Amyloidosis is a generic term referring to extracellular tissue deposition of fibrils with beta-pleated sheets. Deposits in heart, spleen, kidney, liver, gut, skin

-> Primary Amyloidosis (AL): Deposition of fragments of monoclonal light chains. Usually variable portion of light chains. Only disease linked to 10 amyloid is multiple myeloma (plasma cell clone responsible for excess light chain production undergoes malignant transformation). Diseases can co-occur. Proteinuria and serum or urinary paraprotein in 85-90% of AL dz
  - Marrow positive for clonal plasma cells in 10-15% of pts w/o serum or urine paraprotein
  - Rarely progress to overt myeloma if don’t have myeloma at the time of diagnosis or shortly thereafter. (Mayo clinic series 0.4% progression to overt myeloma)
  - Should be considered in all pts>40 with unexplained nephrotic syndrome. Serum M spike seen in 90% of pts
  - Very poor prognosis - Mayo clinic series 15% surv. at 5 yrs, best prog finding is young age
  - Treatment: Pred/melphalan for AL and LCDD, reduces proteinuria, improves survival somewhat. However, can be marrow toxic causing pancytopenia or AML. BMT - very limited data. Survival best with less organ involvement at time of transplant. Cardiac involvement – very poor prognosis

-> AL vs Light Chain Deposition Disease (LCDD): LCDD is similar to AL amyloid in that there are tissue deposits of monoclonal light chains in kidney, heart, liver, and gut, and can also be assoc with mult myeloma. However, LCDD is usually kappa light chains, granular not fibrillar, don’t bind Congo Red, SAP, or thioflavine T. AL - lambda light chains. Development of AL vs. LCDD depends on kind of light chain and differences in the variable region.

-> Secondary Amyloidosis (AA) Also called “reactive amyloid” - response to an inflammatory condition.
  - Causes include bronchiectasis, RA (48-56% of AA), ankylosing spondylitis (5-8%) psoriatic arthritis(5%), chronic infection (osteomyelitis, TB, decubitus ulcers), familial mediterranean fever (2-3%), IBD, CF, neoplasms (esp Hodgkin’s and RCC).
  - Inflammation leads to increased hepatic production of serum amyloid A, which is degraded by macrophages into smaller amyloid A fragments which are deposited in tissues
  - Treat underlying disease process

-> Dialysis Related Amyloid: Beta 2 microglobulin. Linked to duration of dialysis (up to 100% after 13 yrs of dialysis). CTS, bone cysts, spondyloarthropathy, pathologic fx, scapulohumeral periarthritis. Predilection for bones, joints, synovium- B2 microglobulin with high affinity for collagen. B2 removal is minimal with standard cellulosic membranes, has improved with highly permeable hemodialyzers, newer biocompatible membranes, and longer dialysis times.

-> Familial Amyloid: Numerous hereditary amyloid syndromes. Most common: Familial amyloid polyneuropathy (FAP) associated with transthyretin as amyloid protein.

Diagnosis

Tissue biopsy – required for diagnosis
  - Kidney or liver bx positive 90% of cases. Abd fat pad 60-80% positive (many false positives), bone marrow bx (50-55%), skin bx (50%)
  - Amyloid fibrils bind Congo red and have positive green birefringence

Serum amyloid P(SAP) component scintigraphy – amyloid fibrils bind serum amyloid P component. Tc labeled SAP injected. More accurate in AA amyloid. Sensitivity approaching varies by organ involvement (almost 100% if universal splenic uptake to 25-50% with hepatic uptake, less sensitive for cardiac amyloid). However, costly and not widely available