Fig. 4 did not show significant increase in heart size from earlier examinations. E.C.G.s at the time showed no gross changes.

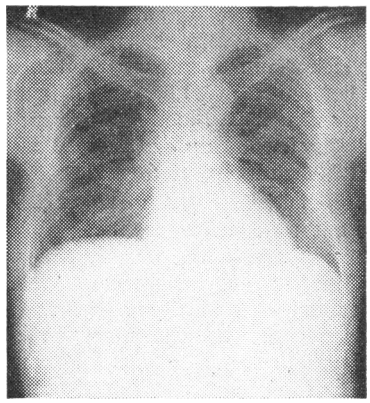

FIG. 4.—Case 3. Chest radiograph.

Discussion

Our experience in three cases of arteriovenous fistulae is described. We have not to date been impressed with the flow rates obtained during dialysis, nor do we consider setting up dialysis a convenient procedure, as compared with our experience with conventional Scribner shunts. The fistula in Case 3 was the only one which in our hands yielded satisfactory dialyses. In Cases 1 and 3 there was no significant distal flow to provide a safety valve as described by Klinkmann *et al.* (1967).

We feel in retrospect that in spite of other cardiovascular and respiratory changes all cases were significantly embarrassed by the circulatory effects of their fistulae (our information is that all the shunts were 5 mm. in size at the time of construction), and it was for this reason we closed the fistula in Case 3. It is interesting that a clinically small shunt may have created such haemodynamic effects, but we feel sure that this shunt was responsible for the patient's symptoms and cardiovascular state.

In the light of our experiences with these three patients we think it is important that such patients have adequate investigation, including measurement of cardiac output after exercise both with the shunt occluded and open.

We are interested in the sudden deaths described by Verberckmoes *et al.* (1967), and, as already mentioned, we know of one similar case. It is possible that Case 2 may be a further example, for, though he was ill from a combination of factors, the suddenness of his death was unexpected.

We wish to thank Professor R. Y. Calne for permission to publish details of patients under his care. We are grateful to the Cardiological Unit at Papworth Hospital for the cardiac output measurement in Case 3. We thank Dr. P. R. Millard for his help in the preparation of this paper.

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Clinical Trial of 6% Hydroxyethyl Starch* (a New Plasma Expander)

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Summary: No adverse effects were seen in 29 patients given an intravenous infusion of 6% hydroxyethyl starch solution. Platelet counts had fallen by eight hours after infusion, but had reached pretransfusion levels by 24 hours. Two patients developed unusual bleeding postoperatively, which was possibly due to the infusion. Further investigations on the first stage of coagulation and prothrombin generation in patients receiving hydroxyethyl starch are required.

Introduction

For some time starch has been known to have a colloid effect when administered intravenously. However, ordinary starch solutions are physically unstable; moreover, rapid enzymatic destruction occurs in the blood stream. In 1959 the use of physically stable branched or waxy polymers of starch and the introduction of hydroxyethylation to resist enzymatic hydrolysis initiated the re-examination of starch as a plasma expander.

The starting-point for hydroxyethyl starch synthesis is waxy sorghum starch, which is composed of over 95% amylopectin. Reaction with ethylene oxide introduced hydroxyethyl groups, which are attached by an ether linkage to the hydroxyl groups of the amylopectin. The number of hydroxyethyl groups attached to a molecule is reflected by a number called the degree of substitution, which is defined as the average number of hydroxyethyl groups per glucose residue. The hydroxyethyl starch used in this trial has a degree of substitution of 0.7, which means it contained on the average seven hydroxyethyl groups per every 10 glucose residues.

The important properties of hydroxyethyl starch from the medical viewpoint are its molecular weight (400,000–450,000) and the intravascular persistence of two weeks which depends

* 6% Hydroxyethyl starch in 0.9% sodium chloride was supplied by Don Baxter Co., Glendale, California, U.S.A.

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on its degree of substitution. Hydroxyethyl starch is a cheap product with reproducible characteristics. In addition, it has the same viscosity in solution as dextran. There are also theoretical considerations based on the similarity to normal body glycogen. In countries where facilities for blood transfusion are not readily available it is worthy of consideration: it does not lose its efficiency on storage over long periods.

Ballinger *et al.* (1966) showed that the administration of a 6% solution of hydroxyethyl starch in saline to dogs subjected to haemorrhagic shock was as effective in restoring arterial blood pressure and maintaining survival as clinical dextran solution. After these results were published preliminary clinical studies were started. The present trial was divided into three phases: (1) to study the effects of infusion of 6% hydroxyethyl starch on patients, (2) to compare 6% hydroxyethyl starch and dextran as plasma expanders in shocked patients, and (3) to study the effects of infusion of large volumes of 6% hydroxyethyl starch. This paper reports the first phase of the trial.

Materials and Methods

Twenty-nine patients admitted to the University College Hospital, Ibadan, for routine investigations and operation were used for this trial. Of these, 21 were males and 8 females. Their ages ranged from 28 to 82 years and the clinical diagnoses are as shown in the Table. Full consent was obtained from all patients, and the experiment was thoroughly explained to them. Five hundred millilitres of a solution of 6% hydroxyethyl starch was given over periods ranging from 5 to 34 minutes. Vital signs were monitored every 15 minutes. Determination of haematocrit, haemoglobin, bleeding-time, clotting-time, platelet counts, serum proteins, and fibrinogen titre were made before and at 10 minutes, 1 hour, and 4, 8, 12, and 24 hours after infusion. Blood and urinary concentrations of hydroxyethyl starch were measured at 10 minutes, 1 hour, and 4, 8, 12, and 24 hours after transfusions (Figs. 1, 2, and 3).

Total plasma carbohydrate concentration was measured in duplicate by the anthrone techniques using trichloroacetic acid filtrates of plasma. Plasma and urinary glucose were determined by the Glucostat enzyme system. Urine total carbohydrate concentrations were measured with the anthrone technique. Fibrinogen titre was determined by the method of Hardisty *et al.* (1964), using Fibrindex. Haematocrit, haemoglobin, bleeding-time, clotting-time, platelet count, and plasma protein concentrations were measured by standard procedures. During the trial there was no restriction on fluid intake, and the patients had the normal ward diet.

Clinical Trial of Hydroxyethyl Starch in 29 Patients

Case No.	Age and Sex	Clinical Diagnosis	Weight lb.	Weight kg.	Duration of Transfusion (min.)
1	60 M	Carcinoma of oesophagus ..	95	43·1	15
2	66 M	Pulmonary tuberculosis. Carcinoma of oesophagus ..	101·5	46·0	15
3	30 F	Grade IV carcinoma of breast	156·5	71·0	10
4	44 M	Madura foot	152	68·9	10
5	45 M	Mycetoma	127	57·6	5
6	36 M	Mycosis fungoides	131	59·4	10
7	33 M	Carcinoma of stomach ..	84	38·1	20
8	45 M	Chronic D.U. elephantiasis ..	122	55·3	10
9	30 F	Chronic ulcer of foot ..	84	38·1	13
10	45 M	Gangrene of scrotum ..	153	69·4	7
11	32 F	Carcinoma of breast	103·5	46·9	10
12	60 M	Benign prostatic hypertrophy	100·3	45·5	15
13	66 M	Advanced carcinoma of bladder	150	68·0	5
14	82 M	Hydrocele	116·5	52·3	11
15	52 M	Elephantiasis of scrotum ..	108	49·0	10
16	39 F	Lipoma	122·5	55·6	10
17	50 M	Strangulated left inguinal hernia	117·8	53·4	15
18	28 M	Pyomyositis	120	54·4	8
19	49 F	Carcinoma of breast	101	45·9	15
20	55 M	Hepatoma	85·5	38·8	8
21	50 M	Post-necrotic cirrhosis of liver	151	68·5	10
22	35 M	Fistula-in-ano	154	69·9	10
23	35 F	Colloid goitre	113	51·3	8
24	29 F	„ „	101	45·8	15
25	60 F	Carcinoma of breast	126	57·2	7
26	62 M	Urethral stricture	155·5	70·5	20
27	60 M	Carcinoma of bladder ..	112	50·8	17
28	70 M	Inguinal hernia	105·5	47·8	22
29	40 M	Inguinoscrotal hernia ..	114·5	51·9	34

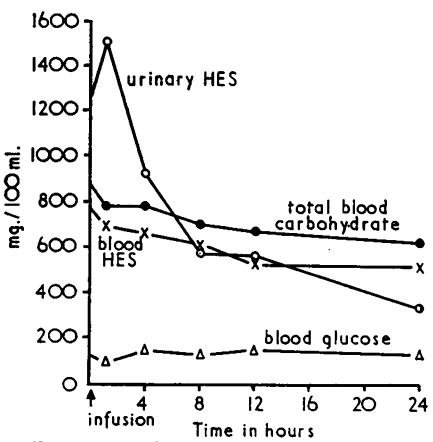
Results

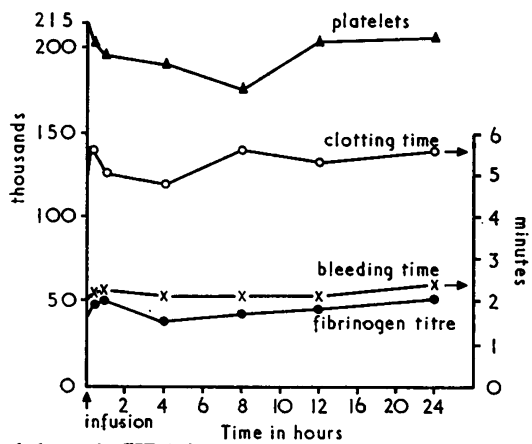
There were no significant changes in the blood pressure readings throughout the experiment. The platelet counts done eight hours after transfusion showed a drop ($0.05<P<0.1$), which returned to pretransfusion levels in 24 hours. The clotting-time showed a corresponding rise at eight hours after transfusion but the difference was not significant ($P=0.10$). The bleeding-times and the fibrinogen titre showed no appreciable changes throughout the experiment. The blood level of 6% hydroxyethyl starch showed a gradual decrease over 24 hours and the substance was rapidly excreted in the urine. The intravascular persistence at four hours was 80% and at 24 hours 60%.

Two patients had unusual bleeding following surgery after infusion with 6% hydroxyethyl starch. A patient with carcinoma of breast (Case 11) had biopsy of the breast done 48 hours after infusion, and the bleeding from the biopsy site was so profuse that transfusion with 1 pint (570 ml.) of blood was necessary. A patient with benign prostatic enlargement (Case 12) bled profusely after prostatectomy four days after infusion with 6% hydroxyethyl starch.

Comment

Infusion with 500 ml. of 6% hydroxyethyl starch appeared to have no adverse effect on the patients. The average dose used was about 10 ml./kg. body weight. This dosage is said to produce dilutional coagulation abnormalities, whereas higher doses (20–30 ml./kg.) increase bleeding by 30 to 40 times more than what one would expect from haemodilution (Garzon,





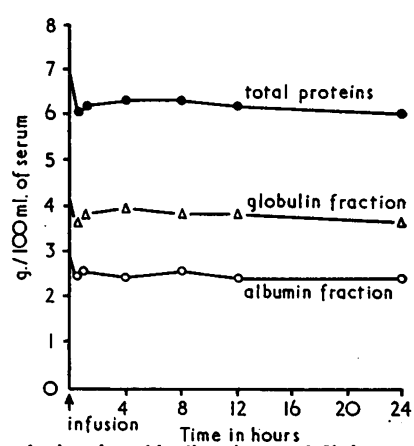


FIG. 1.—Persistence studies of 6% hydroxyethyl starch (HES) in 29 patients. FIG. 2.—Platelet count, clotting-time, bleeding-time, and fibrinogen titre estimations. FIG. 3.—Serum protein estimations before and after transfusion.

1967). Lee (1967) found, in 60 to 70% of 24 patients transfused with hydroxyethyl starch, gross abnormalities in the partial thromboplastin time, which is a useful screening for the first stage of coagulation. It is possible that the abnormal bleeding notice in this trial was due to the hydroxyethyl starch, though the bleeding-time and clotting-time during and after infusion were normal. There is therefore need for further investigation of the first stage of coagulation and prothrombin generation in patients being transfused with this substance.

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Medical Memoranda

Duodenal Haematoma

Brit. med. J., 1968, 3, 785–786

With the increasing awareness that intramural haematoma of the duodenum is a definite clinical and radiological entity it is possible to make a diagnosis of this condition with reasonable certainty on the barium-meal examination. Because road accidents are especially likely to result in upper abdominal injuries through impaction with the steering column (Bruck and Caplan, 1964), this condition will be seen with increasing frequency. Also the use of the Ross biopsy capsule for obtaining specimens of the duodenal mucosa (Tobin *et al.*, 1966) and treatment with anticoagulants (Culver *et al.*, 1961) have added to the incidence of the condition, which may also occur spontaneously in haemorrhagic diatheses (Culver and Pirson, 1959).

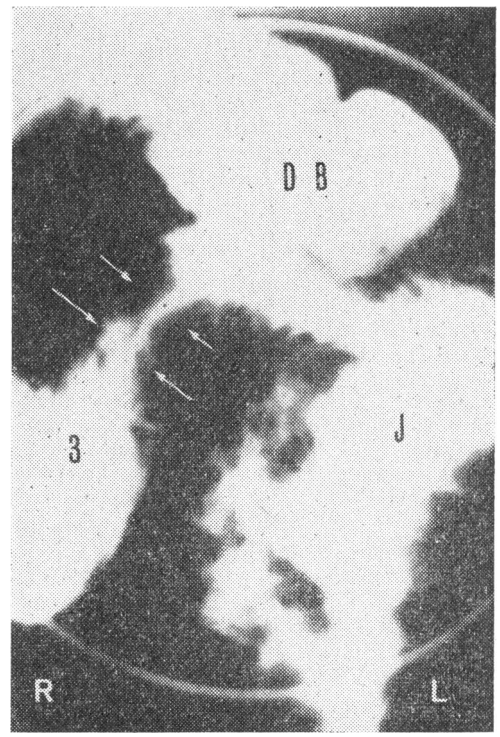
Case Report

A 55-year-old woman was admitted to hospital on 18 November 1966 after being injured in a car accident the previous day, when she had been thrown forward against the windscreen and the steering column. She vomited later that day and again the next morning.

On admission she was alert and co-operative, complaining of pain in the chest and also of headache. There was tenderness and bruising over the sternum, but no other physical signs. Investigations showed Hb 14.9 g./100 ml., intravenous pyelogram normal, cholecystogram normal. The patient improved and three days later was discharged. She remained well for two days, but on the third day after discharge vomiting recurred. The food seemed to stick in the epigastrium, producing a nauseated feeling. On readmission on 1 December she looked well, her B.P. was 120/80, pulse 50, Hb 15.3 g./100 ml., W.B.C. 6,500/cu. mm. There was tenderness in the epigastrium, but no other physical signs were present, and her stools were normal.

Barium-meal examination showed a moderate-sized reducible hiatus hernia. The stomach was otherwise normal. There was delay in propulsion of the barium in the region of the third part of the duodenum with marked churning movements in the second part. Just beyond this, in the third part of the duodenum, there was an area of concentric narrowing with marked irregular margins (see Fig.). The duodenum proximal to the area of narrowing showed widening with accentuation of the tranverse folds. The mucosal pattern in the narrowed area was coarse and markedly irregular. The appearances were very similar to previous published illustrations (Tobin *et al.*, 1966; Gordon and Hauser, 1967), and haematoma of the third part of the duodenum was therefore diagnosed.

The patient was treated conservatively, and after two weeks was discharged completely asymptomatic. Double contrast duodenography (Raia and Kreel, 1966; Kreel, 1968) was performed one month later, when the duodenum was shown to be normal. She has since remained asymptomatic, and has had no recurrence of the vomiting.



Spot film of third part of duodenum showing the concentric narrowing with marked proximal dilatation of the second part of the duodenum. DB=Duodenal bulb. 3=Third part of duodenum. J=Jejunum.

Comment

Early radiological diagnosis of intramural haematoma of the duodenum obviates the necessity for an exploratory laparotomy. If the possibility of this condition is entertained in the differential diagnosis of the "acute abdomen" and there is no evidence of perforation of the bowel, the demonstration in a barium study of the pattern associated with an intramural extramucosal mass will establish the finding. It is, however, most important in cases of upper abdominal trauma, or in those on anticoagulants who present with vomiting, to demonstrate the whole of the duodenum, including the third part. Unless this part of the duodenum, which is usually hidden by the barium in the stomach in the frontal or slightly oblique