Amyloidosis

[1][2]**Amyloidosis** is a condition associated with a number of inherited and inflammatory conditons in which extracellular fibrillar proteins are responsible for tissue damage and functional compromise. Amyloid is a pathological protein , it has precursor proteins in normal conditions but if its in excess it can lead to amyloidosis. Amyloidosis is fundamentally a disorder of protein misfolding , all amyloid deposits are formed of beta sheet polypeptide chains.

Amyloid contains 3 main proteins

AL(amyloid light chain) produced by plasma cells is made of complete immunoglobulin light chains.

AA(amyloid associated) fibril is a non immunoglobin protein derived from a serum precursor called SAA (serum amyloid associated). SAA is synthesized by liver cells under the influence of IL-6 and IL-1 that are produced during inflammation , thus long standing inflammation has elevated levels of SAA. But increased levels of SAA do not lead to deposition of amyloid.

'**Aβ amyloid** is found in cerebral lesions of Alzheimer's disease. It constitutes the core of cerebral plaques and the amyloid deposits in cerebral vessels in this disease. This protein is derived from amyloid precursor protein (APP).

There are also several other proteins that have been found in amyloid deposits;

-Transthyretin is a normal serum protein that binds and trasports thyroxine and retinol. Mutations in the gene encoding TTR leads to deposition of amyloid. The resultant disease is called familial amyloid polyneuropathy.TTR is also deposited in the heart of aged persons – Senile Systemic Amyloidosis.

-β_2 Microglobulin a component of MHC class 1 molecules and a normal serum protein has been identified as amyloid fibril subunit (Aβ2 m) in amyloidosis. It complicated the course of patients on long term hemodialysis. These patients develop amyloid deposits in the synovium , joints and tendon sheats.

Amyloid may be systemic involving several organs or it may be localized where deposits are limited to a single organ. On clinical aspects the systemic pattern is sub classified into Primary Amyloidosis when associated with a monoclonal plasma cell proliferation and Secondary Amyloidosis when it occurs as a complication of an underlying chronic inflammatory process.

Primary Amyloidosis – Immunocyte Dyscrasias Amyloidosis (AL)

Secondary Amyloidosis - Reactive systemic Amyloidosis **its secondary because of its association to an inflammatory condition.**

Localized Amyloidosis - Deposition of amyloid in single organ or tissue without any involvement of any other site in the body.

Amyloid of Aging- - Some well documented forms of amyloid deposition occurs with aging.Senile systemic amyloidosis refers to systemic deposition of amyloid in elderly persons. SA is also related to the dysfunction of the heart, this form is called Senile Cardiac Amyloidosis. In this form the amyloid consists of normal transthyretin.

Clinical course Most common symptoms are weakness , fatigue and weight loss. Later on amyloidosis manifests in one of several ways ; by renal disease, hepatomegaly , splenomegaly or cardiac abnormalities. Renal problem gives rise to severe proteinuria (nephrotic syndrome)

Biopsy and Congo Red staining are the most important tools in diagnosing Amyloidosis.

In all cases of Amyloidosis serum and urinary electrophoresis and immunoelectrophoresis should be performed.

Bone marrow examination usually shows plasmacytosis.

1. Chapter 5 in: Mitchell, Richard Sheppard; Kumar, Vinay; Abbas, Abul K.; Fausto, Nelson. Robbins Basic Pathology. Philadelphia: Saunders. ISBN 1-4160-2973-7. 9th edition
2. Robbins basic pathology 9e Kumar , Abbas and Aster