closely watching patients receiving oxprenolol so that any adverse reactions may be detected at an early stage.

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Department of Dermatology, University Hospital of Wales, Cardiff, CF4 4XN
P. J. A. HOLT, M.B., M.R.C.P., Senior Registrar
E. WADDINGTON, M.D., F.R.C.P., Consultant Dermatologist

Glycerol Therapy for Cerebral Oedema Complicating Fulminant Hepatic Failure

A recent analysis of the main causes of death in a consecutive series of 132 patients (96 deaths) with fulminant hepatic failure (F.H.F.) seen over a seven-year period showed cerebral oedema in 35 (31%) of the 92 cases in which the brain was examined at necropsy. In 20 of these there was associated brain herniation, and in some cases death appeared to be due to cerebral oedema at a time when liver function was improving. The mechanism of the development of the oedema and its relation to the encephalopathy is unknown but clearly an effective means of control might improve the survival rate in this condition. Because of experience in neurosurgery, both dexamethasone and mannitol have been advocated in F.H.F. but the former may lead to gastrointestinal bleeding and the latter is often followed by a rebound increase in intracranial pressure. Glycerol given intravenously as a 10% solution in a dose of 50 g over 24 hours reduces the neurological deficit resulting from a cerebrovascular accident, possibly by limiting cerebral oedema,[1] and there is one report of its successful use in F.H.F.[2] As the liver is an important disposal site of endogenous glycerol liberated during lipolysis we have measured its concentration in blood in patients with F.H.F. and have also investigated the effect of infusion of a 10% solution.

Case Histories

Eighteen untreated patients with F.H.F. who were in grade 4 hepatic coma showed significantly higher ($P<0.05$) basal whole blood glycerol concentrations (mean 0·354 ± SEM 0·118 mmol/l) than fasting control subjects (0·074 ± 0·005 mmol/l). Five further patients with F.H.F. who had deteriorated to grade 4 hepatic encephalopathy were treated with intravenous glycerol in a dose of 50 g/24 hours but we could find no improvement in the level of consciousness. Further studies in two volunteer subjects showed that this dosage led to only a minor rise in blood glycerol concentration and no change in plasma osmolality. To produce an appreciable rise in blood glycerol concentration a further fasted control patient was given a loading dose of 6·5 g followed by 13 g over 40 minutes. With this dosage blood glycerol concentration rose to a maximum of 2·64 mmol/l at 40 minutes but this was not associated with an appreciable increase in plasma osmolality. Definite intravascular haemolysis occurred, however: plasma free haemoglobin rose to 70 mg/100 ml at 40 minutes and plasma haptoglobin concentration fell sharply to less than 10 mg/100 ml at 24 hours.

Discussion

Both endogenous and exogenous glycerol are removed principally in the liver and kidney and possibly this process is impaired in hepatic disease, which explains the significantly increased blood glycerol levels found in patients with F.H.F. The low dosage of intravenous glycerol (50 g/24 hours) given to these patients did not improve their level of consciousness and the benefit seen in patients with stroke given the same dose may be due to a direct effect on infarcted brain. Higher doses of intravenous glycerol may benefit cerebral oedema by an osmotic action and in patients with stroke given 17 g/h there was an associated increase in cerebral hemisphere blood flow and a decrease in the respiratory quotient. Cerebrospinal fluid pressure decreased and no rebound occurred.[3] Our results show, however, that similar doses may result in intravascular haemolysis and this has also been reported using other dosage schedules (60-80 g of glycerol as a 20% solution over 15-60 minutes and also after 50 g as a 10% solution over 60-90 minutes).[4,5]

We conclude that intravenous infusion of 10% glycerol (50 g/day) is ineffective in improving encephalopathy in patients with F.H.F. and that higher doses may result in dangerous intravascular haemolysis.

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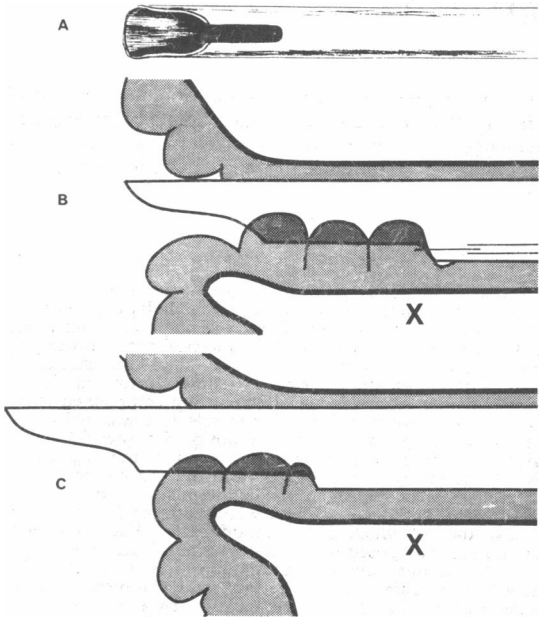
Liver Unit, King's College Hospital and Medical School, SE5 8RX
C. O. RECORD, M.B., M.R.C.P., Honorary Lecturer in Medicine (Present appointment: Senior Registrar, The London Hospital, London E1 1BB)
R. A. CHASE, B.SC., Research Fellow
R. D. HUGHES, B.SC., PH.D., Research Fellow
IAIN M. MURRAY-LYON, M.D., M.R.C.P., Senior Lecturer in Medicine
ROGER WILLIAMS, M.D., F.R.C.P., Director of the Liver Unit

Modified Oesophagoscope for Injecting Oesophageal Varices

Emergency operations for the arrest of bleeding from oesophageal varices carry a high mortality rate.[1-4] Better results have been reported using injection of sclerosants through the oesophagoscope,[5] but manipulating accurately the point of the needle at the distal end of the oesophagoscope is difficult. The technique is greatly simplified by modifying the 50-cm Negus oesophagoscope after the style of the Gabriel proctoscope.

Modification and Technique

The modification consists of cutting a slot 0·5 cm × 4·0 cm in the lower end of the instrument diagonally opposite the beak (see fig. (a)).



Modified oesophagoscope. (a) Slot cut in distal end. (b) Prolapse of varix and overlying mucosa into slot, which allows needle to be advanced directly into mass of varix. (c) Oesophagoscope advanced to compress site where injection has been given.

This allows the varices to prolapse into the lumen of the instrument. It is then a simple matter to advance the needle directly into the varix.

The injection is made as near to the cardia as possible (see fig. (b)). After injecting 5 ml of ethanolamine oleate the needle is withdrawn, and the oesophagoscope advanced to compress the site of the injection for one to two minutes (see fig. (c)). The oesophagoscope is then withdrawn to allow the widened proximal end which carries the lighting to emerge from the mouth so that the instrument can be rotated. It is then advanced again. Five or six sites equally spaced around the circumference of the lumen are usually injected at the first sitting; up to 30 ml of sclerosant may be used. A Sengstaken-Blakemore tube may be passed if there is any significant bleeding; it is usually removed after six to 12 hours.

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King's College Hospital, London S.E.5
M. E. BAILEY, F.R.C.S., Senior Surgical Registrar
J. L. DAWSON, M.S., F.R.C.S., Consultant Surgeon

Bone Marrow Suppression by Antilymphocytic Globulin

The problem of suppressing bone marrow function by preparations of antilymphocytic globulin (A.L.G.) was reported at a recent conference on A.L.G. at the Royal College of Physicians. We report some preliminary studies which show that A.L.G. inhibits human bone marrow colony forming cells.

Case Histories

Burroughs Wellcome A.L.G. was studied as our group has used this preparation in marrow transplantation in two patients where acute graft-versus-host disease followed marrow transplantation from a family donor judged compatible by H-LA typing and the mixed lymphocyte reaction. The first patient, a 6-month-old boy with severe combined immune deficiency disease, was given a single dose of A.L.G., 8 mg/kg. This improved the graft-versus-host disease without impairing marrow function. The second patient, a 27-year-old man with severe aplastic anaemia, received A.L.G., 10 mg/kg, which abolished the graft-versus-host disease. No engraftment occurred and the patient died three days after a second graft was given.

To study bone marrow colony growth bone marrow in heparin was taken from haematologically normal patients. The buffy coat obtained by sedimentation was washed three times in culture medium and the cell count adjusted to 10^6 cells/ml. Marrow was incubated for three hours in the presence of A.L.G. in concentrations varying from 0 μg/ml-100 μg/ml with or without the addition of autologous serum as a source of complement. The marrow was then plated in soft agar on previously prepared peripheral blood leucocyte feeder layers as a source of colony stimulating factor, using the method described by Pike and Robinson.[1] After 10-14 days colony counts were performed on triplicate cultures and the results of two such experiments are shown in the table.

Bone Marrow Colony Growth after Incubation with A.L.G. or Horse Globulin

Marrow	Autologous Serum	Colonies/3 × 10^5 Cells Plated Mean of Three Culture Plates					
		Control No Feeder	Control	A.L.G. μg/ml			
				0·1	1·0	10	100
1	None	0	75	67·6	56·3	31·6	16·0
2	None	1·0	141	—	158	94·6	73·0
1	0·1 ml	0·6	76	52·3	33·3	25·3	5·3
2	0·1 ml	2·0	145	78	71	23	5·5
				Horse Globulin μg/ml			
				0.1	1.0	10	100
2	0·1 ml	2·0	145	97·6	118	163	159

Discussion

The results show that A.L.G. significantly inhibits marrow colony formation at doses as low as 0·1 μg/ml ($P = < 0.05$) and that fresh serum significantly enhances this effect ($P = 0.005$) while horse globulin causes no inhibition. A.L.G. causes depression of rat stem cells[2] but no direct measure of human stem cells is available. The action of A.L.G. on human colony forming cells may be relevant to its harmful effect after marrow transplantation. Our preliminary experience shows that the dose of A.L.G. used may be critical in allowing marrow to take. We hope to use this technique to test a variety of A.L.G.s for marrow toxicity, and to investigate the possibility of removing the anti-stem-cell activity while preserving its anti-lymphocyte action by absorption with myeloid cells in the way Marmont described.[3]

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Department of Haematology, Westminster Hospital, Dean Ryle Street, London SW1P 2AP
A. J. BARRETT, M.B., B.S., Lecturer in Haematology
J. G. HUMBLE, F.R.C.P., F.R.C.PATH., Professor in Haematology
J. R. HOBBS, F.R.C.P., F.R.C.PATH., Professor in Chemical Pathology

Postpartum Rubella Vaccination and Anti-D Prophylaxis

Rubella vaccination of recently delivered women for preventing rubella and congenital malformations in future pregnancies is now routine. Simultaneously some patients run a risk of Rh immunization. As anti-D immunoglobulin preparations from pooled human sera, which should be administered post partum, also contain rubella antibodies, Alderman and Charles[1] have recommended the postponement of rubella vaccination in these cases. This practice has several disadvantages; particularly if conception occurs during the viraemia. We have used an anti-D immunoglobulin preparation with a 1:1024 rubella HI-titre and studied its influence on the development of immunity after rubella vaccination.

Case Histories

We screened 587 antenatal patients for the presence or absence of rubella antibodies by a haemagglutination-inhibition method. No rubella antibodies were detectable (seronegative—that is, titre <8) in 6% of these patients. Twenty one and 25 were investigated in detail three and six weeks after vaccination, respectively. Previous experience had shown that seropositive patients with titres as low as 1:8 did not show an appreciable antibody titre rise after rubella vaccination. Patients in group A received the rubella vaccine—0·5 ml of live, attenuated rubella virus vaccine, duck embryo cell-adapted HPV-77 strain, containing not less than 1000 $TCID_{50}$ of rubella virus (Meruvax, MSD)—on the fifth day of the puerperium. Patients in group B (both rhesus-negative and -positive) were given 250 μg anti-D immunoglobulin in 2 ml of a 16% gammaglobulin preparation intramuscularly (immunoglobulin anti-D SRK) within 48 hours of delivery, followed three days later by the rubella vaccine. Several patients had no alteration of rubella antibody titre three days after administration of this anti-D preparation. Three weeks and six weeks after the rubella vaccination, rubella HI-titres were found in both groups (see table). The conversion rate in both (admittedly small) groups was 100%. Two patients responded poorly, one in group A with a titre of 1:8 six weeks after vaccination, another in group B with a titre of 1:16. The latter had received 3 units of blood at delivery.

Results

We conclude that the rubella antibodies administered with the anti-D immunoglobulin do not delay or prevent active immunity against the rubella virus when the vaccine is given at about the same time. Our