Huntington Disease

Genetics

-Gene: HTT (Huntington, 4p16.3)

-AD

Clinical findings/Dysmorphic features

-Progressive motor disability involving both involuntary and voluntary movement (chorea, dysarthria, dysphagia progress to bradykinesia, rigidity, dystonia)

-Cognitive decline (problems with planning or organization)

-Psychiatric disturbances (personality change, affective psychosis, schizophrenic psychosis)

-Mean age of onset 35-44 yrs (juvenile onset <20yrs ~10%)

Etiology

-HD prevalence varies across world regions: 10:100,000 in Europe; less frequent in Japan, China, Korea, Finland, indigenous African populations from South Africa (0.1 to 2 per 100,000)

Pathogenesis

-Toxic gain of function; non-cell autonomous toxicity; many pathways lead to toxicity

Genetic testing/diagnosis

-CT or MRI: characteristic atrophy of caudate and putamen

-Analysis of repeat by PCR --> heterozygous expansion of CAG (glutamine) in 1st exon of HTT

Others

-> 36 CAG considered HD-causing alleles (risk of developing the disease); 36 to 39 CAG --> incompletely penetrance; > 40 CAG are completely penetrant

-Adult-onset HD usually with 40 to 55 CAGs while juvenile onset with >60 CAGs

-Maternal expansions are extremely rare