Alport Syndrome

Genetics

-Gene: COL4A3, COL4A4, or COL4A5 (Collagen alpha-3(IV) chain/ 4(IV) chain/ 5(IV) chain

-AR/AD: COL4A3 and COL4A4; XLR: COL4A5; 2/3 XLAS; 15% ARAS; 20% ADAS

Clinical findings/Dysmorphic features

-Spectrum: progressive renal disease with cochlear and ocular abnormalities (Alport) to isolated hematuria with benign course (thin basement membrane nephropathy)

-Renal disease progresses: microscopic hematuria (blood in urine) (microhematuria; 100% of affected males and > 90% of affected females with XLAS; 100% of males and females with ARAS) to proteinuria, progressive renal insufficiency, end-stage renal disease (ESRD) in all males with XLAS, and in all males/females with ARAS

-Progressive SNHL is usually present by late childhood or early adolescence

-Ocular findings: virtually pathognomonic: anterior lenticonus (localized, cone-shaped deformation of the anterior or posterior lens surface); maculopathy (whitish or yellowish flecks or granulations in the perimacular region); corneal endothelial vesicles (posterior polymorphous dystrophy); recurrent corneal erosion

-In ADAS: ESRD is delayed until later adulthood, SNHL is late in onset, ocular involvement is rare

Etiology

-Prevalence estimated at 1:50,000 live births

Pathogenesis

-Type IV Collagen: ubiquitously; major collagen component of basement membranes

-Abnormal secretion of collagen alpha 3,4, 5 chains

Genetic testing/diagnosis

-Multigene panel: COL4A5 (80-85% of AS cases; Seq: 85-90%; Indel: 10-15%)