

THYROID UPTAKE STUDIES IN INFECTIOUS HEPATITIS

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Ever since Kendall (1) described that the liver holds a relatively large amount of thyroid hormones, considerable interest has been shown in the functional relationship between the thyroid and the liver. The nature of this interrelationship is not clear, but it is conceivable that the thyroid function may be abnormal in some liver disorders.

An occurrence of an epidemic of infectious hepatitis in Bombay, India, during the year 1967 afforded an opportunity to make a study of thyroid function in patients with severe liver damage. Our observations in these patients showed abnormalities in thyroid function which correlated to some extent with the degree of liver damage.

PATIENTS AND METHODS

Forty-three adult males with varying degrees of jaundice were selected for the investigations. Some were in the acute phase of the disease while others were recovering and their jaundice was waning. The degree of liver damage was estimated by serum bilirubin levels determined by the method of Malloy and Evelyn (2). None of the patients had any apparent thyroid disorder at the time of the investigations or a history of liver disease in the past.

Thyroid-function studies included (A) measurement of radioiodine uptake by the thyroid at 2, 24, and 48 hr and (B) serum PB¹³¹I at 48 hr. It was not possible to carry out many other more sophisticated thyroid-function investigations because facilities for doing them were not available in Bombay at the time of the study. Because these studies were carried out in a field infectious disease hospital, followup studies after the patients recovered completely were also not possible.

RESULTS

The serum bilirubin values in the 43 patients with infectious hepatitis at the time of the study varied from 0.62 to 35.72 mg% with an average of 8.1

mg%. Those having more than 8.0 mg% were considered as having severe liver damage, while those having less than 8.0 mg% were considered as having only a moderate degree of liver damage.

By this criterion, 15 were in the group with a severe degree of liver damage. They had an average serum bilirubin of 15.7 mg% with a range of 8.17–35.72 mg%. The other group with mild or moderate damage consisted of 28 patients who had an average serum bilirubin value of 4.0 mg% and a range from 0.62 to 7.0 mg% (Table 1).

Thyroid ¹³¹I uptake measurements done in our laboratory on 109 adult euthyroid individuals with no liver disorders had an average value of 13.6 ± 6.5 at 2 hr, 38.7 ± 13.8 at 24 hr, and 41.1 ± 13.2 at 48 hr. In patients with infectious hepatitis who had bilirubin values of more than 8.0 mg%, the mean thyroid uptake values at all periods of measurements were found to be lower than those in normal subjects. The uptake in this group averaged

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TABLE 1. SERUM BILIRUBIN LEVELS IN INFECTIOUS HEPATITIS

	No. of patients	Mean bilirubin values (mg%)	Range
Total	43	8.1	0.62–35.72
High degree of liver damage (bilirubin > 8.0 mg%)	15	15.7	8.17–35.72
Mild or moderate degree (bilirubin < 8.0 mg%)	28	4.0	0.62– 7.0

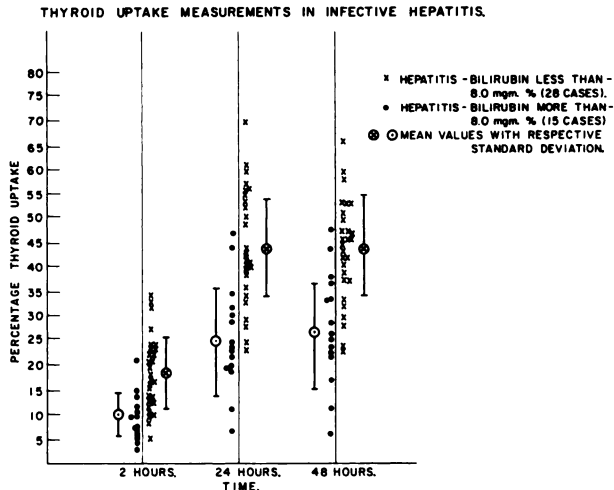


FIG. 1. Percentage values of radioiodine uptake by thyroid at various time intervals in 43 patients with infectious hepatitis.

10.7 ± 4.3 at 2 hr, 25.2 ± 11.0 at 24 hr, and 25.5 ± 10.7 at 48 hr. The differences in these mean values and those in the control group were statistically significant at 24 and 48 hr ($p < 0.001$).

Patients with a moderate or low degree of liver damage with bilirubin less than 8.0 mg% had a normal pattern of radioiodine uptakes. The average values of thyroid uptake in these patients were 18.8 ± 7.8 at 2 hr, 43.8 ± 19.4 at 24 hr, and 44.2 ± 10.2 at 48 hr (Fig. 1).

The differences between the mean values of thyroid uptake of radioiodine in the two groups with infectious hepatitis were statistically significant at all periods of measurements ($p < 0.001$ at 2 hr, $p < 0.001$ at 24 hr, and $p < 0.001$ at 48 hr).

Uptake values at 24 hr for the 43 patients were also compared with their respective serum bilirubin values. A good degree of correlation was found between these two parameters (coefficient of correlation = -0.69). Serum $PB^{131}I$ levels in patients with infectious hepatitis were not significantly altered in comparison to a normal mean value of $0.19 \pm 0.17\%$ of the administered dose per liter of plasma in our laboratory. Mean $PB^{131}I$ in patients of Group I was 0.11 ± 0.064 mg%, while in Group II, the mean was $0.23\% \pm 0.24$ per liter of plasma. While the $PB^{131}I$ in the latter group seemed slightly elevated, there was no statistically significant difference between this value and that of the normal group. Similarly there was no difference in average $PB^{131}I$ values between the two groups of patients with infectious hepatitis.

DISCUSSION

Several clinical and experimental reports have suggested an interrelationship between the thyroid

and liver. Hypothyroidism after neonatal jaundice was described by several workers (3-6). Gross liver damage has been observed on postmortem of patients with severe thyrotoxicosis (7). Animals with liver damage from carbon tetrachloride administration show changes suggestive of thyroiditis on histological examination (8). Levey (9) reported inhibition of radioiodine uptake by the thyroid in vitro in the presence of liver extract, and Overby (10) has reported a protective action by liver extract against the effects of excess thyroxine in rats.

There are several reports of abnormal thyroid function tests in association with liver disorders. In cirrhosis of the liver serum PBI was found to be low or normal (11,12). Radioiodine uptake in some of these patients (13) was reported to be high. In infectious hepatitis, the PBI was found to be elevated (11,14,15) while thyroid uptake was reported to be diminished (14) or high (15) in a small series of patients.

The discrepancies in these observations may be attributed to the fact that in cirrhosis involvement of the liver is variable and processes of destruction and repair are at work simultaneously. Since in infectious hepatitis the damage to the liver is acute and severe, it is likely that biochemical abnormalities may be more marked in this disease than in cirrhosis.

Our patients were divided into two groups, those with serum bilirubin levels above 8.0 mg% and those with less than 8.0 mg%. This dividing line was chosen arbitrarily and served the useful purpose of dividing the patients into those with mild and those with severe liver damage. The thyroid uptake of radioiodine was significantly suppressed in those with severe damage to the liver. The uptake values at 24 hr in the 43 patients showed a good degree of correlation when plotted against the respective serum bilirubin values (coefficient of correlation = -0.69).

A possible explanation can be offered for the changes observed in these studies. A damaged liver could be limited in its ability to store and conjugate thyroxine. As a result of this, a high amount of thyroxine might be retained in the circulation. This would suppress pituitary function, and the thyroid might become underactive with diminished values of thyroid radioiodine uptake. This possibility is supported by the observations of high stable PBI in infectious hepatitis by various workers (11,14) and by the findings of the chromatographic studies of Vannotti (14) that in normal subjects the serum contains thyroxine and the bile contains thyroxine and glucuroconjugates of thyroxine while in infectious hepatitis serum and bile contain only thyroxine but no glucuroconjugates.

SUMMARY

Thyroid-function studies were done in 43 cases of infectious hepatitis with varying degree of liver damage as judged by serum bilirubin levels. A different pattern of thyroid uptakes was seen in patients with moderate liver damage and those with severe liver damage. A good correlation was observed between thyroid uptake and degree of liver damage.

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REFERENCES

1. KENDALL EC: The physiologic action of thyroxin. *Endocrinology* 3: 156-163, 1919
2. MALLOY HT, EVELYN KA: The determination of bilirubin with the photoelectric colorimeter. *J Biol Chem* 119: 481-490, 1937
3. AKERREN Y: Prolonged jaundice in new born associated with congenital myxedema. *Acta Pediat* 43: 411-425, 1954
4. CHRISTENSEN JF: Prolonged icterus neonatorum and congenital myxedema. *Acta Pediat* 45: 367-371, 1956
5. LOWREY GH, ASTER RH, CARR EA, et al: Early diagnostic criteria of congenital hypothyroidism. *AMA J Dis Child* 96: 131-143, 1958
6. BIALKIN G, HARRIS L: Clinical kernicterus and congenital hypothyroidism. *NY State J Med* 58, 101-103, 1958
7. TROTTER WR: *Diseases of the Thyroid*, Oxford, Blackwell Scientific Publications, 1962, p 49
8. LEE GLOVER E, REUBER MD: Chronic thyroiditis in Buffalo rats with carbon tetra-chloride induced cirrhosis. *Endocrinology* 80: 361-364, 1967
9. LEVEY HA: Studies on the mechanism of action of liver extracts in inhibiting uptake of ¹³¹I in vitro by the rat thyroid gland. *Endocrinology* 80: 417-422, 1967
10. OVERBY LR, FREDRICKSON RL, FROST DV: The antithyrototoxic factor of the liver. *J Nutrit* 67: 397-411, 1959
11. KYDD DM, MAN EB: Precipitable iodine of serum in disorders of the liver. *J Clin Invest* 30: 874-878, 1951
12. BORA SS, KAPOOR DC, KRISHNAN PS, et al: Protein bound iodine in cirrhosis of liver. *J Indian Med Assn* 41: 176, 1963
13. MUELLER R, BRAUSCH CC, HIRSCH EZ, et al: Uptake of radioiodine in the thyroid gland of patients with impaired liver function. *J Clin Endocrinol Metab* 14: 1287-1299, 1954
14. VANNOTTI A, BERAUD T: Functional relationship between the liver, the thyroxin binding protein of serum and the thyroid. *J Clin Endocrinol Metab* 19: 466-477, 1959
15. FRIIS T: Thyroxin metabolism in man estimated by means of ¹³¹I-labelled thyroxin. *Acta Endocrinol* 29: 587-601, 1958