lasting remission with immunotherapy. All patients are alive without any relapse six to 14 years after beginning immunotherapy.

HLA phenotypes were determined by microlymphocytotoxicity assay in microtest plates. Selected monospecific or bispecific antisera enabled us to test for 31 HLA antigens. Frozen rabbit serum was used as the source of complement. Antigen frequencies of these patients were compared with those of 591 healthy individuals and of 14 ALL long-term survivors from the initial study by Kourilsky *et al*, which had used chemotherapy exclusively.

The HLA phenotypes are listed in the table. When antigen frequencies among patients treated with BCG immunotherapy were compared with those obtained in normal individuals, a significant increase (Fisher's exact test and χ^2 comparison with Yates's correction) in antigens HLA-BW17 (46.1% *v* 7.3%) and HLA-AW33 (30.8% *v* 1.2%) was observed ($P < 0.001$). These increases remained statistically significant when corrected for the number of specificities tested. Nine patients had at least one of these two antigens (69.2% *v* 8% in controls: $P < 0.001$) but only one patient (No 5) had both antigens. No patient possessed HLA-B5 antigen (*v* 13.2% in controls). Deviations in other HLA antigen frequencies were not apparent.

Long-term survivors treated with chemotherapy alone showed no alteration in HLA-BW17, AW33, or B5 frequencies (0/14 BW17 in the "chemotherapy" group *v* 6/13 in the "immunotherapy" group. χ^2 with Yates's correction: 7.63 ($P < 0.01$)).

Discussion

HLA antigens HLA-BW17 and HLA-AW33 were significantly increased in 13 patients with ALL who were surviving in their first remission for over six years after immunotherapy with BCG. Previous reports have not shown that the frequencies of these antigens were different in patients with ALL, the only alteration in some series being a high incidence of HLA-A2 (or HLA-A2-B12 haplotype), which was not apparent in our patients. Some have suggested that the HLA phenotype may interfere with the clinical course of the disease and prognosis. Nevertheless, in patients treated only with chemotherapy, we found no statistically significant difference between short-term and long-term survivors—though in some prospective series, a better survival time has been found to be associated with HLA-A2⁴ and HLA-A9.⁵ These latter two reports dealt with patients treated by chemotherapy exclusively. In our group of BCG-treated patients, HLA-A2 and B9 were slightly (but not significantly) decreased.

Our patients differ from other series of those with ALL reported in only one obvious point: their treatment. We suggest that the observed difference in HLA phenotypes is in some way related to the fact that these patients were good responders to BCG immunotherapy. Thus our results suggest the existence in man of HLA-linked genes which are concerned with the response to immunotherapy in ALL. Whether these genes govern a specific immune response to some leukaemia antigen, or a non-specific response to BCG immunotherapy cannot be assessed.

Beside its theoretical interest, the finding that a good response to

BCG immunotherapy in ALL is at least in part genetically determined and HLA linked could possibly lead to the use of HLA phenotyping to choose those patients with a good chance of cure with immunotherapy (as BW17 and AW33?), or conversely of patients with a "poor chance" (as B5?) who require long-term chemotherapy without immunotherapy. A prospective study is needed to obtain a clear definition of these groups of good and bad responders to BCG immunotherapy. Moreover, similar studies should be done in patients treated by immunotherapy for malignancies other than ALL.

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Spurious polycythaemia developing during observation

Whether spurious polycythaemia, defined as an increased packed cell volume with a normal red cell mass,^{1,2} is a disease or a variant of normal is not clear. Recent studies have suggested two distinct forms^{2,3}—one characterised by a reduced plasma volume, normal red cell mass, hypertension, vascular disease, and increased mortality; the other by a high-normal red cell mass, low-normal plasma volume, no specific clinical features, and a normal prognosis. The second form was thought to represent the extreme of the normal range.^{2,3} I describe

HLA phenotypes of long-term survivors with ALL

Case No	Sex	Age at diagnosis (years)	Date of diagnosis	Length of chemotherapy	Length of immunotherapy (years)	HLA phenotype	
						A locus	B locus
Patients treated with immunotherapy							
				(months)			
1	F	4	1966	8	4	1	14, W17
2	M	7	1971	8	5	3, W33	7, W27
3	M	2½	1969	10	6 y 6 m	1, 11	W17, W18
4	F	19	1971	6	5	2, W33	7, W15
5	F	10	1968	8	7	9, W33	8, W17
6	F	6	1963	30	10	3	7
7	F	12	1971	6	5	2, W32	W17, W40
8	M	18	1963	30	10	2, 3	8, W17
9	F	8	1971	6	5	2, W33	12
10	M	5½	1966	8	5 y 6 m	9, 28	12, 14
11	F	4	1967	8	5	1, 29	12, W17
12	F	13	1962	15	9 y 2 m	2, 28	W32, W35
13	M	3	1968	12	8	2, W23	12
Patients treated exclusively with chemotherapy							
				(years)			
14	M	4	1966	6	0	2, 3	7, W38
15	F	4½	1965	7	0	11, 29	W35
16	F	6	1968	5	0	2, 11	7
17	M	16	1966	5½	0	2, 11	5
18	M	15	1966	5	0	1, 9	13, W40
19	F	5½	1965	6	0	1, 2	8, 12
20	F	4½	1962	11	0	2	12, W41
21	F	4	1966	5¾	0	2, 19-2	5, W21
22	M	2½	1967	5	0	1, 19-2	7, W40
23	M	3	1964	7	0	9, 28	12, W35
24	F	2½	1968	7	0	1, 9	8, W15
25	F	4½	1968	5	0	3, W32	8, W35
26	F	17	1966	5	0	2, W28	7, 12
27	M	11½	1966	4	0	1, 2	W37, W40

a patient who developed this second form of spurious polycythaemia over a six-month period.

Case report

A 46-year-old man, previously healthy, developed a hemiparesis in April 1976. He smoked 40 cigarettes daily and drank alcohol heavily. He had a dense left hemiparesis, slight hepatomegaly, and was normotensive. Computerised axial tomography showed no intracranial abnormality. A mild initial liver dysfunction returned rapidly to normal. Cerebral thrombosis and alcohol-induced liver dysfunction were diagnosed. After 11 days he developed calf vein thrombosis (confirmed by venography) and a small pulmonary embolism (on lung scan). He was treated with heparin and warfarin, and was discharged on warfarin after six weeks. Thereafter he smoked 15 cigarettes daily and took little alcohol.

When in hospital his blood picture was repeatedly normal (table). The next blood count, five months later, showed a strikingly raised packed cell volume, haemoglobin, and red cell count, and the abnormalities have persisted for over one year (table). Red cell indices, white cell count, serum urate and sodium concentrations, and blood pressure remained constant.

Mean values for haematology, biochemistry, and blood pressure measurements during first admission (April-May 1976), and during 11 months (November 1976 to October 1977) after packed cell volume had risen

	April-May 1976 Mean $\pm$ SD (n)	Nov 1976-Oct 1977 Mean $\pm$ SD (n)
Haemoglobin (g/dl)	13.3 $\pm$ 0.8 (6)	19.5* $\pm$ 0.9 (11)
RBC ($10^{12}/l$)	4.17 $\pm$ 0.32 (6)	6.31* $\pm$ 0.26 (11)
Packed cell vol (%)	38.3 $\pm$ 2.1 (6)	56.7* $\pm$ 2.8 (11)
MCV (fl)	92.0 $\pm$ 3.0 (6)	91.1 $\pm$ 2.7 (11)
MCH (pg)	31.7 $\pm$ 1.2 (6)	31.5 $\pm$ 1.0 (11)
MCHC (g/dl)	34.3 $\pm$ 0.9 (6)	34.4 $\pm$ 0.8 (11)
WBC ($10^9/l$)	8.43 $\pm$ 0.79 (6)	9.58 $\pm$ 1.39 (11)
Platelets ($10^9/l$)	— (0)	193.6 $\pm$ 19.8 (11)
Serum albumin (g/l)	30.2 $\pm$ 3.9 (4)	39.7† $\pm$ 3.1 (4)
Serum protein (g/l)	60.0 $\pm$ 1.8 (4)	70.7* $\pm$ 0.4 (3)
Serum urate (mmol/l)	0.22 (4)	0.21 (2)
Serum sodium (mmol/l)	137.4 $\pm$ 2.6 (8)	137.9 $\pm$ 1.4 (3)
Blood pressure (mm Hg)	138 $\pm$ 15 (22)	137 $\pm$ 7 (12)
	87 $\pm$ 11 (22)	85 $\pm$ 10 (12)

*P < 0.001 } versus results for April-May 1976, Student's unpaired *t* test.

†P < 0.01 }
Conversion: SI to traditional units—Urate: 1.0 mmol/l $\approx$ 20 mg/100 ml. Sodium: 1 mmol/l = 1 mEq/l.

Serum albumin and protein concentrations also increased. Platelets were normal. In August 1977 investigations showed: red cell volume (^{51}Cr -RBC) 35.3 ml/kg, predicted 27.7 ml/kg; plasma volume (^{131}I -albumin) 30.9 ml/kg, predicted 42.9 ml/kg; marrow appearances normal; splenomegaly absent by palpation, ultrasound, and scintiscan; leucocyte alkaline phosphatase raised; respiratory function (FVC, FEV₁, FEV₁/FVC, diffusing capacity) normal; arterial Po₂ 96 mm Hg. Renal disease was excluded by intravenous pyelogram and ultrasound; hepatic disease by scan, ultrasound, and α -fetoprotein; and chronic dehydration by 24-h urine volume (1450 ml) and sodium (173 mmol). The results of chest x-ray examination, and concentrations of lipoproteins, plasma cortisols, and urine normetadrenaline were normal.

Comment

Spurious polycythaemia was diagnosed by definition (raised packed cell volume with red cell mass < 36 ml/kg^{1.2}) and also by excluding polycythaemia vera and recognised causes of secondary polycythaemia. Raised leucocyte alkaline phosphatase has been reported in spurious polycythaemia.³ There was no evidence that a high packed cell volume had been masked in April-May 1976—for example, by iron deficiency (red cell indices were unaltered) or haemodilution (serum sodium was unaltered). The reason for the rise in packed cell volume is unknown. The concomitant rise in plasma albumin could indicate contraction of the plasma volume but more probably reflected improved liver function, for which there was other evidence. The rise in packed cell volume was in any event disproportionate to the rise in albumin. Tissue hypoxia resulting from the pulmonary embolism might have increased the red cell mass, but this seems improbable in view of the normal arterial Po₂ and pulmonary function. Heavy smoking, heavy alcohol intake,⁴ and hypertension⁵ apparently played no part in raising the packed cell volume.

To my knowledge, spurious polycythaemia developing during observation has not been reported. A high-normal red cell mass (< 36 ml/kg) and low-normal plasma volume (> 30 ml/kg), as seen in this patient, typify the more common form of spurious polycythaemia, considered to represent the extreme of the normal range.^{2,3} This view of the condition is difficult to sustain in this case, where

spurious polycythaemia was observed to develop over a six-month period.

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Oesophageal perforation due to paraquat

The severe and often fatal effects of paraquat on the lungs and kidneys are well recognised.¹ The corrosive effect on the upper alimentary tract mucosa² has received less prominence. We report two cases of paraquat ingestion causing oesophageal ulceration and death from mediastinitis.

Case 1

A 59-year-old man was admitted in April 1976 having ingested 50–100 ml Gramoxone three days earlier. The previous day he had consulted his doctor about a sore mouth and throat. Paraquat was present in the urine. On admission he had severe stomatitis and coarse basal crepitations in the chest. Blood urea was 26.2 mmol/l (178 mg/100 ml) creatinine 0.66 mmol/l (7.3 mg/100 ml), and plasma paraquat 0.55 mg/l. Haemodialysis was instituted. Two days after admission he had severe central chest pain; radiography showed mediastinal surgical emphysema. He died 10 hours later.

Necropsy showed surgical emphysema in the supraclavicular fossae, mediastinum, and hila of both lungs. Ulceration of the mucosa of the tongue and oesophagus was present, though no distinct perforation was seen. The stomach was not ulcerated. The lungs were collapsed and showed oedema, congestion, and hyaline membranes around some alveolar walls. Paraquat concentrations in lung and kidney were 1.5 $\mu\text{g/g}$ and 2.6 $\mu\text{g/g}$ respectively.

Case 2

An 18-year-old man was admitted three hours after ingesting 50–75 ml of Gramoxone. After gastric lavage he was given one litre 30% Fuller's Earth. Charcoal haemoperfusion was started six hours after ingestion and continued for 54 hours, including six hours in tandem with a haemodialyser. Fuller's Earth and magnesium sulphate by mouth and a forced diuresis were maintained throughout. Vomiting started after the first dose of Fuller's Earth and continued for 24 hours. Seven hours after vomiting ceased he complained of sudden severe chest pain; chest radiography showed mediastinal emphysema. Oesophagoscopy (Mr Dark) showed generalised necrosis of the oesophageal mucosa. He died 70 hours after ingestion of poison. The initial plasma paraquat concentration was 2.7 $\mu\text{g/l}$.

At necropsy there was surgical emphysema in the mediastinum and bilateral pulmonary collapse with bronchopneumonia. The oesophagus was ulcerated throughout its length (figure) with complete loss of the epithelium

Photograph of oesophagus showing ulceration of mucosa.