

# AMYLOIDOSIS - II

## PATHOGENESIS AND CLASSIFICATION

**Dr.V.Shanthi**

**Associate professor, Pathology**

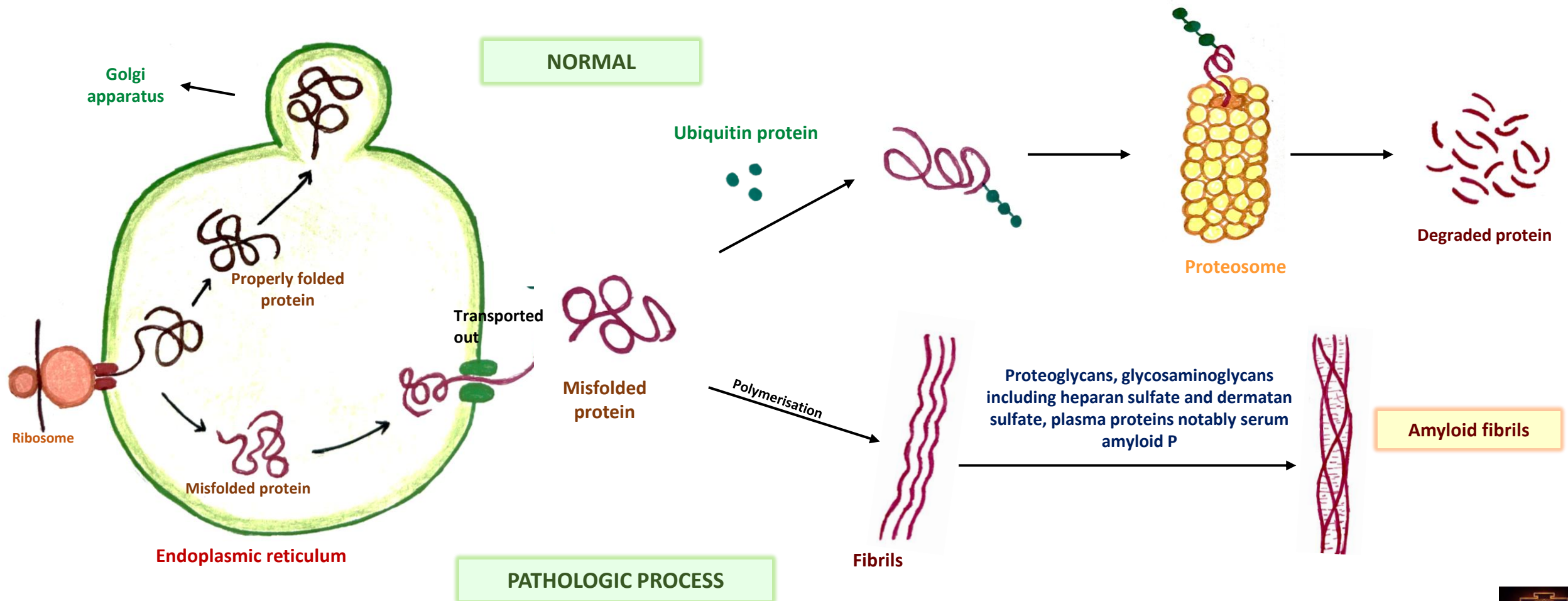
**Sri Venkateswara Institute of Medical Sciences, Tirupathi**



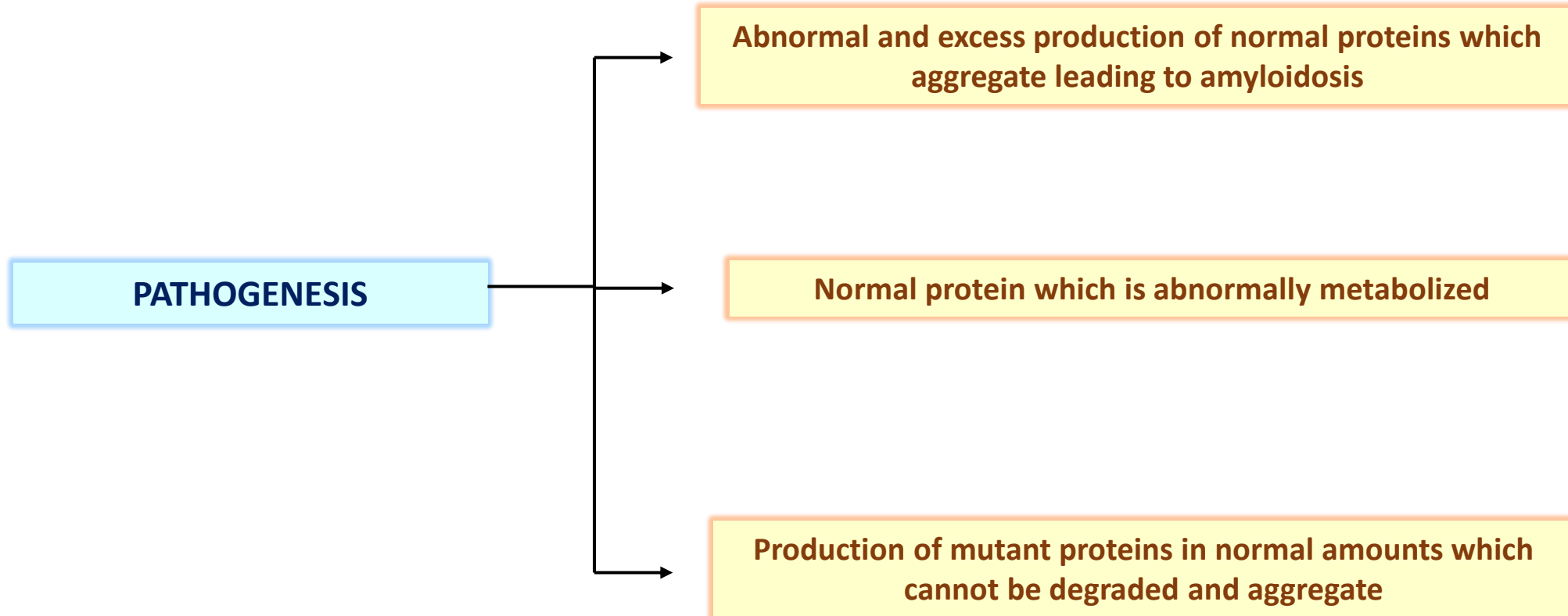
# AMYLOIDOSIS

## PATHOGENESIS

Amyloidosis results from abnormal folding of proteins, which become insoluble aggregates and deposit as fibrils in extracellular tissue

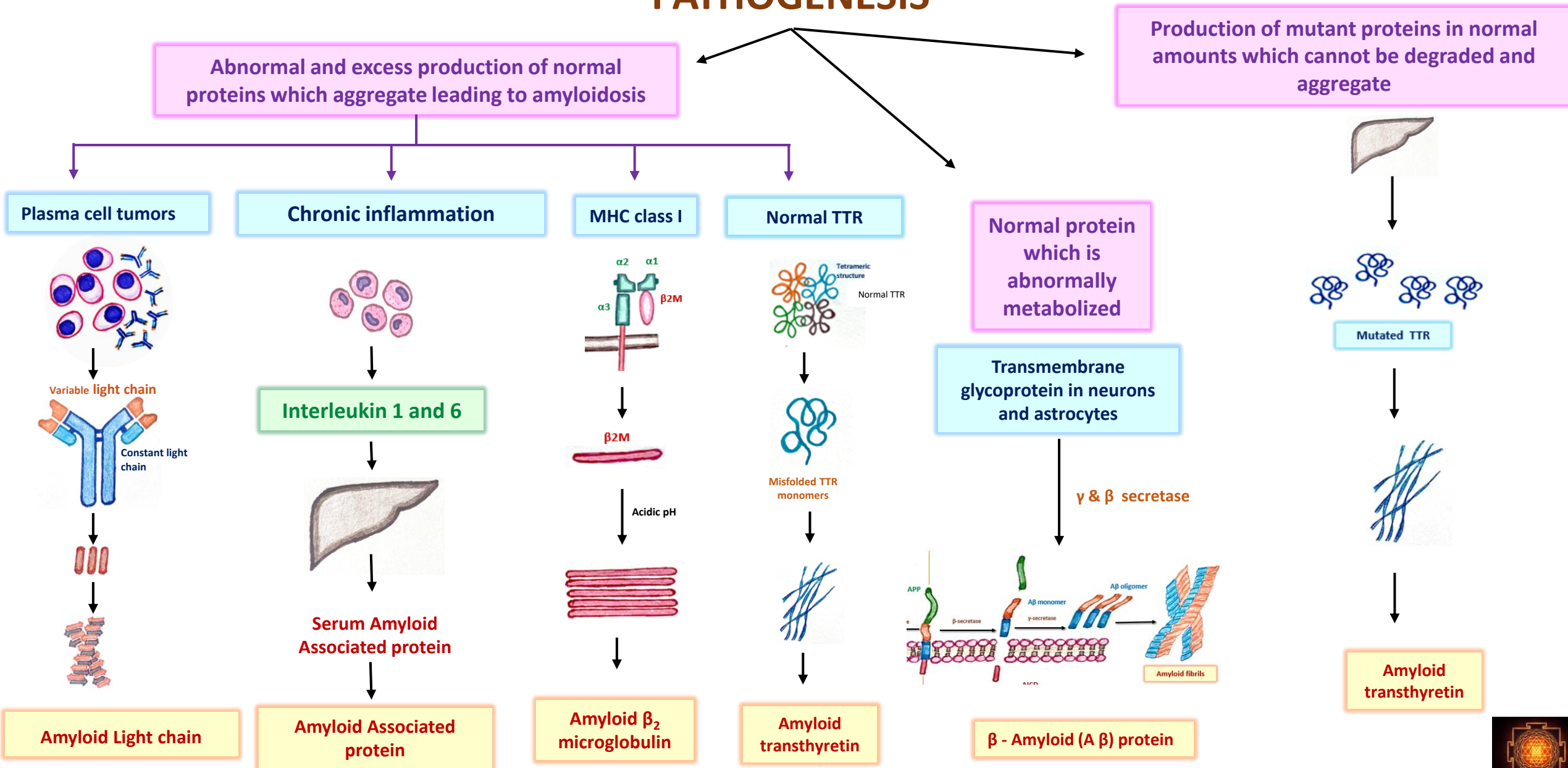


# AMYLOIDOSIS



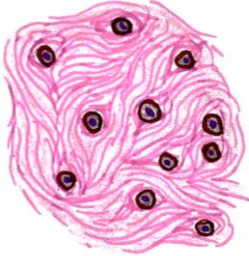
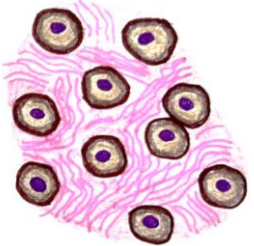
# AMYLOIDOSIS

## PATHOGENESIS

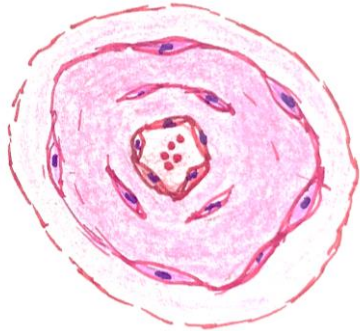
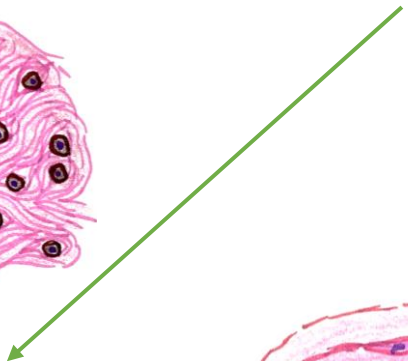


# AMYLOIDOSIS

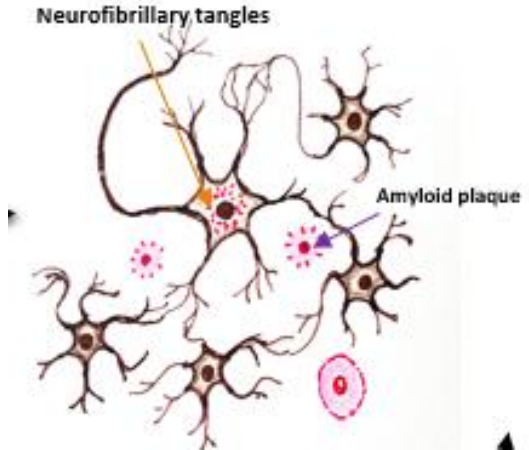
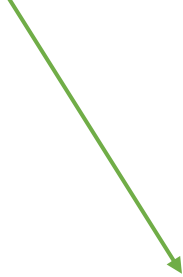
Mechanism of damage



**Pressure atrophy**



**Accumulation of amyloid in the vessel wall causing compression of lumen leading to ischemia and increased vascular permeability**



**Alzheimers disease**  
Prefibrillar oligomers are injurious to cells



**Direct cytotoxicity**  
Amyloid light chain in cardiac muscle



# AMYLOIDOSIS

## Classification

### Generalized / systemic amyloidosis

- Primary amyloidosis
- Secondary amyloidosis
- Hemodialysis associated amyloidosis

### Localized amyloidosis

- Senile cerebral amyloidosis
- Endocrine
  - Medullary carcinoma thyroid
  - Type 2 diabetes - Islets of Langerhans
- Isolated atrial amyloidosis

### Hereditary amyloidosis

- Familial Mediterranean fever
- Familial amyloidotic neuropathies
- Systemic senile amyloidosis



# GENERALIZED / SYSTEMIC AMYLOIDOSIS

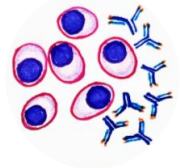
## Primary amyloidosis

## Secondary amyloidosis

## Hemodialysis associated amyloidosis

Conditions associated

Plasma cell disorders



Secondary to chronic inflammation

- Rheumatoid arthritis
- other connective tissue disorders such as ankylosing spondylitis
- Inflammatory bowel disease both Crohn disease and ulcerative colitis
- Drug abusers - . Heroin
- Solid tumors - Most common being renal cell carcinoma and Hodgkin lymphoma

Chronic renal failure patients with hemodialysis

Precursor protein

Synthesizing Ig light chain, chiefly  $\lambda$  chain

Serum Amyloid associated protein produced by liver due to stimulation by IL-1 and 6 produced by macrophages

$\beta$ 2-microglobulin Retained in circulation and serum levels are increased

Major fibril protein

Amyloid Light chain (AL) protein

Enzyme defect leading to incomplete breakdown of SAA  
Structural abnormality in SAA rendering it resistant to degradation

Amyloid associated protein (AA)

Amyloid  $\beta$ 2-microglobulin

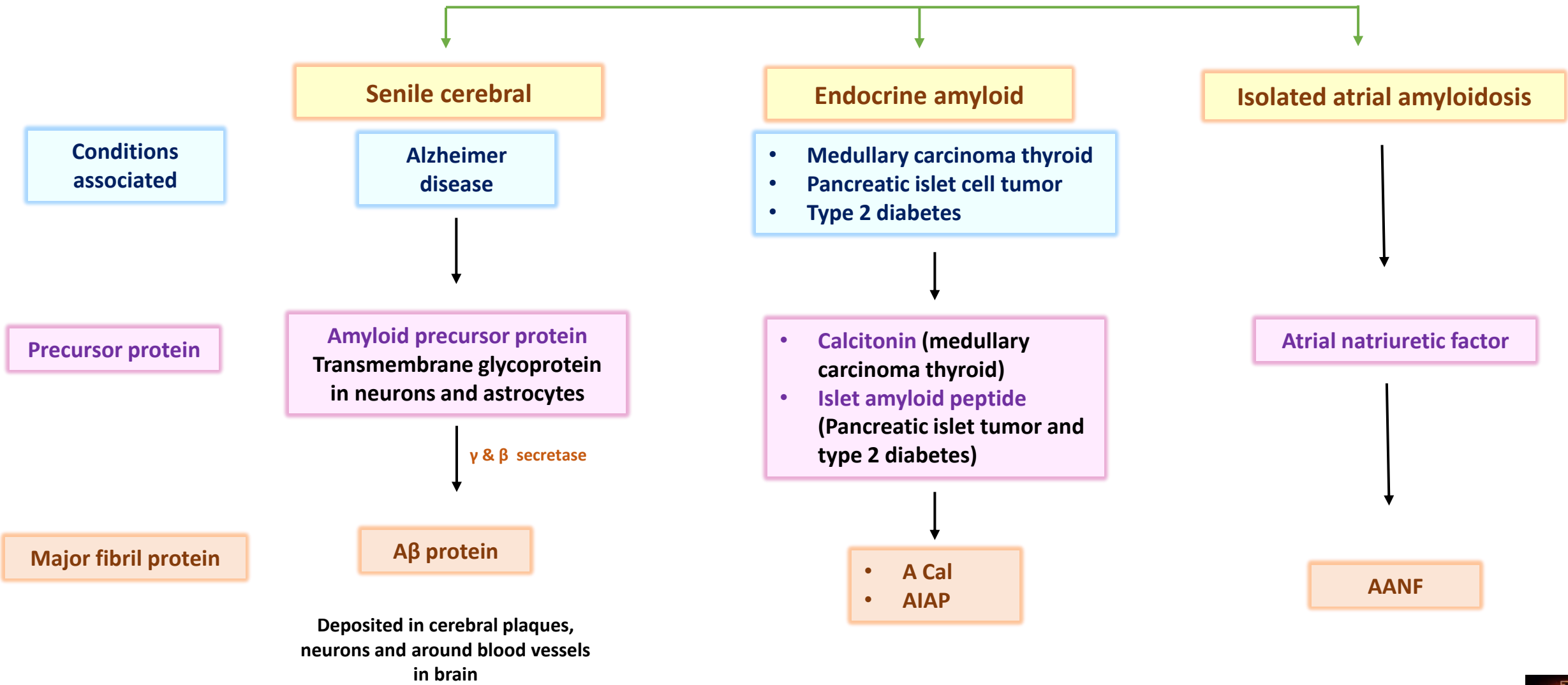
Seen in 5% to 15% of cases of multiple myeloma

Deposited in joints, muscle, tendons or ligaments- CARPAL TUNNEL SYNDROME



# LOCALIZED AMYLOIDOSIS

- Amyloid deposition is limited to single organ or tissue without involvement of any other site
- Deposits are present as nodules in lung, larynx, skin, urinary bladder, tongue and around eye





# HEREDITARY AMYLOIDOSIS

## Familial Mediterranean fever

Autoinflammatory syndrome which is autosomal recessive

Characterized by fever and serosal inflammation involving pleura, peritoneum and synovial surfaces

Increased production of cytokine IL-1

Increased production of SAA

Amyloid associated protein

## Familial amyloidotic neuropathies

Autosomal dominant

Familial amyloidotic polyneuropathies

Deposition of amyloid in peripheral and autonomic nerves

Mutant TTR

ATTR

## Systemic senile amyloidosis

Normal TTR

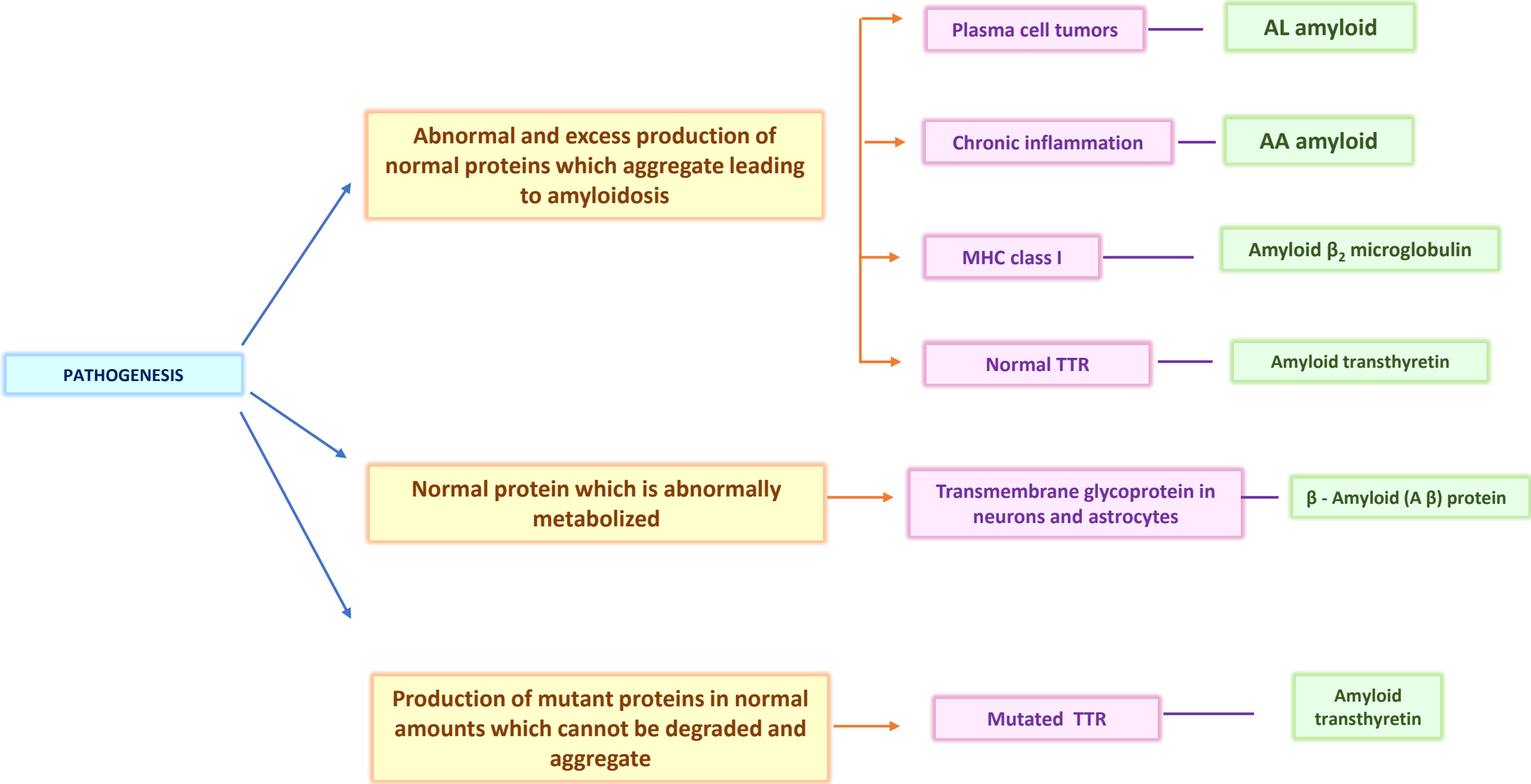
ATTR

Conditions associated

Precursor protein

Major fibril protein





Clinicopathologic category	Associated diseases	Precursor protein	Major fibril protein
<b>SYSTEMIC (GENERALIZED) AMYLOIDOSIS</b>			
Primary amyloidosis (Ig light chain amyloidosis)	Plasma cell tumors	Ig light chains, chiefly $\lambda$ type	AL
Secondary amyloidosis (Reactive systemic amyloidosis)	Chronic inflammatory conditions	Serum Amyloid Associated protein (SAA)	AA
Hemodialysis – associated amyloidosis	Chronic renal failure	$\beta_2$ microglobulin	A $\beta_2$ M
<b>HEREDITARY AMYLOIDOSIS</b>			
Familial Mediterranean fever		SAA	AA
Familial amyloidotic neuropathies		Transthyretin	ATTR
Systemic senile amyloidosis		Transthyretin	ATTR
<b>LOCALIZED AMYLOIDOSIS</b>			
Senile cerebral	Alzheimer disease	Amyloid Precursor protein (APP)	A $\beta$
Endocrine	<ul style="list-style-type: none"> <li>Medullary carcinoma thyroid</li> <li>Islets of Langerhans</li> <li>Type 2 diabetes</li> </ul>	Calcitonin Islet amyloid peptide	A Cal AIAPP
<ul style="list-style-type: none"> <li>Isolated atrial amyloidosis</li> </ul>		Atrial natriuretic factor	AANF



Thank  
You

