# THE RELATION BETWEEN THE LIVER AND THE THYROID GLAND

## I. Blood Iodine as an Indicator of Liver Function

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Control of the level of blood iodine appears to be principally a function of the thyroid gland[1]. Evidence points to the thyroid as an organ for abstraction from the blood and storage of iodine. Radioactive iodine injected intravenously into rabbits accumulated mainly in their thyroids[2]. In hyperthyroidism there is a markedly increased negative iodine balance, with general iodine depletion, partly accountable for by increased urinary iodine excretion[3]. In hypothyroid states an apparently opposite mechanism occurs. The urinary excretion of iodine is decreased in populations of goiter-endemic zones[4]. The blood iodine level has been noted as consistently elevated in a large proportion of hyperthyroidism cases[5]. It is usually high in cases with symptoms of under one year's duration, and tends to be normal in older cases[6].

However, though the thyroid is of unquestioned importance in iodine metabolism, much data indicate that it is not the only influence. Evidence exists which points to the involvement of other organs, particularly the liver. Much of the material indicating relationship between the liver and the thyroid is clinical and pathological.

It has been noted for many years that icterus may occur in thyrotoxicosis[7], and it has been considered a sign of poor prognosis[6, 8]. It was at first attributed to liver damage due to intercurrent disease or heart failure, and not directly to disease of the thyroid gland. Later, cases were described in which no other factor than thyroid disease could be found.

Pathological study revealed further evidences of liver damage. Kerr and Rusk[9] in 1922 described a case of hyperthyroidism with jaundice in which an acute yellow atrophy of the liver was present at post mortem. Earlier, Pettavel[10] had found fatty livers in eight cases of hyperthyroidism, none of which had heart failure. Further pathological descriptions in similar cases have included "central acinar and perivenous necrosis"[11] and "a generalized hyperemia, most marked in the liver, with widening of the central vein and necrosis of parenchymal cells"[12]. Acute liver necrosis has been ascribed as the cause of death in "thyroid crisis"[13].

Liver damage in thyrotoxicosis has been explained on the one hand as of toxic origin[14], and on the other as due to metabolic influences. Chvostek[15] discussed the relationship as one of disturbed carbohydrate metabolism. Markedly lowered liver glycogen has been noted[16] and it has been found that animals given excessive doses of thyroxin show liver fat deposition[17].

Clinically, other liver disturbance signs than jaundice are found in hyperthyroidism. Galactosuria, liver enlargement, and urobilinuria may be present. All of these appear to a greater extent with high basal metabolic rates[8].

Experimental data indicate that the liver is involved in normal iodine metabolism. Iodine is excreted with the bile[18]. The amount so excreted is increased after meals, particularly after iodine ingestion, and by chologogues[19, 20]. Yuzuriha claims that the reticulo-endothelia system is responsible for removal of iodine from the blood[21, 22].

Against such a background De Courcey has attempted to relate elevation of blood iodine to disease of the biliary tract and liver[23, 24, 25]. He reports frequent association of liver and gall bladder disease with elevated blood iodine levels, although his experimental evidence is certainly far from conclusive[25], and attributes such elevation to disturbed liver function. He suggests that iodine determination might be a useful index of the condition of the liver before gall bladder surgery, and proposes that more intensive preparatory treatment be given to patients with elevated blood iodine.

However, Greene and Bruger[26] found that patients with liver and gall bladder disease have normal blood iodine levels if no iodine-containing drugs have been previously administered. They noted that the iodine level may be high for several weeks following the use of radio-opaque iodine-containing dyes in cholecystography. Experimentally they observed that common duct ligation in cats failed to raise the blood iodine.

## EXPERIMENTAL

It seemed important to determine, by more conclusive evidence than De Courcey presents, whether blood iodine analysis is of importance in disease of the liver and gall bladder. We measured blood iodine in normal persons, in patients with liver and gall bladder disease, and in rabbits before and after carbon tetrachloride poisoning. All of the rabbits were on uniform diet throughout the experiment.

Iodine analyses were made by the method of Trevorrow and Fashena[27], using 10 cc. samples of blood from arm veins of the humans and from rabbit hearts. The use of iodine was carefully avoided. Rabbit liver damage was accomplished with carbon tetrachloride inhalation[28]. The animals were maintained in anesthesia for ten minute periods with the drug after induction with ether administered by cone saturation. The poisoning was done at three day intervals over two and three week periods. One day after the final inhalation, blood specimens were taken, and the animals killed. Histological examination was made to confirm the effect of poisoning.*

### *Pathological description of rabbit livers*

No. 3. Early necrosis of parenchymal cells about central vein, with condensation of cells and of fibrous stroma. Extensive vacuolization of central cells.

No. 496. Very extensive necrosis extending from central vein to portal areas. Leucocytic infiltration. Areas of early fibrosis.

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* Courtesy of Dr. G. Y. Rusk, Department of Pathology, Mt. Zion Hospital, San Francisco.

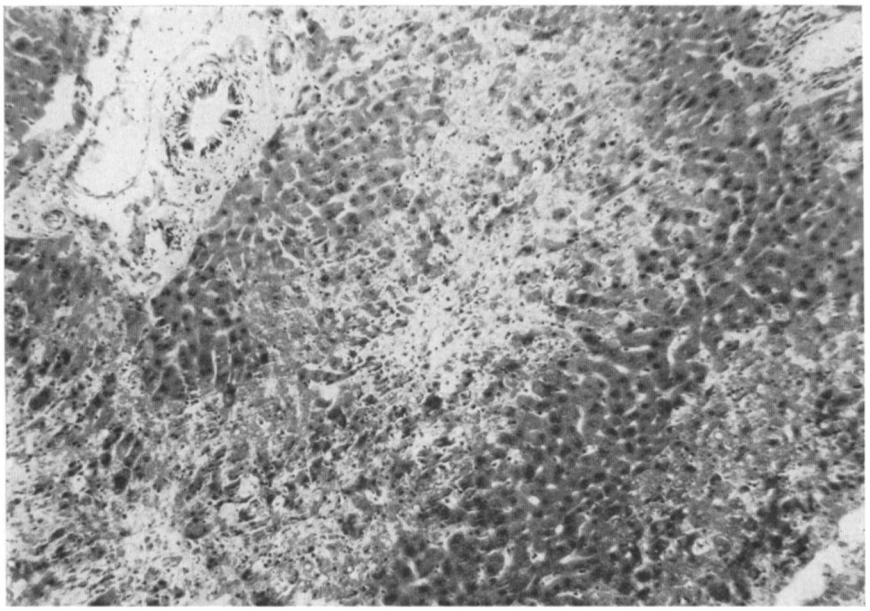

FIG. 1. PHOTOMICROGRAPH OF A SECTION OF LIVER FROM RABBIT 496 AFTER CARBON TETRACHLORIDE POISONING

Blood iodine level within same limits as control rabbit

TABLE 1

| NORMAL HUMANS | AVERAGE BLOOD IODINE |
|---|---|
| | *microgram per cent* |
| 1 | 8.84 |
| 2 | 25.6 |
| 3 | 17.5 |
| 4 | 31.42 |
| 5 | 33.29 |
| Average of normals | 23.33 |

TABLE 2

| PATHOLOGICAL HUMANS CONDITION | AVERAGE BLOOD IODINE |
|---|---|
| | *microgram per cent* |
| 1. Metastatic liver malignancy | 22.60 |
| 2. Post cholecystectomy with probable cholangitis | 23.45 |
| 3. Catarrhal jaundice | 26.25 |
| 4. Advanced cirrhosis | 25.62 |
| Average of patients | 24.48 |

No. 499. Condensation and dark staining of central cells, with granular cytoplasm and deposition of fat.

No. 500. Very similar to No. 499.

As tables 1, 2 and 3 show, there is no significant difference between the iodine levels of our normal cases and those with liver disease. Nor is there any difference between the rabbit blood iodine before and after severe liver damage.

TABLE 3

| RABBITS | BLOOD IODINE, CONTROLS | BLOOD IODINE FOLLOWING CARBON TETRACHLORIDE INHALATION |
|---|---|---|
| | *microgram per cent* | *microgram per cent* |
| 1 | 32.16 | |
| 2 | 34.40 | |
| 3 | 27.00 | |
| 4 | 25.1 | |
| 5 | 24.9 | |
| 6 | 27.6 | |
| 7 | 25.5 | |
| 8 | 31.7 | |
| 9 (Before $CCl_4$) | 25.9 | 25.32 |
| 10 (Before $CCl_4$) | 24.51 | 25.2 |
| 11 (Before $CCl_4$) | 22.4 | 26.02 |
| 12 (Before $CCl_4$) | 24.9 | 24.04 |
| Average control | 27.48 | |
| Average poisoned | | 25.28 |

## DISCUSSION

Our results, clinical and experimental, do not bear out De Courcey's generalization that blood iodine is elevated in liver and gall bladder disease. As Greene and Bruger have demonstrated[26], dyes used in gall bladder X-ray diagnosis may elevate the blood iodine for several weeks and may very well have been responsible for such elevated values as have been reported. Furthermore, we have concluded that the determination of iodine is not a suitable general clinical method because of its technical difficulties. The analysis we feel is restricted to research and should be carried out by trained chemists in oxidizing-vapor-free laboratories.

Though the liver and the thyroid may each play a part in the metabolism of iodine, their relationship is not expressed by blood iodine level, and indeed, may be completely independent of their mutual influences on iodine excretion and absorption.

## SUMMARY

Blood iodine is not elevated per se in liver and gall bladder disease, as claimed by some investigators.

The determination of blood iodine as a routine clinical procedure is not practical.

The functional relationship between the liver and the thyroid is not expressible by the blood iodine level.

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