HUNTINGTON’S DISEASE

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WHAT IS HUNTINGTON'S DISEASE?

- Huntington's disease (HD) is a fatal, inherited, autosomal dominant, neurodegenerative disorder caused by a CAG trinucleotide repeat expansion in the *HTT* gene. This leads to an abnormal elongation of the polyglutamine region which leads to neurodegeneration.
- HD primarily affects the striatum and cerebral cortex, with medium spiny neurons (MSNs) in the striatum and cortical pyramidal neurons showing early vulnerability.
- Striatal MSNs are critical for motor control.
- Cortical neuron degeneration contributes to cognitive decline and psychiatric symptoms.

HOW IS IT CAUSED?

- The *HTT* gene on the short arm of chromosome 4 codes for a protein called Huntingtin (3144 amino acids, approximately 350 kDa), which plays a role in synaptic function and also plays a crucial role in the post-embryonic period.
- The gene has a region of CAG repeats that starts from the 18^{th} amino acid. Expansion of this repeat leads to disease condition.

HTT gene: ……$(CAG)_n$……

n>55: Juvenile HD
36<n<55: HD
27<n<35: No disease phenotype, but prone to repeat instability
n<26: No HD

- This elongation causes the protein to be more prone to aggregation and accumulation, which disrupts cellular function.

SYMPTOMS

1. Motor Symptoms: Patients experience involuntary movements (chorea), muscle rigidity, impaired balance, and difficulty walking. Fine motor tasks become challenging, and speech and swallowing difficulties often develop.

2. Cognitive Symptoms: Declining memory, difficulty concentrating, and impaired decision-making are common. Problem-solving skills diminish, and individuals may struggle with organizing tasks.

3. Psychiatric Symptoms: Depression, mood swings, irritability, and anxiety frequently occur. Behavioural changes like social withdrawal and obsessive-compulsive tendencies may also develop, severely affecting emotional well-being and relationships.

TREATMENT

- There is no cure for HD.
- There are many therapeutic options for suppressing chorea, including dopamine antagonists, benzodiazepines, acetylcholinesterase, lithium, deep brain stimulation, and glutamate antagonists.
- Adjunctive therapies, as well as behavioural plans and cognitive interventions, may also play a role.

THANK YOU