

TABLE II.
Vitamin K Activity Determined with Chicks on Ration K-11.

Substance	No. of animals used	Minimum effective dose in 6-hr test γ
Thyloquinone	154	$\frac{1}{2}$
Thylohydroquinone	233	$\frac{1}{2}$
Phosphate (I)	59	10
" (II)	23	$1\frac{1}{2}$
Amino (2)	26	$1\frac{1}{4}$
" (3)	35	2
Quinoline-quinone	31	10 mg insufficient
Bananas (fresh, ripe) *	100	4 g daily insufficient

*Prophylactic test.

naphthoquinone and methylnaphthohydroquinone have identical biological activities. Apparently, solutions of the latter compound are stable even at elevated temperatures. In regard to the discrepancy in the potencies of the 2 phosphate derivatives, the Hoffmann-LaRoche preparation (Phosphate II) was found to be about as potent as methylnaphthoquinone on a molecular basis, thus confirming the recent data of Fieser, *et al.*¹⁰ As suggested by Lee, *et al.*,⁷ it may be that the Phosphate (I) had a low activity due to the fact that its preparation did not include the isolation and purification of the intermediate diphosphoryl chloride. The observation of Emmett, *et al.*,⁸ that the amino compound with the methyl group in position 2 is more potent than the one with the methyl group in position 3, was confirmed. It is of interest to note also that the quinoline-quinone has apparently no antihemorrhagic activity.

12014

Blood Prothrombin Levels and Hippuric Acid Excretion Liver Function Test in Liver Disease.

ROBERT KARK, FRANKLIN W. WHITE, ALEXANDER W. SOUTER
AND EMMANUEL DEUTSCH. (Introduced by George R. Minot.)

From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, and the Department of Medicine, Harvard School, Boston.

Wilson¹ showed that a close correlation existed between the hippuric acid excretion and the plasma prothrombin levels of 36 patients

¹⁰ Fieser, L. F., Tishler, M., and Sampson, W. L., *J. Biol. Chem.*, 1941, **137**, 659.

¹ Wilson, S. J., *Proc. Soc. Exp. Biol. and Med.*, 1939, **41**, 559.

with liver disease whom he studied. He concluded that "the quantitative levels of plasma prothrombin and the amounts of hippuric acid excreted following the ingestion of a known quantity of sodium benzoate reflected most sensitively and consistently the degree of liver damage existing."

We have observed the hippuric acid excretion and the blood prothrombin level of 12 patients with clinically evident liver disease in the same way as Wilson did, save that in our patients these two tests were made following adequate treatment with synthetic vitamin K analogues.

In these 12 patients the "prothrombin time" was measured by the Quick technic³ and converted to blood prothrombin percentage of normal.⁴ The hippuric acid liver function test² was performed on the patients on the same day as the blood prothrombin level was estimated, or within the next 3 days.

The clinical diagnoses, response to therapy with vitamin K, final blood prothrombin level and hippuric acid excretion of these patients are recorded on Table I.

Conclusion. There was no correlation between the blood prothrombin level and a single estimation of the urinary excretion of

TABLE I.
Comparison of the Prothrombin Levels in Blood of Patients Suffering with Liver Disease (after Correction of Avitaminosis K) with Hippuric Acid Excretion, Measured at the Same Time.

Case No.	Clinical diagnosis	Response to therapy with vitamin K analogues	Blood prothrombin % of normal	Hippuric acid excretion, g
1.	Subacute yellow atrophy	Slight, delayed	35	2.62
2.	Portal ("aleoholic") cirrhosis	None	40	1.12
3.	" " " "	" "	40	1.2
4.	Catarrhal jaundice	Moderate, delayed	40	1.3
5.	Cardiac failure with hepatitis	" rapid	50	1.5
6.	" " " "	" "	58	1.1
7.	Portal ("aleoholic") cirrhosis	None	60	1.3
8.	" " " "	" "	65	<1
9.	Stricture of common duct. Biliary cirrhosis	Complete, rapid	100	<1
10.	Cancer of gall bladder. Biliary cirrhosis	" "	100	1.3
11.	Cancer of head of pancreas. Biliary cirrhosis	" "	100	0.43
12.	Recurrent jaundice. ?Toxic hepatitis. ?Obstruction	" "	100	1.2

² Quick, A. J., *Am. J. Med. Sc.*, 1933, **185**, 630.

³ Quick, A. J., Stanley-Brown, M., and Bancroft, F. W., *Am. J. Med. Sc.*, 1935, **190**, 501.

⁴ Souter, A. W., and Kark, R., *Am. J. Med. Sc.*, 1940, **200**, 603.

hippuric acid after ingestion of known amounts of sodium benzoate in 12 patients with liver disorders after treatment with synthetic vitamin K analogues.

12015 P

Etiological Agents of North and South American Blastomycosis.*

N. F. CONANT AND ARDEN HOWELL, JR.† (Introduced by E. C. Faust.)

From the Department of Bacteriology, Duke University and Hospital, Durham, N.C., and the Department of Tropical Medicine, Tulane University, New Orleans, La.

A granulomatous fungus infection simulating scrofuloderma was described by Gilchrist in 1894. Since the fungus was seen in the diseased tissues as a budding, yeast-like organism, associated with a skin infection, it was called *Blastomyces dermatitidis*¹ and the disease *blastomycosis*. A number of different species of *Blastomyces*² and a number of variously named fungi³ since reported from cases of North American blastomycosis have been shown to be either slight variations of Gilchrist's organism or to be *Coccidioides immitis*,^{4, 5} the causative agent of San Joaquin Valley Fever or coccidioidal granuloma.

South American investigators have described a granulomatous fungus infection as pseudococcidioidal granuloma⁶ caused by a fungus first confused with *Coccidioides immitis*,^{7, 8} later named *Paracoccidioides brasiliensis*.⁹ Moore,¹⁰ however, showed that *Paracoccidioides* reproduced in the tissues by multiple-budding, thus in-

* Aided by a grant from the John and Mary R. Markle Foundation.

† National Research Council Fellow in the Medical Sciences, Duke University School of Medicine, 1939-40.

¹ Gilchrist, T. C., and Stokes, W. R., *J. Exp. Med.*, 1898, **3**, 53.

² a. Moore, M., *Ann. Missouri Bot. Gard.*, 1933, **20**, 49; b. Moore, M., *Ann. Missouri Bot. Gard.*, 1933, **20**, 471; c. Moore, M., *Arch. Derm. and Syph.*, 1933, **27**, 49.

³ Castellani, A., and Jacono, I., *J. Trop. Med. and Hyg.*, 1933, **36**, 297.

⁴ Benham, R. W., *Arch. Derm. and Syph.*, 1934, **30**, 385.

⁵ Ciferri, R., and Redaelli, P., *Att. dell' Ist. Bot. Univ. di Pavia*, 1935, **6**, 55.

⁶ Lutz, A., *Brasil-med.*, 1908, **22**, 121, 141.

⁷ Fonseca, O. da, and Leao, A., *Compt. Rend. Soc. Biol.*, 1928, **98**, 619.

⁸ Almeida, F. de, *Ann. Fac. Med. Sao Paulo*, 1929, **4**, 91.

⁹ Almeida, F. de, *Compt. Rend. Soc. Biol.*, 1930, **105**, 315.

¹⁰ Moore, M., *Arch. Derm. and Syph.*, 1938, **38**, 163.