the gene coding for the HLA system is located on the VI pair. A close association of one of these genes with the erythrocyte membrane abnormality and with hypertension would have been interesting on both theoretical and practical grounds. From our results, however, the abnormal gene(s) responsible for the essential hypertension does not appear linked to any of the major group systems studied.

Our findings suggest that the erythrocyte sodium-potassium cotransport deficiency is a biochemical abnormality characteristic of essential hypertension; this warrants further investigation in genetic studies of the disease.

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SHORT REPORTS

Atypical case of alcohol-induced Cushingoid syndrome

True alcohol-induced Cushingoid syndrome invariably resolves completely after several weeks of abstinence.[12] We report a case of apparent pituitary-dependent Cushing's syndrome in an alcoholic in which there was evidence of hypercorticosteroidism over nine weeks after complete alcohol withdrawal, but which responded to a short course of metyrapone with no relapse.

Case report

A 59-year-old woman with a long history of alcoholism and whose recent intake was one bottle of sherry daily was admitted because of extensive bruising of her legs. On examination she was obese (weight 59 kg) and plethoric, with hirsutism, thin skin, and limb bruising. Blood pressure was 140/80 mm Hg, but subsequent readings were lower. She had numerous spider naevi, facial telangiectasia, hepatomegaly, and ankle oedema.

Haemoglobin concentration was 12·2 g/dl mean corpuscular volume 114 fl (114 μm^3). Serum vitamin B_{12}, folate, and fasting lipid concentrations were normal, as was a chest radiograph. Liver function values, which were abnormal on admission (raised serum bilirubin concentration, low serum albumin concentration, and raised serum alkaline phosphatase, aspartate transaminase, and γ-glutamyltranspeptidase activities), became normal within four weeks. Prothrombin ratio was 1·4. Serum sodium concentration was 138 mmol (mEq)/l, serum potassium concentration 2·9 mmol (mEq)/l, and blood urea concentration 2·0 mmol/l (12·0 mg/100 ml). Blood sugar concentration was 11·3 mmol/l (204 mg/100 ml) with glycosuria.

Serum cortisol concentrations measured by fluorometry during the first week and while receiving spironolactone were 4100 nmol/l (149 μg/100 ml) at 9 am (normal 160-660 nmol/l; 6-24 μg/100 ml) and 4600 nmol/l (167 μg/100 ml) at 10 pm; measured by radioimmunoassay the next week, however, values were 950 nmol/l (34 μg/100 ml) at 9 am (normal 200-700 nmol/l; 7-25 μg/100 ml) and 740 nmol/l (27 μg/100 ml) at 10 pm (normally under 140 nmol/l; 5 μg/100 ml). Two weeks after stopping spironolactone serum cortisol concentrations measured by fluorometry were 1050 nmol/l (38 μg/100 ml) at 9 am and 1130 nmol/l (41 μg/100 ml) at 10 pm; 24-hour urine collection yielded a cortisol concentration (also measured by fluorometry) of 7314 nmol/l (265 μg/100 ml). Serum adrenocorticotrophic hormone concentration at 9 am was 131 ng/l (normal 10-80 ng/l). Three weeks after stopping spironolactone serum cortisol values after 2 mg dexamethasone for two days did not suppress (fluorometry: 760 nmol/l (28 μg/100 ml) at 9 am and 1310 nmol/l (47 μg/100 ml) at 10 pm), but adequate suppression occurred after 8 mg (350 nmol/l (13 μg/100 ml) at 9 am, 150 nmol/l (5 μg/100 ml) at 10 pm).

Two months after total abstinence (she was bedbound with no access to alcohol) there were still physical and biochemical features of apparent Cushing's syndrome, with loss of diurnal variation and raised serum cortisol values, and pituitary adenoma was suspected. Metyrapone 500 mg thrice daily was begun, and the serum cortisol concentration fell to normal within six days. Skull radiography, tomography of pituitary fossa, perimetry, brain scan, and computed tomography showed no evidence of pituitary adenoma. After one month the metyrapone was stopped and she was clinically and biochemically better, with improved facial appearance and skin changes and loss of 8 kg. Electrolyte and blood sugar concentrations were normal. Serum cortisol and biochemical values remained normal three, six, and 12 months later with no treatment except complete abstinence.

Comment

Over 20 cases of alcohol-induced Cushingoid syndrome have been reported, invariably reversing within several weeks of alcohol withdrawal.[1-5] Physical signs or biochemical features, or both, had aroused suspicion of Cushing's syndrome, confirmed by loss of normal diurnal variation and raised serum cortisol values. When measured, adrenocorticotrophic hormone concentrations were raised in some patients.[1 4] Response to low-dose dexamethasone was also variable, some patients showing normal suppression and others not. Response to the high-dose dexamethasone suppression test has not been reported before.

Although hypercorticosteroidism in alcoholics may be due to a lower metabolic clearance rate of cortisol or to decreased production of cortisol-binding globulin resulting from hepatic dysfunction, this does not explain the loss of diurnal variation or that total rather than unbound cortisol values are raised. In our patient adrenocorticotrophic hormone concentration was raised and production of cortisols was suppressed by high-dose but not low-dose dexamethasone, which clearly implicates a central mechanism affecting the pituitary or hypothalamus.

Our patient appeared to fulfil the criteria for typical pituitary-

dependent Cushing's disease but there was no recurrence after a short course of metyrapone and while totally abstaining from alcohol; although the possibility of cyclical true Cushing's syndrome remained, we think this unlikely. Alcohol abuse should always be considered in the differential diagnosis of Cushing's syndrome. Abstinence does not necessarily lead to rapid clinical improvement; in this case the signs and biochemical abnormalities persisted for over two months and closely mimicked pituitary-dependent Cushing's disease.

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Remission of primary pulmonary hypertension during treatment with diazoxide

Until recently primary pulmonary hypertension was an untreatable illness characterised by steady deterioration and death about three years after diagnosis. Short-lived reductions in pulmonary vascular resistance have been obtained by intravenous injections of isoprenaline and tolazoline,[1 2] but not until 1978 was sustained improvement in the pulmonary hypertension described after treatment with oral diazoxide.[3] Of three patients treated two improved, one symptomatically and the other both symptomatically and haemodynamically for more than two years. Further studies have confirmed that pulmonary artery pressures may be reduced by diazoxide and hydrallazine[4 5] but in no patient has a complete remission of the pulmonary hypertension been achieved. We describe a patient with primary pulmonary hypertension in whom pulmonary artery pressures returned to normal during treatment with diazoxide.

Case report

A 31-year-old housewife complained of fainting attacks since her last pregnancy 21 months earlier and exertional breathlessness for 12 months. Physical examination showed signs of severe pulmonary arterial hypertension for which investigation revealed no cause. Pulmonary artery pressure was 65/35 mm Hg and pulmonary wedge pressure was normal. The patient was treated with warfarin for anticoagulation and started on oral diazoxide, the dose being slowly increased to 600 mg a day. Side effects included fluid retention, hyperglycaemia, and hypertrichosis. After three months' treatment the patient's symptoms had improved, radiographs showed a reduction in heart size, and the electrocardiographic changes of right heart strain were less evident. Repeat cardiac catheterisation showed a pulmonary artery pressure of 37/20 mm Hg and normal pulmonary vascular resistance. Nine months after starting diazoxide there were no clinical signs of pulmonary hypertension and the chest radiograph and electrocardiogram were normal. Pulmonary artery pressure after 15 months' treatment was 25/12 mm Hg and the patient was asymptomatic. Diazoxide was then stopped. The patient remained well for six months, when she noticed a return of the dyspnoea. Physical signs of pulmonary hypertension were again evident and the electrocardiogram showed right-sided changes. Cardiac catheterisation confirmed the relapse, the pulmonary artery pressure being 100/40 mm Hg. Since then she has been taking increasing doses of hydrallazine and is once more improving symptomatically. Haemodynamic data are summarised in the table.

Haemodynamic data of patient with primary pulmonary hypertension

	Pulmonary artery pressure (mm Hg)			Pulmonary artery wedge pressure (mm Hg)	Cardiac output (l/min)	Pulmonary vascular resistance (units)
	Systolic	Diastolic	Mean	Mean		
Before treatment	65	35	42	4	5·4	7·0
After five months' treatment	37	20	25	9	6·8	2·4
After 15 months' treatment	25	12	17	3	6·0	2·3
Seven months after stopping diazoxide	100	40	60	8	3·8	13·7

Comment

In one patient with primary pulmonary hypertension we have shown how the effects of the disease may be completely ameliorated by treatment with the vasodilator drug diazoxide. We believe that all patients with this condition should be given a trial of treatment with drugs of this type. Our experience suggests that a successful response is more likely if the illness is treated at an early stage, when the pulmonary hypertension is still labile and before irreversible changes have occurred in the pulmonary arteries.

It is interesting that the pulmonary hypertension in our patient returned when diazoxide was stopped; this suggests that the underlying disease process responsible for the development of pulmonary hypertension is still active.

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Transposons and trimethoprim resistance

The release of trimethoprim for use alone has led to speculation on possible effects on the incidence of trimethoprim-resistant bacteria.[1] The incidence of trimethoprim resistance has been increasing among hospital bacteria but is still low in strains causing urinary infections in the community outside hospital.[1] Nearly all trimethoprim-resistant bacteria isolated from clinical material are also sulphonamide-resistant.

Plasmids are DNA molecules that replicate autonomously in bacteria and may be transferred from one bacterium to another, a replica remaining in the original cell. R plasmids encode antibiotic resistance genes and disseminate resistance among bacteria. Transpo-