HAEMOPHILIA,

BY

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I hereby declare that I have composed the accompanying thesis entirely by myself.

John J. Wilson.
HAEMOPHILIA.

Having now had for several years under my care a patient, suffering from Haemophilia, who has had all the various manifestations of the disease, I shall begin by a description of his case, so far as I know it, and afterwards take up in detail the historical account of the disease, its symptoms, aetiology, morbid anatomy and pathology, prognosis and treatment.

W.O., aged 33. A thin delicate-looking man with pale complexion. His skin has a waxy appearance; the veins on the temporal regions stand out prominently, especially on exertion. He walks with a distinct limp arising from a drawing up of the left heel, consequent on contracture of the muscles after haemorrhage into their substance.

He was born in Anstruther, Fife, and is the only son of his parents, the rest of the family consisting of eight sisters, so that the whole family consists of nine. Both his father's and mother's relatives were long-lived, and no trace of a history of any "bleeders" having existed on either side of the family can be discovered.

His sisters have all rather a pale and waxy appearance, and several have suffered from anaemia at
some time of their life. Two suffer from marked lateral curvature of the spine.

Two sisters are married; one having two sons living, aged five and one, and the other one a son aged one. The mother of the former children, during her second pregnancy, suffered from placenta praevia, and the child, a girl, was still-born. This condition may have just been a coincidence, as she was safely delivered of a boy a year afterwards without any mishap. None of the children of these married sisters have shewn signs of haemophilia.

History.

The patient has never suffered from any illnesses with the exception of the attacks of haemorrhage. In infancy his mother noticed that he was very easily bruised, as large masses of blood formed on the thighs or limbs, when any injury was sustained. His gums bled in infancy and youth with great ease, and when he was losing his temporary teeth, oozing of blood occasionally occurred and was with difficulty stemmed.

When the condition was first noticed, it appears that a correct diagnosis was not made, if any was made at all, and it was not till he was between 10 and 12 years of age that the disease was really recognised as one of haemophilia. Great care was taken of him, and he was not allowed to go to school or mix with other boys.
When about fourteen years of age he had a very severe attack of subcutaneous haemorrhage into the calf of the right leg. The swelling was very large, and was aspirated, and blood drawn off. The skin ultimately burst, and the mass of blood was sloughed out, but from all accounts there was very little haemorrhage after the rupture. At that time he was recommended to begin and take Iodide of Potassium, which he has continued ever since. After this severe illness he had comparative immunity from haemorrhage for ten years, although he had occasional swelling of joints during that time. Four years ago, however, a period set in, during which he has had six serious attacks of haemorrhage into his lower limbs, during the course of which I have attended him. The last occurred in June 1892 and resulted in rupture of the skin and sloughing of the mass of blood; since which attack he has been free from haemorrhage.

Character and history of Attacks of Haemorrhage.

In May 1890 the first of these haemorrhages occurred; the bleeding took place into the gluteal muscles, and was confined to that region. The pain and haemorrhage continued for a week, and after that the swelling rapidly dissolved away. In April 1891 he was again confined to bed, and the following notes, taken at the time, are a detailed account of that attack, as they give a very fair idea of its character.
On April 25th, 1891, the patient experienced a tight feeling at the back of the left knee-joint, as if the tendons were a little tense. He paid no attention to it, however. On Sunday, the 26th, he felt all right; went to church, twice, and took a long walk. In the evening he took a hot bath, a thing he has not done since his previous illness in May, 1890.

On the 27th he felt the calf of his leg a little tight, but went to his office downstairs as usual. In the evening there was a distinct swelling in the calf of his leg.

**Tuesday, April 28th, 1891.**

Left calf very much swollen; there has been, during the night, an increase in circumference at the broadest part of the calf of 1\(\frac{1}{2}\) inches. Slight discoloration at the back of the knee-joint. Tumour on palpation is uniform. There is very marked tenderness about the middle of the inner aspect of the calf. The rest of the calf is very tense, and there is slight tenderness on pressure. Pulse at the ankle is quite perceptible. Slight oedema over the tibia and at the inner aspect of the ankle.

Pulse and temperature normal.

**April 29th.**

Limb much the same. Increase at the middle of calf 1\(\frac{1}{2}\) inch. Discoloration more marked, and extending down the limb. Feels no pain, only a tight sensation.
Tenderness still present.

April 30th.

Patient wakened at four o'clock in the morning with distinct pain over the upper part of the calf a little below the knee-joint. Sleep much disturbed after.

Temperature 100°, pulse 100. Practically no increase in circumference of limb, but tenderness very marked. Patient looks haggard.

1.30, P.M.

Complaining of severe pain which has been increasing in severity since morning. Gave \( \frac{1}{6} \) gr. Morphia hypodermically.

3.30, P.M. Much easier.

7.30. Complaining again of pain. Gave \( \frac{1}{5} \) of Nepenthe.

May 1st, 1891.

4.A.M. Patient was suddenly awakened with acute pain in the calf of the leg. It is very severe and bursting in character. Gave \( \frac{1}{6} \) gr. Morphia hypodermically.

10,A.M. Since injection of morphia was given, patient has slept well. Pulse 112. Temperature 100.6.

11.30, A.M.

He is suffering excruciating pain at present. Gave \( \frac{1}{3} \) gr. Morphia. There is considerable swelling of the left forearm where the morphia has been injected.
6 P.M. Pain has begun again $\frac{1}{6}$ gr. Morphia

11 P.M. Easier, has slept. Temperature 101.6.

Saturday, May 2nd.

2 A.M. Pain again. $\frac{1}{6}$ gr. Morphia.

9 A.M. There has evidently been more haemorrhage, when the severe pain arose, as there is now distinct bulging of the calf over the inner aspect. The hardness of the calf is very marked, and over the bulging area the slightest touch causes severe pain.

Measurements shew increase of one inch. Patient is looking pale. Not taking food well.

2 P.M. Pain began again $\frac{1}{6}$ gr. Morphia.

May 3rd.

Patient had a good night. Was able to do without Morphia till 7 A.M., when $\frac{1}{6}$ gr. was given. Limb has increased 1 inch in circumference.

Evening. Had a day almost free of pain. Feeling rather sick.

May 4th.

12.15, A.M. Pain again. $\frac{1}{6}$ gr. Morphia.

9 A.M. Slept well. Pulse 100. T. 100.1. Pulse is improving in volume.

May 5th.

Gave $\frac{1}{6}$ gr. Morphia during the night. Pain is diminishing in intensity.
May 8th.

Patient is now steadily improving and the swelling of the calf is rapidly going down. He is looking much better. Temperature and pulse normal. A fortnight later the knee joint became rapidly filled with fluid. No discolouration round the joint. The skin over it was painted with iodine and the swelling rapidly subsided.

During October and November 1891 he had a similar haemorrhage, with a corresponding course, into the left calf.

At the end of July 1892 there occurred haemorrhage into the anterior aspect of the left leg amongst the extensor muscles. The pain was very severe and the tension of the limb very marked. As there were evident signs of the skin rupturing, I aspirated the tumour and drew off about 4oz. of blood. This brought about relief at the time, but the limb rapidly filled up again and finally rupture occurred. I cleared out what clots were loose, and left the others to slough out, as I was afraid of tearing through blood vessels. The clots gradually came away with only very slight haemorrhage as I applied continuous elastic pressure.

The wound was not healed till the middle of October.

After each of these severe attacks of haemorrhage there has always been swelling of joints of the
affected limbs.

Since the haemorrhage into the arm consequent on the use of the hypodermic needle, I have always injected the Morphia into the affected limb as there is always considerable oedema and less liability to haemorrhage.

The case is an interesting one for the following reasons.

(1) There is no hereditary history discoverable.

(2) There does not seem to be so much liability to external haemorrhage as to internal.

(3) The patient has lived past the average age.

(4) There is very severe pain during the attacks which is undoubtedly due to the tension of the blood tumour.

(5) There seems to be apparent immunity from haemorrhage after blood has been lost externally; about 10 years freedom from it on one occasion and now 1½ years from the last.

(6) The haemorrhage seems to come on in sudden bursts, as note the sudden accession of pain on several occasions.

Nature of the Disease.

Haemophilia is a congenital disease which in the majority of instances exists during the whole period of the life of an individual. Though in a number of
cases there is little to shew that it does exist in infants under one, still, in most, in fact one might say in all cases, if there is any injury such as a blow or wound, the signs of haemorrhage soon manifest themselves in subcutaneous or external form.

The various synonyms applied to the disease are as classified by Dr Dunn (1). Hereditary Haemorrhage, Haemorrhagic Diathesis, Haemophilia, Idiocyancrasia Haemorrhagica, Haematophilia, Haemorrhaphilia, French Hemophilie, German Bluterkrankheit.

History of the Disease.

Authorities seem all to agree that the report of the first authentic case, a record of which still exists, occurs in the writings of Albucasis or Alzaharavius, an Arab who lived in Cordova and who died there A.D. 1107. Wickham Legg (2), in his monograph gives a doggerel Latin translation of this author's work, the original Arabic version of which exists in the Bodleian at Oxford. From that account there is evidence that there must have been a large number of victims to the disease. The substance of the Latin translation is that there were men, who when phlebotomised or cut, bled to death; and if the boys' gums were rubbed they bled profusely, and that haemorrhage was a common cause of death. From this we gather that apparently bleeding from the gums was more common in boys than adults. There seems to have
been a number of cases of the disease in this homestead or village. In all probability this is quite an authentic record, as the disease is easily propagated and handed down by intermarriage in a small village community.

There is a long period of years in which no mention of the disease can be discovered, until we find the case reported by Alexander Benedictus, in 1539, of the Venetian barber who died of haemorrhage from the nose.

The following is a translation from his work.
"Concerning a flow of blood from the Nostrils."
"At Venice a certain barber, in cutting troublesome hairs in the nostrils with his scissors, incautiously cut a small vein, and the blood rushed out with such force that many physicians could not find a means of staunching it, and he, wretched one, ended his life."

Doubt is thrown by Legg as to whether this is really a true case of haemophilia or not, but I think we must accept it as such.

The next really authentic report is a case noted by Virchow (3), as being related by Hochstetter, a physician of Augsburg, who described the case in 1674.

The following is a literal translation as it gives a very good idea of the disease as it was then reported.
"A rather profuse discharge of blood from the
"navel just after birth and a tendency of the nostrils to bleeding accompanied by livid spots when grown up."

"A certain boy when newly born had a copious issue of blood owing to the navel not being properly tied: the mother on removing the bandages was terrified at the sight of the infant all-stained, fell into a fever and delirium and died; the boy was no worse in condition, but while he was growing up he became particularly liable to bleeding at the nostrils; at the ninth year of age it was so copious as to terrify the bystanders.

"The doctors therefore employing cooling applications, and staunching the blood, the dropping at the nostrils ceased, but the foeces came away with blood liquid and clotted, mottled and livid spots or blood red stains, changing to dark blue, appeared everywhere through the skin, on face, breast, back and limbs, which at last became yellow and disappeared.

"In the following years, when similar bleeding and discolouration presented themselves, they were followed by a scab. While this is being cured by blood purifiers and purgatives, the bleeding is postponed (promoted?) and therefore in the 11th year of his age I opened a vein with advantage not fearing his tender age."

Legg draws attention to three cases which originally were recorded in the Philosophical Transactions.
in 1674. The first of these has been claimed by the Germans and is called Lowthorp's or Coxe's case, but which belongs to neither. The other two cases were never taken note of till Legg discovered the account of them in the Philosophical Transactions of 1743.

The first one, he says, is not true haemophilia, but the second, of which he gives a full account, (4) is an undoubted one, and is fully reported in his Treatise (4). The patient seems to have had subcutaneous haemorrhage, epistaxis, haematuria, and haemorrhage from the bowels, the account given being a most interesting one.

In 1784, Sir William Fordyce described a family living in Northamptonshire in which the father, a daughter and sons were affected with bleeding. (5)

The only other two cases noted about this time is one published in the "Medizinische Ephemeriden" (6) p. 267, in 1793, and the other, by Rave in 1798.

The disease, as such, seems to have been distinctly noted and taken up now by American Physicians, as Otto described a New England family in whom the disease could be traced back for about 80 years. It was he who first applied the term "Bleeders" to those who were so afflicted, and he also took note of the freedom from the disease of the female members of the family, and the liability of the female members to be a cause of the handing down of the condition to future generations of males.
Otto also refers to three other cases reported by Rush and Boardley.

In 1813, Hay reports the Appleton-Swan family, which Legg says is a branch of the same family reported by Otto.

The other cases reported in America are the Collins family by Buel (8), a Pennsylvanian family by Coats (9) in 1828. Since then a number of cases have been reported on that continent by Hughes, Gould, Dunn, and a number of other observers.

Germany now took up the study of the disease, thanks to the paper on the subject by Nasse (10) in 1820. Schönlein also studied the disease and introduced theories as to its causation. Wachsmuth published a monograph on the disease in 1849, and in 1854 Virchow described the disease. In 1855, Grandidier published his now classical Treatise.

In France, Gavey published an account of the microscopical examination of the blood-vessels, and an analysis of the blood, and Simon wrote an article on the subject in 1874.

In England, very little notice seems to have been taken of the disease, except reports of individual cases, until Legg published his treatise in 1872. More lately, Sir William Jenner has related a case with an account of the examination of the joints. Legg has also reported several individual cases with an account of the morbid anatomy of the tissues and joints.
Symptoms.

According to Legg, Fagge and others the symptoms of the disease, as a rule, rarely manifest themselves during infancy; in fact, Legg questions what Virchow and Nasse say in regard to the incidence of the disease, as these two authorities maintain that it exists from birth. I think that probably the reason why some authorities maintain that the disease does not exist from birth is, because so few cases are recorded. The infants have died so young that it has not been considered worth while to report the condition. That the disease is a congenital one, the following cases will show.

"Mrs S., aged 38, primipara, delivered of a male child, apparently strong and healthy. On the third day a small dark spot was observed on either side of the occiput. The day following the child had two black eyes, the discoloration extending symmetrically above the eyebrows and on the malar bones. The eyeballs presented an unusually pearly appearance. Next morning there was a purple swelling on the external aspect of the left humerus, and in the evening the same was observed on the right side. Next day the cord began to bleed, which was stopped by retying. Haemorrhage broke out again in the proximal end, and the child died before it could be stopped."

(11) This case is reported by Dr Macarthur of Sturminster Newton.
The following is reported by Dr Vincent. (12)

"Mrs P. delivered of a male infant on the 8th March. 10th March it was jaundiced, 13th two swellings one behind each axilla. During the next two days swellings appeared on the back of the shoulders, front of chest, elbows and knees. The cord separated on the morning of the 15th, and the child died on the 16th from haemorrhage from the umbilicus. Six years previously the mother gave birth to a male child who died much swollen and covered with 'lumps.'

Dr Eagle (13) relates the case of a child in which the cord separated on the fifth day with no haemorrhage. On the 14th day there was extravasated blood beneath the left scapula. The child was jaundiced. Next day there was bleeding from the umbilicus and the swelling had spread. The bleeding from the umbilicus was stopped by pressure, but in an hour returned. Then oozing from the mouth set in, which ceased, when the umbilical haemorrhage returned. The child died in the London Hospital from haemorrhage 6 hours after admission. There was no history of any diathesis."

The following case is reported by Dr Jardine (14) of Glasgow and it is all the more interesting and remarkable in that the subject of the disease was a female infant.

"Child weakly looking when born. In a day or two it was jaundiced. The cord separated on the eighth day and with it there was oozing. This ceased
for three days, but began again on the thirteenth. On the eighteenth day there was haemorrhage from nose, mouth and anus, and bruises were noticed on the right side of the chest also on the right knee and elbow. On the nineteenth day, there were ecchymosis in the palate. The joints, especially the right elbow, were distended. The mother was not a bleeder, but stated that their other little girl bleeds profusely from the nose. The father is also troubled in the same way."

Another similar case is reported by Dr H. J. Roper. (15) "The child bled from the cord till the 8th day and from the cicatrix till the death on the 24th day. There was bleeding from the mouth, bladder and rectum on the second day. Extravasation of blood on the shoulder and pectoral region. Haematemesis on the 10th day. No Jaundice."

From these cases as examples we must conclude that the disease exists and manifests itself from birth onwards, and is truly a congenital disease. Legg says it is latent at birth and does not shew itself till some injury is sustained, but evidently in all the cases reported above, the haemorrhage was quite spontaneous. Undoubtedly the disease is much more evident after a child has begun to crawl about, walk and buffet with the world, hence it is more taken note of after one or two years. The joint
affection appears as a rule at the 7th and 8th years and again at the 13th and 14th. The latest age at which the disease has been known to manifest itself is at 21 or 22, recorded by Steiner and quoted by Grandidier, (16) in which both a father and son became subject to profuse haemorrhage and died from it.
The symptoms of the disease can be grouped under three distinct heads, and in the more severe cases all the symptoms are present. Legg classifies the cases according to the severity of the manifestations of the disease, but I shall simply take up the symptoms of the disease in order, under three headings.

(1). **External Haemorrhages.** The blood may proceed from the skin, mucous membrane of nose, mouth, stomach bowel, or bladder. It may be either traumatic or spontaneous.

(2). **Internal Haemorrhage.** That is beneath the skin, between or into the muscles or into serous or synovial cavities.

(3). **Arthritic affections.**

According to some authorities, Wachsmuth and Otto, there are often distinct prodromata which occur some days before a haemorrhage, but Legg in his monograph says he has never seen any such premonitory symptoms. I, myself, have never seen any such symptoms in the case I have described. The usual premonitory symptoms described are flushing of the skin, plethora of the face, throbbing of the temples, dyspnoea, headache and giddiness with irritability of temper, also restlessness with irritability of sight and hearing, accompanied by a scanty secretion of urine. There are also spontaneous pains in the limbs, and the bowels are confined. Legg says there are often symptoms
indicating the position of the haemorrhage, as pains in the back when haematuria is to occur, irritability of the nose before epistaxis. The appetite is sometimes very capricious beforehand.

I. External Haemorrhages.

The most frequent seat of haemorrhage, especially in children, is from the mucous membrane of the nose, and according to Grandidier it is four times as frequent from there as from any other position. The figures given by him out of 256 cases are as follows:-

<table>
<thead>
<tr>
<th>Surface</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose</td>
<td>122</td>
</tr>
<tr>
<td>Lungs</td>
<td>15</td>
</tr>
<tr>
<td>Mouth</td>
<td>34</td>
</tr>
<tr>
<td>End of fingers</td>
<td>4</td>
</tr>
<tr>
<td>Stomach</td>
<td>11</td>
</tr>
<tr>
<td>Scalp</td>
<td>4</td>
</tr>
<tr>
<td>Bowel</td>
<td>33</td>
</tr>
<tr>
<td>Tongue</td>
<td>4</td>
</tr>
<tr>
<td>Urethra</td>
<td>13</td>
</tr>
<tr>
<td>Eyelids</td>
<td>1</td>
</tr>
<tr>
<td>Ear</td>
<td>3</td>
</tr>
<tr>
<td>Female genital organs</td>
<td>10</td>
</tr>
</tbody>
</table>

The bleeding may go on from any of those surfaces till the patient bleeds to death.

All the haemorrhages arising from mucous surfaces may arise spontaneously, but in a number of cases, it arises from injury, such as extraction of a tooth, or incision of the gums. Haemorrhage may also occur spontaneously from the skin, as from beneath the finger nail, although Grandidier only quotes 4 cases out of 256. The great majority of cases of bleeding from the skin occurs from some blow
or injury, whereby an abrasion is brought about. There is only one case of death, reported by Henschel as arising from haemorrhage after vaccination. Hughes (17) relates the case of a family in whom the application of blisters produced bullae of blood instead of serum, and he saw death occur twice from this cause.

The slightest injury to the skin may result in the death of the victim. The blood goes on oozing and defies the most powerful styptics which can be employed. Sir William Jenner says that the bleeding seems to be venous, but I have watched the bleeding taking place and have observed that it is distinctly arterial in character. There is a constant oozing as from a sponge if the wound be large. In a case described by Coates, as much as two quarts of blood were lost in 24 hours and three gallons in ten days.

When the bleeding has once ceased, the wound heals up very rapidly and apparently after a certain time, if the patient does not die, the bleeding will cease spontaneously, but it may recur again and again after the patient has so far recovered as to bring up his blood tension.

If the bleeding is going on to a fatal issue, the usual signs of profuse haemorrhage manifest themselves, blanched face, absence of pulse, delirium, hallucinations, general convulsions and death. Legg says that patients recover from their anaemia very
slowly, but in the case I have quoted, the recovery was very rapid, but, of course, in my patient’s case the haemorrhage was not excessive and not external.

II. Internal Haemorrhage.

In a great majority of patients, this form of haemorrhage is very marked, and it may be due to this symptom of the disease that the condition is first recognised.

There occur beneath the skin, between the muscles, or into the muscular substance, or more rarely into serous cavities large haemorrhages. In other cases there may be simply petechiae beneath the cutis. The haemorrhage occurs in those regions which have not much support from fasciae, or in those areas which are liable to injury from exposure, such as the lower limbs, and the shoulders. The face often escapes however. Sometimes they seem to arise spontaneously, but generally some traumatism is the cause.

The bleeding may be very slight, and may cease very rapidly; in other cases, W. O. being an example, large blood tumours may form and during their formation most excruciating pain is endured owing to their tension. The temperature and pulse rise evidently from the nervous disturbance arising from the pain and tension. The blood seems to ooze out slowly from the capillaries, but as the healthy part of the muscle or subcutaneous tissue is torn up by the advancing blood, larger vessels are ruptured and rapid
extravasations occur. I have frequently observed a sudden access of pain in a limb and accompanying it a rapid increase of swelling of the affected part. Distinct fluctuation can be felt for some time in those large masses, but finally the blood coagulates and is generally rapidly absorbed; during the absorption there is a beautiful play of colours all over the diseased part. Surrounding the blood tumour there is a considerable amount of oedema which disappears with the blood.

If the haemorrhage occurs into the subcutaneous connective tissue, so much pressure may be exerted on the skin that gangrene is produced and the blood is sloughed out, after which the wound heals up by granulation tissue. There may be very serious bleeding from such a cavity, but, fortunately, the blood-vessels are often sealed up by the pressure of the effused blood before the rupture of the skin takes place, and thus haemorrhage is prevented. The cicatrix which is left after the wound has healed shews a great disposition to break down and the skin is a long time before it attains such a thickness as to resist any free movement of the injured limb.

Instead of absorption of the effused blood taking place, calcification of the altered blood may occur, resulting in masses similar to the phleboliths sometimes found in the veins of the pelvis.

In addition to these blood tumours, crops of
petechiae may appear on the limbs of the patient and accompanying such crops of petechiae, there is generally the swelling of joints so characteristic of the disease.

Haemorrhage into the serous cavities of the body seems to be rare in the disease, but it does occasionally happen. Immerman records two cases in which there was haemorrhage into the peritoneum, and four in which it occurred into the meninges of the brain. Dr Goodhart performed a post-mortem examination on a case in which he discovered in the right pleural cavity adhesions of a deep orange colour, probably due to extravasated blood undergoing absorption.

It is to be noted as an interesting circumstance that at one time a patient may be able to stand serious blows and injuries which do not induce much haemorrhage, and at other times the slightest contusion or twist of a muscle may induce profuse haemorrhage and large haematoma. Haemorrhage seems often to set in, when an individual is at his best as regards his general health. I have noticed this repeatedly in the case of W. O. After a severe attack of haemorrhage, especially if sloughing has taken place, there seems to be immunity from the liability to haemorrhage for some time.

III. Arthritic Phenomena.

This is a very interesting and remarkable phase
of the disease. There occurs, often without any warning, but sometimes as the result of a strain or twist considerable swelling into the different joints of the body accompanied by pain and stiffness. It is often a late manifestation of the disease, not occurring till the 7th or 14th year of life. It may be the most marked of all the symptoms, the external or internal haemorrhage being quite secondary in importance.

The condition resembles an attack of synovitis as there is pain, swelling, fluctuation, and inability to use the limb. The temperature may also rise. It occurs most frequently in the joints, which are most often in use, the order of attack being the knee, hip, elbow, ankle, wrist, and shoulder. It rarely occurs in the joints of the fingers or toes. According to Legg, it seems to be most frequent in spring and autumn, especially in cold damp weather, and, therefore, has resemblances to rheumatism in that respect.

Formerly it was thought that the fluid which was poured out was ordinary synovial effusion, but as the result of post-mortem examinations it has been ascertained that the effusion is a bloody one. There is never or very rarely any discoloration of the skin over the joint, and that is probably the reason why it was considered to be synovial in character. I have examined the skin over a swollen joint on
several occasions, but have never been able to discover any discoloration as yet.

The swelling may disappear very rapidly or may persist for months, and in some cases it alternates with haemorrhage in some other locality.

This arthritic manifestation is very prone to arise after a patient has been confined to bed for a time, for as soon as he begins to use his limbs again there is invariably swelling into the knee or ankle joints, especially if one of the lower extremities has been affected with haemorrhage.

Closely allied to the joint swellings are the frequent attacks of severe pain in the muscles of the body and limbs. The patient may be attacked with pains simulating lumbago or sciatica, or the pain may affect the chest. In cases of Vieli's quoted by Grandidier, the pains were very acute and lasted about 9 days; the patient being very much prostrated and weakened by the attacks. As showing the relationship between these pains and swelling into the joints, haemorrhage may alternate with the pains as well as with the swelling.

Aetiology of the disease.

(a) Heredity.

As an example of a hereditary disease, haemophilia is one of the most marked, but the remarkable peculiarity of its hereditary nature is, that the female
members of a family are practically always exempt from the disease.

It may apparently arise in a member of a healthy family with no trace of the disease amongst the ancestors, as in the case I have recorded, but as a rule some trace can be discovered. When the disease does crop up or exist in a family, if there is marriage the disease is rapidly propagated.

Dr Dunn has collected statistics of 250 families in which there were 751 cases, and he adds to these 19 cases of Immerman, occurring in 6 families giving a total of 770 cases in 256 families, or an average of 3 bleeders to each family.

As shewing the great liability for the disease to be handed down from one generation to another, the annexed is copied from a chart of a family called Yeaton in America. It was constructed by Dr Gould and appears in Pepper's System of Medicine.

Yeaton.


Son-Bleeder. Three Daughters.

Son-Bleeder.


Son-Bleeder. Son, bled to death.


Twin Boys. Son, not a Bleeder. Son, not a Bleeder. Daughter.
From an examination of this tree, we see that the disease is not handed down directly but is propagated through the female side of the house. A father "bleeder" may give birth to a son who is a "bleeder", but his daughters may escape. The unfortunate phase that the disease takes, however, is that those daughters who apparently are quite healthy themselves may give birth to sons who are bleeders and they, the sons, again may hand down the disease to another generation, in which the sons suffer and the daughters escape. Again, a daughter of the original "bleeder" may give birth to a daughter, both of whose sons and daughters escape, but whose grandsons through the daughter are victims to the disease. It does not necessarily follow that all the sons and grandsons are "bleeders," but there is a great liability and tendency for them to be affected. It has been noted that direct transmission from a father's generation to a son's is more common, where the father's brothers have been affected, and where the father himself has escaped. The disease may exist for a great number of years in the members of one family and its descendants; Hay (19) has recorded a family in which the disease can be traced back for 95 years, and Legg (20) shows a family tree in which the condition has extended back for 200 years.

Sex.

Closely related to heredity as an aetiological
factor of the disease is the sex of the members of a family. It is, perhaps, an unfortunate circumstance in the prevention of the propagation of the disease, that so few females are affected and that the disease is passed on through them, as they consider, that because they are not affected with the disease they may marry with impunity, and so be a cause of fresh generations suffering. The male members who are subject to the disease, refrain from marrying and so prevent new cases arising. Females are not always exempt from the disease. According to Dr Dunn, only about 8% of females are affected, or about 1 woman to 11 men in haemophilic families.

Langes in 1849 says the proportion was as 1 to 7. Grandidier in 1855 says 1 to 14, and in 1863 1 to 11.

Legg says that the proportion of 1 to 11 is too high, as even in Grandidier's first calculation there were a number of cases included which should not have been.

Although females are affected with the disease in that proportion, the condition is not manifested in such a severe form, and, as a rule, the haemorrhage manifests itself as menorrhagia or metrorrhagia.

In a case reported to me by a friend, the mother suffered from severe haemorrhage for about five months after giving birth to the child, who died of exhaustion from subcutaneous haemorrhages all over
the body.

Another peculiarity of the female members of a family who may not be subjects of the disease is, that they are much more prolific than other women. The average number of children in a haemophilic family is 9, whereas the average in ordinary healthy families is 5. There are generally more daughters born than sons. In the case of W. O., both these characteristics are very well marked.

Legg says that where all the boys in a family are not affected by the disease, that the first born are more liable to be exempt than the others.

(γ) Age.

The disease, seeing that it is a congenital and hereditary one, may shew itself from birth onwards. From the cases I have quoted, it undoubtedly shews itself in early infancy much earlier than many authors admit.

Of 95 cases quoted in Grandidier's tables, it appeared in 58 during the first year; in 9 during the second, in 8 during the third, 2 during the fourth, 5 during the fifth and in 5 during the 6th year.

In the cases collected by Dr Dunn, in thirty-four, bleeding shewed itself before the eighth year, while in only two did it begin after that date. He maintains that it rarely occurs after the twelfth year; but Grandidier quotes two cases of father and son, in which the disease manifested itself between
21 and 22.

I can discover no statistics shewing whether it occurs earlier in boys or in girls.

(7) Race.

By some authorities, it is maintained that the disease belongs to the Teutonic race, and by others that the Semitic races are more liable to it than all others.

There can be no doubt that a great deal of the reporting and tabulating of cases depends on the teaching in the schools at which the medical men are educated. Legg, in his treatise, brings this out very clearly; as he shews in the history of the disease how first Bonn, through the Writings of Nasse was shewn to be a seat of the disease, and then as students at that school spread over the country, we have a record of it among other races than the Teutonic. There are more cases reported from Germany, however, than from any other country. Of 219 families affected with haemophilia, Germany supplies 94, Great Britain 52, North America 23, France 22, and other European countries the remainder.

It has been observed that the Jews are very liable to it, and it is first readily recognised in them, owing to the ceremony of circumcision.

We therefore see that race seems to have very little to do with the occurrence of the disease.

(8) Climate.
(6) **Climate.**

It appears in all altitudes from the low lying plains and river beds of Germany to the mountains of Switzerland, 5,000 feet above sea-level.

Cold and damp weather seems to predispose to attacks of haemorrhage, while the occurrence of warm weather has the opposite effect. The joint affections are also more liable to occur in spring and autumn, especially in damp cold weather.

(5) **Social Position.**

It may attack people in all classes of society from the highest to the lowest. Patients suffering from it may be fat or lean, but generally they are thin, having a nervous temperament. The skin is thin and transparent, and the veins stand out prominently. The intellect is sharp and the mental capacity above the average.
Morbid Anatomy.

The morbid conditions found in patients who have died of the disease has as yet not yielded very much information. If the individual has died as the result of haemorrhage, the usual appearances of such a death are apparent. The body is pale and rigor mortis well marked; it rapidly decomposes.

The internal organs are bloodless, and, if there has been haemorrhage into the muscles or joints the result is visible.

I shall take up all the morbid appearances which have been discovered and treat of them in the following order:

- (1) Changes in the heart.
- (2) Changes in the blood-vessels.
- (3) Morbid anatomy of the joint affection.
- (4) Changes in other organs.

(1) Changes in the heart.

There have been discovered a number of peculiarities both in regard to the shape and size of the heart. One observer (21) has recorded that the heart was four or five times larger than its usual size owing to "inordinate development of its muscular fibres."

In the case of a boy aged 17, quoted by Schneider, the pleural and pericardial cavities were filled with
serum; the left ventricle was enlarged, the wall of the right ventricle thin and delicate, and the coronary veins full of blood.

Escherich found in the case of a student who died of bleeding from a scratch received in a duel that the auricular septum was unnaturally thin. Sehlemann records a similar condition, in addition to which the pulmonary artery was very thin.

These are all the morbid conditions of the heart reported as yet, and to sum up they are Hypertrophy of the left ventricle, thinness of the walls of the right ventricle, thinness of the interauricular septum with, in one case, patency of the foramen ovale.

(2) Changes in the blood-vessels.

Blagden (22) in 1817 was the first to draw attention to any peculiarity of the blood-vessels. The patient was a man aged 27, in whom "the temporal artery and some branches of the external carotid were nearly transparent. There were in the coat of the carotid several white opaque spots which were evidently areas of fatty degeneration." The spots however, are quite accounted for by the mode of death from haemorrhage, and are not necessarily a cause of the disease. The next observer to note a similar condition was James Wilson (23) in 1819. Legg quotes this authority in full.

The subject was a boy between three and four
years of age who bled to death after biting his tongue; post mortem examination revealed the fact that the aorta and the branches from it were very thin and resembled veins more than arteries; the aorta instead of remaining cylindrical after removal from the body collapsed and in the popliteal artery no muscular fibres could be discovered.

In a case in which the post mortem examination was made by Virchow in 1857, in which the patient was aged 24, there was found fatty degeneration of the fibres of the heart; the aorta was narrow and it is also noted, which I think is important, that the thymus gland was persistent.

Schüneman also noted fatty degeneration of the heart and an unnatural transparency and thinness of the vascular walls.

The most important changes, however, and which may enable more light to be thrown on the disease, than any other changes, are those related by Dr Percy Kidd in the case of a child aged 6 years who died as the result of haemorrhage from the gums. The heart was fatty in the inner half of its wall. The aorta, the iliac veins and arteries were found to be unusually thin.

He examined microscopically the mucous membrane of the mouth from an area where the bleeding had taken place. He found that the epithelium was very
considerably altered from the normal. It was less thick and the individual cells were very indistinctly marked with no or very few nuclei. It had also the appearance as if it were being separated into layers and undergoing necrotic changes.

In the blood-vessels of the sub-mucous layer, he found very distinct changes. The smaller vessels especially the veins shewed a marked proliferation of the endothelial cells, so great as almost in some cases to block up and obliterate the lumen of the vessel. In the region of the necrotic area the blood-vessels were very few in number, as if they had been obliterated.

In some of the arteries he discovered that there were very few muscular fibres, and when they were to be seen the nuclei were undergoing subdivision. The coats of the vessels in which subdivision of the nuclei was taking place, shewed an indefinite indistinct appearance which was evidently a sign of degeneration and which caused an obliteration of the lumen of the vessel from swelling.

The endothelium of the aorta and Venae Cavae was normal but the vasa vasorum of these vessels shewed endothelial proliferation and consequent obliteration of the lumen of the arteries.

In two cases reported by Legg (25) in the Pathological Transactions, in which careful microscopic examination was made, no morbid appearances were
discovered.

In a case examined by Dr Acland, no abnormal conditions were found in the blood-vessels, but there were changes in the thymus which will be described later on.

(3) **Morbid Anatomy of the Joint Affection.**

Poncet was the first observer to record the exact condition of the joint affection, being followed later by Sir William Jenner.

Legg describes the morbid anatomy of two different cases.

In a joint recently affected there is a small amount of blood-clot discoverable without any apparent structural change in the cartilage.

The following is the account of the results of the post mortem examination of the knee joints of a boy aged 13 who died of the disease. The case is recorded by Legg (25) in the Transactions of the Pathological Society.

"In the left knee joint there was no recent blood found, but there were traces seen in the deep russet brown colour of the lining membrane. The cartilages preserve their pearly white aspect. At the under aspect of the external femoral condyle, where it meets the pressure of the tibia, the cartilage is worn thin and granular over a space of half
an inch in diameter.

The Ligaments are unaltered. In the right knee the connective tissue of the joint is also deeply stained of a brown colour, but changes in the cartilage are far more advanced than in the left knee. The cartilage is wanting over the points of pressure and bone thinly covered by cartilage has developed at the periphery of the joint. At the under-surface of the femoral condyles about the central points, the cartilage is thin, worn and rough. It is fissured in various directions and laminated. It has lost its close attachment to the bone so that a knife can be passed here and there beneath for a distance of two or three lines. The edges of this partly detached cartilage when raised are seen to be ragged and fibrous and split into layers like that in the joint of chronic rheumatic arthritis. Around each condyle is a prominent lip of bone somewhat nodular and thinly covered with cartilage. The same description holds good for the articular surfaces of the tibia and patella. In the femur there is a gap in the cartilage of the external condyle in its front surface at the line of division between the articular surfaces and on the tibia and patella. The gap extends to the bone and is widest at the outer part. The edges of the cartilage bounding the gap were smooth and rounded.
On microscopic examination of the cartilage of the joints, there is found fibroid degeneration of the matrix with multiplication of cells and breaking up of the capsules."

I have quoted this description in full as it gives a good account of the morbid condition found in all cases examined within recent years and which are not described even in Legg's Treatise published in 1872.

(4) Changes in the Thymus Gland.

In a case recorded by Lemp in 1857, in which the post mortem examination was performed by Virchow, it is noted that the Thymus gland was persistent, but no further particulars are given. The patient was aged 24 which is an unusual age for the thymus gland to be found still present. Wickham Legg reports persistence of it in a boy aged thirteen, but he does not relate any microscopic changes.

Dr Acland(26) gives an account of the only changes in the thymus gland which have as yet been reported. The patient was aged seven and died as the result of haemorrhage from a small wound of the tongue.

There were present in the thymus "rounded apparently spherical masses so large as to be readily visible to the naked eye. In some cases they were related to the corpuscles of Hassall and in others
surrounded a blood-vessel.

Microscopically they were surrounded by a layer of flattened elongated cells with well-defined nuclei. The fibrous tissue of the gland was much increased and the gland was large for a child of seven. That these changes must have some relation to haemorrhage or, in any case, to a morbid condition of the blood is evident from the fact that the same bodies were observable in a patient suffering from purpura, and in a number of glands from patients dying from other disease, no such morbid appearances could be observed.

(5) Changes in the blood.

The morbid appearances which have been quoted by one author after another and handed down from one treatise to another are that the blood after death is more watery, is pale, and has an excess of white blood corpuscles. Such changes, however, can be accounted for by the general mode of death, that is, haemorrhage.

Formerly it was considered that the blood did not coagulate, but this idea is now departed from. The various analysis of the composition of the blood by Ritter, Otto and Leconte throw practically no light on the pathology of the disease. The most important addition to our knowledge of the state of
the blood has been made by Professor Wright (27) of Netley. He has investigated the state of the blood in a patient aged 11 years suffering from haemophilia and finds the following changes.

(a) "Reduced number of white blood corpuscles."

He thus upsets the previous observations of others.

(b) "Diminished proportion of polynuclear leucocytes (54 per cent of the total number of leucocytes instead of 75 per cent.)"

(c) " Apparently altogether subnormal degree of coagulability (coagulation time 9 to 10 minutes instead of in normal blood 2 to 5 minutes or rarely 6 minutes.)"

The number of red corpuscles ranged from 4,280,000 to 5,200,000 or practically normal."

He tested the coagulability by finding out the time blood took to coagulate in carefully prepared graduated capillary tubes.

Pathology

We now approach the most difficult and at the same time the most interesting part of the subject, the pathology of the disease.

Various theories have been brought forward to account for the disease, and I shall briefly refer to those which were originally advanced, but which must now be discarded.
A number of observers, among whom are Nasse and Ricken, lay stress on the fact that it is closely allied to gout, but investigations shew no relationship between the two diseases.

Later the idea was propogated that it was an intermediate morbid condition between cyanosis and scrofula, but as no definition is given of these so-called diseases we are as much in the dark as ever.

Vogel considered that the cause of it might be a scorbutic state of the blood; there are certainly resemblances, but from a consideration of the various symptoms, this theory must be passed over. The more rational theories for which there is some foundation are very fully discussed by Legg and briefly may be summed up under the three following heads.

(1) That there is an alteration in the blood from its normal condition. Nasse maintained that there was an unnatural fluidity of the blood arising from a deficiency in the growth, so that it did not attain its full strength and consistence, the result being that coagulation with difficulty took place.

This theory of unnatural fluidity has recently been advanced again by Gavey and Prussak, but they hold that it is due to the presence of an alkaline salt. We shall see that probably Nasse was approaching the truth though he had not many data to come and go upon.
(2) The theories of others are that the disease is a nervous one depending on some alteration in the vasomotor centres whereby certain areas of the body become congested and haemorrhage occurs. For my part I can hardly see in what way this accords with all the symptoms and morbid conditions.

(3) Legg himself advances the views that there is in the disease an imperfect development of the whole vascular system, this being an advance from the theory of Nasse. This imperfect development leads to a liability of blood-vessels to rupture. He says that the occasional recovery from and disappearance of the disease may be explained on the grounds that as the vascular system is fully developed the disease disappears.

I think we must consider the disease to be one arising from

(1) a defective development of the blood-vessels which in many cases is not observable to the eye;

(2) a deficiency in the coagulability of the blood and as a consequence a grave want of relationship between the blood and blood-vessels. Woolridge says "The blood and the Vascular wall may be looked upon as a protoplasmic unit." This is practically Osler’s theory, to which conclusion I had come before reading his views; he says that "two circumstances combine in haemophilia - congenital
fragility of the vessels and a defect in coagulability of the blood; but whereon these depend we are as yet entirely ignorant." As regards the last phrase I hope to shew that we are not now so ignorant and that advances have been made within the last few years in our knowledge of the disease.

The disease therefore cannot be considered as a simple one arising from one cause, but one in which the whole vascular system is at fault; by the term vascular system I mean both blood and blood-vessels.

Although very few really important post mortem changes have been shewn, we must consider those described by Dr. Kidd as probably a type of the morbid condition of the blood-vessels which is partly the cause of the disease. Although such minute changes have been rarely described, there is an undoubted thinness of the blood-vessels and a consequent friability and liability to haemorrhage. There must also be, I think, a friability of both muscular and subcutaneous tissue, as the blood effused seems to plough up those tissues very readily.

The condition of the blood described by Professor Wright helps, I think, to throw light on the pathology of the disease. It has been shewn by Woolridge (28) in his "Chemistry of the blood" that coagulation of the blood is not necessarily caused by the action of a ferment resulting from breaking down of leucocytes, but may be due to an interaction and coagulation...
of the "fibrinogens" of the blood as he calls them. "The processes of coagulation are the result of the union in definite proportions of complex proteid-lecithin compounds." He shews that if extracts of the thymus and other glands be taken so that lecithin was retained in the extract and some of this "Tissue-fibrinogen" was injected into the blood, intravascular clotting was produced, this being the "positive phase" of coagulation as he called it.

If, however, a smaller quantity of such extract were introduced, there was produced an opposite effect namely the "negative phase." The blood in this latter condition was found when tested to be more fluid and coagulated less easily than before, in fact, as he said, there was produced "a temporary and mild sort of haemorrhagic diathesis."

Following from these experiments of Woolridge, may we not deduce that the condition of the blood is one of deficient growth in those "tissue-fibrinogens" which are a cause of the coagulation of the blood. This, coupled with the morbid condition of the vessel-wall, will account for the haemorrhage, for, the two, the vessel-wall and the blood may, as Woolridge says, be looked upon as a "protoplasmic unit," and if one is wrong both are.

The persistence of the thymus may be looked upon as a sign of the retarded development of the vascular
system and it may remain, simply because the blood and vessels have need of it. Woolridge has shewn that the probable composition of these "tissue-fibrinogens" is

<table>
<thead>
<tr>
<th>Substance</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumen</td>
<td>44%</td>
</tr>
<tr>
<td>Lecithin</td>
<td>4 or 5%</td>
</tr>
<tr>
<td>Salts</td>
<td>1 or 2%</td>
</tr>
</tbody>
</table>

The salts are calcium in character. Arthus and Pages have shewn that if the soluble calcium salts are removed from the blood by decalcifying them with oxalate of potash, the blood so decalcified remains fluid. Wright has brought out that by the administration of calcium chloride to a patient suffering from haemophilia the coagulability of blood is increased, but not brought up to the normal. If, however, we could introduce into the system a sufficient amount of these fibrinogen substances, we should be able to help to overcome the disease from the blood side, though not from the vascular.

The joint affection I think can be explained as simply being a manifestation of the general disease. The blood-vessels around the joint are ill-supported and are liable to injury from the amount of movement which takes place. Proof of this is shewn in the fact that the knee joint is the one most frequently affected as we may consider that it has more to do
than almost any other joint in the body. The pain and subsequent enlargement and stiffness of the joints is a secondary sequence to the haemorrhage into the joint cavity. The blood acts as a foreign body, causing thickening and all the changes which are similar to those of chronic rheumatic arthritis. This theory which I have formulated, agrees with that of Nasse and Legg and is a union of the two. It, however, carries us I think a few steps further on in advancing distinct pathological data as a cause of the disease. By it can be explained the occasional recovery of subjects from the disease, in that the glands, the thymus probably, go on functionating and so bring up the vascular system to its normal strength.

I cannot, however, advance any explanation as to why the disease should be handed down from males through females to males.
Diagnosis.

In the great majority of cases there is little difficulty in the diagnosis, as the symptoms are so evident and distinctive, the external haemorrhage, the subcutaneous haemorrhage and the joint swellings. In a few cases in which the disease is in a milder form, there may be a little difficulty, but the family history will as a rule guide one. The principal diseases which may at first be confounded with it are purpura in its different forms and scurvy, but the transitory nature of these conditions soon aids us.

Prógnosis.

The prognosis in all cases must be grave, as death as a rule takes place from haemorrhage at some time or other. No doubt a few patients have recovered from the disease, but that is a rare exception. Few people live after 21 years of age. Grandidier gives a list of 212 boys suffering from the disease and shews the ages at which death occurred.

<table>
<thead>
<tr>
<th>Within the 1st year</th>
<th>22 males</th>
<th>7 females</th>
</tr>
</thead>
<tbody>
<tr>
<td>From 1 to 7 years</td>
<td>89</td>
<td>3</td>
</tr>
<tr>
<td>&quot; 8 to 14 &quot;</td>
<td>39</td>
<td>1</td>
</tr>
<tr>
<td>&quot; 15 to 21 &quot;</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>&quot; 22 to 50 &quot;</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Over 50</td>
<td>6</td>
<td>-</td>
</tr>
</tbody>
</table>
In a series of cases reported by Dr Dunn there were 16 deaths, nine occurring before eight.

Legg says that out of a list of 152 patients only 19 lived to be 21. He quotes a number of cases in which there was an apparent disappearance of the disease, but in the majority of them there were always left one or two signs that the condition was not quite away; they might have slight swelling of joints or neuralgic pains throughout the body.

He says that there are only nine authentic cases of recovery. The longer a person lives, the greater chance he has of recovering or at least suffering from the disease in a less mild form. When external haemorrhage occurs the prognosis of course is much more grave, as it is with the greatest difficulty that the haemorrhage can be stemmed, and it is often only when the heart's action becomes very feeble that the haemorrhage ceases.

On the other hand, when subcutaneous haemorrhage takes place, the great pressure of the effused blood compresses and obliterates the surrounding vessels and so there is less likelihood of continuous oozing. I have noticed that when a large clot has been cleared out of a cavity formed by the mass of blood that there may be very little haemorrhage from the raw surface. The joint affection leads to enlargement and stiffening of those joints which are implicated, with impairment of their function, which,
however, is gradually restored in time if no subsequent attacks supervene.

Treatment.

In the treatment of this disease we must look at it from many points of view.

(1) Preventive.

In considering the preventive treatment, we are faced by a social problem of great importance, namely, the prevention of marriage in families in which the disease exists. It is our duty, as medical men, in this disease, as in many others, to dissuade, if possible, matrimony among both the male and female members of a family who may be afflicted with haemophilia. As an example of the efficacy of this means of prevention it is related (29) that among two families at Senna haemophilia had been known to exist for about a century. In 1855 the female members of the families resolved not to marry and in 1879 there were no well-marked cases of the disease in the community.

The patients should be taken great care of and not allowed to enter into boisterous games. School teachers should be warned not to strike them on any pretext whatever. The extraction of teeth should be avoided and all means whereby the skin might be broken should be prevented.

When manhood has been reached, the patient's
employment should be a sedentary one, one in which there is least liability to injury. If possible he should reside in a warm climate avoiding any damp region where there is a liability to rheumatic affections. The clothing should be warm, with flannel next the skin, but should not be excessive in amount. The diet should be light with plenty of fresh vegetables and varied in quality; alcoholic liquors should be avoided, especially if there are prodromata of haemorrhage. There is no doubt that haemorrhage seems to be more liable when the patient is at his best, so that too stimulating a regimen should not be insisted upon.

If there are any prodromata very often a saline purgative and free depletion do good.

(2) **Joint Affection.**

The patient should be enjoined rest for the swollen joint, light pressure with a bandage, and after the pain ceases, counter-irritation with tincture of Iodine. If the fluid is not rapidly absorbed, strapping with Scott's dressing is often efficacious.

(3) **Treatment of haemorrhage.**

As has been described, death may take place from haemorrhage from the slightest wound, which is an indication that the greatest difficulty may be experienced in stopping the haemorrhage.

If a patient receives a wound, absolute rest must
at once be enjoined. If possible pressure should be employed, but it must be remembered that if the compression be too great, additional haemorrhage may result into the surrounding tissues, and as a consequence extensive sloughing arise. All the known styptics have been employed in the disease and at one time or another some may have proved effective, but sometimes all fail. Probably the most efficacious is the actual cautery at a dull red heat. If epistaxis occurs, plugging of both anterior and posterior nares must be resorted to.

In bleeding from the gums Some recommends Matico leaves, while Ranger advises that plaster of Paris should be applied to the gums and the jaws kept in position by a bandage.

**Internal administration of medicine.**

In the subcutaneous forms of haemorrhage, as I have shewn, the bleeding ceases generally of its own accord, and as the pain is very severe, the only indication, till the haemorrhage ceases, is morphia administered hypodermically. I have found that hypodermic administration is much more satisfactory, as the haemorrhage and pain arise often very suddenly but the pain is easily subdued by small doses of morphia. I find that it is much safer injecting morphia into the swollen limb where oedema is present,
as there is less liability to haemorrhage at the point of puncture. On one occasion before adopting this method I caused extensive haemorrhage into the forearm.

I have administered Ergot and digitalis internally and have found them of little, if of any service. As a preventive and aperient Otto has recommended Sulphate of Soda, and Fordyce Sulphate of Magnesium. Legg has employed 30 to 40 minim doses of perchloride of Iron, and he maintains that by its use haemorrhage is prevented, and if a patient does suffer from it, it is of a less severe type. I myself, however, after an attack of haemorrhage, in order to cure the anaemia put a patient on the Compound Syrup of the Hypophosphites, and immediately afterwards he was seized with another severe haemorrhage into his limb, which I ascribed rightly or wrongly to the too rapid increase of his general strength and blood pressure.

Professor Chiene has recommended Iodide of Potash as a means of reducing the blood pressure and certainly in the case of W. O. he was practically free from haemorrhage for almost 10 years after he began and continued to take it.

Professor Wright has shewn that when Calcium Chloride was added to the extravascular blood of a patient suffering from haemophilia, the rate of coagulation was increased and he also found that when administered internally, the time of coagulability
was reduced by a half. Care had to be taken, how¬
ever, that the doses were not too large as the time
was very much increased if that was the case.

The principal indication in treatment, if the
time of the disease I have advanced holds good, is
to increase those "tissue-fibrinogens" of Woolridge
and of course along with them the lime salts, and by
that means we may attack the disease from the blood
side.

I believe that if we can bring up the blood to its
normal condition by the addition of these substances,
which help coagulation, and in which the blood is
apparently deficient, we may do much also to combat
the morbid state of the vessel-wall, and so amelior¬
ate to a certain extent, if not altogether, the un¬
fortunate condition of a patient suffering from the
disease.
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