days. The urines were evaporated and extracted with the same alcohol ether mixture. From this extract or from the water solution of the residue of this extract, we recovered 2.3 grams of the ingested hippuric acid without difficulty.

It would seem then that starving hens do furnish a very small amount of ornithine when this is necessary for the detoxication of benzoic acid. Contrary to the claims of Suga however, we were unable to find even a trace of hippuric acid in the urine of well fed birds after the feeding of benzoic acid but instead only benzyl ornithine or free benzoic acid and like Yoshikawa we believe that birds are unable to furnish glycocoll for detoxication purposes and even unable to make use of it, if it is furnished them from exogenous sources.

63 (2023)

The experimental production of gall-stones in dogs, in the absence of infection, stasis, and gall bladder influence upon the bile.

By PEYTON ROUS, P. D. McMASTER, and G. O. BROUN.

[*From the Rockefeller Institute for Medical Research, New York City.*]

Numerous circumstances and influences which favor the development of gall-stones are now recognized, but uncertainty exists as to which of them are contributory in character and which critical, and as to whether indeed the decisive causes for cholelithiasis are to be found amongst them. In this connection, observations under controlled conditions in animals possess interest.

By a method elsewhere reported,[1] it is possible to join a rubber tube to the common duct of a dog and collect the bile under sterile conditions for months. The gall bladder should be removed at the time of intubation. Our animals thus treated remained in

[1] Rous, Peyton, and McMaster, P. D., *Jour. Exp. Med.*, 1923, xxxvii, 11.

excellent condition, but the observations on several of them were cut short by calculus formation in the collecting system. Twelve dogs have been studied with relation to this development. Calculi were found in six, and in three of these the bile had been sterile. In two of the three instances, the calculi gradually filled the 2 mm. lumen of a glass canula on the wall of which they were sessile, and gave rise to obstruction. Once this happened within twenty-one days of intubation.

The calculi were found only on the walls of the collecting system of rubber and glass, never in the ducts themselves; and they occurred in none of five instances in which this system remained clear of organic débris (dead cells and mucinous matter), but in six out of seven in which there was lodgment of such material,—from which the ducts were always practically free. The stones were multiple, discrete,—at least to begin with,—of approximately the same size at any given level in the tube system, but larger toward the glass canula inserted into the common duct, and more numerous and larger on the lower side of the tube lumen and wherever there existed the possibility for an eddy in the bile current or a dead space, as where glass and rubber joined. The calculi that had formed on the glass connections could be examined directly with the microscope. Early stages were studied in this way.

The stones were made up of calcium bilirubinate and calcium carbonate, with a scaffolding of organic material. Cholesterol was not demonstrable in them. The majority had a center of calcium bilirubinate surrounded by an envelope of crystalline, slightly pigmented carbonate; but stones consisting almost wholly of one or the other substance were encountered. Frequently a number of pigment stones were secondarily united in a matrix of carbonate. The relation of the calculi to the organic débris associated with them differed significantly. Those formed primarily out of carbonate originated in the midst of lumps of the débris, as the microscope showed, whereas the minute pigment stones were so situated as to suggest that they, or their original nuclei, had once been free in the bile but had been caught in the débris and retained. Some of the pigmented calculi were large and of such shape as to leave no doubt that deposition had occurred upon them *in situ*.

The relation between calcium bilirubinate and calcium car-

bonate in the stones of the dog has similarities to that between calcium bilirubinate and cholesterol in human calculi. There is the same tendency in both instances for a nucleus of the pigment material to be overlaid with another substance.

The observations here reported show that infection is not the essential factor in cholelithiasis. That it frequently plays the determining rôle is equally certain.[2] This it would seem to do by damaging the duct wall with result in desquamation,—which the sterile canula did in our experiments,—and by lessening the ability of the bile channels to rid themselves of the cell débris. The débris induces, or furthers, the direct deposition of solids, and may catch and retain potential nuclei for stone formation, in the shape of pigment particles from higher up in the biliary system, which would under ordinary circumstances be voided with the bile.

64 (2024)

The paradoxical shortening of blood coagulation after intravenous administration of sodium citrate.

By NATHAN ROSENTHAL and GEORGE BAEHR.

[*From the Department of Pathology and the First Medical Service, Mount Sinai Hospital, New York City.*]

Sodium citrate, when administered intravenously in large doses (0.5 grams for dog or cat, 3.0 to 6.0 grams for man), produces a pronounced and progressive shortening in coagulation time of the blood which usually reaches its maximum within one hour and may persist for many hours. As a rule, the coagulation time slowly returns to normal within twenty-four hours.

This action of sodium citrate upon the coagulation of the blood *in vivo* is exactly opposite to what occurs *in vitro*. We

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[2] Gilbert, A., et Fournier, L., *Sc. et mém. de la Soc. de Biol.*, 1897, iv, 10 Ser., 936; Mignot, R., *Arch. gen. de Med.*, 1898, i, 129.