REPORT OF THE EDINBURGH COMMITTEE ON THE ACTION OF MERCURY, PODOPHYLLINE, AND TARAXACUM, ON THE BILIARY SECRETION.

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PART II.

THE number of this JOURNAL for July, 1868, contains the first part of this report, which was altogether historical. The concluding part, containing the researches of the Committee, is now given. With a view of completing the subject, additional investigations have been made as to the action of podophylline and of taraxacum on the liver. The whole inquiry occupied two years, and, so far as the Committee believe, is quite exhaustive, and leaves nothing to be desired.

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 collection of the bile for a period of at least twenty-four hours at a time was considered incumbent, to insure accuracy and to avoid error. The proceeding caused much trouble, and was attended with frequent 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 each 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. In 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 cannula 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 cyst with the hepatic duct, and that the intervening portion should be excised. The object is to prevent as much as possible the re-establishment 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; full-grown strong good-tempered dogs of any breed should alone 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 cannula. 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 cannula 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 cannula, 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 cannula, provided a perfectly free exit be allowed through it. The cannula 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 permitted 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 cannula 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 cannula by means of a large sponge. In this way no resistance was offered to the flow of bile through the cannula, such as is apt to occur when the bag is used, by its flowing over the free end of the tube. This acted by 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 immovably 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 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 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 diluted hydrochloric acid, in order that they might be thoroughly disinfected, 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 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 sporgy gums in three dogs out of five (*Mercur und Syphilis*, Berlin, 1861, pp. 110-114), and Murray in his experiments with large doses of calomel also produced salivation in one dog (*Transactions of Med. and Phys. Society of Bombay*, 1841, p. 11) 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 so little result, that it was resolved to adopt the more commodious method of subcutaneously injecting a solution of corrosive sublimate. This investigation was undertaken by Dr. W. Rutherford, who carried it to a successful termination.

[A Table is here given, showing the daily progress of the experiment in each of the six dogs operated on. The following is a summary.]

1. Dog A; retriever, 12 months old, weight 30½ lbs.; animal in excellent health; feces light brown, semi-solid. Corrosive sublimate was given during 18 days; the dose being $\frac{1}{10}$ th of a grain on the first day, gradually increased up to $\frac{1}{10}$ th grain on the 14th, 15th, 16th, and 17th days. On the latter two days, 20 and 30 minims of tincture of opium were administered; and on the 18th day, $\frac{1}{10}$ th of a grain of corrosive sublimate were given. Nasal discharge set in on the 15th day, and diarrhoea on the 16th; and both increased. Salivation was first noticed on the 18th day; and on the next day the animal was found dead, with a copious stream of fluid, evidently from the mouth, on the floor of the cage. The weight of the dog, when dead, was 22 lbs.

2. Dog B; collie, 5 months old, weight 18½ lbs.; animal in excellent health; feces solid, brown. Corrosive sublimate was given during 8 days, in doses increasing from $\frac{1}{10}$ th to $\frac{1}{5}$ th of a grain. On the 9th day, $\frac{1}{4}$ grain of muriate of morphia was given; on the 10th and 11th, 30 minims of tincture of opium on each day; on the 12th, no medicine was given; and on the 13th day the dog was found dead. There was decided salivation on the 11th day, less on the 12th. A slight nasal discharge appeared on the 10th day, and had become very abundant and muco-purulent on the 12th. Diarrhoea set in on the 9th day, was very profuse on the 10th and 11th, but had nearly ceased on the 12th. The dog, when dead, weighed 14½ lbs.

3. Dog C; Skye terrier, 15 months old, weight 24½ lbs.; animal in excellent health; feces solid, light brown. During 7 days, corrosive sublimate was given, in doses increasing from $\frac{1}{10}$ th grain to $\frac{1}{10}$ th grain. On the 7th day, 30 minims of tincture of opium were also given; on the 8th day, the dog had no medicine; on the 9th, $\frac{1}{10}$ th grain of corrosive sublimate were administered. Profuse salivation, with slight nasal discharge, was observed on the 8th and 9th days; and on the 10th the dog was found lying with a stream of saliva flowing from the mouth, and ulceration of the gums, tongue, and lips. It died in the afternoon, with slight convulsions. Weight 21½ lbs.

4. Dog D; young retriever, 6 months old, weight 11½ lbs.; animal rather weak; feces clay-coloured. $\frac{1}{10}$ th grains of corrosive sublimate was given in two doses, with an interval of twenty hours. Twenty hours after the first dose of $\frac{1}{10}$ th grain, a nasal discharge of mucus was observed. Two hours after the second dose, the dog was in a state of constant tremor, and staggered in attempting to walk. Liquid clay-coloured feces, mixed with blood, were passed. The nasal discharge was increased. There was no apparent salivation, nor factor of breath. The dog was found dead 36 hours after the first dose; weight 11 lbs.

5. Dog E; bulldog, 2 years old, weight 38½ lbs.; animal in excellent health; feces clay-coloured. During 13 days, corrosive sublimate was given, in doses increasing from $\frac{1}{10}$ th grain to $\frac{1}{2}$ grains daily; and on the 14th day no mercury was given. The appetite first became impaired, on the 13th day. On the 14th, there was a slight nasal discharge; profuse salivation; no purging; feces clay-coloured, free from blood. The animal died during the night of the 15th day; it weighed 31½ lbs.

6. Dog F; collie, 18 months old, weight 37 lbs.; animal in excellent health; feces semi-solid, clay-coloured. Corrosive sublimate was given during 7 days, in doses increasing from $\frac{1}{10}$ th grain to 6 grains in a day. The appetite was first noticed to be much impaired on the 6th day; on the 7th day, the feces were slate-coloured and semi-solid; this character they retained, but on the ninth day they contained some blood. On the 8th day (no mercury), there were slight nasal discharge; foetid breath; salivation; and ulceration of the skin where the injections were made. On the 9th day, the nasal discharge and salivation were more decided; the dog vomited everything it took. It died during the night. The weight was 30 lbs.]

Of the six dogs experimented on, three had, and three had not biliary fistulae 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 the drug; of these three (A, B, and C) were small dogs without fistulae, while two (E and F) were large strong dogs with fistulae.

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 fistula—aged 5 (B), 12 (A), and 15 (C) months respectively—all of them small animals, decided salivation followed the administration of $4\frac{1}{2}$ grains of corrosive sublimate, extending over a period of eight days, to the dog aged 5 months; of $12\frac{1}{2}$ grains, extending over a period of eighteen days, to the dog 12 months old; and of $7\frac{1}{2}$ grains, extending over a period of nine days, to the dog 15 months old.

In two large strong dogs (E and F) with biliary fistulae, 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 (D) was a retriever six months old, which was poisoned by $1\frac{3}{4}$ 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 any one that the doses required to produce salivation in these dogs were much larger than those usually required in the case of man. The dose required in the dog is, however, perhaps not nearly so large as the Table (as analysed above) would make 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 foetid. 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 faeces of all the dogs, excepting dog E. Profuse diarrhoea was produced in all the dogs without biliary fistulae; it was slight in the 'little dog D, while it was entirely absent in the other two dogs with fistulae, although these, like all the other dogs, were killed by corrosive sublimate. During the administration of the drug, the faeces 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 ileum. 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 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 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 into 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.*

* The daily results of each series of observations are recorded in tables, giving (1) the date; (2) the weight of the dog; (3) the amount of food—water, bread, milk,

Observations with Pilula 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 faeces became clay-coloured. The general health of the animal was excellent when, on June 10th, the apparatus for collecting the bile was applied, and the observations were commenced.

The observations were undertaken with a view to ascertain the average amount of bile secreted daily before 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 the secretion was very inconstant. Thus on June 15th the quantity secreted (75.7 grammes fluid bile) was only about a half of what it was upon the 11th (150.4 grammes).

[The observations commenced on June 11th, and ended on June 19th]. Three days (the 13th, 14th, and 16th) have been omitted, owing to a portion of the bile having been lost. This resulted from the slipping of the apparatus. Despite every care in its adjustment, it was sometimes so shifted by the movements of the animal that the cannula 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; [being milk, 567 grammes; bread, 170.1 grammes; meat, 283.5 grammes]. 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.

The amount of fluid bile, bile-solids, and salts secreted has been estimated with regard to each kilogramme-weight of the animal, and each 100 grammes of dry food consumed by it. [The amounts in relation to each kilogramme of the animal were, in grammes: fluid-bile—maximum, 8.12; minimum, 4.09; average, 6.47: bile-solids—maximum, 0.478; minimum, 0.313; average, 0.412: bile-salts—maximum, 0.066; minimum, 0.045; average, 0.068. For each 100 grammes of dry food the quantities were, fluid bile—maximum, 65.5; minimum, 32.9; average, 52.18: bile-solids—maximum, 3.85; minimum, 2.52; average, 3.32: bile-salts—maximum, 0.53; minimum, 0.36; average, 0.548. The amount of dry food consumed during the six days amounted to 22.5 grammes, or 12.3 grammes for each kilogramme of dog.] The experience of the Committee has shown that there is no relation between the amount of bile secreted and the weight of the animal; nor is the relation between the amount of food consumed and the quantity of bile secreted a very close one; 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 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 29th June, and continued for other six consecutive days. 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; this expectation, however, was not realised; 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 previously to the administration of a drug were seldom prolonged beyond four or five days.

The average amount of fluid bile secreted daily during this series of

and meat; (4) the quantity of fluid bile, bile-solids, and bile-salts, secreted in twenty-four hours; (5 and 6) the amount of fluid bile, bile-solids, and bile-salts, secreted in proportion to each kilogramme of the animal and to each 100 grammes of dry food. In columns 5 and 6, the 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 estimated from the average quantities of columns 2, 3, and 4.

* 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.

† By the term bile-salts is meant the inorganic solids of the bile left after its incineration.

observations (131.31 grammes) was slightly above the average amount secreted during the preceding series; but there was a great diminution in the bile-solids. The average quantity during the first series was 7.62 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, during the second series, the inorganic solids (*bile-salts*) were somewhat greater in amount (1.343 grammes) than they were during the first series of observations. [The maximum, minimum, and average quantities (in grammes), in proportion to each kilogramme of dog, were: fluid bile, 11.01, 4.85, and 7.82; bile-solids, 0.392, 0.177, and 0.28; bile-salts, 0.119, 0.049, and 0.079. For each 100 grammes of dry food they were: fluid bile, 80.6, 35.5, and 57.21 grammes; bile-solids, 2.87, 1.29, and 2.05; bile-salts, 0.87, 0.35, and 0.58. The total amount of dry food consumed was 229.5 grammes, or 13.6 grammes for each kilogramme of the animal.] 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 July.

As it seemed impossible to obtain a better standard of comparison than that here afforded, it was resolved to commence the administration of mercury. Five grains of pilula hydrargyri were given as one dose daily during eight days; the pill was always given twenty-four hours previously 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. [The weight of the dog was now 15 kilogrammes. The daily quantity of food was the same as in the preceding two series of observations; the total amount of dry food in nine days being 229.5 grammes or 15.27 to each kilogramme of dog. The maxima, minima, and averages were: in proportion to each kilogramme of the animal, fluid bile, 13.6, 4.46, and 8.50 grammes; bile-solids, 0.39, 0.19, and 0.344 grammes; bile-salts, 0.152, 0.042, and 0.09; for each 100 grammes of dry food, fluid bile, 88.8, 29.19, and 5.56; bile-solids, 3.52, 1.246, and 2.24; bile-salts, 0.99, 0.31, and 0.601.] 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, more fluid and solid bile (204 grammes and 8 grammes) 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 the amount of fluid and solid bile (67 grammes and 2.86 grammes) was less than it had 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. 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.

Pilula hydrargyri was again given. Extraordinary variations occurred in the amount of bile obtained during its administration, 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 faeces. Although it did not lose weight to any notable extent, 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 ap-

plied, 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 faeces 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.

In this case, as well as in several others, 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 cannula having permitted a freer exit to the bile than the fistulous opening which the contraction of the recti abdominis always tended to close. At first, therefore, after the introduction of the cannula, 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 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 (varying from 230.0 grammes of fluid-bile, 12.9 of bile-solids, and 2.51 of bile-salts, on the first day, to 73.9 grammes of fluid bile, 5.60 of bile-solids, and 1.18 of bile-salts, on the fifth day.) The general health of the animal had not materially suffered by the continued application of the apparatus, although it at first occasioned much distress.

It was now decided to observe the effects of calomel. During six days, calomel was given internally in varying doses. [The amounts were: 1st day, 3 doses of 2 grains=6 grains; 2nd day, 1 dose of 2 grains; 3rd day, 3 doses of 2 grains=6 grains; 4th day, 4 doses of 2 grains=8 grains; 5th day, 6 doses of 2 grains=12 grains; 6th day, 2 doses of 2 grains=4 grains.] 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 (5th and 6th days), and died on October 5th, apparently from inanition. Purgation, foetor 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 (second day). Under the action of the calomel, less bile was secreted than there was previously to its administration; 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 was healed satisfactorily, the faeces 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 ($\frac{1}{12}$ th of a grain) frequently repeated. The bile was collected on four successive days previous to, and on four consecutive days during the administration of the drug, without any break between the two series.

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.

On October 30th seven pills, each containing $\frac{1}{12}$ th 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.

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 3rd, apparently from inanition. No salivation, foetid breath, ulceration of gums, or purgation was produced by the medicine.

The average of the second series of observations shews 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 [fluid bile 70.32 grammes, bile-solids 3.732

* The table shews that the quantities of fluid bile on the seven days comprised in this series were, in grammes, 231.9, 56.7, 95.0, 42.1, 38.2, 175.0, and 69.3; of bile-solids, 7.55, 1.61, 2.86, 1.73, 1.47, 4.88, 2.64. No estimate of bile-salts could be given for the 1st, 2nd, and 4th days; but the quantities ranged from 0.443 gramme on the 5th day to 1.66 on the 6th.

grammes, bile-salts 0.89 *gramme*]; thus distinctly showing that the calomel cannot be said to have affected it at all. [For each *kilogramme* weight of the dog, the average quantities were: before calomel was given, fluid bile 5.47, bile-solids 0.293, bile-salts 0.064; after calomel was given, fluid bile 5.76, bile-solids 0.305, bile-salts 0.072.] 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 of the next experiment show that such is not the case.

Dog 4 was a healthy collie, about eighteen months old, weighing 19 *kilogrammes*. 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 cannula was not introduced. Instead of the cannula 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 feces became clay-coloured soon after the fistula was established. The general health of the animal was excellent when the observations were begun.

The bile was collected for five consecutive days previously 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*. [The amounts for each *kilogramme* of dog were, fluid bile, 3.53 *grammes*; bile-solids, 0.146; bile-salts, 0.044; for each 100 *grammes* of dry food, fluid bile, 40.13; bile-solids, 2.148; bile-salts, 0.503]. 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 the bile on that day, ten pills, each containing one-twelfth of a grain of calomel, were given, one pill at a time, at intervals of an hour. On the next day twelve such pills were given. On November 10th ten grains of pilula hydrargyri were administered in one dose. On the 11th and 12th no mercury was given. On the 13th the ten grains of pilula 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, the mean amount of bile secreted was diminished to 35.46 *grammes*, or nearly one half of what it was in the period preceding the administration of the mercury; although nearly as much food was consumed during as before the administration of the drug. [The mean amount of bile-solids was 1.812 *grammes*, of bile-salts 0.436 *grammes*. The average amounts for each *kilogramme* of dog were, fluid bile, 1.93 *grammes*; bile-solids, 0.099; bile-salts, 0.023; for each 100 *grammes* of dry food, fluid bile, 24.18 *grammes*; bile-solids, 1.23; bile-salts, 0.29]. Moreover, during the second period, the average amount of bile secreted was, on the whole, greater on the days when no mercury was given than on the other days. No purgation or any other 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 of purgative doses upon the biliary secretion. 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 re-obtained on the 11th of July. The fistulous opening had closed, the dog was jaundiced, the conjunctiva and skin yellow, and the urine loaded with bile. As the feces 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 feces

were clay-coloured, and the wound was sufficiently healed to permit of observations being begun.

The bile was collected perfectly on six days [July 22nd to 28th inclusive, except the 27th] in order to ascertain the normal secretion. The average daily quantity during this period was 357.4 *grammes* of fluid bile, 13.11 *grammes* of bile-solids, and 3.12 *grammes* of bile-salts. [The average amounts for each *kilogramme* of dog were, fluid bile, 21.8 *grammes*; bile-solids, 0.801; bile-salts, 0.190; for each 100 *grammes* of dry food, fluid bile, 92.9 *grammes*; bile-solids, 3.49; bile-salts, 0.811]. During the first four days the dog was in excellent health. On July 26th it was seized with a smart attack of diarrhoea; on that day both the fluid and solid portions of the bile were diminished. The diarrhoea 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 previously to the collection of the bile on the 29th, ten grains of blue pill were administered. During the succeeding three days ten grains of calomel were given daily in one dose, on each occasion twenty-four hours previously 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 last two 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*. [The mean quantities were, for each *kilogramme* of the dog, fluid bile, 17.4 *grammes*; bile-solids, 0.496; bile-salts, 0.131; for each 100 *grammes* of dry food, fluid bile, 89.2 *grammes*; bile-solids, 2.54; bile-salts, 0.674]. It will be seen that the diminution was quite as marked in the solid as in the fluid bile. The high amount (390.2 *grammes*) 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 solid constituents of the bile are, however, those which are of paramount importance in the present inquiry; and the diminution of these on the same day (to 9.59 *grammes* bile-solids and 2.77 bile-salts) is unmistakable.

The bile was finally collected for two days, August 2nd and 3rd, on which no mercury was given. There was no purgation on those 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. [viz. on August 3, fluid bile, 2.43 *grammes*; bile-solids, 7.59; bile-salts, 2.43].

Previously to the exhibition of mercury the feces were of a clay-colour, mixed with slate-colour 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 diarrhoea 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 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's 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 ten-grain dose of blue pill given on July 29th, although it diminished the bile-solids, increased the fluid-bile. 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. Hence 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 Chologogue Action of
Pilula Hydrargyri and Calomel.*

1. Pilula hydrargyri, when given in doses which did not produce purgation, caused no increase of the biliary secretion.
2. Pilula hydrargyri, when given in doses which produce purgation, diminished the biliary secretion.
3. Calomel, given in doses of one-twelfth of a grain, from six to fourteen times a day, and in doses of two grains from two to six times a day, did not produce purgation or increase the biliary secretion.
4. Calomel, when given in doses which produced purgation, diminished the biliary secretion.

Observations with Corrosive Sublimate.

Dog 6 (already referred to as dog D), a retriever, 6 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 by the effects of the fistula.

During the three days previous to the administration of the mercury, the secretion of fluid and solid bile was remarkably constant, notwithstanding great variation in the amount of food taken. The mean quantities were: 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 four-fifths 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 semi-solid 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; and 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 fetid. 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 could no longer 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 cannula. The result of this experiment was briefly this: 1½ grains of 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. On dissection, the stomach 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 administration of small doses.

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.

During five days previous to the administration of corrosive sublimate, the amount of food consumed was constant: [water, 846 grammes; milk, 564 grammes; bread, 225.6 grammes; tripe, 1353.5 grammes]. On May 31st the bile was 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.

During three days, one-sixth 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 16th), the dose was increased to one-third of a grain at the second injection.

During these ten days, the biliary secretion underwent marked varia-

tions; 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 17th, the increased dose of one-third of a grain twice a day was given. Although these doses produced no purgation, fetid breath, or salivation, yet the dull eye and general drooping uneasy aspect of the animal shewed that the general health was decidedly impaired. [The fluid bile fell from 115.7 grammes on the 16th to 32.7 grammes on the 17th; and the bile-solids from 7.39 to 2.62 grammes.] The amount of food consumed, however, had been but slightly diminished; but 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 18th, only one-third 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. The dog looked miserable and lifeless; there was no salivation, fetid breath, nasal discharge, nor 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 18th, the biliary secretion, instead of undergoing a still further diminution, consequent on 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 average proportions to each kilogramme of dog from June 6th to 16th were, fluid bile, 4.414 grammes; bile-solids, 0.217; bile-salts, 0.036; on June 18th, fluid bile, 1.97; bile-solids, 0.10; bile-salts, 0.014. To each 100 grammes of dry food the proportions were, from June 6th to 16th, fluid bile, 37.4 grammes; bile-solids, 1.44; bile-salts, 0.239; on June 18th, fluid bile, 73.6 grammes; bile-solids, 3.01; bile-salts, 0.56. The mean daily amount of dry food from June 6th to 16th inclusive was 414.11 grammes; on the 18th, it was reduced to 73.9 grammes].

The collection of the bile was in this case quite perfect on every day, with one exception (May 31). 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 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 2d of June, 1868. The recovery was rapid, and observations, with a view to determine the normal secretion of bile, were commenced June 17th.

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 diarrhoea, 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. A diminution of the biliary secretion, which occurred on the 21st, cannot be ascribed to the diarrhoea, 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 average daily amount of dry food from June 18th to June 25th, was 181.3 grammes; on the 26th, 389.06 grammes were given. For each kilogramme of dog were secreted an average of fluid bile, 9.24 grammes; bile-solids, 0.305; bile-salts, 0.054. The proportions to each 100 grammes of dry food were, fluid bile, 51.84; bile-solids, 1.714; bile-salts, 0.307 grammes]. 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.

During the first eight days, one-sixth of a grain of corrosive sublimate was given twice a day. On July 5th and 6th, three-sixths of a grain were given in the day. On July 7th and 8th, the dose was one-third 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 of 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; the amount of the *inorganic* solids was slightly increased. [The proportion to each *kilogramme* of dog were, fluid bile, 7.62 *grammes*; bile-solids, 0.171 *grammes*; bile-salts, 0.057 *grammes*: to each 100 *grammes* of dry food, fluid bile, 49.2; bile-solids, 1.105; bile-salts, 0.372.]

On July 9th, two-thirds of a grain were given, as on the previous two 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 foetid; 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 recognise as mercurial. The faeces, which, previously to the administration of the mercury, had been white, were, during the greater period of administration, 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 *kilogrammes*. 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, foetid 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 that, 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 faeces, 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 Chologogue 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 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.

Influence of Partial Starvation on the Biliary Secretion.—For the following experiment, dog 7 was used, which had thoroughly recovered its health and strength. 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 [560.9 *grammes*].

On July 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. [The amount of dry food was 104.2 *grammes*.] 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. The bile-salts were scarcely at all increased. On July 29th, 543 *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*, of bile-solids to 5.11 *grammes*, and of 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 of 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 shew that the biliary secretion is greatly influenced by the great amount of food consumed, and it permits 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 biliary secretion observed in the case of dog 7 on June 17; for 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 Chologogue Action of Mercury.

The foregoing observations seem to us clearly to shew that blue pill, 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 produce 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 shewn 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 fistulae 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 in all probability would ren-

der it impossible to establish biliary fistulæ in them. In pigs, the hepatic secretion differs from that of man, inasmuch as it contains hycolic 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 dogs are superior to most other animals, 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 and vinegar stimulate 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 shewn, 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. 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 the 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 24th, 1868. The recovery was rapid. Shortly after the operation, the fæces were clay-coloured.

On August 7th and 8th, the bile was collected to ascertain the normal secretion, previously to the exhibition of the drug. On the 9th, 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 twenty-four hours after the dose was given: 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 [to 287 *grammes*], while the solid bile rose to 13.31 *grammes*. On the 11th, 4 grains of podophylline were given. Decided purgation followed. A marked diminution in the fluid and the 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. The fluid bile now rose to 238.4, the bile-solids to 12.87 *grammes*.

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 when 207 *grammes* of food were consumed but it cannot possibly apply to the great fall upon the 13th [when the animal had 104 *grammes*].

Little attention need be paid to the increase in the fluid bile 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 of the previous day, without any drug having been given. Moreover, on the 9th the bile-solids fell to a decided extent.

The next series of observations was made on dog 7, after he had regained his health.

The bile was collected for five days previously to the administration of podophylline. On one of these (August 8th), 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. [The fluid bile fell from 246.95 to 148.3 *grammes*, and the bile-solids from 13.91 to 9.33 *grammes*.]

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 twenty-four hours after the dose was given. Both fluid and solid bile had undergone a great diminution. [The fluid bile had fallen from 256.8 to 156.1 *grammes*; the bile-solids from 12.48 to 9.88 *grammes*.] 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 these observations, the fæces were of a slate-colour. The observations were discontinued, owing to the weakness of the animal.

The next series of observations was 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*, the bile-solids 10.42 *grammes*. On the following day, the fluid bile was 154.5 *grammes*, the bile-solids 4.20 *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.

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 twenty-four hours previously 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 following three days, the amount of fluid bile fluctuated greatly. On September 2nd, it was 355.5 *grammes*—a larger quantity than that secreted during the twenty-four hours after the second dose of the tarax-

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

acum 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. [The daily amount of food consumed by the animal from August 22nd to September 3rd was the same; being 566 *grammes* of water, 563 of milk, 225.6 of bread, and 906.8 of spleen.]

Taraxacum was also given in dog 7, which had recovered his health. After the bile had collected for two days, 60 grains of solid extract of taraxacum were given. Twenty-four hours afterwards (August 28th), the fluid bile rose to the extent of 38 *grammes* [from 176 to 214 *grammes*] while the bile-solids fell to the extent of 1.59 *gramme* [from 10.52 to 8.93 *grammes*]. Next day (28th), 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 1st), the bile was lost, owing to slipping of the apparatus. On September 2nd, 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 4th, the apparatus was left off, owing to ulceration of the skin. On September 7th, it was re-applied, and the bile was collected on the four subsequent days. A large quantity of bile [251.1 *grammes* fluid bile and 12.17 *grammes* of bile-solids] was collected on September 8th; this was most probably due to the escape of the bile pent up in the bile-ducts, owing to the cannula not having been used during the previous four days. Twenty-four hours previously 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* [169.4 to 180.6 *grammes*]; and the bile-solids to the extent of 0.23 *gramme* 8.61 to 8.84 *grammes*. 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 feces were always solid. The dog was in most excellent health when these observations were discontinued. [It had increased in weight from 29.4 *grammes* to 31 *grammes*. The daily amount of food was uniform: viz., water, 846 *grammes*; milk, 564 *grammes*; bread, 225.6 *grammes*; and tripe, 1353.6 *grammes*: except on August 31st, when no tripe was given, and on September 2nd, when 652 *grammes* of water only were given to the animal.]

The observations recorded in this case show even more conclusively than those in the preceding that taraxacum did not influence the biliary secretion in any way whatever.

Results of the Observations on Podophylline and Taraxacum.

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 diarrhoea, dysentery, purgation produced by pilula hydrargyri, by calomel, by corrosive sublimate, and by podophylline, always diminished the solid constituents of the bile, and, with one exception, 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 diarrhoea, etc., the amount of bile was nearly a half and even four-fifths less 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 the observations on dog No. 6, 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* 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 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.

NO. OF DOG.	FLUID BILE.	BILE-SOLIDS.
1	6.47 <i>grammes</i> .	0.412 <i>grammes</i> .
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 " "	0.35 " "
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 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 proportion 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 animals, 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 24th, 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, 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 at which the Committee have taken so much pains to arrive. If the refutation of a wide-spread 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 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 opinion every where 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 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.

PROFESSOR HUXLEY'S HUNTERIAN LECTURES ON THE ANATOMY OF THE VERTEBRATA.

Delivered at the Royal College of Surgeons of England.

LECTURE XI.

In his eleventh lecture, Professor Huxley began by calling attention to the main points in the cranial structure of Reptiles and Birds, illustrating the former by the skull of the Crocodile. In these classes we have the four occipital elements—the basioccipital, the two exoccipitals, and the supraoccipital. The penultimate cranial segment exhibits the basisphenoid, the alisphenoid, and the parietals. The segment in front of this is much less perfect in bony development, as it consists of but the presphenoid and the frontal, or of the latter only. The prootic is constantly ossified, and the opisthotic remains a distinct bone (the occipital externe of Cuvier) in Chelonians, but in them only amongst Sauropsida.

The bones of the face of Lizards consist of small premaxillæ in front, and immediately behind them, in the middle line, the vomer; while behind them, on each side, are the maxillæ. The palatine bones bound posteriorly the openings, which are termed the "posterior nares," but which, in reality, answer to the median part of the nasal passages of Mammals. Behind the palatines are the pterygoids, while, external to them, is placed, on each side, an os transversum.

In Chelonians, all the cranial and facial bones are firmly united to each other by sutures, but the os transversum is wanting. The Turtles have a supplementary cranial arch formed by such an extension of the several bones that the temporal fossa is completely roofed over, the skull having thus, as it were, a double wall.

In the Crocodiles, the maxillary and palatine bones develop plates in such a way that the posterior nasal openings are thrown far back, as in Mammals; and, indeed, not these bones only, but the pterygoids also.

The Eustachian tubes are singularly complicated, and are brought down to the base of the skull. Air-cavities are formed in the cranium, and are connected with the tympanic cavity, and penetrate the os articulare, reaching the latter by the fibrous tube before noticed, passing to the last-named bone from the os quadratum. It is very surprising to see these air-cavities in the skull of the Crocodile, where they are found even in individuals not yet hatched. They are remarkable anticipations of what we meet with in Birds.

The Ophidian skull has not only the os quadratum very moveable, but even also the squamosal which supports it, and which is united to the skull by ligament only in the adult, though in the embryo it is more in its normal condition. The hyoidean arch nearly aborts altogether, a mere rudiment of it being left in the adult in the shape of a small arch of cartilage in front and on each side of the glottis. In the poisonous snakes, the pterygo-palatine osseous rod is so connected with the small poison-fang bearing maxilla that, by the opening of the mouth, and consequent thrusting forwards of the distal end of the quadrate, the fang becomes erected. This fang, as is well known, is traversed by a canal formed by the bending round of the tooth, and having nothing to do with the pulp-cavity.

Snakes have the different bones of the face so mobile and loosely articulated, that the jaws and gape can be immensely dilated; and the process of swallowing may more accurately be spoken of as the drawing of the swallower over the body of his victim.

In Birds, the premaxilla is enormously produced, while the maxilla is reduced to a slender rudiment, though it does not abort. The latter is continued on to the quadrate by a small quadrato-jugal bone; and in some Birds—notably in the Parrots—this structure, together with a great flexibility of the root of the upper jaw, elevates the latter when the mouth is opened, somewhat as has been mentioned in speaking of poisonous serpents.

As regards Mammals, the Professor called attention to the great size of the Malleus, and the rudimentary state of the Incus in the Echidna—conditions according well with its other Sauropsidan affinities, on the system of interpretation before advocated respecting these small ear bones. The remarkable peculiarities of the Cetacean skull—which seems at first so very abnormal—were then explained by Professor Huxley by means of the black-board, an outline of the human skull, in profile, being first made, and then modified till the essential Cetacean structure was displayed, and the exact relations of its component parts to those of Man demonstrated; the foramen magnum being made to look backwards, the frontal and occipital made to meet (the