A REPORT

ON

THE BILIARY SECRETION OF THE DOG:
WITH REFERENCE TO THE ACTION
OF CHOLAGOGUES:*Presented to the Scientific Grants Committee of the
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ACTION OF ACETATE OF LEAD.

THE well-known astringent effect of lead-acetate in cases of diarrhoea renders it desirable to know whether or not it has the power of diminishing the secretion of bile. Röhrig ("Experimentelle Untersuchungen über die Physiologie der Gallenabsonderung", *Stricker's Jahrbuch*, 1873, p. 270) experimented with acetate of lead, and found that 0.6 gramme (9.2 grains), dissolved in four ounces of warm water and injected into the small intestine of a dog, diminished the secretion of bile. The erroneous nature of some of Röhrig's results, due to his very imperfect mode of experiment—as pointed out in the introduction to our first series of experiments—rendered necessary a reinvestigation of the effects of lead-acetate.

It has already been stated that, in Experiment 2 (Fig. 2), the administration of eight grains of lead-acetate was followed by a diminution of the bile-secretion, but that the result was of an equivocal nature. In Experiment 3 (Fig. 3), ten grains produced no effect. In Experiment 6 (Fig. 6), a first dose of eight grains, with a second dose of twelve grains, was indeed followed by a diminished bile-secretion; but, as stated in the description of that experiment, the result was entirely equivocal, and therefore other experiments were obviously required.

Experiment 9.—Dog that had fasted seventeen hours. Weight not ascertained. (Fig. 9) Owing to great difficulty in introducing the biliary cannula, and consequent serious disturbance of the bile-duct

Fig. 9.

Secretion of bile before and after lead acetate: 2 grains in 15 cc. of water injected into the duodenum at t_1 , and at t_1 ; 4 grains in 32 of water at t_2 ; 4 grains in 15 cc. of water at t_3 ; 8 grains in 15 cc. of water at t_4 ; and 10 grains in 15 cc. of water at t_5 (30 grains given in all).

and its surroundings, the secretion of bile became, as mostly happens in such a case, very irregular; so much so, indeed, that the record of the first three hours is omitted from the chart. Two grains of lead-acetate in 15 cc. of water were injected into the duodenum at t_1 and t_1 ; four grains in 32 cc. of water at t_2 ; four grains in 15 cc. of water at t_3 ; eight grains in 15 cc. of water at t_4 ; and ten grains in 15 cc. of water at

t_5 . Thirty grains were given in all. The irregularity of secretion rendered the experiment unsatisfactory, and the discovery that the acetate of lead used in this and the previous experiments was impure necessitated another experiment.

Experiment 10.—Dog that had fasted eighteen hours. Weight, 14.6 kilogrammes. (Fig. 10.) Ten grains of pure lead-acetate, dissolved in 10 cc. of distilled water, were injected into the duodenum at t_1 , t_1 , t_1 , and t_1 ; fifty grains in all being given. The decided fall in secretion towards the close of this experiment is abnormal, and may fairly be ascribed to a depressant effect of the lead; but it is obvious that the first doses did not produce the effect which might have been anticipated from Röhrig's experiments. That the liver was not exhausted, however, and was capable of increased action, was proved by injecting into the duodenum twenty grains of sodium-salicylate dissolved in 10 cc. of water. Although it was the ninth hour of the experiment, the biliary secretion became greatly accelerated, and reached a point decidedly higher than it had been at the beginning of the experiment. All the more, therefore, may the previously diminished secretion be ascribed to the depressant action of the lead; while it is obvious that an ordinary dose of sodium-salicylate can excite the liver poisoned and depressed by lead.

Result of Experiments with Lead Acetate.—In large doses, it has a depressant effect on the secretion of bile. Sodium salicylate can overcome that effect. The obstinate constipation observed in cases of lead-poisoning may, to some extent, be owing to the depressant effect of lead on the liver; but it is probably chiefly owing to a depressant action on the intestinal glands; for, in view of the astringent effect of a dose of from one to four grains in diarrhoea, it seems highly probable, from the above experiments, that it affects the intestinal canal much more than the liver. It is a remarkable fact that, of all the substances employed in this research, lead-acetate is the only one which depresses the action of the liver without producing purgation. It seems to be a direct hepatic depressant. As explained in the former series, every purely intestinal purgative agent depresses hepatic action, in a manner which is probably, however, purely indirect, and to which allusion will again be made in the sequel.

ACTION OF AMMONIUM PHOSPHATE AND TANNIC ACID:

In the second series of experiments (this JOURNAL, 1877), it was proved that sodium phosphate is a powerful hepatic stimulant, which can raise the bile secretion to a coefficient of 0.44 cc. per kilogramme of body-weight per hour. It appeared desirable to test the action of ammonium-phosphate. This substance is used in cases of chronic gout, and in urinary affections where uric acid calculi exist or threaten. Nothing is known of its action on the liver, probably because it is not a purgative; and, therefore, the excessive secretion of bile which probably occurs has hitherto passed unobserved. The dose for a man is from five to twenty grains.

The first experiment with this substance yielded a negative result; but it has been thought right to discard it, because the ammonium-phosphate was injected after liquor bismuthi into the same part of the intestinal canal.

Experiment 11.—Dog that had fasted seventeen hours. Weight, 9.7 kilogrammes. (Fig. 11.) Twenty grains of ammonium-phosphate dissolved in 22 cc. of water, were injected into the duodenum at t_1 . The subsequent increased bile secretion was decided and prolonged. Since tannin is employed as an astringent in cases of diarrhoea, twenty grains, dissolved in 20 cc. of warm water, were injected into a fresh portion of the small intestine (t_2); but, as it did not affect the bile-secretion, it was not thought worth while to repeat the dose. Twenty grains of sodium salicylate, in 10 cc. of water, were then injected into a fresh portion of the small intestine (t_3), and, within half an hour, its never-failing effect was evident. Obviously it stimulated the liver much more powerfully than the ammonium-phosphate. At the beginning of the experiment, the coefficient of secretion was 0.19 cc. per kilogramme of body-weight per hour: a fair average for a fasting dog. After the ammonium-phosphate, it rose to the unusually high figure of 0.634 cc.; and after the sodium-salicylate, it rose still higher to 0.89 cc. The result of this experiment being apparently so unequivocal, it was not thought necessary to repeat it. Nevertheless, considering the small size of the animal (21.5 pounds), and that the dose was the maximum dose for a man, it seems reasonable to regard the effect of the ammonium-phosphate in this case as perhaps unduly exaggerated. Probably, now that attention is directed to the matter, it will be found to be a stimulant of the liver in the human subject also.

NECROPSY.—Nothing notable was observed in the intestine.

Result of Experiments with Ammonium-Phosphate and Tannic Acid.—Ammonium-phosphate is a hepatic stimulant, that produced a power-

* Continued from page 912 of last number.

Experiment 10.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog : per hour.
cc.	
1.80	
1.15	
1.25	
1.80	
1.55	
1.70	
1.49	
1.85	
1.55	
1.20	
1.60	
1.15	
1.25	
1.25	
1.20	
1.20	} 0.331 cc.
1.15	
1.10	
0.99	
1.05	
1.00	
0.75	
0.90	
0.95	
0.95	
0.95	
0.80	
0.70	
0.60	
0.80	
0.70	
0.75	} 0.171 cc.
0.65	
0.55	
0.55	
0.55	
0.55	} 0.452 cc.
1.55	
2.10	
2.40	

Experiment 11.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog : per hour.
cc.	
0.35	
0.50	
0.45	
0.40	
0.50	
0.75	} 0.19 cc.
0.80	
1.10	
1.25	
1.10	
1.25	
1.30	
1.50	
1.50	
1.55	
1.60	
1.50	} 0.634 cc.
1.20	
1.05	
1.00	
0.99	
0.99	
0.85	
0.80	
0.80	
0.75	
1.25	} 0.329 cc.
2.50	
2.65	
2.25	
2.25	} 0.89 cc.
2.25	
2.25	
2.25	

Fig. 10.

Secretion of bile before and after lead acetate and sodium salicylate. 10 grains of lead acetate in 10 cc. of water injected into the duodenum at *t* and *t'*: 10 grains in 10 cc. of water at *t''*, *t'''*, and *t''''*; 20 grains of sodium salicylate in 10 cc. of water injected into the duodenum at *s*.

Fig. 11.

Secretion of bile before and after ammonium phosphate, tannin, and sodium salicylate. 20 grains of ammonium phosphate in 22 cc. of water injected into the duodenum at *a*; 20 grains of tannin in 20 cc. of water injected at *t*: 20 grains of sodium salicylate in 10 cc. of water injected at *s*.

ful effect in the single experiment above recorded. It is not an intestinal stimulant.

Tannin does not appear to affect the liver.

[To be continued.]

Erratum.—In the JOURNAL for December 14th, page 861, column 2, line 8 from bottom, for “after” read “before”. In the JOURNAL for December 21st, page 909, column 2, line 26 from bottom, for “1069” read “1869”; page 910, Experiment 3, at sixth horizontal line between numbers, insert letter *b*; page 911, col. 1, Table II, for “0.223” read “0.233”; page 912, col. 1, line 2, for “869” read “1869”.

ON THE IMPORTANCE OF AN EARLY DIAGNOSIS OF STONE IN THE BLADDER, AND THE MEANS OF EFFECTING IT.*

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I HAVE been led to the choice of the subject I to-day bring before you by the sad instances I have seen in our profession in which the existence of a stone in the bladder has been overlooked, and the patient's life endangered or sacrificed thereby. I think it will be admitted by all that there are a number of diseases which are largely under our control; and, if patients would only apply early enough, and their doctors were to exercise reasonable skill and patience in interpreting the phenomena presented to them, we might almost exterminate those complaints, or, at all events, greatly diminish their evil effects. Amongst such diseases I would include stone in the bladder. We all know that the operation of cutting out a stone from a man is a very serious affair. It was Sir Benjamin Brodie's opinion that one-half of all the adult males cut for stone died after the operation. All inquiry goes to prove that his opinion was a tolerably correct one, thus showing a terrible mortality. Cannot we do something to improve the results of the operation? I am afraid not. Surgeons have posed before man's perinæum for centuries, and have entered his bladder by every conceivable route; but the results, take them all in all, have not varied very much. Happily, however, for mankind, everything must have a beginning, and stone is no exception to the rule. Unfortunately, the physician can do little or nothing to prevent the formation of a calculus, and it is reserved for the surgeon to wait for the enemy till it has made its descent into the bladder and to there attack it. Luckily, a stone is a long time growing to a considerable size, and it usually gives a good warning of its presence, so that ample time is afforded to attack and crush it while it is yet young, with absolute safety to the patient. Everything, consequently, turns on the diagnosis of the complaint. It may be said that the risk attached to stone in the bladder depends on its size; the larger the calculus, the more disease it occasions, and the greater the risk, therefore, attached to its removal. A big stone means much disease and great risk; whereas, if a small one, it may be affirmed, little disease, small risk. Hence it ought to be our aim to discover a calculus while it is yet young, and to crush it in its infancy. Now, the symptoms which should lead us to suspect the existence of a stone in the bladder are often obscure and ill-defined when taken singly, but, if grouped together and subjected to the crucial test questions which I shall hereafter refer to, we get together a mass of evidence which is usually strong enough to enable us to say whether a patient be the subject of stone in the bladder before we sound him.

1. *Frequency of Micturition.*—So soon as there is a foreign body in the bladder, it gives rise, by the movements impressed on it by changes of position, exercise, and the muscular efforts of micturition, to some irritation; and the earliest expression of that irritation is increased frequency of micturition. The increase in frequency will depend greatly on the character of the stone. A small oxalate of lime calculus, which jumps about the bladder with every change in the patient's position, may give rise to excessive frequency; whereas a large smooth phosphatic stone, lying quietly behind the prostate, may occasion but little increase. This symptom *per se* is not of much value, because nearly every disease of the bladder, prostate, or urethra is accompanied by increased frequency of micturition. Then, again, very few men note how often they urinate in the day; so that the interposition of some half-dozen acts of micturition in the day may pass unnoticed, whereas, if it occurred at night, it would be sure to attract attention. Now, as a stone usually gives rise to but little annoyance at night, you see that frequency of micturition, taken *per se*, carries but little weight.

2. *Difficult Micturition* is a common symptom in the early stage of the complaint. The smaller the stone the greater the chance that the flow of urine will carry it into the neck of the bladder, and even into the urethra. The larger the calculus, the more it tends to settle down behind the prostate, especially if the gland be enlarged, and there to lie quietly. The prostate acts as a barrier when enlarged between the neck of the bladder and the stone. Boys really have no prostates; that is to say, the gland in them is so rudimentary that it may be disregarded. Consequently, boys usually have a great deal of pain in micturition; the stone rolling to the neck of the bladder, and forming an impediment to the escape of the urine. One of the marked effects of this interference is exhibited in the way of priapism, rare in adults, but very common in boys.

3. *Pain.*—This is a very variable symptom, though usually present in some degree or other. Whether it be severe or not will depend on the character of the calculus and the nature of the exercise taken. For instance, a clerk, who walks to and from his office at a quiet pace, and sits on a stool all day, will suffer but little inconvenience; whereas a hunting man will be made aware of the presence of a stone. Ten to one that, when he gallops on horseback, he will experience some disagreeable sensation at the end of the penis, and will be frequently obliged to dismount to pass urine. Although hunting has caused many deaths, yet I am sure that, on the other hand, it has saved many lives. Men who hunt are just the subjects for uric acid calculi; and in them the existence of a stone usually makes itself known at a very early period, so that, by the intervention of lithotripsy, they are spared the risk of losing their lives by lithotomy. In children, pain makes itself very evident, for they cry out when passing urine, and rub the penis or squeeze it to mitigate their sufferings.

4. *Blood.*—Whether blood is seen or not will almost entirely depend on the nature of the stone and the character of the exercise taken. A small oxalate of lime calculus in a man who rides will almost certainly cause the escape of a few drops of blood, whereas a large smooth stone in one who leads a sedentary life may not cause any hæmorrhage. It is well to remember that the blood is usually passed in drops at the end of micturition; and that it generally has a florid aspect, different from bleeding from the kidney. The man whose kidney bleeds passes bloody urine, whereas the patient with a stone in his bladder passes urine and then blood.

5. *Altered Condition of Urine.*—This is probably the most untrustworthy symptom. Perfectly clear urine is quite compatible with the presence of a large stone, whereas a little mulberry-calculus may cause great alterations. Remember, I am alluding to the earlier symptoms of stone, not the later ones.

6. *Retention of Urine.*—This very common in boys, but rare in adults. If a boy suffer from retention, and there be no phimosis to account for it, depend upon it a stone is the cause of the stoppage.

7. *Prolapse of the Rectum.*—This is common in boys, but very rare in adults, although they often complain of tenesmus when urinating or defæcating.

8. *Incontinence of Urine.*—This is a symptom but little known or attended to. It was pointed out by Civiale, and a knowledge of the fact has enabled me to suspect, detect, and remove calculi in boys who had been subjected to a course of sea-bathing and tonics. When a stone is impacted in the commencement of the prostatic urethra, it gives rise to retention; for the sphincter of the bladder embraces the foreign body tightly, and accurately fills up the sinuities in the stone, so that the urine cannot escape. If, however, the calculus advance half an inch further, it acts as a gag and prevents the sphincter vesicæ from closing, so that the urine continually escapes along the sinuities in the stone.

Lastly, there are a certain number of aches and pains which may be ranked under the head of “Anomalous Symptoms”. I mention them simply as surgical curiosities, such as pain in the scrotum or down the arm or thigh.

So much for the symptoms of stone. We now come to the difficult point. It is very rare that the presence of a calculus gives rise to more than four of the above symptoms; and, inasmuch as the same four symptoms may be presented by other diseases than stone, we are far off from a correct diagnosis. In stricture, for instance, we may have frequent, difficult, painful, and muco-purulent micturition; and in inflammation of the prostate we may have frequent, difficult, painful, and bloody urination; and in children the presence of worms in the rectum, a fistula, phimosis, or contracted meatus, may closely simulate stone. Happily for us, there is a key to the puzzle, and that key is movement. Let us see how it clears up the case. A stone in the bladder is a foreign body lying unattached, and the symptoms of calculus are chiefly the results which would be produced by any foreign body shifting its position every hour through movements impressed on it. Every

* Read before the East Kent District of the South-Eastern Branch.