Patients, methods, and results

We studied the frequency and type of ventricular extrasystoles as well as the intracellular and extracellular concentrations of sodium, potassium, and magnesium in 50 hypokalaemic patients taking long-term diuretic treatment before and after correction of the serum potassium concentration. The arrhythmias were recorded on a three-hour ECG tape. In 16 patients, eight of whom were hypokalaemic at the start of the study, we also investigated the frequency and type of ventricular extrasystoles, and the intracellular and extracellular electrolyte concentrations after an infusion of 30 mmol magnesium sulphate.

Percutaneous muscle biopsy specimens were obtained from the lateral portion of the quadriceps femoris with a needle biopsy technique. After repeated weighing, drying, and fat extraction, the dried muscle tissue was wet ashed in 1N nitric acid. The magnesium, potassium, sodium, and chloride contents were then determined by atomic absorption spectrophotometry, chloride after precipitation with silver nitrate. The intracellular and extracellular spaces were calculated by the chloride method, given that chloride is freely diffusible across the cell membrane and distributed according to Nernst's equation.³ Paired *t* tests were used to compare the serum and muscle electrolyte concentrations as well as the frequency of ventricular extrasystoles before and after correction of the serum potassium concentration and before and after the magnesium infusion.

Mean extracellular and intracellular potassium before and after magnesium infusion

	Serum potassium (mmol/l)	Muscle potassium (mmol/100 g FFDS)	Intracellular potassium (mmol/kg water)
Before	4.0	39.2	153
After	3.8	40.6	170
P	NS	NS	<0.01

Conversion: SI to traditional units—Potassium: 1 mmol = 1 mEq.

The preliminary results showed that there was no increase in the intracellular potassium concentration or the muscle potassium content after correction of the serum potassium concentration despite a significant increase in this. Nor was there any change in the frequency or type of ventricular extrasystoles after correction of the serum potassium concentration. After the magnesium infusions, however, the intracellular potassium concentration significantly increased, from a mean value of 153 to a mean value of 170 mmol(mEq)/kg intracellular water (*P*<0.01). There was also an increase, although not significant, in the muscle potassium content (see table). All patients had also a lower frequency of ventricular extrasystoles after the magnesium infusions (*P*<0.05).

Discussion

Our preliminary results imply that giving increased potassium supplements to patients taking long-term diuretic treatment does not necessarily augment the cellular uptake of potassium. This may be explained by a concomitant cellular magnesium deficiency with an insufficient activation of Na-K-ATP-ase. This theory is further supported by the increase in cellular potassium concentration obtained after magnesium infusion. This has been shown in studies of magnesium depletion in man⁴ and in animal experiments.²

We believe that the urinary losses of magnesium after long-term treatment with most diuretics are of great importance and may impede the cellular accumulation of potassium and thus lead to increased cardiac excitability. Could this be the explanation for the increased frequency of ventricular extrasystoles found in patients treated with diuretics.⁵ Completion of these studies and further studies are in progress.

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HLA and DRW antigens in insulin-dependent diabetes

The existence of an association between certain diseases and the HLA system has stimulated considerable interest. In insulin-dependent diabetes (IDD) associations with HLA-A, B, or C antigens have been shown.¹ In contrast, no correlation has been found with insulin-independent diabetes. B lymphocytes have been shown to possess antigens that are distinct from HLA-A, B, and C antigens.² Antisera that react with B lymphocytes but not with T lymphocytes have been grouped into antigenic specificities, now called DRW.³ This study aimed to examine whether a relationship also exists between HLA-DRW specificities and IDD, taking into consideration certain complications such as retinopathy and neuropathy.

Patients, methods, and results

A total of 123 insulin-dependent diabetics were studied and compared with 176 normal controls. All patients were Caucasian and unrelated. The group comprised 56 women and 67 men (mean age 25). With the standard NIH-Terasaki microlymphocytotoxicity test 17 HLA-A, 18 HLA-B, and 6 HLA-C were defined. To detect DRW antigens, the internationally accepted microcytotoxicity test was used.³ A total of 180 sera selected by the Seventh International Histocompatibility Workshop and 60 local sera defining accurately seven DRW specificities were used. Differences in HLA antigen frequencies between patients and controls were calculated by χ^2 analysis.

The table shows the main differences of the distribution of HLA-A, B, C, and DRW antigens. Previous findings of an increased frequency of B8 and B18 and of a decreased frequency of B7 were confirmed. Furthermore, the antigens B8 and B18 seem to have a cumulative effect to increase susceptibility to IDD (RR=5.25). In addition, we found important differences in the frequencies of A11, B5, and BW35. Although these differences are no longer significant if the ordinary *P* values are corrected by the number of comparisons made, they agree with the data compiled by the HLA and Disease Registry.¹ The most significant associations are with DRW antigens and particularly with DRW3. No noticeable differences in the distribution of HLA antigens were observed for patients with or without neuropathy. Some 39 (32%) patients had retinopathy, of which 31 were benign and eight malignant (proliferative retinopathy). In the eight patients with malignant retinopathy, six had the antigen B8 and four the antigen DRW3.

HLA-A, B, and DRW antigen frequencies in IDD which show notable differences from control population

Antigen	Patients (%) (n = 123)	Controls (%) (n = 176)	P value	RR
A11	8 (6.5)	30 (17.1)	<0.01	0.34
B5	6 (4.9)	28 (15.9)	<0.01	0.27
B7	16 (13.0)	39 (22.2)	<0.05	0.53
BW35	10 (8.1)	41 (23.3)	<0.005	0.29
B8	46 (37.4)	30 (17.1)	<0.0005	2.91
B18	22 (17.9)	17 (9.7)	<0.05	2.04
DRW2	9 (7.3)	35/160 (21.9)	<0.001	0.25
DRW3	73 (59.4)	22/160 (13.8)	<0.00025	9.16

Discussion

The data of Thomsen,⁴ derived from using the mixed lymphocyte culture (MLC), suggest that the IDD susceptibility gene is probably closer to the D locus than the B locus of the HLA region. It appears likely that the B-lymphocyte antigens (DRW) are coded for by a locus identical or closely linked to the HLA-D locus as defined by the MLC. Our data using a serological approach indicate a strong association of the antigen DRW3 with IDD. The fact that the RR value of DRW3 (9.2) is much higher than that of B8 (2.9) suggests that the former is more strongly associated with IDD, and that the increase of B8 is secondary to that of DRW3 due to the well-established linkage disequilibrium between the two antigens. DRW2 could be a protection marker and the decrease of B7 is also secondary to that of DRW2 due to linkage disequilibrium. In contrast to the results obtained by Thomsen with the MLC technique,⁴ we did not find an increase in DRW4, but this agrees with the lack of increased frequency of B15 and CW3 with which DRW4 is in linkage disequilibrium. In our study no firm relation between certain HLA antigens and neuropathy or retinopathy seemed to exist, except perhaps for an increase of B8 in malignant retinopathy.

The precise genetic basis of IDD is still controversial. Nevertheless, the results of our study suggests that a marker of the disease (HLA-

DRW3) may now be identified in more than half of the patients by a relatively simple serological technique.

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Patients' attitudes to measuring their own blood pressure

Patients with diabetes mellitus commonly monitor their disease by simple urine analysis and adjust their treatment on the basis of these observations. Wilson¹ has argued that patients with hypertension should measure their own blood pressure at home, but if this concept is widely applied it must be acceptable to those using it.² For several years patients attending our hypertension clinic have measured their own blood pressure,³ but while we were aware of the advantages from the doctors' viewpoint we had no definite information on the patients' attitudes. We therefore decided to test their reactions by means of a questionnaire.

Patients, methods, and results

Ninety-five consecutive patients attending the hypertension clinic were trained to measure their own blood pressure, oral instruction being reinforced by written advice. The equipment used was a Littman Nursescope and an anaeroid sphygmomanometer. All patients had been taking their own blood pressure for some months when they answered the questionnaire.

Ninety-five questionnaires were sent out and 82 (86%) returned. Forty-three of the patients were men and 39 women; their ages ranged from 26–68 years and their occupations from the professional to the unskilled. Twenty-six of the patients learnt the technique in under one day, 40 took 2–7 days, and 16 took 7–14 days. Very few were unable to master the technique. Forty-three patients took under five minutes to take their blood pressure both lying and standing, while a further 26 accomplished this in less than 10 minutes. Problems with the apparatus were mainly those of applying the cuff, but with a Velcro strip it could be left rolled up and slipped on the arm without opening. Other difficulties included not hearing the Korotkoff sounds clearly and not being able to inflate the cuff to a sufficient pressure. Thirty-three patients had persuaded a relative or friend to help in taking their blood pressure, and in most cases the assistant dealt both with inflating the cuff and listening with the stethoscope. Twenty-five patients felt encouraged to take their tablets more regularly, particularly when they observed a fall in blood pressure with treatment. Surprisingly, 34 patients were so confident of their readings that they were willing to change their medication on the basis of the figures they obtained. Over half the patients (48) were willing to continue taking their blood pressure at home indefinitely—usually every day. One third of the patients took someone else's blood pressure, usually their spouse's. One patient took a colleague's pressure and on finding it higher than his own pretreatment figure recommended that he saw his doctor for further advice.

The great majority of patients were reassured by taking their blood pressure and most expressed satisfaction from understanding more about the

problem for which they were being treated. Some decided to relax consciously when their pressure was high, providing biofeedback.

Comment

The place of home blood-pressure readings in managing hypertension remains unclear, as the relationship of these readings to clinic records has not been clarified. Burns-Cox *et al*⁴ have shown that home blood-pressure measurement is practicable, and our patients clearly found it easy to master the technique and took little time to perform it.

We think that home blood-pressure estimation is acceptable to many patients, and suggest that each patient with hypertension should be encouraged to take his or her own blood-pressure at the start of treatment. Measurements should continue for at least three months, by which time the blood pressure should be under control. If the patient wants to continue he should be encouraged to buy his own equipment. Home blood-pressure recording used in this way should improve patient compliance and give greater personal insight into the disorder.

We thank Boehringer Ingelheim for providing the equipment.

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Ectopic ACTH-secreting tumour of the bronchus and agammaglobulinaemia

Ectopic ACTH production is one of several well-recognised endocrine manifestations of carcinoma of the bronchus.¹ I report one such case that is unusual in two respects: firstly, the patient was already receiving corticosteroids for asthma; and, secondly, he developed agammaglobulinaemia.

Case report

A 46-year-old man was first admitted to hospital because of asthma. He gave a three-week history of cough, wheezing, and breathlessness, and responded rapidly to corticosteroids and salbutamol by mouth. Respiratory function was normal when tested after discharge. Skin tests gave positive reactions to common allergens, and the results of precipitin tests for aspergillus and avian proteins were negative, as were those of other investigations including plasma electrolytes and protein electrophoresis. He remained well but six months later was seen to be Cushingoid and the dose of prednisolone was reduced to 7 mg daily. Ten months after his first admission he was again admitted to hospital, on this occasion because of severe weakness of one week's duration. He had developed oedema of the legs a few weeks earlier; this had responded to frusemide and had been attributed to a combination of cor pulmonale and the steroids. He was grossly Cushingoid, with striae, hyperpigmentation, a widespread acneiform rash, and oral candidiasis. Plasma concentrations were as follows: sodium 140 mmol(mEq)/l, potassium 2.5 mmol(mEq)/l, bicarbonate 34 mmol(mEq)/l, and urea 8.3 mmol/l (50 mg/100 ml). A chest x-ray film showed some prominence of the left hilum but had not changed over the previous two years. Hypokalaemia was attributed to a combination of inadequate potassium supplements and the steroids, and initially with oral and intravenous potassium he improved. Further investigations disclosed glycosuria with a plasma glucose concentration of 32.8 mmol/l (591 mg/100 ml) and he received insulin. Plasma protein electrophoresis now showed agammaglobulinaemia: IgG was 0.3 g/l (normal value 8.0–17 g/l), while IgA and IgM were normal. A further chest x-ray film showed lingular consolidation, but tomograms were normal. At this stage, because of the chest x-ray appearances and his worsening metabolic state, an ectopic ACTH-producing tumour was suspected. The plasma