

INVESTIGATIONS ON THE PHYSIOLOGY OF BILE SECRETION*
EFFECT OF ADRENALINE AND NORADRENALINE
ON BILE SECRETION

By

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Stimulation of the sympathetic nerve supply of the liver has been shown to decrease the bile secretion by Tanturi and Ivy¹. Hence it is to be expected that the administration of the chemical mediators of the sympathetic system would exhibit the same type of result. But Engstrand's² results indicated that adrenaline in large doses initially increases the bile secretion and finally diminishes the output. Etienne Chambrol and Jean Sallet³ have shown that continuous infusion of adrenaline decreased the bile secretion to $\frac{1}{3}$ its original volume. In order to elucidate the problem, since it is now known that nor-adrenaline is also one of the mediators of the sympathetic system, the effect of both adrenaline and nor-adrenaline on the biliary secretion in dogs has been investigated.

Adrenaline was used as tartrate and nor-adrenaline as (isopropyl nor-adrenaline sulfate) kindly supplied by Boots and Co., in the form of d1-1(3'.4'-dihydroxyphenyl)-2-isopropylaminoethanol sulphate, an N-isopropyl derivative of nor-adrenaline.

Dogs generously supplied by the Bangalore Corporation were used in these experiments. The method of cannulation and collection of bile, anaesthesia used and procedures for estimation of bile salts, bilirubin, cholesterol and fatty acids as also the pharmacodynamic techniques have been described in earlier papers^{4,5}.

The effect of adrenaline on bile secretion is shown in figure 1. Detailed readings are given in Tables I and II. The influence of noradrenaline is indicated in Table III.

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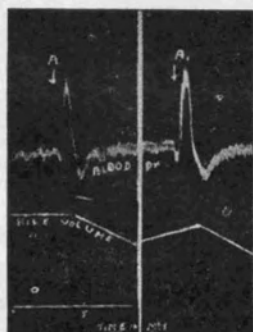


Fig. 1.
Effect of Adrenaline on bile secretion.

TABLE I

Effect of adrenaline on bile secretion

Dosage	Normal (ml.)	Volume of bile in ml. after administration of adrenaline at 5 minutes interval.			
		0-5	5-10	10-15	15-20
4 γ /kg.	0.15	0.10	0.09	0.12	0.14
6 γ /kg.	0.14	0.09	0.07	0.11	0.13

TABLE II.

Continuous infusion of adrenaline at a rate of 4 ml. per minute
(1 γ /ml.)

Dosage	Normal (ml.)	Volume of bile in ml. while infusing adrena- line continuously for 30 minutes.					
		0-5	5-10	10-15	15-20	20-25	25-30
1 γ /ml.	0.18	0.13	0.05	0.03	0.05	0.07	0.07
1 γ /ml.	0.18	0.16	0.15	0.11	0.11	0.10	0.10

TABLE III

Effect of nor-adrenaline on bile secretion

Dosage	Normal (ml.)	Volume of bile in ml. collected at 10 minutes interval after administration of nor-adrenaline.					
		0-10	10-20	20-30	30-40	40-50	50-60
3 γ /kg.	0.70	0.60	0.65	0.62	0.67		
6 γ /kg.	0.67	0.55	0.55	0.57	0.57	0.6	
Continuous infusion for 6 minutes 1 γ /ml Rate: 6 ml/mt.	0.60	0.50	0.5	0.35	0.42	0.47	0.50

The bile secretion is found to be diminished immediately after the injection of adrenaline and nor-adrenaline and returned to normal in about 30 minutes time. The result of continuous infusion was a steady lowering of the volume throughout the period of infusion (Fig. 2). As marked dyspnoea and arrhythmia developed during nor-adrenaline infusion, it could not be persisted for the same period as adrenaline. The systemic blood pressure rise with adrenaline was found to be greater than that induced by nor-adrenaline. But in both the cases alteration of the secretion was in only one direction, i.e., reduction. Whether this alteration is due to haemodynamic changes in the liver or a specific action on the cellular elements needs further elucidation.

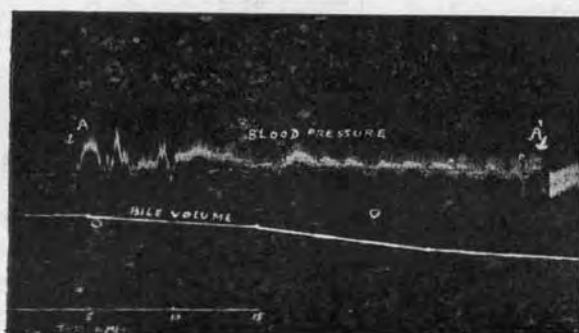


Fig. 2.

Effect continuous infusion of the drug.

QUANTITATIVE CHANGES IN BILE SECRETION AFTER ADRENALINE ADMINISTRATION

Since quantitative changes induced by various drugs are known to cause specific alterations in bile composition as shown by Werner and Parhan,⁶ Sasaki,⁷ Quinones,⁸ Leits and Isabolinskaya,⁹ Besuglor *et al.*¹⁰ Toshiynki Tenka,¹¹ and Paraschiv¹², the analysis of the bile constituents on single and continuous administration of adrenaline has been carried out and shown in Table IV.

The specific effects noticed after single injections are :

- (1) Decrease in total solids
- (2) Decrease in bile salts
- (3) Decrease in fatty acids
- (4) Slight decrease in bilirubin

The same trend is observed with continuous infusion of adrenaline also (Table IV).

TABLE IV
Analysis of biliary constituents

Weight of the dog : 3.5 kg. Seconal sodium 3 mg./kg.

Sample	Solids %	Bile salts gms./100 ml.	Bilirubin mgms./100 ml.	Cholesterol mgms./100 ml.	Fatty acids mgms./100 ml.	Specific gravity
Normal ..	3.5	2.0	32.1	51.0	375	1.35
Adrenaline 4 μ /kg.	2.3	1.25	21.3	54.0	250	1.29
Adrenaline 6 μ /kg.	2.5	1.12	16.0	55.2	200	1.29
Normal ..	2.1	1.8	29.2	50.8	204.3	1.20
(Specimen II)						
Continuous infusion of adrenaline (1 μ /ml.) at a rate of 4 ml./min.						
Weight of the dog	3.64 kg.			Seconal sodium : 30 mg./kg.		
Normal ..	3.4	1.2	32.0	66.4	400	1.21
Continuous infusion	2.1	0.8	24.5	45.5	325	1.23
Normal	2.4	0.99	27.5	53.4	341	1.23
(Specimen II)						

Specimen II: Obtained after the bile flow had regained normal volume.

SUMMARY

Though primarily bile secretion is a function of the liver, the exact role played by the liver cells and biliary canaliculi epithelium in the secretion and excretion of the various constituents of the bile is still undecided. The bile secretion is influenced by the autonomic nervous system, the circulatory haemodynamics, hormones and various other physiological and pathological substances like histamine, normally found in the tissues of the body. The precise role of these regulatory mechanisms in the normal secretion of bile is difficult to assess as they are all closely inter-related and disturbances in one system leads to alteration in many others.

The effects of adrenaline and noradrenaline either by single intravenous injection or continuous infusion, is one of decreased bile secretion. The sympathetic system is considered to be secretory in nature and by some to cause increased bile secretion. But under our experimental conditions, adrenaline and noradrenaline are found to inhibit bile secretion in dogs. Unlike the stimulation of only the sympathetic nerves which innervate the liver and

release the adrenaline and nor-adrenaline in the liver, the intravenous administration of adrenaline causes both systemic and local circulatory changes which is reflected in bile secretion and might explain the variations observed in bile secretion between sympathetic stimulation and adrenaline and noradrenaline administration.

The qualitative and quantitative alterations in the individual constituents of the bile after adrenaline and noradrenaline administration present some interesting features. Not only is the total volume diminished but also the concentrations of bile salts, bile pigments and fatty acids are reduced. The cholesterol content is not affected to any extent, thus indicating some specificity in the biological effect of adrenaline and noradrenaline.

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