

indicates again an overlap in physiological activity as well as the stimulating effect on the glands of animals receiving the various androgens.

The slighter mammary response in animals receiving the larger amounts of estradiol benzoate and also triphenylethylene and stilbestrol reaffirms the "stunting effect" on mammary tissues of large amounts of estrogens.⁶

10685

Effect of Sodium Dehydrocholate (Decholin) on Bile Salt, Chloride and Cholesterol of Bile in Dogs.

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Bile salts have been used for a number of years as choleretics. While it is generally accepted that the volume of bile after the administration of bile acids is increased,^{1, 2} few reports are available on the effect of these substances on the various constituents of the bile.^{7, 9} It is important to know whether or not following administration of certain bile salts, the patient excretes an increased amount of bile salt in the hepatic bile or whether the choleretic action is merely expressed by an increased water content. One of the most widely used choleretics is sodium dehydrocholate (Decholin). The following experiments were undertaken to determine what effect sodium dehydrocholate (Decholin) has on the 24-hour excretion of certain constituents of the bile.

Method. Two to 3 g sodium dehydrocholate (Decholin) were given daily for a period of 3 to 4 days to each of 5 dogs whose common duct had been doubly intubated by the method of Rous and McMaster,³ and whose cystic duct had been doubly ligated. Twenty-four-hour specimens of hepatic bile were collected before, during, and after the Decholin feeding. Bile was analyzed for chloride by the Wilson-Ball⁴ method, for cholate by the Gregory-Pascoe method

¹ Neubauer, E., *Klin. Woch.*, 1924, **3**, 883.

² Powelson, P., and Wakefield, E. G., *Ann. Int. Med.*, 1929, **3**, 572.

³ Rous, P., and McMaster, P., *J. Exp. Med.*, 1923, **37**, 11.

⁴ Wilson, D. W., and Ball, E. G., *J. Biol. Chem.*, 1928, **79**, 221.

⁷ Schmidt, C. R., Beazell, J. M., Atkinson, A. J., and Ivy, A. C., *Am. J. Digest. Dis.*, 1938, **5**, 613.

⁹ Doubilet, H., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 687.

TABLE I.
Changes in Composition of Bile After Administration of Sodium Dehydrocholate (Decholin) to Dogs.

Dog	Changes in Composition of Bile after Administration of Sodium Bile-salts (200 mg.) to Dog.												
	Volume cc			Chloride mg/24 hr		Cholate mg/24 hr		Cholesterol mg/24 hr		Grams Decholin ingested and period of ingestion			
	Before	During	After	Before	During	After	Before	During	After				
247	121	195	92	329	617	237	3047	2051	2005	20	18	22	8 g 4 days
248	134	193	164	440*	581	439	2545	2704	3797	22	20	16*	9 g 3 "
346	75	100+	217	148	507	789	2030	3653	1389	13	8	8	6 g 3 "
						165			1233			9	
415	74	139	49	214	433	196	950*	1277	270	7	10	20	8 g 3 "
416	37	142	89	102	449	301	994	3834	1820	2	14	13	10 g 4 "
						231			2002			11	
Av.†	85	146	113	217	512	368	2114	2546	1721	12	14	15	

* One determination only.

† Average of all individual determinations.

as described by Reinhold and Wilson,⁵ and for cholesterol by a combined digitonin precipitation-colorimetric procedure.⁶

The period of control collection before Decholin administration was usually 4 days. The period of collection during Decholin feeding varied in the different dogs from 6 hours before the first Decholin feeding to 12 hours after the first Decholin feeding. The collection period after cessation of Decholin administration was from 2 to 4 days. In 2 animals bile was collected for a second "after" period, beginning about 8 to 10 days after Decholin feeding was terminated.

Table I gives mean figures for the volume and 24-hour excretion of cholate, chloride and cholesterol for each of the animals, and mean values for all 5 animals together.

The volume of bile increased after Decholin, and decreased in the "after" period. This increase is in agreement with that reported by all other workers, although it is greater than the 25% increase reported by Schmidt, Beazell, Atkinson and Ivy⁷ for a somewhat larger dosage of Decholin.

The concentration of chloride, as well as the volume of bile, rose with the result that the 24-hour output of chloride was enormously increased. The increase in chloride excretion is interesting in connection with a recent report by Rubin and Rapaport.⁸ They found that in animals with marked reduction in the plasma chloride concentration the mortality from anaphylactic shock was significantly reduced. Previous work in this laboratory had shown that the intravenous administration of sodium dehydrocholate for several days before a shocking dose of horse serum to sensitized dogs greatly reduced the symptoms of anaphylactic shock and the mortality consequent to a shocking dose of horse serum.

There was considerable variation in cholate excretion in different animals and in the same animal from day to day, but the mean values indicate that, after feeding Decholin, in 4 of 5 animals the cholate excretion increased, and in one it decreased. Mean values for the 5 animals together show an increase in cholate excretion of 20%. This is at variance with the results reported by Schmidt, *et al.*,⁷ who found Decholin to decrease the average 24-hour excretion of cholate in 3 dogs, and of Doubilet,⁹ who also reported cholic acid excretion to be decreased after feeding dehydrocholic acid, but found total bile acid to be increased, due to an increase in the desoxycholic acid fraction.

⁵ Reinhold, J. G., and Wilson, D. W., *J. Biol. Chem.*, 1932, **96**, 637.

⁶ Riegel, C., and Rose, H. J., *J. Biol. Chem.*, 1936, **113**, 117.

⁸ Rubin, M. I., and Rapaport, M., *Am. J. Med. Sc.*, 1939, **197**, 435.

The effect on cholesterol was extremely variable, there being in some cases an increase, in some a decrease.

Summary. Feeding sodium dehydrocholate to dogs with biliary fistulae resulted in an increase in volume of bile excreted in a 24-hour period. Associated with the increase in bile volume there was an increase in the chloride excretion and in 4 of 5 dogs an increase in the cholate excretion. There was no significant change in 24-hour excretion of cholesterol.

10686

Experimental Catatonia in a Chimpanzee.*

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Experimental catatonia, as defined by de Jong and Baruk,¹ consists of the following phenomena, which may be considered as an analogue of the syndrome of human catatonia: (a) After administration of an average dose of bulbocapnine or of other drugs having similar effect there occurs: (i) *Catalepsy, i. e.*, the tendency to retain for abnormally long periods of time postures imposed passively or assumed by the animals themselves. (ii) *Negativism, i. e.*, passive or active resistance against change of position, especially position in space. (iii) *Autonomic phenomena, i. e.*, polypnoea, salivation, etc. (b) After administration of a larger dose, hyperkinesia and abnormal postures are present. (c) After administration of a still larger dose epileptoid seizures may occur and lead ultimately to death.

Hitherto bulbocapnine had not been administered to an animal as closely related to human beings as a chimpanzee. Doctor John F. Fulton, to whom I am greatly indebted, gave me the opportunity to use 2 of his chimpanzees for this purpose. Two animals were injected (intramuscularly) with a dose of 10-15 mg per kg of body weight, 20 mg per kg being the average dose for the common macaque. The first animal, Chimpanzee "Ronald" (decorticated on one side one

* I am indebted to Doctor H. G. Barbour for providing me with the bulbocapnine used in this experiment.

¹ de Jong, H., and Baruk, H., *La catatonie expérimentale par la bulbocapnine*, Masson et Cie, Paris, 1930.