A REPORT ON THE BILIARY SECRETION OF THE DOG: WITH REFERENCE TO THE ACTION OF CHOLAGOGUES:

*Presented to the Scientific Grants Committee of the
British Medical Association.**

By WILLIAM RUTHERFORD, M.D., F.R.S.,
Professor of the Institutes of Medicine in the University of Edinburgh;

ASSISTED BY

M. VIGNAL AND WM. J. DODDS, M.B., D.Sc.

ACTION OF SODIUM-BICARBONATE.

Experiment 18.—Dog that had fasted eighteen hours. Weight, 16.3 kilogrammes. (Fig. 18.) 5 cc. water and 2 cc. bile were injected into the duodenum at *b* (a needless precaution), and thirty-one grains of sodium-bicarbonate in the same fluid were injected at *s*, *s'*, and *s''*, and one hundred and twenty-four grains in 15 cc. water and 2 cc. bile were injected at *s'''*, 217 grains being given in all. Only after the last dose did the secretion of bile begin to rise slightly.

Experiment 19.—Dog that had fasted eighteen hours. Weight, 19.9 kilogrammes. (Fig. 19.) Five cc. of water and 2.5 cc. of bile were injected into the duodenum at *b* (a needless precaution); and the same fluid, with 64 grains of sodium-bicarbonate, was injected at *s*, *s'*, and *s''*—192 grains being given in all. The secretion of bile rose slightly after each dose.

Result of Experiments with Sodium-Bicarbonate.—In Experiment 18, the hourly coefficient of secretion per kilogramme of body-weight during the first hour was 0.294 cc.; during the seventh hour, it was 0.287 cc.; and during the last hour, after 217 grains of the salt had been given, it was 0.341 cc. In Experiment 19, the coefficient during the first hour was 0.23 cc.; during the fifth hour, when the secretion was at its height, it rose to 0.28 cc.—128 grains of sodium-bicarbonate having been given. It is, therefore, evident that, though the blood of the portal vein was, comparatively speaking, laden with this very readily decomposable sodium-salt, the hepatic cells were scarcely at all excited thereby. It may, therefore, be inferred that, although sodium is required to form the salts of the bile-acids, a liberal supply of sodium has a feeble influence in leading to an increased formation of bile. Sodium-bicarbonate is, therefore, an exceedingly feeble hepatic excitant even in large doses; and it may, therefore, be inferred that the ordinary dose of ten or twenty grains, given to the human subject, produces no appreciable influence on his bile-secretion. It should be stated that the introduction of bile into the intestine—though of great service when resinous substances are given, as has been already explained—was in Experiments 18 and 19 entirely needless. Indeed, the introduction of 10 cc. of bile in the case of dog 18 was of itself calculated to slightly increase the bile-secretion; but in Experiment 19 the distinct rise of secretion after each dose of the sodium-salt was combined with the 2 cc. of bile and water that had previously had no effect, clearly shows that the sodium-bicarbonate was the cause of the increased hepatic activity.

ACTION OF POTASSIUM-BICARBONATE.

In the second series of these experiments, potassium-sulphate was shown to be a powerful though uncertain stimulant of the liver. The following experiment shows the influence of potassium-bicarbonate.

Experiment 20.—Dog that had fasted eighteen hours. Weight, 19.3 kilogrammes. (Fig. 20.) Thirty-one grains of potassium-bicarbonate in 8 cc. of water were injected into the duodenum at *p*, *p'*, and *p''*, and 108 grains in 8 cc. of water were injected at *p'''*—201 grains being given in all. The bile-secretion was distinctly increased.

NECROPSY.—Fifty-three cc. of a clear brownish liquid, with numerous mucous flakes, found in small intestine. Vascularity of its mucous membrane was considerably increased.

Result of Experiment with Potassium-Bicarbonate.—Before the alkaline salt was given, the hourly coefficient of secretion per kilogramme of body-weight was 0.238 cc.; and, after 201 grains had been given, it rose to 0.384 cc. Seeing that 31 grains produced no effect, it may be safely assumed that, when a dose of 10 or 15 grains is taken by the human subject, his biliary secretion is not sensibly affected.

* Continued from page 71 of last number.

ACTION OF IODIDE OF POTASSIUM.

Potassium-iodide is sometimes administered in hepatic affections, in the hope that it may produce an "alterative" effect. On that account, it seemed desirable to ascertain whether or not it affects the biliary secretion.

Experiment 21.—Dog that had fasted eighteen hours. Weight, 17 kilogrammes. (Fig. 21.) Ten grains of potassium-iodide in 3 cc. of water were injected into the duodenum at *p*, 20 grains at *p'*, and 30 grains at *p''*. There was no increase of secretion, but, on the contrary, a rather greater fall than is usually observed in a normal case. A repetition of the experiment was, therefore, necessary.

Fig. 21.

Secretion of bile before and after potassium-iodide. At *p* 10 grains, at *p'* 20 grains, and at *p''* 30 grains, in 3 cc. of water injected into the duodenum.

NECROPSY.—Fifty-four cc. of a thick yellowish mucous fluid found in the small intestine, thus affording evidence of a slight purgative action.

Experiment 22.—Dog that had fasted nineteen hours. Weight, 16.9 kilogrammes. (Fig. 22.) Five grains of potassium-iodide in 2 cc. of water were injected into the duodenum at *p*, 10 grains in 2 cc. of water at *p'*, 20 grains in 5 cc. of water at *p''*, 30 grains in 5 cc. of water at *p'''*, and 40 grains in 8 cc. of water at *p''''*. The trifling increase of secretion after the second and fourth doses may be discarded, and the fall of secretion as the experiment advanced might very probably have been equally marked had nothing been given.

NECROPSY.—Small intestine contained 25 cc. of a clear mucous fluid, indicating a slight purgation; for, though 22 cc. of water had been injected, much of it had doubtless been absorbed.

Fig. 22.

Secretion of bile before and after potassium-iodide. At *p* 5 grains in 2 cc. of water, at *p'* 10 grains in 2 cc. of water, at *p''* 20 grains in 5 cc. of water, at *p'''* 30 grains in 5 cc. of water, and at *p''''* 40 grains in 8 cc. of water, injected into the duodenum.

Result of Experiments with Potassium-Iodide.—This substance does not appear to affect the biliary secretion.

ACTION OF SULPHATE OF MANGANESE.

It is stated by Pereira (*Materia Medica*, 1854, vol. i, p. 667) that "C. G. Gmelin tried the effect of sulphate of the protoxide of manganese on animals, and found that it caused vomiting, paralysis with convulsions, and inflammation of the stomach, small intestines, liver, spleen, and

Experiment 20.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.
cc.	
1.30	} 0.238 cc.
1.35	
1.10	
1.15	
1.20	
1.15	
<i>p</i>	
1.20	} 0.287 cc.
1.15	
1.15	
1.25	
1.30	
1.45	
1.30	
1.50	} 0.384 cc.
1.30	
<i>p''</i>	
1.25	
1.30	
1.40	
<i>p'''</i>	
1.45	
1.40	
1.45	
1.50	
1.50	
1.60	
1.50	
1.67	
1.70	
1.50	
1.80	
1.85	
1.85	
1.90	
1.70	
1.40	
1.45	
1.30	

Experiment 25.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.
cc.	
2.00	} 0.238 cc.
1.90	
1.95	
1.85	
1.95	
2.00	
2.00	
1.90	} 0.140 cc.
1.95	
1.90	
1.85	
1.90	
1.90	
<i>m</i>	
1.90	
1.95	
1.90	
1.90	
2.00	
<i>m'</i>	
1.90	
1.90	
2.00	
<i>m''</i>	
1.90	
1.95	
1.80	
1.70	
1.65	
1.60	
1.70	
<i>m'''</i>	
1.50	
1.45	
1.55	
1.30	
1.00	
1.15	
1.20	

Fig. 18.

Secretion of bile before and after sodium-bicarbonate. 5 cc. of water and 2 cc. of bile injected into the duodenum at *b*; the same, with 31 grains of sodium-bicarbonate injected at *c*, *c'*, and *c''*; 15 cc. of water with 2 cc. of bile and 124 grains of sodium bicarbonate injected at *c'''*.

Fig. 19.

Secretion of bile before and after sodium-bicarbonate. 5 cc. of water and 2.5 cc. of bile injected into the duodenum at *b*; the same, with 64 grains of sodium-bicarbonate, injected at *s*, *s'*, and *s''*.

Fig. 20.

Secretion of bile before and after potassium-bicarbonate. 31 grains with 8 cc. of water injected into the duodenum at *p*, *p'*, and *p''*; 108 grains in 8 cc. of water injected at *p'''*.

heart. He notices the remarkable fact, the extraordinary secretion of bile produced by it, and which was so considerable that nearly all the intestines were coloured by it, and the large intestines had a wax-yellow colour communicated to them." (Gmelin, *Versuche über die Wirkungen des Baryts*, etc., 1824.) At the suggestion of Pereira (*loc. cit.*), its effects on the human subject were tested by Mr. Ure, who found that, in doses of from 60 to 120 grains, it acts as a purgative and cholagogue. In a recent communication to the *Lancet* (1878, i, 882), Dr. R. H. Goolden states that he has been in the habit of using this substance as a cholagogue for more than thirty years. He finds that, in doses of from ten to twenty grains, it produces large bilious evacuations. Ten grains he regards as a sufficient dose for ordinary purposes. This he dissolves in a tumbler of water, and adds some citrate of potash or magnesia. These statements rendered it desirable for us to test the action of this substance by our method of experiment.

Experiment 23.—Dog that had fasted eighteen hours. Weight, 15 kilogrammes. (Fig. 23.) Thinking, from Pereira's statement of the amount given to the human subject by Ure, that sixty grains of manganese-sulphate would not be too large a dose for a dog, we injected that amount in 30 cc. of water into the duodenum at *m*. So far from any increase of the bile-secretion resulting, there was a decided fall, the secretion coming nearly to a standstill. The weak pulse of the animal suggested that collapse had been occasioned by the drug, and the necropsy fully confirmed the idea that too much had been given. The fall of secretion, however, was in the first instance indirectly due to the effect of the powerful purgation that was induced, though the very low secretion at the close was, in all probability, due to collapse.

NECROPSY.—Evidence of powerful purgation in the upper third of small intestine. Very violent irritation of the mucous membrane of this region of the gut, the surface of which was covered with a yellowish white pulpy matter, as if the epithelium had been dissolved by a caustic alkali.

Fig. 23.

Secretion of bile before and after sulphate of manganese. 60 grains of manganese-sulphate in 30 cc. of water injected into the duodenum at *m*.

Experiment 24.—Dog that had fasted eighteen hours. Weight, 17.7 kilogrammes. (Fig. 24.) As the dose in the previous case had evidently been too large, only twenty grains of manganese-sulphate were given, in the same manner as before, in this instance (*m*). But there was not the slightest rise in the bile-secretion; on the contrary, there was a decided fall, as is the rule under the influence of a substance that produces purgation without exciting the liver. It now came to be the question, Would the bile-secretion rise in spite of the purgative drain from the portal vein, if a hepatic stimulant were administered? To determine this, 21 grains of sodium-benzoate in 15 cc. of water were injected into the duodenum at *s*; and, in spite of the disadvantageous circumstance of its being introduced into a column of intestinal juice actively being secreted, it excited the liver to secrete more bile, showing that the liver could be excited by a substance possessed of the property of so doing.

NECROPSY.—Copious watery purgation throughout the whole length of small intestine, whose mucous membrane was, however, scarcely at all reddened. The dose had, therefore, been efficient as an intestinal, but not as a hepatic, stimulant.

Result of Experiments with Manganese-Sulphate.—Experiments 24 and 25 entirely bear out the statement that manganese-sulphate is an intestinal stimulant, but lend no support to the idea that it is a hepatic stimulant. The effect on the biliary secretion is, indeed, similar to that of magnesium-sulphate, or any other pure intestinal stimulant; that is, it diminishes the biliary secretion, probably by draining the portal system. Yet Dr. Goolden's statements are explicitly to the effect (*lib. cit.*) that the same result was not produced by sulphate of magnesium as by

sulphate of manganese. We cannot, of course, from the above experiments, deny that the manganese-salt is a cholagogue in man; but, looking to the general harmony between our observations on the dog and those on man, we think we are entitled to throw very grave doubts upon the idea that manganese-sulphate excites the human liver. It might, indeed, be maintained that it has the power of inducing contractions of

Fig. 24.

Secretion of bile before and after manganese-sulphate and sodium-benzoate. 20 grains of manganese-sulphate in 15 cc. of water injected into the duodenum at *m*; 21 grains of sodium-benzoate in 15 cc. of water injected at *s*.

the gall-bladder and larger bile-ducts, and of thus increasing the amount of bile in the dejections; but we can only commend to the attention of physicians Dr. Goolden's positive observations as to the increased amount of bile in the dejections of man, and our negative results as to its action on the biliary secretion of the dog.

[To be continued.]

CLINICAL MEMORANDA.

SCARLATINA AND SEPTICÆMIA.

THERE can be little doubt, I think, that a rash, hardly to be diagnosed from that of scarlatina, is often the consequence of a septicæmic condition.

On March 25th, 1876, a single woman, aged 28, was confined of her first child at the full term in Queen Charlotte's Hospital. The labour was quite natural; there was no laceration of the perinæum. She was a healthy woman, but had suffered much from sickness and nausea during her pregnancy. The child died soon after birth, very dusky. On the 26th, the patient's pulse was 112; temperature 100.4; the tongue was furred; the lochia natural. On the 27th, the pulse was 136; temperature 104. After confinement, she was very flushed, and had continued so. There was general suffusion of the skin, most marked on the face; the tongue was moist and furred; the papillæ were not prominent. There was no sore-throat or redness of the fauces. There was a very tender red spot, about the size of a small walnut, on the extensor surface of the right arm. The calf of the right leg was very tender. No history of infection from scarlatina could be obtained after the closest questioning. On the 28th, the pulse was 120; temperature 103.2. At times, she was more flushed than at others. The calf of the leg was swollen, and pain there was much increased. There was distinct fluctuation in the swelling on the right arm. The lochia were natural. On the 29th, she was very restless, suffering much from pain in the leg. She died on this day.

A patient, who was at first in the same ward, had a very distinct red rash, but the colour appeared in patches, and was not always present. She did not desquamate, but an abscess formed over the shoulder, and afterwards another over the hip. The perinæum in this case sloughed on the third day, though the labour had been a short one and no laceration of parts had occurred.

It not unfrequently happens that patients, during the secondary fever of small-pox (especially if the attack have been a severe one), develop an erythematous rash which is occasionally very difficult to distinguish from that of scarlatina: it is, I believe, an indication of a septicæmic condition; it is not usually followed by desquamation.

F. W. STRUGNELL, Resident Surgeon Small-pox and Vaccination Hospital, Highgate.