*Gut*, 1960, **1**, 169.

# HEPATIC NECROSIS DUE TO MARSILID

BY

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In the patient reported here severe jaundice and death resulted from treatment with iproniazide ("marsilid") given for only three days.

Iproniazide ("marsilid") is now well recognized as a cause of jaundice due to liver cell damage. The following case report is exceptional in that death followed the administration of a very small dose of iproniazide given over 72 hours.

## Case History

A 64-year-old woman was admitted to Wood Green Hospital on August 7, 1959. For the previous 18 months she had suffered from severe angina pectoris, and on July 10, iproniazide, 50 mg. T.D.S., had been prescribed. Two days later, on account of anorexia and slight nausea, the dose was reduced to 12·5 mg. T.D.S. for one further day and then stopped. Two weeks later slight jaundice developed and her urine became dark. There was no pruritus and no previous history of jaundice or of contact. She was observed at home for two weeks but was then admitted to hospital in view of deepening jaundice. She had lost a stone in weight over the month just before admission.

On examination she was deeply jaundiced but mentally alert. Neither liver nor spleen were palpable and the area of liver dullness was reduced. She was slightly tender in both hypochondria. Her blood pressure was 160/90 mm. Hg. No other physical signs were obtained.

Investigations.—The serum bilirubin test was 40 mg.%, the Van den Bergh reaction positive, serum alkaline phosphatase 27 King-Armstrong units. Flocculation tests were negative. S.G.O.T. was 44 units. Blood urea was 84 mg.%. Hb was 12·8 g. (87%) and W.B.C.s numbered 6,000 per c.mm. The differential count was normal. Some target cells were present on the blood film. Radiographs of the chest and abdomen were normal.

Treatment.—Glucose drinks, vitamin supplements, and triamcinolone, 5 mg. T.D.S., were given.

On August 15 slight mental confusion was noticed for the first time. The bilirubin level had now fallen to 30 mg.%. On August 28, in view of increasing mental confusion, she was transferred to Hammersmith Hospital. On admission she was semi-comatose. Deep jaundice was present and slight foetor hepaticus was noted. There was no flapping tremor or muscular hypertonia. There were no skin stigmata of chronic liver disease. Neither liver nor spleen was palpable and there was resonance to percussion over the entire liver area. There was no ascites but slight sacral oedema. Blood pressure was 160/90 mm. Hg. A few basal rales were present. There were no further physical signs.

Investigations.—An analysis of the urine showed bile but not urobilinogen. Microscopically the urine was normal.

Prothrombin time was 19 sec. (26-35%), Hb 15·8 g. (107%), P.C.V. 56%, M.C.H.C. 28%, platelets 150,000 per c. mm., W.B.C.s 22,000 (neutrophils 93%, lymphocytes 4%, monocytes 3%, reticulocytes 3%).

Liver function tests showed that bilirubin was 30mg.%, cholesterol 149 mg.%, alkaline phosphatase 31 King-Armstrong units, thymol turbidity 1 unit, zinc sulphate 1 unit. Total protein was 5·8 g. (albumin 3·0 g., globulin 2·8 g.). Electrophoresis was normal. S.G.O.T. was 77 units and S.G.P.T. 55 units.

The bicarbonate level was 24 m.Eq./l., sodium 111 m.Eq./l., potassium 3·5 m.Eq./l., chlorides 78 m.Eq./l., and urea 130 mg./100 ml.

Treatment.—Neomycin, potassium chloride, and high doses of steroids were given. Glucose 20% was given intravenously and vitamin supplements intramuscularly. Regular bowel motions were ensured by oral magnesium sulphate and bowel washouts as required.

On the morning after admission her blood pressure fell over a few hours to 80/60 mm. Hg. As the haemoconcentration, low serum sodium, and raised blood urea, in addition to the fall in blood pressure, pointed to a low sodium state, 500 ml. of 5% sodium chloride was given intravenously. This caused no change in the level of blood pressure, which was later temporarily raised by a noradrenaline infusion. There was no improvement in her general condition, however, and she died 36 hours after admission.

A liver biopsy taken a few minutes after death showed ballooning and hyaline change of the liver cells, quite large numbers of which were necrotic. Considerable biliary retention was present, particularly in the canaliculi. There was slight infiltration of the portal tracts (Prof. C. V. Harrison).

Post-mortem examination confirmed that the liver

was very small; in fact it weighed only 700 g. (normal 1,450 g.). Microscopy of liver sections obtained at necropsy showed that the liver cell destruction was patchy and periportal; it was not centrilobular.

## Discussion

In this case, as in most of the recorded cases, it is not possible to distinguish the clinical picture from that of acute hepatic necrosis due to infective hepatitis. The absence of centrilobular necrosis in the liver sections from this patient shows, however, that this was not hepatic necrosis due to infective hepatitis. Another important point is that in this patient 337·5 mg. of iproniazide caused death. No case history could be found in the literature in which so small a dose of iproniazide caused a fatal result. Floody, Dixon, and Mattia (1958) state that the amount of iproniazide given to 13 fatal cases ranged from 300 to 8,000 mg. They give no details and most of the information seems to have been obtained from questionnaires. Benaim and Dixon (1958) quote Marks as saying that jaundice may occur with as little as 25 mg. and that the duration of therapy is not important.

It has been said (Pare and Sandler, 1959) that in patients on iproniazide serial transaminase values may rob the drug of one of its great hazards to life. From our experience with this case it would seem that it may be too late to stop the drug when the transaminase values become raised.

We wish to thank Professor Sheila Sherlock for permission to publish this case.

## References

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