# Amyloidosis

*Amyloidosis is an infiltrative multisystem disorder that is characterized by the presence of abnormal monoclonal serum proteins which are deposited in involved organs; it can be primary (AL - lymphoproliferative) or secondary (AA) to other inflammatory diseases (RA, ankylosing spondylitis, multiple myeloma); kidney involvement is most common, and is manifested by proteinuria, progressing to the nephrotic syndrome, renal failure, or both; cardiac deposits result in CHF, arrhythmias, or anginal syndromes; peripheral nerve infiltration produces symptomatic neuropathy, whereas central nervous system deposition may produce dementia or cerebral hemorrhage when deposits are primarily vascular; macroglossia is of particular interest and is seen in primary amyloidosis*

**ANESTHETIC CONSIDERATIONS:**

- Potential difficult airway: (macroglossia, laryngeal / tracheal / bronchial obstruction)
- Potential full stomach: (GI infiltration and decreased esophageal motility)
- Organ Dysfunction
  - Renal: nephrotic syndrome, ESRD
  - Cardiac: Cardiomyopathy, CHF, dysrhythmias (VT / sudden death), heart block
  - GI: Gastroparesis, pseudo-obstruction
  - Heme: Bleeding diathesis, factor X deficiency
  - Neuropathy: mixed sensory / motor, neuropathic pain, autonomic dysfunction
- Associated Illness
  - Inflammatory: RA, ankylosing spondylitis, psoriatic arthritis
  - Hypothyroidism
  - Multiple myeloma
- Side effects of medication therapy

**ANESTHETIC GOALS:**

- Assess and optimize end organ dysfunction

**HISTORY**

- Identify extent of disease and end organ involvement
- Assessment of end-organ dysfunction
  - Functional Capacity
  - Airway: hoarseness, stridor
  - Nephropathy: nephrotic syndrome (protein loss), ESRD, dialysis
  - Cardiovascular disease: CHF (Restrictive or dilated cardiomyopathy), VT, conduction defects / heart block, pacemaker
  - Neuropathy: peripheral (sensory& motor), distribution, neuropathic pain, autonomic dysfunction (postural hypotension)
  - Gastrointestinal: gastroparesis, GERD, pseudo-obstruction, decreased absorption
  - Heme: bleeding diathesis, factor X deficiency
- Identify associated illness (RA etc.)
- Treatment of underlying illnesses

**PHYSICAL**

- **GENERAL**
  - Postural vitals (orthostatic hypotension from autonomic dysfunction)
- **HEENT**
  - Airway assessment (macroglossia, laryngotracheobronchial obstruction)
  - Assess patency & ease of intubation (MP, hoarseness, stridor etc.)
- **CVS**
  - Restrictive myopathy, LV / RV dysfunction, conduction abnormalities (S3, bradycardia)
- **RESP**
  - CHF (rales)
- **HEME**
  - Factor X deficiency (periorbital bruises)
- **CNS**
  - Autonomic neuropathy (orthostasis)

**INVESTIGATIONS**

- Degree of investigation determined by complexity of surgery
- **Labs**
  - CBC, Lytes, BUN, Cr, INR, PTT (anemia, thrombocytopenia, electrolyte abnormalities, renal insufficiency, coagulopathy)
  - Factor X assay
- **Imaging**
  - ECG (evidence of conduction defects / arrhythmias)
  - ECHO (if history of amyloid heart or history or physical suggestive of CHF)

**OPTIMIZATION**

- Identify, assess and optimize organ dysfunction as indicated by severity of disease and complexity of surgery / anesthetic
  - Optimize heart failure
  - Avoid dehydration (renal failure)
- Pacemaker management

**ANESTHETIC OPTIONS**

- Local, Regional and GA all acceptable

- Decision should be based on patient / surgery / co-morbidities
- Specific consideration should be made with the use of regional in amyloidosis, esp. if presence of peripheral neuropathy as:
  - Block duration may be prolonged (decreased LA requirements),
  - Higher risk of nerve injuries

## ANESTHETIC SETUP

- **Drugs**
  - Standard emergency drugs
- **Equipment**
  - CAS monitors (+5 lead ECG)
  - Arterial line (if CHF)
  - Difficult airway cart
  - Pacemaker magnet / reprogramming

## MANAGEMENT OF ANESTHESIA

- **Induction**
  - Airway
    - Macroglossia or tracheal stenosis
    - Increased risk of bleeding into airway from capillary fragility and possible coagulopathy
  - May develop reduced CO and hypotension
  - Coagulopathy may contraindicate regional anesthesia
- **Maintenance**
  - No agent or technique shown superior
  - Maintain adequate urine output
- **Emergence**
  - Patient fully awake to minimize risk of reintubation
  - Caution with nasal airway – may cause hemorrhage

## DISPOSITION & MONITORING

- Close monitoring of CV & renal status
- Consider ICU setting for postoperative care

## COMPLICATIONS

- Difficult airway
- CHF
- Hypotension
- Renal failure

## PATHOPHYSIOLOGY

- **Etiology**
  - Both acquired and hereditary forms exist
  - Major risk factors for acquired disease: multiple myeloma, chronic infectious or inflammatory disease (osteomyelitis, RA, juvenile RA, Ankylosing spondylitis)
  - Hereditary forms very rare
- **Treatment**
  - Acquired: treat underlying disease; colchicines, DMSO, chemotherapeutic agents (azathioprine, cyclophosphamide, methotrexate etc)
  - Hereditary: colchicines, chemotherapeutic agents (melphalan) +/- steroids, liver transplantation
- **Organ involvement:**
  - **Renal disease**
    - Most often presents as asymptomatic proteinuria or clinically apparent nephrotic syndrome
    - Primary deposition can be limited to blood vessels or tubules; such patients present with renal failure with little or no proteinuria
    - End-stage renal disease is the cause of death in a minority of patients
  - **Cardiomyopathy**
    - Cardiac involvement can lead to systolic or diastolic dysfunction and the symptoms of heart failure
    - Other manifestations include syncope due to arrhythmia or heart block, and angina or infarction due to accumulation of amyloid in the coronary arteries
  - **Gastrointestinal disease**
    - Hepatomegaly with or without splenomegaly is a common finding in some forms of amyloidosis
    - Other GI manifestations include bleeding (due to vascular fragility and loss of vasomotor responses to injury), gastroparesis, constipation, bacterial overgrowth, malabsorption, and intestinal pseudo-obstruction resulting from dysmotility
  - **Neurologic abnormalities**
    - Mixed sensory and motor peripheral neuropathy and / or autonomic neuropathy may occur
    - Numbness, paresthesia, and pain are frequently noted, as in peripheral neuropathy of many other etiologies
    - Compression of peripheral nerves, especially the median nerve within the carpal tunnel can cause more localized sensory changes
    - Symptoms of bowel or bladder dysfunction and findings of orthostatic hypotension may be due to autonomic dysfunction
    - CNS involvement unusual in patients with the more common AL and AA amyloidosis
    - Amyloid deposits can lead to extensive cortical pathology and dementia in patients with sporadic or familial Alzheimer's disease, while cerebral amyloid angiopathy can cause spontaneous cortical and subcortical intracranial bleeding, primarily in the elderly
  - **Musculoskeletal disease**
    - Amyloid infiltration of muscles may cause visible enlargement (pseudohypertrophy)
    - Large tongue (macroglossia), or lateral scalloping of the tongue from impingement on the teeth, is characteristic of AL amyloid

        - Arthropathy may be due to amyloid deposition in joints and surrounding structures
        - "Shoulder pad" sign is visible enlargement of the anterior shoulder due to fluid in the glenohumeral joint and / or amyloid infiltration of the synovial membrane and surrounding structures
            - This type of shoulder involvement is characteristic of AL amyloid and dialysis related amyloidosis due to deposition of beta-2 microglobulin
        - Other musculoskeletal features of dialysis-related amyloidosis include scapulohumeral periarthritis, spondyloarthropathy, bone disease, and carpal tunnel syndrome
    - **Hematologic abnormalities**
        - May be directly associated with a bleeding diathesis
            - Two major mechanisms have been described: factor X deficiency due to binding on amyloid fibrils primarily in the liver and spleen; and decreased synthesis of coagulation factors in patients with advanced liver disease
            - Some patients have no abnormality in any coagulation test; amyloid infiltration of blood vessels may contribute to the bleeding diathesis
        - Factor X deficiency results from binding of factor X to amyloid fibrils
        - Factor X levels improve, obtaining partial remission, following high-dose melphalan chemotherapy and autologous hematopoietic cell transplantation
        - Other hematologic manifestations are related to the degree of organ involvement, including anemia in patients with renal failure or multiple myeloma, and thrombocytopenia due to splenomegaly
    - **Pulmonary disease**
        - Pulmonary manifestations of amyloidosis include tracheobronchial infiltration, persistent pleural effusions, parenchymal nodules (amyloidomas), and (rarely) pulmonary hypertension
        - Tracheobronchial infiltration can cause hoarseness, stridor, airway obstruction, and dysphagia; bronchoscopic or surgical resection of airway abnormalities may be required

**REFERENCES**


- Uptodate
- Roizen & Fleisher – Essence of Anesthesia Practice – p 13