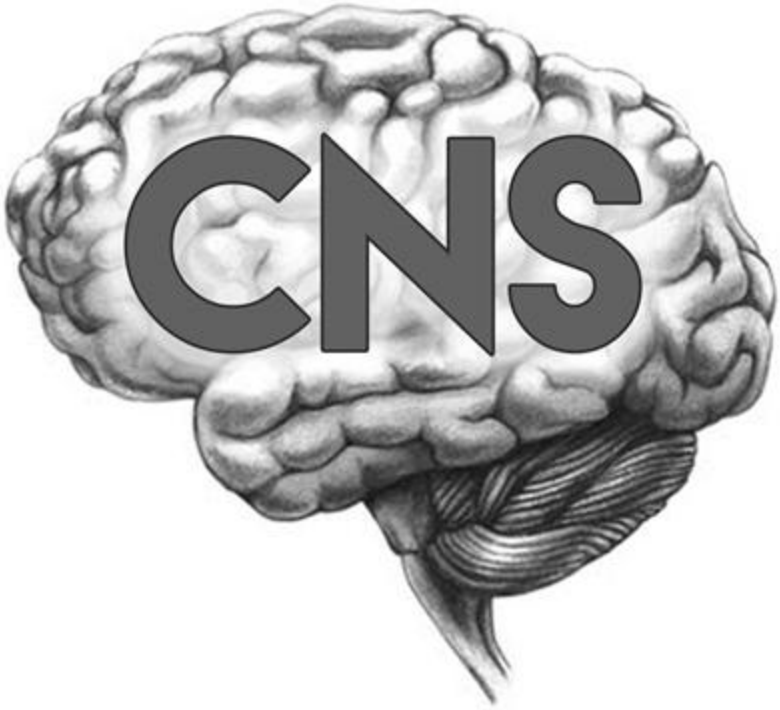

☑ Sheet ○ Slide ○ Handout

Number

7

Subject

Parkinson's, Huntington's chorea diseases

Done By

Hussein El-smadi II

Corrected by

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Doctor

Dr-Heyam Awad

Date: **00/00/2016**

Price:

1- If not feeling motivated, watch this video
https://youtu.be/c1VGFOAERgY
2- This sheet was written based on the recording of section 1.
3- This sheet is to simplify the Drs slides.
4-Have fun!!

In this lecture, we are going to talk about "Neurodegenerative diseases that cause motor dysfunction":
• 1. Parkinson disease • 2. Huntington chorea

Parkinson's disease

Parkinson's KEYWORDS:
Neurodegenerative, bradykinesia, stooped posture, rigidity, pill rolling tremor, late dementia, Lewy body dementia, sporadic and some familial, alpha-synuclein, substantia nigra, L-Dopa

Symptoms are related to the motor function.
Tremors, rigidity, bradykinesia(Walking slowly), and instability(probability of falling while standing).
those symptoms all as a syndrome are called (PARKINSONISM).
Parkinsonism can be caused by:
1-Parkinson's disease
2-toxins
3-dopamine antagonists
So, when a patient comes to you with those typical symptoms of parkinsonism you should investigate for toxins, dopamine antagonists as you think about Parkinson's disease.
you can't tell the patient "you have Parkinson's disease" unless you eliminate other causes.

Now what are the symptoms of (PARKINSON'S) disease?
-Masked face "expressionless face", the patient doesn't have facial movement.
-Stooped posture "forward tilt of the trunk", look at this picture.
-Bradykinesia "slow voluntary movement".
-Rigidity "stiffness".
-Pill rolling tremor "a tremor in the wrist joint while he/she is in rest, if the patient moves this tremor is slightly relieved", it means that the tremor disappears when the patient moves.
-Festinating gait "shortened steps", basically, he is shuffling his legs.
-Reduced arm swinging.

If a patient comes to you with those symptoms; forward tilt of the trunk, bradykinesia, shuffling of the legs and tremor. You think about Parkinsonism and its major cause "Parkinson's disease".

The accumulation of the proteins begins at the lower parts of the brain, then it affects the basal ganglia and also affects the upper cortical regions; affecting the cortical regions means dementia will be developed in those patients (it's one of the very late stages). The characteristics features of it are fluctuating course and hallucinations.

But if a patient developed dementia in the first year of being diagnosed with Parkinson's (normally, dementia is developed late) we call this condition: Lewy body dementia.

Lewy body dementia is a subtype of Parkinson's disease.

Normally, Parkinson's patients live free of dementia for about 10-15 years, they have good memory, cognition with perfect behavior.

Parkinson's disease starts with movement problems, at the beginning cognition of the patient is normal.

So, at the first stage only problems of the voluntary movement.

Then progression of the disease takes place over 10-15 years ends with severe motor slowing. usually, Parkinson's patients cause of the death is:

1- Infections; any disorder causes dementia will increase the incidence of death due to infections, because the patient can't take care of [him/her]self.

2- Trauma; because they have very unstable movement, so they fall easily.

Pathogenesis:

Mainly, sporadic (occurs irregularly). There are some familial cases because of a mutation in the gene that codes for ALPHA SYNUCLEIN. both types Autosomal recessive and autosomal dominant.

-what is the cause of Parkinson's disease?

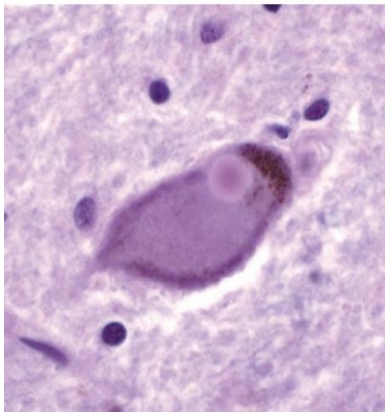
-accumulation of alpha-synuclein protein.

-what is the normal function of the alpha-synuclein?

-it is a protein involved in the synaptic transmission.

The mechanism is that alpha-synuclein is involved in the synaptic transmission, once there is accumulation of this protein, the protein loses its function and it is immune against digestion by proteases (can't be destroyed), and accumulates in Lewy bodies. Look at this photo.

Lewy body: intracytoplasmic eosinophilic round to elongated inclusions that have a dense core surrounded by a pale halo.



Lewy bodies are pink bodies represent the accumulated proteins, Lewy bodies are surrounded by clear (Halo) around it.

Parkinson's disease is not restricted to the basal ganglia, it affects (substantia nigra) making it pale in color. Normally, substantia nigra is black in color.

Substantia nigra is responsible for the production of dopamine, if substantia nigra is damaged by this disease. What is the treatment for this disorder?

We give the immediate precursor of dopamine which is (L-Dopa) to control the symptoms ONLY!

Which means we can't treat the (accumulation of the protein), and with progression of the disease. The therapy will become less effective and the symptoms will become more difficult to manage.

So, L-Dopa is given to manage the symptoms at the beginning of the disease.
Recent studies show that there is a hope in treating Parkinson's disease with (Medical Marijuana).

As we said before, Parkinson's disorder begins at the lower part of the brainstem (Medulla) without clear symptoms, then it affects (substantia nigra) where the symptoms start to appear, going through the (basal ganglia) and end by infecting the cortex causing dementia.

Morphology:
-Pale substantia nigra.
-loss of pigmented neurons and associated gliosis.
-Lewy bodies are seen in the remaining neurons in these regions.

Huntington chorea

*Chorea: means the circle dancing.

It's a neurodegenerative disease. So, the cause should be accumulation of a protein.

What makes the disease unique is that it's the only neurodegenerative that is inherited as autosomal dominant, without any sporadic forms of this disease.

-This disease is familial (inherited). So, what is the inherited mutation on the case of Huntington chorea?

- Trinucleotide repeat expansions CAG (cytosine-adenine-guanine), which are found inside the gene that encodes for the Huntington protein, which has a role in long term memory storage. So, at the end Huntington patient will suffer from memory loss.

Abnormal Huntington protein contains polyglutamine tract; because of the increased content of glutamine.

Trinucleotide repeat expansions are nucleotides that are repeated in a certain gene very many times.

Huntington's KEYWORDS:
Neurodegenerative, Inherited, Trinucleotide repeat expansion, CAG, Glutamine, born with it, Autosomal dominant, Jerky movement, Dance-like movement, suicide, small brain, abnormal Huntington protein, Progressive, long term memory storage, caudate and putamen

Normally, CAG is repeated in a normal human being between 5 -35 times (Dr slides: 11-35 times, also in section 3 the Doctor says it's between 11-35 times). But in the case of Huntington disease you inherit very huge number of glutamines through the repeat expansion, the more the glutamine molecules you have, the earlier you develop symptoms of Huntington disease.

VERY IMPORTANT NOTE:
You have to pay attention that the baby is born with the Huntington disease, but doesn't develop the symptoms until the 20s or 30s of age (In the slides it's 40s to 50s), but as the baby inherits more glutamine amino acids, the earlier the symptoms appear. Course of disease isn't affected by number of repeats.

Remember that every 3 nucleotides encodes for 1 amino acids,, in the case of CAG, CAG encodes for the amino acid Glutamine.

Autosomal dominant in this disease: that one of the parents at least should have the disease so children to have the it.

Here, there is an increase in the movement (Jerky movement, Dance-Like movement), unlike the case of Parkinson's disease when we talked about less movement and slowed movement.

The parts which are degenerated are the caudate and the putamen.

Dr-Heyam didn't talk about the pathogenesis and the morphology of Huntington chorea in this lecture, but I will list them here the way they are in the slides.

Pathogenesis, Clinical course:

- The abnormal Huntington protein contains polyglutamine tracts as a result of the inherited mutated "Trinucleotide repeat expansion CAG".
- They will form large aggregates inside the nucleus.
- Those aggregates are the ones responsible for the Huntington symptoms.

*Those symptoms -like any other neurodegenerative disorder hits the cortex- begin with motor disturbances and choreiform movements.

This disease is progressive so symptoms begin with motor problems, eventually, develops to memory loss, dementia, behavioral changes which could lead to the patient committing suicide.

VERY IMPORTANT NOTE:
***Infections is the leading cause of death among patients who suffer from dementia; because they can't take a good care of themselves. Other causes of death like: suicide(behavioral changes) and trauma(Movement disturbances).

Morphology:

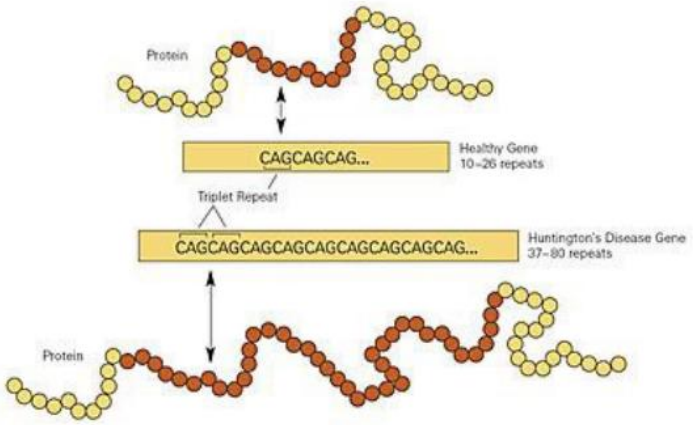
Just like any other neurodegenerative disease:

-Small brain

-Atrophy of the caudate and putamen.

-Severe loss of the neurons; because of the accumulation of the abnormal Huntington protein.

-This is the CAG trinucleotide repeat expansion seen in abnormal Huntington protein.



If you are not making someone's else life better, then you are just wasting your time.!.