3. In pregnant patients with severe anaemia (whether iron-deficiency or megaloblastic in type) who are near term. The potential hazards of post-partum haemorrhage or an operative procedure exists, as in every parturient.

In the haemolytic type of anaemia due to sickle-cell disease and malaria seen in Western Nigeria Fullerton and Turner (1962) have also shown the value of exchange transfusion.

Summary

A study is presented of the indications and effects of exchange transfusion in gynaecology and obstetrics.

The investigation includes a detailed study of 50 consecutive patients who on admission had a haemoglobin level below 4.4 g./100 ml. (30%). These patients were assigned by the method of random sampling to receive either an exchange transfusion or a slow packed-cell transfusion.

In no case was the cardiac function, clotting mechanism, or electrolyte balance in any way impaired, nor was there any evidence of citrate toxicity.

Subsequent exchange transfusion of a further 31 patients lends support to our finding that exchange transfusion is a safe procedure, the indications for which have been discussed. Thus exchange transfusion is of great value to the woman in anaemic cardiac failure, and to the severely anaemic patient who is pregnant, is approaching delivery, or requires an urgent gynaecological or obstetrical operation.

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Preliminary Communications

Epsilon-aminocaproic Acid Therapy for Dental Extractions in Haemophiliacs

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Much has been written regarding local and systemic measures to prevent and arrest dental haemorrhage in haemophiliacs (Matheson, 1949 ; Wishart *et al.*, 1957 ; Winstock and Ingram, 1961 ; McIntyre *et al.*, 1964). The present generally accepted regimen involves frequent transfusions of fresh frozen plasma combined with the local use of dental splints to protect the sockets, which are packed with oxidized cellulose soaked in bovine thrombin. Antihaemophilic globulin concentrates of human, bovine, or porcine origin have also been used with considerable success (Macfarlane *et al.*, 1954 ; Biggs *et al.*, 1965).

Lucas *et al.* (1962) advocated the use of hypnosis, combined with extensive local measures, as a means of obtaining haemostasis without the need of replacement therapy. Reid *et al.* (1964) suggested that hypnosis possibly prevented a rise in fibrinolytic activity resulting from mental stress. It was argued that artificial reduction of the activity of the fibrinolytic system should produce a similar effect, and success was claimed in normalizing the thrombelastograph tracings of haemophilic blood in vitro by the addition of epsilon-aminocaproic acid (E.A.C.A.). A series of dental extractions on haemophiliacs with the use of systemic E.A.C.A. combined with extensive local measures was carried out, obviating the need for replacement therapy.

In view of this apparent success it was decided to repeat the experiment in the United Bristol Hospitals on haemophiliacs requiring dental extractions. It was felt that the effectiveness of E.A.C.A. had not been proved beyond doubt by the previous series, since the local measures were so extensive that these alone might well have been responsible for much of the haemostasis. Though at the outset exactly corresponding local measures were used in the series reported here, an attempt was made to reduce them progressively and to place increasing reliance on E.A.C.A.

Since E.A.C.A. has no corrective influence on the thromboplastin generation test, it seemed reasonable that any beneficial result of the therapy would be equally apparent in both classical haemophilia and Christmas disease ; the present series therefore includes male patients with both these conditions.

Method

When a patient who was known or thought to have haemophilia or Christmas disease presented for dental surgery, a definite diagnosis was first established on the basis of a personal and family history of bleeding and a clearly defined deficiency in the thromboplastin generation test. A full dental assessment was carried out and dental haemorrhage splints were constructed immediately before admission to hospital and held in readiness as a precautionary measure.

On the patient's admission a full medical examination was carried out to ensure that there was no contraindication to dental surgery, general anaesthesia, or the use of E.A.C.A. Each adult patient was given E.A.C.A. by mouth at the rate of 24 g./day in four or six divided doses, beginning 12 hours preoperatively. Children were given proportionally the same amount on a weight-ratio basis.

Planned dental extractions were performed under general anaesthesia, with progressively fewer local measures aiding haemostasis as the series proceeded.

Though all patients began E.A.C.A. therapy at a rate of 24 g./day, this rate was raised if oozing occurred, and attempts were made to lower it if haemostasis was entirely satisfactory. The final adult dose varied between 16 and 36 g./day, with an equivalent lower range for children. The E.A.C.A. therapy was maintained until 24 hours after the sutures had been removed, normally for a total period of six or seven days. The first patients in the series received all their E.A.C.A. by mouth in a syrup ; to the later patients it was given by mouth for 12 hours, then in a saline drip intravenously from a few hours preoperatively until about 24 hours postoperatively, after which it was again given by mouth.

RESULTS

Table I shows the progressive reduction in local measures employed throughout the series. As an initial step dental haemorrhage splints were replaced by sutures, then bovine thrombin and oxidized cellulose were discontinued in that order. The final cases had silk sutures only. It is not intended to attempt elimination of this final local measure, since it is normal to use sutures as an aid to haemostasis and healing in the normal individual.

Replacement therapy was necessary in only one case, and this is worthy of further comment. Ten teeth were extracted from a mouth which had been sorely neglected for many years.

TABLE I.—*Haemostatic Measures Employed in the Present Series.*

Case No.	E.A.C.A.	Sutures	Oxycel or Surgical	Bovine Thrombin	Dental Splints	Blood or Fresh Frozen Plasma
1	+		+	+	+	
2	+	+	+	+		
3	+	+	+	+		
4	+	+	+			
5	+	+				
6	+	+				
7	+	+				
8	+	+	+			+
9	+	+				
10	+	+				
11	+	+				
12	+	+				

An extremely unhealthy gingival condition was present which had failed to respond to local treatment, and it might have been expected that a postoperative ooze would occur even if the patient had been a normal individual. As expected, the ooze took place, but the patient swallowed the blood, and the first postoperative dose of E.A.C.A. by mouth may not have been absorbed because of the quantity of blood in the stomach. A typical haemophilic bleed occurred some hours postoperatively. As an emergency measure transfusion of fresh frozen plasma and whole blood was given and E.A.C.A. administration in saline was begun intravenously. Within an hour the haemorrhage had almost ceased, and on the following day administration of E.A.C.A. by mouth was resumed without significant recurrence of the haemorrhage. This particular case showed the danger of relying on absorption of E.A.C.A. from administration by mouth in the immediate postoperative period. Of the 12 patients treated this was the only one requiring replacement therapy to secure haemostasis.

The ages of the patients ranged from 5 to 58 years and the number of teeth extracted from 1 to 16. In one case of Christmas disease two horizontally impacted wisdom teeth were removed surgically.

Side-effects of E.A.C.A. were noted in three patients in the series—two experienced diarrhoea and the third both diarrhoea and "dizziness." But in no case was it necessary to discontinue therapy.

DISCUSSION

Previous experience in the dental treatment of haemophiliacs had convinced us that it was not possible to forecast how severe the bleeding would be or how much parenteral fluids would be required. In particular, no correlation seemed possible between these variables and the frequency of bleeding incidents, or the results of laboratory assessments. Even previous dental experience in a given patient was not invariably informative. We have not, therefore, attempted to grade the patients in the two series according to estimates of severity, either clinical or pathological.

Comparison of these 12 E.A.C.A.-treated cases with the immediately previous 12 cases treated by replacement therapy and local measures (Table II) shows that the average post-operative time in hospital was reduced from 18 to 7 days, while the average number of teeth extracted in the present series was six, as opposed to five in the previous series. The replacement therapy consisted of an average of 6 litres of fresh frozen plasma and $2\frac{2}{3}$ units of whole blood. In the present series only one patient received any replacement therapy, and this consisted of only 450 ml. of fresh frozen plasma and 2 units of blood. All the adult patients, except two who had never experienced dental extractions (one of whom required the replacement method), remarked on the comparative ease with which they were able to undergo a procedure which they had previously found to be an ordeal. This experience was shared by those responsible for the patients and is illustrated by the amount of attention required under each regimen by the patients appearing in both series (see Table II).

TABLE II.—*Dental Extractions on 24 Consecutive Cases of Haemophilia and Christmas Disease*

Patients Treated by Replacement Therapy					Patients Treated by E.A.C.A. Therapy				
Case No.	No. of Teeth Extracted	Days in Hospital After Operation	Units of Blood Transfused	Fresh Frozen Plasma Transfused (ml.)	Case No.	No. of Teeth Extracted	Days in Hospital After Operation	Units of Blood Transfused	Fresh Frozen Plasma Transfused (ml.)
1	1	8	—	650	13	2	7	—	—
2†	4	16	—	5,100	14	12	7	—	—
3*	8	19	—	9,000	15*	7	7	—	—
4	2	14	—	7,230	16	9	7	—	—
5	1	14	—	5,260	17	3	5	—	—
6	2	12	—	800	18	4	6	—	—
7	5	42	5	10,000	19†	16	10	—	—
8	9	16	1	7,400	20	10	12	2	450
9	1	17	—	7,000	21	1	4	—	—
10	16	27	8	6,600	22	1	7	—	—
11	5	12	12	1,600	23	2	5	—	—
12	6	19	8	10,000	24	4	7	—	—
Average	5	18	2·6	5,900	Average	6	7	0·16	37·5

* Patient appearing in both series. † Patient appearing in both series.

The results obtained suggest that the use of this inexpensive drug may well eliminate much of the burden previously experienced by the Blood Transfusion Service in attempting to provide adequate supplies of whole blood and fresh frozen plasma for these necessary planned procedures. The shorter period in hospital is a self-evident advantage. The results obtained in this small series are so encouraging that we feel justified in giving this treatment further trial.

SUMMARY

A technique described by Lucas *et al.* (1962) for obtaining haemostasis after dental extractions in haemophiliacs, without recourse to replacement therapy, was modified in a series of 12 cases by reducing the number of local measures recommended. It was found that adequate E.A.C.A. therapy combined with sutures produced more satisfactory haemostasis in both classical haemophilia and Christmas disease than did conventional replacement therapy combined with full local haemostatic measures.

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