

# COAGULOPATHIES

**A coagulopathy (bleeding disorder) may be inherited (a diathesis) or acquired.**

## RISK FACTORS

In virtually all cases of inherited bleeding abnormalities, both parents must be carriers in order for a person to be affected.

Any interference with the complex chain of clotting factors and cells may lead to an acquired coagulopathy.

## SYMPTOMS - HISTORY

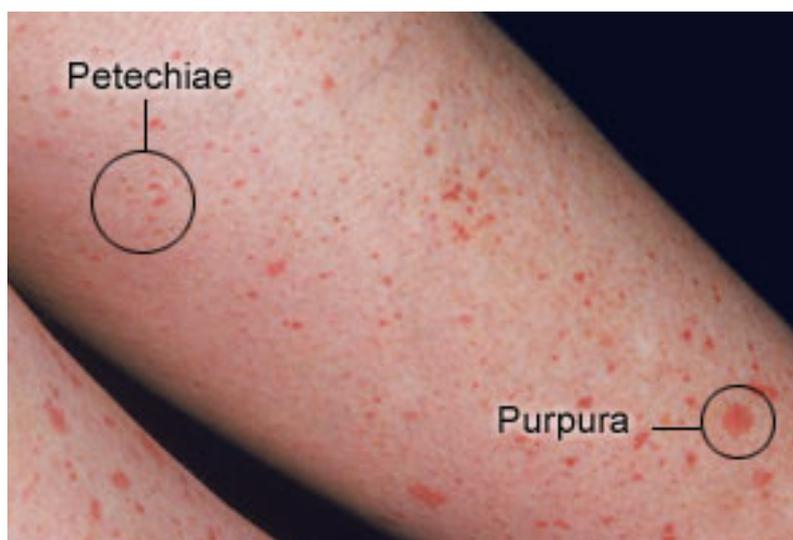
Those with a coagulopathy may :-

- bruise easily
- develop petechiae or purpura
- bleed for a prolonged time when cut
- develop painful joints
- become fatigued due to anaemia
- bleed into the intestine (melaena), lungs (haemoptysis) or genitourinary tract (haematuria).
- have excessively prolonged and heavy menstrual periods

## SIGNS - EXAMINATION

### PETECHIAE

Petechiae are tiny flat red spots that are scattered across the skin. They are caused by bleeding from capillaries in the skin, which occurs in diseases such as generalised viral infections, bleeding disorders (eg. thrombocytopenia), meningococcal infections, capillaritis and advanced typhoid fever.



### PURPURA

Purpura are small red or dark blue marks made in the skin by abnormal bleeding from capillaries. The most common cause is a low level of platelets in the blood (thrombocytopenia).

## BLEEDING DIATHESSES

### HESS TEST

A sphygmomanometer cuff inflated to 80 mmHg (10.6 kPa) around the upper arm for five minutes causes purpuric spots to appear below the cuff when the patient suffers from diseases associated with purpura (eg. thrombocytopenia, diseases of vascular endothelium, thromboasthenia, uraemia). Tests the resistance of capillaries to increased venous pressure. Obsolete test that should not be performed if more sophisticated tests for vascular disease available

## INVESTIGATIONS - PATHOLOGY

RI = Reference interval (normal result) Int = Interpretation Phys = physiology

### Screening tests include :-

#### Bleeding Time

RI: 1 - 7 minutes

Int: HIGH - Drugs (eg. aspirin, NSAIDs), thrombocytopenia, thromboasthenia (platelets?), haemophilia, Christmas disease, von Willebrand's disease, Bernard-Soulier syn., Glanzmann syn.

Phys: Normal with anticoagulant therapy (eg. heparin, warfarin). Measures platelet function.

#### Clotting Time

RI: < 10 minutes

Ind: Bleeding disorders

Int: HIGH - Anticoagulant therapy, lack of blood clotting factors

Phys: Covers intrinsic and common pathway from factor XII to fibrinogen. Screening test for bleeding disorders

#### Platelet Count, Blood

RI: 150-450 x 10<sup>9</sup>/L (150,000-450,000/mm<sup>3</sup>)

Int: HIGH (**thrombocytosis**) - Myelofibrosis, chronic leukaemia, polycythaemia rubra vera, essential thrombocythaemia, infection, trauma, post-splenectomy, strenuous exercise, labour of childbirth, familial

LOW NUMBER, NORMAL TYPE (**thrombocytopenia**) - Marrow suppression or infiltration, carcinoma, myeloma, cytotoxic drugs, infections, megaloblastic anaemia, SLE, acute leukaemia, disseminated intravascular coagulation, haemolytic-uraemic syn., massive transfusion, autoimmune diseases, hypersplenism, rheumatoid arthritis, Fanconi syn., HELLP syn., sticky platelet syn., Wiskott-Aldrich syn., alcohol, viral or bacterial infections (eg. rubella, infectious mononucleosis), idiopathic, congenital, post-transfusion, drugs (eg. quinidine, quinine, heparin, aurothiomalate, NSAIDs)

NORMAL NUMBER, ABNORMAL TYPE (**thromboasthenia**) - Glanzmann's disease

LOW NUMBER, ABNORMAL TYPE - May-Hegglin anomaly

Phys: Platelets are essential for blood clotting.

#### Fibrinogen, Blood (Factor 1)

RI: 2 - 6 g/L

Int: LOW - Defibrination syn., Waterhouse-Friderichsen syn., endotoxic shock, abruptio placentae, intrauterine fetal death, amniotic fluid embolism, disseminated intravascular coagulation

HIGH - Nephrotic syn., Hodgkin's disease, pemphigus, pulmonary embolism, pregnancy

Phys: Fibrinogen is involved in the first stage of the blood clotting cycle

#### Full Blood Count [FBC]

##### (Complete Blood Examination [CBE]; Full Blood Examination [FBE])

This includes the following investigations: Haemoglobin; White Cell Count; mean corpuscular volume (MCV); mean corpuscular haemoglobin (MCH); mean corpuscular haemoglobin concentration (MCHC); Haematocrit; Platelet Count; Red Cell Count

#### Activated Partial Thromboplastin Time, Plasma [APTT]

RI: Adult : 28 to 38 seconds

11-16 years : 31 to 44 seconds

6-10 years : 30 to 46 seconds

## BLEEDING DIATHESSES

1-5 years : 29 to 45 seconds

<1 year : 26 to 50 seconds

Int: HIGH - Heparin therapy, coagulopathy requiring further investigation

Phys: Nonspecific test measuring numerous factors except numbers VII and XIII

### **Prothrombin Time [PT]**

RI: 12-16 seconds

Therapeutic range 20-30 seconds on anticoagulant

Int: LONG - Lack of fibrinogen, prothrombin, factors V, X, or VII.

Liver disease, anticoagulant therapy, vit. K deficit

Phys: Tissue factor (brain extract), calcium chloride, and test plasma are incubated and compared to a control. The time for clotting is noted

### **Thrombin Clotting Time, Plasma**

RI: 10-15 seconds

Int: HIGH - Low fibrinogen levels, heparin therapy

## **Further detailed investigations may include :-**

### **Factor VIII, Blood**

RI: Very wide variation in normal levels. Assay of the molecular components of factor VIII (a and c) may give a more accurate diagnosis, but interpretation is difficult and false positives and negatives occur. Consult with haematologist

Int: LOW - Haemophilia, von Willebrand's disease. Diagnosis of these diseases and the carrier state may be determined with careful analysis. Increased in pregnancy.

### **von Willebrand Factor, Plasma (vWf)**

**(Ristocetin Cofactor; Collagen Binding Assay, von Willebrand Factor)**

RI: Variable

Int: von Willebrand's disease

Int: LOW - von Willebrand's disease

Phys: ELISA test, measuring qualitative and quantitative abnormalities of von Willebrand factor. Subtypes of disease can be identified by variables within test

### **Vitamin K, Serum**

**(Phytomenadione)**

RI: Refer to laboratory

Int: LOW - Malabsorption, cholestasis, small bowel diseases, haemorrhagic disease of newborn, dietary insufficiency, long term antibiotics

Phys: Lack of vitamin K causes excessive bleeding and bruising.

## **POSSIBLE CAUSES OF COAGULOPATHIES (ABNORMAL EXCESSIVE BLEEDING)**

### **BLEEDING DIATHESSES**

Haemophilia A (factor VIII deficiency)  
Haemophilia C (factor XI deficiency)  
Christmas disease (factor IX deficiency)  
von Willebrand's disease  
Other blood factor deficiencies  
Bernard-Soulier syndrome (inherited platelet defect)

### **ACQUIRED COAGULOPATHIES**

AIDS (splenomegaly, fever, cachexia)  
Aplastic anaemia (lassitude, pallor, purpura)  
Bacterial endocarditis (heart murmur, fever)  
Bone marrow suppression (may be iatrogenic)  
Cushing syndrome (moon face, obese, amenorrhoea)  
Defibrination syndrome  
Disseminated intravascular coagulation (rare, secondary to severe disease, clotting occurs within normal arteries and veins in one area of the body to deplete platelets and clotting factors)  
Following massive blood transfusions  
Glanzmann syndrome (mucocutaneous bleeding)  
Henoch-Schönlein syndrome (abdominal pain, excess bleeding)  
Hepatic failure  
Idiopathic thrombocytopenia (bruising, purpura)  
Insect and snake bite  
Ionising radiation (eg. X-rays, gamma rays)  
Leukaemia, acute (abnormal white cell count, malaise, arthralgia, fever)  
Meningococcal meningitis (fever, headache, vomiting)  
Meningococcal septicaemia  
Renal failure  
Scurvy (inflamed and bleeding gums)  
Subacute bacterial endocarditis  
Typhus (fever, malaise)  
Vitamin K deficit  
Waterhouse-Friderichsen syn. (petechiae, pallor)  
Drugs (eg. warfarin, heparin, aspirin, steroids, arsenic, quinine, chlorothiazide)

# BLEEDING DIATHESSES

**A diathesis is an inherited tendency towards a specific condition.**

There are some people who are born with defects in the chemical pathways that cause blood to clot, or who develop a lack of one of the essential elements for clotting, and become bleeders. Instead of stopping within a few minutes of an injury, bleeding may persist for hours, and the slightest injury may cause massive bruises, or bleeding into joints that leads to arthritis.

**The serious bleeding diatheses are X-linked and occur only in males**

## HAEMOPHILIA A

Haemophilia A is an inherited lack of factor VIII, one of the essential factors responsible for the clotting of blood. The gene for the disease is carried by women on the X chromosome, but can only affect men.

These people have excessive bleeding from a cut, severe bruising from a minor injury, bleeding into joints to cause arthritis, internal bleeding into the gut and other organs. The excessive bleeding may result in arthritis, infertility, damage to other organs from bleeding, chronic weakness, and a shorter than normal life span. Specific blood tests can confirm the diagnosis.

Injections of the missing coagulation factor must be given to prevent excessive bleeding when it occurs. Insufficient is available to be given regularly to prevent bleeding at present, but genetic technologies are likely to change this in the near future. The factor is obtained from blood donations at present. Recombinant factor VIII is available also, but in the future may be obtained from genetically modified pig milk. There is also some evidence that the use of the medicine desmopressin (which is normally used to treat bed wetting and diabetes insipidus) can increase the level of circulating factor VIII, but the mechanism for this is unknown.

The severity may vary from one patient to another and no permanent cure available. Statistically, half the children of a woman who carries the responsible gene will have the disease, but the overall incidence is only 1 in 10,000, which means there are about 1000 men in Australia with the condition.

## CHRISTMAS DISEASE

Christmas disease (factor IX deficit or haemophilia B) is named after the patient Stephen Christmas, who was a child with the disease. It is an inherited lack of factor IX, one of the essential factors responsible for the clotting of blood. The gene for the disease is carried by women on the X chromosome, but can only affect men (sex linked inheritance). Statistically, half the children of a woman who carries the responsible gene will have the disease. The incidence is one in 40,000 people.

Symptoms include excessive bleeding from a cut, severe bruising from a minor injury, bleeding into joints to cause arthritis, internal bleeding into the gut and other organs. Specific blood tests can confirm the diagnosis.

Injections of the missing coagulation factor are given to prevent excessive bleeding when it occurs. Insufficient supplies are available for it to be given regularly to prevent bleeding, as the factor can only be obtained from blood donations.

Arthritis, infertility, damage to other organs from bleeding, chronic weakness, and a shorter than normal life span may occur.

## HAEMOPHILIA C

Haemophilia C (Rosenthal syndrome) is an inherited form of haemophilia caused by a lack of factor XI, and found mainly in Ashkenazi Jews. It causes a minor degree of abnormal bleeding and bruising, heavy menstrual bleeding and excessive bleeding with surgical procedures and childbirth. It is not life threatening or nearly as severe as haemophilia A, and life expectancy is relatively normal.

## von WILLEBRAND DISEASE

Von Willebrand disease (vascular haemophilia) is an autosomal dominant inherited cause of prolonged bleeding that may be detected in as many as one in every one hundred people, but only one in every thousand people has significant symptoms. It affects both sexes. Patients lack the von Willebrand factor, a protein that mediates platelet adhesion.

There are six different types of the disease that vary in their severity depending on the level of vWF and factor VIII. Interestingly, it is less common in people with blood type O.

## BLEEDING DIATHESSES

Most cases are mild, and patients experience nose bleeds, heavy periods, bleeding gums and bleeding into the gut. Excessive bleeding also occurs with any cut or surgery, bleeding into joints may cause premature arthritis, and the condition is dramatically worsened by aspirin. The diagnosis is confirmed by appropriate blood tests (eg. bleeding time, von Willebrand factor).

No treatment is required in the majority of patients, but aspirin and NSAID (arthritis drugs) must be avoided. Iron supplements may be necessary for those who bleed regularly, and contact sports are not the best form of recreation. An injection of a blood extract that contains the missing factors is given before surgery and to those who experience excessive bleeding from a severe case of the disease. The long-term prognosis is excellent.

### **BERNARD-SOULIER SYNDROME**

The Bernard-Soulier syndrome is an uncommon inherited defect of platelets (blood cells essential for clotting), which fail to stick together to form a clot. Excessive bleeding occurs, particularly from mouth and nose. Bruises and red spots and patches under skin, particularly on feet. The condition is aggravated by aspirin.

Blood tests on platelet function and bleeding time are diagnostic.

Blood transfusions on a regular basis are the only treatment for this lifelong defect that may cause significant disability.

## ACQUIRED BLEEDING DISORDERS

### **APLASTIC ANAEMIA**

Aplastic anaemia is a rare, but extremely serious form of anaemia caused by a failure of the bone marrow and spleen to produce new red blood cells (erythrocytes). As old red blood cells die, they are not replaced, leading to a rapidly progressive and severe anaemia. Reasons for the failure of the blood cell production include poisons, toxins, insecticides, nuclear irradiation, severe viral infections and some drugs. In more than half the cases, no cause can be found.

In addition to the normal symptoms of anaemia of weakness, tiredness and pallor, these patients have a fever, bleeding into the skin, a rapid heart rate, and increased susceptibility to infection. Heart, lung and other organ failure may occur suddenly. It is diagnosed by examining a blood film under a microscope.

Repeated blood transfusion can keep the patient alive in the short term only, so any cause must be eliminated if it can be found. Steroid drugs and oxandrolone may control the condition, but the only effective long-term cure is a bone marrow transplant. The donor must be closely related to the patient, but cannot be one of the parents. Brothers and sisters are usually the best donors. The procedure involves taking a small amount of bone marrow from the pelvic bone or breastbone of the donor, and injecting it into the bone marrow of the patient. Unfortunately, rejection is a far greater problem with a bone marrow transplant than with other forms of transplant, and as a result, up to half the patients will eventually die from the condition.

### **DEFIBRINATION SYNDROME**

The defibrination syndrome is an uncommon life threatening abnormality of blood clotting.

It may be caused by a very severe infection, or shock after an accident may cause inappropriate blood clotting within arteries and veins. This causes the level of fibrinogen in the blood to drop to a low level. Fibrinogen is essential for the clotting of blood, so patients with this critical problem then start to bleed profusely. Rarely it may follow childbirth.

After suffering excessive internal clotting which may affect their brain, heart, lungs, limbs and other organs, patients start to bleed excessively internally (eg. into the gut and kidney), externally (eg. intractable nose bleeds) and into the skin (eg. massive bruises). The condition can be diagnosed by specific blood tests.

Treatment involves the rapid transfusion of freshly donated compatible blood and other blood concentrates to stop bleeding, heparin given intravenously to stop abnormal clotting, and treating the underlying cause of the syndrome if possible. Unfortunately, permanent organ damage is common in the few survivors.

### **DISSEMINATED INTRAVASCULAR COAGULATION**

Disseminated intravascular coagulation (DIC) is a rare and horrendous blood reaction to many different types of severe disease (eg. septicaemia, cancer). Excessive blood clotting occurs within normal arteries and veins in one area, which uses up all the available blood clotting factors in the body, so that excessive bleeding occurs elsewhere.

The blood supply to an organ (eg. kidney, liver, brain), finger or limb may be cut off partially or completely to cause loss of function, gangrene or scarring. This is followed by severe and damaging bleeding internally to other

## BLEEDING DIATHESSES

organs, externally into the skin and from most body openings.

The diagnosis can be confirmed by specific blood tests.

Transfusion of fresh blood to replace lost clotting factors is the only treatment. Amputation of affected fingers, toes, or limbs may be necessary, and permanent organ (eg. stroke if brain affected) or limb damage is probable.

Sudden death occurs in severe cases, and most survivors are damaged in some way.

### HENOCH-SCHÖNLEIN SYNDROME

The Henoch-Schönlein syndrome (anaphylactoid purpura) is a generalised inflammation of small blood vessels resulting in the formation of small red spots in the skin (Henoch-Schönlein purpura). It may be a complication of a number of different diseases (eg. after a *Streptococcal* bacteria infection), but its cause is often unknown, although it is more common in children.

Small, slightly raised dilated blood vessels (purpura) appear on the skin as red or purple patches about five to ten millimetres across. There may also be bleeding into the skin, intestine, lungs, kidneys and joints to cause belly pain, coughing of blood, blood in the urine and arthritis.



HENOCH-SCHÖNLEIN SYNDROME

It is diagnosed by biopsy of one of the purpura in the skin, but no treatment is normally necessary as the condition is self-limiting and usually settles without serious long-term problems in one to six weeks. If the kidneys become involved medical treatment is necessary, as long-term kidney damage may occur.

Eduard Henoch (182-1910) and Johannes Schönlein (1793-1864) were German physicians.

### MENINGOCOCCAL MENINGITIS

Meningococcal meningitis is an uncommon, serious bacterial infection of the meninges (membranes around the brain) and blood stream (septicaemia). Sporadic outbreaks occur worldwide, usually in winter, but up to 40% of the population carry the responsible bacteria in their nose and throat without any symptoms. Infection is more common in closed communities such as military camps and boarding schools. It affects about one person in every 100,000 every year.

The infection is caused by the bacteria *Neisseria meningitidis*, which occur in 5 common strains, and several dozen uncommon strains. The C strain is the most serious, while strains M, W and Y are probably next in severity, but this varies between patients. It is spread by prolonged close contact with a person who has the disease by inhaling their sputum or phlegm in coughs and sneezes.

Symptoms include a high fever, severe headache, vomiting, neck and back stiffness, limb pains, confusion, convulsions and a rapidly spreading bruise like rash that starts on the arms and legs. The rash does not go white with pressure under a glass slide, a symptom that is critical in differentiating Meningococcal infections from other rashes, although there are some other infective rashes that do the same thing. In terminal stages the patient becomes delirious, and goes into a coma. Rarely, abscesses may form in the brain, and pneumonia may develop.

Cultures of blood and/or spinal fluid from the lower back can confirm the presence of the responsible bacteria, then penicillin, or more potent antibiotics, are given by injection as soon as the diagnosis is suspected. The patient should be admitted to hospital for confirmation of the diagnosis, and continuation of antibiotics given through a drip into a vein. Life support in an intensive care unit may be necessary. The infection may be rapidly progressive

## BLEEDING DIATHESSES

causing death within hours, but overall 80 to 90% of all cases survive, with only 5% of survivors developing long-term consequences such as epilepsy.

Two vaccines are available. One is against strain C only, but lasts long-term, the other prevents four strains of the bacteria, but lasts for only two years. The former can be given to infants, and is now part of most routine vaccination schedules. This form of meningitis is particularly common in the Sahel region of Africa (South of the Sahara Desert) and travellers to this region should consider vaccination.

### THROMBOCYTOPENIA

Thrombocytopenia (idiopathic thrombocytopenic purpura) is a complex uncommon condition due to a lack of platelets (also known as thrombocytes), the blood cells that are responsible for controlling the rate at which blood clots. In children the condition often follows a viral illness and settles quickly, but in adults it is usually an autoimmune condition (body rejects its own cells) in which platelets are inappropriately destroyed by the spleen for no apparent reason. It can also occur as a result of adverse drug reactions, infections and other rare disorders.

Patients are unable to clot their blood as quickly as normal, and they bleed excessively. They develop purpura across a wide area, bleed internally to cause melena, have nosebleeds that are difficult to stop, may vomit and cough blood, bruise very easily, bleed around their teeth after eating and may bleed very heavily during a menstrual period. Bleeding into the brain may cause a stroke, or very rarely, death. The diagnosis is confirmed by a simple blood test.

In some children, rest and time are the only necessary treatments. In all adults and most children, high doses of prednisone are given to settle the condition and allow more platelets to be made in the bone marrow. Immunoglobulin injections may also be used. As the spleen is the organ destroying the platelets, surgical removal of this can cure the disease in resistant cases. Other exotic medications may be used in severe cases.

The disease may last for a long time in adults, but the vast majority of patients respond well to treatment, although there are significant dangers before the patient presents to a doctor and in the first few days of treatment. It may occasionally recur in adults, but rarely in children.

An inherited form of thrombocytopenia is also known in which the low platelet count is found in numerous family members. These people have a low platelet count, usually between 80 and 110 x 10<sup>9</sup>/L (normal is 150 to 450 x 10<sup>9</sup>/L), but have minimal problems with abnormal bleeding or bruising.

### WATERHOUSE-FRIDERICHSEN SYNDROME

Waterhouse-Friderichsen syndrome (fulminant meningococcaemia) is a catastrophic infection of the adrenal glands, which sit on top of each kidney and secrete steroids to sustain the body. It is caused by a severe *Meningococcal* bacterial infection, which causes bleeding into both adrenal glands, destroying them and causing an acute Addisonian crisis.

The patient collapses, and develops bleeding into and under the skin, a blue tinge to skin around the mouth, and a pale complexion. This is followed by coma, heart failure and death. A blood culture can identify the bacteria responsible and blood tests show numerous body chemistry abnormalities.

Immediate treatment is critically urgent. Large doses of antibiotics are given by a drip into a vein, followed by hydrocortisone injections and fluids into the drip.

The prognosis is poor. Death may occur within a few hours, and even in patients who survive, permanent Addison disease, brain or heart damage may occur.

Rupert Waterhouse (1873-1958) was a British physician and Carl Friderichsen (b. 1886) was a Danish physician.

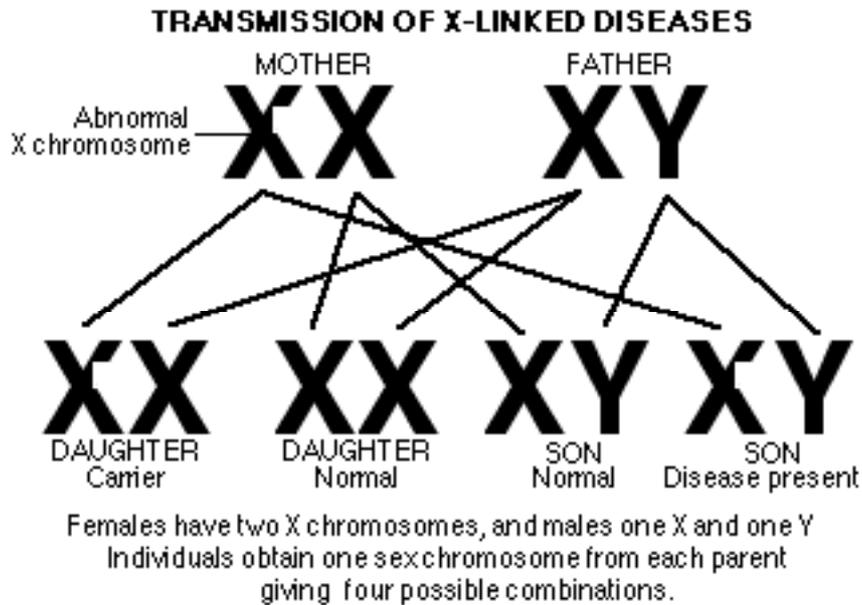
## USELESS INFORMATION

*The adrenal glands change size throughout life. The adrenal glands are responsible for releasing stress hormones like cortisol and adrenaline. In the seventh month of a foetus' development, the glands are roughly the same size as the kidneys. At birth, the glands have shrunk slightly and will continue to do so throughout life. By the time a person reaches old age, the glands are so small they can hardly be seen.*

## ADDITIONAL INFORMATION

### X-LINKED CONDITION

Women have two X chromosomes, while men have one X chromosome and a much smaller Y chromosome. If one X chromosome is defective, in women the other X chromosome can compensate. In males this compensation cannot occur, so there are a number of X-linked inherited conditions that only affect males. Statistically one half of sons will have the disease and one half of daughters will be carriers.



### FACTOR

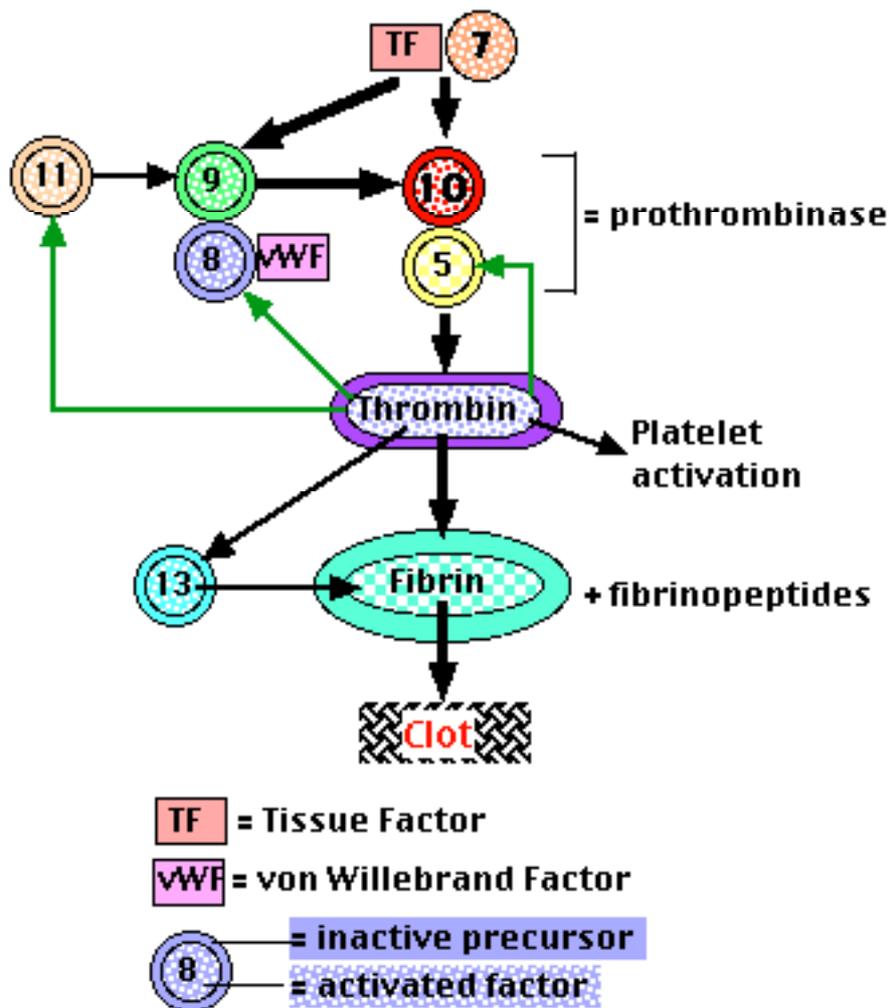
The factors within blood are any one of the 13 substances that allows the process of blood clotting to occur. They include:-

- Factor I - fibrinogen
- Factor II - prothrombin
- Factor III - thromboplastin
- Factor IV - the calcium used in blood clot formation
- Factor V - converts prothrombin to thrombin
- Factor VI - an as yet unidentified but essential component in the clotting process
- Factor VII - proconvertin
- Factor VIII - a compound factor made from two components. The lack of one causes von Willebrand disease, while a lack of the other is responsible for haemophilia A
- Factor IX - a deficiency causes Christmas disease (haemophilia B).
- Factor X - thrombokinasase or the Stuart-Prower factor.
- Factor XI - a deficiency causes haemophilia C
- Factor XII - activation factor or Hageman factor
- Factor XIII - fibrinase.

## BLEEDING DIATHESSES

### The Clotting Process

- \* Damaged cells display a surface protein called tissue factor (TF)
- \* Tissue factor binds to activated Factor 7.
- \* The TF-7 heterodimer is a protease with two substrates:
  - o Factor 10 and
  - o Factor 9
  - o Let's follow Factor 10 first.
- \* Factor 10 binds and activates Factor 5. This heterodimer is called prothrombinase because it is a protease that converts prothrombin (also known as Factor II) to thrombin.
- \* Thrombin has several different activities. Two of them are:
  - o proteolytic cleavage of fibrinogen (aka "Factor I") to form:
    - + soluble molecules of fibrin and a collection of small
    - + fibrinopeptides
  - o activation of Factor 13 which forms covalent bonds between the soluble fibrin molecules converting them into an insoluble meshwork — the clot.



## CURIOSITY

### **SCURVY**

*Scurvy was the scourge of sailors on long voyages over two centuries ago, when fresh food supplies could not be relied upon. The cause is a lack of ascorbic acid (vitamin C) in the diet, and it may occur in people on unusual fad diets or in malnourished alcoholics. Captain James Cook made a name for himself early in his career by insisting that all his crew had rations of lime juice (which contains high levels of vitamin C) every day.*

*In early stages patients develop vague tiredness and weakness. As the vitamin deficiency becomes more severe, **bleeding** into the skin, rashes, **bleeding** gums, joint pain and **bleeding** into joints, slow wound healing and tender bones are experienced. The patient becomes severely anaemic, and **bleeds** readily. In advanced cases the kidneys fail, the body swells, **bleeding** occurs in the brain, and death follows.*

## TOTALLY, COMPLETELY AND UTTERLY USELESS INFORMATION

*The application of a quantity of cobweb may be resorted to in stopping the bleeding of obstinate cuts.*

Assoc. Prof. Warwick Carter  
[wcarter@medwords.com.au](mailto:wcarter@medwords.com.au)

# BLEEDING DIATHESSES

