THE MANAGEMENT OF FRACTURES IN HAEMOPHILIA
AND CHRISTMAS DISEASE


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Haemophilia is uncommon and therefore fractures in haemophilic patients are not often met. The case reports that follow of patients with fractures illustrate various aspects of the clinical problems that were seen at the Nuffield Orthopaedic Centre, Oxford, where haemophiliacs and patients with Christmas disease are treated for orthopaedic conditions in collaboration with the Blood Coagulation Research Unit of the Medical Research Council.

CASE REPORTS

Case 1—A man aged fifty years was a mildly affected haemophiliac with 9 per cent of AHG and he had not previously suffered haemarthroses despite heavy work as a naval stoker, which shows the protective effect of the low level of AHG in preventing spontaneous bleeding. He had, however, bled excessively on several occasions after injury and operations. While working as a slater he fell from a roof and sustained a fracture-dislocation of the left elbow, which was reduced elsewhere. On admission the elbow was held in 90 degrees of flexion and the forearm

in mid-pronation. There was considerable bruising and finger movements were restricted by pain, there was no sensory loss and the radial pulse was present. Radiographs showed simple fractures of the olecranon and of the coronoid process of the ulna and a comminuted fracture of the head of the radius (Figs. 1 and 2). The patient was given a litre of fresh frozen plasma on each of the first two days to establish haemostasis and to encourage some reduction of swelling of the elbow. On the third day the fragmented head of the radius was excised; the fractured olecranon process was reduced and fixed by a screw. The limb was immobilised in a plaster back splint. The operation involved considerable soft-tissue damage and to avoid post-operative bleeding it was considered justifiable to provide maximal AHG cover by employing a potent concentrate; porcine AHG was given immediately before the operation and then daily for nine days. Convalescence was uneventful. After eight weeks the plaster was removed and cover with fresh frozen plasma was given for the first two days of mobilisation.
Case 2. Figure 3—The fracture of the left ankle on admission. Figure 4—Three months later. Figure 5—The supracondylar fracture of the right femur at the time of admission. Figure 6—Three months later. Figure 7—The fracture of the left tibial plateau on admission. Figure 8—Three months later.
Case 2—A man aged forty-four, a severe haemophiliac with no circulating antihaemophilic globulin (AHG or Factor VIII), was involved in a road accident and sustained a supracondylar fracture of the right femur, and fractures of the left tibial plateau and the left ankle (Figs. 3 to 8), with impaction of a tooth and cuts and bruises. The ankle fracture was manipulated and all three fractures were immobilised in split plaster casts. In view of the multiplicity of his injuries he was given four large daily infusions of human AHG followed by three daily infusions of plasma. The steady clinical recovery and the absence of bleeding from the dental and other superficial injuries indicated that adequate haemostasis had been obtained. Three months later all the fractures were united.

Case 3—A man aged forty-two, a severe haemophiliac with no circulating AHG, had suffered many previous haemarthroses, particularly of the left knee, which showed a characteristic arthropathy and limitation of movement. He was admitted eight days after a stumbling fall in which he had sustained a comminuted fracture of the left tibial plateau, a fracture of the neck of the left fibula and a transverse fracture of the left patella (Figs. 9 to 11). On admission there was extensive bruising. Skin sensibility was lost distal to the mid-calf and there was no active movement of the foot. The peripheral pulses were present. Four days before admission he had been given one litre of fresh plasma. Clinical assessment indicated that bleeding had stopped, although previous blood loss must have been considerable because the haemoglobin level was of 57 per cent. He was given two days' treatment with a litre of fresh frozen plasma on each day and four pints of packed red cells. The fractures were in good position and were immobilised in a long posterior plaster splint. There was no further bleeding. Union of the fracture was not delayed and sensory and motor function ultimately returned to normal.

Case 4—A man aged forty-nine, a severe haemophiliac with no circulatory AHG, had had repeated haemarthroses affecting at one time or another most of the larger joints, and the knee joints in particular in which active flexion was restricted to 15 degrees in each. Two days before admission he had fallen, injuring the right hip. On examination there was a large diffuse haematoma distending the anterior aspect of the thigh. The hip was held in flexion, abduction and lateral rotation, with severe pain on movement. Radiographs showed

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**FIG. 9**
Case 3—The fractures of the left tibial plateau and left fibula. The patella was also fractured. Figure 9—Three weeks after injury. Figure 10—Twelve weeks after injury. Figure 11—One year after injury.
an intertrochanteric fracture of the right femur. The patient’s haemoglobin was 62 per cent and for this reason packed cells were transfused. Soft-tissue damage was assumed to have occurred at the time of fracture, so initially human AHG was given. The hip was supported in a padded plaster spica which was split. Daily infusions of plasma were given for a further four days. Twelve weeks later the fracture was consolidated and the patient was mobilised without complications.

Case 5—A man, aged eighteen, had very severe haemophilia and his blood lacked AHG completely. Other males in his family were similarly afflicted. He had suffered many previous haemarthroses, especially in the right knee, which could not be flexed above a right angle. Four days before admission he had fallen heavily on to his right side. He rose unassisted and drove a considerable distance home. He attended hospital because of increasing pain in the right hip. On examination the hip was observed to be flexed, laterally rotated and abducted, with passive flexion limited to about 15 degrees by pain and muscle spasm. There was no soft-tissue swelling. Radiographs showed an undisplaced linear fracture of the neck of the femur. Because there was no reason to suspect excessive bleeding into the tissues, no infusion treatment was given and a well padded plaster spica was applied. The subsequent progress was uneventful.

Case 6—A boy of eleven had been diagnosed as a haemophiliac at the age of eighteen months. He had had numerous haemarthroses and the left knee was severely affected. Nine days before admission he fell and sustained a spiral fracture of the right femur (Figs. 12 and 13). He had been transfused with a pint of fresh plasma and a pint of packed cells before admission. Despite this, on admission his haemoglobin level was only 53 per cent, so a further pint of packed cells and a single dose of human AHG were given. The anaemia proved refractory.
and two further blood transfusions were given but no further treatment with plasma or AHG was needed. The fracture was treated by balanced traction in a Thomas's splint and six weeks later it was uniting with some malalignment; he was subsequently sent home in a plaster spica on crutches, walking with a patten under the left shoe. When he was readmitted six weeks later the fracture was soundly united but mobilisation was twice complicated by a haemarthrosis of the right knee, aspirated on each occasion under cover of human AHG. After each of these episodes physiotherapy was restarted cautiously under cover of plasma, given on each of the first three days. Subsequent recovery was uneventful.

Case 7—A boy of fourteen had been diagnosed as a severe haemophiliac at the age of five months. His blood was completely deficient in AHG. The history of excessive bleeding included many episodes of haemarthrosis affecting various joints. In 1957 he had been admitted to the Centre for the correction of bilateral flexion deformities of the knees. While on traction he had sustained a spontaneous supracondylar fracture of the right femur. Correction of the deformity had been obtained by this time and, as the fracture was in good alignment, traction was continued. On the assumption that the fracture would heal well without undue bleeding and that the soft-tissue damage was relatively slight, it was thought sufficient only to give a concentrate of human AHG on the first day for haemostasis and fresh frozen plasma was given on the second day. Five weeks later there was radiological evidence of union. At ten weeks the fracture was sufficiently consolidated to permit gentle mobilisation in the swimming pool. The patient was able to walk in a caliper at thirteen weeks.

Case 8—A boy of nine had severe Christmas disease and his blood was completely deficient in Christmas factor (Factor IX). He had had many haemarthroses of all the commonly affected joints. Three months before admission he had a severe bleed into the left knee which caused a flexion contracture of 90 degrees. This was successfully treated elsewhere by traction.

The patient was being actively mobilised when he tripped and fell, fracturing the upper end of the left tibia and fibula (Figs. 14 and 15). He was transfused with a litre of fresh plasma to control bleeding and a pint of packed cells to restore the haemoglobin level. When transferred to the Centre four days later he had a flexion deformity of the knee of 90 degrees because of bleeding into the soft tissues. The fractures were relatively undisplaced. Infusions of a concentrate of Christmas factor were given on several occasions to prevent bleeding during surgical manipulations to extend the knee joint. Union of the fracture was not delayed and the patient was discharged with a residual flexion deformity of only 10 degrees.
PRINCIPLES OF ANTIHAEMOPHILIC TREATMENT

Transfusion therapy—The problem always presented by the injured haemophiliac is that of replacing the deficient factor which involves infusing AHG or Christmas factor. The materials used are fresh frozen plasma, concentrates of AHG prepared from human or animal plasma, and concentrates of Christmas factor prepared from human plasma. The duration of the activity of the infused factor is short and, because haemostasis is dependent on the maintenance of high blood concentrations, it may be necessary to give infusions at least once a day. Treatment is limited by the volume of fluid which can be given intravenously, by the shortness of supply of materials derived from human plasma, or by the risk of the development of inhibitors to AHG following the administration of animal concentrates.

In general, there are certain principles in treatment. Fresh human plasma has the easiest availability because it can be stored in the frozen state and 15 to 20 millilitres are given per kilogram of body weight. Within an hour it produces a rise in AHG from nil to about 20 per cent. Plasma is used to prevent bleeding from minor injuries, as a continuation treatment during the later stages of healing of more severe injuries, and to cover such procedures as wound dressing or the removal of sutures. When plasma is the only available treatment it can be given twice daily in order to obtain high AHG levels in the blood, but care must be taken to prevent fluid retention.

Concentrates of AHG, prepared by alcohol, ether or cold precipitation from fresh human plasma, are several times more potent, volume for volume, than fresh plasma, and are capable of producing high levels of AHG. The large number of blood donors required to produce this material may render its use in adults impracticable except for short courses. Its main application is in the treatment of children, in whom high levels of AHG may be economically obtained with little disturbance of the blood volume.

AHG is also prepared commercially from pig and ox plasma. This is approximately ten times more potent than human plasma. Suitably administered to adults a normal AHG level can be achieved once or twice a day. However, the patient tends to become refractory to its use, usually after a week to ten days of treatment. Administration of concentrate from the alternate animal source may then produce a further period of response until sensitisation again develops. Severe reactions are now uncommon with these materials though occasionally such reactions may necessitate a change of treatment. The materials are potentially antigenic because they contain protein of animal origin. Repeated courses of the same animal concentrate should be administered with the greatest caution.

The main indications for the use of animal AHG is in the management of very severe injuries and to cover surgery in the more severely affected adult haemophiliacs who need long and continuous high level protection, which cannot be achieved with human extracts.

The presence of circulating inhibitor to AHG contra-indicates treatment with any material containing AHG as this may increase the titre of the inhibitor. If blood is needed in such a case it is administered as saline-washed packed cells.

The materials used in the treatment of Christmas disease are plasma and Factor IX concentrate. Plasma, which need not be freshly collected, may be used for the same indications as in haemophilia but it is less effective in the treatment of Christmas disease. The Factor IX concentrate of Christmas factor is prepared in the M.R.C. Research Unit laboratory. It is a potent material which is in short supply and is not presently available for use outside the controlled supervision of the Unit.

General management—Three important principles are involved in the haemostatic management of any injury in haemophilia: production of initial haemostasis, maintenance of haemostasis during healing, and immobilisation of the injury.

First, appropriate materials should be infused in a dose sufficient to maintain haemostasis until the next transfusion is given. It is important when planning treatment to consider the lowest level to which the patient’s clotting factor will fall, because a recurrence of bleeding
will be largely determined by this level. It is known from past observation that some damaged tissues need higher clotting factor concentrations than others and that, in general, the more extensive the injury the higher the concentration required.

Secondly, daily infusions should be continued over the shortest time usually necessary for the healing of the particular injury, because there is a considerable risk of recurrent bleeding during this period.

Finally it is necessary to emphasise the importance of absolute immobilisation and protection of the injured part. This applies equally to fractures, haemarthroses and soft-tissue injuries because movement often causes a recurrence of bleeding. The anaemia associated with fractures in haemophiliacs may be considerable, and it may be necessary to administer transfusions of whole blood or packed cells. In undisplaced fractures, however, the amount of bleeding is usually small.

Infection did not complicate any of the cases of this series. Infection would, however, be expected to delay healing, and infusion therapy and immobilisation in such cases would need to be extended. Maneouvres such as changing a plaster should be covered by infusion of the appropriate factor. When wounds are sutured, the sutures are left for a longer period than is usual, and if they are removed carefully bleeding is usually insignificant. Occasionally it is considered justifiable to give the appropriate factor before the removal of sutures. To avoid this problem it is good practice to approximate the edges of the incision with interrupted subcutaneous catgut and to close the skin edges with "Steri-strip."

Soft-tissue bleeding in the limb of a haemophiliac may produce compression of nerves and vessels with consequent neurapraxia and ischaemia. Peripheral gangrene and Volkman's ischaemia have been observed complicating untreated soft-tissue injuries. Such effects have been described by Fraenkel (1957) and by others. Because of these hazards no fracture or other lesion in a haemophilic limb should be immobilised in a complete plaster unless haemostasis is absolute and the swelling is diminishing. Consequently, all plasters should be adequately padded and completely split. During the period of immobilisation it is essential to exercise the unaffected limbs, because disuse may render the joints more susceptible to subsequent haemarthroses.

Fracture healing in haemophilia is not delayed, even in patients who have not received treatment with coagulation factors during the whole period of fracture repair. However, the radiographs show little periosteal callus formation. In one of our cases there was a limited periosteal reaction but widespread calcification of the surrounding periosteal haematoma (Fig. 13).

**DISCUSSION**

The literature on fractures in haemophiliacs is sparse. Several authors have overemphasised the association of fractures with haemophilic cysts or pseudotumours. Ghormley and Clegg (1948) and Egeberg, Borchgrevink and Hjort (1960) described such cases. Harrison (1964) suggested that following non-union pseudotumour formation is inevitable. Jordan (1958) in a comprehensive review of 110 patients reported fractures in twelve, and he said that fractures in haemophilia unite well and with solid bonyunion, usually in less than the average time: he postulated that "the speed of callus formation in haemophilia is probably due to the same influence that stimulates growth of affected epiphyses." However, Boldero and Kemp (1966) suggested that the overgrowth that occurs in the affected epiphyses is a local response to hyperaemia, a factor which is common to fractures in both the normal and the haemophilic patient. Five of Jordan's six cases, for which the radiographs were published, showed relatively slight callus formation, the exception being virtually identical with our Case 6.

Although the reported cases are few in numbers we believe that haemophiliacs are more susceptible to fracture because of the limitation of joint movement, poor muscle function and associated osteoporosis. Consequently the fractures tend to be stress lesions near joints
showing evidence of haemophilic arthropathy. In only two of our cases were fractures caused by severe trauma and these were in apparently normal bone.

As Jordan pointed out, the most surprising feature of fractures in haemophilic patients is that union is not delayed, despite the osteoporosis and the absence of plasma clotting factors. Basing his hypothesis on the work of Rizza (1961), who showed that the plasma level of AHG is raised in both normal persons and in haemophiliacs as a result of intensive exercise, Trueta (1966) postulated that AHG may possibly be fixed in the medullary tissue and that clotting may therefore take place locally at the fracture site even though bleeding continues in the neighbouring soft tissues. An associated observation is the relative lack of periosteal callus. This suggests that fracture healing in these cases is largely endosteal. This observation supports the contention of Urist and McLean (1941) that it is the haematoma, rather than the periosteal response to trauma, which initiates fracture healing.

SUMMARY

1. The management of fractures in seven haemophiliacs and one patient with Christmas disease is described.
2. The problems of management are essentially those associated with haemorrhage into the soft tissues.
3. There is no delay in the healing of fractures, which usually occurs with a relative lack of periosteal callus.
4. The principles of transfusion therapy are discussed.

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REFERENCES


