscesses under the skin in some of the sites of injection. Other organs normal.	Pancreas very vascular. Suppuration under the skin of the whole back and sides where the injections had been made. Ulcers in the skin. Other organs normal.

or leather straps with buckles. If the dog be a male, means must be taken to prevent the urine from reaching the sponge. This is effectually done by a sheet of thin india-rubber, laced round the posterior part of the shield and body in front of the penis, so as fairly to prevent the access of a single drop of urine. The whole apparatus was removed, washed and reapplied once in the twenty-four hours. The sponge was then weighed and placed in the shield dry. At the end of the period it was removed and weighed again, to ascertain the amount of bile. Two sponges are necessary for observations on a single dog, each sponge used on alternate days. They must be cleaned, after the collection of bile, with great care. It was found best to wash them in dilute hydrochloric acid, in order that they might be thoroughlydisinfected, for putrid matter soon produces decomposition of the bile.

The shield should be firmly secured on the animal to prevent its being moved. The Committee have in only one instance found it necessary to muzzle a dog while it wore the apparatus.

The dogs were kept in large cages, the lower half of the sides and entire floor of which consisted of sheet zinc. The floor sloped to a central hole, through which the urine was collected. The dogs were mostly taken out to the open air for a few hours daily.

Observations to determine how far Dogs are subject to the action of Mercury.

The Committee had not proceeded far with their experiments, before it became evident that a preliminary investigation was necessary, in order to determine how far dogs are capable of being influenced by mercurials. Although in veterinary and other works it is admitted that this animal may be salivated, although Overbeck states that by means of frictions with mercurial ointment he succeeded in producing marked salivation with spongy gums in three dogs out of five *, and Murray in his experiments with large doses of calomel also produced salivation in one dog †, the Committee were of opinion that further careful observations should be made on this point.

Accordingly great pains were taken by Dr. Gamgee to produce salivation in two dogs, by means of inunction of mercurial ointment, during the winter and spring of 1867. The hair of the animal was shaved from the back, and daily frictions made with the hand on the naked skin with strong mercurial ointment. In one dog a drachm of the ointment was rubbed in daily for twenty-eight days, and in another for eight days. No marked symptoms were produced, nor was their health impaired. In the first of these dogs a most elaborate series of observations on the urine was made to determine whether that secretion was in any way influenced. These consisted of careful analyses before and after the inunction, but with a negative result.

The frictions occasioned so much trouble and loss of time, and appeared to be attended with such little result, that it was resolved to adopt the more commodious method of subcutaneous injection of a solution of corrosive sublimate. This investigation was undertaken by Dr. W. Rutherford, who carried it to a successful termination, as seen in Table I.

It will be seen from Table I. that of the six dogs experimented on, three had, and three had not biliary fistulæ established. This selection was made with a view to ascertain whether or not the existence of a biliary fistula affected the action of the mercurial. Of the six dogs, five were salivated by

* Mercur und Syphilis (Berlin, 1861), pp. 110–114.

† Transactions of Med. and Phys. Society, Bombay, 1841, p. 11.

the drug; of these, three (Dogs A, B, and C) were small dogs without fistulæ, while two (Dogs E and F) were large strong dogs with fistulæ.

In dogs A and B the action of the drug upon the salivary glands was inferred from the occurrence of unusual wetness of the mouth merely; while in dogs C, E, and F a stream of saliva was observed flowing from the mouth.

In the three dogs without fistulæ—aged 5 (Dog B), 12 (Dog A), and 15 (Dog C) months respectively,—all of them small animals, decided salivation followed the administration of $4\frac{1}{4}$ grains of corrosive sublimate, extending over a period of eight days, to the dog aged 5 months; of $12\frac{1}{5}$ grains, extending over a period of eighteen days, to the dog 12 months old; and of $7\frac{1}{5}$ grains, extending over a period of nine days, to the dog 15 months old.

In the two large strong dogs (Dogs E and F) with biliary fistulæ, much larger quantities of the drug were required to produce well-marked salivation. $19\frac{1}{10}$ grains, extending over a period of seven days, to dog F, aged 18 months, and $19\frac{1}{2}$ grains, extending over a period of thirteen days, to dog E, aged 24 months. The dog which was not salivated (Dog D) was a retriever 6 months old, which was poisoned by $1\frac{3}{5}$ grain of corrosive sublimate, given in two doses during twenty hours.

In all the six dogs a discharge of mucus from the nostrils was observed during the administration of the drug; in some cases it preceded, in others it was coincident with decided salivation. In dog D the nasal discharge was decided, although salivation was not observed.

It can hardly fail to strike anyone that the doses required to produce salivation in these dogs are much larger than those usually required in the case of man. The dose required in the dog is, however, perhaps not nearly so great as Table I. makes it appear; for it must be remembered that a dog cannot, like a man, tell us when it feels unusual moisture in the mouth. When, therefore, we have noted salivation as having been produced, it has only been when the salivation had become very marked, giving rise to unusual wetness of the mouth, or to a stream of saliva flowing from it.

In all the dogs, excepting dog D, the appetite became much impaired, and the breath remarkably fœtid. In dogs A, C, and E the mucous membrane of the mouth became ulcerated. Mere sponginess of the gums was never observed.

All the dogs, with the exception of dog D, became much emaciated. During the very decided action of the drug, blood appeared in the fæces of all the dogs, excepting dog E. Profuse diarrhœa was produced in all the dogs without biliary fistulæ; it was slight in the little dog D, while it was entirely absent in the other two dogs with fistulæ, although these, like all the other dogs, were killed by corrosive sublimate. During the exhibition of the drug, the fæces in dog A changed from a light to dark brown, brownish yellow, and greenish brown; in dog B they changed from brown to greenish brown, greenish yellow, and slate-brown; while in dog C they hardly underwent any change in colour. In dogs D and E there was no change in the colour, while in dog F they changed from a clay to a slate-colour: this dog, like the two previous ones, had a biliary fistula.

Appearances found on Dissection.

In all the dogs the mucous membrane of the stomach was found healthy. In all there were numerous bright red vascular patches found on the mucous membrane of the small intestine, extending from the pylorus to the ileo-colic valve. In dog B there were patches of lymph on the inner surface of the mucous membrane of the ilium. In dogs C and F this redness was most marked in the duodenum, but the orifice of the common bile-duct was not redder than the other portions of the duodenum. In all the dogs, except

dog B, the mucous membrane of the large intestine was streaked with bright red lines running longitudinally throughout its entire length.

In all the dogs, except dog D, there was unusual vascularity of the pancreas, but in none was there any abnormal appearance of the salivary glands.

In no case did the liver present any unusual appearance.

These facts show that on the dog mercury has the same action as it exerts on man.

Results of the Experiments made on Dogs with Biliary Fistulæ to determine the action of Mercury as a Cholagogue.

During the two years over which the Committee's inquiries extended, forty-one dogs were subjected to the operation for establishing a biliary fistula. Of these, four died during its performance from the effects of chloroform. In four others the operation was not proceeded with after opening the peritoneum, in consequence of the impossibility of bringing the fundus of the gall-bladder in contact with the abdominal wall. The operation was completed in thirty-three cases, but from various causes, which the Committee consider it unnecessary to detail minutely, satisfactory observations could only be carried on in nine dogs. These have been numbered consecutively from one to nine, but it has been thought better to arrange the numerous observations made upon them according to the preparation of mercury employed.

Observations with Pil. Hydrargyri.

The first dog (No. 1) in which a biliary fistula was successfully established by the Committee was a healthy retriever about eighteen months old, weighing 18·5 kilogrammes, for which we are indebted to Mr. Nunneley of Leeds. The operation was performed on the 29th of May, 1867. The wound in the abdominal wall healed rapidly. Shortly after the operation the fæces became clay-coloured. The general health of the animal was excellent when on the 10th of June the apparatus for collecting the bile was applied, and the observations recorded in the following Table (Table II.) were commenced.

As the metrical system of weights is used in all the Tables with regard to everything except the doses of drugs, it may be of service to remind the English reader that—

1 gramme = 15·434 grains, 28·34 grammes = 1 ounce, 1 kilogramme = 2·2 pounds.

Table II.—First Series of Observations on Dog 1. Daily amount of Bile secreted without Mercury.

1	2	3				4			5			6		
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted		
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.
1867.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grms.	grm.
June 11.	18·5	None.	567	170·1	283·5	150·4	8·843	1·221	8·12	0·478	0·066	65·5	3·85	0·53
„ 12.		„	„	„	„	125·0	8·400	1·355						
„ 15.		„	„	„	„	75·7	5·791	0·836	4·09	0·313	0·045	32·9	2·52	0·36
„ 17.		„	„	„	„	121·8	6·954	1·280						
„ 18.		„	„	„	„	115·0	7·290	1·345						
„ 19.		„	„	„	„	130·7	8·456	1·520						
Mean						119·76	7·622	1·259	6·47	0·412	0·068	52·18	3·32	0·548

Note.—The amount of dry food consumed daily during the above period amounted to 22·5 grammes.
„ „ „ for each kilogramme of dog amounted to 12·3 grammes.

The above series of observations was undertaken with a view to ascertain the average amount of bile secreted daily previous to the administration of mercury to the animal. It was thought necessary to collect the bile for six consecutive days before calculating its average daily amount; for, as is evident from the Table, the secretion was very inconstant. Thus on June 15th the quantity secreted was only about a half of what it was upon the 11th.

In the above Table three days (the 13th, 14th, and 16th) have been omitted, owing to a portion of the bile having been lost. This resulted from slipping of the apparatus. Despite every care in its adjustment, it was sometimes so shifted by the movements of the animal that the canula was dragged out of the fistula, and the bile consequently lost.

The average daily amount of bile secreted during the six days was 119·76 grammes of fluid bile, 7·622 grammes of bile solids, and 1·259 gramme of bile salts*. The daily amount of food consumed during the whole period was uniform. This was due to the fact that for some days previous to the commencement of the bile-collections the dog was offered an excess of food; the amount consumed was estimated, and this amount was given on subsequent days, and always entirely eaten by the animal. With a view to assimilate all the Tables, a column for water is introduced, although in this case none was given.

In this and all the following Tables, the amount of fluid bile, bile solids, and salts secreted is estimated with regard to each kilogramme-weight of the animal, and each 100 grammes of dry food consumed by it. In columns 5 and 6 of the foregoing Table these estimates are made on the days when the maximum and minimum quantities of bile were secreted; and the average quantities given at the foot of these columns are, in this and all the subsequent Tables, estimated from the average quantities of columns 2, 3, and 4. Columns 5 and 6 have a special physiological interest, and will be afterwards referred to at length. For the present the attention of the reader need not be directed to column 5, for the experience of the Committee has shown that there is no relation between the amount of bile secreted and the weight of the animal; the relation between the amount of food consumed and the quantity of bile secreted is not a very close one either (as the foregoing Table is sufficient to show), yet in some cases it seems to be such as to render necessary its being taken into account when the influence of any agent upon the biliary secretion is under consideration †.

During all the observations on this animal, however, the same amount of food was taken daily; therefore any variation in the biliary secretion cannot be ascribed to variation in the diet, so that the relation between the secretion of bile and amount of food may in this case for the present be disregarded.

On the 19th of June it was found necessary to discontinue the observations, as the pressure of the apparatus had caused ulceration of the skin over the sternum, and the fistula had assumed a very irritable appearance. The wound having healed, and the fistula become more healthy, the observations were resumed on the 28th of June, and continued for other six consecutive days.

The results are given in the following Table:—

* By the term bile *salts* in this and all subsequent Tables is meant the *inorganic* solids of the bile left after its incineration.

† To give completeness to the Tables the absolute amount of dry food taken daily or on some particular day, together with the amount consumed per kilogramme of dog, has been given.

TABLE III.*—Second Series of Observations on Dog 1. Daily amount of Bile secreted without Mercury.

1	2	3				4			5			6		
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted		
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.
1867.						grms.	grms.	grms.	grms.	grm.	grm.	grms.	grms.	grms.
June 29.	16·8	None.	567	170·1	283·5	106·2	3·865	1·15						
„ 30.		„	„	„	„	148·0	†	†						
July 1.		„	„	„	„	117·5	4·31	1·116						
„ 2.		„	„	„	„	185·1	6·60	2·010	11·01	0·392	0·119	80·6	2·87	0·87
„ 3.		„	„	„	„	81·6	2·978	0·824	4·85	0·177	0·049	35·5	1·29	0·35
„ 4.		„	„	„	„	149·5	5·80	1·615						
Mean						131·31	4·71	1·343	7·82	0·28	0·079	57·21	2·05	0·58

The amount of dry food consumed daily during the above period amounted to 229·5 grammes.
„ „ „ for each kilogramme of dog amounted to 13·6 grammes.

* In columns 5 and 6 the maximum, minimum, and mean quantities are calculated; the last, however, are estimated from the mean quantities of column 4.
† Not determined.

This second series of observations was again directed to ascertain the normal secretion of bile, in the hope that the secretion would become more constant; the Table, however, shows that this expectation was not realized, the variation in the daily quantity of bile was indeed even greater. Owing to the experience gained in this experiment, all subsequent observations directed to ascertain the normal secretion of bile previous to the administration of a drug were seldom prolonged beyond four or five days.

Table III. shows that the average amount of fluid bile secreted daily during this series of observations was slightly above the average amount secreted during those in Table II.; but it shows that there was a great diminution in the bile solids. The average quantity during the first series was 7·622 grammes, during the second series only 4·71 grammes. This was entirely due to a falling off in the amount of the organic constituents of the bile; for the Tables show that during the second series the inorganic solids (*bile salts*) were somewhat greater in amount than they were during the first series of observations. The animal had lost weight to the extent of 1·7 kilogramme, but was nevertheless in excellent health generally, although the irritable state of the fistula rendered necessary an interruption of the observations until the 8th of July.

As it seemed impossible to obtain a better standard of comparison than was afforded by Table III., it was resolved to commence the administration of mercury. Table IV. shows the results.

Five grains of Pil. Hydrargyri were given as one dose daily during eight days; the pill was always given twenty-four hours previous to the collection of the bile.

On July 11th, the apparatus having shifted, the bile escaped. On the other seven days, however, the collections were perfect, and the results show that the administration of the drug was accompanied by slight diminution (3·71 grammes) in the average quantity of fluid bile secreted daily, and a slight augmentation (0·45 gramme) in the average quantity of bile solids. This slight increase in the bile solids cannot be regarded as a proof of the power of blue pill to increase the biliary secretion, when the extreme variations of the secretion in this case are taken into account. In favour

of the idea it may, indeed, be alleged that on July 14th (Table IV.) more fluid and solid bile was secreted under the influence of blue pill than had been secreted on any day without it; but as a counterpart to this it can be said that on July 17th (Table IV.) the amount of fluid and solid bile was less than it had ever been on any previous day. On the whole, therefore, it may be concluded that in this case there was no evidence that the administration of blue pill affected the biliary secretion.

TABLE IV.*—Third Series of Observations on Dog 1. Amount of Bile secreted in twenty-four hours when 5 grs. of Pil. Hydrargyri were given daily.

1	2	3				4			5			6		
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted		
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.
1867.						grms.	grms.	grms.	grms.	grm.	grm.	grms.	grms.	grm.
July 9.	15	None.	567	170·1	283·5									
„ 10.		„	„	„	„	100	4·27	1·10						
„ 11.		„	„	„	„									
„ 12.		„	„	„	„	89	3·729	1·023						
„ 13.		„	„	„	„	170·6	6·19	1·74						
„ 14.		„	„	„	„	204·0	8 9	2·29	13·6	0·39	0·152	88·8	3·52	0·99
„ 15.		„	„	„	„	139 0	5·86	1·52						
„ 16.		„	„	„	„	127·6	5·13	1 50						
„ 17.		„	„	„	„	67·0	2·86	0·73	4·46	0·19	0·042	29·19	1·246	0·31
Mean						127·6	5·16	1·38	8·50	0·344	0·09	55·6	2·24	0·601

NOTE.—The amount of dry food consumed daily during the above period amounted to 229·5 grammes.
„ „ „ for each kilogramme of dog amounted to 15·27 grammes.

* In columns 5 and 6 the maximum, minimum, and mean quantities only are calculated. The last, however, are estimated from the mean quantities of column 4.

The above-mentioned doses of blue pill did not purge the animal.

On July 17th the observations were interrupted on account of renewed ulceration over the sternum by the pressure of the apparatus. At that date the animal was in excellent health.

The observations were resumed after an interval of six days. The results are given in the following Table :—

TABLE V.†—Fourth Series of Observations on Dog 1. Amount of Bile secreted in twenty-four hours when 5 grs. of Pil. Hydrargyri were given daily.

1	2	3				4			5			6		
Date.	Weight of dog.	Amount of food, in grammes.				Quanty of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted		
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.
1867.						grms.	grms.	grm.	grms.	grms.	grms.	grms.	grms.	grms.
July 23.	15	None.	8·46	282	225·6	231·9	7·55	lost.						
„ 24.	„	„	„	„	„	56·7	1·61	lost.						
„ 25.	„	„	„	„	„	95·0	2·86	0·931						
„ 26.	„	„	„	„	„	49·1	1·73	lost.						
„ 27.	„	„	„	„	„	38·2	1·41	0·443						
„ 28.	„	„	„	„	„	175·0	4·88	1·66						
„ 29.	14·9	„	„	„	„	69·3	2·64	0·691						

† In this and all subsequent Tables the amount of medicine said to be given on any day was always given during the twenty-four hours *previous* to the bile collection of the same date.

Pil. Hydrargyri was again given. Extraordinary variations occurred in the amount of bile obtained during its exhibition, and the quantities appear to show that the secretion of bile was diminished; but they are in truth rendered valueless by the circumstance that a considerable quantity of bile was separated by the kidneys, owing, most probably, to its free exit by the fistula having been interfered with. The animal was never purged until July 30th, when it twice passed a considerable quantity of liquid fæces. Although it did not lose weight to any notable extent during the period embraced by Table V., its strength diminished. In order that the dog might rally, the observations were suspended, and a more liberal diet allowed. It grew gradually weaker, however, and died on the 5th of August. On dissection a layer of recent lymph was found over the whole surface of the peritoneum. The cause of the peritonitis was not evident *.

Observations with Calomel.

The second dog (No. 2), with a biliary fistula, was a full-grown half-bred collie, weighing 15·6 kilogrammes. The operation was performed on the 5th of September, 1867. The wound healed perfectly, and collection of the bile was begun on the 20th of September. The general health of the animal was, however, indifferent; its appetite was uncertain, and its general strength feeble. When the apparatus was applied, the animal appeared to be much distressed by its weight, and by the constriction of the thorax and abdomen, which its proper application rendered necessary. After the operation the fæces became clay-coloured.

During seven days, from September 21st to 27th inclusive, observations were made with a view to determine the normal secretion of bile: the results are given in the following Table (Table VI.):—

TABLE VI.—First Series of Observations on Dog 2. Daily amount of Bile secreted without Mercury.

1	2	3				4			5			6		
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted		
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.
1867.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grms,	grms.
Sept. 21.	15·6	None.	561	None.	None.	130	7·29	1·41	8·333	0·467	0·09	230·0	12·9	2·51
„ 22.		„	564	„	„	81	4·48	0·907						
„ 23.	...	Not accurately noted. State ment in book is "scarcely any food taken."				94·15	6·072	1·205						
„ 24		None.	225·6	None.	None.	94·70	5·750	1·01						
„ 25.	15·6	„	282	„	310·2	78·80	5·92	1·25	...	...	...	73·9	5·60	1·18
„ 26.		„	197·4	„	225	62·50	5·70	1·08						
„ 27.		Has only taken a little milk				35·50	1·99	0·436	2·27	0·12	0·027			
Mean for seven days						82·46	5·31	1·042	5·27	0·34	0·066			

NOTE.—On the 25th September the dry food consumed amounted to 105·7 grammes, or 6·7 grms. per kilog. of dog; on the 21st, 56·4 grms., or 3·6 grms. per kilog. of dog.

In this Table, as well as in several others, it will be observed that the amount of bile collected was greater on the first than on other days—a rule, however, by no means invariable. The occurrence was probably due to the canula having permitted a freer exit to the bile than the fistulous opening

* For further observations on the action of Pil. Hydrargyri see Tables IX. and X.

which the contraction of the recti abdominis always tended to close. At first, therefore, after the introduction of the canula, a large quantity of bile pent up in the ducts may have escaped, or the larger quantity may have been due to increased biliary secretion.

The average quantity of bile secreted daily by dog 2 during the seven days embraced by Table VI. was of fluid bile 82·46 grammes, of bile solids 5·31 grammes, of bile salts 1·042 gramme. During the whole period the animal took a very variable quantity of food; on two days the amount was not accurately recorded; the average quantity of dry food consumed daily could not therefore be estimated. The biliary secretion was, when compared with the amount of food, extremely variable, however, as column 6 of the Table suffices to show.

The general health of the animal had not materially suffered by the continued application of the apparatus, although it at first occasioned so much distress.

It was now decided to observe the effects of calomel. Table VII. (p. 209) gives the results.

During the six days embraced by Table VIII. calomel was given internally in varying doses. The effect of the medicine upon the general health of the animal was very decided; it grew daily weaker and thinner, it lost its appetite, had attacks of vomiting on October 2nd and 3rd, and died on October 5th, apparently from inanition. Purgation, fœtor of the breath, or ulceration of the gums were never produced by the drug, nor was there any evidence of salivation.

On October 2nd the bile was lost, and on the 3rd, two days before the death of the animal, and when it took no food, only 2·2 grammes of bile were secreted. An average has been taken from the first four days during which the animal took food. The average quantity of fluid bile secreted during these four days was 60·02 grammes.

The average quantities of bile solids and salts have not been estimated seeing that they were not ascertained on September 29th. The Table shows that under the action of the calomel less bile was secreted than there was previous to its exhibition; but as the amount of calomel given had seriously, indeed fatally, injured the health of the animal, it was determined to try in the next case the effect of minute and frequently repeated doses.

Dog 3 was a young healthy retriever, weighing 12·9 kilogrammes. The operation for biliary fistula was performed on the 13th of October, 1867. A few hours afterwards the dog pulled the india-rubber tube out of the fistula, and the external opening of the fistula closed, so that on October 15th the fistulous opening had to be reestablished by an incision. The wound in the abdominal wall healed satisfactorily, the fæces were clay-coloured, and the animal was in excellent health when the collection of bile was begun, October, 26th 1867. It was decided to observe the effects of very small doses of calomel ($\frac{1}{12}$ of a grain) frequently repeated. The bile was collected on four successive days previous to, and on four consecutive days during the exhibition of the drug without any break between the two series. Table VIII., p. 209, gives the results of both series of observations.

During the four days previous to the administration of the calomel the animal secreted daily on an average 70·62 grammes of fluid bile, 3·792 grammes of bile solids, and 0·83 gramme of bile salts. The health of the animal during these days was excellent.

Table VII.—Second Series of Observations on Dog 2. Daily amount of Bile secreted when Calomel was given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Amount of Calomel given.
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts	Fluid bile.	Bile solids.	Bile salts.	
1867.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grms.	grms.	
Sept. 28.	14·3	None.	846	None.	None.	61·6	3·54	0·67	4·307	0·24	0·46	72·8	4·18	0·79	2 grains three times in the day=6 grains.
„ 29.	„	„	253·8	„	112·8	7·3	..	...	...	...	...	...	...	...	2 grains in the day = 2 grains.
„ 30.	„	„	141·0	„	253·8	85·7	5·69	1·11	5·99	0·39	0·07	164·2	10·9	2·12	2 grains three times in the day=6 grains.
Oct. 1.	...	„	253·8	„	None.	65·5	3·76	0·85	...	...	...	...	...	...	2 grains four times in the day=8 grains.
„ 2.	...	„	282	„	„	Lost.	...	...	...	...	...	...	...	...	2 grains six times in the day=12 grains.
„ 3.	12·24	„	none.	„	„	2·2	...	...	...	...	...	...	...	...	2 grains twice in the day=4 grains.
Mean quantity during first four days						60·02									

Note.—On 28th Sept. the dry food consumed amounted to 84·6 grammes, or 5·9 grammes per kilog. of dog.
30th „ „ „ „ „ „ 77·55 grms., or 5·30 grms. per kilog. of dog.

Table VIII.—Observations on Dog 3. Daily amount of Bile secreted before and after Calomel was given.

1	2	3				4			5			6			7
Oct. 26.	12·9	None.	564	None.	338·4	91	4·83	1·19							
„ 27.	...	„	„	„	„	111	6·14	1·26	8·60	0·476	0·097	78·7	4·354	0·839	Before calomel was given.
„ 28.	...	„	„	„	„	22	1·16	0·27	1·70	0·080	0·002	15·6	0·822	0·191	
„ 29.	...	„	„	„	None.	58·5	3·04	0·60							
Mean of the above observations			564	...	253·8	70·62	3·792	0·83	5·47	0·293	0·064	58·9	3·165	0·692	
Oct. 30.	12·2	None.	none.	None.	None.	36	1·88	0·45	2·96	0·154	0·036	...	...	...	Seven pills, each containing one-twelfth of a grain of calomel, were given one at a time, with an hour's interval between each.
„ 31.	...	„	„	„	„	89·9	4·79	1·15	...	...	...	...	...	...	Seven pills as above.
Nov. 1.	...	„	„	„	338·4	108·5	5·76	1·36	8·89	0·472	0·111	...	...	...	Fourteen pills as above.
„ 2.	...	„	„	„	None.	46·9	2·51	0·6	...	...	...	...	...	...	Six pills as above.
Mean of the second series of observations						70·32	3·732	0·89	5·76	0·305	0·072				

Note.—On October 26th, 27th, and 28th, the dry food consumed amounted to 141 grammes, or 10·9 grms. per kilog. of dog; the mean quantity consumed daily on the first four days amounted to 119·8 grms., or 9·13 grms. per kilog. of dog.
The amount of food consumed when the mercury was given was so small (taken on one day only) that no calculation has been made from it.

On October 30th seven pills, each containing $\frac{1}{12}$ of a grain of calomel, were given with an hour's interval between each. On October 31st seven pills, on November 1st fourteen pills, and on November 2nd six pills were administered in the same way as above mentioned.

The effect on the general health was very marked. Soon after the administration of the drug was begun the appetite failed, and the animal took no food of any kind during three of the four days. The strength became rapidly exhausted, and the animal died on November 3, apparently from inanition. No salivation, fœtid breath, ulceration of gums, or purgation were produced by the medicine.

The average of the second series of observations shows that during the four days on which the calomel was given the secretion of bile was not influenced. It was almost exactly the same in the second as during the first period, thus distinctly showing that the calomel cannot be said to have affected it at all. It is also to be observed that although during the second four days the animal took food only once, the amount of bile secreted was on an average very nearly the same as during the first four days when it ate well. This might at first sight be considered as supporting the notion that mercury increases the biliary secretion. But were it true that in the present case the mercury had kept up the secretion notwithstanding the diminution in the food, then certainly it ought to increase the secretion when a due supply of food is taken; for it cannot be held that the influence of food is anything but highly favourable to the secretion. The results given in Table IX. will show that such is not the case.

Dog 4 was a healthy collie, about eighteen months old, weighing 19 kilogs. The operation for biliary fistula was performed on the 19th of October, 1867. The wound in the abdominal wall healed slowly. As the fistulous opening was very irritable, the canula was not introduced. Instead of the canula and india-rubber bag previously employed, a sponge was used to collect the bile; it was secured in a tin box below the fistulous opening. The fæces became clay-coloured soon after the fistula was established.

The general health of the animal was excellent when the observations recorded in Table IX. p. 211, were begun.

The bile was collected for five consecutive days previous to the administration of mercury, in order to ascertain the average amount secreted daily. This was: of fluid bile 67·1 grammes, of bile solids 3·592 grammes, of bile salts 0·842 gramme. At the end of this period the dog was in excellent health.

On November 8th the administration of mercury was begun. During the twenty-four hours previous to the collection of bile on that day, ten pills, each containing one-twelth of a grain of calomel, were given, one pill at a time, with an hour's interval between each. On the next day twelve such pills were given. On November 10th ten grains Pil. Hydrargyri were administered in one dose. On the 11th and 12th no mercury was given. On the 13th the ten grains of Pil. Hydrargyri were repeated. On the 14th nine calomel pills were given as above; and on the last day of the observations the mercury was withheld.

During the five days on which calomel or blue pill was administered in the above modes, the amount of bile secreted was diminished to nearly a half of what it was in the period preceding the administration of the mercury; and this, although nearly as much food was consumed during as before the exhibition of the drug. Moreover, during the second period, the average amount of bile secreted was, on the whole, greater on the days when no mercury was

TABLE IX.—Observations on Dog 4. Daily amount of Bile secreted before and after Calomel and Pil. Hydrargyri were given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Amount of Mercury given.
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1867.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grms.	grm.	
Nov. 3.	19	338·4	282	112·8	338·4	71·2	3·84	0·85							
„ 4.	...	„	„	„	„	61·9	3·34	0·81							
„ 5.	...	„	564	56·4	„	88·9	4·78	1·14	4·67	0·251	0·06	50·85	2·703	0·652	} Before mercury was given.
„ 6.	...	„	282	„	„	72·0	3·80	0·90							
„ 7.	...	„	„	„	„	41·5	2·23	0·514	2·18	0·117	0·027	28·308	1·521	0·350	
Mean		338·4	338	78·96	338·4	67·1	3·592	0·842	3·53	0·146	0·044	40·13	2·148	0·503	
Nov. 8.	18·3	338·4	282	56·4	338·4	*76·0	4·13	1·01	4·15	0·225	0·055	51·84	2·817	0·688	Ten pills given, each containing one-twelfth of a grain of calomel; one pill every hour.
„ 9.	...	„	„	„	„	*47·0	2·54	0·56	...	...	...	...	...	...	Twelve pills as above.
„ 10.	...	„	„	„	„	*12·5	0·06	0·01	0·68	0·003	0·0005	8·525	0·048	0·006	10 grains Pil. Hydrargyri given.
„ 11.	...	„	„	„	„	45·0	2·41	0·54	...	...	...	...	...	...	No mercury given.
„ 12.	...	„	„	„	„	58·0	3·07	0·754	...	...	...	...	...	...	No mercury given.
„ 13.	...	„	„	„	„	*24·0	1·33	0·34	...	...	...	...	...	...	10 grains Pil. Hydrargyri given.
„ 14.	...	„	„	„	„	*17·8	1·00	0·26	...	...	...	...	...	...	Nine pills, each containing one-twelfth of a grain of calomel given; one pill every hour.
„ 15.	...	„	„	„	„	45·0	2·40	Lost.	...	...	...	...	...	...	No mercury.
Mean of the five days (marked*) on which mercury was given.		338·4	282	56·4	338·4	35·46	1·812	0·436	1·93	0·099	0·023	24·18	1·23	0·29	

NOTE.—The average amount of dry food consumed during the first period amounted to 167·2 grammes, or 8·8 grammes per kilogramme of dog. The average amount of dry food consumed during the first period amounted to 146·6 grammes, or 8·01 grms. per kilogramme of dog.

given than on the other days. No purgation or any signs of specific action were produced by the mercury; but shortly after its first administration the strength of the animal began to decline. Sores, produced by the pressure of the apparatus, formed upon the back, in consequence of which the observations were interrupted on November 15th. The appetite failed, and the animal became so much emaciated that it was killed on the 28th of November.

It is evident that in this case the mercury diminished the biliary secretion, and it is remarkable that it did so without impairing the appetite, and without producing purgation.

In the foregoing experiments purgation had never been produced by the mercurials while the bile was being collected; it seemed, therefore, desirable to ascertain the effect upon the biliary secretion of purgative doses. This was done in the following experiment.

Dog 5 was a strong collie, twelve months old, weighing 16·7 kilogrammes. The operation for biliary fistula was performed on the 2nd of June, 1868. The fistula became satisfactorily established, but on June 28th the dog escaped. It was reobtained on the 11th of July. The fistulous opening had closed, the dog was jaundiced, conjunctiva and skin yellow, urine loaded with bile. As the fæces were, however, clay-coloured, an attempt was made to open the fundus of the gall-bladder. This was found distended with a thick, gelatinous, colourless fluid like white of egg. About ten ounces of this fluid at once flowed from the opening. It was not in the least tinged with bile. The glairy fluid continued to drop from the opening for several hours, after which the bile began to flow, and continued to do so.

In ten days every symptom of jaundice had disappeared, the fæces were clay-coloured, and the wound was sufficiently healed to permit of observations being begun. In Table X., p. 213, are recorded the results obtained before, during, and after purgative doses of calomel and Pil. Hydrargyri were given.

The bile was collected perfectly on six days in order to ascertain the normal secretion. The average daily quantity during this period was 357·4 grammes of fluid bile, 13·11 grammes bile solids, and 3·12 grammes of bile salts. During the first four days the dog was in excellent health. On July 26th it was seized with a smart attack of diarrhœa. On that day both the fluid and solid portions of the bile were diminished. The diarrhœa did not recur after the 26th. On the 27th the collection of bile was rejected, owing to urine having mingled with it. On the 28th it had risen to a little above the average quantity.

Twenty-four hours previous to the collection of the bile on the 29th, ten grains of blue pill were administered. During the three succeeding days ten grains of calomel were given daily in one dose on each occasion twenty-four hours previous to the bile collection. The dose of blue pill and the first dose of calomel produced slight purgation, while decided purgation followed the administration of the two last doses. There was a marked diminution in the biliary secretion during this period, the average daily amount being: of fluid bile 272·67 grammes, of bile solids 7·78 grammes, of bile salts 2·06 grammes. It will be seen from the Table that this diminution is quite as marked in the solid as in the fluid bile.

The high amount which the fluid bile attained when ten grains of blue pill were given might be supposed to indicate an increase in the secretion. The variations in the amount of solid constituents of the bile are, however, those

TABLE X.—Observations on Dog 5. Daily amount of Bile secreted before and after purgative doses of Mercury were given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Observations.
	Kilogs.	Water.	Milk.	Bread.	Liver.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grms.	grms.	grm.	grm.	grms.	grms.	grm.	
July 22.	16·7	566	566	226·4	906·8	412	16·06	3·21	24·67	0·961	0·192	102·7	4·00	0·800	Dog in good health.
„ 23.	16·6	„	„	„	„	331·8	13·20	2·91	...	...	...	...	...	...	Dog in good health.
„ 24.	16·4	367·9	226·4	„	„	375·4	9·20	3·26	...	...	...	...	...	...	Dog in good health.
„ 25.	16·2	566	566	„	„	379·1	14·78	3·07	...	...	...	...	...	...	Dog in good health.
„ 26.	16·0	„	„	„	665·9	282·7	12·80	2·68	17·66	0·80	0·167	81·3	3·74	0·775	Decided diarrhœa.
„ 27.	...	...	...	...	...	Lost.	...	...	...	...	...	...	...	...	Diarrhœa has ceased.
„ 28.	16·3	„	566	212·2	906·8	363·7	12·62	3·60	...	...	...	...	...	...	Dog in good health.
Mean...	16·36	532·9	509·4	224	866·6	357·4	13·11	3·12	21·8	0·801	0·190	92·9	3·49	0·811	No mercury given during the above period.
July 29.	15·9	566	495·2	198·1	807·6	390·2	9·59	2·77	23·9	0·603	0·174	110·2	2·7	0·782	10 grains blue pill given twenty-four hours previous to the collection of bile to-day; slight purgation.
„ 30.	15·7	„	523·5	183·9	906·8	249·7	7·71	1·97	...	...	...	...	...	...	10 grains calomel given as above; slight purgation.
„ 31.	...	„	254·7	84·9	424·5	229·0	6·89	1·74	...	...	...	...	...	...	10 grains calomel given as above; decided purgation.
Aug. 1.	15·4	„	566	226·4	566	221·8	6·94	1·77	14·4	0·450	0·114	68·9	2·15	0·54	10 grains calomel given as above; decided purgation.
Mean of the above 4 days	15·66	566	459·8	173·3	676·2	272·67	7·78	2·06	17·4	0·496	0·131	89·2	2·54	0·674	
Aug. 2.	...	566	396·7	141·7	906·8	293·9	8·17	Lost.	...	...	...	...	...	...	No mercury given.
„ 3.	15·2	„	253·8	„	„	297·5	7·59	2·43	19·4	0·499	0·15	93·3	2·38	0·76	No mercury given.

NOTE.—From July 22 to July 28 the mean amount of dry food consumed daily was 384·6 grammes, or 23·4 grammes per kilogramme of dog. From July 29 to August 1 the mean amount of dry food consumed daily was 305·3 grammes, or 19·23 grammes per kilogramme of dog.

which are of paramount importance in the present inquiry, and the diminution of these on the 29th is unmistakeable.

The bile was finally collected for two days, August 2nd and 3rd, on which no mercury was given. There was no purgation on these days, and the amount of bile secreted suddenly increased. Though the amount was not nearly so great as before mercury was given, it was nevertheless much above the last two days during its administration.

Previous to the exhibition of mercury the fæces were of a clay-colour, mixed with slate-coloured patches. During and on the two days after the mercury was given they were more uniformly slate-coloured. During the whole experiment the health of the animal was excellent, neither the diarrhœa nor the mercurial purgation seemed to affect it.

This series of observations is most conclusive as to the influence of purgative doses of calomel upon the biliary secretion. Under their influence there was a steady diminution in the secretion, and the moment the administration of the drug was suspended, the secretion underwent an increase.

It is important to observe that in this case purgation, whether spontaneous as on the 26th, or as the result of mercurials, diminished the secretion of bile. Other observations will be given further on (see Tables XVII., XVIII., and XIX.), which show that when induced by other drugs it likewise diminishes the biliary secretion.

The amount of bile secreted by this dog was very large, greater in proportion to the weight of the animal than in any other case. At first we were inclined to suppose that this might be due to the animal being fed upon *liver*; but in the case of dog 6, to be described presently, the amount secreted per kilogramme of dog was nearly as great, although the animal ate no liver; and the amount per 100 grammes of dry food was very much greater.

In the foregoing experiment the dose of blue pill given, although it diminished the bile solids, increased that of the bile fluid. It was important to ascertain whether or not the same result would be obtained on another trial. In another dog (No. 7) ten grains of blue pill were given on one day, and fifteen grains on the day following. Slight purgation was produced by the first dose, decided purgation by the second. On the day preceding the administration of the mercury, the amount of fluid bile was 173·9 grammes, of bile solids 9·35 grammes. The bile was lost on the day that the first dose of blue pill was given, but on the next day it had fallen to 119·9 grammes, and the bile solids to 7·5 grammes.

On both days the animal consumed about the same quantity of food. It is therefore clear that the observation recorded in the case of dog 5 on the 29th of July cannot be held as indicating the power of blue pill to increase the fluid portion of the bile; while this observation on dog 7 only confirms the result in the case of dog 5, viz. that a purgative dose of blue pill diminishes the amount of bile solids secreted.

Results of the preceding observations on the Cholagogue Action of Pil. Hydrargyri and Calomel.

1. Pil. Hydrargyri, when given in doses which did not produce purgation, caused no increase of the biliary secretion (Tables IV. and IX.).

2. Pil. Hydrargyri, when given in doses which produced purgation, diminished the biliary secretion (Table X., and non-tabulated observations on dog 7).

3. Calomel, given in doses of $\frac{1}{12}$ of a grain from six to fourteen times a day,

TABLE XI.—Observations on Dog 6. Daily amount of Bile secreted before and after Corrosive Sublimate was given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Amount of Corrosive Sublimate given.
	Kilogs.	Water.	Milk.	Bread.	Meat.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grms.	grms.	
Mar. 9.	5·1	None.	567	113·4	None.	105	4·158	0·934	20·58	0·815	0·183	142·3	5·64	2·48	Four-fifths of a grain of corrosive sublimate were given at 1 o'clock P.M., immediataly after the collection of bile was made on the 11th, and another dose of four-fifths of a grain was given at 9 o'clock A.M. on the 12th, and the last collection of bile was made at 1 P.M. on the same day.
„ 10.	„	„	141·6	None.	„	106·5	4·313	0·969	20·88	0·845	0·190	748·0	30·4	6·84	
„ 11.	„	„	56·7	„	226·8	104·7	4·062	0·942	20·52	0·796	0·184	167·8	6·9	1·51	
„ 12	4·98	„	850·5	56·7	None.	78	3·178	0·717	15·67	0·638	0·142	65·5	2·67	0·60	

NOTE.—On March 9th the dry food consumed amounted to 73·7 grammes, or 14·45 grammes per kilog. of dog; on the 10th, 14·16 grammes, or 2·776 grammes per kilog. of dog; on the 11th, 62·37 grammes, or 12·22 grammes per kilog. of dog; on the 12th, 119·07 grammes, or 23·9 grammes per kilog. of dog.

TABLE XII.—First Series of Observations on Dog 7. Daily amount of Bile secreted before Corrosive Sublimate was given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			
	Kilogs.	Water.	Milk.	Bread.	Tripe.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grm.	grm.	
May 30.	27·4	846	564	225·6	1353·5	136·3	6·97	1·22	4·97	0·25	0·044	26·52	1·31	0·23	
„ 31.	...	„	„	„	„	Lost.									
June 1.	...	„	„	„	„	132·8	not detd.	not detd.							
„ 2.	...	„	„	„	„	114·0	6·04	0·97	4·16	0·22	0·039	21·55	1·139	0·17	
„ 3.	...	„	„	„	„	125·5	6·28	0·91							
Mean	27·4	846	564	225·6	1353·5	127·15	6·43	1·03	4·64	0·23	0·037	23·99	1·21	0·19	

NOTE.—During the whole of this period the dry food consumed amounted to 530·1 grammes, or 19·34 grammes per kilog. of dog.

and in doses of two grains from two to six times a day, did not produce purgation or increase the biliary secretion (Tables VII., VIII., and IX.).

4. Calomel, when given in doses which produced purgation, diminished the biliary secretion (Table X.).

Observations with Corrosive Sublimate.

Dog 6, a retriever, six months old, weighing 5·1 kilogrammes, was operated on for biliary fistula, February 26th, 1868. The recovery was in this case speedy and perfect. Soon after the operation the fæces became clay-coloured. The health of the animal was excellent, and was not appreciably injured by the operation or the effects of the fistula.

Table XI. p. 215, gives the results of the observations, with corrosive sublimate on four consecutive days, three previous to, and one during the administration of the drug.

During the three days previous to the administration of the mercury, the secretion of fluid and solid bile was remarkably constant, and this notwithstanding great variation in the amount of food taken. The mean quantity was, of fluid bile 105·4 grammes, of bile solids 4·144 grammes, of bile salts 0·948 gramme. The constancy in the secretion rendered the case a very valuable one for observing whether or not it was affected by the drug. On the fourth day two doses of $\frac{4}{5}$ of a grain of corrosive sublimate were injected under the skin. The first dose was given at 1 P.M. on the 11th, immediately after the collection of bile had been made on that day. The second dose was given at 9 A.M. on the 12th, and the last collection of bile was made at 1 P.M. on the same day. The amount of fluid bile on this the fourth day was 78 grammes, of bile solids 3·178 grammes, of bile salts 0·717 gramme. Twenty hours after the first dose of the drug was given, a slight discharge of mucus from the nostrils was observed, and a patch of semisolid clay-coloured fæces mingled with a few drops of blood was found upon the floor. Two hours following the administration of the second dose, the animal was observed to be exceedingly weak; it was in a state of constant tremor, and staggered on attempting to walk. At 1 P.M. on the 12th, four hours after the second dose of mercury was given, the last collection of bile was made; at that time the nasal discharge had become more marked. There was no apparent salivation, nor was the breath fœtid. The animal was last seen alive at 5.30 P.M. on the 12th, eight and a half hours after the second dose had been given. At that time there was no apparent change in its condition, further than that it had become so weak that it was no longer able to stand, unless supported. It died during the following night. In the morning (13th) a patch of liquid fæces of a clay-colour was found upon the floor. Ten grammes of bile were found in the bag attached to the canula.

The result of this experiment was briefly this:—$1\frac{3}{5}$ grain corrosive sublimate, given in the course of 24 hours to a dog 6 months old, caused purgation with liquid bloody fæces, nasal discharge, diminution of the biliary secretion, general tremor, and finally death.

For dissection of this dog see Table I., Dog D. It will be observed that the stomach still contained a portion of undigested food.

As the animal had been poisoned by the drug, it was determined to observe the effects of smaller and gradually increasing doses. It was thought that if the drug can increase the biliary secretion, we, by beginning with a very small dose and gradually increasing its strength, would certainly hit upon the amount necessary to do so ere poisonous symptoms set in; moreover we should observe the effects of the repeated exhibition of small doses.

TABLE XIII.—Second Series of Observations on Dog 7. Daily amount of Bile secreted when Corrosive Sublimate was given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Amount of Corrosive Sublimate administered.
	Kilogs.	Water.	Milk.	Bread.	Tripe.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grms.	grm.	
June 6.	27·5	846	564	225·6	1353·6	95	4·89	0·90	3·45	0·17	0·03	17·92	0·92	0·16	One-sixth of a grain.
„ 7.	...	846	564	225·6	1353·6	104·5	5·14	*	...	...	...	...	...	...	One-sixth of a grain.
„ 8.	...	846	564	225·6	677·8	104·7	5·94	0·93	...	...	...	...	...	...	One-sixth of a grain.
„ 9.	...	846	564	225·6	916·5	143·3	4·90	1·21	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 10.	27·44	846	564	225·6	1128·0	159·6	7·32	1·41	5·82	0·26	0·05	33·6	1·54	0·297	One-sixth of a grain twice in the day.
„ 11.	...	846	564	225·6	677·8	104·8	5·83	*	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 13.	...	846	564	225·6	677·8	114·45	5·21	0·68	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 14.	...	Not accurately noted				89·0	5·39	0·80	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 15.	...	761·4	564	225·6	296·1	107·1	7·71	0·87	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 16.		846	564	225·6	916·5	115·71	7·39	1·13	...	...	...	...	...	...	One-sixth of a grain in the evening, and one-third of a grain in the morning.
Mean .	27·47	836·4	564	225·6	888·6	113·8	5·972	0·99	4·14	0·217	0·036	37·4	1·44	0·239	
June 17.	...	846	564	225·6	789·6	32·70	2·62	0·401	...	...	...	...	...	...	One-third of a grain twice in the day.
„ 18.	27·6	789	564	None.	70·5	54·60	2·93	0·40	1·97	0·10	0·014	73·6	3·01	0·56	One-third of a grain.——Total quantity, 4 grains.

* Not estimated.

NOTE.—On June 6th the dry food amounted to 530·1 grammes, or 19·27 grammes per kilog. of dog; on the 10th, 473·8 grammes, or 17·20 grammes per kilog. of dog; on the 18th, 73·9 grammes, or 2·67 grammes per kilog. of dog. Mean amount of dry food consumed daily from June 6–16 inclusive, 414·11 grammes, or 15·07 grammes per kilog. of dog.

TABLE XIV.—First Series of Observations on Dog 8. Daily amount of Bile secreted without Mercury.

June 18.	19·3	850	567	226·8	453·6	263	8·28	0·89	13·62	0·429	0·046	145	3·56	0·49	At the time of commencing observation the dog was in perfect health. Fæces quite white and semisolid.
„ 19.	...	„	„	„	„	241·6	6·76	1·40							
„ 20.	...	„	„	„	„										
„ 21.	...	„	„	„	„	200·0	5·34	1·30	...	...	...	...	...	...	Dog does not look very well. A little diarrhœa.
„ 22.	...	„	„	„	„	124·0	7·34	1·22	...	...	...	...	...	...	Diarrhœa has ceased. Dog looks well.
„ 23.	...	„	„	„	„	160·5	6·24	1·22							
„ 24.	...	„	„	„	„	158·6	5·12	0·77							
„ 25.	...	„	„	„	„	113·7	5·25	*	5·37	0·272	...	62·71	2·89		
„ 26.	19·7	676·8	846	225·6	676·8	180·3	3·40	0·70							
Mean...	19·5	763·4	706·5	226·2	565·2	180·2	5·96	1·07	9·24	0·305	0·054	51·84	1·714	0·307	

* Accidentally lost.

NOTE.—The amount of dry food consumed daily from June 18th to June 25th amounted to 181·3 grammes, or 9·3 grms. per kilog. of dog; on the 26th, 389·06 grammes, or 19·74 grms. per kilog. of dog.

Dog 7 was a strong full-grown retriever, weighing 27·4 kilogrammes, for which we were indebted to Dr. Kelburne King, of Hull. The operation for biliary fistula was performed on the 24th of April, 1868. The healing of the wound around the fistula was so slow that observations could not be begun before the 29th of May. Table XII. p. 215, gives the results previous to the administration of corrosive sublimate.

During the five days embraced by Table XII., the amount of food consumed was constant. On May 31st the bile was unfortunately lost, owing to the apparatus having slipped. The average quantity secreted during the remaining four days was of fluid bile 127·15 grammes, of bile solids 6·43 grammes, of bile salts 1·03 gramme. The observations were interrupted on account of repairs needed in the apparatus. When resumed on the 5th of June, the dog was in excellent health. Table XIII. p. 217, gives the results of observations during the administration of small and gradually increasing doses of corrosive sublimate.

During the first three days $\frac{1}{6}$ of a grain of corrosive sublimate was injected under the skin once a day. During the next six days the same quantity was injected twice a day, and on the tenth day (June 16) the dose was increased to $\frac{1}{3}$ of a grain at the second injection.

During these ten days the biliary secretion underwent marked variations; the average daily quantity was 113·8 grammes of fluid bile, 5·972 grammes of bile solids, and 0·99 gramme of bile salts. These figures show that there was a slight diminution in the biliary secretion during this period. At the same time, however, the amount of food consumed had undergone a considerable decrease, but the health of the animal had not suffered, and its weight remained almost exactly the same. On June 17, the increased dose of $\frac{1}{3}$ of a grain *twice* a day was given. Athough these doses produced no purgation, fœtid breath, or salivation, yet the dull eye and general drooping uneasy aspect of the animal showed that the general health was decidedly impaired. On that day (17th) there was a great decrease in the biliary secretion. The bile solids fell to about a third, and the fluid bile to about a fourth of what it had been on the previous day. The amount of food consumed, however, had been but slightly diminished, as compared with the previous day; but a glance at the Table will suffice to show that more food was consumed on the 17th than on the 11th, 13th, and 15th. On all these days at least thrice as much fluid bile, and about twice as much bile solids had been secreted. On June 18 only $\frac{1}{3}$ of a grain was given; and after the collection of bile on that day the observations were suspended, on account of the very marked impairment of the general health occasioned by the mercury. On that day the following is the note that was taken of the condition of the animal:—"The dog looks miserable and lifeless, his health is evidently much impaired, there is no salivation, fœtid breath, nasal discharge, or purgation." The quantity of bile secreted on the 18th, though above that of the previous day, was nevertheless very low. The consumption of food had greatly diminished; and it should be noticed that on the 10th the biliary secretion, instead of undergoing a still further diminution, consequent on the decreased consumption of food, was, in fact, augmented. This, in our opinion, could only be attributed to the influence of a smaller dose of the drug.

The collection of the bile was in this case quite perfect on every day, with one exception (May 31), recorded in Table XII. The observations distinctly show that corrosive sublimate, given in small gradually increasing doses, did not augment the biliary secretion. On the contrary, they point out

TABLE XV.—Second Series of Observations on Dog 8. Daily amount of Bile secreted when Corrosive Sublimate was given.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Amount of Corrosive Sublimate given.
	Kilogs.	Water.	Milk.	Bread.	Tripe.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grm.	grms.	grm.	grm.	grms.	grm.	grm.	
June 27.	19·70	676·8	846	225·6	676·8	172·2	4·30	1·60	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 28.	„	676·8	846	225·6	676·8	137·0	3·20	1·10	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 29.	„	676·8	846	225·6	676·8	142·8	3·55	1·02	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 30.	„	846·0	846·0	225·6	676·8	162·7	4·23	1·31	...	...	...	...	...	...	One-sixth of a grain twice in the day.
July 1.	„	846·0	846·0	225·6	None.	113·3	2·09	0·69	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 2.	19·82	1071	846·0	225·6	451·2	179·47	4·77	0·879	9·06	0·24	0·044	53·9	1·43	0·264	One-sixth of a grain twice in the day.
„ 3.	„	1241	846	225·6	366·6	147·1	3·30	1·381	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 4.	„	1241	846	225·6	141·0	145·0	2·68	1·19	...	...	...	...	...	...	One-sixth of a grain twice in the day.
„ 5.	„	1241	338·4	54·6	239·7	145·0	2·68	1·19	...	...	...	...	...	...	One-sixthof a grain in the evening, one-third in the morning.
„ 6.	19·59	1241	846·0	225·6	239·7	157·2	2·11	0·48	8·02	0·107	0·024	56·19	0·75	0·171	One-sixth of a grain in the evening, one-third in the morning.
„ 7.	...	1241	846·0	225·6	423	153·0	3·67	1·346	...	...	...	...	...	...	One-third of a grain twice in the day.
„ 8.	...	1241	308·9	183·3	56·4	147·51	4·115	1·44	...	...	...	...	...	...	One-third of a grain twice in the day.
Mean...	19·7	1019	754·4	207·8	420·4	150·19	3·374	1·135	7·62	0·171	0·057	49·2	1·105	0·372	
July 9.	...	1241	126·9	42·3	None.	74·2	2·04	0·570	...	...	...	...	...	...	One-third of a grain twice in the day.
„ 10.	16·10	Taken a little milk.		42·3		17·5	0·133	0·05	1·086	0·008	0·003	...	...	...	One-third of a grain.——Total quantity, six grains.

NOTE.—On July 2nd the dry food consumed amounted to 332·76 grammes, or 16·70 grammes per kilogramme of dog; on the 6th, 279·8 grammes, or 14·2 grms. per kilog. of dog; on the 10th, salivation and ulceration of gums appeared; on the 1st the tripe was stinking when given.

TABLE XVI.—Third Series of Observations on Dog 7. Daily amount of Bile secreted before, during, and after partial starvation.

July 26.	29·5	311·7	226·7	141·7	1813	140·8	5·04	0·88	4·7	0·170	0·029	2·15	0·89	0·15	Dog in excellent health.
„ 27.	„	850·2	„	„	1728·7	139·9	5·14	1·00	...	...	...	...	...	...	Dog in excellent health.
					Liver.										
„ 28.	„	None.	None	None.	453·4	104·8	7·73	1·03	...	...	...	100·5	7·4	0·98	Dog in excellent health.
„ 29.	28·6	453·4	„	„	None.	41·6	2·77	0·40	1·45	0·096	0·013	...	...	...	Dog in excellent health.
„ 30.	...	850·2	226·7	141·7	None.	85·7	5·11	0·87	...	...	...	79·57	4·74	0·808	Dog in excellent health.
					Tripe.										
„ 31.	28·6	425·0	„	„	1813·7	173·9	9·35	1·68	6·08	0·326	0·058	31·0	1·66	0·29	Dog in excellent health.

NOTE.—On July 26 the dry food amounted to 560·9 grammes, or 19·01 grammes per kilogramme of dog; on the 28th the dry food amounted to 104·2 grammes, or 3·64 grammes per kilogramme of dog; on the 29th no dry food was given; on July 30th the dry food amounted to 107·7 grammes, or 3·7 grammes per kilogramme of dog; on the 31st the dry food amounted to 560·9 grammes, or 19·9 grammes per kilogramme of dog.

that so long as the general health remained good, the amount of bile was not changed, but as soon as the animal became weak, diminution of the secretion at once took place.

Dog 8 was a strong mongrel collie, about five years old, weighing 19·3 kilogrammes. The operation for biliary fistula was performed on the 2nd of June, 1868. The recovery was rapid, and observations, with a view to determine the normal secretion of bile, were commenced June 17th. The results are given in Table XIV. p. 217.

The bile was perfectly collected for eight days. On one day (20th) the apparatus was not applied. When the observations were commenced, the animal was in perfect health, the fæces were quite white and semisolid. On the 21st it had a slight attack of diarrhœa, which had, however, disappeared on the following day. With this exception, the health of the animal was exceedingly good during the whole period, and instead of a loss there was a slight gain in weight. The diminution of the biliary secretion on the 21st cannot be ascribed to the diarrhœa, seeing that on the next day, when it had ceased, a still greater decrease took place. The average daily amount of bile during the above period was, of fluid bile 180·2 grammes, of bile solids 5·96 grammes, of bile salts 1·07 gramme. The dog's appetite was remarkably good. It was decided that corrosive sublimate should now be given in small and gradually increasing doses as in the previous case. Table XV. p. 219, gives the results.

During the first eight days $\frac{1}{6}$ of a grain of corrosive sublimate was given twice a day. On July 5th and 6th $\frac{3}{6}$ of a grain were given in the day. On July 7th and 8th the dose was $\frac{1}{3}$ of a grain twice a day. Until July 8th the animal continued in good health; then its appetite began to fail.

The average amount of bile secreted daily during the twelve days from June 27th to July 8th inclusive was, of fluid bile 150·19 grammes, of bile solids 3·374 grammes, and of bile salts 1·135 gramme. During this period the amount of fluid bile was one-sixth less than during the premercurial period; but the diminution in the bile solids was still more marked, the average quantity not being much more than a half of what was secreted during the premercurial period. This diminution was entirely due to a decrease in the organic solids of the bile, indeed the amount of the *inorganic* solids was slightly increased.

On July 9th two-thirds of a grain were given, as on the two previous days. The falling off in the appetite now became more marked, and the animal looked ill. There was a great failure in the biliary secretion; fluid and solid bile were reduced to about a half of what they had been on the previous day. One-third of a grain was given upon the following day (10th). This was the last dose. Symptoms of seriously deteriorated health were very apparent some hours after it was given. The animal refused almost all food; it looked very languid; its breath was fœtid; there was slight salivation, and on the mucous membrane inside the upper lip there was an incipient ulcer, which experience regarding the effects of mercurials on the mouths of other dogs enabled us to recognize as mercurial. The fæces, which previous to the administration of the mercury had been white, were during the greater period of exhibition sometimes white, at other times grey, and during the two last days of a slate-colour. There never was purgation. Latterly the animal became rapidly emaciated. Up to the 6th it maintained its weight well, but during the last four days it lost 3·49 kilo-

grammes. The amount of bile secreted on the 10th was still further diminished, the fluid bile being little more than a ninth of the average quantity secreted during the twelve days from June 27th to July 8th inclusive; while the bile solids were little more than a thirtieth of the average quantity secreted during the same period.

In the case of dog 8 six grains, in that of dog 7 four grains of corrosive sublimate were required to bring about the same result as regards the biliary secretion. This was apparently due to the fact that dog 8 was an older and a stronger dog. But although the biliary secretion held out longer against the drug in this animal, the constitutional symptoms were more marked. Thus salivation, fœtid breath, and ulceration of the gums were present, while these were wanting in dog 7. This fact adds greatly to the value of the observations on dog 8; for it shows when mercury is given to an extent sufficient to increase the function of the salivary glands, it diminishes the biliary function of the liver.

The impression produced by the drug upon the health of dog 8 was deep and lasting. Although its administration and the collection of bile were stopped on July 10th, the emaciation of the animal continued to increase rapidly. The appetite was very poor on the 14th, there was coffee-ground vomiting, blood was passed in the fæces, and there was a decided muco-purulent discharge from the left nostril. The ulcer in the mouth became larger. The animal, which previous to the administration of the mercury had been so strong and vigorous, grew so weak that it could hardly walk, and it was killed July 25th. On dissection six hours after death nothing abnormal was found. The hepatic cells seemed healthy. The intestine, pancreas, and salivary glands were not unduly vascular.

Results of the preceding Observations on the Cholagogue Action of Corrosive Sublimate.

These two series of observations on dogs 7 and 8 so closely resembled each other, and were so perfectly carried out, that there was no possibility of fallacy. They show:—

1. That corrosive sublimate, when given in small doses, gradually increased in strength, does not augment the biliary secretion, but that it diminishes it the moment the dose reaches a strength sufficient to deteriorate the general health.

2. That corrosive sublimate given in the above method may diminish the biliary secretion, while it does or does not produce an evident action on the salivary glands and mouth, and without producing purgation.

3. Case 6 shows that the biliary secretion is likewise diminished when this drug is given in a dose sufficient to produce purgation.

The next subject which engaged our attention was the mode in which the mercury had caused a diminution of the biliary secretion in dogs 7 and 8.

The experiment on dog 8 seemed strongly to point to the diminished consumption of food as the cause of the diminished biliary secretion. With a view to throw further light on this matter, we performed the following experiment on the

Influence of Partial Starvation on the Biliary Secretion.

For the following experiment dog 7 was used, which had thoroughly recovered its health and strength.

Table XVI., p. 219, shows the results of the observations before, during, and after partial starvation.

During the first two days the amount of bile fluid and solids secreted was very nearly the same. The amount of dry food consumed was also nearly alike.

On the 28th, bread, milk, and water were withheld. It was intended to give the usual allowance of tripe, but as it could not be obtained, liver was given instead. On this day the amount of fluid bile fell to 104·8 grammes, as compared with 140 grammes on the two previous days, but the bile solids rose to about a half more than they had previously been. This was almost wholly due to increase of the organic constituents of the bile; for it will be seen from the Table that the bile salts (inorganic solids) were scarcely at all increased. July 29th 453 grammes of water were given without any dry food.

The quantity of fluid bile secreted was only 41·6 grammes, less than a third of the quantity on the days previous to starvation. The amount of bile solids was 2·77 grammes, rather more than a half of the quantity secreted during the first period, while the inorganic constituent of the bile fell to 0·40 gramme, less than a half of the amount during the first period. On the 30th of July it was intended that the animal should return to the diet of July 27th, but the tripe was accidentally withheld. The amount of fluid bile rose on that day to 85·7 grammes, bile solids to 5·11 grammes, and bile salts to 0·87 gramme. Although the dry food consumed on this day was hardly one-fifth of what it was on July 26th, the amount of bile solids and salts was almost the same. On July 31st the partial starvation was discontinued; the animal consumed the same amount of dry food as on July 26th, with nearly a fourth more water. The fluid bile on that day reached a quantity 33·1 grammes above what it was on the 26th, when the same quantity of food was given, while the amount of bile solids and salts was nearly doubled. It is difficult to account for this marked increase in the biliary secretion when the full diet was again given. During the whole experiment the animal was in excellent health, and lost only 0·9 kilogramme in weight.

The preceding observations are sufficient to show that the biliary secretion is greatly influenced by the great amount of food consumed, and it permits of the inference that diminution in the biliary secretion observed in the case of dog 8 under the influence of corrosive sublimate may have been due to impaired appetite. The same explanation cannot apply to the diminution in the biliary secretion observed in the case of dog 7 on June 17 (see Table XIII.); for, as has been previously pointed out, on that day the animal took more food than it had done on many previous days on which it had secreted a larger amount of bile.

On the whole, therefore, the legitimate conclusion seems to be that mercury, when administered so as to impair the general nutrition, lessens the biliary secretion. This may result without impairment of the appetite; but when there is a diminished consumption of food, the failure in the biliary secretion is all the more marked.

Conclusions regarding the Cholagogue Action of Mercury.

The foregoing observations seem to us clearly to show that Pil. Hydrargyri, calomel, and corrosive sublimate, when given to dogs in either small, gradually augmented, or in large doses, do not increase the biliary secretion; they do not even influence it so long as neither purgation nor impairment of health are produced, but they diminish it as soon as they do either or both. It may be

urged that, although we have proved this regarding dogs, it does not follow that on man these drugs will have the same action. It must be admitted that some animals are altogether insensible to remedies which produce powerful effects on others, that different doses are often requisite to occasion similar results, and that there may be peculiarities so very decided as to render it impossible to infer what will be the action of a remedy on one animal from its influence upon another. But have we any reason to conclude that in the present instance there exists such difference in the action of mercury as to prevent any inference being drawn from the dog regarding man? All the facts with which we are acquainted show that it is legitimate to infer that the action of mercury ought to be regarded as similar in both cases. We have demonstrated that, as regards its action upon the salivary glands, mouth, intestine, appetite, and general nutrition, the influence of mercury is the same. We therefore infer that it is in the highest degree probable that its action on the hepatic secretion will also be the same. The only difference that there seems to be between the dog and man, as regards the action of mercury, consists in the fact that in the dog larger doses are generally required to produce the same effects as those observed in man. But even here it may be argued that more marked results are required to satisfy the observer, and hence the greater dose necessary. These circumstances, therefore, cannot be held as affecting the conclusion at which we have arrived.

We have not deemed it worth our while to experiment upon any other animal, for we are unable to see how such experiments could materially strengthen our position. Even though we had shown that mercury when given to a rabbit, cat, pig, donkey, or horse diminishes the biliary secretion, it might still be said that this does not apply to man. But there are several special reasons which render experiments on these animals either impracticable or less reliable than those on the dog. Bidder and Schmidt failed to establish biliary fistulæ in cats, we therefore thought it not worth our while to spend money and time in making the attempt. Horses and donkeys are too unwieldy for the purpose and have no gall-bladders, a peculiarity which would in all probability render it impossible to establish biliary fistulæ in them. In pigs the hepatic secretion differs from that of man, inasmuch as it contains hyocholic acid, and according to Strecker no sulphur. It might, therefore, not unfairly be objected to any inferences from experiments on pigs that, inasmuch as the porcine differs from the human hepatic secretion, it could not be held as altogether probable that mercury would influence both in the same way. Everything seems to show that the animals used by the Committee are those best suited for the observations they have made. In addition to the therapeutical facts previously mentioned, which after all are the most important, there are these, that the qualitative composition of canine is the same as that of human bile, and that the dog, like man, can be fed on a flesh, vegetable, or mixed diet. In this respect they are superior to most others, even to the Quadrumana, which though in conformation most resembling man are vegetable feeders. So far, therefore, as direct experiment and exact observations are capable of determining the influence of mercury upon the biliary secretion, the Committee have no doubt that the dog is superior to the animals above mentioned.

But it may be supposed that mercurials possess some specific power of exciting the biliary secretion by acting on the orifice of the common bile-duct, and so stimulating the secretion through the nerves which connect it with the liver, just as pyrethrum or vinegar stimulates the salivary glands when they are applied to the orifices of the salivary ducts. It might also be objected that,

inasmuch as in our experiments the common bile-duct had been divided, the nerves alluded to might have been so injured that stimulation of the orifice of the common bile-duct could no longer excite the secretion. It remains to be shown, however, that mercurials do specially excite the orifice of the bile-duct. It is not probable, at any rate, that their influence on the biliary secretion was, in the cases of dogs 6, 7, and 8, prevented by division of hepatic nerves. In these experiments the common bile-duct was simply divided with as little injury to neighbouring parts as possible (in previous experiments a portion of the bile-duct was removed), and these animals did not suffer in the least from the shock after the operation; so that nervous injury could not have been extensive. Moreover, in the case of dog 7, the parts around the common bile-duct were dissected after death, and the nerves proceeding from the solar plexus to the liver were found at some distance from the duct, and had apparently suffered no injury at the place where it had been divided. The Committee, therefore, do not attach any value to this objection.

But some may say that although we have proved that mercury diminishes the biliary secretion in dogs and that in man its action will in all probability be the same, yet our experiments have been performed on animals in a state of health, and that had they been made on dogs with diseases such as those in which mercury has been *supposed* to increase the hepatic secretion, it would possibly, in the case of such dogs, have been increased. With such an hypothesis we need not seriously occupy ourselves until the objectors *prove* that, in any case whatever, mercury can increase the biliary secretion in man.

We have been unable to discover any facts brought to light in this or any other age which prove that mercury stimulates the biliary secretion. So far as we can make out, the notion that it does so originates in some vague statement made by Paracelsus*, or the authors of his time, as to the good effects of mercury in what he has called "icteritia." But, we repeat, not only do we not know how such a notion has arisen, but we are ignorant how to make direct observations on the subject in man. We have already stated that such observations are, in the present state of physiological chemistry, impossible (see p. 187). We do not deny the possibility of mercury being useful in some diseases of the liver; we simply say that the notion of its doing good by increasing the biliary secretion is untenable.

Observations on Podophylline and Taraxacum as Cholagogues.

Before concluding our observations on dogs with biliary fistulæ, the Committee thought it would be important to try the effect of two other drugs which have been supposed to exercise a cholagogue influence on the liver, viz. podophylline and taraxacum.

Observations with Podophylline.

Dog 9 was a retriever, about three years old, weighing 26·6 kilogrammes, and the operation for biliary fistulæ was performed upon July 24, 1868. The recovery was rapid. Shortly after the operation the fæces were clay-coloured. Table XVII., p. 225, shows the results of the bile collections previous to, during, and after the administration of podophylline.

* Paracelsus (Aur. Phil. Theoph.), Opera Medico-Chemica, 3 tom. 4to, Francof. 1603-1605. De Icteritiis, vol. i. p. 329.

TABLE XVII.—Observations on Dog 9. Daily amount of Bile secreted before and after the administration of Podophylline.

1	2	3				4			5			6			7
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			For each kilogramme of dog there were secreted			For each 100 grammes of dry food there were secreted			Observations.
	Kilogs.	Water.	Milk.	Bread.	Liver.	Fluid bile.	Bile solids.	Bile. salts.	Fluid bile.	Bile solids.	Bile salts.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grms.	grms.	grm.	grm.	grms.	grms.	grm.	
Aug. 7.	26·6	564	346·6	141·0	676·8	273·0	15·47	1·91	10·2	0·58	0·07	99·3	5·6	0·69	Dog in excellent health. No medicine given.
„ 8.	...	„	141·0	84·6	846·0	285·8	14·54	2·47	...	...	...	...	...	...	Dog in excellent health. No medicine given.
„ 9.	...	„	282·0	112·8	564·0*	304·2	12·98	2·22	...	...	...	...	...	...	2 grains Resina Podophylli given 24 hours previous to this collection. *Bowels not moved.*
„ 10.	26·4	„	84·6	56·4	„	287·0	13·31	2·75	...	...	...	...	...	...	Bowels moved once. Fæces solid.
„ 11.	25·7	„	None	None.	902·4†	203·2	10·85	1·95	7·9	0·42	0·07	97·9	5·2	0·93	4 grains given 24 hours previous to this collection. *Decided purgation.*
„ 12.	...	„	225·6	141·0	None.	238·2	6·62	1·65	...	...	...	...	...	...	Bowels not moved.
„ 13.	24·5	„	„	„	338·4†	151·2	4·00	0·98	6·1	0·16	0·04	82·0	2·1	0·53	6 grains podophylline given 24 hours previous to this collection. *Decided purgation.*
„ 14.	...	„	„	„	676·8	238·4	12·87	1·95	...	...	...	...	...	...	Dog in good health.
„ 18.															

* The collection which followed the administration of the purgative when it did not produce purgation. † Those which followed purgation.

NOTE.—Amount of dry food consumed on August 7, 274·8 grammes, or 10·3 grms. per kilog. of dog; on the 11th, 207·5, or 8·0 grms. per kilog. of dog; on the 13th, 184·0 grammes, or 7·5 grms. per kilog. of dog.

TABLE XVIII.—Fourth Series of Observations on Dog 7. Daily amount of Bile secreted before and after Podophylline was given.

Aug. 7.	28·6	507·6	225·6	141·0	1325·4	246·95	13·91	2·09	..	..	..	..	..	..	Dog in excellent health.
„ 8.	„	„	„	„	1579·2	148·3	9·33	1·40	5·1	0·32	0·04	30·3	1·9	0·29	Has had a smart attack of dysentery; 5 grains Pulv. Doveri removed it.
„ 9.	28·4	451·2	„	„	„	210·5	13·78	1·97							
„ 10.	..	310·2	„	„	„	249·5	12·64	2·04							
„ 11.	..	..	„	..	..	..	..	..	..	..	..	..	..	..	Canula could not be introduced owing to false passages.
„ 12.	..	..	..	..	..	..	..	..	..	..	..	..	..	..	Canula could not be introduced owing to false passages.
„ 13.	..	..	..	..	..	..	..	..	..	..	..	..	..	..	Canula could not be introduced owing to false passages.
„ 14.	28·7	846·0	„	„	„	256·8	12·48	2·01	8·9	0·43	0·07	52·6	2·5	0·41	
„ 15.	28·4	„	„	„	None.	156·1	9·88	1·41	5·4	0·34	0·04	180·0	11·3	1·6	8 grains podophylline given 24 hours previous to this collection. *Profuse purgation.* Dog looking very ill. Staggers when it walks.

NOTE.—The amount of dry food on August 8th was 486 grammes, or 16·9 grms. per kilog. of dog; on the 14th, 486 grammes, or 16·9 grms. per kilog. of dog; on the 15th, 86·8 grammes, or 3·0 grms. per kilog. of dog.

On August 7th and 8th the bile was collected to ascertain the normal secretion previous to the exhibition of the drug. On the ninth day 2 grains of Resina Podophylli (prepared by Messrs. Gardner and Ainslie, druggists, Edinburgh) were given. This amount did not produce purgation. The bile was collected 24 hours after the dose was given, and it was found that the fluid bile had risen from 285·8 to 304·2 grammes, but the solid bile had fallen from 14·5 to 12·9 grammes. On the 10th no medicine was given. On that day the fluid bile fell somewhat, while the solid bile rose. On the 11th 4 grains of podophylline were given. Decided purgation followed. A marked diminution in the fluid and solid bile was the result—the fluid bile fell from 287 to 203·2 grammes, the bile solids from 13·31 to 10·85 grammes. On the 12th no medicine was given: the fluid bile rose to 238·2 grammes, while, strange to say, the bile solids fell to 6·62 grammes. On the 13th 6 grains of podophylline were given. Decided purgation followed. The fluid bile fell to 151·2, the bile solids to 4 grammes. On the 14th no medicine was given, and, notwithstanding the purgation, the dog was in excellent health. On the 14th the fluid bile rose to 238·4, the bile solids to 12·87 grammes.

These observations clearly show that in this case podophylline, when it produced purgation, diminished the biliary secretion. This decrease cannot be accounted for by diminution in the amount of food taken. Certainly such an explanation might be advanced to account for the fall in the quantity secreted on the 11th, but it cannot possibly apply to the great fall upon the 13th.

Little attention need be paid to the increase in the bile fluid on the 9th, when 2 grains of podophylline were given without purgation resulting; for it was only 18·4 grammes, whereas on the 8th there had been a rise of 12·8 grammes over the quantity on the previous day, without any drug having been given; moreover, on the 9th the bile solids fell to a decided extent.

The observations recorded in Table XVIII. p. 225, were made on dog 7, after he had regained his health.

The bile was collected for five days previous to the exhibition of podophylline. On one of these (August 8) the dog had a smart attack of dysentery; on that day the solid and fluid bile was much below what it was on any other day of the period—another evidence of the lowering influence of purgation upon the biliary secretion.

On August 15th 8 grains of podophylline were given; it produced profuse purgation, and so weakened the animal that it staggered when it walked. The bile was collected 24 hours after the dose was given; both fluid and solid bile had undergone a great diminution. It is curious to observe that the purgation produced by the podophylline, although it was accompanied by a diminished consumption of food, did not lessen either the fluid or solid portions of the bile to the extent effected by the attack of dysentery, although the latter was accompanied by comparatively slight depression of the general health and appetite. Throughout the observations in Table XVIII. the fæces were of a slate-colour.

The observations were discontinued owing to the weakness of the animal. The observations recorded in Table XIX. p. 227, were made on dog 5 after it had regained its health.

The bile was collected for two days, August 23rd and 24th, to ascertain the normal secretion. On August 25th and 26th 6 grains of Resina Podophylli were given; both doses occasioned decided purgation. The effect on the biliary secretion was unequivocal. On the day preceding that on which

the first dose was given the fluid bile was 220·9 grammes, bile solids 10·42 grammes; on the following day the fluid bile was 154·5 grammes. After the second dose the fluid bile was 150 grammes, the bile solids 1·95 gramme. The next day (27th) no medicine was given, and the fluid bile rose to 297 grammes, and the bile solids to 11·99 grammes, most conclusively showing that doses of podophylline which produce purgation diminish the fluid and solid constituents of the bile.

TABLE XIX.—Second Series of Observations on Dog 5. Daily amount of Bile secreted before, during, and after Podophylline and Taraxacum were given.

1	2	3				4			5
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			Observations.
	Kilogs.	Water.	Milk.	Bread.	Spleen.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grms.	
Aug. 23.	14·7	566	566	225·6	906·8	282·8	11·56	3·0	Dog in good health, though rather lean. Fæces semisolid.
„ 24.	..	„	„	„	„	220·9	10·42	2·84	Dog in good health, though rather lean. Fæces semisolid.
„ 25.	..	„	„	„	„	154·5	4·20	1·58	6 grains Resina Podophylli given 20 hours previous to the collection of bile. *Profuse purgation.*
„ 26.	14·6	„	„	„	„	150	1·95	0·52	6 grains Resina Podophylli given 23 hours previous to this collection of bile. *Decided purgation.*
„ 27.	..	„	„	„	„	297	11·99	3·21	No medicine given.
„ 28.	..	„	„	„	842·1	396	10·21	2·42	60 grains solid extract of taraxacum given 24 hours before this collection of bile. *No purgation.*
„ 29.	14	„	„	„	906·8	340	9·36	2·12	60 grains solid extract of taraxacum given 24 hours before this collection of bile. *No purgation.*
„ 30.	..	„	„	„	„	Lost.	..	..	No medicine given.
„ 31.	..	„	„	„	„	Lost.	..	..	No medicine given.
Sept. 1.	..	„	„	„	„	317	9·42	2·46	No medicine given.
„ 2.	..	„	„	„	„	355·5	10·61	3·02	No medicine given.
„ 3.	14·3	„	„	„	„	298	9·53	2·27	No medicine given.

NOTE.—As the weight of the dog and the amount of food eaten by it were so constant in this case, we have not thought it necessary to calculate the amount of bile secreted per kilogramme weight of dog, or per 100 grammes of food consumed.

Observations with Extract of Taraxacum.

After dog 5 had had a day's rest from the action of podophylline, 60 grains of solid extract of taraxacum were given 24 hours previous to the collection of bile on August 28th; on that day the fluid bile rose to the extent of 99 grammes, but the bile solids fell to the extent of 1·78 gramme. Next day the same dose was repeated; the fluid bile fell to the extent of 56 grammes, the bile solids to the extent of 0·85 gramme. Neither dose produced any effect upon the bowels. After this no more medicine was given. The bile was unfortunately lost on August 30th and 31st, owing to slipping of the apparatus; on the three following days the amount of fluid bile fluctuated greatly. On September 2nd it was 355·5 grammes,—a larger quantity than that secreted during the 24 hours after the second dose of the taraxacum was given; on that day also (September 2nd) the amount of bile solids secreted was greater than on either of the days on which taraxacum was given. It is therefore evident that the taraxacum did not increase the solid constituents of the bile; and it is extremely probable that the large amount of fluid bile secreted after the first dose was

due to other causes. On September 2nd, when no taraxacum was given, the bile rose to the extent of 38·5 grammes over the amount on the previous day, and on September 3rd it fell to the extent of 57·5 grammes without any assignable cause. On the whole, therefore, it seems that taraxacum exercised no influence upon the biliary secretion. On September 3rd the observations were discontinued, as the margins of the fistula had become much ulcerated.

Taraxacum was also given to dog 7, which had been the subject of the observations recorded in Tables XII., XIII., XVI., and XVIII., which had recovered his health.

TABLE XX.—Fifth Series of Observations on Dog 7. Daily amount of Bile secreted before and during the administration of Extract of Taraxacum.

1	2	3				4			5
Date.	Weight of dog.	Amount of food, in grammes.				Quantity of bile secreted in 24 hours.			Observations.
	Kilogs	Water.	Milk.	Bread.	Tripe.	Fluid bile.	Bile solids.	Bile salts.	
1868.						grms.	grms.	grms.	
Aug. 26.	29·4	846	564	225·6	1353·6	192	8·53	2·10	Dog in excellent health. Fæces solid.
„ 27.	..	„	„	„	„	176	10·52	2·36	Dog in excellent health. Fæces solid.
„ 28.	29·5	„	„	„	„	214	8·93	1·94	60 grains solid extract of taraxacum given twenty-four hours before this collection of bile. *No purgation.*
„ 29.	..	„	„	„	„	188	9·64	2·12	120 grains solid extract of taraxacum given twenty-fours before this collection of bile.
„ 30.	..	„	„	„	„	151	9·99	2·45	
„ 31.	29·3	„	„	„	None.	140	8·43	1·64	
Sept. 2.	..	652	„	„	1353·6	212·2	12·9	3·76	No medicine given. Dog in excellent health.
„ 3.	29·2	846	„	„	„	138	8·04	2·51	
„ 8.	31·2	„	„	„	„	251·1	12·17	3·21	
„ 9.	..	„	„	„	„	169·4	8·61	2·61	
„ 10.	..	„	„	„	„	180·6	8·84	1·98	120 grains solid extract of taraxacum given twenty-four hours before this collection of bile. *No purgation.*
„ 11.	31	„	„	„	„	159	9·12	2·31	240 grains solid extract of taraxacum given twenty-four hours before this collection of bile. *No purgation.* Dog in excellent health.

After the bile had been collected for two days 60 grains of solid extract of taraxacum were given; twenty-four hours afterwards (August 28) the fluid bile rose to the extent of 38 grammes, while the bile solids fell to the extent of 1·59 gramme. Next day (29) 120 grains were given, and the fluid bile fell to the extent of 26 grammes, while the bile solids rose to the extent of 0·71 gramme as compared with the previous day. These doses had no effect upon the bowels. After this, the bile was collected for five consecutive days, on which no medicine was given; on one of these days (September 1) the bile was lost owing to slipping of the apparatus. On September 2 the fluid bile reached a figure very nearly as high as it had attained during the administration of taraxacum, and the bile solids were higher than they had ever been on any of the previous days. On September 4 the apparatus was left off owing to ulceration of the skin; on September 7 it was reapplied, and the bile was collected on the four subsequent days. The large quantities obtained (September 8) the first of these days need not be paid attention to; it was most probably due to escape of bile pent up in the bile-ducts, owing to the canula not having been used during the previous four days. Twenty-four hours previous to the collection on the 10th, 120 grammes of solid extract of taraxacum were given; on that day the fluid bile rose to

the extent of 11·2 grammes, and the bile solids to the extent of 0·23 gramme. Next day 240 grains were given, and the fluid bile fell to the extent of 21·6 grammes, while the bile solids rose to the extent of 0·38 gramme. These doses produced no effect upon the bowels. The fæces were always solid. The dog was in most excellent health when these observations were discontinued.

The observations recorded in Table XX. show, even more conclusively than those recorded in Table XIX., that taraxacum did not influence the biliary secretion in any way whatever.

Results of the Observations recorded in Tables XVII., XVIII., XIX., *and* XX.

1. Doses of podophylline, varying from 2 to 8 grains, when given to dogs diminished the solid constituents of the bile, whether they produced purgation or not.
2. Doses which produced purgation lessened both the fluid and solid constituents.
3. During an attack of dysentery both the fluid and solid constituents of the bile were greatly lowered.
4. Doses of the solid extract of taraxacum, varying from 60 to 240 grains, affected neither the biliary secretion, the bowels, nor the general health of the animal.

Influence of Purgation upon the Biliary Secretion.

The observations of the Committee conclusively show that purgation produced by a variety of causes diminished both the fluid and solid constituents of the biliary secretion. Spontaneous diarrhœa (Table X.), dysentery, (Table XVIII.), and purgation produced by Pil. Hydrargyri (Table X., and non-tabulated observations on dog 7, see p. 214), by calomel (Table X.), by corrosive sublimate (Table XI.), and by podophylline (Tables XVII., XVIII., and XIX.) always diminished the solid constituents of the bile, and with one exception (see July 29, Table X.) the fluid portion of the bile also. That purgation diminishes the biliary function of the liver is one of the most important facts established by the Committee. It is, however, nothing more than what might have been expected, seeing that purgation drains the portal blood from which the bile is almost entirely formed.

Relation of Biliary Secretion to Consumption of Food.

The observations of the Committee show that the relation between the biliary secretion and the amount of food consumed is by no means such a close one as Bidder, Schmidt, Arnold, and others have supposed. On looking at the collections of bile in the healthy animal previous to the administration of drugs, it will frequently be seen that while eating the same food, and without there being any apparent disturbing cause, such as diarrhœa, &c., the amount of bile was nearly a half (Tables II. and III.) and even four-fifths less (Table VIII.) than on previous and subsequent days. Further, it was frequently observed that although the amount of food consumed varied greatly the secretion of bile was remarkably constant. In Table XI. are observations which illustrate this fact. During three days of perfect health the animal secreted very nearly a constant amount of bile fluid and bile solids, although the amount of food varied greatly. Thus on the first day it took 73·7 grammes of dry food, on the second day it took 14·16, and on the third day 62·37 grammes; on these days the amount of bile secreted per

100 grammes of dry food was on the first day 5·64 grammes, on the second day 30·4 grammes, and on the third day 6·9 grammes. The observations recorded in Table XVI. show, however, that the biliary secretion was in the case of dog 7 greatly influenced by the amount of dry food; it will there be seen that the amount of bile secreted was greatly diminished by starvation. It therefore appears that the biliary secretion is in some cases greatly influenced by the amount of food taken, while in other cases it is not influenced at all.

Relation between Biliary Secretion and Weight of Animal.

The close relation supposed to exist between the amount of the biliary secretion and the size or weight of the animal has not been supported by the observations of the Committee. The amount of bile secreted for every kilogramme weight of dog varied greatly in different cases, as the following Table shows.

Table XXI.—Average amount of Bile secreted per Kilogramme Weight of the Dogs observed by the Committee before drugs were administered.

No. of dog.	Fluid bile.	Bile solids.
	grms.	grm.
Dog 1.....	6·47	0·412
„ 1.....	7·82	0·28
„ 2.....	5·27	0·34
„ 3.....	5·76	0·293
„ 4.....	3·53	0·146
„ 5.....	21·8	0·801
„ 6.....	20·66	0·818
„ 7.....	4·64	0·23
„ 8.....	9·24	0·305
„ 9.....	10·2	0·58

The foregoing Table gives the per kilogramme biliary secretion only when the dogs were healthy, and not subjected to the action of drugs. The Table shows how fallacious are the calculations which have been made regarding the human biliary secretion, from observations upon dogs, by Bidder and Schmidt. We at one time thought that the large secretion in the case of dog 5 might be due to the fact that it ate liver instead of muscle like the other dog 9; it secreted nearly as much bile, however, when, instead of liver, it ate spleen. Moreover, such an explanation could not be offered in the case of dog 6, which secreted nearly as much bile per kilogramme as dog 5. This dog was fed on a diet the same as that given to dogs 1, 2, 3, and 4, so that no peculiarity in the nature of the diet can be alleged as the cause of the large secretion in the case of dog 6. Nor can the quantity of food it took have been the cause; for the animal secreted more bile per 100 grammes of dry food than any other dog under the observation of the Committee. Seeing, then, that in the case of dog 6 neither the food nor the size of the animal can at all account for the amount of bile secreted, we must look for the cause elsewhere. One member of the Committee suggested that perhaps the amount of bile secreted may have a closer relation to the size of the liver than to the size of the animal. Unfortunately this idea did not occur until after dog 6 was killed, so that its liver was not weighed; but there is this much to be said, that dog 6 was a young dog (six months' old); and we know that in young animals the liver is larger in pro-

portion to the rest of the body than it is in more advanced age. To ascertain whether or not there be anything in this idea would require observations to be made on dogs of various sizes and ages. The biliary secretion, amount and nature of food, and weight of the animal would require to be observed for three or four days; the animal ought then to be immediately killed and its liver weighed, and calculations based on such data. It is, however, improbable that the size of the liver determines the amount of the biliary secretion; the great variation which we frequently observed in the secretion from day to day in the same animal is opposed to such an idea.

Effect of the loss of Bile upon the Health of the Animal.

Although an animal may live in perfect health for a considerable time without any bile passing into its alimentary canal, it would appear, from the observations of all who have experimented on the subject, that, even when a fistula has been established without accident, the health sooner or later begins to suffer. Emaciation comes on, and death results from inanition. Much depends on the strength of the animal, which, when vigorous, usually preserve their health.

Dog 7, the retriever sent us by Dr. Kelburne King of Hull, had the operation for biliary fistula performed on April 24, 1868. Notwithstanding the wearing of apparatus for collecting the bile during a period of nearly two months, partial poisoning with corrosive sublimate, purgation with podophylline, and dosing with taraxacum, the animal was on the 11th of September, 1868, when our observations terminated, as strong as it was before the fistula was made; and so far from exhibiting any signs of emaciation, it had gained nearly 4 kilogrammes (8·8 pounds) in weight during the five months it lived, without a drop of bile passing into the intestines. Such a case favours the view of Blondlot and Arnold, as to the inutility of the bile for the purposes of digestion. It is in itself quite sufficient to show that the entrance of bile into the alimentary canal is not essential for the health of the animal, and supports the idea that the bile is a secretion destined to be little more than a mere excretion.

Effect of Muscular Movements upon the Flow of the Bile.

It was frequently observed that when the dogs were taken out of their cages, in which their movements were much circumscribed, and allowed to run about, that during the first half hour or so of their increased movement the amount of bile discharged by the fistula was greatly augmented. This was in all probability due to the bile being more rapidly expelled from the hepatic ducts by the pressure upon the liver of the contracting abdominal muscles, which must, when in action, compress the liver like a sponge, and so expel its contained fluid. This fact is valuable in serving to show that exercise may have an important influence upon the liver. It further points out, however, how utterly fallacious must the results have been had we endeavoured to estimate the daily secretion of bile from collections made during a few minutes at a time, such as were made by Bidder and Schmidt, regarding which, however, we have previously expressed our opinion.

It is unnecessary to dwell upon the importance of the results which the Committee have taken so much pains to arrive at. If the refutation of a widespread error be as important as the establishment of a new truth, the practical advantage of demonstrating that mercury is not a cholagogue cannot be too highly estimated. Although in recent times the administration of

mercurials for hepatic diseases has greatly diminished, their employment is still very general, and in India almost universal. Recent cases demonstrate that long-continued salivation and great loss of health have been produced in the attempt to remove old abscesses or other chronic diseases of this organ, and there are few of its lesions in which it is still not thought advisable to try small or full doses of the drug.

On this subject, however, it is unnecessary to dwell at present; the real question is, whether the evidence is satisfactory, or whether further researches are necessary. On this and many other topics connected with therapeutics, what we require are not unfounded assumptions and vague speculations, but positive knowledge based on unquestionable data; these we have furnished, and consider them amply sufficient to demonstrate the fallacy of the opinions everywhere prevalent as to the cholagogue action of mercury.

It would be vain attempting to convey an adequate idea of the great labour, wearisome repetition of observations, numerous disappointments, and loathsome manipulations which have tested the zeal, endurance, and courage of Drs. Rutherford and Gamgee, on whom the entire labour of the experiments devolved.

The difficulties and expense have been greatly increased by the want of a proper locality for carrying on such investigations, and by the necessity of combating the well-meaning but, we humbly think, mistaken notions of those who maintain that physiologists are not justified in experimenting on animals, even with the objects of determining more accurately the use of poisonous drugs and of preserving the life of man. A very different doctrine might have been expected to exist in a great University like that of Edinburgh; but its Senatus, led astray by the reasoning, we regret to say, of an influential member of the Medical Faculty, unquestionably, by its resolutions, greatly added to the toil and annoyance of the Committee's proceedings. On the other hand our warmest thanks are due to Mr. Nunneley of Leeds, to Dr. Kelburne King of Hull, and Dr. Andrew Buchanan of Glasgow, for their kind assistance in forwarding animals to us.