Amyloidosis

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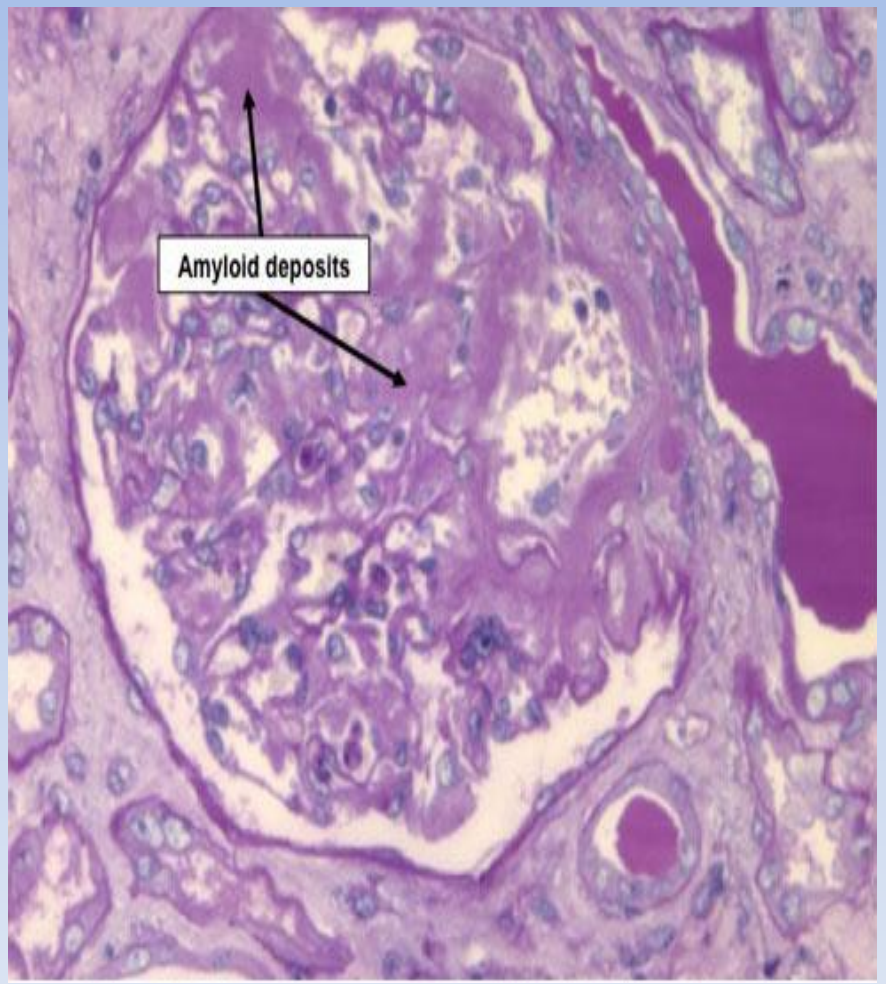
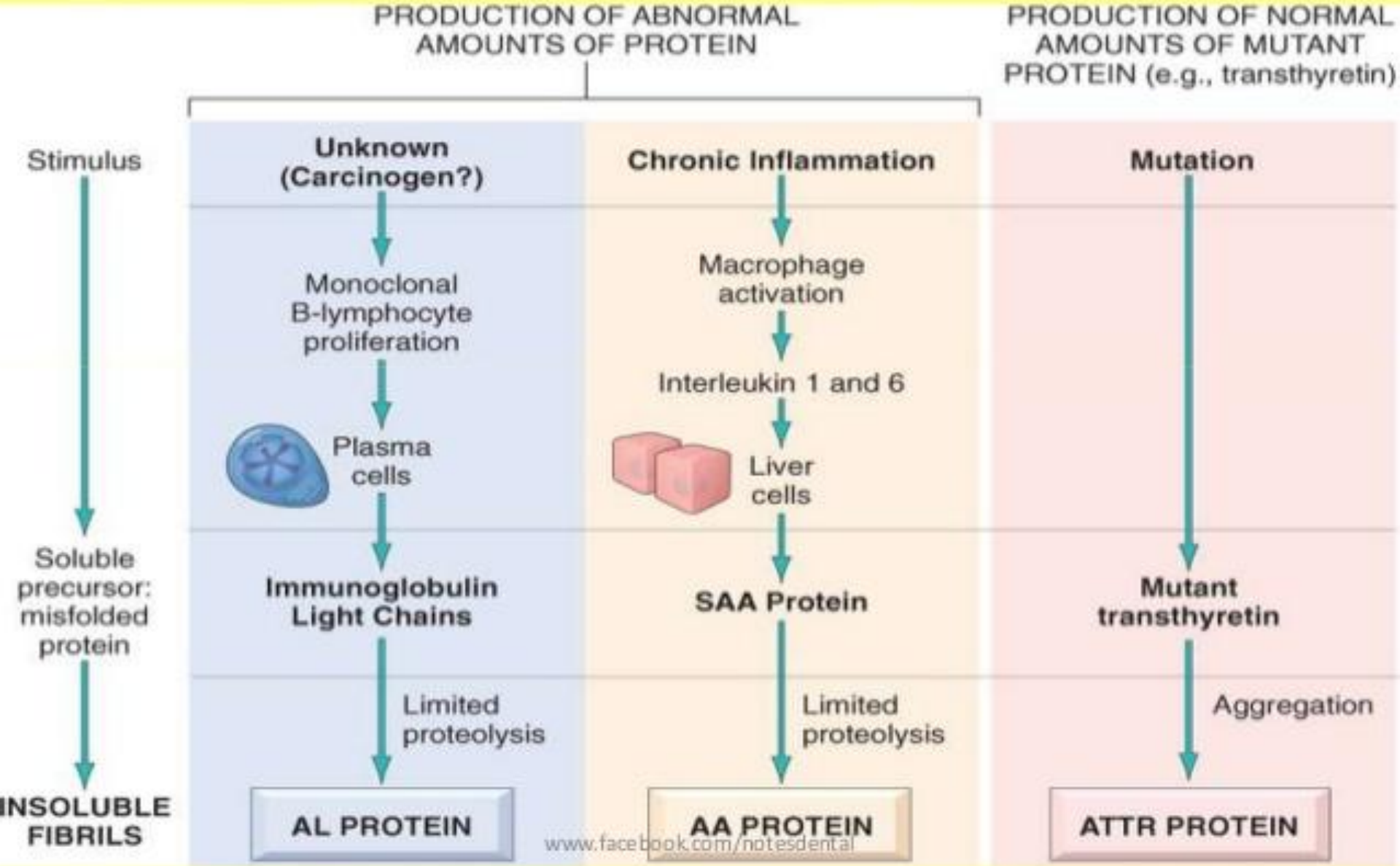
Amyloidosis

- **Amyloidosis is a rare and serious disease caused by accumulation of proteins in the form of abnormal, insoluble fibres, known as amyloid fibrils, within the extracellular space in the tissues of the body. Amyloid deposits can be confined to only one part of the body or a single organ system in 'local amyloidosis' or they can be widely distributed in organs and tissues throughout the body in 'systemic amyloidosis**



PATHOGENESIS OF AMYLOIDOSIS



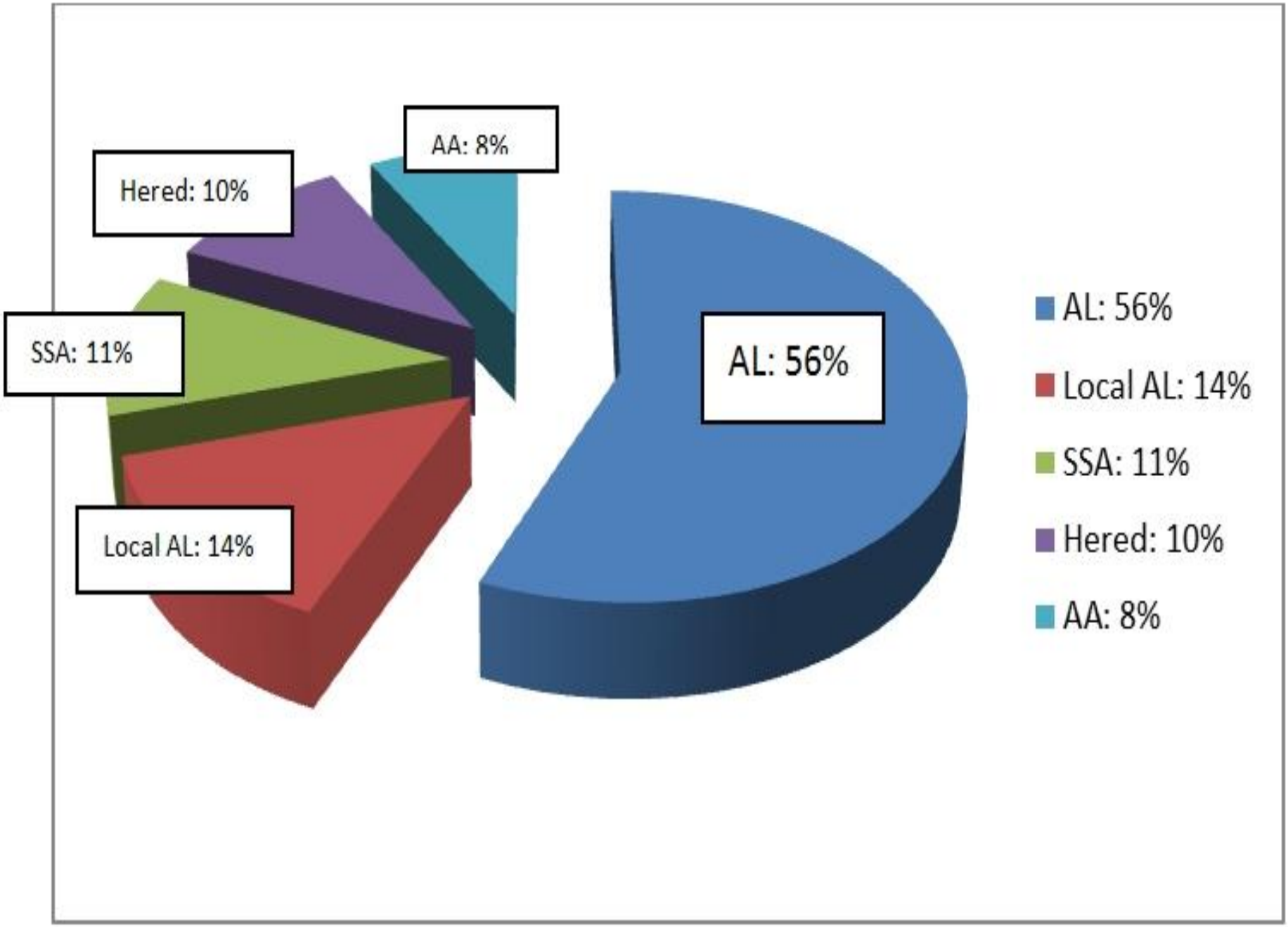
CLASSIFICATION OF AMYLOIDOSIS

- **Based on cause**
  - **Primary :** with unknown cause and the deposition is in the disease itself
  - **Secondary:** as a complication of some underlying known disease
- **Based on extent of amyloid deposition**
  - ***Systemic (generalised)*** involving multiple organs
  - ***Localised amyloidosis*** involving one or two organs or sites
- **Based on histological basis**
  - **Pericollagenous***:* corresponding in distribution to primary amyloidosis
  - **Perireticulin:** corresponding in distribution to secondary amyloidosis

MAIN TYPES OF AMYLOIDOSIS

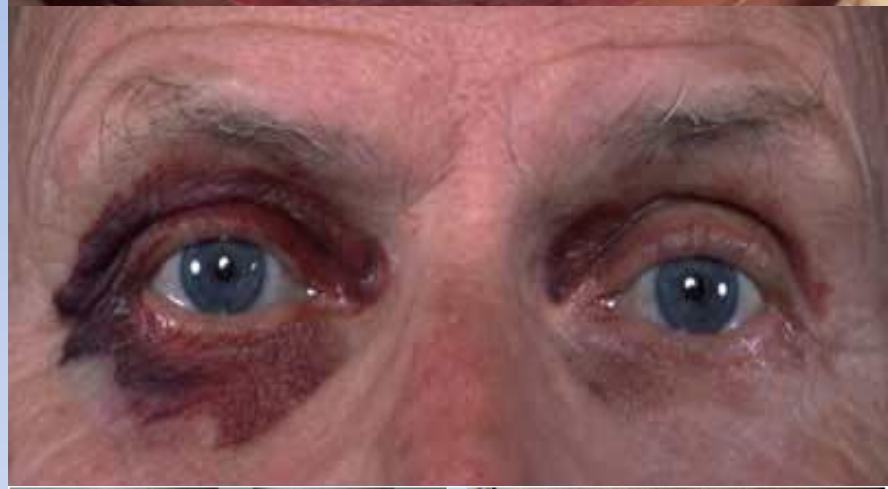
Isolated Deposits

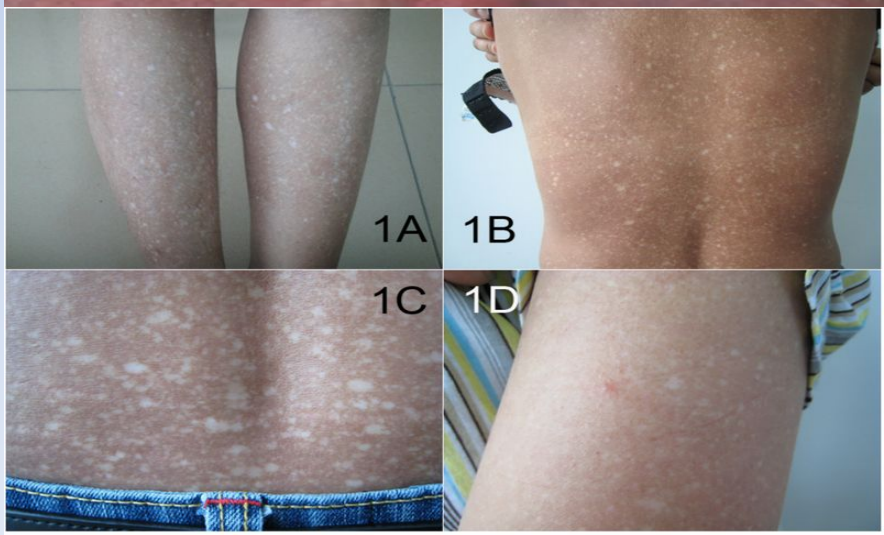
TYPE	SOURCE of AMYLOID	ORGANS INVOLVED
AL (Primary) Amyloidosis Amyloid Light-Chain	**Bone Marrow (Light chains produced by plasma cells)**	**Kidneys, Heart, Liver, GI system, Nervous system**
AA (Secondary) Amyloidosis Amyloid A Protein	**Circulating inflammatory protein (Serum amyloid A)**	**Kidneys, Liver**
TTR (Familial) Amyloidosis Mutant Transthyretin	**Unstable, mutant transthyretin produced in the liver**	**Nervous system, Heart**
SSA (Senile systemic) Amyloidosis Seniors	**Wild-type (normal) transthyretin**	**Heart**


AA: 8%
Hered: 10%
SSA: 11%
Local AL: 14%
AL: 56%
AL: 56%
Local AL: 14%
SSA: 11%
Hered: 10%
AA: 8%

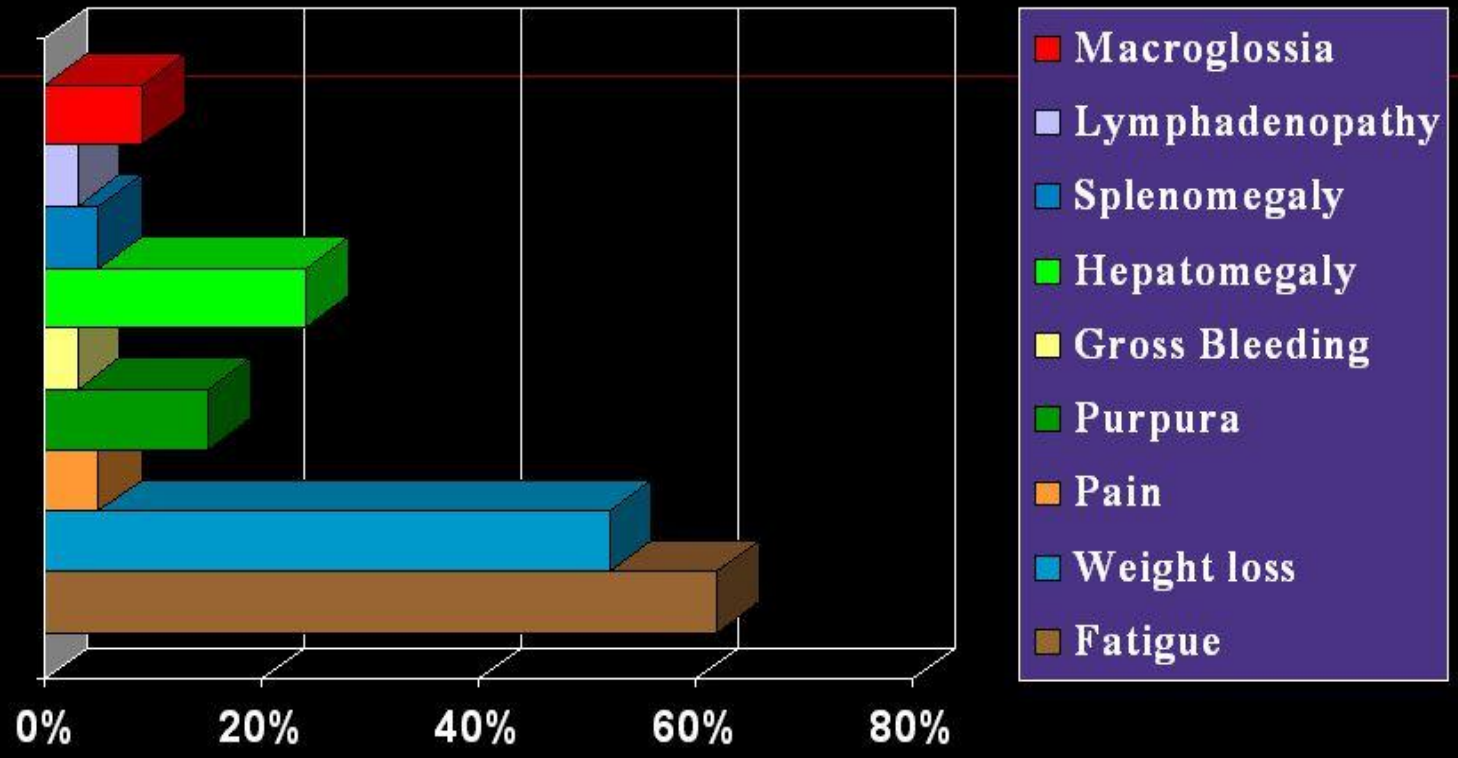
Signs and symtoms

- The presentation of amyloidosis is broad and depends on the site of amyloid accumulation. The kidney and heart are the most common organs involved
- Signs and symptoms of amyloidosis may include:
- Swelling of your ankles and legs
- Severe fatigue and weakness
- Shortness of breath
- Numbness, tingling or pain in your hands or feet, especially pain in your wrist (carpal tunnel syndrome)
- Diarrhea, possibly with blood, or constipation
- Feeling full quickly when eating, and significant weight loss
- An enlarged tongue
- Skin changes, such as thickening or easy bruising, and purplish patches around the eyes
- An irregular heartbeat
- Difficulty swallowing





Symptoms & Signs in Amyloidosis



- Median Wt loss ~ 23 #
- Renal insufficiency in 45% usually without hypertension
- Proteinuria in 73%

Diagnosis

- **Laboratory tests.** Your blood and urine may be analyzed for abnormal protein that can indicate amyloidosis. Depending on your signs and symptoms, you may also have thyroid and liver function tests.
- **Biopsy.** A tissue sample may be taken and checked for signs of amyloidosis. The biopsy may be taken from your abdominal fat, bone marrow, or an organ such as your liver or kidney. Tissue analysis can help determine the type of amyloid deposit.
- **Imaging tests.** Images of the organs affected by amyloidosis can help establish the extent of your disease. Echocardiogram may be used to assess the size and functioning of your heart.

Table 2 Recommended Diagnostic Testing for a Histologic Diagnosis of Amyloidosis

- CBC, creatinine level, alkaline phosphatase level
- Serum and 24-hour urine total protein, electrophoresis, and immunofixation
- Serum immunoglobulin free light chain assay
- Marrow biopsy
- Quantitative immunoglobulins
- N-terminal pro-B natriuretic peptide level, serum troponin levels, uric acid level
- Echocardiography with Doppler
- Confirmation that amyloid deposits are of Ig origin (ie, laser capture microdissection followed by mass spectroscopy)

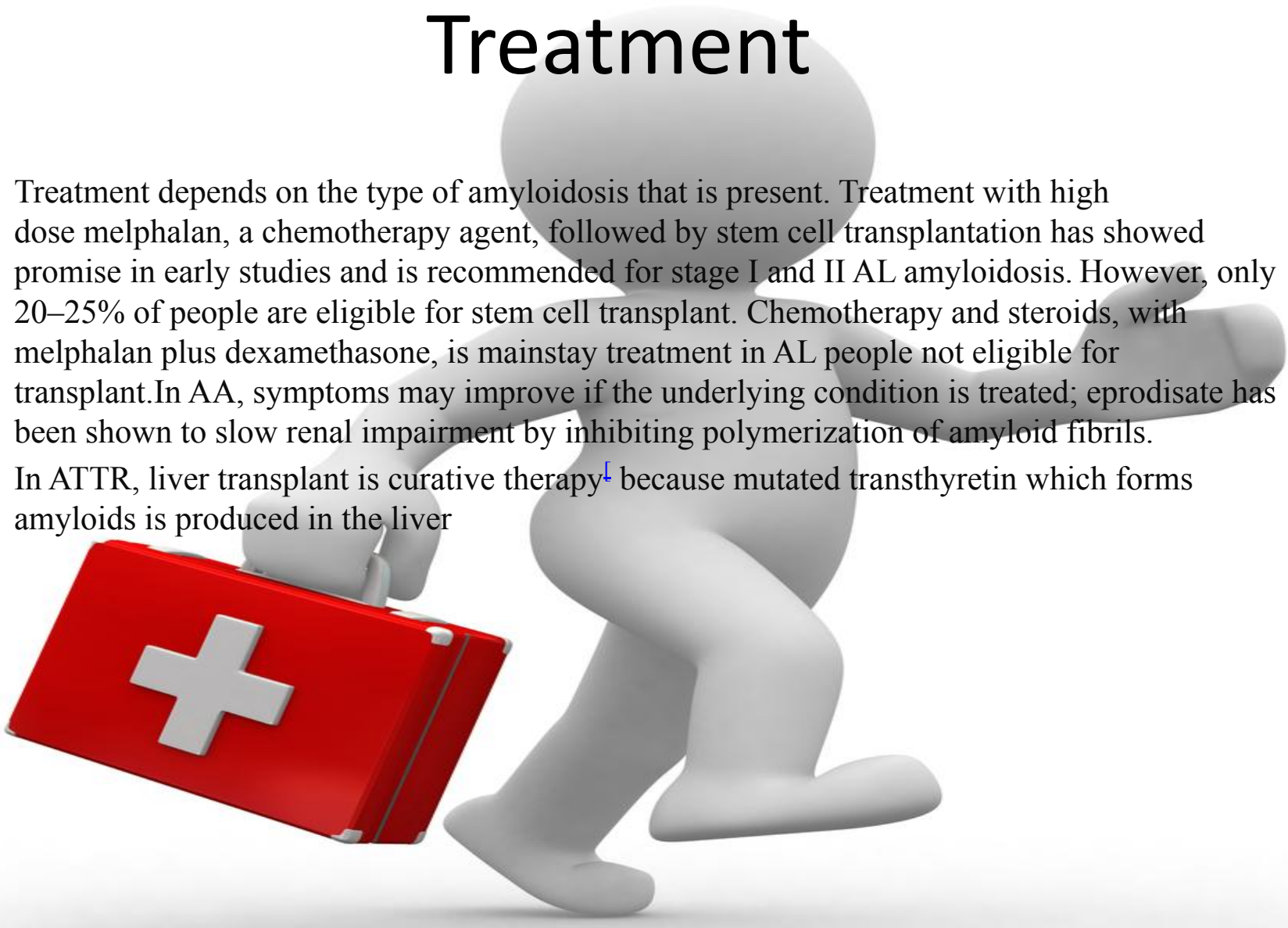
CBC = complete blood cell count.

TREATMENT..

- Treatment of the different types of amyloidosis varies with the cause of fibril production.
- **Secondry AA amyloidosis:** Therapy is aimed at the underlying infectious or inflammatory disorder
- **(AL) amyloidosis:** treating the underlying plasma cell dyscrasia in primary
- **Dialysis-related amyloidosis:** either altering the mode of dialysis or considering renal transplantation
- **Hereditary amyloidoses** in which the mutant amyloid precursor protein is produced by the liver (eg, transthyretin, apolipoprotein A-I, and fibrinogen Aa), liver transplantation may in some instances prevent further deposition of amyloid and may lead to regression of established deposits. Transplantation during the first year after appearance of symptoms is ideal. Patients with sporadic or undiagnosed hereditary amyloidosis who present with advanced end-organ damage may benefit from combined hepatorenal or hepatocardiac transplantation.

Treatment

- Treatment depends on the type of amyloidosis that is present. Treatment with high dose melphalan, a chemotherapy agent, followed by stem cell transplantation has showed promise in early studies and is recommended for stage I and II AL amyloidosis. However, only 20–25% of people are eligible for stem cell transplant. Chemotherapy and steroids, with melphalan plus dexamethasone, is mainstay treatment in AL people not eligible for transplant.In AA, symptoms may improve if the underlying condition is treated; eprodisate has been shown to slow renal impairment by inhibiting polymerization of amyloid fibrils.
- In ATTR, liver transplant is curative therapy because mutated transthyretin which forms amyloids is produced in the liver

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