

## THE CHOLERETIC ACTION OF GENEBILE\* IN A DOG

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### SUMMARY

A procedure for cannulating the bile duct of the dog is described. An intramuscular injection of Genebile increased the bile flow rate. A possible mechanism for this increase is suggested.

### INTRODUCTION

The use of Genebile in cattle<sup>2</sup> has been described and critical trials carried out in sheep<sup>4</sup> and goats<sup>3</sup>. Its effect in the dog has not previously been evaluated.

This communication describes the cannulation procedure of the bile duct in a dog and the collection of bile before and after administration of Genebile. The bile was analysed to investigate the possible mode of action of this compound as a choleric.

### MATERIALS AND METHODS

A clinically normal Alsatian bitch, 3 years old and weighing 26 kg was used. The diet consisted of a commercial ration containing 20% crude protein, fed once daily. Water was available *ad libitum*.

#### Cannulation Procedure

After 24 hours fasting the dog was prepared for surgery. Anaesthesia was induced with thiopentone and maintained, after intubation, with 2% Halothane B.P. in oxygen in a closed circuit. A right paracostal incision exposed the liver, pyloric part of the stomach and the duodenum. The gallbladder was located and manual pressure applied to it to facilitate identification of the common bile duct. The latter was then ligated immediately distal to the point where the duct from the right lateral lobe of the liver entered it, and transected distal to the ligature. Care was taken not to injure the portal vein closely associated with the duct.

A polythene tube of suitable diameter was inserted in an antegrade direction into the lumen of the duodenum through the distal part of the common bile duct and its sphincter. The method illustrated in figure 1 was employed to secure the tube firmly in the lumen of the duct.

Partial cholecystectomy was performed and a polythene tube secured in the lumen of the remaining part of the neck of the gallbladder and the cystic duct, again using the method illustrated in figure 1.

One end of each of the polythene tubes was brought to the exterior through small stab incisions in the different layers of the abdominal wall, care being taken to leave as little as possible of the tubes in the abdominal cavity and not to cause kinking of the tubes. They were anchored to the peritoneum, subcutaneous tissue, and to the skin externally by using a slight modification of the method shown in figure 1.

The shaft of a large-bore hypodermic needle

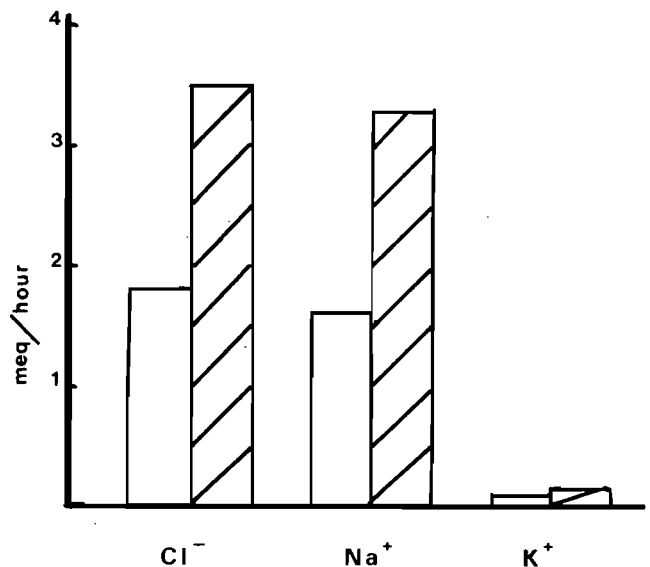


Fig. 1. Method used to secure artificial tubes in ducts.

served as a connection between the tubes externally. This arrangement allowed the collection of total bile flow as desired on certain days, while on other days bile flowed continuously into the duodenum thus obviating the problems associated with continuous bile loss from the body.

After the operation the dog remained clinically normal but showed some inappetence, consuming about half the amount of food eaten prior to the operation. She was allowed a 72 hour recovery period before experimentation began.

Pilot trials conducted with previous dogs had shown that normal bile flow was greatest in the morning, decreasing to a minimum in the afternoon. As this is probably related to the mid-morning feeding regimen followed routinely, it was decided to collect samples hourly over a 6 hour period before feeding the animal.

Initially a 6 hour series of control samples was taken by disconnecting the two polythene cannulae and collecting the bile coming directly from the tube inserted into the neck of the gall bladder. The following day Genebile was injected intramuscularly at a dose of 10mg/kg body weight and a further series of samples collected. The samples from these 2 days were compared (Trial 1). This procedure was repeated twice with a 72 hour rest period between each trial (trials 2 and 3).

#### Sample Analysis

After noting the flow rate per hour, the samples were analysed for sodium and potassium by flame photometry, chloride by mercurimetric chloride titra-

\* Diethano-Lamino Salt of 4-(4-Methoxy-Naphthalene-(1)-4-Oxy-Butyric Acid.

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tion (Merckotest), bilirubin by the van den Berg reaction and the osmolality determined by freezing point depression (Knauer ostometer).

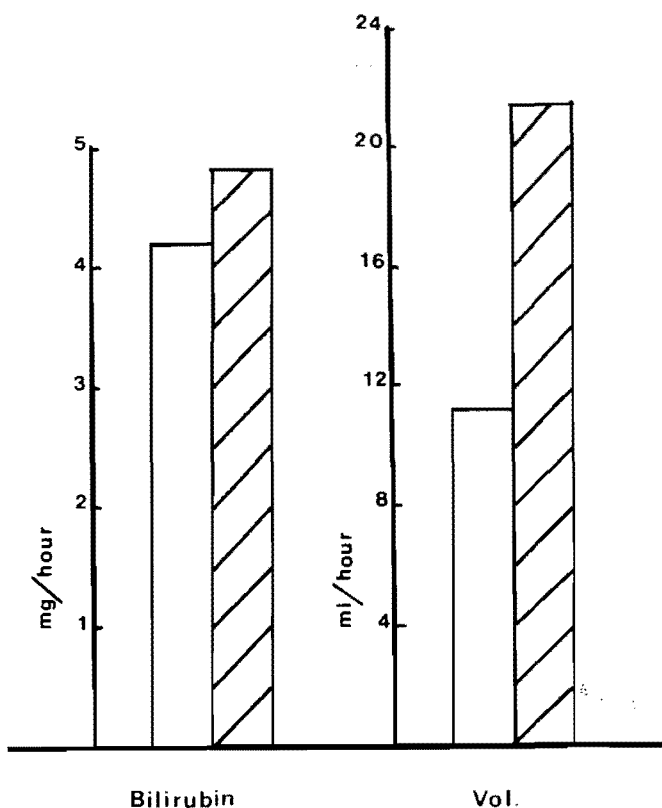


Fig. 2 The effect of treatment on bile composition and flow rate. The height of each column represents the mean value for the three trials.

- Before treatment
- ▨ After treatment

## RESULTS

The mean flow rates per hour before and after administering Genebile are shown in figure 2. The results clearly indicate that the mean rate of bile under control conditions (11,2ml/hour) was considerably less than the mean flow rate after administering Genebile (22,7ml/hour).

The mean values for the excretion of bilirubin and electrolytes into the bile per hour are compared in figure 2.

The results show that the amount of bilirubin excreted per hour increased slightly after treatment, while the amounts of sodium and chloride excreted per hour increased markedly. The excretion of potassium was also somewhat elevated.

The mean values obtained for the individual trials were analysed statistically (Student t test) and are set out in Table 1. In all cases there was a highly significant increase in flow rate as well as sodium and chloride excretion while the excretion of potassium was unaltered in one trial, but significantly increased in the other two trials. Bilirubin excretion remained unaltered during two of the trials but was significantly increased in the other.

## DISCUSSION

The results obtained suggest that the cannulation procedure employed in this trial is suitable for the study of factors affecting biliary excretion. In some preliminary trials where the cannula was passed retrograde fashion into the common bile duct of dogs and sheep (unpublished data) the bile flow has been very variable.

The results indicate that Genebile has a choleric action in that the bile flow rate was consistently elevated after intramuscular injection at a

Table 1: ANALYSIS OF BILE COLLECTED BEFORE AND AFTER INTRA-MUSCULAR ADMINISTRATION OF GENEBILE (10MG) KG BODY WEIGHT

Analysis	TRIAL I			TRIAL II			TRIAL III		
	Control	After treatment	Significant levels	Control	After treatment	Significant levels	Control	After treatment	Significant levels
Flow rate (ml/hour)	7 $\pm$ 3,2	13,9 $\pm$ 1,7	P<0,01	15,2 $\pm$ 2,7	26,8 $\pm$ 6,4	P<0,001	11,3 $\pm$ 3	25,9 $\pm$ 4,4	P<0,001
Bilirubin excretion mg/hour	1,09 $\pm$ 0,23	1,65 $\pm$ 0,26	P<0,01	5,83 $\pm$ 1,6	6,70 $\pm$ 2,64	N.S.	5,63 $\pm$ 3,24	6,01 $\pm$ 0,99	N.S.
Cl excretion meq/hour	0,82 $\pm$ 0,29	1,76 $\pm$ 0,39	P<0,001	2,51 $\pm$ 0,41	4,61 $\pm$ 1,04	P<0,001	2,08 $\pm$ 0,60	4,13 $\pm$ 0,70	P<0,001
Na excretion meq/hour	1,1 $\pm$ 0,59	2,11 $\pm$ 0,58	P<0,05	2,29 $\pm$ 0,51	3,94 $\pm$ 0,73	P<0,001	1,76 $\pm$ 0,55	4,04 $\pm$ 0,78	P<0,001
K excretion meq/hour	0,044 $\pm$ 0,029	0,063 $\pm$ 0,015	N.S. <sup>x</sup>	0,089 $\pm$ 0,021	0,154 $\pm$ 0,024	P<0,001	0,077 $\pm$ 0,032	0,164 $\pm$ 0,051	P<0,01
Osmolality Average	299,6 $\pm$ 6,1	304,7 $\pm$ 5,7	N.S.	292,7 $\pm$ 4,7	301 $\pm$ 10,9	N.S.	306,1 $\pm$ 4,5	302,6 $\pm$ 4,7	N.S.

x N.S. = not significant

dosage of 10mg/kg body weight. It may be postulated that the drug stimulates a sodium pump mechanism and that chloride follows passively down an electrochemical gradient. As the osmolality remains unaltered, passive water movement along with the sodium chloride would seem to explain the findings. Such a mechanism is in agreement with that

postulated by Diamond<sup>1</sup> (1969) for the isotonic reabsorption from the gallbladder. The results suggest that the drug does not actively stimulate bilirubin excretion, the increased excretion in trial 1 possibly being secondary to the increased water movement into the bile. A similar situation may hold for potassium excretion.

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## BOOK REVIEW

## BOEKRESENSIE

### ÜBER KAPSELKÖRPER UND GLEITDRUCKSTRUKTUREN — EIN BEITRAG ZUR SESAMBEINFRAGE

F. PREUSS AND A. WÜNSCHE

Supplement 21 to *Zentralblatt für Veterinärmedizin*. Paul Parey, Berlin. 1974. Price R10.

The authors analyse a 130 odd publications on the question of sesamoid bones – their origin, structure and function. Their views are further based on their own dissections which cover the domesticated animals, laboratory animals and birds. Sesamoid bones in the digital joints of the pig are described for the first time. They consider true sesamoid bones to develop in synovial capsules of joints, bursae and tendon sheaths. Three groups are recognized *viz.*: those in close proximity to joints, *e.g.* the patella and fabellae; those associated with bursae and tendon sheaths, *e.g.* the peroneal sesamoid in man; those not associated with synovial capsules and which are not true sesamoid bones, *e.g.*

the ossified tendons of certain birds. The primary function is thought to be protection of the joint capsule, stabilization of the joint, and improvement of the effectiveness of muscular action.

Until such time as it would be possible to devise and introduce suitable experimental methods, conflicting views will be rife. This is an almost philosophical treatise on corresponding and conflicting views held by various authors since 1888 in regard to sesamoid bones. It makes interesting reading but its appeal will probably be limited.

J.M.W. LE R.