

KIMYO INTERNATIONAL UNIVERSITY IN TASHKENT

Faculty of Pediatrics

Student: **Maxamedova Saodat Yoqubjon kizi**

Scientific supervisor: **Musayeva Shahlo Najatovna**

Topic: Prions and the Diseases They Cause, Prevention, Treatment, and Diagnostic Methods

Annotation: Disruption of biosynthetic processes occurring within the cell caused by infectious agents, changes in prions, the effects of mutations, and diseases arising from alterations in prion structure, as well as their prevention, are discussed in this paper.

Introduction:

Methods for studying the main biological properties of pathogenic microorganisms (bacteria, fungi, protozoa, intermediate microorganisms, later viruses, and now prions), isolating them, and classifying them into different species, have been developed.(1) Prions are a special class of infectious agents composed of misfolded protein molecules that lack nucleic acids such as DNA or RNA. They cause transmissible spongiform encephalopathies (TSEs) in humans and animals — rare, incurable, and fatal neurodegenerative diseases.

In this process, PrP^{sc} (scrapie prion protein) is an infectious, misfolded isoform of the normal prion protein PrP^c.

These proteins cause prion diseases such as Creutzfeldt–Jakob disease (CJD) in humans and scrapie in sheep.(2)

Mechanisms of Prion Conversion:

A. Spontaneous Conversion

In spontaneous conversion, the protein structure changes — the alpha-helical configuration is replaced by beta-sheet formations. This leads to the accumulation of proteins and neurodegeneration (destruction of nerve cells).

B. The Role of Mutations

Mutations promote the transformation of the normal cellular prion protein (PrP^c) into the pathogenic, abnormal form (PrP^{sc}). Mutations make the protein less stable and more prone to misfolding.

These changes increase hydrophobicity, alter structure, and enhance aggregation, typical of prion diseases such as familial CJD (fCJD), Gerstmann–Sträussler–Scheinker syndrome (GSS), and fatal familial insomnia (FFI).

C. Template-Assisted Model of PrP^{sc} Formation

The template-assisted model explains how abnormal, infectious PrP^{sc} is produced.

An existing PrP^{sc} molecule acts as a template, forcing a normal PrP^c to misfold into the same abnormal shape.

This conversion is the core process in prion diseases such as scrapie, causing damage to neurons.

D. Deformed PrP^{sc} Discussion

This model explains how misfolded prions can self-propagate and evolve into more pathogenic forms.

The discussion includes the “protein-only” hypothesis, differences between PrP^c and PrP^{sc}, mutation and viral effects, and the potential for non-pathogenic prions to become infectious.(3)

Types of Prion Diseases: Creutzfeldt–Jakob Disease (CJD):

- The most common early symptoms of CJD include memory loss and mental confusion, similar to Alzheimer’s disease.
- Some patients first show loss of coordination (ataxia).
- Variant CJD (vCJD) may start with psychiatric symptoms like anxiety or depression.
- Over time, cognitive and behavioural decline intensifies.
- After about six months, myoclonus (involuntary muscle jerks), tremors, and unsteady gait appear.
- Patients often experience hallucinations, seizures, and extreme sensitivity to sound.
- Breathing and swallowing muscles weaken, increasing the risk of pneumonia.
- Symptoms worsen quickly, leading to severe dementia.
- Most patients die within 6–12 months of onset; in variant CJD, survival averages 18 months.
- Diagnosis of Creutzfeldt–Jakob Disease
- Magnetic Resonance Imaging (MRI)
- MRI reveals characteristic brain changes, especially for variant CJD.
- Cerebrospinal Fluid Examination (Lumbar Puncture)
- CSF testing detects even trace amounts of prions and is highly reliable.
- Similar detection can be done through urine analysis.
- Electroencephalography (EEG)
- EEG shows characteristic electrical patterns in 65% of patients, usually in late stages.
- Exclusion of Other Diseases
- CJD diagnosis involves ruling out other dementia types and reversible conditions.(4)
- **Doctors suspect CJD if:**
- Rapid mental deterioration,
- Myoclonus,
- Unsteady gait,
- Other dementias excluded by testing.
- Variant CJD is suspected in young patients exposed to BSE-contaminated beef.
- Familial CJD is linked to a positive family history.
- Autopsy remains the only definitive confirmation method.
- Prevention of Creutzfeldt–Jakob Disease
- Currently, there is no cure for CJD, making prevention essential.(5)

Preventive measures include:

- Wearing gloves and masks when handling infectious materials

- Destroying or decontaminating surgical tools that contact prions;
- Using only synthetic human growth hormone;
- Avoiding donations from at-risk individuals.(6)

Public health controls for variant CJD include:

- Regular testing of cattle for BSE (“mad cow disease”);
- Culling infected animals;
- Monitoring animal feed for contamination.
- The USDA conducts monthly testing of selected cattle for BSE.(7)

Kuru Disease:

Symptoms:

Loss of coordination (ataxia), tremors, muscle spasms, headaches, and emotional instability (e.g. sudden laughter).

Late stages cause paralysis and inability to speak.(8)

Stages:

1. Prodromal Stage: Partial loss of balance.
2. Sedentary Stage: Inability to walk, severe tremors, involuntary movements.
3. Terminal Stage: Bedridden, incontinence, speech loss, dementia, and death within a year, often from pneumonia.(9)

Cause:

Kuru is a transmissible spongiform encephalopathy (TSE) affecting the cerebellum.

Caused by infectious prion proteins, not bacteria or viruses.

Spread through consumption of infected brain tissue, historically during Fore tribe rituals in Papua New Guinea.

Diagnosis

Neurological exam, EEG, MRI, and blood tests to exclude other causes.(10)

Conclusion:

Biosynthesis, transport, degradation, and conversion of PrP protein in the cell:

PrP^C is synthesised in the endoplasmic reticulum, modified post-translationally, and transferred via the Golgi apparatus to the cell membrane.

Signal peptides are removed, N-linked glycans and a GPI anchor are added, and a disulphide bond forms.

At the membrane, some PrP^C is internalised into endosomes, while the rest recycles.

Conversion to PrP^{Sc} occurs at the membrane or in lysosomes, accumulating near the nucleus.(11/12)

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