about 1 in 500 cases in this series and caused death in 1 in 1000. The exact pathogenesis is not clear, but the necrosis is presumably ischaemic in origin and caused by the laying bare of most of the lesser curvature. It may be attributable to the relatively poor submucosal blood supply in that region as compared with the rich anastomotic network in the submucosa of the anterior and posterior walls of the stomach.[16-18] Whatever the cause may be, knowledge of this potential complication should help in its prevention. Devascularisation of the stomach should be kept to a minimum by careful preservation of all arteries to the stomach except the branches of the left gastric artery, which must be sacrificed. The uppermost short gastric arteries should be preserved when possible, and if the spleen has to be removed on account of iatrogenic trauma the increased risk of subsequent lesser-curve necrosis must be borne in mind. At the end of the operation it might be wise to cover the raw area on the lesser curvature with peritoneum by suturing the cut edges of serosa.

Necrosis of the lesser curvature seems to be particularly likely to occur when HSV is used prophylactically for duodenal ulceration in patients about to undergo renal transplantation. Death due to necrosis of the lesser curvature occurred in two such patients in Zurich[19] and in one in Munich.[20] The total number of transplant patients treated by HSV in these two centres was not ascertained precisely, but the mortality of HSV in such patients certainly seems to be high. Hence the use of HSV in these patients is contraindicated, at least until more information is available. Finally, awareness of the possibility of lesser-curve necrosis should prompt surgeons to re-explore the abdomen of any patient who develops signs of an intra-abdominal disorder during the first 10 days after the operation.

Twelve of the 17 deaths after HSV in this series were not due to gastric necrosis, no fewer than eight being due to thrombosis, embolism, or myocardial infarction (table II). Thus it seems reasonable to suggest that the use of prophylactic low-dose heparin might lower the operative mortality of HSV still further.[21 22]

The third main conclusion is that when vagotomy is confined to the proximal two-thirds or so of the stomach, as in HSV, troublesome gastric stasis is rare, only 0·8% of the patients in this study subsequently needing drainage. Thus provided that in the long term HSV proves as effective as vagotomy with drainage in curing the ulcer, the use of drainage procedures could be abandoned and their attendant complications such as dumping, diarrhoea, and bilious vomiting could be largely prevented.[5 23 24]

I wish to thank all the surgeons listed in table I for kindly furnishing details of their patients treated by HSV.

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Local infusion of urokinase and heparin into renal arteries in impending renal cortical necrosis

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Summary

Two patients with presumed impending cortical necrosis, after haemolytic uraemic syndrome in one and after concealed accidental haemorrhage in the other, were treated by local infusion of urokinase and heparin into the renal artery. Both recovered and one regained normal renal function. Local infusion of anticoagulants or thrombolytic drugs into one renal artery offers the possibility of a controlled examination of the efficacy of this treatment in preventing cortical necrosis.

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Introduction

The mortality rate among patients with the haemolytic uraemic syndrome has fallen with the availability of supportive measures, particularly peritoneal dialysis,[1] but there remain patients in whom bilateral cortical necrosis leads to irreversible renal failure. Heparin has been advocated for arresting intravascular coagulation, and more recently thrombolytic treatment in the form of streptokinase has been used in an attempt to lyse intrarenal fibrin.[2 3] Both these treatments may lead to generalised haemorrhage, and the risks of treatment may outweigh the

possible advantages. Randomised controlled trials of anticoagulant or thrombolytic treatment have for various reasons proved difficult to organise[3] and an alternative approach to assessing treatment in this condition is needed. We report two patients in whom cortical necrosis was thought to be imminent and who received urokinase infusions into the renal arteries,[4] with improvement in the arteriographic appearances after infusion in one and with eventual clinical recovery in both.

Case 1

A 9-year-old boy (weight 22·2 kg, surface area 0·84 m^2) with Hirschsprung's disease had numerous abdominal operations but had been well with a terminal left iliac fossa colostomy for the last four years. He presented with a 10-day history of diarrhoea and vomiting; he was depleted of fluid, anuric, anaemic, and thrombocytopenic, and red cell fragmentation was seen on his blood film. He was transfused, but 24 hours later had become unconscious and remained volume depleted with severe hyponatraemia (Na+ 105 mmol/l (105 mEq/l)). He had a respiratory arrest from which he was resuscitated. In spite of rehydration and large doses of intravenous frusemide he passed only a few drops of urine containing protein and blood. Multiple periotoneal adhesions from previous abdominal surgery precluded successful peritoneal dialysis and he was transferred to Guy's Hospital for haemodialysis. Investigations on admission showed the following results: haemoglobin 5·0 g/dl; platelets 30×10^9/l (30 000/mm^3); reticulocytes 4%; prothrombin time 12 seconds (control 12); kaolin-cephalin time 32 seconds (control 33); thrombin time 17 seconds (control 12); reptilase time 23 seconds (control 13); fibrinogen titre 1/64; fibrin degradation product (FDP) titre 1/40 (ThromboWellco test. Wellcome Reagents Ltd, normal <1/5). The blood film showed definite red cell fragmentation, and blood cultures were sterile.

He regained consciousness within 24 hours of the start of haemodialysis. His bowel was shown to be distended with fluid levels on x-ray examination and he vomited for several days. He complained of severe central chest pain, and the electrocardiogram showed S-T depression and T-wave inversion in leads II, III, aVF, and V_2 and V_6, and 24 hours later a loud pericardial rub was heard. Renal plasma flow was estimated by dynamic renal scintillography using ^{99m}Tc-diethylenetriamine penta-acetic acid (DTPA)[5]; this showed poor blood flow, and low uptake of tracer in the left kidney, none in the right, and none in the bladder.

It was decided to infuse the right kidney with urokinase through a catheter passed up from the femoral artery. A preinfusion right renal arteriogram showed poor filling of peripheral branches and poor nephrographic opacification. Urokinase (Leo Laboratories) 100 000 units and heparin 2000 units per 24 hours were infused via the catheter for the next two days. A repeat renal scintillogram immediately after the infusion showed little change but it was noted at repeat renal arteriography that though the catheter had slipped back into the aorta at some undetermined time there was now good peripheral vessel filling and a virtually normal nephrographic blush. The right renal artery catheter was replaced and a left renal artery catheter inserted. Urokinase 50 000 units and heparin 1500 units per 24 hours were infused via each catheter for a further two days.

Subsequent renal scan showed significant improvement in blood flow to both kidneys, the vascular phase appearing much earlier than in the previous scan with an increased accumulation of tracer. Ten days later he began to pass significant volumes of urine, his blood urea and plasma creatinine gradually fell, and no further haemodialysis was needed. At the time of writing renal function was normal.

He was treated throughout with oral dipyridamole (75 mg eight hourly) and, after the cessation of intra-arterial infusions with low-dose subcutaneous heparin so that the kaolin-cephalin time did not exceed the control value. At no time during the urokinase infusion did he have any haemorrhagic side effects, and there was no evidence of a systemic effect of the local activation of the fibrinolytic system: the fibrinogen titre remained at 1/64, and there was no further prolongation of the thrombin time or reptilase time and no increase in the FDP titre.

Case 2

This 28-year-old woman was admitted to Guy's Hospital as an emergency on 28 July 1974, during the 38th week of her second pregnancy. Four years earlier she had a normal twin pregnancy, with no evidence of hypertension. At the start of antenatal care (18 weeks) her blood pressure was normal (110/75 mm Hg) and her urine was free of protein. At 35 weeks however, she was admitted to another hospital because of proteinuria and hypertension. Six days later she discharged herself against medical advice; at this time her blood pressure was 140/100 mm Hg but her proteinuria had resolved. Three hours before admission to Guy's Hospital she developed abdominal pain and vaginal bleeding. On examination she was shocked (blood pressure 90/60 mm Hg, with a hard tender uterus. The fetal heart was initially slow and irregular but soon became inaudible.

The results of tests of haemostasis were: prothrombin time 12 seconds (control 12); kaolin-cephalin time 38 seconds (control 32); thrombin time 11 seconds (control 11); reptilase time 15 seconds (control 15); fibrinogen titre 1/64; FDP titre 1/40; platelet count 82×10^9/l (82 000/mm^3).

Abruptio placentae was diagnosed, the membranes were ruptured, and she was transfused a total of 3·5 litres of blood. Nine hours later she had a forceps delivery of a fresh stillbirth.

After delivery she was noted to be passing small amounts (10 ml/6 h) of iso-osmolar urine (307 mmol/l (307 mosmoles/kg)). There was no response to intravenous frusemide 1 g, a diagnosis of renal cortical necrosis was suspected, and she was started on dipyridamole 200 mg three times a day, aspirin 300 mg twice a day, and subcutaneous heparin 5000 units eight hourly. A ^{99m}Tc-DTPA dynamic renal scintillogram showed extremely poor renal perfusion, and on 31 July, 54 hours after delivery, renal arteriography showed that the kidneys were of normal size and that peripheral perfusion was reduced with a sparse and patchy nephrogram. A catheter was placed in the left renal artery, and during the next 48 hours a total of 400 000 units of urokinase was infused into the renal artery. No complications of this treatment were observed and there was no evidence of a systemic effect of the local activation of the fibrinolytic system; at the end of the infusion the following results were obtained: fibrinogen titre >1/128; thrombin time 15 seconds (control 11); reptilase time 17 seconds (control 13); FDP titre 1/20. The position of the catheter was checked before it was withdrawn.

She passed virtually no urine for 11 days and was treated with intermittent peritoneal dialysis, the last treatment being on 12 August. At urography on 13 August there was faint bilateral nephrographic opacification, which did not increase at three and a half hours; the later films showed calyceal opacification, and the right kidney measured 13·5 cm and the left 15 cm. Subsequently her renal function improved slowly, and three months after delivery her plasma urea and creatinine were both raised at 12·3 mmol/l and 203 μmol/l (74 mg/100 ml and 2·3 mg/100 ml) respectively.

Isotopic studies suggested that the left kidney recovered earlier and more completely than the right. On 7 August perfusion was marginally better on the left and on 12 September the left kidney was noted to be larger than the right. This difference was confirmed radiologically and persisted though at the time of writing they were both much smaller than on 13 August, with the right kidney measuring 10·5 cm and the left 12 cm with a considerable reduction in volume. Eight months later, renal scintillography suggested that the left kidney provided 70% of total renal function.

Discussion

Infusion of urokinase and heparin into the aorta at the level of the renal arteries was associated with full recovery of renal function in an anuric child with presumptive evidence of impending cortical necrosis associated with the haemolytic uraemic syndrome. In an adult with concealed accidental haemorrhage and impending cortical necrosis thrombolytic treatment applied locally to one kidney was associated with better perfusion on the scan, suggesting that there was less severe damage to the perfused kidney. Subsequently this kidney was appreciably larger than the opposite non-perfused kidney, and though such a difference in length can be seen in normal people the difference in the renal bulk was outside the normal range. We cannot ascribe these results directly to the treatment, and further experience is necessary but a fresh approach to these difficult problems has been shown.

There has been no controlled study showing that heparin or thrombolytic treatment affects the mortality of the haemolytic uraemic syndrome,[1] and, indeed, good results have been

obtained without using such treatment.[6] Moreover, it has not always been possible to show any effect of treatment from kinetic studies of platelet and fibrinogin turnover.[7] Recently the importance of fibrin deposition in the kidney in the pathogenesis of the disease has been questioned.[8 9] The undoubted risk of fatal haemorrhage in association with anticoagulation or thrombolytic treatment makes the need for adequate controlled trials imperative, but the complexity of the trial design and the problem of unnecessary treatment of mildly affected patients have so far proved insurmountable.[3] A further consideration pointing to the need for proper trials is the apparent low incidence of residual hypertension in patients treated with streptokinase.[3] Local infusion, as used in our cases and in those of others,[1] has an advantage of providing the drug in high concentration in the kidney without affecting haemostasis in the rest of the body, and, moreover, if only one kidney is perfused the other can serve as a control. A similar approach to evaluating treatment in cortical necrosis in conditions other than the haemolytic uraemic syndrome is suggested by the second case. The use of the gamma-camera for frequent assessment of renal perfusion and function in impending cortical necrosis would enable only the more seriously affected cases to be treated in this way, whereas those with presumed tubular necrosis alone might be treated conservatively. We cannot yet conclude that the fall in renal perfusion as estimated by dynamic renal scintillography will necessarily lead to cortical necrosis but it is possible to identify these patients with tubular necrosis who have normal or only slightly diminished renal blood flow.

Close collaboration between various disciplines within the hospital service is needed, for without this essential teamwork the treatment of acute renal failure is unlikely to improve.

ADDENDUM—Since this report was prepared we have treated two further children, one aged 14 months and the other 5 months. Both were referred in established renal failure from haemolytic uraemic syndrome and in both cases renal perfusion as judged by the appearance on renal scintillography was extremely poor. It was not known at what time renal perfusion had begun to deteriorate. One child remained alive and well but with chronic renal insufficiency, and there was no difference in individual renal function. The other child died of chronic renal failure after some recovery in renal function, but at necropsy the perfused kidney was smaller than the non-perfused kidney.

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Plastic isolators for treatment of acute leukaemia patients under "germ-free" conditions

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Summary

A gnotobiotic isolation system based on those developed in veterinary research has been constructed for hospital use. Fifteen patients with leukaemia and neutropenia spent a total of 110 weeks in plastic isolators, and none acquired any infection. Endogenous flora was effectively suppressed by topical antiseptics and gastrointestinal decontamination effected with nonabsorbable antibiotics. The isolator system was acceptable to patients and staff and much cheaper than the use of sterile rooms. Other advantages of the system are portability, easy storage, and use on ordinary open wards without prejudice to the microbiological protection afforded. It is as yet uncertain whether protective environments of this type will substantially improve the outcome of treatment for the acute leukaemias.

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Introduction

For the past 60 years microbial isolators have been used to maintain a sterile environment in which germ-free animals may be produced for laboratory investigations.[1] These animals are free from bacteria, moulds, and other contaminants in the environment, but some carry vertically transmitted viruses, and the term "gnotobiotic," signifying that their flora is known, is more accurate than the term "germ-free." Colonies of gnotobiotic rats and mice have been maintained continuously since 1954 and a great many species, including calves and foals, have been reared in sterile isolators.[2 3] Experience gained from veterinary gnotobiotic research enabled the development of closed isolator systems using barriers made of flexible plastic film in which many tasks may be performed without violating the microbiological integrity of the system.

Closed-system isolators that are used for the care of patients who are at special risk of infection[4-8] impose restrictions on medical and nursing care because of the interposition of a mechanical barrier between patient and attendants.[9] Hence isolation systems in which a linear flow of sterile air is combined with partial mechanical barriers and reverse barrier nursing techniques have been preferred, even though such systems are microbiologically less secure than closed-system isolators.[9-12] We have designed a patient isolator in which the limitations imposed by the flexible film barrier have been reduced and a linear flow of sterile air has been used solely to protect the port through which sterile supplies are introduced.[13] The security