Prions and Neurodegenerative Disorders

PRION DISEASES

- Prion diseases are neurodegenerative disorders. They have 100% fatality in humans and there are no treatments
- A long incubation period is typical (sometimes many decades), followed by rapid progression of the disease
    - Within weeks to months, a person can go from having no symptoms to severe disability / death
- Prion disorders share a common pathogenic process
    - The pathology involves the degeneration and death of neurons
    - This neuronal death occurs in the absence of an immune response
- The disorder is transmissible without requiring a conventional infectious agent

AETIOLOGY OF PRIONS

- Prion diseases are associated with the misfolding of a normal cellular protein
    - The normal cellular protein involved is called PrP
- Prions are small, proteinaceous infectious particles
- These infectious particles are resistant to inactivation by most procedures designed to modify nucleic acids
- **Sporadic** cases occur when there is no known aetiology
- **Familial** cases are caused by a mutation of the prion protein gene
- **Acquired** cases happen either through iatrogenic means or through zoonotic transmission

EXAMPLES OF PRIONS

- **Scrapie** affects sheep and goats
- **Bovine Spongiform Encephalopathy** is also known as mad cow disease and impacts cows
- **Chronic wasting disease** affects deer and elk
- Prion diseases have also been observed in exotic ungulates, felines, and mink

VARIANT CJD

- Bovine Spongiform Encephalopathy was first identified as a Scrapie-like disease during routine neuropathologic examination of food animals
- Increased surveillance for Creutzfeldt-Jakob Disease was initiated
- A variant form of CJD (vCJD) was described in 1996
    - This 1996 variant showed striking differences in clinical presentation and neuropathology compared to CJD previously described
    - The pathology observed in variant CJD was similar to the pathology found in BSE

SIGNS AND SYMPTOMS

- **Signs** are things a doctor can physically **measure**
    - For example, taking a patient's temperature to determine if they have a fever

- **Symptoms** are things the patient has to be able to **tell** someone about (they must be observable at a minimum)

CELLULAR ADAPTATION

- **Physiological adaptation** is the cell responding to normal kinds of stimulation
    - This is typically caused by hormones or endogenous chemicals
- **Pathological adaptation** is when the cell responds to stimulation that is happening because of an underlying disease or is trying to avoid injury

HYPERTROPHY

- This is when the cell size increases, which leads to the organ size increasing
- It happens because of increased workload, which can come from physiological or pathological stimuli
- The organ gets larger because the individual cells get larger
- There are no new cells created, only cells that are bigger
- This process happens in non-dividing cells, like myocytes or skeletal muscle
- ***Example:*** If someone has hypertension (often due to atherosclerosis), the increased workload makes the heart enlarge, which initially improves performance but can eventually lead to degeneration

HYPERPLASIA

- This involves an increase in the number of cells, resulting in an increase in organ size
- It means there is an increase in the number of cells within a tissue or an organ
- Hyperplasia only happens in cell populations that are capable of dividing
- It can occur as both a physiological and a pathological response
    - **Physiological Hyperplasia:**
        - **Hormonal:** Like changes seen during puberty
        - **Compensatory:** Such as when the liver regenerates after a resection
        - **Increased demand:** Like when low atmospheric oxygen causes an increase in erythrocytes (which could also be argued to be induced by medication, making it pathological)
    - **Pathological Hyperplasia:**
        - **Hormonal:** Such as endometriosis
        - **Viral infection:** Like the process that causes skin warts
        - **Chronic stress:** Such as developing a callous

ATROPHY

- This is a decrease in cell size or cell number, which causes the organ size to decrease
- It means the organ shrinks because the cells within it decrease in either size or number
    - ***Example:*** Muscle atrophy seen in paraplegic limbs
- **Physiological atrophy** is pretty common during normal development
    - This includes the breakdown of embryonic structures, like the structures that form webbed fingers or toes
    - It also includes the uterus shrinking back down following pregnancy
- **Pathologic atrophy** depends entirely on whatever the underlying cause is