Hashemite University
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Medical School Committee

Scientific Team
الفريق العلمي

# PATHOLOGY

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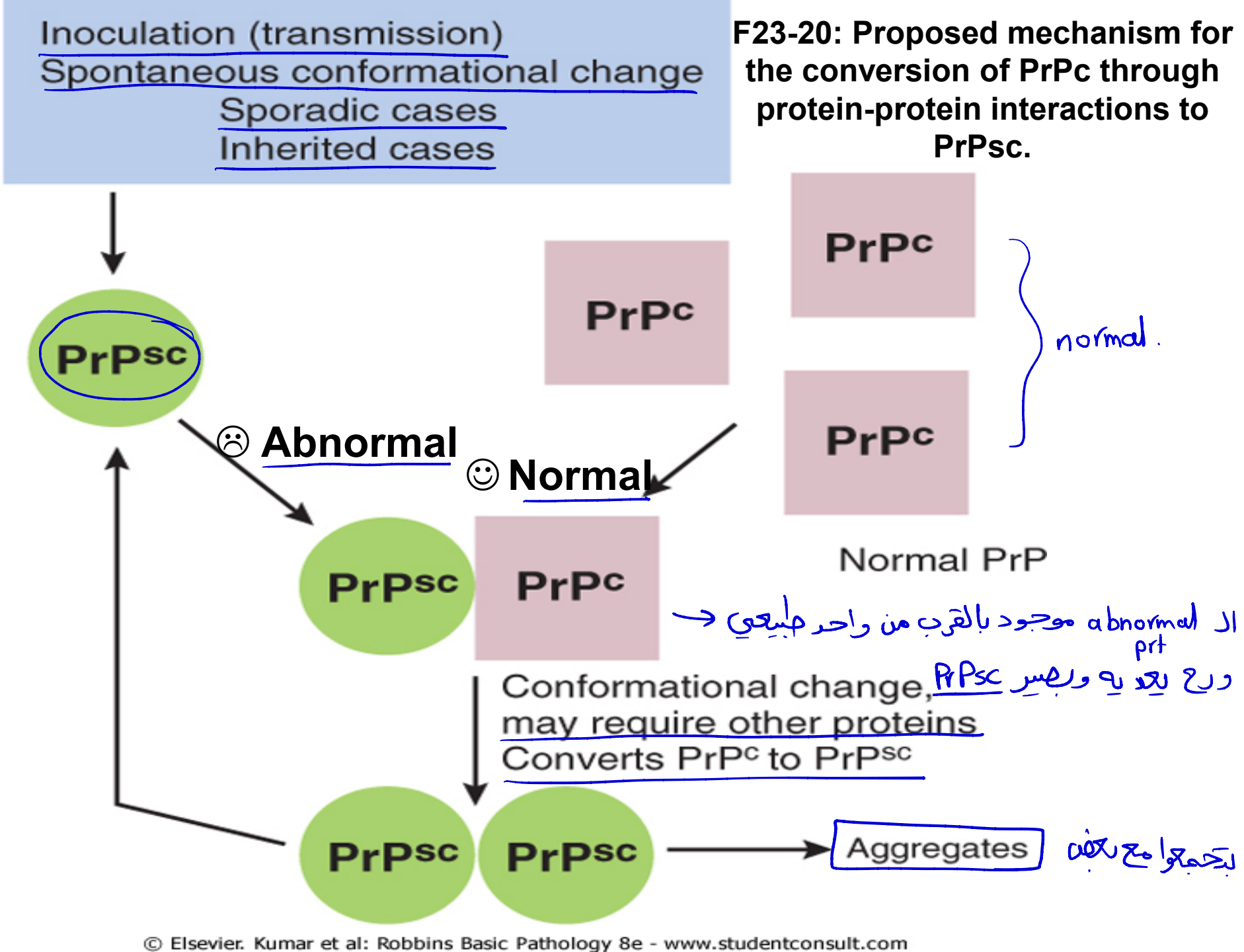
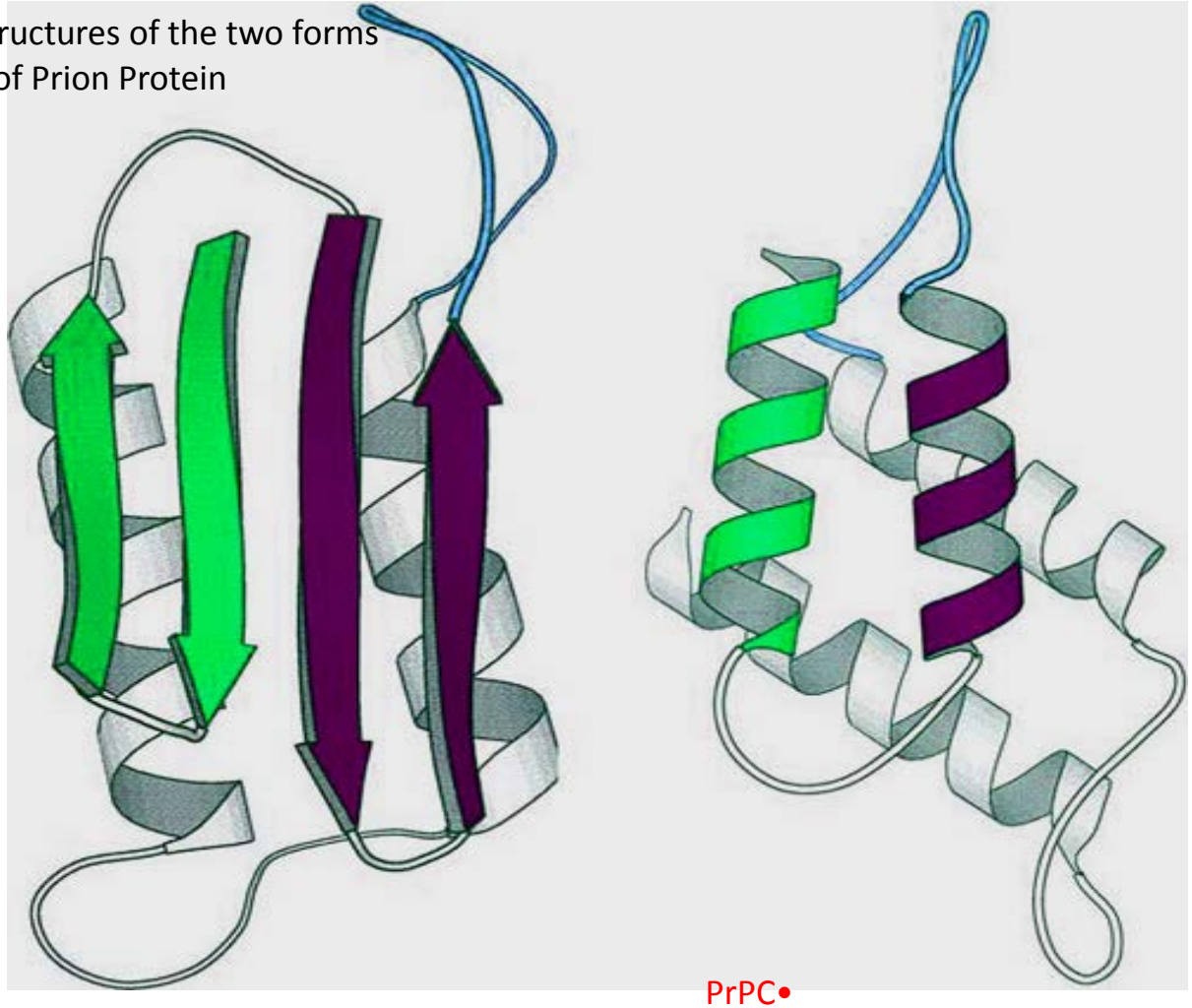
**F23-20: Proposed mechanism for the conversion of PrPc through protein-protein interactions to PrPsc.**



Protein Structures of the two forms of Prion Protein



PrPSc

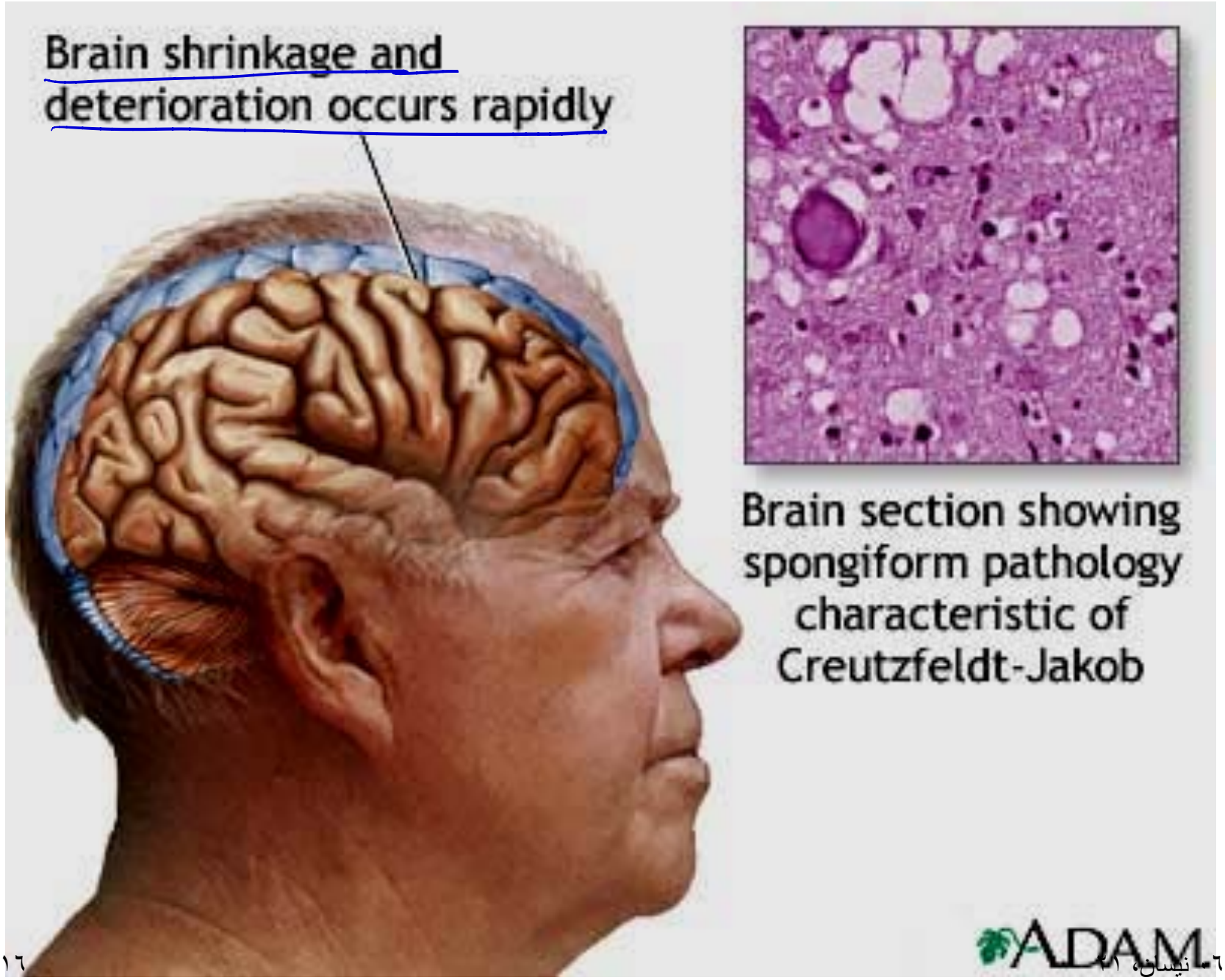
Infectious form(normal form of protein folded incorrectly)..

*Sc*= 'scrapie

PrPC•

The normal form of the protein.•

*C*= 'cellular' or 'common •


Brain shrinkage and deterioration occurs rapidly
Brain section showing spongiform pathology characteristic of Creutzfeldt-Jakob
A.D.A.M.

★ Accumulation of PrPsc in neural tissue seems to be the cause of cell injury, but **how** this material leads to the development of cytoplasmic vacuoles & eventual neuronal death is still **unknown!** مش معروف كيف بيو تكوين الـ vacuoles و الـ abnormalities للمرض.

## Creutzfeldt-Jakob Disease (CJD)

- CJD is a rare (first described in 1920, up till 1980 was of unknown cause!) but well-characterized prion disease that manifests clinically as a **rapidly progressive dementia**.
- It is sporadic in about 85% of cases, with a worldwide annual **incidence of about 1 per million**; familial forms also exist. The disease has a peak incidence in the 7th decade. Elderly people.

☹ There are well-established cases of **iatrogenic transmission** by **deep implantation electrodes** & **contaminated preparations of human growth hormone (GH)** (1) (2) 15% is familial سابقاً كان يعمل

★Presentation begins with mild changes in *memory & behavior* that rapidly progress to **dementia**. The disease is **uniformly fatal**, with an average duration of only 7 months.

◘ H, the pathognomonic finding is a **spongiform transformation of the cerebral cortex & deep gray matter structures** (caudate, putamen); this consists of a multifocal process that results in the uneven formation of **small, empty, microscopic vacuoles** of varying sizes within the cerebral substance(" **neuropil**" ◘ 4.17) & sometimes in the perikaryon of neurons (F23-21A).

• In advanced cases, there is **severe neuronal loss, reactive gliosis**, & sometimes expansion of the vacuolated areas into **cystlike spaces** ("status spongiosus").

✱ **No inflammatory infiltrate is present !**

▼ In all forms of prion disease, **immunohistochemical staining** demonstrates the presence of proteinase K-resistant **PrPsc in tissue** (◘ 4.16).

▼ **Western blotting of tissue extracts** after partial protease digestion allows detection of diagnostic PrPsc.

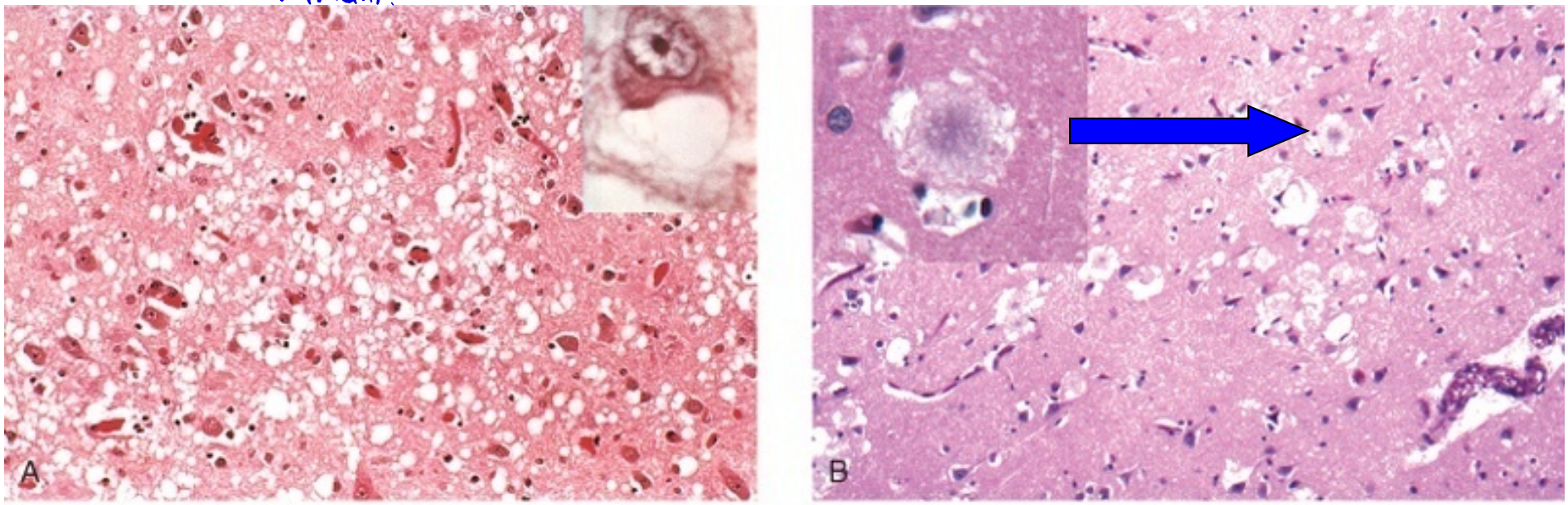
F 23-21: **Prion disease.**

**A,** Histology of CJD showing spongiform change in the cerebral cortex.

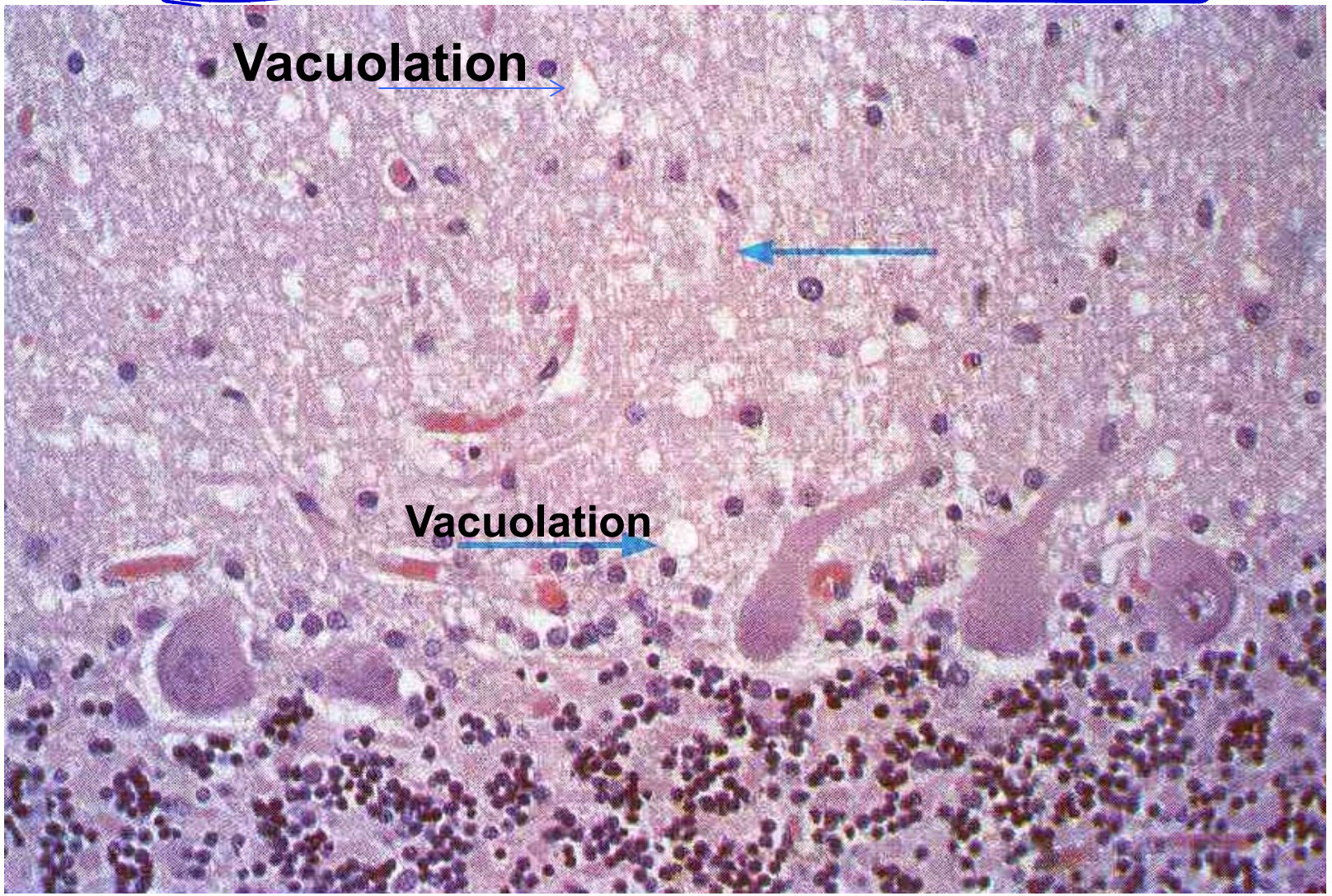
**Inset,** High magnification of neuron with vacuoles.

**B,** Variant CJD (vCJD) is characterized by abundant cortical **amyloid plaques** (see **inset**), **surrounded by spongiform change**.

هذا هو الفرق بين CJD العادي والـ variant

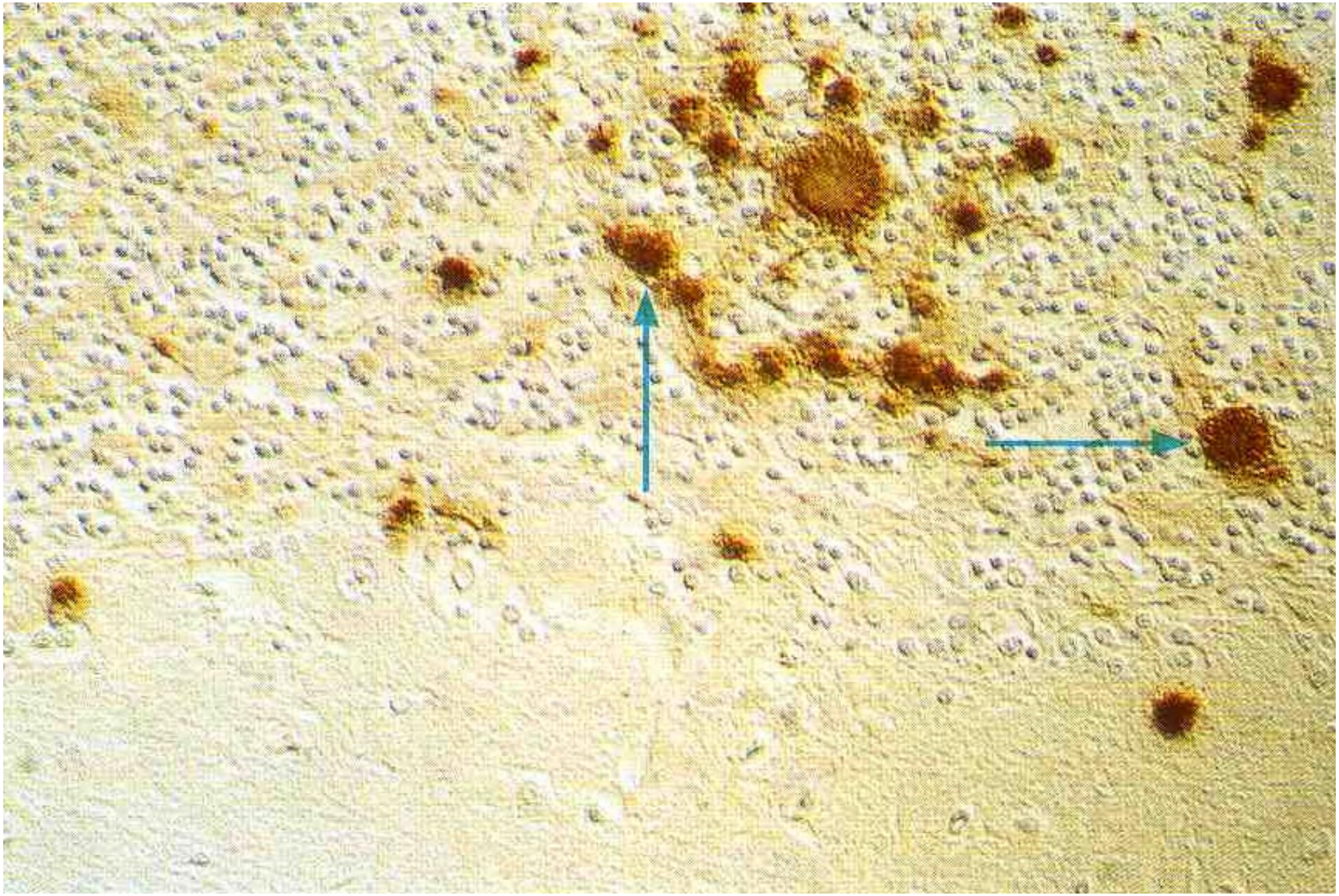


◘ 4.17: **Creutzfeldt-Jakob disease: Brain.** The main features are **loss of neurons**, **demyelination** & spongiform change (confluent **vacuolation** {thin arrow} of the cerebral white matter "neuropil"). However there is **no inflammatory reaction**!



* Neuropil (Vacuolization) is pathognomic to CJD? True.

◘ 4.16: **Creutzfeldt-Jakob disease: Brain.**
Immunohistochemical stain demonstrating the presence of proteinase K-resistant Prion Protein (**PrPsc) in tissue** {arrows}.



# Variant Creutzfeldt-Jakob Disease

➔ **Starting in 1995**, a series of cases with a CJD-like illness appeared in the United Kingdom. They differed from typical CJD in several important respects: the disease affected
**(1) Young adults**, → مستحيل يصيرعندهم CJD ال
**(2) Behavioral disorders** are prominent in the early stage; &
**(3)** the neurologic syndrome **progressed more slowly** than in individuals with other forms of CJD.
↑ مهم
بعض ما بموت بسرعة زي ال CJD .

😐 The neuropathologic findings & molecular features of these new cases were similar to those of CJD, suggesting a close relationship between the two illnesses.

😐 Multiple lines of evidence indicate that this new disease is a consequence of **exposure** to the prion disease of cattle, **Bovine spongiform encephalopathy**. → Eating meat / Drinking milk.

مهم جدا
vCJD has a similar pathologic appearance, in general, to other forms of CJD, with spongiform change & absence of inflammation. In vCJD, however, there are abundant cortical amyloid plaques, surrounded by spongiform change (F23-21B).