Haemorrhagic fever (Dengue Fever)

Histopathological effects of haemorrhagic fever

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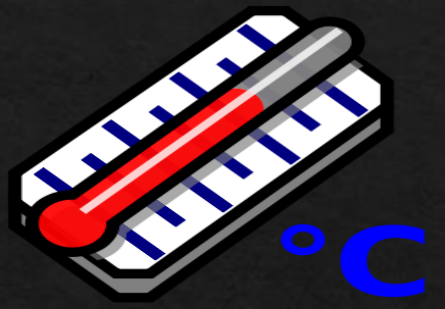
- Most people with Dengue virus infection remain asymptomatic or develop only very minor symptoms.
- Only about 25% of the people infected experience a self-limited febrile illness, accompanied by mild to moderate haematological and biochemical abnormalities.
- Clinically relevant complications develop in a small proportion of the patients, which include a systemic vascular leak syndrome, coagulation abnormalities that can be **associated with bleeding, and organ involvement, typically hepatic or neurological.**

Clinical phases

- After an incubation period of 4-7 days (maximum 14 days), symptoms typically begin abruptly and follow three phases.
- Febrile phase
- Critical phase
- Recovery phase

Febrile phase



- It begins with sudden onset of high fever and chills – typically persistent or unremitting although a saddle back pattern can be observed. Fever lasts for 3-7 days from illness onset.
- Systemic symptoms such as headache, malaise, retro-orbital pain, arthralgia, myalgia, bone pain, nausea, vomiting and altered taste sensation.
- Examination findings can include rash, flush, conjunctival or pharyngeal injection, mild bleeding manifestations, generalised lymphadenopathy and a palpable liver.

Critical phase

- Develops around the time of defervesence during which various complications occur . The various complications include:

- **Vascular leak syndrome** – Characterised by increased vascular permeability, plasma leakage and intravascular volume depletion which can progress to life threatening dengue shock syndrome. Plasma leakage can lead to hypoproteinaemia and serosal effusions.

- **Bleeding** – Minor bleeding is common – eg: skin petechiae, easy bruising, gingival, GI or PV bleeding – but not universal. Patients also have intrinsically lower platelet counts increasing the risk of bleeding with dengue.
- **Liver impairment** – Hepatomegaly and liver dysfunction are very common but rarely clinically important. AST titres typically exceed ALT titres.
- **CNS impairment** – Seizures, encephalitis, neuropathies , Guillain-Barre syndrome and transverse myelitis have all been reported.

- **Cardiac impairment** – Sinus bradycardia and minor or asymptomatic arrythmias are common.

- **Eye impairment** - Ocular manifestations include retinal haemorrhages, retinal oedema, macular ischaemia and optic neuritis. Patients usually complain of painless visual impairment, often around the time of platelet nadir.

- **Impairment of other organs** – Microscopic haematuria has been noted in 20-30% of patients with dengue. Renal failure is seen in profound DSS or in association with rhabdomyolysis.

Histopathologic findings

Dengue infection can cause a wide spectrum of presentations extending from simple self-limiting febrile illness to severe dengue, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Dengue associated **hemophagocytic lymphohistiocytosis (HLH)** is a rare, life-threatening condition

characterized by the uncontrolled activation of macrophages and T cells, eliciting clusters of symptoms and signs and abnormal biochemical parameters.

On microscopic examination studies , histological changes were seen in the liver , lungs, spleen, brain , kidney and heart.

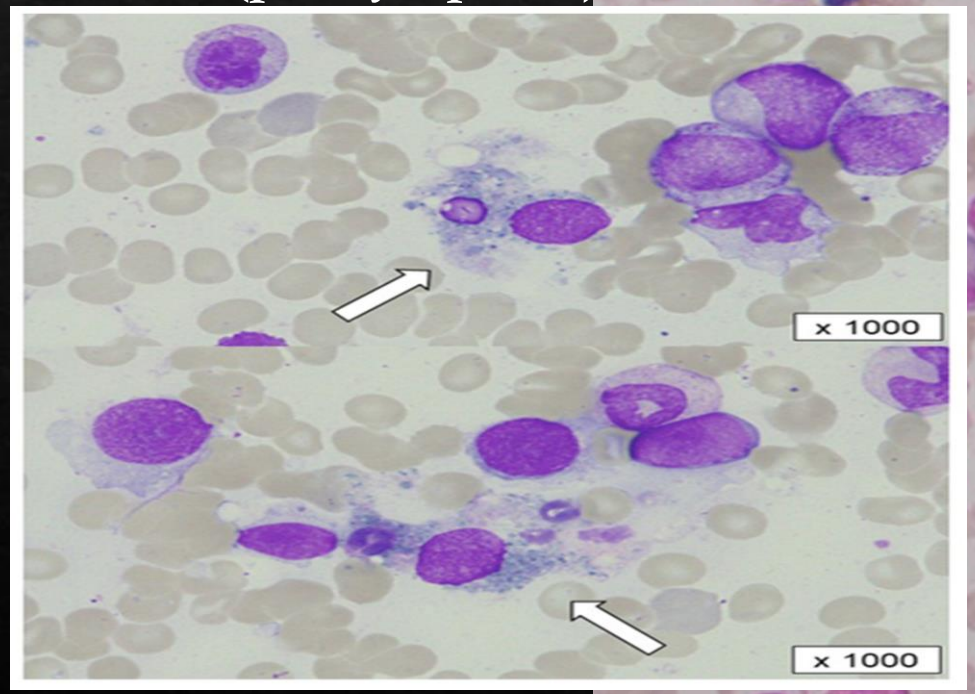
The liver was the most commonly affected organ (Figures). 77% cases showed a liver pathology .

❖ Blood

HLH is a rare but leth

HLH as a possible co

counts (pancytopenia)



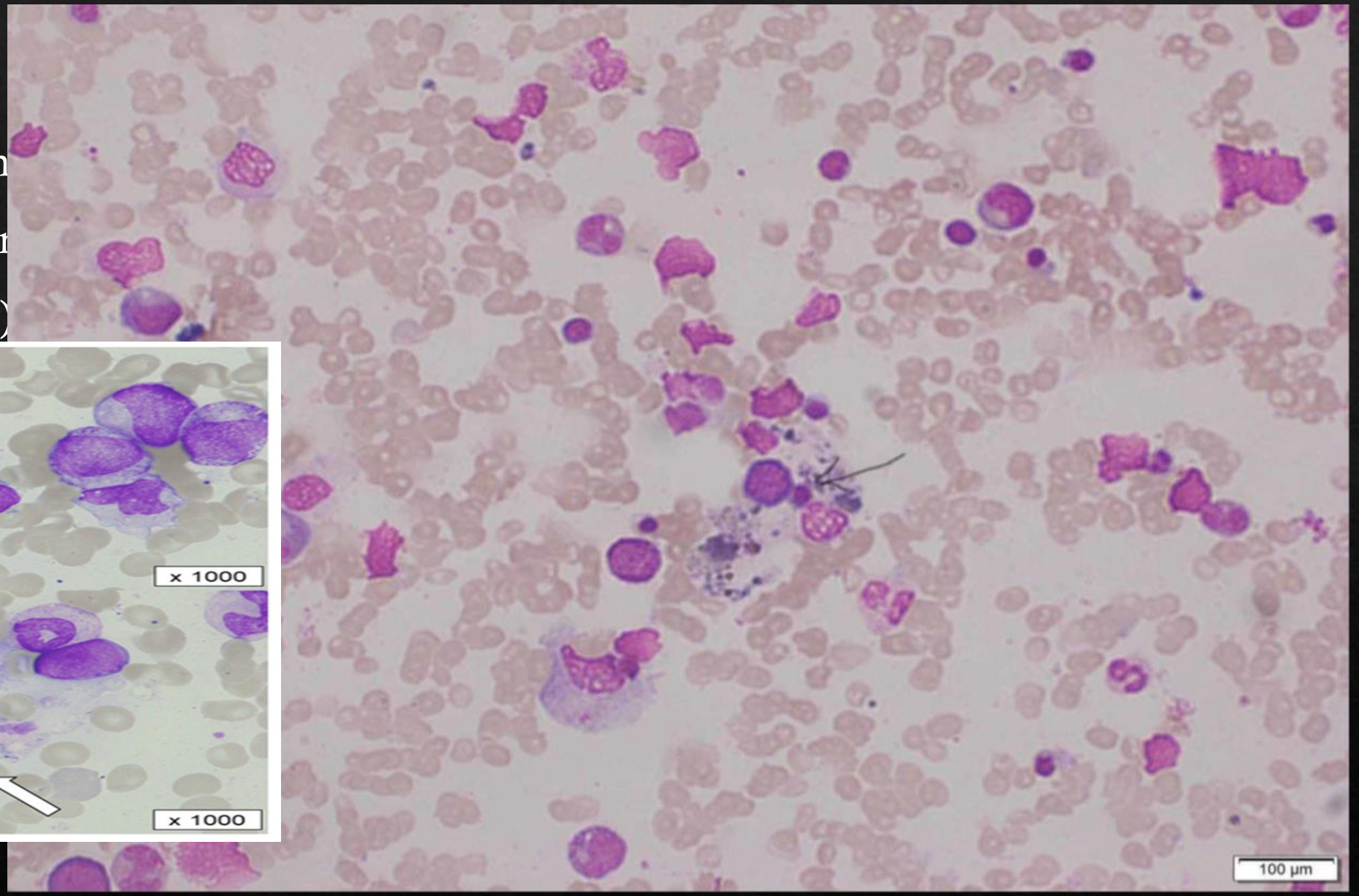
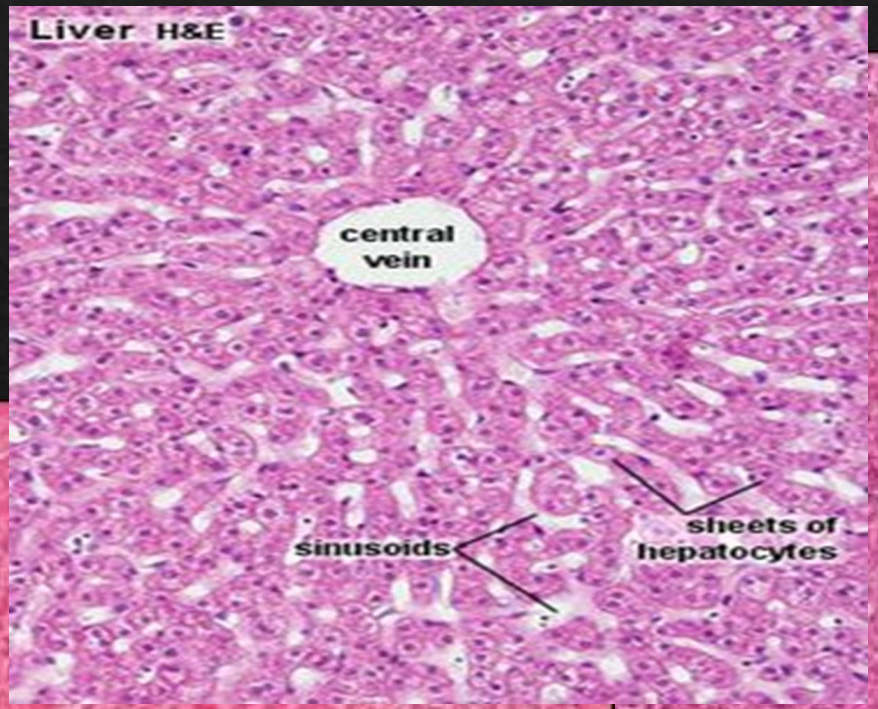
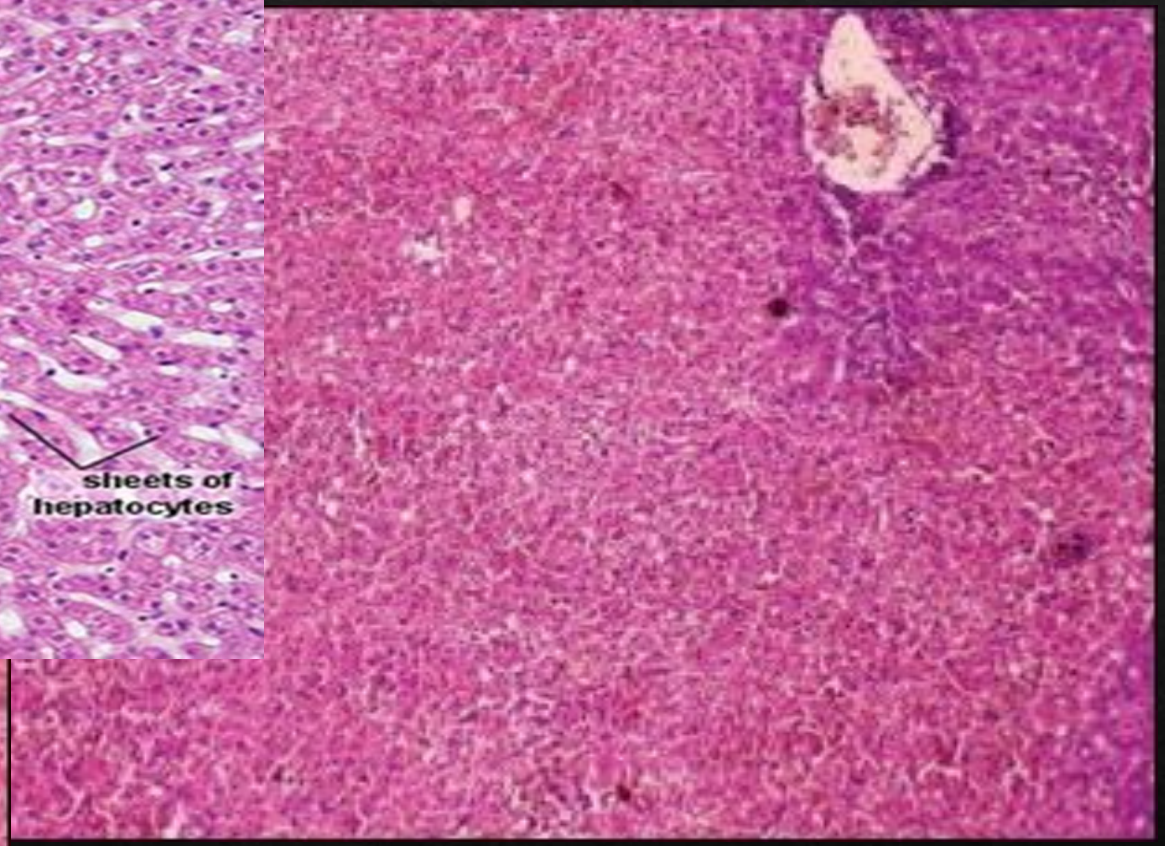


Figure 1: Bone marrow aspirate showing macrophage with marked hemophagocytic activity (arrowhead)

Liver

- Submassive necrosis
- Bridging necrosis
- Centrilobular necrosis





2. Liver- Submassive necrosis. (H&Ex100) 42 years. gue PCR positive

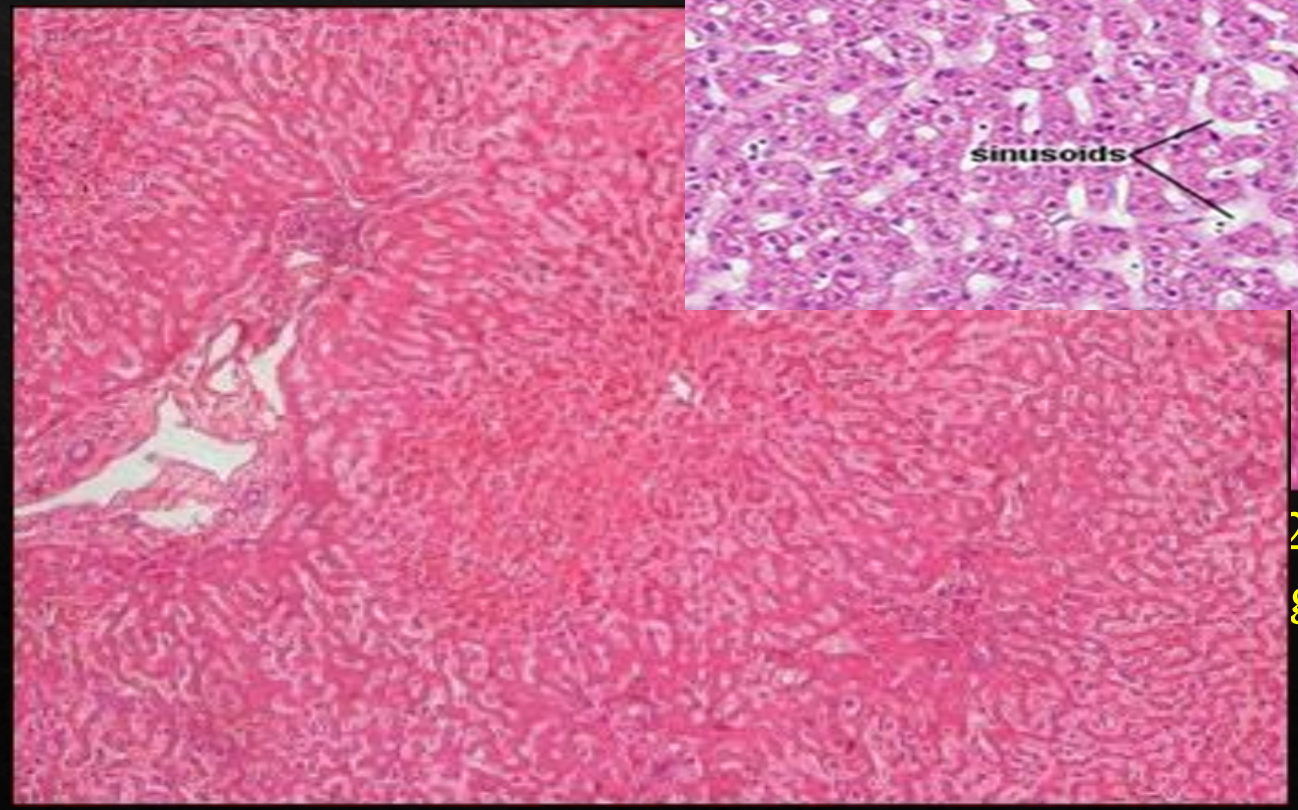


Figure 3. Liver-Centrilobular necrosis (arrow) (H&Ex100) 7 years. Dengue IgM positive.

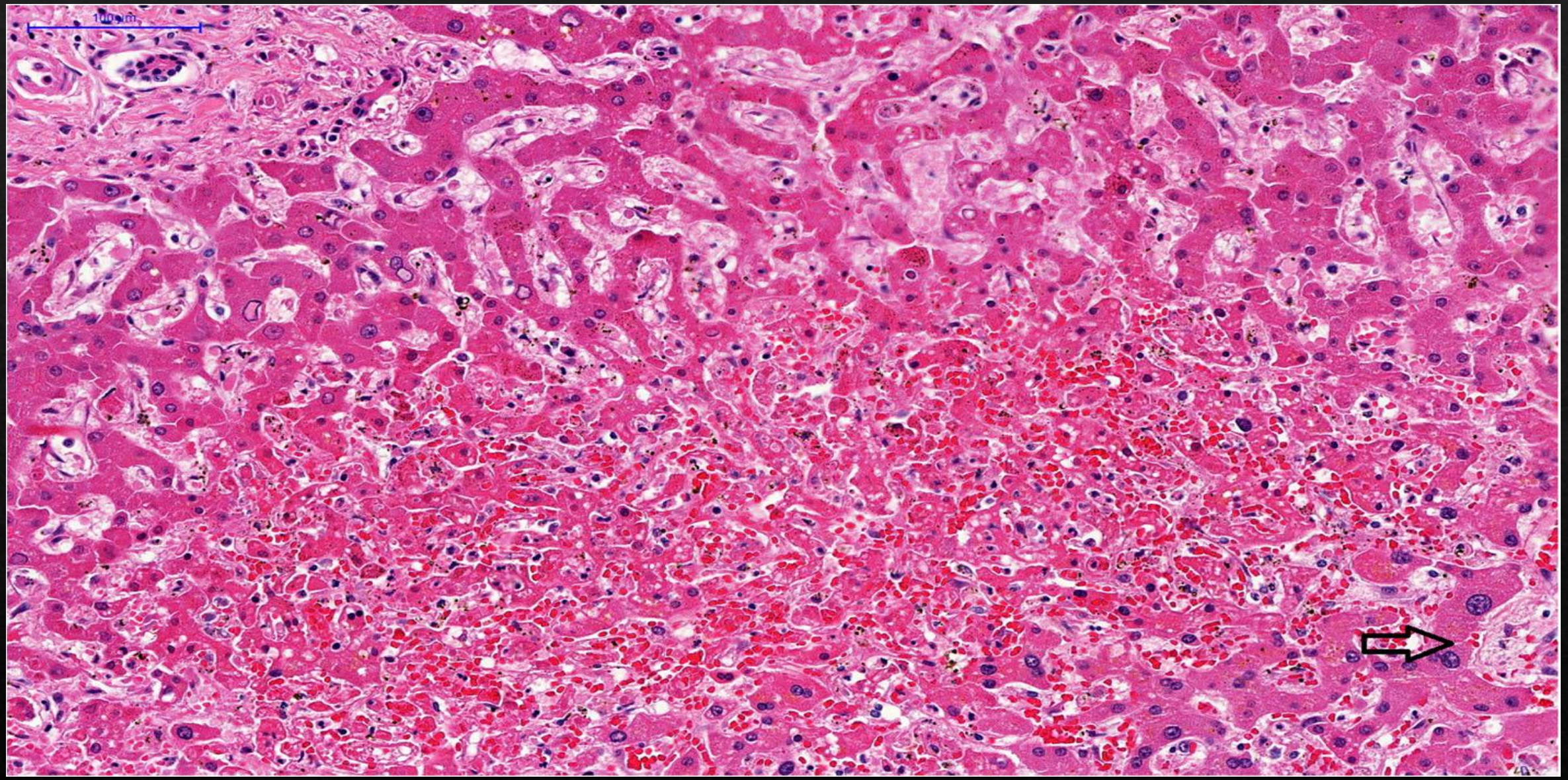
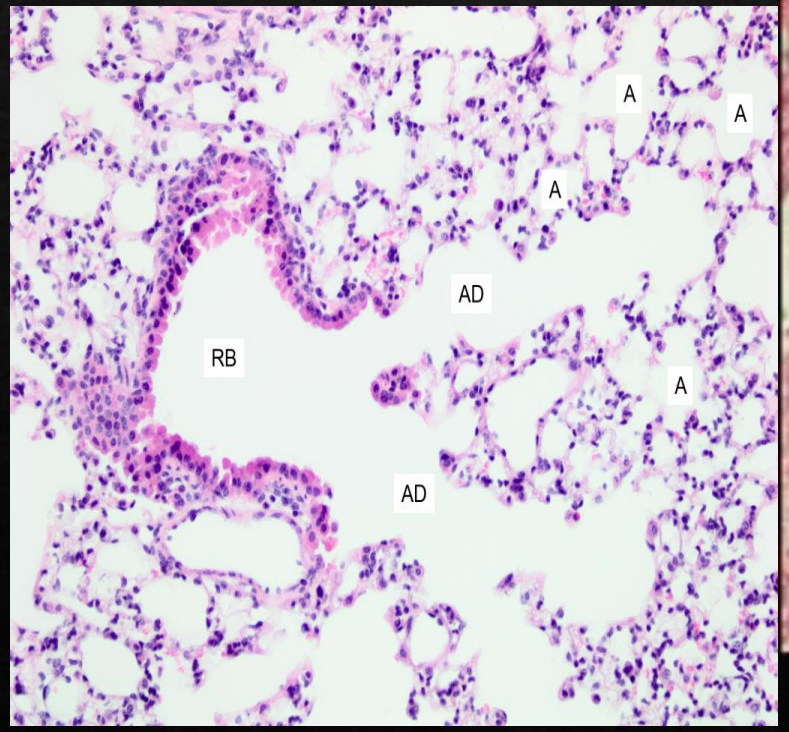


Figure . 4 . Micrograph of the liver in a fulminant case of dengue fever: midzonal hepatitis, with **apoptotic** hepatocytes and sinusoidal congestion associated with a scarce inflammatory reaction. The portal area on the left top; arrow indicates centrilobular vein. HE 200x

- **Lung**

Pulmonary haemorrh

Pulmonary oedema



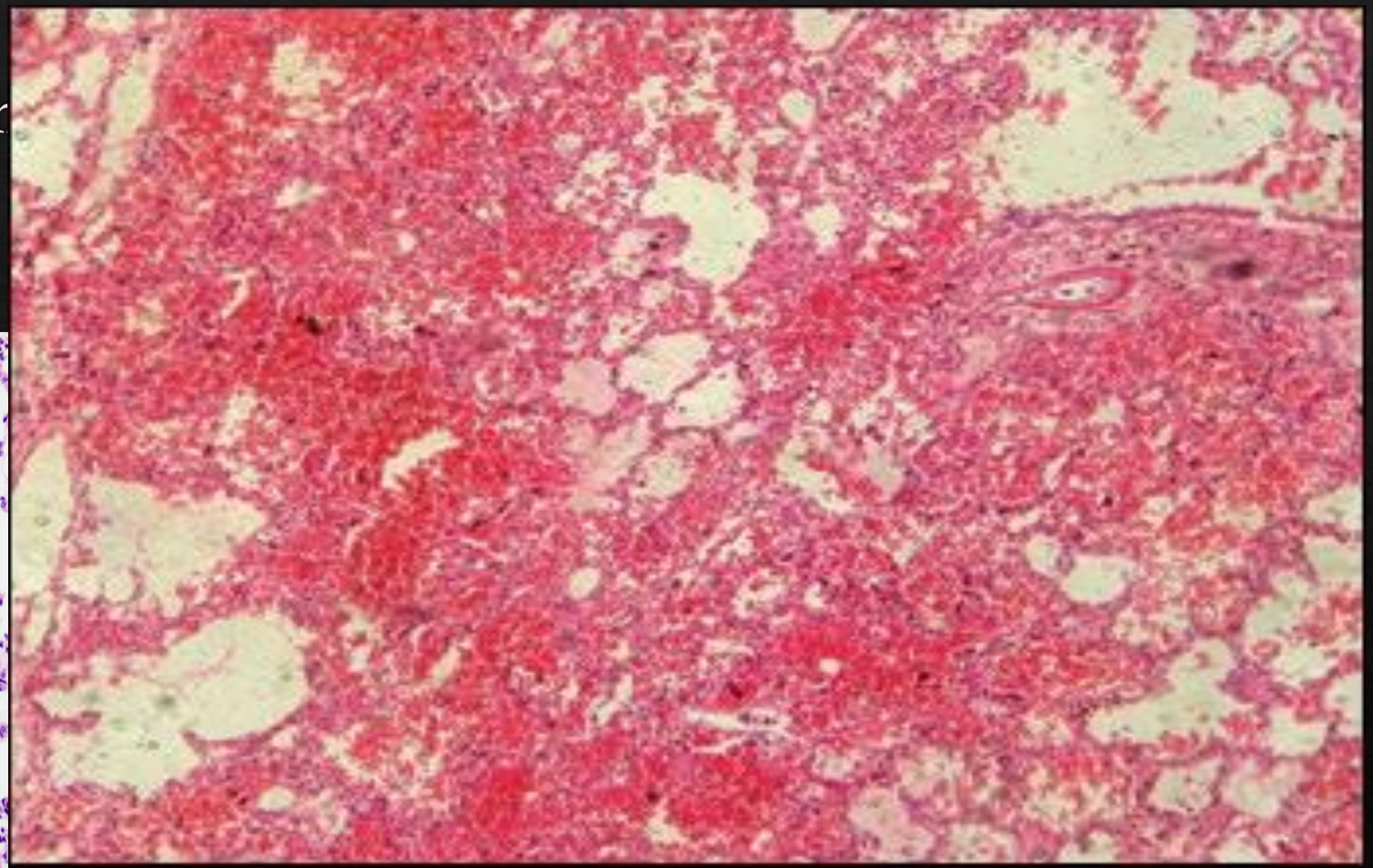
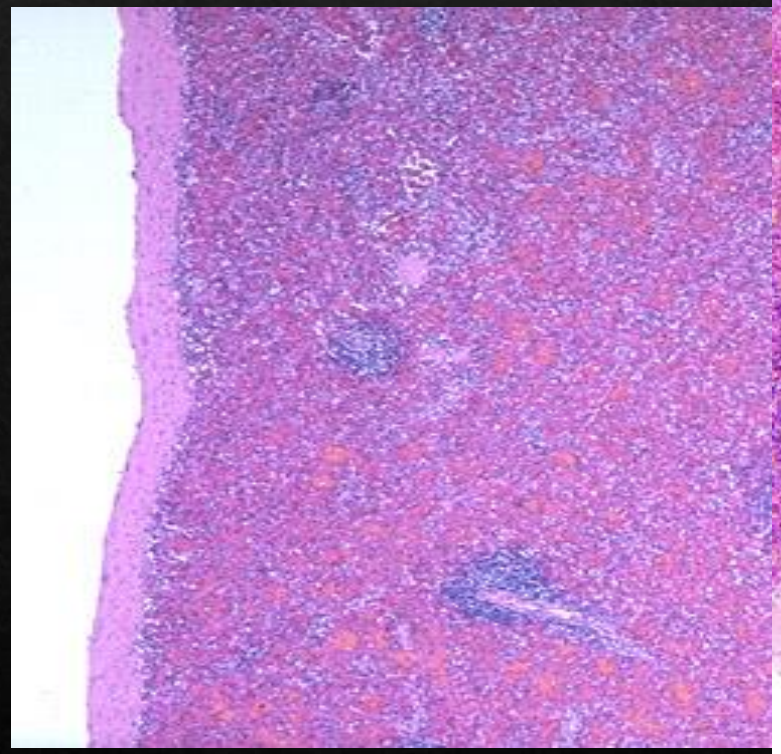


Figure 5. Lungs: Pulmonary haemorrhages (H & E x100) 7 years. Dengue IgM positive

Spleen

- **Red pulp congestion a**



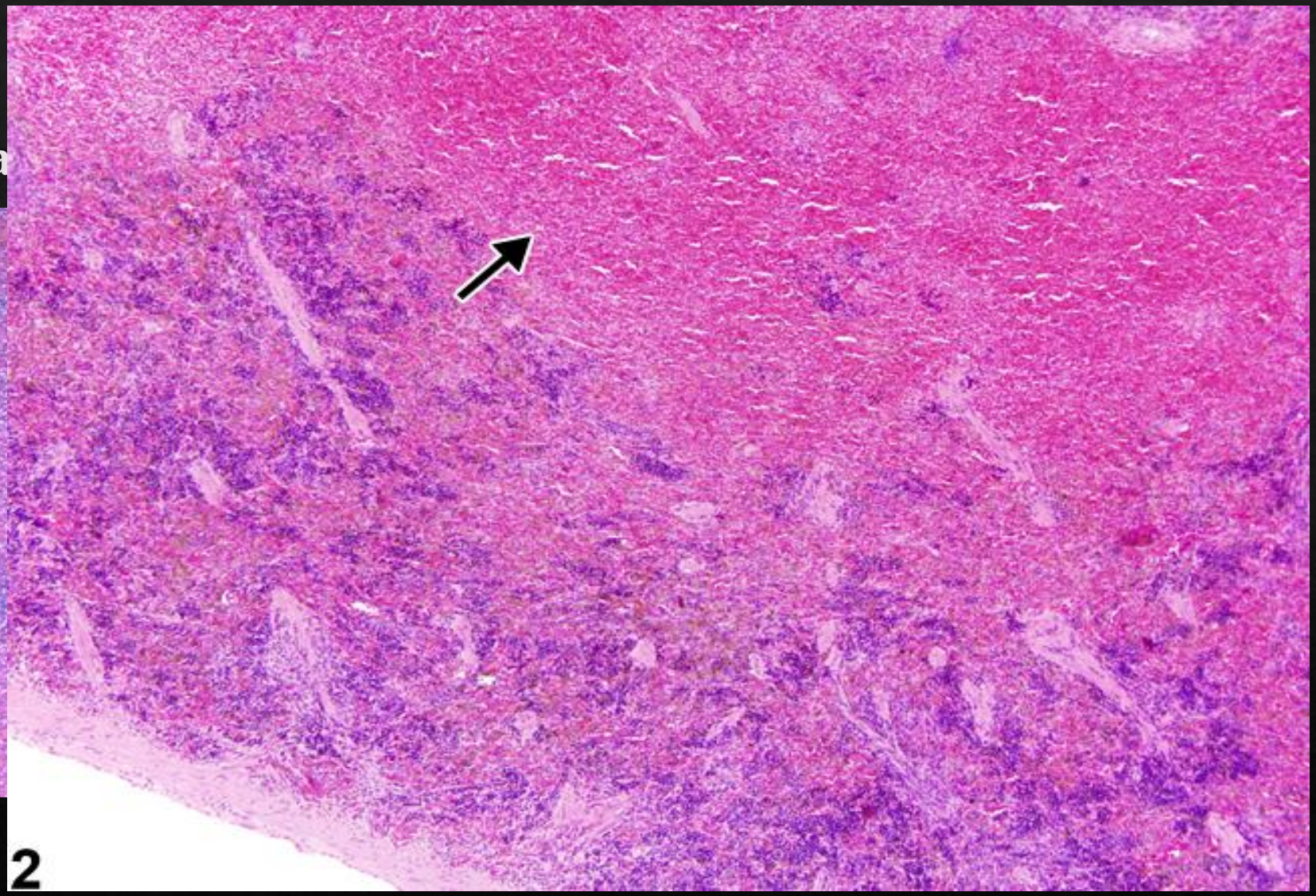
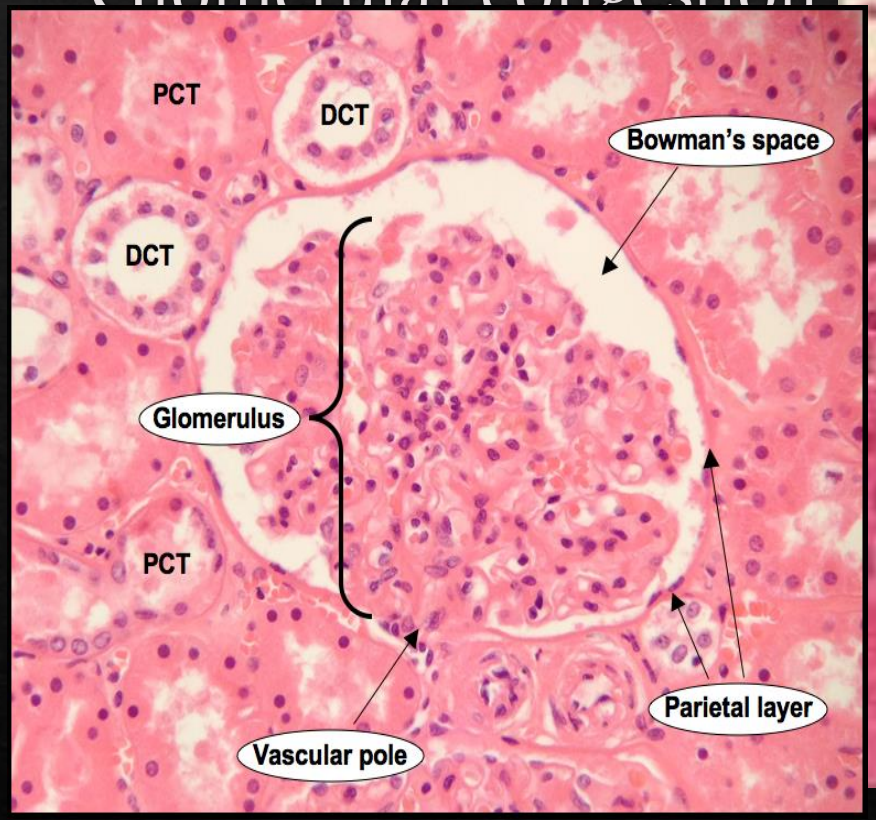


Figure 6. Spleen : Red pulp congestion and haemorrhage = ((H & E x100) in female . Dengue IgM positive

◈ Kidney

Glomerular congestion



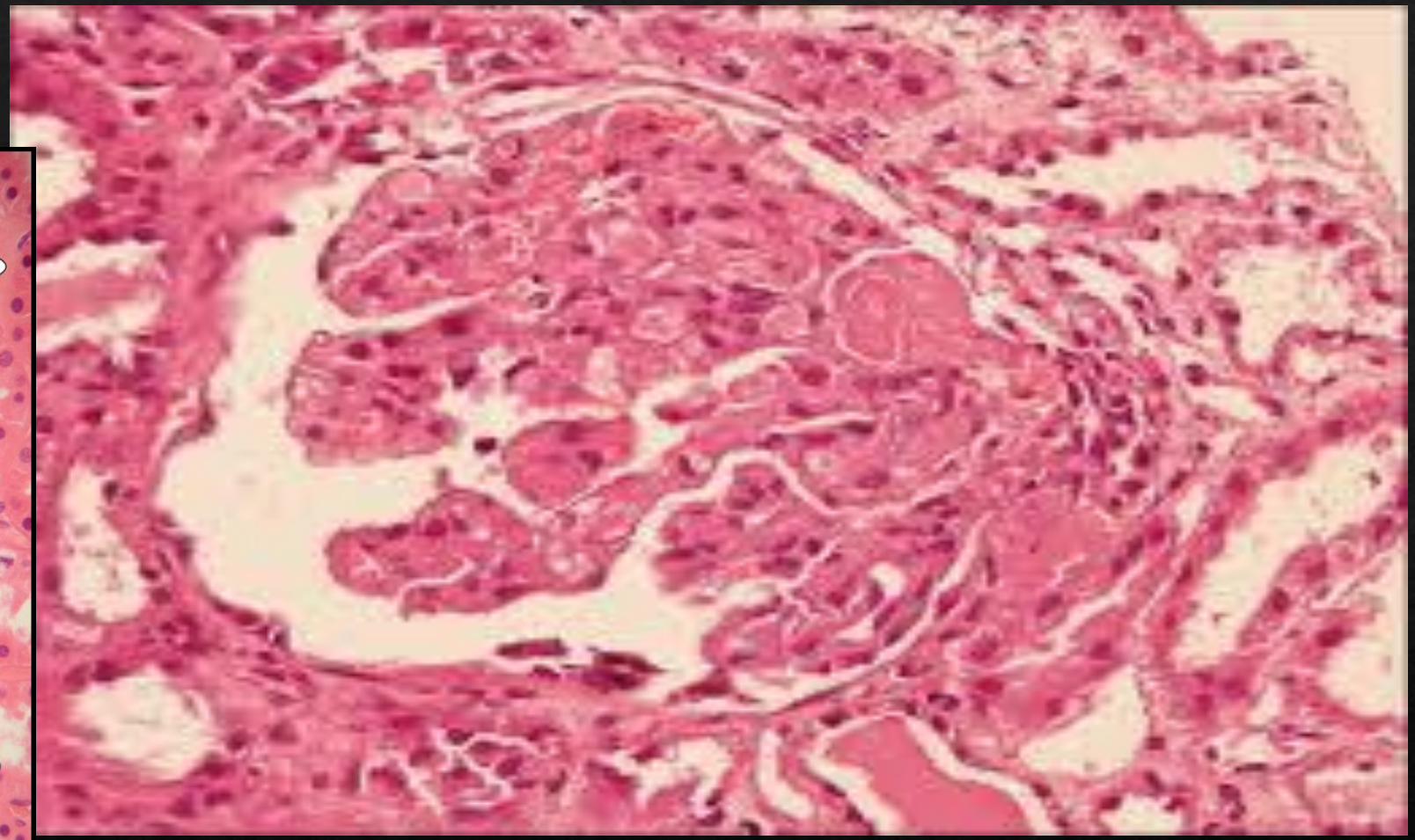
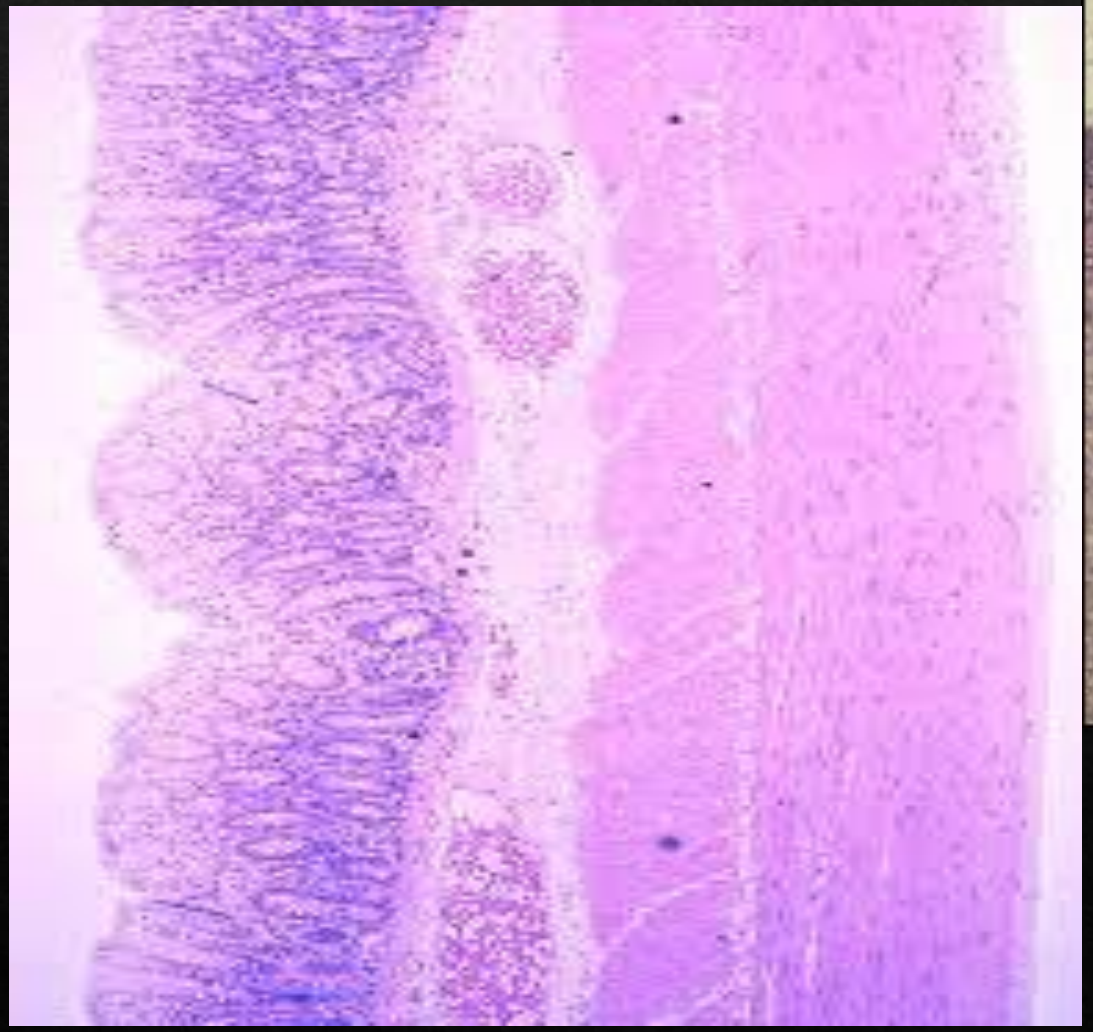


Figure 7. kidney tissue. The cortical region shows hemorrhage in glomerulus capillaries and proximal convolute tubules , interstitial edema in both cortical and medullar region. (H & E x 100) .

◈ Gastrointestinal tract

Mucosal haemorrhage = (47%



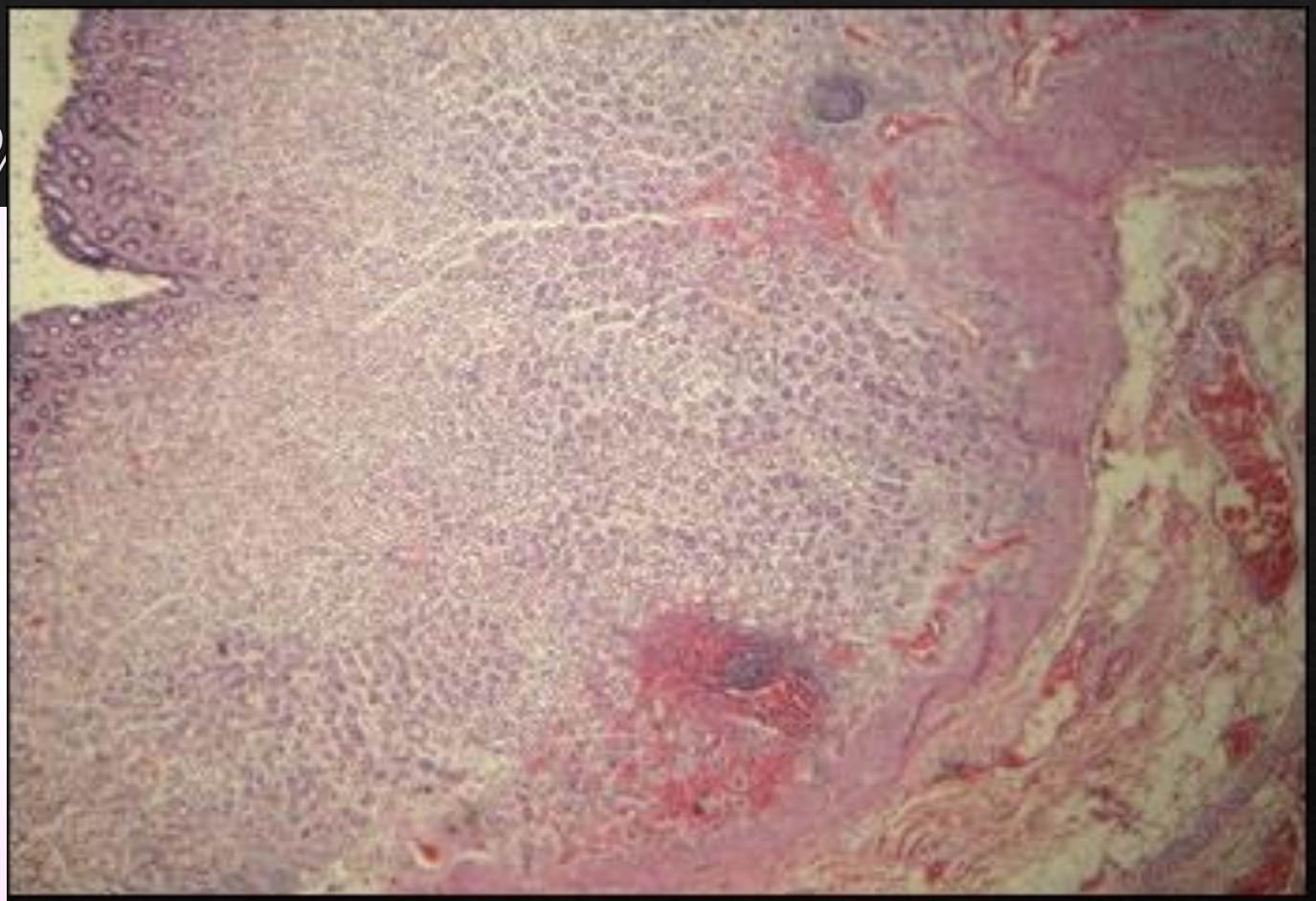
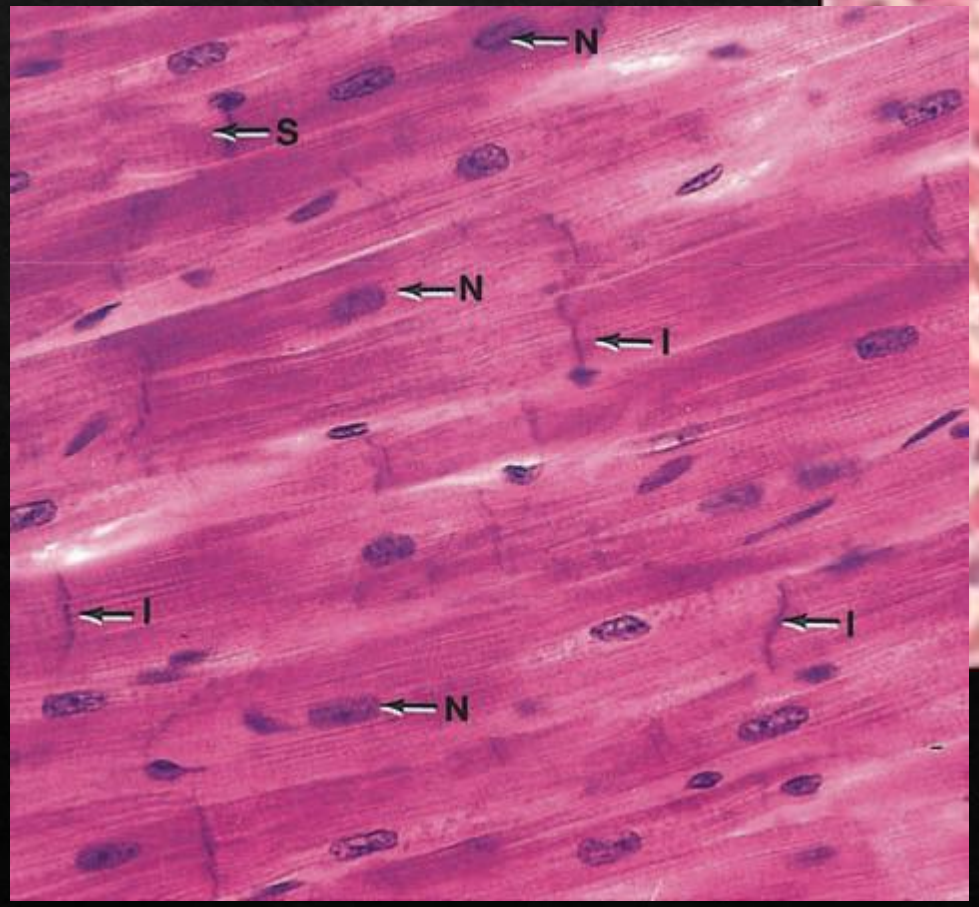


Fig. 8.GIT: Gastric mucosal haemorrhages (H & Ex100) 12 years. Clinically diagnosed as DHF

◈ Heart

Myocarditis = (6

Myocardial haemorrha



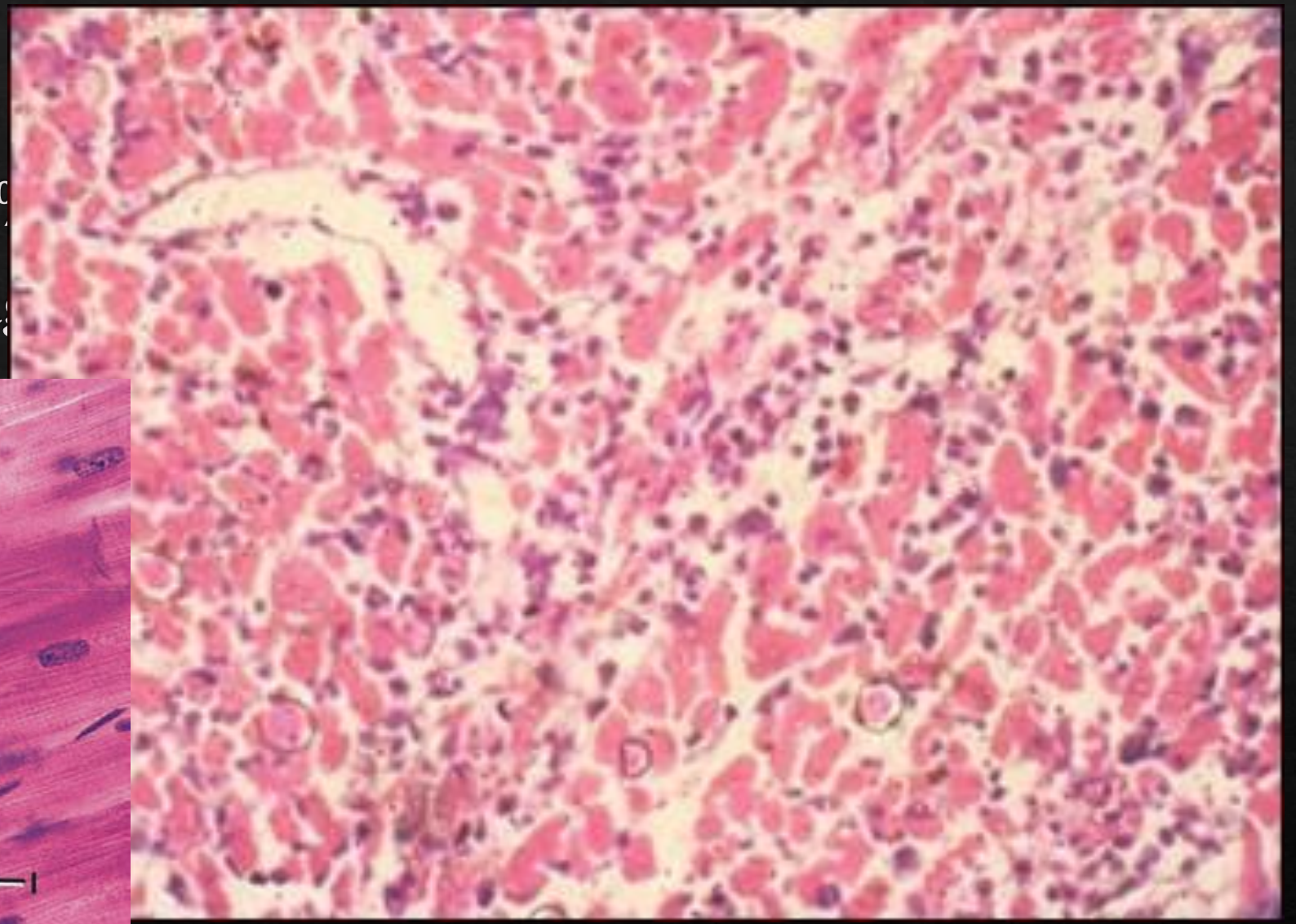
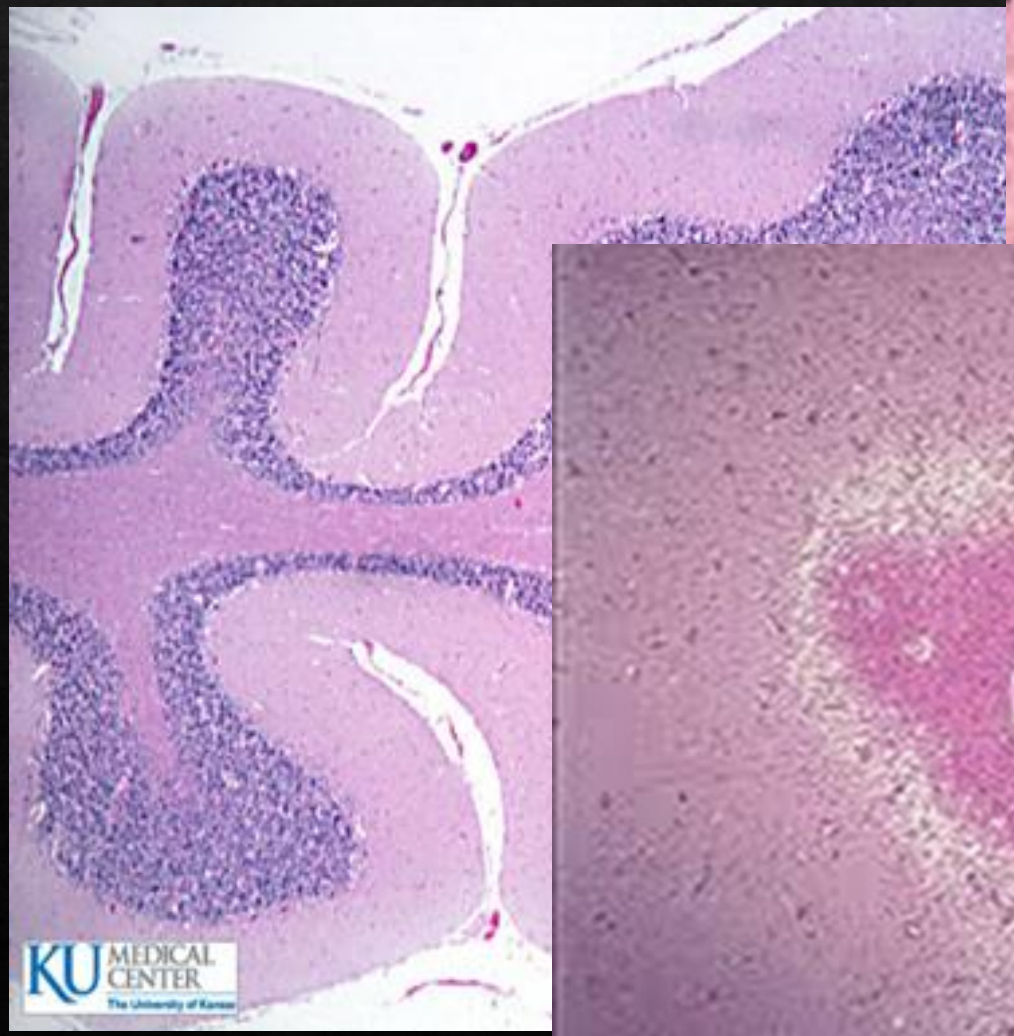
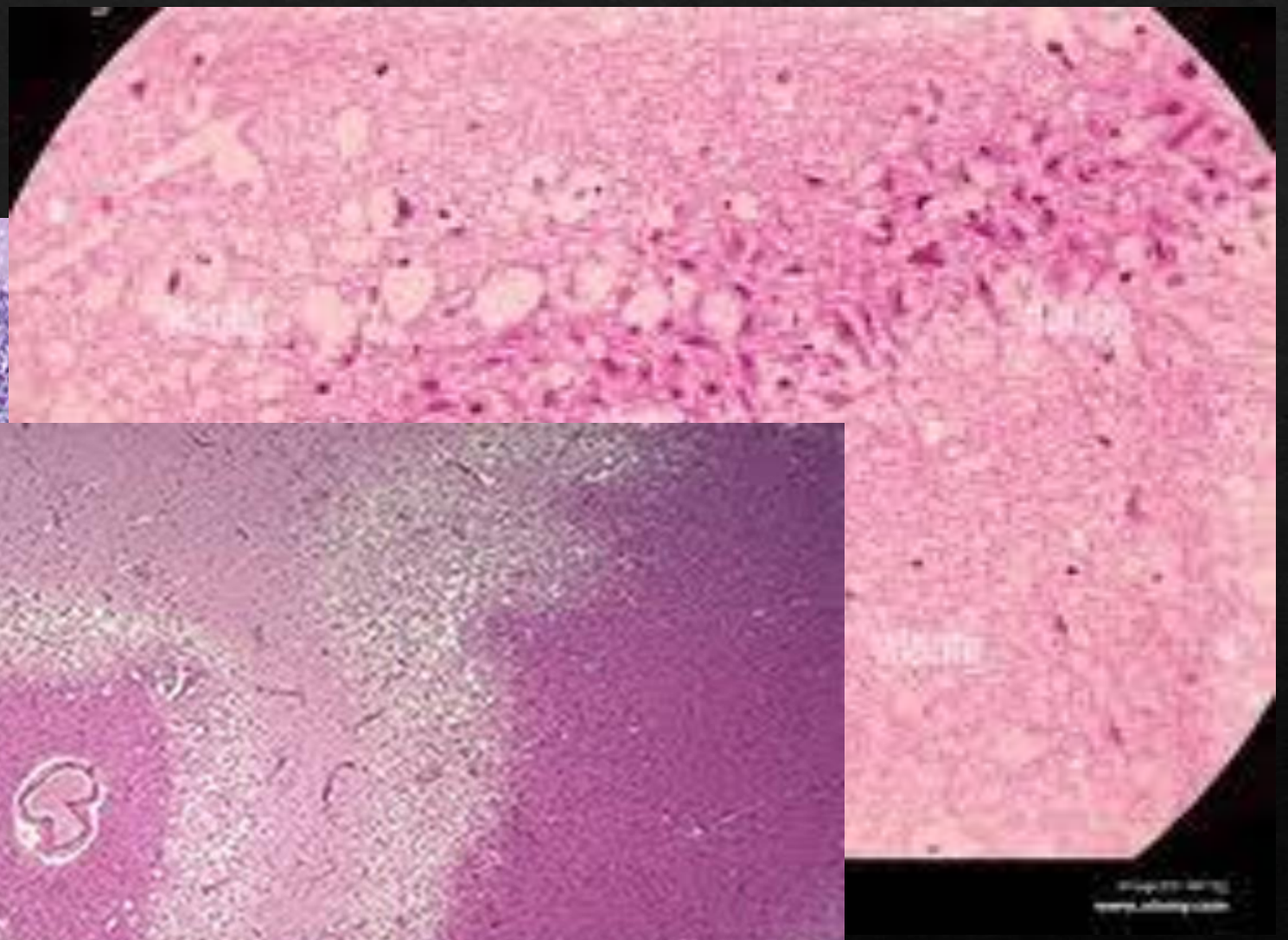


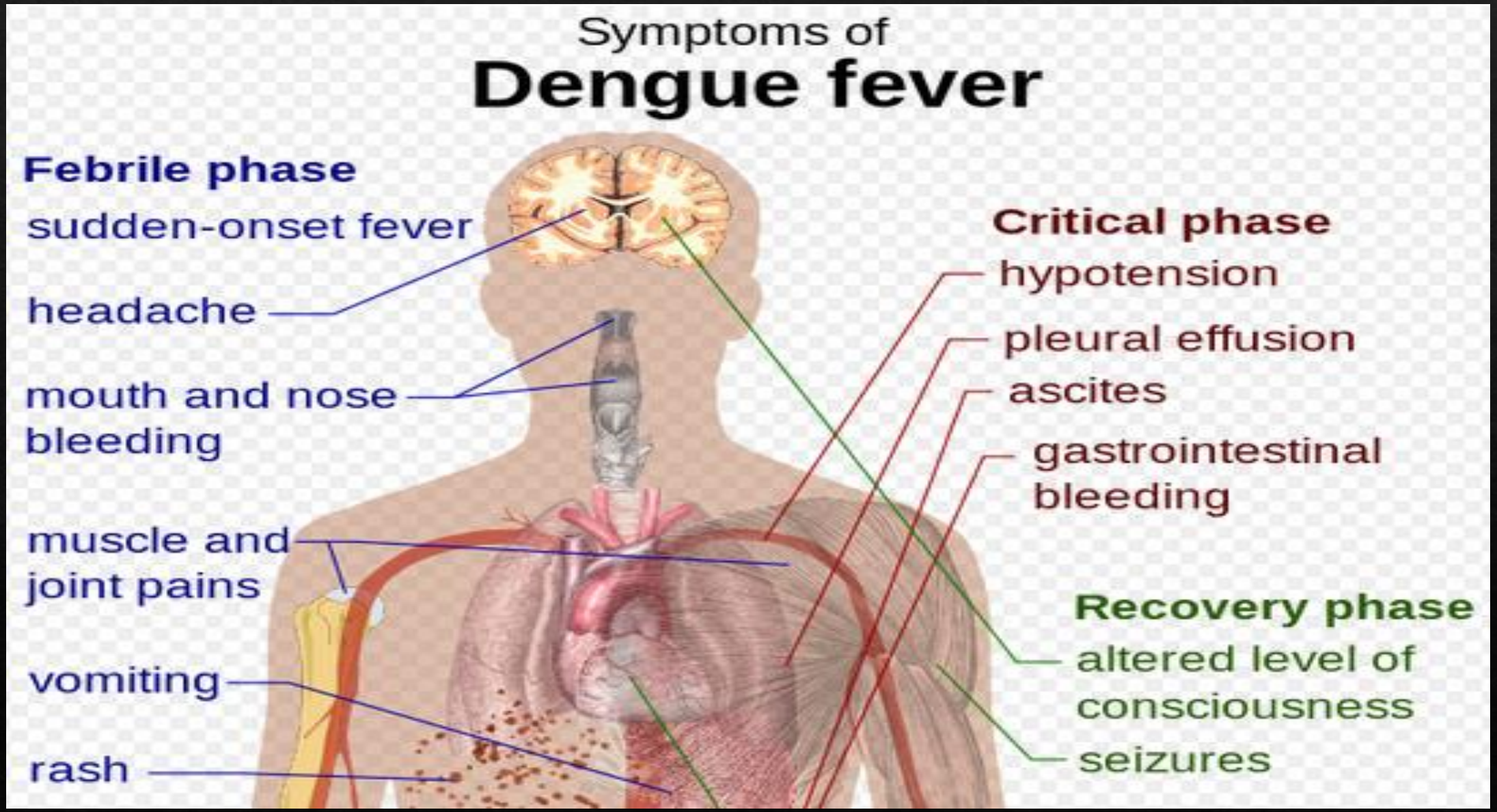
Fig. 6. Heart: Myocarditis. (H & E x100). 19 years. Clinically diagnosed as DHF.

◈ Brain

Cerebral oedema = (47%)






Symptoms of
Dengue fever
Febrile phase
sudden-onset fever
headache
mouth and nose bleeding
muscle and joint pains
vomiting
rash
Critical phase
hypotension
pleural effusion
ascites
gastrointestinal bleeding
Recovery phase
altered level of consciousness
seizures

Thank You