1.0. Aims

- To understand the nature and factors influencing formation of thrombus in blood vessels.
- To explore the outcomes of thrombosis such as recanalization and embolism.
- To recognise the appearances of infarction in lung and heart.
- To recognise the appearances of an atherosclerotic plaque.
- To practice writing descriptive and interpretative reports on previously unseen histological sections, concluding with identification of the pathological process.

2.0. Thrombosis

**Thrombus** is a mass, formed inappropriately, within the circulation from the normal constituents of blood. It consists of fibrin and aggregates of platelets; both formed through the activation of the blood coagulation cascade, together with entrapped leukocytes and red blood cells. Thrombus is formed in flowing blood. It may be distinguished from blood that has solidified after death, which is referred to as blood clot.

**Thrombus** has a firm texture and a non-shiny surface, which is usually grey and rough or even ridged. A piece of thrombus may break off and be carried through the circulation to impact in a vessel at a distant site. This is known as an embolism. The mobile fragment of thrombus is one type of embolus. Any thrombus within a blood vessel is soon invaded by macrophages, endothelium and smooth muscle cells and organisation occurs. With time, new channels form within the thrombus, allowing blood flow to continue – this is called recanalisation.

Recent thrombi contain the following:

- **fibrin** – delicate fibrils
- **platelets** – granular masses
- **white blood cells** – often degenerating
- **red blood cells** – passively entrapped

2.1. Veins: thrombosis

**NDP Image:** 21.1: 67.27  
**Glass Slide:** 21.1: 67.27  
**Image Maps:** A_VA_TI_VN_16; A_VA_TI_VN_08; A_VA_TI_VN_10

In the veins, thrombi with different appearances can be seen. The oldest thrombus has endothelium over the surface and is penetrated by new channels. More recent thrombus retains its laminated structure. The laminated structure of the recent thrombus is composed of alternating zones of deeper pink red blood cells and paler pink platelet aggregates with fibrin strands. White blood cells are caught up in the thrombus, often concentrated at the margins of the zones.
This slide is from a 31-year-old woman who died one month after receiving a renal transplant. This vein was close to an abscess in the renal pelvis.

Q1 Why do you think the endothelium did not act in its usual anti-thrombotic manner in this case?

Q2 What are the risk factors for thrombosis? Can you explain at a cellular / molecular level how each risk factor operates.

2.2. Femoral vein: Recent thrombus (Trichrome stain)

**NDP Image:** 21.2: 27.22  
**Glass Slide:** 21.2: 27.22

Platelets are not easily distinguished in the H&E section but appear as tiny grey-blue granules, contrasting with the scarlet fibrin in the trichrome stain. (Collagen is blue and red cells may appear yellow to orange)

3.0. Embolism – Venous thrombo-emboli: pulmonary embolus causing pulmonary infarction

Here is a clinical history that is typical of a pulmonary embolus of venous origin:

An obese, 64 year old lady became suddenly short of breath while walking to the hospital entrance for a cigarette, 8 days after surgery for appendicitis. Within minutes, she had collapsed and could not be resuscitated.

There is a photograph P21.1 on the bench, of this lady’s lung at post mortem (compare to CR8: 70.16A normal lung).
Q3 Where did the original thrombosis occur? What course did this thrombo-embolus take to reach the lady’s lung?

Q4 Why did this lady die within minutes of the onset of symptoms?

4.0. Lung: pulmonary infarction

NDP Image: 21.3: 80.871
Glass Slide: 21.3: 80.871
Image Maps: A_VA_IF_LU_11; A_VA_IF_LU_12; A_VA_IF_LU_13; A_VA_IF_LU_14

Look at section 21.3, which is a section of lung tissue taken at post mortem. Can you see a red zone in the lung tissue, compared to the section of normal lung? This main histological feature is due to severe haemorrhage into the alveoli (alveoli filled with red blood cells). Examine the alveolar walls within this red area – can you see evidence of karyolysis indicating necrotic cell death in a zone of infarction? Some of the alveolar epithelial cells have begun to take on a ghost-like appearance due to this necrosis, although the overall architecture of the tissue is preserved. Inflammatory cells, particularly neutrophils are beginning to invade the infarcted tissue. Pleurisy (inflammation of the overlying pleura) is also visible on some sections. Look at the large pulmonary arterial vessels adjacent to the red area – are any of them blocked by thrombo-embolus? Necrosis and inflammation could not occur within a few minutes of the embolic event. Therefore this section is from an earlier event, in which a pulmonary embolus occurred about 24-48 hours prior to death.

Q5 Why does haemorrhage occur into the tissue, given that the pulmonary artery is occluded?

Q6 What risk factors does this lady have for pulmonary thrombo-embolism?

Large pulmonary emboli that block the main pulmonary arteries are a common cause of death in hospital patients and are thought to occur in up to 30 – 65 % of trauma and burns patients. Although large emboli can be fatal, medium-sized emboli usually cause pulmonary infarction (as in this slide), and small emboli may not cause infarction (and may be lysed by fibrinolysis) and thus are often not detected and are probably clinically insignificant.

5.0. Arterial thrombo-emboli causing infarction

As well as arising in veins, thrombo-emboli may also arise in the heart or arterial system. These can then travel through the arteries and eventually lodge in arterial vessel and occlude the vascular supply to the relevant organ, causing ischaemia (functional impairment due to low blood flow) or infarction (zones of continuous necrotic cell death due to hypoxia from very low blood flow or its complete obstruction). One of the commonest sites of arterial thrombus formation is over atherosclerotic plaques – atherosclerosis will be dealt with in more detail in the next practical (PSE). In essence, an abnormal collection of fatty material builds up in the wall of an artery to form a “plaque”. This plaque has a fibrous covering (the “fibrous cap”) which is prone to rupture. At the site of rupture there is exposure of fibrous tissue and fatty material that excites thrombus formation. If a large enough thrombus
forms over the ruptured plaque, it can block the lumen, preventing blood flow, leading to infarction of the zone of heart muscle that was previously supplied by that artery – called a myocardial infarction. Sometimes, rupture of the plaque can release the fatty material into the artery lumen. This fatty material can then flow down the artery as an embolus until it reaches an artery with a small calibre lumen and block it, causing an infarction.

5.1. Infarction - Heart: Myocardial Infarction

NDP Image: 21.4: 67.640
Glass Slide: 21.4: 67.640
Image Maps: A_VA_IF_HT_63; A_VA_IF_HT_68; A_VA_IF_HT_69

This is a slide of myocardium taken at post mortem from a 57 year old, obese, male smoker with high blood levels of lipids and high blood pressure who died 3 days after the onset of severe crushing chest pain. The myocytes have lost their characteristic striations and many are eosinophilic, due to coagulative necrosis of the proteins within them, increasing the uptake of eosin. Some nuclei exhibit karyolysis (fading of the nuclei) and karyorrhexis (nuclear disintegration). Many nuclei have already disappeared. Infiltration with neutrophils can be seen, indicating that the necrotic cells have released signals initiating acute inflammation. On the pericardial surface there is fibrin formation (pink strands of protein) as part of the acute inflammatory response (fibrinous pericarditis). At the endocardial surface there is thrombus formation (platelets, fibrin and entrapped red blood cells) on the ventricular wall (called a mural thrombus), due to release of pro-thrombotic factors by the necrotic tissue. Therefore this section shows the microscopic appearances of the myocardium 72 hours after an acute myocardial infarction.

Q7 Name the 2 pathological processes that are the most likely to have caused this infarct and in which blood vessel have they occurred?

Q8 What further complications may follow from the development of endocardial (mural) thrombosis over the site of a myocardial infarct?

Museum specimen P88.001 shows a normal heart from an 18 year old girl, (heart weight 210 g); longitudinal section

Museum specimen P80.825 also shows a normal heart

Museum specimen P86.752 shows a recent infarct from a 72 year old woman with a history of hypertension (heart weight 546g). Dilated and hypertrophied left ventricle with a posterior, recent infarct (yellow with dark red rim). Around its edges, grey patches indicate where organization is taking place. A shrunken scarred area in the lateral wall is the site of a previous, healed infarct.

Museum specimen P79.766 is from a 71 year old man, breathless and unwell on the day before he died. The pericardial sac was distended by about 400 ml of fluid blood and clot: the heart weighed 448g. An old infarct in the lateral wall of the left ventricle and a recent posterior infarct near the septum can be seen. It is not easy to distinguish but the myocardium is thin and disrupted.
Museum specimen P59.442 shows an aneurysm: The thin stretched fibrous scar of a healed infarct forms an aneurysmal dilatation filled by laminated thrombus. Some old fibrous pericardial adhesions are present.

Museum specimen P63.468 shows a kidney infarction in a man of 70 with hypertensive heart failure and thrombi in the atrial appendages. The kidney contains arterial emboli and wedge shaped infarcts, (reflecting vascular distribution).

6.0. Atherosclerosis

Aorta Atherosclerotic plaque: NDP Image: 21.5: 85.512
Aorta Atherosclerosis: NDP Image: 21.5: 85.75 (Coronary Atherosclerosis)
For comparison - Normal Aorta: NDP Image: 21.5: 80.517

The aorta is an elastic artery with 3 layers: tunica intima (inner layer in contact with blood in the lumen), tunica media (middle layer containing smooth muscle cells and elastic fibres), and tunica adventitia (outer layer composed of supporting fibroconnective tissue with capillaries and nerves). The 3 layers are separated by 2 elastic laminae. In H&E sections, the elastic laminae appear pink and usually have a wavy appearance. The intima is the innermost layer and lies between the inner elastic lamina and the endothelium and it is here where atherosclerotic plaques develop.

The process of atherosclerosis leads to formation of atherosclerotic plaques, which have a fibrous cap overlying a soft centre, composed of lipid and necrotic material forming a lipid pool (the fibrous cap and the lipid pool are the 2 main features to identify in this section). The lipid pool forms within the plaque, usually as a clear central area, which originally contained necrotic tissue and lipid, (the latter dissolved out during the processing of the tissue). This lipid-rich central necrotic material contains many cholesterol clefts (crystal-like formations of cholesterol that dissolve out during tissue processing leaving cleft-shaped holes behind).

Macrophages are present within the plaque, usually in the shoulders (where the fibrous cap meets the aortic wall) and their cytoplasm is filled with many lipid-laden vacuoles. These appear after tissue processing as clusters of clear bubbles, hence the descriptive term “foam cells”.

Q9 Which cells secrete the fibrous connective tissue in the fibrous cap of the atherosclerotic plaque?

Q10 Where does the extracellular lipid in the lipid pool come from?
7.0. Section for reporting and pathological process identification and description

Calf veins

NDP Image: 21.6: 54.354
Glass Slide: 21.6: 54.354

This is a cross section of veins and an artery within the calf muscles, from a 73-year-old man who developed swelling of the leg after a bladder operation.

Please write a report along the usual lines:

(1) Diagram (labelled)
(2) Description
(3) Interpretation – concluding with identification of the pathological process.

Show your report to a demonstrator

8.0. Words used

Infarction = stuffed (Latin) (as in lung infarct stuffed with haemorrhage).