10745 P

Quantitative Prothrombin and Hippuric Acid Determinations as Sensitive Reflectors of Liver Damage in Humans.*

SLOAN J. WILSON. (Introduced by Charles A. Doan.)

From the Division of Medical Research, Department of Medicine, Ohio State University, Columbus, Ohio.

With the development of quantitative methods for the determination of plasma prothrombin by Quick[1] and Warner, Brinkhous and Smith,[2, 3] it has been established that the liver is an extremely important intermediary in the production of this important coagulation element. Smith, Warner and Brinkhous[3] report a marked decrease in prothrombin after severe chloroform-induced liver damage in dogs. The extirpation of 60 to 75% of the liver in rats[4] resulted in a temporary decrease in the plasma prothrombin to 30 or 40% of normal with a subsequent gradual return to normal during the 10 days to 3 weeks required for the regeneration of the liver to its normal weight.

In the present study observations have been made on normal human subjects and on patients with various degrees of liver damage without biliary obstruction or fistulae. The two-step method of Warner, Brinkhous and Smith was used to determine the level of the plasma prothrombin. The prothrombin, expressed in per cent of normal, was then compared with the plasma fibrinogen and the galactose, bromsulphalein and hippuric acid liver function tests.[5]

The quantitative level of the plasma prothrombin was found to correlate closely with the quantity of hippuric acid excreted. (See Chart 1). In those individuals with proven liver damage in which the hippuric acid excretion was 0.91 to 2.0 g, the prothrombin was found to be 19 to 37% of normal; with 2.0 to 3.9 g, the level was 33 to 90% of normal; and with 3.9 to 4.56 g hippuric acid excre-

* Aided by a grant from the Comly Research Fund, Ohio State University.

1 Quick, A. J., Stanley-Brown, M., and Bancroft, F. W., *Am. J. Med. Sci.*, 1935, **190**, 501; Quick, A. J., *Am. J. Physiol.*, 1936, **114**, 282; Quick, A. J., *J. A. M. A.*, 1938, **110**, 1658.

2 Warner, E. D., Brinkhous, K. M., and Smith, H. P., *Am. J. Physiol.*, 1936, **114**, 667.

3 Smith, H. P., Warner, E. D., and Brinkhous, K. M., *J. Exp. Med.*, 1937, **66**, 801.

4 Warner, E. D., *J. Exp. Med.*, 1938, **68**, 831.

5 Quick, A. J., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 12; *Am. J. Med. Sci.*, 1933, **185**, 630.

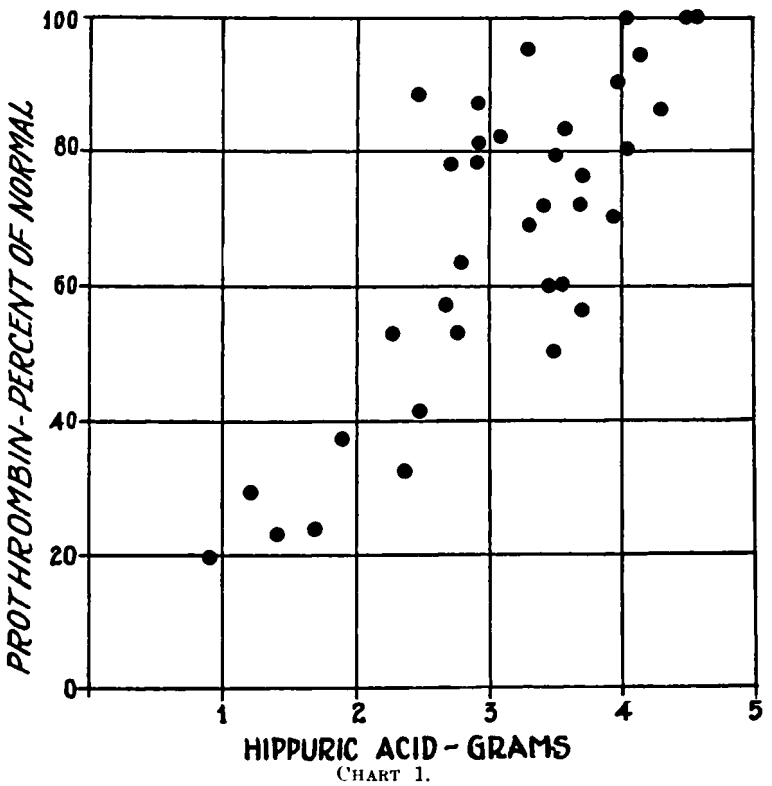

CHART 1.

Illustrating the close correlation of plasma prothrombin determination (ordinate) and the Quick hippuric acid test (abscissa) in terms of liver damage as measured by these respective tests. Any decrease in hippuric acid output was always accompanied by a proportionately diminished prothrombin level in the blood. Each point represents a different patient.

tion, the prothrombin level was 70 to 100% of normal. In 2 patients with severe cirrhosis of the liver and a consistently low plasma prothrombin level of 23 and 29% respectively, the hippuric acid excretion in one was only 1.2 g, in the other 1.9 g, and large amounts of vitamin K and bile salts were without demonstrable effect on the prothrombin.

There was no consistent relationship found between plasma prothrombin and plasma fibrinogen. In one of the patients with cirrhosis of the liver, a consistently low prothrombin and an initially low fibrinogen, the latter became elevated during an acute parotitis, the prothrombin remaining unchanged. In another subject with an aplastic anemia, oral sepsis, continuous high fever of 104°F. and acute hepatic damage, the prothrombin was only 30% of normal but the fibrinogen was discovered to be elevated to 0.531 g %. Smith,

Warner and Brinkhous[3] noted a similar phenomenon during an episode of canine distemper which complicated the convalescence in one of their dogs following chloroform-induced hepatic damage.

The galactose tolerance test was within normal limits in all of the individuals studied. There was a wide variation in the results recorded for the bromsulphalein dye test.

Conclusion. In the human subjects here studied, without biliary obstruction of biliary fistulae, the quantitative levels of plasma prothrombin and the amounts of hippuric acid excreted following the ingestion of a known quantity of sodium benzoate would seem to have reflected most sensitively and consistently the degree of liver damage existing. There was no such suggestive correlation or relationship observed between these tests and the plasma fibrinogen levels, the bromsulphalein dye clearance or galactose utilization, either singly or collectively, when all were studied in the same patient.

10746

Determination of Ascorbic Acid in Feces. Its Excretion in Health and Disease.

HERMAN CHINN AND CHESTER J. FARMER.

From the Department of Chemistry, Northwestern University Medical School, Chicago, Illinois.

In studying the absorption of ascorbic acid from the gastrointestinal tract, we found it necessary to develop a method for the estimation of ascorbic acid in feces. Although reference to ascorbic acid in feces has been made by 2 authors,[1, 2] no description of the method used was given in one case[1] and in the second,[2] only an abstract was available which referred to a colorimetric procedure. In the method to be described, the total indophenol reducing substances of the feces are estimated, an aliquot is then treated with an ascorbic acid oxidase, after which the reducing value is again determined. The difference represents the ascorbic acid present.

Feces upon excretion are immediately weighed to the nearest gram and transferred to a mortar in which they are rubbed to a homogeneous sludge with a minimum volume of freshly prepared 5%

[1] van Eeckelen, M., *Biochem. J.*, 1936, **30**, 2291.

[2] Ishibashi, T., *Acta Pædiat. japon*, 1937, **43**, 187. Abstracted by *Am. J. Dis. Child.*, 1937, **54**, 1101.