particularly difficult cases in whom standard treatment had failed. In three of them mexiletine alone controlled the arrhythmia, but only at the cost of intolerable adverse effects. Combined treatment with mexiletine and propranolol, which have different actions and different adverse effects, enables arrhythmia to be suppressed through co-operative antiarrhythmic action. Since adverse effects have been a major limitation to widespread use of mexiletine^{3,4} combined therapy with propranolol may broaden its usefulness as an antiarrhythmic drug by two means—by decreasing its adverse effects and by more effective arrhythmia suppression through co-operative drug action.

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Minimal-change glomerulonephritis associated with circulating anticoagulant to factor XII

Circulating anticoagulants to factor XII have been described in two patients. In one the anticoagulant was associated with discoid lupus erythematosus¹ and in the other with systemic lupus erythematosus.² In both there was also anticoagulant activity to factor XI. Furthermore, the nephrotic syndrome may occasionally be associated with a selective leak of factors IX,³ XI, and XII.^{4,5} We report a case of a circulating anticoagulant to factor XII associated with the nephrotic syndrome secondary to minimal-change glomerulonephritis.

Case report

A 16-year-old boy presented with puffiness of the face and eyes and swelling of the legs. He had a history of childhood asthma and eczema but nothing suggestive of a bleeding disorder. On examination he had oedema of the face and legs and bilateral pleural effusion. His haemoglobin concentration was 16.6 g/dl with normal blood indices. Blood urea and electrolyte concentrations were normal. Serum protein and serum albumin concentrations were low at 34 g/l and 15 g/l respectively. Results of antinuclear and other autoantibody tests were negative. DNA binding activity was less than 20 U/ml serum and C3 and C4 concentrations were normal. Urine microscopy showed red cells and granular casts. Urinary protein excretion was 30 g/24 h and was very selective (differential protein clearance 0.04). The prothrombin time was normal but the kaolin cephalin clotting time (KCCT) was prolonged at 93 s as opposed to a control of 52 s. Factor XII activity was reduced at 12%. Factor XI, IX, X, VIII, VII, V, II, and I concentrations were well within the normal range. The KCCT was corrected to within normal limits with an equal mixture of patient's and pooled normal plasmas, but the results on incubation were characteristic of a progressive inhibitor to factor XII (table). A biopsy specimen of renal tissue obtained under cover of corticosteroid therapy showed no abnormality on light microscopy and tests for immunofluorescence were negative.

The patient's nephrotic syndrome remitted with corticosteroid treatment. His circulating anticoagulant disappeared after 14 days of treatment and his

factor XII concentrations reverted to normal (80%). He relapsed on two occasions when the dose of corticosteroids was being reduced. The circulating anticoagulant activity returned with each relapse but rapidly disappeared when the corticosteroid dose was increased.

Clotting studies in patient with circulating anticoagulant to factor XII

Incubation time (s)	Control pooled normal plasma		Equal volumes of patient and control plasma		Patient's plasma	
	KCCT (s)	Factor XII (%)	KCCT (s)	Factor XII (%)	KCCT (s)	Factor XII (%)
0	53	120	58	115	93	12
30	59	—	70	60	140	—
60	60	115	80	23	172	3

KCCT = Kaolin cephalin clotting time.

Comment

This patient had typical minimal-change glomerulonephritis. The clotting studies indicated the presence of an inactivator of factor XII, whose activity increased on incubation. The nephrotic syndrome may occasionally be associated with a selective leak of coagulation factors, and acquired deficiencies of factors XI and XII have been described.^{4,5} The patient's urine was not assayed for factor XII but the repeated haematological investigations during relapse of the nephrotic syndrome strongly favoured the presence of an inactivator rather than a selective urine leak. So far as we know the association of a circulating anticoagulant and minimal-change glomerulonephritis has not been noted. The close association of the presence of circulating anticoagulant with the activity of the patient's nephrotic syndrome seems more than fortuitous. There was no clinical evidence of a bleeding diathesis to accompany the factor XII deficiency.

This case shows the importance of checking for bleeding and clotting abnormalities when performing a renal biopsy, a procedure which already has an inherent risk of haemorrhage.

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Persistence of defective hypothalamic control of prolactin secretion in some obese women after weight reduction

In animals the hypothalamus is of fundamental importance in regulating food intake and disorder of its function, which may be congenital or acquired, results in obesity.¹ We have previously reported^{2,3} evidence for a disorder of hypothalamic function in some massively obese women. We found two distinct patterns of prolactin response