

There was a positive but non-significant correlation between the B.M.R. and the urinary thiamine excretion. The weights of these men ranged from 137 to 168 lbs. Here also, there is no correlation between weight and thiamine excretion. Variations probably exist in the way that these individuals metabolize thiamine. We know that only about 30% of the thiamine intake at these 2 levels can be accounted for as the sum of the urinary thiamine and pyrimin excretions.² Break-down products of thiamine other than pyrimin probably vary inversely as the thiamine excretion.

No accurate prediction of the magnitude of one subject's excretion at a higher or lower level can be made from data of any one control period. For instance, in the 2 different groups D and A had approximately the same level of excretion on an intake of 1.0 mg per day whereas there was a marked difference in the excretion levels when the intake was 2.0 mg (313 versus 411). The overall excretion of the group on 2.0 mg thiamine in December 1945 was considerably higher than that of the other group when it was on this intake. The excretion of the subjects on 1.0 mg was approximately the same for both groups.

There are a few references to the variations of individuals on the same level of thiamine intake.^{9,10} In these reports the great variation in the thiamine excretion is apparent

¹⁰ de Jong, S., *Arch. néerl. de physiol.*, 1940, 25, 57.

but the data do not permit any more detailed analysis. In both of these reports, there is a strong suggestion that the thiamine excretions of their subjects are characteristic of the individuals. De Jong states that "The mean of the daily excretions of a weekly period is, for the same individual, more or less constant."¹⁰, p 127

Summary. 1. The thiamine and pyrimin excretions by 2 groups of normal young men maintained on 1 and 2 mg of thiamine per day have been determined on 2 different occasions when the same diet was served on 3 successive days. Each of these periods occurred only after the men had been stabilized at their respective intakes.

2. The thiamine excretion on a constant diet shows a 2 to 3 fold variation for the men within each group and an overlapping of the 2 groups. The pyrimin excretion is much more constant and shows no tendency for the values of the 2 groups to overlap.

3. The excretion of thiamine is characteristic of the individual as shown by the rank correlations of the excretion values. This was true over the entire 8 months of the dietary regime and was also true when the above thiamine intakes were reversed. There is no such correlation for the pyrimin excretions.

4. The explanation of the thiamine excretion as a characteristic of the individual cannot be found in the fecal excretion of thiamine, the physical activity of the subjects, in the B.M.R. nor in their body weights.

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Persistence of Elevated Values for the Thymol Turbidity Test Following Infectious Hepatitis.*

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The thymol turbidity test introduced by Maclagan,¹ because of its simplicity and the

ease with which results can be reproduced, is finding wide application in the study of patients with liver disease.^{2,3} It is extremely

* The Bureau of Medicine and Surgery of the U. S. Navy does not necessarily endorse the ideas set forth in this paper.

¹ Maclagan, N. F., *Nature*, 1944, 154, 670.

² Recant, L., Chargaft, E., and Hanger, F. M.,

TABLE I.
Values for Plasma Bilirubin, Bromsulphalein Retention, and the Thymol Turbidity Reaction in Patients 6 Months or More Following an Attack of Infectious Hepatitis.

	No. cases	% with increased plasma bilirubin	% with increased bromsulphalein retention	% with increased thymol turbidity values
Persistent symptoms	27	41	44	67
No symptoms	30	10	0	7

sensitive and may be of special use in evaluating mild symptoms that persist in patients who have had an attack of infectious hepatitis. A study of a group of cases presenting vague complaints more than 6 months after an attack of infectious hepatitis was made in the out-patient department of the Hospital of The Rockefeller Institute, and it was found that the thymol turbidity test was positive more often than any other test of liver function (Table I). It would seem to be of considerable importance, therefore, to determine the significance of this reaction. A study of the results of serial determinations of the thymol turbidity test throughout the course of infectious hepatitis, in cases with and without complications, has furnished certain information.[†]

In the acute stage of the disease values of the thymol turbidity test showed a delayed rise reaching a peak at least a week later than did values for plasma bilirubin and bromsulphalein retention, and at a time when symptoms of the disease had almost disappeared. These values then fell to normal more slowly than did those of any other test of liver function, several months sometimes being

required for a return to normal. Fig. 1 illustrates the delayed rise and fall in the intensity of the thymol turbidity reaction in a typical case.

Approximately 18% of the cases of infectious hepatitis studied at the Hospital of The Rockefeller Institute developed definite recurrences during convalescence. These usually followed the first period of unrestricted activity and were characterized chiefly by an increase in bromsulphalein retention and a return of mild clinical symptoms. Values of the thymol turbidity test reflected all of these recurrences by a delayed rise one to 3 weeks after the onset of the recurrence. Extremely high values were sometimes found, frequently higher than those observed in the initial attack. These high values persisted for as long as 6 months after other objective signs of relapse had disappeared, and did not appear to give a true indication of the clinical state of the patient. Fig. 2 and 3 show the delayed rise and markedly prolonged elevation of the thymol turbidity values following typical recurrences during convalescence. In these cases, the second attack, although extremely mild, produced a more marked response in the thymol turbidity reaction than did the initial attack.

Results of the cephalin flocculation test paralleled the thymol turbidity values in most of the cases. Because quantitative measurements were more difficult, serial determinations of the cephalin flocculation test did not give curves that could be clearly interpreted. However, this test also remained positive for a greater period following relapse than after the first attack.

Certain patients with infectious hepatitis had marked persistence of symptoms and abnormalities in other tests of liver function for long periods without demonstrating definite recurrences; these cases showed only slightly

PROC. SOC. EXP. BIOL. AND MED., 1945, **60**, 245.

³ Watson, C. J., Rappaport, E. M., *J. Lab. and Clin. Med.*, 1945, **30**, 983.

[†] Estimation of the thymol turbidity reaction was carried out by the method of MacLagan⁴ modified for the use of the Coleman Jr. spectrophotometer; Evans blue dye (T-1824) was used as a standard of reference. A concentration of 3 γ per cc is equivalent to 20 thymol turbidity units. The Evans blue standard appears to have certain advantages over the barium sulfate standard previously employed in this laboratory.⁵

⁴ MacLagan, N. F., *Brit. J. Exp. Path.*, 1944, **25**, 234.

⁵ Shank, R. E., and Hoagland, C. L., 1946, **162**, 133.

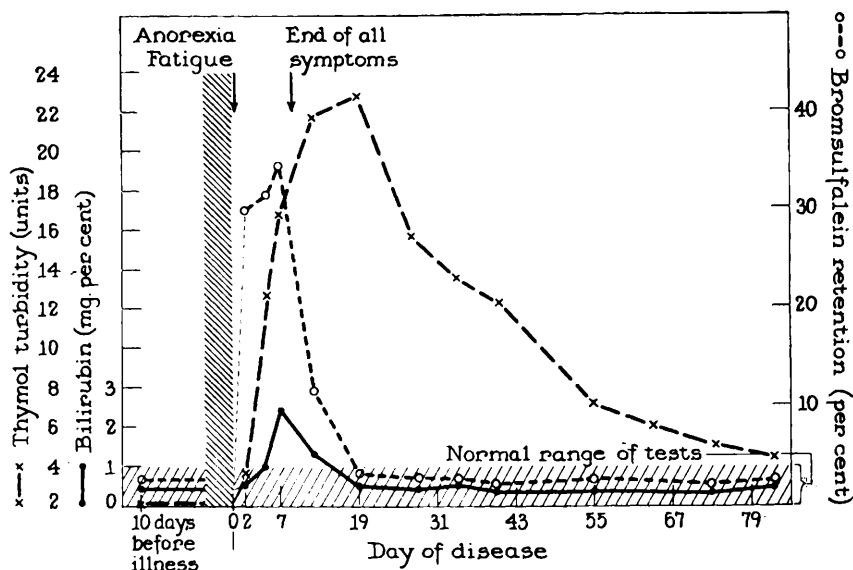


FIG. 1.

Comparative results on the serial determination of plasma bromsulfalein, the level of plasma bilirubin, and the thymol turbidity reaction of the serum in infectious hepatitis (mild uncomplicated case).

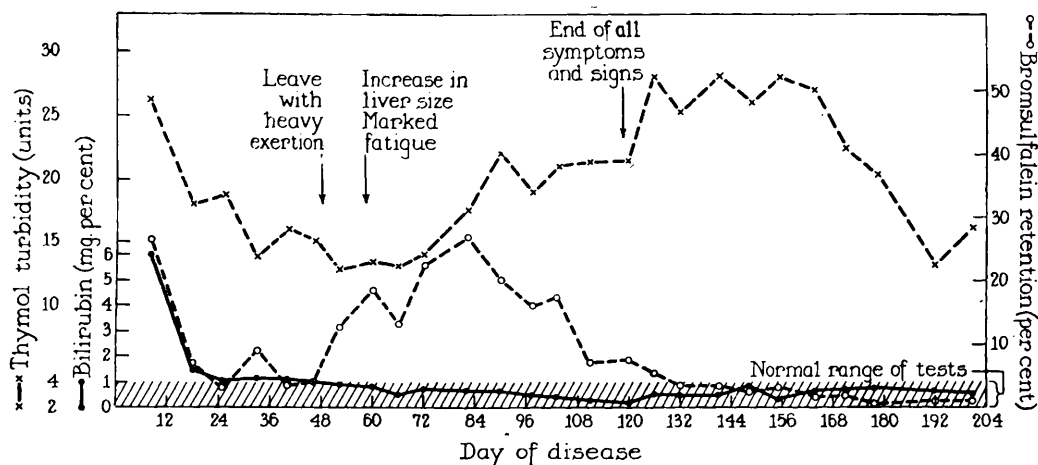


FIG. 2.

Comparative results on the serial determination of plasma bromsulfalein, the level of plasma bilirubin, and the thymol turbidity reaction of the serum in infectious hepatitis (recurrence during convalescence).

increased values for the thymol turbidity test. The greatest and most prolonged elevations were seen following recurrences of the disease and in these cases the values appeared to be out of proportion to the condition of the pa-

tient as judged by the mild clinical symptoms and the results of other tests of liver function. The significance of these high values is not clear. It may be that a selective function of the liver is measured which re-

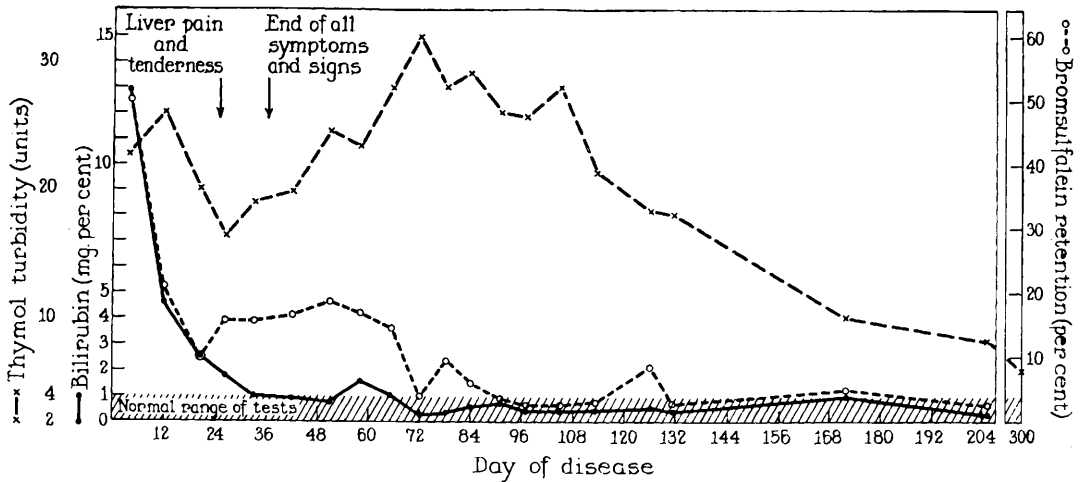


FIG. 3.

Comparative results on the serial determination of plasma bromsulfalein, the level of plasma bilirubin, and the thymol turbidity reaction of the serum in infectious hepatitis (recurrence during convalescence).

mains impaired for a prolonged period. The fact that these patients developed a recurrence of hepatitis shows that there was persisting activity. On the other hand, since the maximal response in the thymol turbidity reaction occurred coincident with the period of recovery following recrudescence, the possibility that the reaction is related in some manner to reparative phenomena in the liver should be entertained.

Studies of the protein precipitated by the thymol reagent are now in progress and the results may aid in understanding the significance of the reaction. At present it may be said that values of the thymol turbidity test should be interpreted with special care

because they often appear to reflect previous events in a patient's illness. However, because of the simplicity and marked sensitivity of this test, it is very useful for following patients with liver disease, if the above limitations are kept in mind.

Summary. Values for the serum thymol turbidity test show a delayed rise and fall following an acute attack of infectious hepatitis. Recurrences of the disease produced a marked increase in the thymol reactivity of the serum which persisted long after other objective signs had disappeared. These findings indicate that the thymol turbidity reaction may show a delayed and prolonged response to liver injury.