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Thyroid function and interferon treatment in chronic hepatitis C

EDITOR.—We read with much interest the article by Marcellin *et al* (*Gut* 1992; 33: 855-6) about two cases of sustained hypothyroidism induced by recombinant α interferon in patients with chronic hepatitis C. The presence of antithyroid antibodies in both patients suggested an autoimmune cause of the hypothyroidism.^{1,2}

We have recently seen a 51 year old woman with chronic active hepatitis C proved on biopsy examination randomised to receive 3 MU of recombinant interferon alfa 2-b (INTRON-A, Schering-Plough Corporation) subcutaneously three times a week for six months. The patient had no history of thyroid disease and had not received any drug known to be toxic to the thyroid. Serum triiodothyronine, thyroxine, free thyroxine, and thyroxine binding globulin were determined by RIA kits (Farnos Diagnostica Ltd, Turku, Finland); serum thyroid stimulating hormone,

thyroid microsomal antigen autoantibodies, and thyroglobulin autoantibodies were measured by IRMA kits (Biocode, Switzerland). Serum samples were collected before treatment and every month for 12 months thereafter.

A transient reduction in triiodothyronine, thyroxine free thyroxine values started at month 4 and an increase in thyroid stimulating hormone values was recorded (Figure). The patient had no clinical signs of hypothyroidism; thyroid autoantibodies remained negative. On this basis, we suggest a multifactorial cause of thyroid function change induced by recombinant α interferon. In our case, a direct inhibition of thyroid hormone synthesis and secretion, or both by recombinant α interferon could have played a determinant role. This mechanism has been shown by *in vitro* experiments with γ interferon.^{3,4}

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Reply

EDITOR.—We read with interest the comment by Picciotto *et al* on our paper reporting another case of hypothyroidism, probably induced by recombinant interferon alfa 2-b in a patient treated for chronic hepatitis C. No antithyroid antibodies were found and the authors suggest a multifactorial mechanism by which thyroid abnormalities are induced.

We agree that, in the absence of antithyroid antibodies, the role of a direct inhibition of thyroid hormone synthesis and secretion by α interferon, or both, might be considered. Indeed, among 22 patients developing thyroid abnormalities while receiving interferon, we found antithyroid antibodies (anti-thyroglobulin and anti-peroxydase) in only half of them (unpublished data). *Ex vivo* studies of patients' thyroid cells, if considered ethical, might provide pertinent information about the mechanisms of the cell damage induced by interferon in these patients.

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Biliary endoprosthesis and common bile duct stones

EDITOR.—The report from Peters *et al* (*Gut* 1992; 33: 1412-5) of a group of patients with bile duct stones treated with a biliary endoprosthesis is of considerable interest. This technique has been used by many centres, provides excellent immediate drainage, and reasonable medium term results – but I wish to sound a note of caution. The justification for using stents as permanent treatment must depend on the results in the long term, indeed can only be assessed by lifetime follow up which no one has yet reported. Our own series with a follow up of 2-5 years was encouraging,¹ but more than half of the patients were still alive (despite being apparently at very high risk initially),¹ and many problems may have occurred subsequently.

The number of patients having stenting for bile duct stones in the King's series seems very high – no fewer than 40 of 146 of a consecutive series, including 27 (18%) as projected permanent treatment. The authors suggest that their low rate of duct clearance reflected their referral practice but referral centres should have special expertise. Of 343 patients with duct stones referred to this unit during the last two years, the clearance rate using standard techniques and mechanical lithotripsy was 94%. Stents were used as 'permanent' treat-

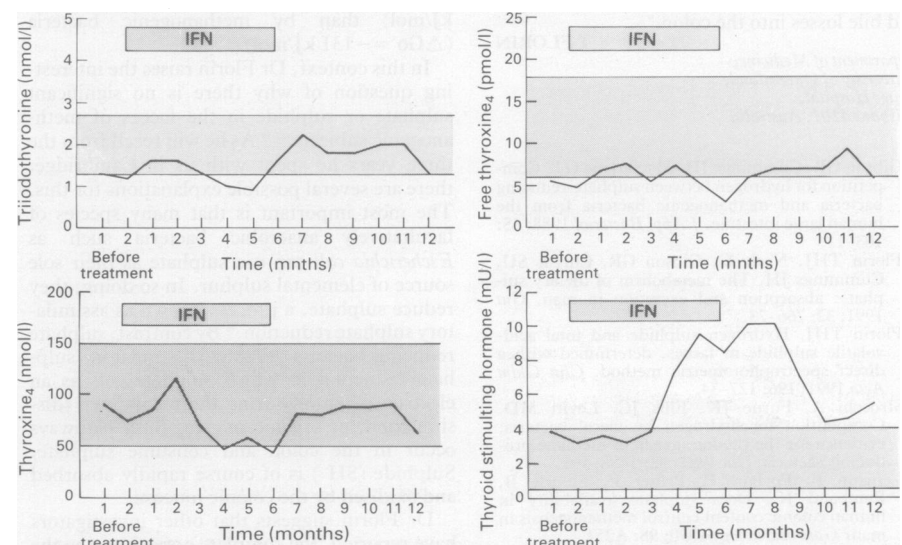


Figure: Triiodothyronine, thyroxine, free thyroxine, and thyroid stimulating hormone behaviour in a patient with chronic hepatitis C treated with 3 MU of IFN alfa 2-b for six months.