Alagille syndrome

Genetics

-JAG1 (20p12, 95% of cases) and NOTCH2 (1p13-p11)

-AD, 50-70% de novo

Clinical findings/Dysmorphic features

-Bile duct paucity --> Cholestasis (stop of bile [Galle] flow)

-Cardiac defect (most commonly stenosis of the peripheral pulmonary artery and its branches)

-Skeletal abnormalities (most commonly butterfly); pulmonic stenosis

-Eye: posterior embryotoxin (thickened and centrally displaced anterior border ring of Schwalbe)

-Butterfly vertebrae

-Developmental delay, failure to thrive

-Facial: broad forehead, deep-set eyes, pointed chin, straight nose with bulbous tip

Etiology

-1:70,000

Pathogenesis

-Truncated JAG1 unable to bind to the cell membrane resulting in functional haploinsufficiency

Genetic testing/diagnosis

-Sequencing of JAG1 (>89%), JAG1 20p12 del FISH (~7%), NOTCH2 sequencing (1-2%)

Others

-Variable expressivity with clinical features ranging from subclinical to severe

-Clinical Tests: Bile duct paucity on liver biopsy

-NOTCH signalling