Bardet-Biedl syndrome

Genetics

-At least 19 genes: BBS1 (11q13; 23%), BBS10 (12q21.2; 20%), BBS2 (8%)

-AR, 10% triallelic; no identifiable variant in 20% of individuals

Clinical findings/Dysmorphic features

-Rod-cone dystrophy (night blindness by age 7-8 yrs, legally blind by age 15.5 yrs); truncal obesity; postaxial polydactyly (pinky or toe); ID

-Male: hypogonadotropic hypogonadism; female: complex genitourinary malformations

-Renal abnormalities: renal disease is a major cause of morbidity and mortality

Etiology

-1:100,000 (North America), 1:160,000 (Switzerland)

Pathogenesis

-Defects in cilia or intra-flagellar transport

-Defects in the transport of phototransduction proteins from the inner to the outer segments of photoreceptors --> cell death underlies pathogenesis of retinitis pigmentosa in BBS

-Aberrant sonic hedgehog signaling --> polydactyly in BBS

Genetic testing/diagnosis

-Diagnosis on clinical findings

-Gene panel, mostly missense; p.M390R variant in exon 12 of BBS1 (30% of individuals)

Others

-Majority have significant learning difficulties, only a minority have severe impairment