HAEMOPHILIA 2:

SOME MANIFESTATIONS OF HAEMOPHILIA

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Present day concepts on haemophilia have altered since Bullock and Fildes (1911) established the disease as clinical entity Since then Christmas disease (Biggs et al, 1952) was separated from classical haemophilia, and other distinct conditions such as P.T.A. (Plasma thromboplastin antecedent) by Rosenthal et al (1953). Originally haemophilia was restricted to excessive bleeding disorders manifested from infancy, restricted to the male sex and transmitted by apparently normal females. Now, evidence of similar conditions arising in adult patients is forthcoming and apparently, 25-30% of all cases appear to have no family history of the condition. (Biggs and Macfarlane, 1957). The nomenclature of congenital deficiencies of blood coagulation factors and mode of inheritance is shown in Table 1. This paper is restricted to a consideration of some manifestations of classical haemophilia, (Haemophilia A, Biggs and Macfarlane, 1957) and illustrated by means of three family histories, two Maltese and one an Italian family resident in Malta.

EARLY LIFE AND CHILDHOOD

The inherited type of haemophilia is almost invariably manifested in early childhood and then persists for life. Umbilical cord bleeding appears to be rare but severe haemorrhage following circumcision is more common. During the first year of life the child is to some extent protected in his environment of bed or cot. Some episode is frequent in this period even if only a tendency to bruise easily. Craw-

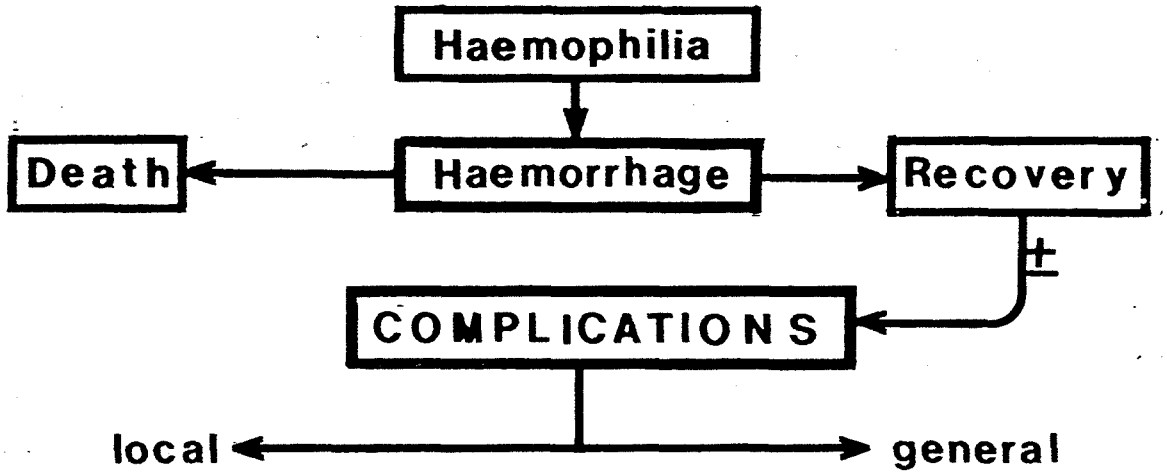
ling or walking multiplies the chances of trauma against hard or sharp objects or by falls. Commonly this type of injury affects the face resulting in epistaxis, or bleeding from a lacerated tongue, frenulum or gum. This bleeding may be profuse and necessitate blood transfusion, or even be the cause of death. In fact, no source of haemorrhage, no matter how trivial, may be regarded of little import in an haemophiliac.

The eruption of the deciduous teeth and their subsequent exfoliation present a further hazard to the growing child. Until recently the chances of trauma or haemorrhage of dental origin were responsible for the death of a large number of haemophiliacs during the first few years of life. As will be seen, today the picture has changed considerably.

Bleeding may be spontaneous or secondary to trauma or infection. It may be external, affecting skin, nose, mouth, gastro-intestinal or renal tracts, or it may be internal into a body cavity or tissues. The amount of blood lost into the tissues may be very large. The consequences of this haemorrhage are shown in Fig. 1 Severe bleeding, if uncontrolled will result in death. If mild, or if controlled energetically the patient may survive, usually to face recurrent bouts of haemorrhage from time to time. It is the complications of these repeated episodes that the haemophiliac has to face today. This is the price of survival.

TABLE I

FACTOR		CONGENITAL DEFICIENCY		
Inter. Nomen.	**Some Synonyms**	**Name**	**Synonyms**	**Inheritance**
I	Fibrinogen	Afibrinogenaemia		Autosomal Recessive
II	Prothrombin	Prothrombin deficiency	Hypoprothrombinaemia	"
V	Proaccelerin, labile factor	Factor-V deficiency	Parahaemophilia	"
VII	Proconvertin, stable factor	Factor-VII Deficiency	Hypoproconvertinaemia	"
VIII	Antihaemophilic factor (AHF) Antihaemophilic factor A. Antihaemophilic globulin (AHG)	Haemophilia	Haemophilia A	Sex-Linked Recessive
IX	Christmas factor, plasma thromboplastin component (PTC), antihaemophilic factor B	Christmas disease	PTC deficiency, Haemophilia B, deuterohaemophilia	"
X	Stuart-Prower factor.	Factor-X deficiency	Stuart defect, Prower defect.	Autosomal Recessive
XI	Plasma thromboplastin antecedent (PTA), antihaemophilic factor C	Factor-XI deficiency	PTA deficiency haemophilia C, Rosenthal's syndrone	"
XII	Hageman factor	Hageman trait		Autosomal Recessive
XIII	Fibrin stabilizing factor (FSF)	Factor-XIII deficiency	FSF deficiency	"



Haemarthrosis → impaired function / crippling deformities

Obstruction → necrosis, atrophy - limbs / abd organs

Haem. → mouth / neck → asphyxia

Haem → brain → CNS disturbances

Social problems → male → private life / work

Social problems → female → children – ?

FIG 1.

HAEMARTHROSIS

Of the many complications, haemarthrosis is one of the most common. Haemorrhage into the joints is usually accompanied by great pain and swelling. The commonest joints affected are the ankles, the knees and elbows. The shoulders, wrists and hips are also affected but to a lesser extent. (Smith, 1966). In acute haemarthrosis there is severe pain, swelling, heat, tenderness and limitation of movement. The early haemorrhages are resorbed, however recurrence usually causes extensive damage. There is thickening of synovial membranes, destruction of articular surfaces and bone. Repeated attempts at repair lead to fibrous tissue formation. Contractures then cause permanent crippling and/or limitation of function. This picture is so common that it has been used as a grading method for the severity of the disorder. Frequent or severe haemarthrosis indicate a severe haemophilia with usually completely absent Factor VIII. Less frequent or less severe joint involvement indicate the moderate case while the patient with only rare haemarthrosis is a mild one.

REORGANISATION OF HAEMATOMAS

As in the case of joints, the reorganization of haematomas in other areas can result in further abnormalities. Such a process occurring in or around a nerve bundle can lead to paralysis of the area supplied. Such a nerve may also be outside the site of haemorrhage but still be involved in subsequent contractures. In the brain spontaneous haemorrhages damage directly and their effect is dependent on the site of injury.

PRESSURE EFFECTS

Haemorrhage into the tissues or body spaces can result in manifestations due to pressure effects. Thus the arterial supply to a limb or organ may be impeded by such pressure effects. Necrosis or atrophy of the limb or organ could follow. In the region of the neck, haemorrhage into the lax tissue spaces can embarrass the respiration sufficiently to cause asphyxia.

In some cases the haemorrhage may present problems of differential diagnosis. An example is haemorrhage into the retroperitoneal space, or mesentery. The symptoms may simulate an acute abdominal emergency such as an appendicitis or perforating ulcer. A mild leucocytosis may add to the diagnostic difficulties.

Haematuria is common and usually persistent in spite of treatment. It may be spontaneous or follow trauma, eg., a fall or motor vehicle accident.

CASE HISTORY I

The patients belonging to the Maltese family shown in Fig. 2 are proved haemophiliacs with a Factor VIII level of 0%. The nine patients to be described have all been traced to one common source, their grandfather, A.M., who was a known bleeder and who died at the age of 58 years from a severe epistaxis. The family is a good example of the mode of inheritance of a sex-linked recessive gene and shows how it can skip a generation because all the male children of a generation are normal, while all the female children are carriers of the gene but are clinically normal. The family also illustrates the better prognosis for haemophilia today. All ten children in generation 2 died soon after birth, while of generation 4, all except two are alive and the deaths were a consequence of a severe fall in one case and a car accident in the other.

The family illustrates well the classic ways of presentation of haemophilia. The first three children of these families only came to the attention of a medical practitioner after the age of one year when they started walking and so had the chance of falling on their faces. All three suffered laceration of their upper labial frenulum which bled profusely. Later children were observed more closely and were noticed to bruise easily in the cot or pram.

The following patients are 4th generation members of the family shown in Fig. 2:

Patient no. 1.

First child. Died at age of 6 years following an intra-cranial haemorrhage after a car accident. He presented at the age of $1\frac{1}{2}$ years because of a cut upper labial frenulum. Required admission.

Patient no. 2.

14 years old, alive.

First episode prior to 12 months old — joint swelling from trauma in pram. Also cut upper labial frenulum with prolonged bleeding. Repeated admission to St. Luke's Hospital for bleeding episodes.

Patient no. 3.

12 years, alive.

Parents became more attentive and noticed that the child bruised very easily at about the age of 6 months when he became more active. At 2 years episodes of marked epistaxis.

Patient no. 4.

9 years old, alive.

At 7 months noticed tendency to bruise easily when exerting himself in bed. At the age of $1\frac{1}{2}$ years fell from table and has since been suffering from paraplegia.

Patient no. 5.

14 years old, alive.

First episode at 10 months when he cut his upper labial frenulum following a fall.

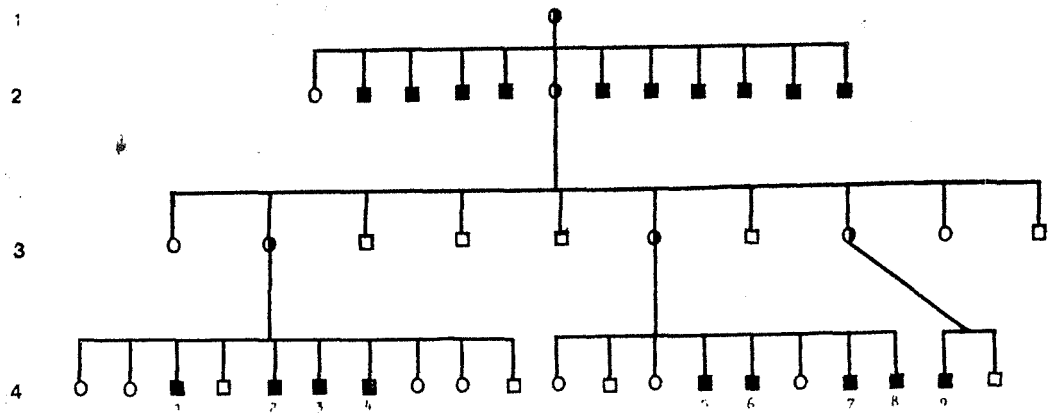


FIG. 2 Maltese family

Patient no. 6.
Died at 10 years after a severe fall.
St. Luke's Hospital. Internal haemorrhage, ruptured spleen, haematuria.

Patient no. 7.
7 years old, alive.
First episode = joint swellings following minor trauma.

Patient no. 8.
$4\frac{1}{2}$ years old, alive.
First episode = joint swellings following minor trauma.

Patient no. 9.
6 years old, alive.
First episode = joint swelling following falls in cot.

DENTISTRY IN HAEMOPHILIA

Apart from the above manifestations of this disease, iatrogenic causes add to the list. Major surgical procedures have no place in this paper, however minor oral surgery is almost inevitable in the life of the ordinary person and unfortunately the haemophiliac is no exception. The patient or his parents have a natural dread of the dentist. Neglect of the mouth makes future extractions inevitable with resulting grave problems in oral surgery. The importance of dentistry in haemophilia commences in early life with eruption of the deciduous dentition, as the following case history testifies:

CASE HISTORY II

Patient: Male, 23 years

Haemophiliac. First episode of bleeding occurred at the age of seven years. The boy noticed a loose temporary tooth during school. He played with it with his tongue and it was loosened completely. Bleeding followed at a slow but steady oozing. In order not to attract attention he swallowed the blood until time came to go home. He fainted three times on the way home and only reached there with assistance. At home the situation called for blood transfusion. Today, after a lifetime of hospital admissions for haemarthrosis and other complications the patient has a neglected mouth that necessitates extensive dental extractions.

CASE HISTORY III

The permanent dentition has an even worse record in haemophilia. The Italian family described in Figure 3 illustrates this well. In generation 3, the five members who manifested haemophilia have all died, two of them as a result of dental intervention.

Member no. 1. Died at 4 years; fell, internal haemorrhage.

Member no. 2. Died at 6 months; melaena and haematemesis.

Member no. 3. Died at 14 years; *tooth extraction*

Member no. 4. Died at 1 month; Haematemesis.

Member no. 5. Died at 28 years; *tooth extraction.*

Since going to print, one of the 4th generation males, aged 13 months until now presumed free of the condition and shown as such in the Figure 3, has shown severe bleeding tendencies. Following a fall, he cut a frenulum. This necessitated admission to hospital and blood transfusion.

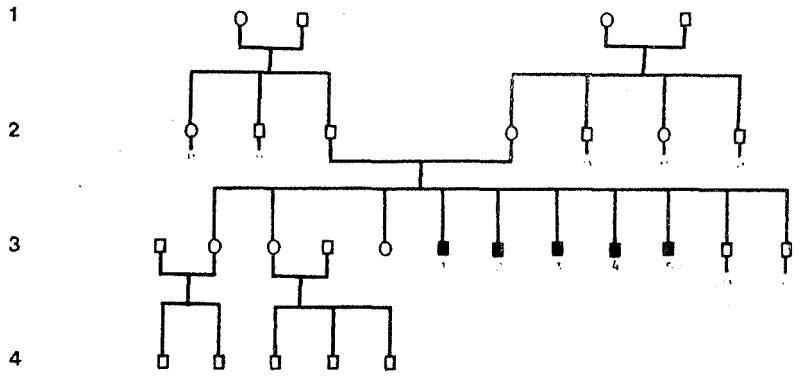


Fig. 3. ITALIAN FAMILY n=apparently normal

Local regional anaesthesia may also be accompanied by disastrous consequences. Block injection of the inferior dental nerve has been followed by death on occasion due to intractable haemorrhage into the soft tissues around the pharynx and in the neck. (Archer and Zubrow, 1964; Parnell, 1964). One of the authors has experience of blood transfusion being necessary following a prick in the ear of a haemophiliac for a blood count.

SOCIAL FACTORS

Secondary manifestations of haemophilia may take the form of social problems. The consequences of a life with possible disaster round the corner and frequent in-patient episodes cannot be without some mental trauma. The "carrier" girl who is otherwise normal also may face grave problems made worse since she cannot know beforehand whether her future children will be haemophiliacs or not. In these Islands these personal problems are augmented by the social stigma which the disease carries. Frequent hospitalization makes employment difficult and it is easy to develop feelings of inferiority and depression under these circumstances. A case such as this occurred recently at St. Luke's Hospital. The attempted suicide was treated successfully but the problem remains.

An attempt has been made to discuss some aspects of the manifestations of haemophilia, direct, indirect, social or psychological. Today rapid advances in therapy may soon eliminate the drip and blood transfusion. Concentrated preparations of Factor VIII may lead to outpatient treatment for all but a few cases of haemorrhage. This would mean less absenteeism from work and a greater feeling of self reliance. However much remains to be done in the way of education of the people to accept these patients as useful members of society. Dental education is also required to emphasise the need for continuous prophylactic and preventive measures in order to avoid the dangers of oral surgical procedures.

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