

AMYLOIDOSIS

MORPHOLOGY, SPECIAL STAINS AND DIAGNOSIS

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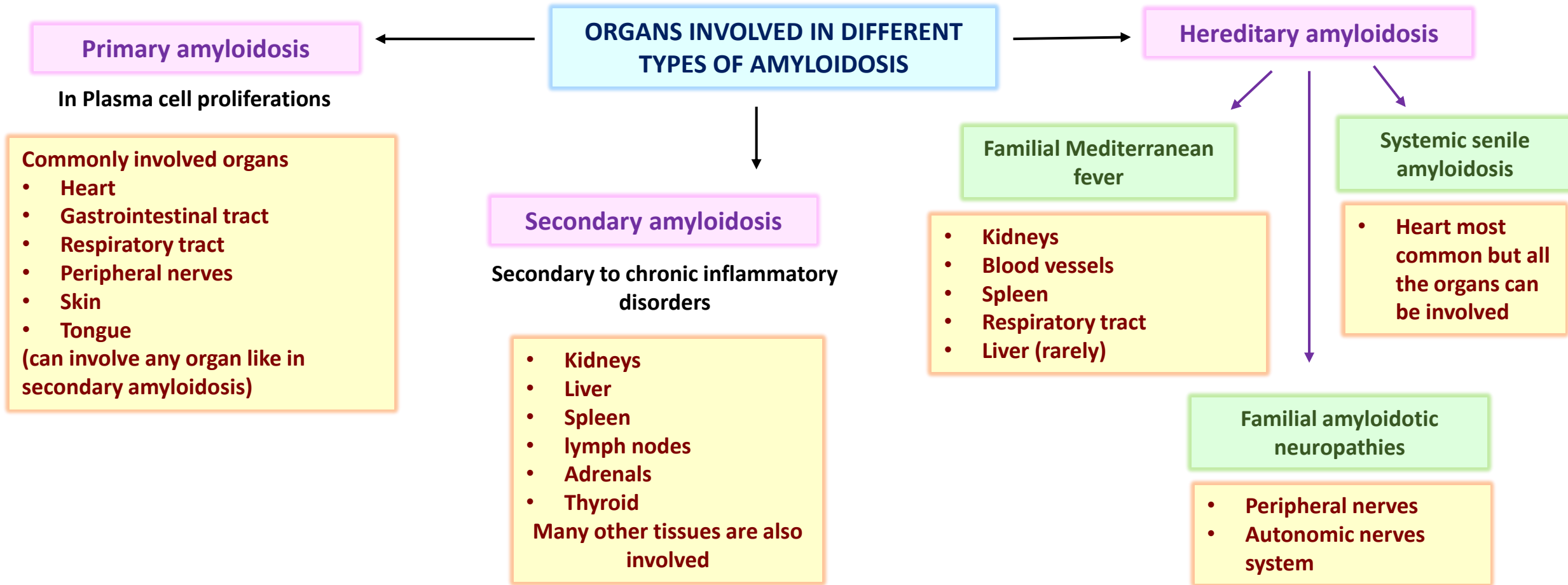
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AMYLOIDOSIS

MORPHOLOGY



AMYLOIDOSIS

MORPHOLOGY

Gross

- Macroscopically amyloid may or may not be seen
- When it accumulates in larger amounts organ is enlarged and the tissue appears **gray with a waxy, firm consistency**

Histologically

- Amyloid deposition is **extracellular** and begins **between cells**, often closely adjacent to basement membranes
- As the amyloid accumulates, it encroaches on the cells, in time surrounding and destroying them
- In the form associated with plasma cell proliferation, perivascular and vascular deposits are common



AMYLOIDOSIS

KIDNEY

- Most common organ involved in amyloidosis
- **Gross-**
 - Kidneys may be of normal size and color
 - In advanced cases, they may be shrunken due to ischemia caused by vascular narrowing induced by the deposition of amyloid within arterial and arteriolar walls



Amyloidosis of blood vessels leading to ischemia

Shrunken kidney



AMYLOIDOSIS

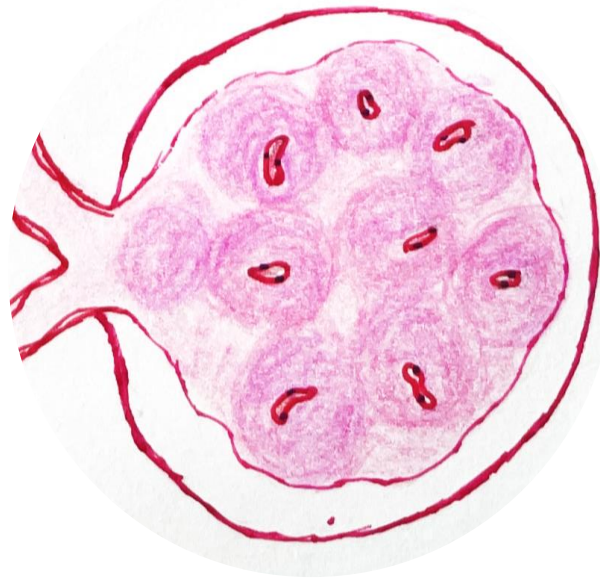
KIDNEY

Microscopy

Amyloid is deposited primarily in the glomeruli



Glomerular deposits first appear as subtle thickenings of the mesangial matrix, accompanied usually by uneven widening of the basement membranes of the glomerular capillaries



Deposits along the basement membranes cause capillary narrowing and distortion of the glomerular vascular tuft



With progression of the glomerular amyloidosis, the capillary lumens are obliterated, and the obsolescent glomerulus is flooded by confluent masses or interlacing broad ribbons of amyloid

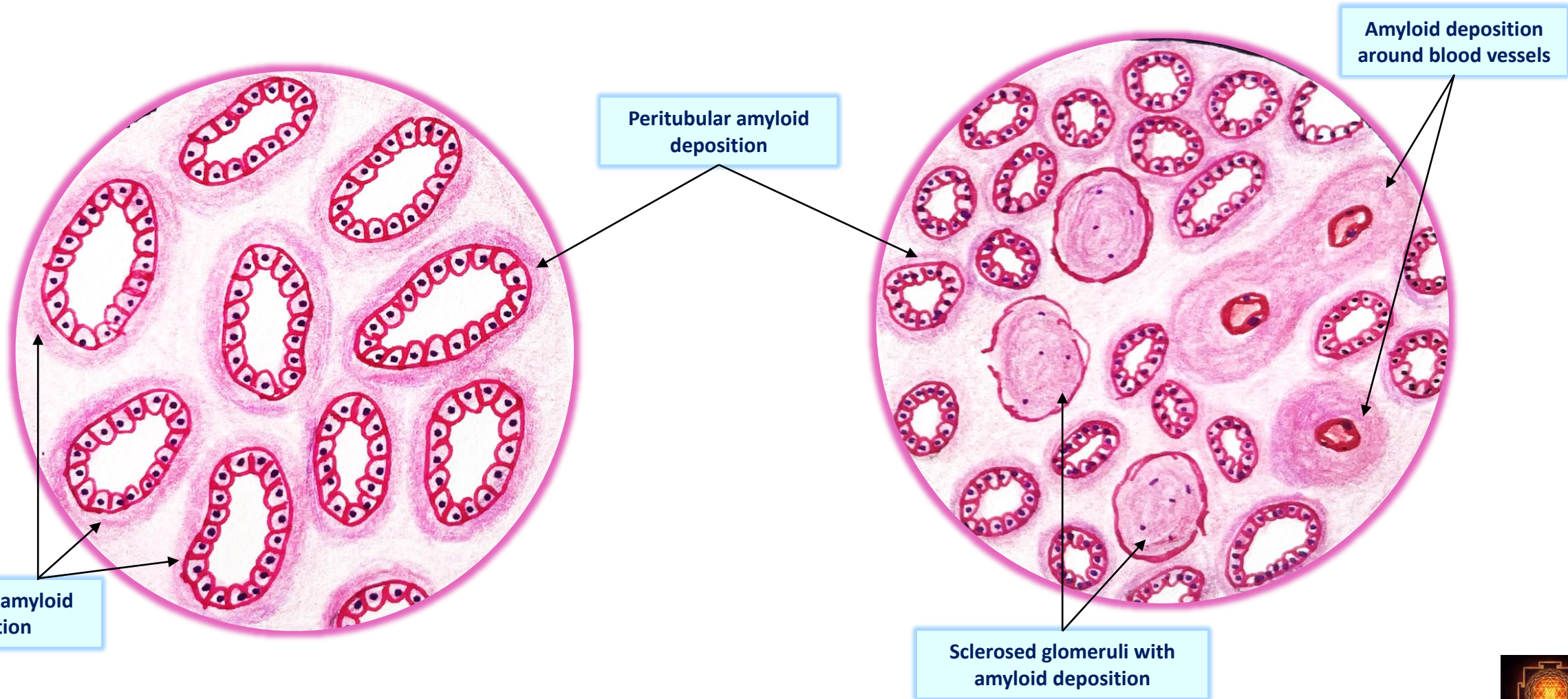


AMYLOIDOSIS

KIDNEY

Microscopy

Interstitial peritubular tissue, arteries, and arterioles are also affected



AMYLOIDOSIS

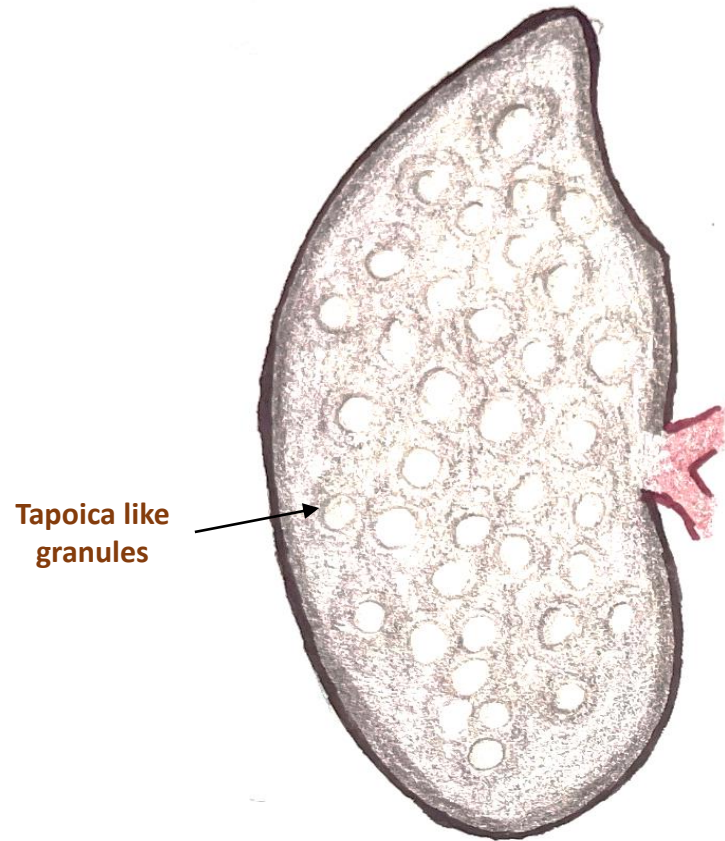
SPLEEN

- **Gross** - inapparent or may cause moderate to marked splenomegaly (up to 800 g)
- **Histologically** – two patterns of amyloid deposition
 - Sago spleen
 - Lardaceous spleen



AMYLOIDOSIS

SAGO SPLEEN



Tapioca seeds



Gross

Amyloid deposits are largely limited to the splenic follicles, producing tapioca-like granules on gross inspection designated 'sago spleen'



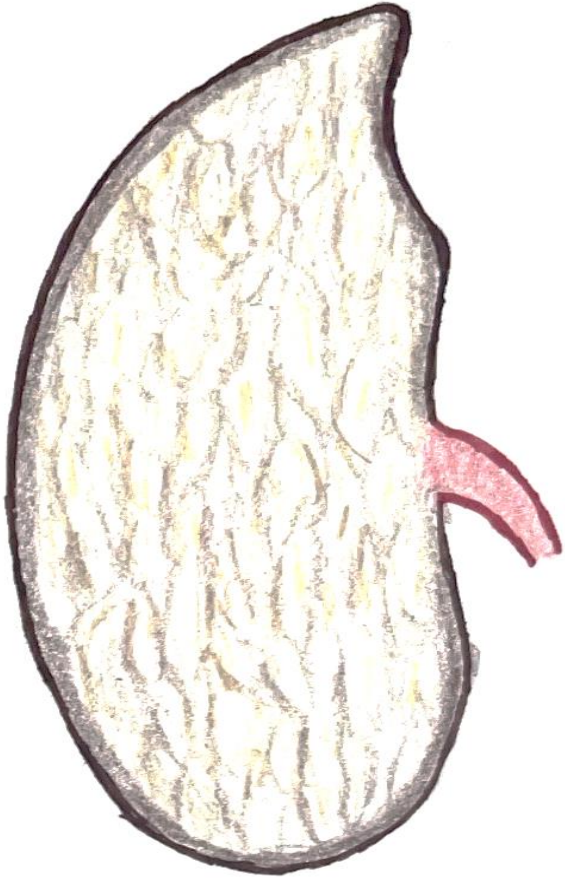
Microscopy

Amyloid deposits are limited to the splenic follicles of white pulp



AMYLOIDOSIS

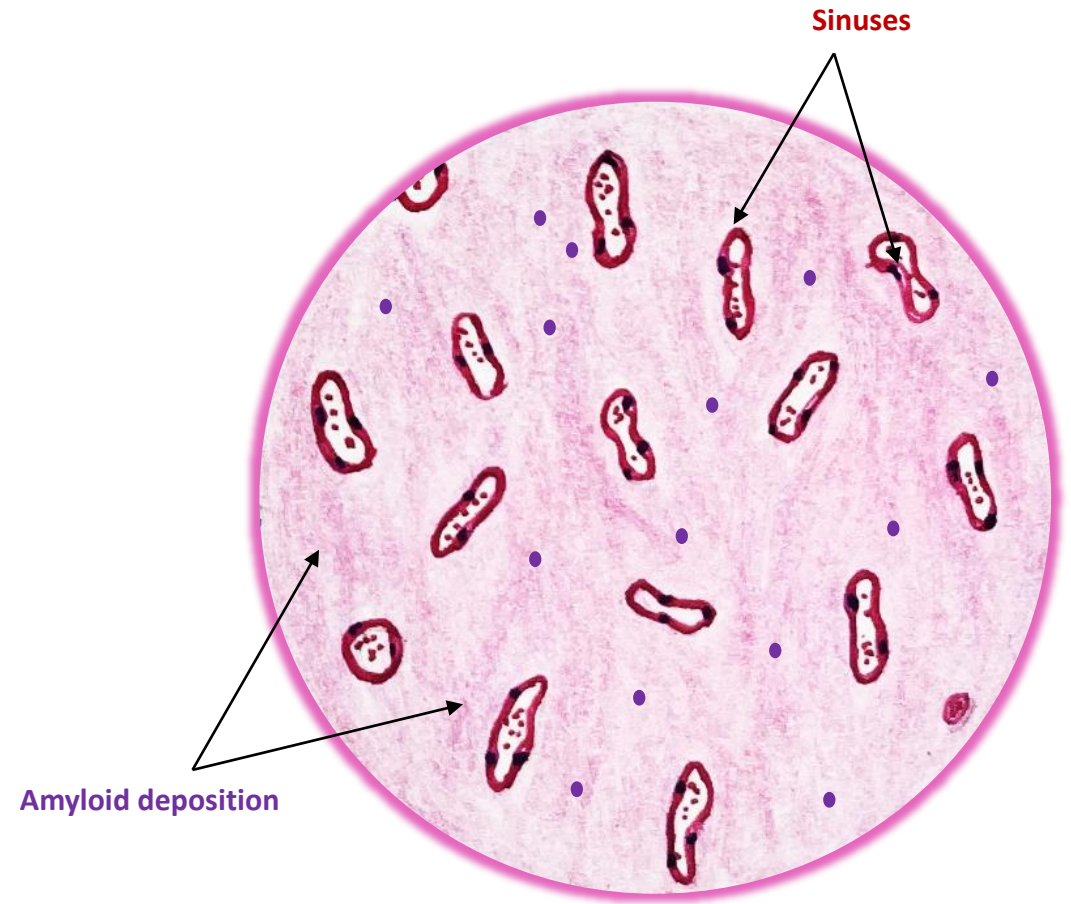
LARDACEOUS SPLEEN



Lard: Pork abdomen fat

Gross

Fusion of amyloid deposits creates large, map like areas of amyloidosis giving spleen fatty or waxy texture resembling lard (Fat at the abdomen of the pig)



Microscopy

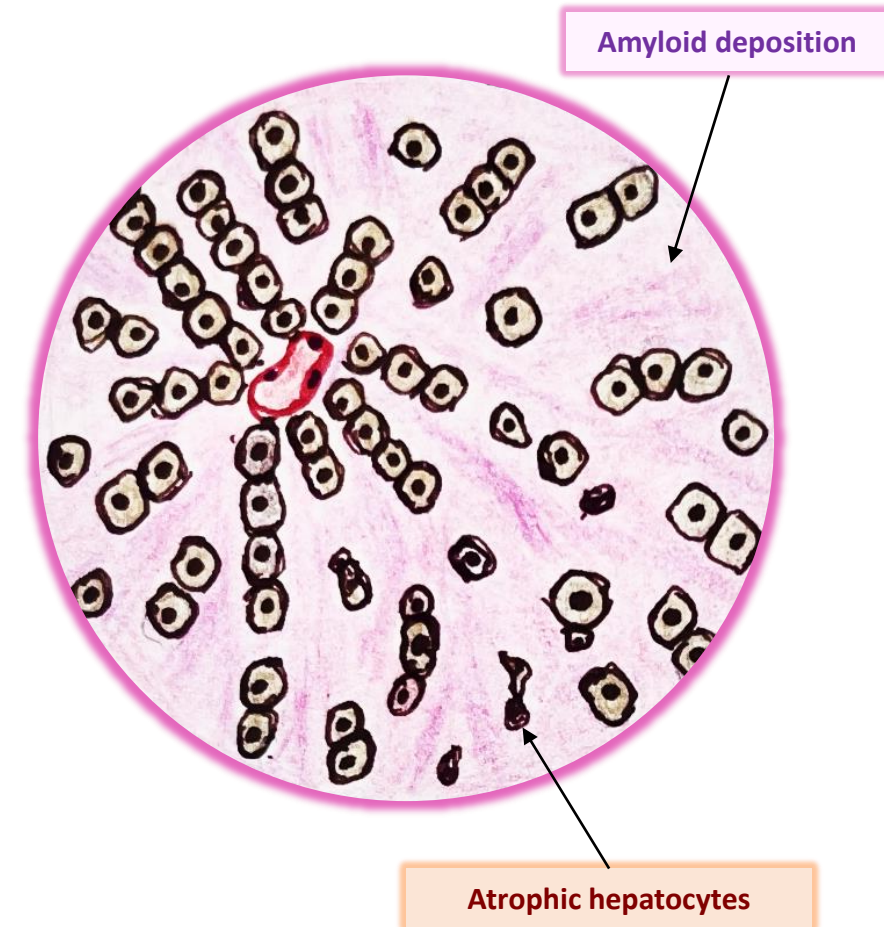
Amyloid involves the walls of the splenic sinuses and connective tissue framework in the red pulp



AMYLOIDOSIS

LIVER

- **Gross** - inapparent or may cause moderate to marked hepatomegaly
- **Microscopy** - Amyloid appears first in the **space of Disse** and then **progressively encroaches on adjacent hepatic parenchymal cells and sinusoids**
- **Pressure atrophy**, and **disappearance of hepatocytes** occur causing **total replacement of large areas of liver parenchyma**
- **Vascular involvement is common**
- **Even with extensive involvement, liver function is usually preserved**

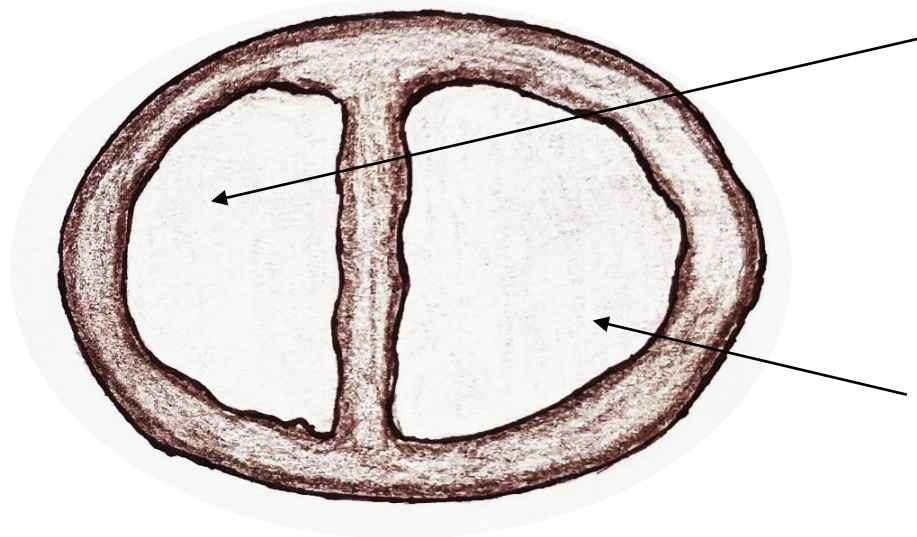


AMYLOIDOSIS

HEART

- Major organ involved in senile systemic amyloidosis
- **Gross** - heart may be enlarged and firm or may not show significant changes

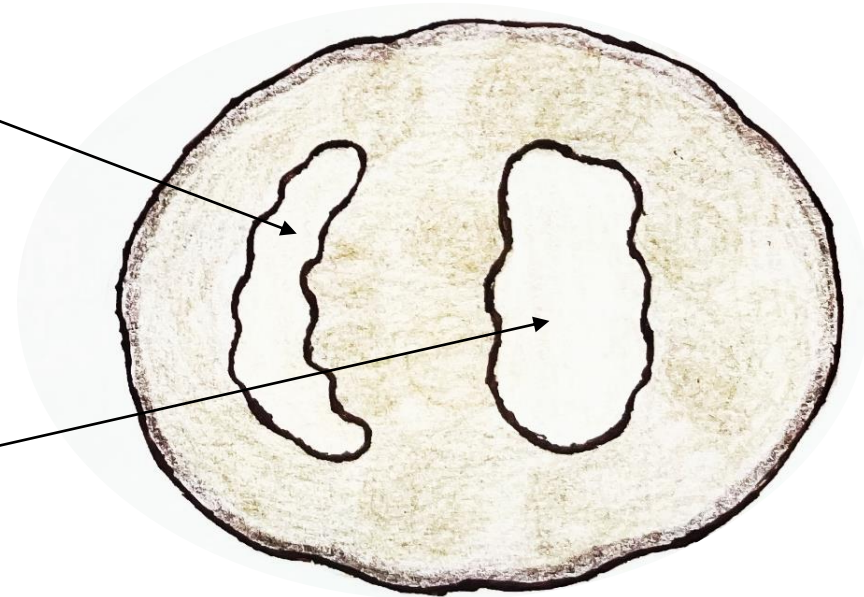
Cut section of normal heart



Atria

Ventricles

Amyloidosis heart



Amyloid deposition with increased thickness of heart wall having firm waxy appearance

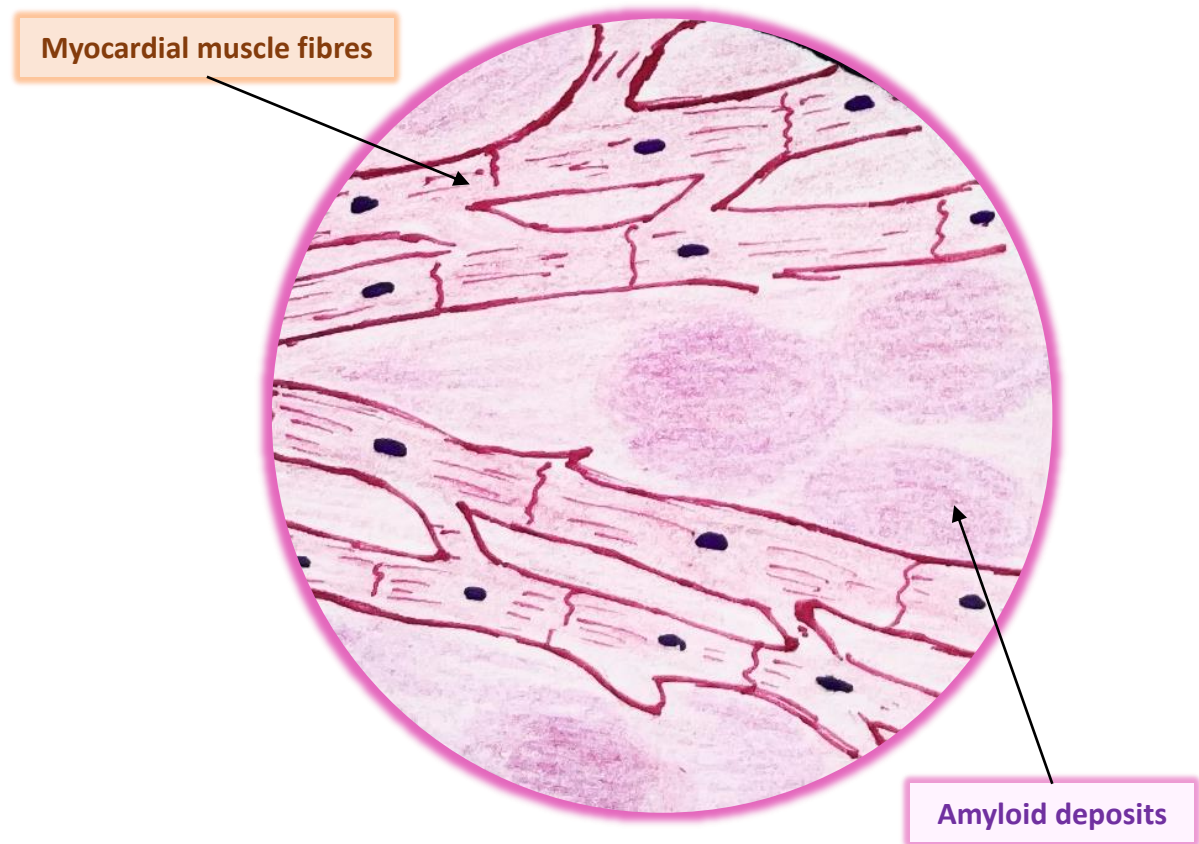


AMYLOIDOSIS

HEART

- **Microscopy –**

- Deposits begin as **focal subendocardial accumulations and within the myocardium between the muscle fibers**
- Myocardial deposits eventually causes **pressure atrophy of myocardial fibers**
- Amyloid deposits in subendocardium causes damage to the conduction system, accounting for the **electrocardiographic abnormalities**

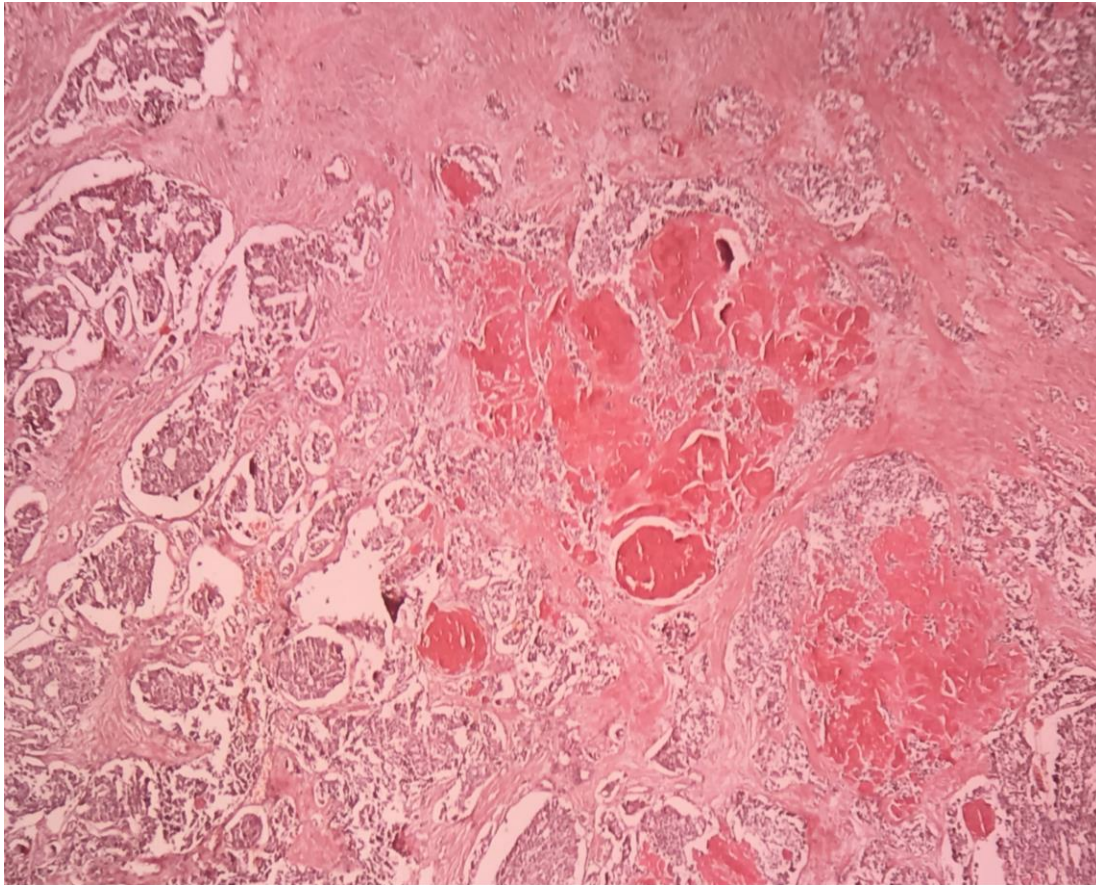


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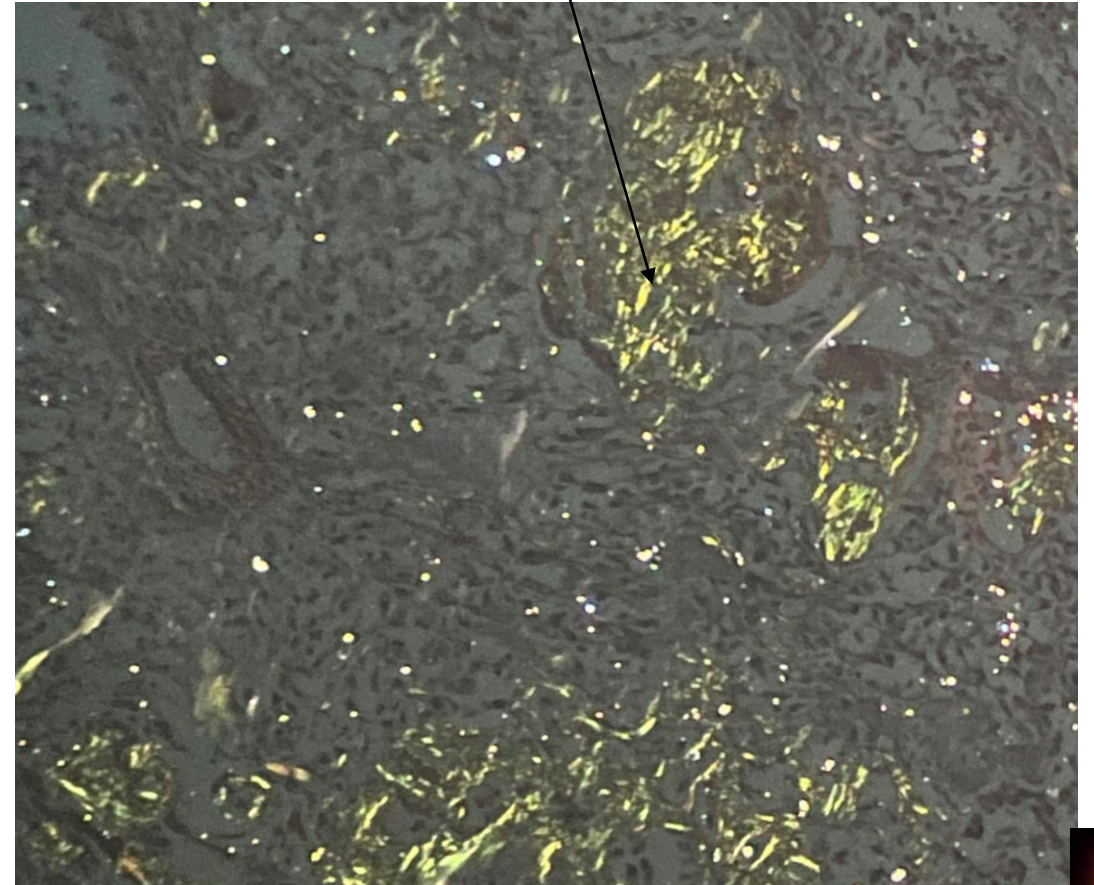
SPECIAL STAINS

Congo Red

Red pink (Salmon pink) on light microscopy



Apple green birefringence on polarized microscopy



AMYLOIDOSIS

OTHER SPECIAL STAINS

- **Methyl and Cresyl violet** – rose pink color
- **Thioflavin T and S** – exhibits fluorescence on ultraviolet light
- **Alcian blue** – stains blue-green to the presence of glycosaminoglycans
- **Periodic Acid Schiff (PAS)** – pink
- **Immunohistochemistry** – used for distinguishing AA, AL, ATTR
- **Special stain on gross** – Lugol's iodine imparts mahogany brown color to the amyloid in tissue. On further adding dilute sulphuric acid it turns blue



AMYLOIDOSIS

Lab diagnosis

- **Common sites biopsied for diagnosis**
 - **Abdominal fat**
 - **Rectal biopsy**
 - **Gingival biopsy**
 - **Kidney biopsy**



AMYLOIDOSIS

Lab diagnosis

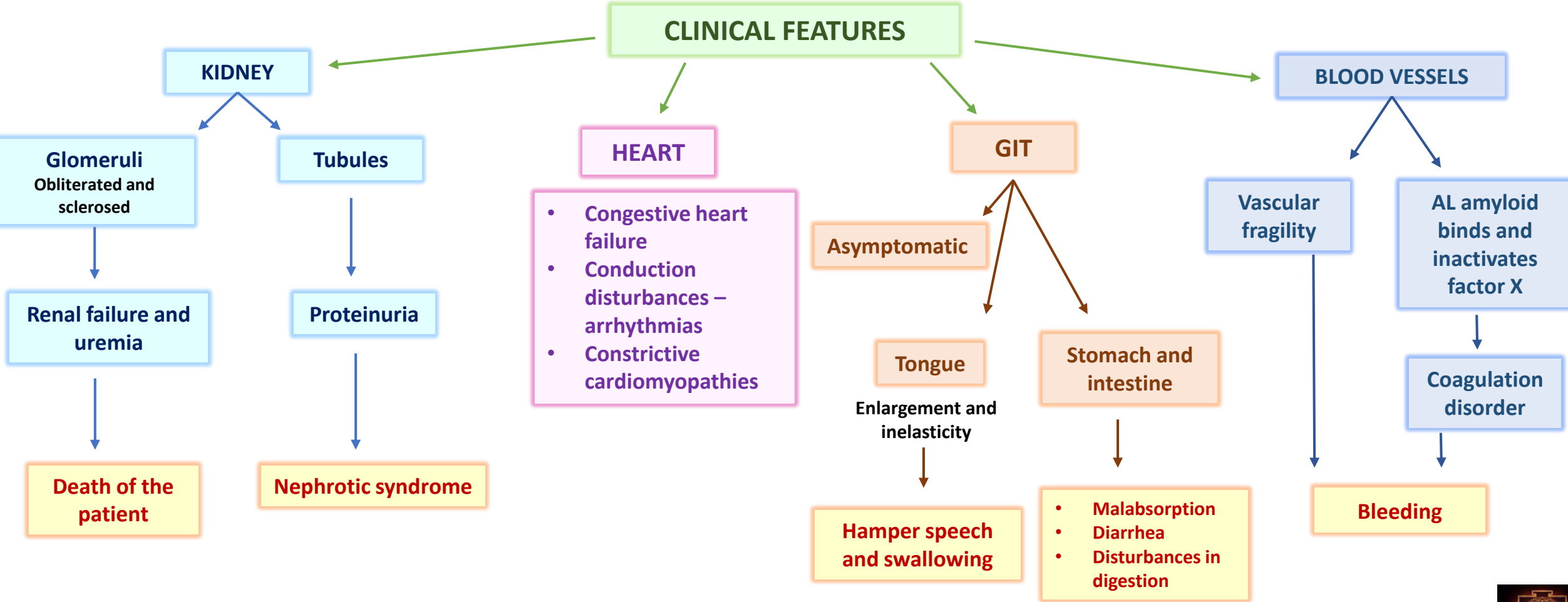
- **AL amyloidosis**
 - serum and urine protein electrophoresis
 - Immunoelectrophoresis should be performed
 - Bone marrow aspirates in such cases often show monoclonal plasmacytosis, even in the absence of overt multiple myeloma
 - Scintigraphy with radiolabeled serum amyloid P component is a rapid and specific test, since it binds to the amyloid deposits and reveals their presence
 - It also gives a measure of the extent of amyloidosis and can be used to follow patients undergoing treatment



AMYLOIDOSIS

CLINICAL FEATURES

Symptoms depend on the amount of the amyloid deposited in the different sites or organs affected



AMYLOIDOSIS

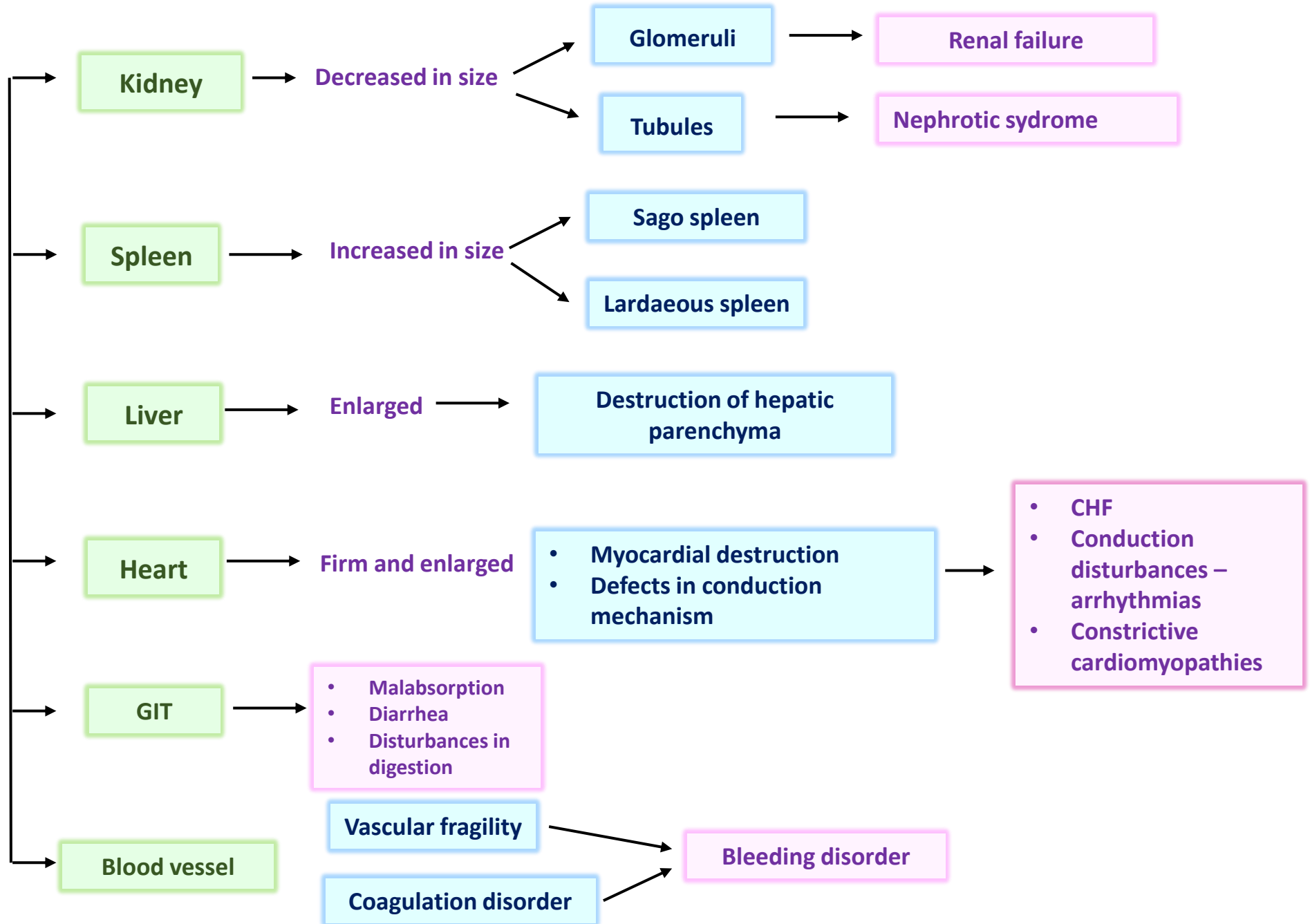
Prognostic factors

- **Generalized amyloidosis** – prognosis is poor when compared to localized amyloidosis
- **Reactive systemic amyloidosis** – prognosis is better
- **AL amyloidosis** –
 - **Prognosis is poor**
 - **Median survival is 2 years after diagnosis**



SUMMARY

Morphology of organs involved and clinical features



Common Biopsy sites

- Abdominal fat
- Rectal biopsy
- Gingival biopsy
- Kidney biopsy

Special stains

Gross

- Iodine – brown
- Further sulphuric acid -blue

Microscopy

- Congo red – red pink; apple green birefringence
- Thioflavin T & B – ultrasound fluorescence
- Methyl and Cresyl violet – rose pink
- Alcian blue – blue green
- PAS - pink
- Immunohistochemistry



