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.**

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ACTION OF MORPHIA.

As morphia has the well-known power of arresting diarrhoea and of producing constipation, it is desirable to know whether this is to be ascribed to its effect on the intestine alone, or also to a power of diminishing the secretion of bile.

Experiment 25.—Dog that had fasted eighteen hours. Weight, 33 kilogrammes (Fig. 25). One grain of morphia-hydrochlorate in 3 cc. of bile and water were injected into the duodenum at *m*, *m'*, *m''*, and *m'''*, four grains being given in all. The first two doses had no obvious effect on the bile-secretion; but it began to fall after the third, and continued to do so after the fourth, doses. As it was impossible to know, from this single experiment, whether or not this fall in the secretion was due to the morphia, a second experiment was performed.

NECROPSY.—The mucous membrane of the small intestine was almost perfectly dry.

Experiment 26.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.
cc.	
1.15	
0.85	
0.80	
0.70	
0.70	
0.80	
<i>m</i> —	
0.95	
1.10	
0.95	
<i>m'</i> —	
0.90	
0.85	
0.75	
1.05	
0.90	
<i>s</i> —	
1.05	
3.05	
3.35	
2.45	
2.40	
2.15	
2.30	
2.30	
2.30	
2.60	
2.60	

Experiment 27.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.
cc.	
1.7	
1.75	
1.55	
1.65	
1.65	
1.65	
1.65	
1.60	
1.65	
<i>h</i> —	
1.60	
1.65	
1.70	
1.65	
<i>k'</i> —	
1.65	
1.60	
1.55	
1.45	
1.55	
<i>k''</i> —	
1.50	
1.45	
1.30	
1.20	
1.35	
1.25	
<i>k'''</i> —	
1.20	
1.10	
1.20	
1.10	
0.90	
0.80	
0.90	

Experiment 26.—Dog that had fasted eighteen hours. Weight, 19.9 kilogrammes (Fig. 26). One grain of acetate of morphia in 5 cc. of water was injected into the duodenum at *m*, and 2 grains in 10 cc. of water were injected at *m'*. No diminution of secretion was the result; in short, the morphia did not appear to affect the secretion. As it seemed desirable to know whether or not the liver of an animal so narcotised could be excited by an appropriate stimulant, 20 grains of

sodium-salicylate in 10 cc. of water were injected into the duodenum at *s*. Powerful and prolonged excitement of the liver was the result.

Fig. 25.

Secretion of bile before and after morphia-hydrochlorate. 1 grain with 2 cc. of bile and 1 cc. of water injected into the duodenum at *m*, *m'*, *m''*, and *m'''*.

NECROPSY.—Slightly increased redness of the duodenal mucous membrane. Evidence of slight purgative action in the upper part of the small intestine.

Fig. 26.

Secretion of bile before and after morphia and sodium-salicylate. 1 grain of morphia-acetate in 5 cc. of water injected into the duodenum at *m*; 2 grains in 10 cc. of water at *m'*; 20 grains of sodium-salicylate in 10 cc. of water injected into the duodenum at *s*.

Result of Experiments with Morphia.—Three grains of morphia-acetate did not affect the secretion of bile.

ACTION OF HYOSCYAMUS.

As extract of hyoscyamus is often administered with cholagogue substances, it is important to know whether or not it diminishes the secretion of bile. The dose of this substance for a man is from five to ten grains.

Experiment 27.—Dog that had fasted eighteen hours. Weight, 21 kilogrammes (Fig. 27). Two grains of aqueous extract of hyoscyamus

* Continued from page 107 of last number.

in 3 cc. of water were injected into the duodenum at *h*, *h'*, *h''*, and *h'''*, eight grains being given in all. It was impossible, from this single experiment, to say whether or not the fall in the secretion was due to the hyoscyamus; but the unusually high coefficient of secretion in the earlier part of the experiment (0.311 cc. per kilogramme per hour) favoured the conclusion that the fall was not due to the drug.

Fig. 27.

Secretion of bile before and after hyoscyamus. 2 grains of extract of hyoscyamus with 3 cc. of water injected into the duodenum at *h*, *h'*, *h''*, and *h'''*.

NECROPSY.—Mucous membrane of small intestine pale and dry.

Experiment 28.—Dog that had fasted eighteen hours. Weight, 16.8 kilogrammes (Fig. 28). To decide the point left in doubt by the previous experiment, larger doses of the drug were administered. Eight grains of extract of hyoscyamus triturated with 1 cc. of bile and 10 cc. of water were injected into the duodenum at *h*, and the same dose was again injected into a lower part of the intestine at *h'*. It is difficult to account for the slight rise of secretion that followed both doses. It may be safely assumed that it was due neither to the bile nor to the water. At all events, there was no fall of secretion, notwithstanding the administration of sixteen grains of the drug.

Experiment 28.		Experiment 30.	
Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.	Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.
cc.		cc.	
1.30		1.40	
1.10		1.42	
1.10		1.40	
0.90	0.214 cc.	1.40	0.265 cc.
0.85		1.45	
0.90		1.40	
0.95		1.40	
<i>h</i>		<i>h</i>	
1.10	0.268 cc.	1.40	0.310 cc.
1.25		1.40	
1.25		1.50	
1.25		1.50	
1.20		1.55	
1.00		1.50	
<i>h'</i>		1.60	
1.15		1.60	
1.30		1.45	
1.25		<i>i</i>	
1.20		1.50	
<i>a</i>		1.50	
0.80	0.231 cc.	1.60	0.310 cc.
0.95		1.70	
1.00		1.60	
1.00		1.72	
<i>a'</i>		1.55	
1.00		1.55	
0.90		1.80	
<i>s</i>		1.55	
0.85		1.05	
2.05		1.50	
4.50		1.40	
		1.70	
		1.50	
		1.35	

As the experiment was entirely conclusive regarding the effect of hyoscyamus, it was proposed to investigate the action of pure alcohol; accordingly 5 cc. of absolute alcohol, diluted with 32 cc. of water, were injected into a fresh portion of the small intestine, and, as there was no notable effect, 8 cc. of absolute alcohol in 32 cc. of water were injected into another part of the gut. Notwithstanding the administration of 13

cc. of alcohol (219 minims), the bile-secretion was virtually unaffected. It was now sought to determine what such a liver could do if stimulated. Twenty grains of sodium-salicylate in 10 cc. of water were injected into the duodenum at *s*, and speedily thereafter the bile-secretion was enormously increased, and that so late as the ninth hour of the experiment.

Fig. 28.

Secretion of bile before and after hyoscyamus and absolute alcohol. 8 grains of extract of hyoscyamus in 10 cc. of water and 1 cc. of bile injected into the duodenum at *h*; the same, injected into a lower part of the small intestine, at *h'*; 5 cc. of absolute alcohol in 20 cc. of water injected into the small intestine at *a*; 8 cc. of absolute alcohol in 32 cc. of water injected into the small intestine at *a'*; 20 grains of sodium salicylate in 10 cc. of water injected into the duodenum at *s*.

Result of Experiments with Hyoscyamus.—Sixteen grains of extract of hyoscyamus, prepared according to the *British Pharmacopœia*, did not notably affect the biliary secretion, and did not prevent such a stimulant as sodium-salicylate from augmenting it. From observations on the human subject, we are also able to state that hyoscyamus does not seem to interfere with the stimulating effect of euonymin on the liver, and very probably it may be safely given with all hepatic stimulants that are also intestinal stimulants and happen to cause griping.

ACTION OF ALCOHOL.

It is a matter of common opinion that alcoholic drinks affect the action of the liver; but, whether their hepatic effects may be ascribed to the alcohol, ethers, or other substances they contain, no one has hitherto sought to determine. The results of the preceding experiment already go far to determine the question as regards pure alcohol; but, as hyoscyamus had in that experiment been previously administered, it was desirable to perform another experiment in which nothing but pure diluted alcohol was administered.

Experiment 29.—A small dog (not weighed) that had fasted eighteen hours (Fig. 29). Fifteen cc. of water were injected into the stomach through an œsophagus-tube (*w*); then 5 cc. of absolute alcohol diluted

with 15 cc. of water were injected into the stomach in the same manner at a , a' , a'' , and $a''' = 20$ cc. (338 minims) being given in all.

Result of Experiments with Alcohol.—In Experiment 28, 13 cc. of absolute alcohol, and in Experiment 29, 30 cc. of absolute alcohol, moderately diluted and introduced into the alimentary canal, did not produce any apparent effect on the biliary secretion. These experiments, however, furnish no evidence of what might be the effects of prolonged action of alcohol on the liver; and, in consideration of the great labour and length of this research, we could not undertake experiments designed to show the effects of various sorts of alcoholic drinks, or of the substances other than alcohol which they con-

Fig. 29.

Secretion of bile before and after alcohol. At w , 15 cc. of water; at a , a' , a'' , a''' , 5 cc. of absolute alcohol with 15 cc. of water injected into the stomach through an oesophagus-tube.

tain. Such a research could scarcely be of great practical importance, for we already know that certain alcoholic drinks—such as 'ale, stout, etc.—tend to produce "biliousness"; and, by experiments on the human subject, we have ascertained that this condition, thus induced, may be cured by giving iridin or euonymin (second series of experiments, this JOURNAL, 1877)—substances which powerfully stimulate the liver. As far as they go, however, our experiments show that *pure alcohol* has, at all events, *no immediate* action on the liver of the dog.

ACTION OF JABORANDI.

Jaborandi being a powerful stimulant of the salivary and sweat-glands, we thought it desirable to ascertain its influence on the liver. The mean dose for a man is a watery infusion of sixty-four grains of the leaves.

Experiment 30.—Dog that had fasted eighteen hours. Weight, 21.5 kilogrammes (Fig. 30). Eight cc. of water with 2 cc. of bile were injected into the duodenum at b , and 8 cc. of a concentrated aqueous infusion containing the active principle of sixty-four grains of jaborandi leaves was injected at j , and the same dose was again given at j' . Powerful salivation began half an hour after the first dose (at s), and it is to be observed that shortly afterwards the bile-secretion also underwent a slight increase; that became more marked after the second dose.

Fig. 30.

Secretion of bile before and after jaborandi. 2 cc. of bile and 8 cc. of water injected into the duodenum at b ; 8 cc. of infusion of jaborandi with 2 cc. of bile injected at j and j' ; salivation began at s .

NECROPSY.—Ninety-seven cc. of liquid were found in the small intestine (30 cc. had been injected), but whether most of it had been secreted by the pancreas or by Lieberkühn's follicles was undetermined. There was no unusual redness of the intestinal mucous membrane.

Experiment 31.—Dog that had fasted eighteen hours. Weight, 21.5 kilogrammes (Fig. 31). Ten cc. of water with 2 cc. of bile were injected into the duodenum at b , and the same fluid, with 10 cc. of aque-

ous infusion of jaborandi, was injected at j , and again at j' . As each cubic centimetre of the infusion contained the active principle of seven grains and a half of the leaves, one hundred and fifty grains had been given. Salivation began half an hour after the first dose, and soon thereafter the bile-secretion rose, but to no great extent. It was observed in this experiment that the *bronchial glands were much stimulated* by the jaborandi, the respiratory cannula being completely obstructed by a watery mucus, which must have been secreted in the bronchi and trachea.

Fig. 31.

Secretion of bile before and after jaborandi. At b , 2 cc. of bile and 10 cc. of water; at j and j' the same fluid, with 10 cc. infusion of 75 grains of jaborandi leaves injected into the duodenum. Salivation began at s .

NECROPSY.—The jaborandi had traversed the whole length of the small intestine, which contained 107 cc. of a clear greenish fluid without mucous flakes. Thirty-six cc. of fluid had been injected; but how much of the remainder had been secreted by the pancreas and how much by Lieberkühn's follicles could not be determined.

Experiment 31.

Secretion of bile per 15".	Secretion of bile per kilogramme of dog: per hour.
cc.	
1.80	
1.70	
1.67	
1.70	
b —	
1.70	} 0.314 cc.
1.72	
1.65	
1.70	
j —	
1.70	
1.60	
s —	
1.60	} 0.355 cc.
1.70	
1.60	
1.75	
1.80	
1.75	
1.90	
1.95	
2.00	
1.80	
2.00	
2.05	
1.85	
1.72	
1.60	
j' —	
1.50	
1.52	
1.62	
1.67	
1.70	
1.75	

Result of Experiments with Jaborandi.—In doses that were much more than sufficient to excite the salivary glands, jaborandi produced only a slight increase in the biliary secretion. It is therefore to be regarded as a very feeble hepatic stimulant.

[To be continued.]