

Effect of Anoxic Anoxia on Bile Secretion in the Rat.

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Studies on the effect of anoxic anoxia on the absorption of fat from the alimentary tract of rats have shown that the amount of fat absorbed by animals subjected to partial pressure of oxygen of 63 mm and 53 mm Hg (8.35 and 7.03% oxygen, respectively) was significantly less than for control animals.¹ This cannot be explained on the basis of a prolonged gastric emptying time since it was found that rats fed corn oil showed an initial acceleration of the emptying of the stomach on exposure to diminished oxygen tension.²

Glikson and Rubel^{3,4} reported that exposure of dogs with a biliary fistula to pressures equivalent to altitudes of 6,000 and 8,000 m (9.78 and 7.68% oxygen, respectively) resulted, as a rule, in a decrease in the volume of bile secreted with an increase in the content of organic solids and the viscosity. To a lesser degree and less constantly there was an increase in the bile acid content. They attributed the changes to oxygen starvation of the hepatic cells. Schnedorf and Orr⁵ found that increasing degrees of anoxemia produced by inhalation of 15, 10, and 5% oxygen in nitrogen resulted in a marked and progressive decrease below normal in the flow of bile in nembutalized dogs.

Since it is generally recognized that bile salts play an important role in the digestion and absorption of fat, the decreased rate of fat absorption observed in rats subjected to

reduced barometric pressure might reasonably result from a diminished flow of bile. It was considered of interest, therefore, to investigate the effect of anoxic anoxia on the secretion of bile salts in the rat.

Methods. Young adult albino rats were found to be the most suitable for the experiments. Using the bile fistula technique of Harrington, Greaves, and Schmidt,⁶ the bile duct was anastomosed to the vas deferens by means of a stainless steel cannula about the size of a No. 24 hypodermic needle. Thus the bile was completely excluded from the intestinal tract and excreted in the urine instead. Six rats were successfully operated by this technique and remained in apparent health for a period of 3 to 5 months. The low-fat diet recommended by Greaves and Schmidt⁷ for bile fistula rats was fed, with the exception that meat meal supplemented with 0.25% cod liver oil concentrate was substituted for fish meal which was unavailable at the time. After the rats had recovered from the operative procedure, they were exposed to simulated high altitude for 4-hour periods in individual metabolism cages. At the end of each period the volume of urine was measured and analyzed for its content of bile salts. Exposure to altitude was carried out not more often than once a week to avoid the possibility of acclimatization. Alternating with exposures to altitude control experiments were performed. In the early experiments the rats were subjected to a simulated altitude of 28,000 ft. (53 mm Hg oxygen tension). This resulted in the death of two animals, consequently in the subsequent ex-

¹ MacLachlan, P. L., and Thacker, C. W., *Am. J. Physiol.*, 1945, **143**, 391.

² MacLachlan, P. L., *Proc. Soc. Exp. Biol. and Med.*, 1946, **63**, 147.

³ Glikson, E. B., and Rubel, V. M., *Arch. sci. biol. (U.S.S.R.)*, 1940, **58**, 76.

⁴ Glikson, E. B., and Rubel, V. M., *Bull. biol. med. exptl. U.R.S.S.*, 1940, **9**, 334.

⁵ Schnedorf, J. G., and Orr, T. G., *Am. J. Dig. Dis.*, 1941, **8**, 356.

⁶ Harrington, F. G., Greaves, J. D., and Schmidt, C. L. A., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 611.

⁷ Greaves, J. D., and Schmidt, C. L. A., *J. Biol. Chem.*, 1933, **102**, 101.

TABLE I.
Effect of Anoxic Anoxia on Excretion of Bile Salts and Urine in 6 Bile Fistula Rats. (Average values for four-hour control and experimental periods.)

	No. of Exp.	Bile salts, mg	Urine vol., cc	Corr. coefficient bile salts/urine
Control	32	0.37	2.3	-0.4
Anoxia	32	0.34	3.9	+0.3
Std. Dev.		0.107	1.575	
P (Fisher's)		>0.2	<0.001	

periments the altitude was reduced to 24,000 ft. (63 mm Hg oxygen tension).

The urine was analyzed for its content of bile salts by the procedure of Morrison and Swalm⁸ and Morrison.⁹ This method was found to give satisfactory results on known solutions of cholic acid, as well as urine samples containing bile supplemented with known amounts of cholic acid.

Results and Discussion. The data, Table I, show that there was no significant difference in the amount of bile salts excreted by bile fistula rats when subjected for 4-hour periods to diminished oxygen tension as compared to control periods. In agreement with the findings of Stickney,¹⁰ there was a statistically significant increase in the output of urine as a result of exposure to simulated altitude. Since there was no correlation between the amount of bile salts and the volume of urine excreted, the values for each were expressed in terms of the amount excreted per 4-hour period.

The range in the volume output of urine was 0.8 to 5.0 cc for the control periods, and 1.2 to 7.7 cc for the periods of exposure to altitude. Apparently the urine, irrespective of

its volume, flushed out the bile which had collected in the urethra.

Although the amount of bile salts excreted during the control and experimental periods varied considerably, (0.15 to 0.62 mg and 0.16 to 0.68 mg respectively), the output over a 2- to 3-month interval did not show any noticeable decrease with increasing age of the chronic biliary fistula, as found by Boyd in dogs.¹¹

Haney, Roley, and Cole,¹² as a result of studies on dogs with Thiry Vella loops, suggested that bile salts may play an important role in the normal regulation of the propulsive movements of the small intestine. Ackerman, Curl and Crandall,¹³ however, working with bile fistula dogs found that in general their data did not lend support to the concept that bile salts are an important factor in the regulation of small intestine motility. Since in rats anoxic anoxia was found to be without effect on the secretion of bile salts, a changed motility of the small intestine as a result of deficient bile secretion cannot be considered of importance as far as the effect of anoxia on fat absorption is concerned.

Summary. No significant difference was found in the amount of bile salts excreted by 6 bile fistula rats when exposed for 4-hour periods to decreased oxygen tension (63 mm and 53 mm Hg) as compared to control periods. There was a statistically significant increase in the volume output of urine as a result of exposure to simulated altitude. No correlation existed between the amount of bile salts and the volume of urine excreted.

⁸ Morrison, L. M., and Swalm, W. A., *J. Lab. Clin. Med.*, 1940, **25**, 739.

⁹ Morrison, L. M., *J. Lab. Clin. Med.*, 1943, **28**, 1503.

¹⁰ Stickney, J. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1946, **63**, 210.

¹¹ Boyd, E. M., Earl, T. J., Jackson, S., Palmer, B., and Stevens, M. E. T., *Am. J. Physiol.*, 1945, **145**, 186.

¹² Haney, H. F., Roley, W. C., and Cole, P. A., *Am. J. Physiol.*, 1939, **126**, 82.

¹³ Ackerman, R. F., Curl, H., and Crandall, L. A., Jr., *Am. J. Physiol.*, 1941, **134**, 32.