TABLE I.

Substance	Quantity	Rat Assay: Dose in cc. or mg.	Rat Assay: No. of rats	Rat Assay: % cured	Calculated Total doses
1. Vit. B_1 solution	100 cc.	0.04 cc.	11	64	2500
2. Fullers' earth adsorbate	22 gm.	14.0 mg.	15	73	1570
3. Quinine extract of 2.	≃ 22 gm.	≃ 9.16 mg.	11	73	2400
4. Filtrate from F.E.	100 cc.	1.0 cc.	6	0	<100

were treated with 20 gm. of English fuller's earth. The recovered fuller's earth after careful drying weighed 22 gm. The filtrate, together with a portion of this fuller's earth, was set aside for direct feeding to the test animals. Another portion of the earth adsorbate was extracted with quinine sulfate after the method of Williams, *et al.*[3] Table I gives the results of our assay of these preparations.

These data show that the vitamin was completely removed by the fuller's earth since the spent filtrate from the adsorption was practically devoid of vitaminic activity. When a comparison of the original vitamin solution with the fuller's earth adsorbate prepared from it is made, it appears that some 900 doses were lost in the simple process of adsorption. However, the results obtained with the quinine sulfate extract of this fuller's earth indicate a complete recovery of the vitamin.

The fact that only about 60% of the vitamin can be accounted for when the activated fuller's earth is administered directly makes it apparent that the vitamin B_1 depleted rats cannot fully utilize the vitamin present in preparations such as fuller's earth adsorbates. This is in agreement with our results with the international standard.

9359 P

Hepatic Excretion in the Dog Following Oral Administration of Various Bile Acids.

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Cholic and desoxycholic acids when administered orally to man in large amounts increase both the volume of hepatic bile excretion as well as the concentration of the bile acids.[1] It was found that

[3] Williams, Waterman and Keresztesy, *J. Am. Chem. Soc.*, 1934, **56**, 1187.

* Ralph Colp Fellow in Physiology.

[1] Doubilet, H., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 50.

TABLE I.
Average Bile Acid Excretion in Biliary Fistula Dogs after Oral Administration of Various Bile Acids.

Bile Acid Given gm.	% Concentration			Gm. Bile Acid Excreted			Vol. of Bile cc.
	Cholic Acid	Desoxycholic Acid	Total Bile Acid	Cholic Acid	Desoxycholic Acid	Total Bile Acids	
(Normal Excretion)	1.52	0.75	2.27	2.25	1.12	3.37	150
4 Cholic	1.82	1.31	3.13	4.46	3.21	7.67	245
4 Desoxycholic	0.34	1.39	1.73	0.95	3.91	4.86	281
8 Cholic	1.56	0.93	2.49	5.65	3.14	8.79	356
3 Desoxycholic	0.53	2.20	2.73	1.52	7.07	8.56	321
8 Glycocholic	1.90	1.43	3.33	5.23	3.76	8.99	282
6 Pure Ox Bile Salts	1.39	1.70	3.09	3.68	4.50	8.18	265
8 " " " "	1.92	1.67	3.59	6.11	5.15	11.26	317
6 Dehydrocholic	0.22	0.71	0.93	1.12	3.62	4.74	510
8 "	0.32	0.60	0.92	1.40	2.62	4.02	440
8 Dog Gall Bladder Bile Acids	2.51	1.93	4.44	5.63	4.29	9.92	230

cholic acid was much more effective in raising the concentration of the bile acids in hepatic bile. Similar experiments were carried out in the dog.

A common duct fistula, which drained all the hepatic bile sterilely into a rubber bag, was prepared in 3 female dogs. At various intervals the bags were emptied and the bile discarded after analysis. Pure cholic, desoxycholic, glycocholic and dehydrocholic acids, as well as pure ox bile salts were used. Various amounts of the bile acids were dissolved in equivalent amounts of alkali and administered to the dogs by stomach tube. The ox bile salt powder was mixed with milk for administration. To wash down the bile salt solution about 100 cc. of milk was used. In addition, collected canine gall bladder bile was analyzed for bile acids and an amount containing 8 gm. of bile acids was fed to the dogs. The dogs were kept on the ordinary animal room diet of oatmeal and meat scraps. The bile was analyzed for cholic acid, desoxycholic acid, total bile acids, taurine-conjugated bile acids, and glycine-conjugated bile acids by a method previously described.[2]

The average figures are summarized in Table I. The animals excreted 150 cc. of bile containing 3.37 gm. bile acids in a concentration of 2.27%. Feeding 4 gm. of cholic acid increased the concentration of both cholic and desoxycholic acid. When 4 gm. of desoxycholic acid were administered, the concentration of cholic acid fell, while that of desoxycholic acid rose. When the administration of these 2 bile acids was doubled in amount, each acid tended to depress the excretion of the other acid. The result was that the total excretion of bile acids was approximately the same, 8.79 gm. after cholic acid, and 8.56 gm. after desoxycholic acid.

When 8 gm. of glycocholic acid were administered, the concentration of bile acids rose to 3.33% and 8.99 gm. of bile acids were excreted. Glycocholic acid was found in the bile. On administering 8 gm. of pure ox bile salts (containing about 80% cholic and 20% desoxycholic acids) the concentration of bile acids rose to 3.59% and the total output to 11.26 gm. When only 6 gm. of ox bile salts were given, both the concentration and total output of bile acids were somewhat lower. Glycocholic acid appeared in the bile on ox bile salt administration. After the administration of 8 gm. dehydrocholic acid, the volume of bile rose to 440 cc. but the concentration of bile acids was only 0.92% while the total output was 4.02 gm. Six gm. of dehydrocholic acid gave approximately the same results.

The administration of 8 gm. of natural canine bile salts as found

[2] Doubilet, H., *J. Biol. Chem.*, 1936, **114**, 289.

in normal gallbladder bile led to the excretion of a rather small volume of bile with a bile acid concentration of 4.44%. The total bile acid output was 9.92 gm.

It has been shown by various investigators[3, 4] that the liver often responds to injury by the excretion of a very large volume of dilute bile. As the function of the liver improves, the bile becomes more concentrated and decreases in volume. When such an index of efficiency in the hepatic excretion of bile acids is used, *i. e.*, the largest excretion of bile acids in the smallest volume of bile, it would appear that the various bile acids used can be grouped in the following order of decreasing efficiency: canine bile acids, ox bile salts, glycocholic acid, cholic acid, desoxycholic acid, dehydrocholic acid.

Summary. Oral administration of large amounts of the various bile acids to dogs with a common duct fistula indicate that, from the point of view of largest excretion of bile acids in most concentrated form, the natural bile acids of the dog were probably the most efficient. Under the conditions of these experiments pure ox bile salts and glycocholic acid were found to be more efficient than the unconjugated cholic and desoxycholic acids. The natural bile acids (cholic and desoxycholic acids, and their various conjugated forms) were more effective than dehydrocholic acid.

9360

Hemolytic Streptococcus Toxins and Antitoxins. VI. A Strain of Hemolytic Streptococcus of High Toxicogenicity.

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During an investigation dealing with the titration of hemolytic streptococcus toxins by the flocculation reaction,[1] one strain was found to produce unusually potent toxin. This strain was received from Dr. Alice C. Evans of the National Institute of Health, who designated it as "Streptococcus 594".* The interest of Doctor

[3] Walters, W., Greene, C. H., and Fredrickson, C. H., *Ann. Surg.*, **91**.

[4] Bergareche, J., *Arch. de med., cir. y especialid*, 1933, **36**, 189.

[1] Rane, L., and Wyman, L., *J. Immunol.*, 1937, **32**, 321.

* "Streptococcus 594 was received from Dr. Krause of the Franz-Josefspital, Vienna, Austria. It was isolated from a case of scarlet fever." *Public Health Rep.*, 1934, **49**, 1385.