THE INCIDENCE AND HEREDITY OF HAEMOPHILIA IN INDIA

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INTRODUCTION

There has been, so far as the present writer's knowledge goes, only one study of haemophilia in India (Ghosh, 1942) in which one Bengali family from Calcutta was described. Further studies on this family have been presented here. The other study relating to a Muslim family of Indian stock was made in 1859 by Heymann (*cit.* Gates, 1946) from Palembang, Sumatra.

Apart from the clinical symptoms peculiar to haemophilia, its sex-linked recessive behaviour has been accepted to be one of its diagnostic features. This hereditary behaviour has been emphasized so much that in many cases, in spite of the typical clinical findings of the disease, haemophilia has been ruled out because the typical sex-linked heredity is not seen in the family. The latest case on record is from Australia (Fantl and Margolis, 1955). It is a genetic puzzle since haemophilia in both the mother and the son has been confirmed through the latest clinical examination of the blood. Gates (1946) in a detailed genetic study of this disease has shown that haemophilia, like many other diseases and abnormalities, may not always follow the sex-linked recessive type of inheritance and that y-linked, simple dominant or recessive forms of inheritance may also occur. According to Gates the inheritance of haemophilia may also vary within the same sib due to the cross-over of the gene from x-chromosome to the y-chromosome or vice versa. This fact should not be lost sight of in giving weight to the hereditary behaviour as a diagnostic feature of haemophilia.

Since 1947, a number of cases with haemorrhagic diathesis has been called parahaemophilia (1952). It differs from the classical haemophilia in having a prolonged prothrombin time, which is normal in the case of haemophilia. Like haemophilia it does not affect the joints. It is not sex-linked in inheritance since both the sexes are known to be affected and does not always show a family history. It is associated with the deficiency of the accelerator globulin and should be regarded as a separate syndrome.

Recent discovery of 'Christmas disease' or PTC deficiency (Biggs *et al.*, 1952) shows all the genetic and clinical features of haemophilia but differs from the latter in the presence of anti-haemophiliac globulin, and in the deficiency of some other factor, essential for the formation of thromboplastin. This has led to the assumption of an allelomorphic variant of the gene responsible for haemophilia. Even a series of allelic genes, which determine the plasma level of the anti-haemophiliac factor, has been postulated in the case of mild haemophiliacs. Improved laboratory methods of diagnosis have been established by Biggs and Macfarlane (1953) and Fantl (1954) and these should be followed in this country as well. Fantl proposes that classical haemophilia be called alpha-prothromboplastin deficiency while Christmas disease or PTC deficiency that of beta-prothromboplastin deficiency.

Haemophilia in homozygous females is now an established fact (Merskey, 1951) although Gates (1946) made a case of it through Treves' pedigree of 1886 and its later studies by Bulloch and Fildes in 1911 and Handley and Nussbrecher (1935)

and recently by Merskey (1951). Lloyd (1925) showed that incomplete dominance of the normal condition may also show female bleeders.

It is peculiar, however, that Andreassen (1943), who carried out a complete survey of haemophilia in Denmark and published 63 pedigrees of this disease, has neither found any deviation from the classical form of the disease nor in its sex-linked inheritance. He has not found any genuine haemophilia in the females, though he has noted a tendency to haemorrhage in several heterozygotes, whose blood showed a slight protraction of the coagulation time. This, however, is not confirmed by Merskey and Macfarlane (1951).

Method

In order to find out the incidence of haemophilia in India, a questionnaire was first of all sent to 40 hospitals throughout the country. After the replies were obtained, attempts were made to enquire into the genealogy of each case. For this purpose a tour to Bombay, Nagpur and Ahmedabad, was undertaken and family histories from the above three places were collected. For other cases, enquiries were made through correspondence. The Bengal pedigree was collected after personal interviews from various sources.

The Data

Out of 40 questionnaires sent to various hospitals only 21 replies were received. The number of haemophiliacs reported therefrom is given in Table 1.

TABLE 1

Number of Haemophiliacs reported from Hospitals.

Serial No.	Hospital	City	Period	No.
1	Sarojini Naidu	Agra	1951–54	0
2	Civil	Ahmedabad	1953–54	1
3	Victoria Jubilee	Amritsar	1951–54	5
4	S. S. General	Baroda	1954	0
5	S. G. S. Medical College	Bombay	1945–54	13
6	Dental College	Calcutta	1954	0
7	Medical College	,,	1952–54	0
8	N. R. Sircar Medical College	,,	1954	0
9	S. C. B. Medical College	Cuttack	1954	0
10	Assam Medical College	Dibrugarh	1953–54	1
11	G. R. Medical College	Gwalior	1949–54	0
12	M. G. M. Medical College	Indore	1950–54	0
13	S. M. S. Medical College	Jaipur	1954	0
14	G. M. & Associated	Lucknow	1951–53	0
15	Medical College	Madras	1950–54	3
16	Stanley Medical College	,,	1952–54	0
17	University Medical College	Mysore	1934–54	0
18	Medical College	Nagpur	1954	1
19	Irwin	New Delhi	1954	1
20	Christian Medical College	Vellore	Past several years.	2
21	Andhra Medical College	Vishakapatnam	1944–54	0
				27

It will be seen from Table 1 that out of 21 hospitals, haemophilia has been reported from Ahmedabad, Amritsar, Bombay, Dibrugarh, Madras, Nagpur, New

Delhi and Vellore. The rest has not treated any case of haemophilia. The longest record of absence of any case is from Mysore during the period 1934–54, followed by that of Vishakapatnam during 1944–54. Gwalior and Indore had no cases during the past 5 and 4 years respectively.

The highest incidence appears to be from Bombay during the last 9 years (1945–54). It is likely that there are more cases since only one, out of the seven Bombay hospitals approached, has replied to our query. The next incidence with 5 cases is from Amritsar during the years 1951–54. Amritsar appears to have a higher incidence as the pedigree data will reveal afterwards. Madras Medical College hospital has reported 3 cases during 1950–54 while the Stanley Medical College hospital, Madras, has not treated any case of haemophilia during 1952–54. The Christian Medical College hospital, Vellore, has treated two cases during the past several years but none of them could be traced according to the addresses given by the hospital. Each of the other four hospitals, namely Civil hospital, Ahmedabad, Assam Medical College hospital, Dibrugarh, Medical College hospital, Nagpur, and the Irwin hospital, New Delhi, has treated one case during the year 1953-54. Their previous records could not be obtained.

Due to the highest incidence of haemophilia from Bombay, detailed enquiries of the 13 cases reported by the K. E. M. hospital, Bombay, were undertaken during January 1955.

(a) Haemophilia cases from Bombay

Case No. 1. M. R., male, aged 19 years, was admitted on 12th December, 1945, with swollen knee joints and bleeding gums. Past history revealed that the patient bleeds for a long time whenever he is hurt. Family history revealed no such condition in any member of the family. The patient has 12 normal brothers. Clinical examination of the patient's blood showed: bleeding time—2½ min.; coagulation time—30 min.; platelets—217,600/ccm.; blood group—O.

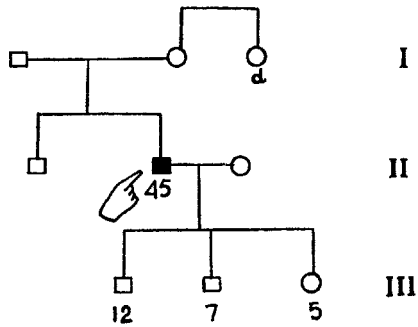
Personal enquiries revealed that the above patient is a resident of the village of Libola, Panchmahals. He obtained admission through a cook of the hospital, who informed the writer that the patient was seen alive about 6 months ago. The patient was married but the cook could not inform anything of his issues; neither could he say anything regarding the disease in the heredity of the patient. The patient is a farmer by occupation.

Case No. 2. K. M. M., male, aged 30 years, was admitted on 5th February, 1948, with bleeding gums and previous history of bleeding from trivial cuts from childhood. The past history also revealed that at the age of 6 he was operated on the forehead when the bleeding was controlled with great difficulty. Every 2-3 months he bleeds and about 6 years ago he had a bleeding which lasted 21 days. The clinical details of the blood are: bleeding time—1 min.; coagulation time—22 min.; platelets—94,000/ccm.

On interview the patient (Ped. 1, 11_2) was found to be quite healthy. He had a defective leg, probably a case of dislocation of the thigh, which the patient said has nothing to do with haemophilia. He was then having homoeopathic medicines, which were doing him good. He does not remember to have known anybody suffering from this disease among his relatives, specially on the mother's side. He is a businessman by occupation and is married, with three minor children. The pedigree is given below.

Case No. 3. G. E., male, aged 17 years, was admitted on 10th June, 1950, with both the knee joints swollen and the kidney affected. He had this recurrent swelling of the knee joints since the last 10 years apart from bleeding from trivial injuries. About a year ago he had haematuria which lasted for about 15 days. The clinical details of the blood are: bleeding time—2 min.; coagulation time—19 min.; platelet count—195,200/ccm.; prothrombin time—20 sec.

PEDIGREE 1*



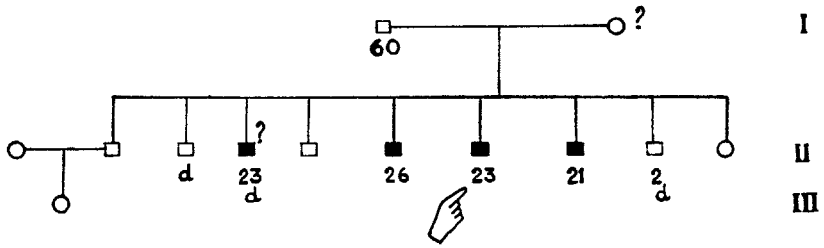
This patient could not be traced at Bombay. The hospital records also do not show any details of the family history.

Case No. 4. N. N., male, aged 7 years, was admitted at the hospital on 18th January, 1951, with recurrent attack of bleeding from nose since 1 year of age. The clinical details of the blood are: bleeding time—4½ min.; coagulation time—3 min.; platelets—198,240/ccm.

This patient could not be traced at Bombay. The hospital records, however, mention two brothers of the patient having died of similar complaints at the ages of 8 and 10 respectively.

Cases Nos. 5 and 7. These two cases, though separately shown by the hospital, have been combined together because the author's investigations showed that they are related as brothers (Ped. 2, II 6 and 8). C. H. (Ped. 2, II 8), male, aged 17 years, was admitted on 17th May, 1951, with the symptom of bleeding from rectum. The clinical picture of the blood was: bleeding time—1 min. 50 sec.; coagulation time—13½ min.; platelets—281,600/ccm.; prothrombin time—45 sec.; blood group—B.

PEDIGREE 2



* *Key to the Symbols used.*

Normal male	□
,, female	○
Haemophiliac	■ ●
Carrier	⊙
Months	*m*
Dead	*d*
Propositus	☞
Twin	⅄
Figures indicate age	
No ch.	No children

M. H. S. (Ped. 2, II 6), male, aged 19 years, was admitted on 22nd August, 1951, with the history of repeated swelling of both the knees. No external haemorrhages were noticed. Nothing is known of the clinical details of the blood except that he belonged to blood group B and that the patient was discharged on 24th August, 1951, after a blood transfusion.

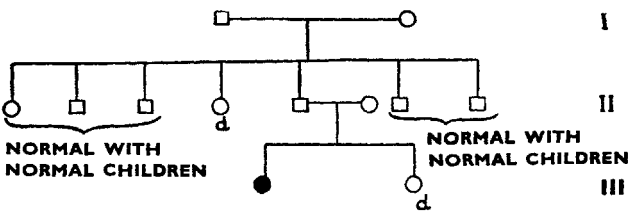
Personal enquiries into the family revealed that a brother (II 4) also died in 1948 from the same disease at about the age of 23, while there is another haemophiliac brother (II 7) who is still suffering. All the brothers have affected knee and elbow joints and the former are said to be more troublesome than the latter. External haemorrhages are not apparent and all the three brothers are now grown up and conscious to avoid injuries. The mother (I 2) is affected with very frequent petichéal haemorrhages but none of her relatives show any symptoms of the disease. The family is a refugee one from Karachi and the father of the family, an old man of about 60 years, informed the writer that this disease is the only case of its kind among the Sindhi Hindus. His son (II 8) was first treated in a Karachi hospital and because of the rare nature of the disease he was demonstrated before a medical conference comprising the local medical men. He was extremely emphatic on the point that his was a small community and he has never heard of this disease in any of its members.

Case No. 6. S. T., male, aged 5 years, was admitted on 13th June, 1951, due to bleeding after an operation for phymosis. His blood picture was: bleeding time—2 min. 10 sec.; coagulation time—7 min. 40 sec.; blood group—O.

On interview the boy was found to be quite normal. The mother and the father's sister of the boy informed the writer that neither the boy nor any member of their families has ever suffered from any kind of haemorrhage. The boy is the eldest issue of the family and is followed by two brothers, all in normal health.

Case No. 8. S. K. (Ped. 3, III 1), female, aged 1½ years, was admitted on 6th November, 1955, with bleeding gums. She had a previous history of bleeding from an incisor abscess and from trivial injuries, which gave no response to coagulants. Her blood picture was: bleeding time—4 min. 53 sec.; coagulation time—3 min. 5 sec.; platelets—268,000/ccm.; blood group—A.

PEDIGREE 3



On interview the child was seen to be quite healthy. Her father's eldest sister (II 1) informed the present writer that she last bled from the nose and gums about 6 months ago and her bleeding tendency was noticeable from a very early age. Each time she bleeds profusely; the joints are not affected. The severity of bleeding has caused the child to be treated in three different hospitals, one after the other, just with the idea of improved treatment. There is no affected individual in the family and the father's eldest sister (II 1), an old woman of about 65 years, was emphatic about it.

Case No. 9. M. S., male, aged 5 years, was admitted on 10th June, 1952, with the symptom of spontaneous bluish indurated swelling on any part of the body. He showed this symptom since 1 year of age. His blood showed: bleeding time —1 min. 25 sec.; coagulation time—not clotted at the end of one hour; platelets—206,720/ccm.

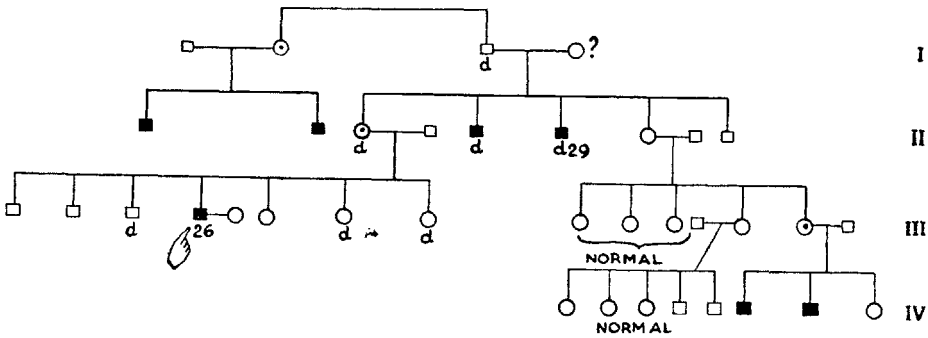
On interview at the address given by the hospital, it was found that the family had gone out of Bombay about 6 months ago, when the child was living. A friend

of the family informed that the boy was treated in another hospital after his discharge from the K. E. M. hospital.

Case No. 10. H. G., male, aged 24 years, European (?) (Ped. 4, III 4), was admitted on the 31st October, 1952, with swollen knee joints. He had it about 10 days ago and gave a history of bleeding from trivial injuries since birth and had haemophysis about 1 year ago. His blood showed: bleeding time—2 min. 7 sec.; coagulation time—6 min. 20 sec.; platelets—232,200/ccm.; blood group—A.

This patient could not be contacted although his church became interested in him. The hospital records, however, contained a genealogy, lacking in many details, which is given below:

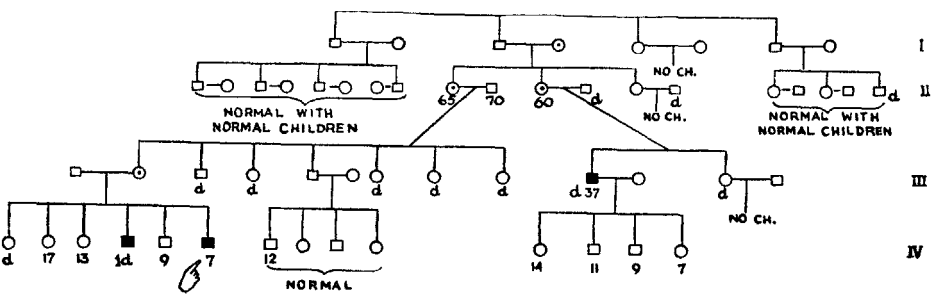
PEDIGREE 4



It will be seen from the pedigree that haemophilia is present in two brothers of the mother and they died of this disease probably. II 5 used to bleed very often from cuts and bruises and died during lifting a weight, while II 6 died of bleeding from an abscess, operated upon the neck at the age of 29. The father (I 3) is known to be normal but has a carrier sister, while the behaviour of the disease in the children of I 3 indicates that the mother was also a carrier. There appears to have been some amount of inbreeding in the family. No first hand information could be gathered on this family and nothing definite can therefore be said.

Case No. 11. K. Y. J. (Ped. 5, IV 6), male, aged 4 years, was admitted on the 15th December, 1952, with affected skin. His father gave histories of echymoses since birth and one of his elder brothers (IV 4) died of prolonged haemorrhage after a trivial injury on the foot at 1 year of age. His blood showed : bleeding time—1 min. 45 sec.; coagulation time—27 min.; prothrombin time—30 sec.; platelets—345,600/ccm.

PEDIGREE 5

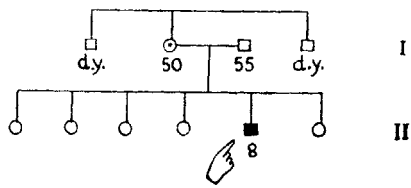


On interview the boy (IV 6) was found to be quite active and healthy. He bled from his gums three days ago and echymosis appears quite frequently. The

maternal uncle of the boy (III 3) died at the age of 8 from an accidental fall while the other uncle (III 5) is normal and is employed out of Bombay in a transport service. All the maternal aunts died young and unmarried. It will be seen from the pedigree that another maternal uncle (III 10) of the boy was also a haemophiliac and the hospital papers relating to the boy also contain some references of III 10. This patient was also treated at the K. E. M. hospital but his papers could not be traced. The present writer was informed by a distant relative, an old employee of the hospital, of the above patient (III 10) that the latter was admitted into the hospital by him while he was about 12 years old. He was constantly suffering from echymosis and haemorrhages and died in 1954 at about the age of 37 leaving 2 sons and 2 daughters. Unfortunately, both II 9 and II 11 are living in two different places outside Bombay city and could not be contacted. Their third sister (II 13) is a widow without any children. The probability of I 4 being a carrier is however great. The family is a native of the state of Bombay.

Case No. 12. P. D. (Ped. 6, II 5), male, aged 5½ years, was admitted on 17th March, 1953, with affected knee joints. He had this swelling several times during the past 1 year and before coming to the hospital he was bleeding from the gums for about 5 days. Previously, he was treated in another hospital in the city. His blood showed: bleeding time—1 min. 55 sec.; coagulation time—more than 1 hour; platelets—246,400/ccm.; prothrombin time—noted as 'quick'; blood group—A.

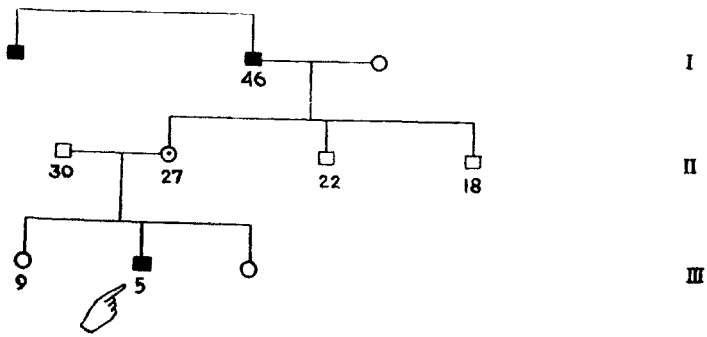
PEDIGREE 6



On interview the boy was seen suffering from swollen knees and was bleeding from the gums. The mother of the boy could not say the cause of death of her two brothers. The family is a native of the state of Bombay.

Case No. 13. S. G. (Ped. 7, III 2), male, aged 4 years, was admitted on the 23rd April, 1954, with bleeding gums and teeth. He had repeated attacks of bleeding since the last 1 year. His blood showed: bleeding time—3 min.; coagulation time—6 min.; platelets—350,000/ccm., blood group—A.

PEDIGREE 7



On interview the boy was found to be quite healthy. The father of the boy also said that he has been keeping well for some time past. The pedigree shows both

the mother's father and his brother as haemophiliacs. The union of a haemophiliac male and a normal woman results in normal sons and carrier daughters. In the present case this is seen very well. The only daughter of the union has been a carrier, the mother of the child in this case. The family is a native of Ramnad, S. India.

(*b*) *Cases from Ahmedabad*

Case No. 14. A. C., male, aged 24 years, was admitted at the Civil hospital, Ahmedabad, on 21st January, 1953, with pain and an intra-abdominal lump in the right iliac fossa during the last 4 days. His past history revealed an injury at the age of 6 years on the forehead from which he bled continuously for 15 days. Then at the age of 12 he injured his finger which also bled for 10–12 days. His joints were affected. His blood showed: bleeding time—2 min.; coagulation time—23 min.; platelets—206,000/ccm.; prothrombin time—18 sec.; blood group—A. The patient was not colour blind.

The patient refused to give any details of his family history. His parents are normal and healthy and are living in a distant village. His eldest brother got the similar complaint of pain with lump in the abdomen and died on the 3rd day of attack at the age of 28. He had also similar bleeding tendency. The patient has two more younger brothers, who are said to be normal and healthy. There are no sisters. The patient is married and is a native of Gujarat.

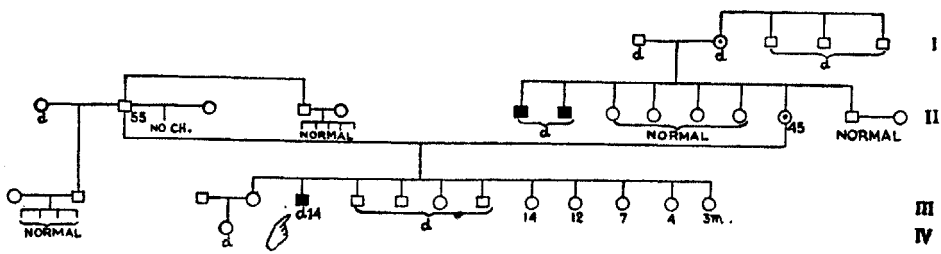
Case No. 15. K. D., male, aged 8 years, was treated privately at Ahmedabad. The patient came for medical treatment in June 1946 owing to an injury on the forehead caused by accidental fall. Bleeding continued for 5-6 days till the boy succumbed. His early history revealed echymosis on all parts of the body as a result of slight injury or pressure. Epistaxis was frequent at the early ages. No clinical examination of the blood was done.

The two elder brothers of the patient also died of haemophilia. The eldest had severe bleeding tendency from his very childhood. He, however, died from internal haemorrhage as a result of a fall from a wooden staircase. One of the younger brothers also died on the 6th day after his birth. In an attempt at sneezing on the 4th day of his birth he began to bleed from his nose which continued at intervals till his death 2 days afterwards.

(*c*) *Case from Nagpur*

Case No. 16. R. T. (Ped. 8, III 5), male, aged 14 years, was admitted on 31st March, 1952, at the Nagpur Medical College hospital with swollen knee and shoulder joints and epistaxis. He gave a history of prolonged epistaxis and severe bleeding on slight injury since 5 years of age, before which he was normal. His blood showed: bleeding time—2 min.; coagulation time—10 min. 15 sec.

PEDIGREE 8



It was found out after local enquiries by the present writer that the above boy was rushed into the above hospital on 31st December, 1953, where he expired the same day at 1-5 p.m.

It will be seen from the above pedigree that III 5 has also two affected maternal uncles (II 6 and 7) who also appear to have died from haemophilia. The latter were never treated medically. The patients belong to an illiterate weaver family. Both II 2 and his wife (II 12) described their diseases as similar to that of their son III 5. All the sisters of II 12 are said to have normal children; so also her only surviving brother. None of the other dead children of II 12 appears to be affected with haemophilia. III 6 died at the age of 7 years while the other three died within 3 years. It also transpired from the statement of II 12 that three of her maternal uncles also died at an early age. Her parental home was in Ramtek, Nagpur.

The above 16 cases were investigated by the writer as a result of a tour in Bombay, Nagpur and Ahmedabad. Their case histories were studied from the hospital records and wherever possible personal enquiries were made to complete the genealogical data.

Case No. 17. This case is shown in Ped. 9, which is from Bengal. The family has scattered about in various parts of the state and some of its members are settled in the city of Calcutta. The family was partly described by Ghosh (1942), who treated V 4 and thereby gathered some genealogical data from the father of the child. Ghosh was good enough to get the present writer introduced to the above family just before his premature death.

The child (V 4) was admitted to the Carmichael Medical College (now R. G. Kar Medical College) on 17th March, 1939, with bleeding gums and a small wound on the left margin of the tongue due to accidental biting. Echymoses was seen in the different parts of the body. His blood on 17th March showed: bleeding time—2½ min.; coagulation time—11½ min.; blood group—AB. In September 1940 the boy was again brought to Dr. Ghosh with swollen left knee joint which appeared after a fall. Then again in November 1940 he bit his tongue and came under Dr. Ghosh's treatment. At this time his blood was again examined and the following results obtained:

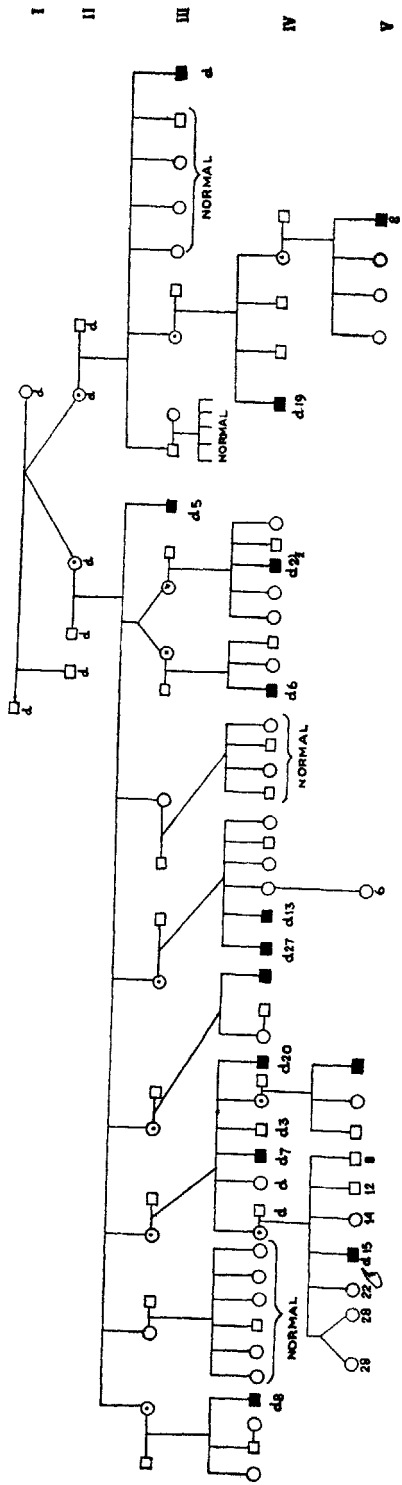
Date	Bleeding time	Coagulation time
26. 11. 40	4 min.	9 min.
29. 11. 40	4 ,,	9 ,,
18. 3. 42	3 ,,	15 ,,

Dr. Ghosh last examined the patient on 18th March, 1952, when the boy was about 6 years of age. He died in 1952.

It will be seen from the pedigree that the whole sib originated from a pair of twin sisters (II 3 and 4) one of whom has given birth to a pair of twins herself. There is also another pair of twins in the V generation who are diagnosed as monozygotic by the present writer. They are not yet married. It was difficult to trace the ancestry of the family but III 10, an old man of about 60, informed the writer that he remembers to have seen a brother of II 3 and 4, who was perfectly normal and had normal children. He lived up to an age of about 70 years. This point however could not be verified from other sources though there is no reason to doubt the statement of III 10.

It will be seen from the pedigree also that the severity of the disease is not similar in the family of the two twin sisters (II 3 and 4). II 3 shows only two normal daughters as against 6 carriers while II 4 shows only one carrier daughter against 3 normals. Haemophilia in the only child (III 17) of II 3 appears to have been correctly diagnosed. The father (II 2) was a medical man and left practically no stone unturned to save the life of his only son. While running, he accidentally hit a fish-knife and sustained a deep wound on the toes from which he bled to death.

PEDIGREE 9


I
II
III
IV
V
NORMAL
NORMAL
NORMAL
NORMAL
d5
d6
d13
d19
d20
d3
d7
d15
d8
12
14
22
28
29

The details of the children of II 4 were extremely difficult to obtain due to the reluctance on the part of the family members. At present there is only one child (V 14) who is still suffering from haemophilia. A few months ago (June 1954) he was seriously laid up with echymosis all over the body, specially the knee joints were affected and there was profuse bleeding from the gums. His tongue was paralysed, thereby preventing any intake of food with ease. His clinical details could not be secured and the case is being treated privately. The boy is now about 8 years old.

Haemophilia is almost certain in the cases of IV 22 and IV 23. Both of them used to bleed from the gums and to have echymosis and bleeding from slight injuries. The knee and elbow joints of IV 22 were severely affected and although treated privately he received the best possible medical attention available in the city of Calcutta. IV 23 died as a result of an accident. Chased by a dog he rushed into the room and while doing so he struck his head on the door lintel and died from the same injury.

It will be seen from the pedigree that in III generation there were 4 male issues of whom 2 were haemophiliacs and died of it. In the IV generation from the available information there were 19 male children of whom 9 were haemophiliacs and 10 normals. Of the 9 haemophiliacs only IV 21 is living and he is reported to have married.

Similarly there are 19 female issues of whom 7 are normals and 3 have proved to be carriers. In the V generation the present author has been able to know of 6 male issues of which 3 are haemophiliacs. None of the females of the V generation is yet married. Out of the total number of 14 haemophiliacs in the whole sib the ages at death of 10 individuals are known which gives an average longevity of 12·5 years (range: 2½ years–27 years).

The above 17 cases have been treated separately because almost all of them were initially reported from hospitals and attempts were made to gather further information on them through personal contacts. The rest of the cases will be described according to the hospitals and in the majority of cases preliminary contacts could not be established by correspondence.

(*a*) The V. J. hospital, Amritsar, reported to us of 5 haemophilia cases, of which two cases appeared to belong to the same individual though nothing definite can be said without a field study of the particular family. The details of these two cases are as follows:—

(i) J. (surname not recorded), male, aged 9 years, was admitted on 28th April, 1952, with epistaxis for 6 days, history of excessive bleeding from cuts and high effusion in both the knees. Clotting time—8 min. Father's name not recorded. Family history showed one brother having died of the same disease while two other brothers bleed often from minor injuries.

(ii) J. T., aged 8 years, male, was admitted on 27th April, 1953, with epistaxis for one week; haematemesis and haemorrhage into the left knee. Bleeding time—2½ min.; clotting time—8 min. 30 sec. Father's name not recorded. Family history shows one brother having died of the same disease and another suffering from it.

The similarity in the name and address of the above two patients raises firstly the doubt of their being two separate individuals. Other details are also similar to some extent. It has already occurred in the experience of the present writer that the same patient came for treatment more than once in the same hospital and has been recorded as separate cases. In such cases only field investigations can determine the true state of affairs.

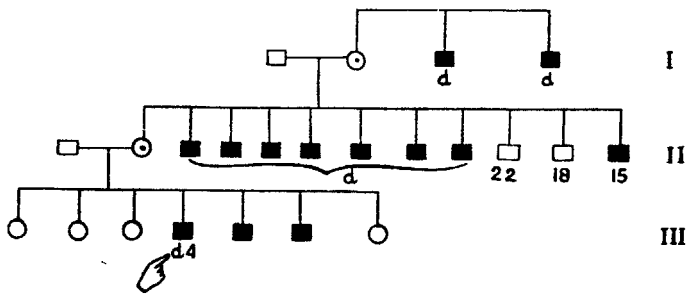
(iii) P. S., male, aged 6 years, was admitted on 6th August, 1954, with bleeding from the upper lip. He gave a history of excessive bleeding from minor injuries. The family history revealed a history of one brother also suffering from the same complaint. Two maternal uncles were also suffering from the disease.

None of the above two cases replied to our queries. No letter was sent to (i) due to the incomplete nature of the names of the patient and his father.

(iv) I. S., male, aged 12 years, was admitted on 24th October, 1952, with bleeding gums. He showed this bleeding tendency from the age of 6 months at the slightest injury. Echymosis was very frequent all over the body and the ankles appear to have been very much affected. Whenever the milk teeth were shed he used to bleed heavily. His early history was sent to us by his father. The younger brother of the child succumbed to this disease at the age of 6 years. It was revealed from the father's letter that the boy was given blood transfusion at the hospital which did not yield any satisfactory improvement. He is now being treated privately and vitamins C and K with coagulin has been effective in his case. The youngest brother, now about 4 years old, appears to be normal. No details of the family history was sent by the father.

(v) R. C. L. (Ped. 10, III 4), male, aged 3 years, was admitted on the 31st August, 1951, with bleeding gums. The hospital records show that he was suffering from peticheal haemorrhages since the age of 6 months. The father of the boy was good enough to send us some details of his family and those of his father-in-law. As regards III 4, the father informed us that in October or November 1951, while playing, the boy injured his head and began to bleed. He was rushed into the hospital where he expired the following morning. The next brother also showed symptoms of the disease from the age of 5 months. Echymosis was frequent all over the body and this symptom also appeared on the testis. The third son is also suffering from the same disease.

PEDIGREE 10



It will be seen from the above pedigree that 7 maternal uncles of the boy (III 4) have also died of this disease and the youngest (II 2) is still suffering from it. The 7 brothers died within 10 years and all were treated in a hospital, which has not replied to our queries. II 1 informs us that in all of them death followed very quickly. He also informed us of the death of two maternal uncles (I 3 and 4) of his wife from the same disease. I 1 was also contacted at the instance of II 1 but no replies were received.

(*b*) The Christian Medical College, Vellore, sent us records of two haemophiliacs but unfortunately none of them could be traced and our letters were returned by the Dead Letter Office.

(i) K. C., male, aged 50 years. The patient was admitted with a sudden attack of inability to talk and haemophilia into the vocal cords was diagnosed. His blood showed: clotting time—6 min. 11½ sec.; bleeding time—2 min. 1 sec.; platelets—88,800/ccm. The patient had frequent epistaxis and haematoma used to be formed at the injection spots. No family history was available.

(ii) M., male, aged 2 years. The child had a fall and injured the scalp wherefrom bleeding could not be controlled. The child was anaemic and had injured

both the liver and the spleen. His blood showed: bleeding time—2 min.; clotting time—32 min.; platelets—495,000/ccm. No family history was available.

(*c*) The Medical College hospital, Madras, reported of three cases of haemophilia, the details of which are as follows:

(i) M., male, aged 5 years, was admitted on April 27, 1954, with a tooth lost as a result of a fall from which he was bleeding for the last one month. Previous to it he bit his tongue and bled for 10 days. He also once bit his lip and bled from it for one month. The family history, as given by the hospital, showed an uncle had suffered from the same disease. The patient had an elder sister, who was about 7 years of age. No reply was received to our letter.

(ii) K., male, aged 30 years, was admitted on May 20, 1954, with bleeding gums. He was the only son of his parents and no such complaint is known in the family.

(iii) T. D., aged 1 year, was admitted on November 15, 1953. The other details of the patient are not available. The last two patients could not be contacted due to the absence of any address.

(*d*) The Irwin hospital, New Delhi, reported of only one case, the details of which are as follows:

(i) A. K. D., male, aged 14 years, was admitted on January 7, 1954, with affected joints. The coagulation time of the patient's blood has been noted as 'delayed'. No other details are known, neither was our letter replied to.

(*e*) The Assam Medical College hospital, Dibrugarh, reported of one case of haemophilia in an Indian Christian.

(i) P. J., male, aged 19 years, was admitted on January 18, 1953, with haematemesis. His maternal uncle was a chronic bleeder. No other details could be gathered from correspondence.

Discussion

It will be seen from Table I that out of the 21 hospitals participating in our enquiry the majority, *i.e.* 13 hospitals, have not treated any case of haemophilia. The longest period involved is that of 20 years for the Mysore University Medical School followed by 10 years for the Andhra Medical College, Vishakapatnam. The G. R. Medical College, Gwalior, had no cases during the past 5 years while the neighbouring town of Indore had similarly no haemophilia cases during the past 4 years. The other 9 hospitals showing no haemophilia cases have reported only for periods varying between one to two years.

The incidence of haemophilia, however, appears to show a higher concentration along the western part of the country than that of the other regions. Starting from Amritsar on the north, we come to New Delhi to Sind (Ped. 2), to Gujarat (case No. 1, Ahmedabad cases) and then to Bombay. Out of the total number of 28 cases, excluding Bengal, 21 cases fall on the western region of the country. It is too premature to say anything definitely on this point from the present small data but a trend towards the higher incidence of haemophilia along the western region of the country is indicated.

The diagnosis of haemophilia may not be correct in all the cases. The laboratory tests on the blood are incomplete in the majority of the cases. The recent discoveries of parahaemophilia and Christmas disease necessitate detailed laboratory tests of the blood and a re-examination of the existing haemophilia cases. The majority of the pedigrees show the sex-linked recessive inheritance of the disease. The inheritance of the pedigrees 1, 2 and 3 cannot be explained due to the paucity of data. There might have been some concealment of facts in pedigrees 1, 2 and 6, while pedigree 3 is an exceptional one in having a female haemophiliac. The existing cases should be re-investigated according to the modern diagnostic methods.

There have been three marriages of haemophiliacs. In pedigree 1, II 2 has three issues, two sons and a daughter. In pedigree 5, III 10 has four issues, two sons and two daughters. In pedigree 7, I 2 has two normal sons and one carrier daughter. The last pedigree thus shows what is expected of the children of a haemophiliac father. The three haemophiliacs thus have a total number of 10 children showing an average of 3 33 children per family.

The average longevity of the haemophiliacs has been found to be 14·11 years, the maximum and the minimum being 37 years and 1 year respectively. The age at death was known in the case of 14 haemophiliacs only, of which 10 are from pedigree 9 alone. The average longevity in the latter case works up to 12·25 years. The pedigree data show that 15 haemophiliacs are still living among the affected number of 42 in 8 families. Pedigrees 3 and 4 have been excluded. The affected number of individuals increases to 52 when those from other hospitals are included. One death out of these 10* affected from other hospitals is definitely known (Amritsar case (v)). Thus when the two data are combined together it is seen that there has been at least 28 deaths in a total number of 52 affected cases.

Summary

1. In order to find out the incidence of haemophilia in India a questionnaire was first of all sent to several hospitals throughout the country requesting them to inform the details of the haemophilia cases treated by them during a certain period.

2. 21 hospitals participated in the enquiry of which 13 have treated no cases of haemophilia while the rest 8 have treated haemophiliacs varying between the numbers 1 and 13. The largest number was treated by the K. E. M. hospital, Bombay, while the second largest number of 5 cases was from the V. J. hospital, Amritsar. A few cases from private medical practitioners have also been included.

3. After the addresses of the haemophiliacs were obtained attempts to contact each case were made for the purpose of collecting their family histories. A tour to Bombay, showing the largest number of cases, Ahmedabad and Nagpur was undertaken for this purpose and personal contacts with the patient or his family were made, where possible. 10 pedigrees have been collected.

4. The average longevity, based on 14 haemophiliacs, has been found to be 14·11 years. Out of the above 14 cases, 10 belong to a pedigree from Bengal, in which the average longevity works up to 12·25 years.

5. 15 haemophiliacs were living at the time of enquiry among the affected number of 42 from 8 families. The affected number increases to 52 when the total hospital data are taken into account. One death out of the latter 10 is known. Thus when the family and the hospital data are combined there have been at least 28 deaths in a total number of 52 affected ones.

6. 3 haemophiliacs are married, having a total number of 10 children.

7. A female haemophiliac child has been recorded, though the diagnosis should be confirmed by latest laboratory methods.

8. The incidence of haemophilia appears to show a higher concentration along the western regions of the country.

9. Improved clinical diagnosis is required, whereby the other two variants of the disease, namely parahaemophilia and Christmas disease, which are assumed to be allelomorphic variants of haemophilia, can be differentiated.

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* Case No. 15 has been excluded from calculation. 3 cases have been counted for Amritsar.

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