of the head of pancreas about half had RES clearance values that were definitely abnormal before operation for relief of the obstruction. After operation the values were lower, and this was so even for patients whose previous values lay within the normal range. Hence Kupffer-cell clearance was increasing postoperatively, and the same phenomenon was seen in the patients with acute cholecystitis, who actually had accelerated RES clearances during their recovery.

Table II shows the results of the serial RES saturation test in 12 control patients (recovering after a coronary thrombosis) and 10 patients with various liver diseases. Half of these patients had abnormal results, as shown by reference to the clearance time for the 10-mg/kg dose, for which the normal values were under 30 minutes. Among these abnormal patients were four with obstructive jaundice and two with alcoholic cirrhosis.

Discussion

The results show that at least half of a group of patients with obstructive jaundice will have defective Kupffer-cell clearance of microaggregated albumin. Although poor liver perfusion may play a part, this is not the whole explanation. The serial RES saturation test shows that we are actually assessing the phagocytic capacity of the Kupffer cells. Support for this comes from the many studies of this type that have been performed in animals.[13] Using a test based on the sample principles, but very different in details, Cooksley *et al*[14] found that RES phagocytic capacity was reduced in some patients with alcoholic cirrhosis. At that time the relevance to obstructive jaundice was not well known, although we had shown in rat experiments that in obstructive jaundice a single dose of endotoxin is sufficient to produce a Shwartzman-type acute renal failure.[15]

Interest in the Kupffer cell in obstructive jaundice centres mainly on the relevance of dysfunction to more severe sequelae of endotoxinaemia and disseminated intravascular coagulation, such as acute renal failure and the respiratory distress syndrome.[16] In the adverse environment created by raised concentrations of bile acids, which are detergents, and of conjugated bilirubin, which is a metabolic poison,[7] it would not be surprising if the Kupffer cells could not perform their normal detoxifying function.[17 18] Furthermore, the phagocytic capacity of the RES may be depressed during and after abdominal surgery.[19] The state of RES perfusion and efficacy in the liver is crucial to the outcome of haemorrhagic, traumatic, and bacterial shock.[20] So far we have not been able to study any patient under more critical circumstances, but our results show that the subject of RES phagocytic capacity is of developing interest.

The adverse complications of obstructive jaundice probably arise when the body is "caught unaware" by the sudden onset of bacteraemia or endotoxinaemia. The first effect of endotoxin is to impair the function of the Kupffer cells, but thereafter there is Kupffer-cell hyperplasia and endotoxin tolerance. The increased RES activity that is symptomatic of this latter phase may be seen to develop in patients with cholecystitis. Rather than reflecting a change in liver blood flow, which should not be the explanation for changes in albumin clearance,[3] the increased RES activities on the third day after operation probably illustrate this same adaptative change in the Kupffer cells.

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SHORT REPORTS

Tumour-induced autoimmune haemolytic anaemia

Anaemia in patients with carcinoma is usually multifactorial. Autoimmune haemolytic anaemia in such patients is rare, however, and tests for autoantibodies almost always give negative results.[1] We report a case of adenocarcinoma of the caecum associated with haemolysis due to a "warm" type of IgG autoantibody within the rhesus blood group system. Haemolysis ceased after removal of the tumour, and lyophilised tumour material was shown to absorb completely the erythrocyte autoantibody.

Case report

A 71-year-old woman was admitted to hospital for investigation of anaemia. She complained only of increasing lethargy and dyspnoea for two months, having previously been in excellent health. There was no drug history, and she had not been exposed to any toxic agents. Examination showed severe pallor and a small mobile mass in the right iliac fossa. No lymphadenopathy or hepatosplenomegaly was found. Investigations showed autoimmune haemolysis (see table) with moderate numbers of spherocytes in the peripheral blood. Faeces were positive for occult blood, and barium enema confirmed the presence of a tumour in the caecum. Serological

Haematological and biochemical data

Days after admission:	0	11 (before operation)	28
Haemoglobin (g/dl)	6·8	13·2	10·9
Reticulocytes (%)	16	27	2
Direct antiglobulin test result	Strongly positive	Strongly positive	Negative
Bilirubin (μmol/l)	39	56	20
Haptoglobin (g/l)	0·10		0·81

Conversion: SI to traditional units—Bilirubin: 1 μmol/l ≈ 0·06 mg/100 ml.

investigations showed her to be group B, Rh-positive, most likely genotype cDE/cde. Serum and red-cell eluates contained two IgG autoantibodies, one a strong anti-c and the other a weaker, non-specific autoantibody. Immunoglobulin levels were normal.

Transfusion preoperatively with group B, CDe/CDe blood under cover of steroids was well tolerated. A right modified hemicolectomy was performed and a tumour 3·5 × 3·5 × 2·0 cm removed. There was no evidence of metastases. Histological examination showed a villous adenocarcinoma with abundant mucin secretion and areas of ossification in the stroma. Residual unfixed tumour was freeze-dried, and the lyophilised material completely neutralised the erythrocyte autoantibody. Dried erythrocyte stromata were not responsible, because antibodies to antigens known to be present on the red cells were not absorbed. Steroids given during the operation were stopped immediately afterwards, and reinvestigation 16 days later confirmed

remission of haemolysis, with a negative direct antiglobulin test result; only weak serum autoantibodies were detectable. No autoantibodies were detected six weeks after the operation.

Comment

Warm autoimmune haemolytic anaemia is not uncommon in the course of lymphomas and other lymphoproliferative disorders[2] but is seldom seen in carcinomas. Ovarian tumours associated with immune haemolysis are well documented, and remission may be expected after removing the tumour, with the rapid disappearance of autoantibodies, some of which may have rhesus specificity.[3] The mechanism by which autoantibody production is stimulated is uncertain. The tumour may liberate substances that alter the red-cell surface, rendering it antigenic, or antibody may be produced by the tumour itself.[4] Alternatively, the tumour may stimulate production of an antibody that cross-reacts with erythrocytes. Immune haemolysis in other carcinomas is rare. Only two cases were listed in a classification of 187 patients seen over an eight-year period in Britain (carcinoma of breast and carcinoid of small bowel),[2] and two cases were reported in a five-year analysis in one of Sweden's health-care regions (bile-duct carcinoma and gastric carcinoma).[5] No serological information or response to treatment was given. In this case the rapid disappearance of antibody after removal of the tumour supports a cause-effect relationship, but the mechanism by which this occurred remains uncertain. Complete absorption of the autoantibody by the tumour is possibly in keeping with tumour material having stimulated the production of an antibody that cross-reacted with the host's erythrocytes.

We thank Dr D A Heath for permission to report on a patient under his care.

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Departments of Medicine and Haematology, Queen Elizabeth Hospital, Birmingham B15 2TH

P A GORDON, MRCP, MRCPATH, senior registrar in haematology
P H BAYLIS, MB, MRCP, registrar in medicine

Regional Blood Transfusion Service, Birmingham B15 2SG

G W G BIRD, DSC, FRCPATH, director

Effect of virus infections on polymorph function in children

Many viruses have been shown to have an effect on the immune system in animals and in man.[1] Surprisingly little is known of the effects of virus infections on human polymorphs despite the occasional tendency for secondary bacterial infection to occur—for example, after measles and in the elderly with influenza.

As part of a wider study of immune mechanisms in children undergoing treatment for leukaemia and other malignancies, we have studied polymorph function at monthly intervals and at times of obvious infection and have correlated the results of these with infective episodes. Several children in the study have shown some depression of polymorph function during episodes of infection, and this study will be reported separately. These results, together with the finding by Larson and Blades[2] of an impaired response in normal human polymorphs treated with influenza virus in vitro, prompted us to look at normal subjects with viral infections.

Patients, methods, and results

Six children, aged 7 weeks to 18 months, with respiratory syncytial virus (RSV) infection and seven children, aged 5 months to 5 years, with influenza virus infection were studied. Diagnosis was by immunofluorescence,[3] and blood was taken during the acute phase of their illness. A stimulated nitroblue tetrazolium reduction test (NBT)[4] was performed on whole blood. Polymorphs were separated by centrifugation on Ficoll-Triosil gradients. Chemotaxis was measured in modified Boyden chambers using casein as the attractant, and killing ability was measured by incubating polymorphs with *Candida albicans*.[5] Individual experiments were controlled with polymorphs from laboratory staff and normal values derived from data obtained on 47 occasions from the staff. Nine babies, aged 1-28 days, admitted to a neonatal surgical unit with non-infective conditions and six other children, aged 4-14 years, were also studied. The means (± 1 SD) of the three tests are shown in the table.

Summary of results of polymorphonuclear leucocyte function tests. Results are means (± 1 SD), and numbers of individual tests are shown in parentheses

	NBT test (arbitrary units)	Chemotaxis (μm)	Killing ability (%)
Normal adults	12·3 : 5·1 (47)	75 : 6·5 (47)	22 : 7 (47)
Other children	13·4 : 4·8 (6)	78 : 4 (6)	24 : 6 (6)
Neonates	13·5 : 2·9 (8)	61 : 13 (7)	23 : 3 (5)
Children with RSV	7·0 : 3·8 (5)	46·9 : 21 (6)	12 : 5 (4)
Children with influenza	13·3 : 4·9 (7)	62 : 9·6 (7)	8·7 : 3·2 (7)

The NBT reduction test result was expressed in arbitrary units (100 · the formazan extinction value per 10^6 phagocytes). Chemotaxis was expressed as the distance in μm travelled by the leading front of polymorphs through the micropore filter. Polymorph killing ability was expressed as the percentage of the *Candida albicans* population that were killed. A standard *t* test was performed between the virus infected children and the normal adult controls. There was a significant difference between RSV-infected children and controls in the NBT reduction test result ($P<0·01$) and polymorph killing ability ($P<0·001$) and between the influenza-infected children and controls in polymorph killing ability ($P<0·001$).

Discussion

Polymorphonuclear leucocytes are an important part of the body defences against bacterial and fungal infection. The demonstration of defective function during episodes of viral infection would help to explain the occasional occurrence of secondary bacterial infection at these times, although there is no firm evidence that in the common viral infections in children, apart from measles, there is a significant incidence of such complications.

Larson and Blades[2] have recently reported defective ingestion of staphylococci by polymorphs treated in vitro with influenza virus. We have shown diminished candidacidal activity, which might also be due to a defect in ingestion. In addition, the normal NBT test result supports their findings of normal hexose monophosphate shunt activity in polymorphs treated with influenza virus. In the children with RSV infection both killing ability and NBT reduction were suppressed, which suggested a more general toxic effect on the polymorphs.

The advent of substances such as levamisole that may be able to improve the function of the immune system, including phagocytosis, makes the finding of depressed polymorph function in children whom we presume to have been previously normal of perhaps more than theoretical interest.

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Department of Child Health, Royal Victoria Infirmary, Newcastle upon Tyne

A W CRAFT, MRCP, senior registrar
M M REID, MB, research associate

Department of Haematology, Royal Victoria Infirmary, Newcastle upon Tyne

W T LOW, FIMLS, senior technician