The Removal and Inactivation of Prions

WFHSS

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STERIS

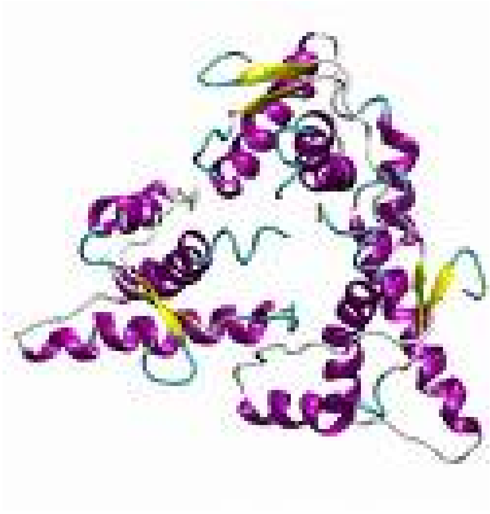
Agenda

1. *Introduction*
    1. *Subject*
    2. *Risks*
    3. *Standards*

1. *Prion introduction*

3. *Cleaning*
    1. *Decontamination*
    2. *Prion inactivation*

Target



Inactivation of prions on infectious proteins

The subject

- **Contaminated surgical instruments need to be cleaned to remove soil and infectious items and proteins**

Soil-A Dirty Subject

- **Implications of inefficient cleaning**
  - Visually unacceptable devices
  - Ineffective disinfection and sterilization
  - Device damage
  - Adverse patient outcomes
  - Accidental prion transmission

Increased Attention

- **Visually unacceptable devices**
  - Cancelled procedures
- **Device damage**
  - Dried on soil / salt deposits
- **End toxins**
- **TASS**
  - Toxic Anterior Segment Syndrome
  - Outbreak in the USA
  - Cataract surgery
  - Inadequate cleaning and/or water residuals

What has Changed since 2000 ?

- The Science of cleaning
- Understanding of “Prions”
- Revolution in Prion Decontamination
  - New Investigations
  - New products

- New Regulatory Focus

What has changed……

…….and reasons for the development of

new and more effective decontamination methods:

- Patient risks
- New Standards
- Increased attention

Patient risks

- **Inadequate disinfection and sterilization**
- **Toxin risks**
- **Prion diseases**
  - Other protein disease concerns

Standards for decontamination

- EN/ISO 15883 series
  - Published
    - *Part 1: General requirements, definitions and tests*
    - *Part 2: Requirements and tests for washer-disinfectors employing thermal disinfection for surgical instruments, anaesthetic equipment, hollowware, utensils, glassware, etc.*
    - *Part 3: Requirements and tests for washer-disinfectors employing thermal disinfection for human waste containers*
  - In final draft (FDIS)
    - *Part 4: Requirements and tests for washer-disinfectors employing chemical disinfection for thermo-labile endoscopes*
  - Technical Specification (TS)
    - *Part 5: Test soils and methods for demonstrating cleaning efficacy of washer-disinfectors*

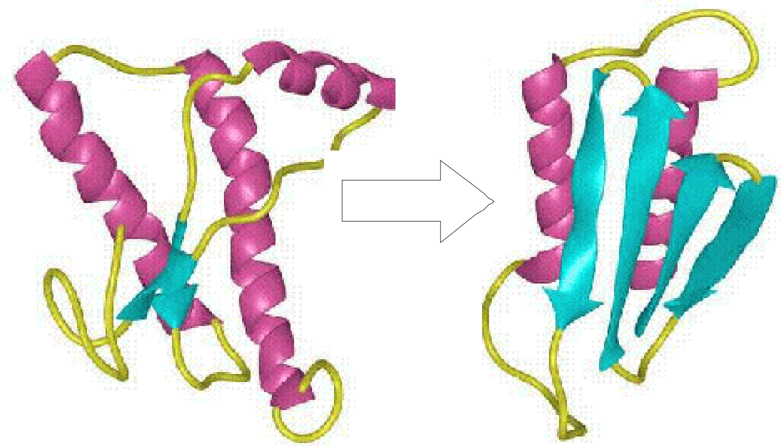
Standards for sterilization

- EN/ISO 17665, *Sterilization of medical devices- Information to be provided by the manufacturer for the processing of resterilizable medical devices*

- Others
  - Biocides directive (98/8/EC; April, 1998)
  - Detergents Directive (648/2004;October, 2005)
  - REACH (Com(03) 644)
    - ‘Registration Evaluation and Authorisation of Chemicals’

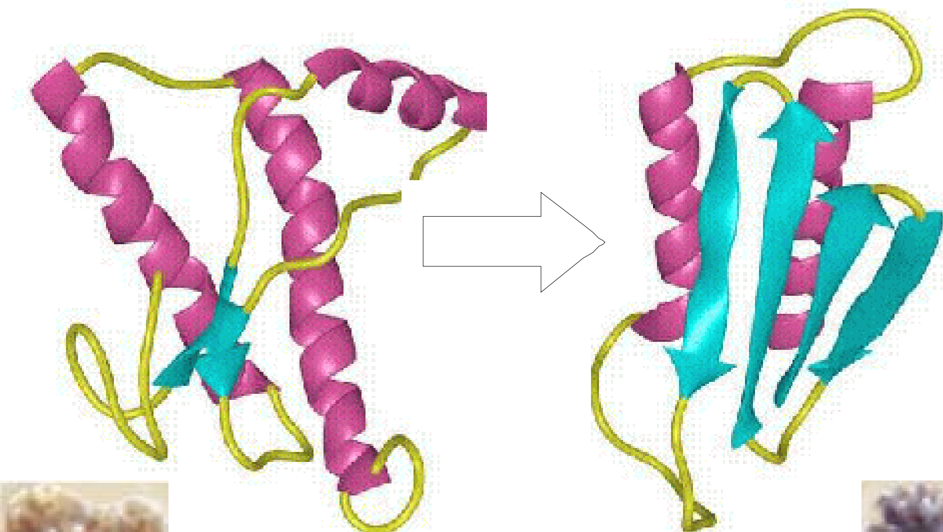
Prion introduction

- What are 'Prions'?
  - Identified as the causative agents for a group of central nervous system diseases
    - TSEs (Transmissible Spongiform Encephalopathies)
    - vCJD, CJD (Creuzfeldt-Jacob disease)
  - *Still debated!*
    - Proteins
    - Appear to be devoid of nucleic acid

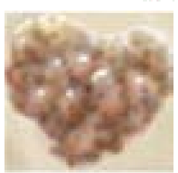


Prion introduction

Prions and protein folding: The cause of vCJD appears to be the presence of an abnormal forms of normal protein, known as a **prion**. This structure makes them hard to be removed from the instruments.

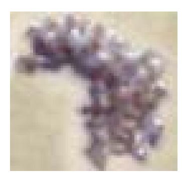


- Accumulate in the body and Causing cell death (brain).
- No more cell growth



Good Protein
Normal Helical form

Bad Protein
Abnormal Sheet form



Prion decontamination

- Intrinsic resistance
  - Prions demonstrate resistance to routine methods of decontamination and sterilization
  - Prions are proteins, not microorganisms

Enveloped Lipid Viruses (HIV)

Large Non-Enveloped Visruses

Vegetable Bacteria

Fungi

Non-Enveleoped Lipid Viruses

Mycobacteria

Bacterial Spores

PRIONS ?

Accidental transmission in practice

Source of CJD	Case 1	Case 2	Implantation
			Assay 
Patient (female) Age: 69	Patient (female) Age: 23	Patient (male) Age: 17	Chimpanzee Age: 17
Exposure Sept. 1974	Exposure Nov. 1974 Death 20 month later	Exposure Dec. 1974 Death 16 month later	Exposure Dec. 1977 Death 20 month later

1-2 new diseases per 1 Mio. People a Year / Global

STERIS Research Facility

- Fontenay-aux-Roses, Paris
  - Laboratory facilities
    - Microbiology (Biosafety 1-3), histology and biochemical laboratories
  - Atypical pathogen research
    - Including Prions

<u>In Vivo</u> and ***<u>In vitro</u>*** sets where carried out
In collaboration with STERIS

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CLEANING

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The science around cleaning

- The chemistry of soil
- How much and what is present
- Detection of soil
- Cleaning indicators
- ‘New’ cleaning methods

- ….How clean is clean?

Concerns with cleaning

- Infectivity is difficult to remove from instrument surfaces
- Drying of soil increases risk
- Improper handling increases risk
- Some standard cleaning processes may also increase risk
- Impractical recommendations

Considerations

- Efficacy
  - Data is conflicting
  - Testing on surfaces
- Compatibility
  - Surface damage
- Safety
  - Handling

<u>WHO process:</u> Emerge instruments in a High concentration of Sodium Hydroxide

The cleaning process

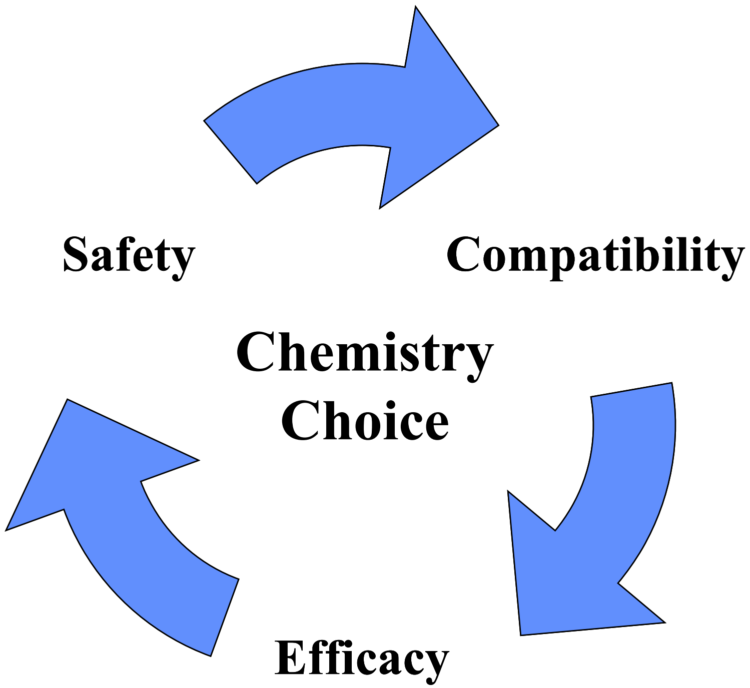
Where should reprocessing begin?

- Point of use (OR)
- WHO, NICE, AORN Guidelines- recommend instruments should not be allowed to dry

Instrument transportation gel / pre-soak

Important Detergent Concepts

- **Regulations**
  - Claims
- **Safety**
- **Process**
  - Contact Method, Time, Temperature, Concentration
  - Water quality
- **Formulation**
  - A combination of ingredients, including active and inert ingredients, into a product for its intended use



New Cleaning Technology

- Enzymatic formulations
  - Genencor
  - Alkaline proteases
  - Effect of formulation
- Advances in alkaline cleaning
- Physico-chemical cleaning
  - e.g., plasma

Cleaning performance

- Cleaning performance test on static emulsion

***Enzymatic* Methods**	***„Log“ Reduction***
Klenzyme	**~4.5**
Enzyme Cleaner 2	**~1**
Porous load autoclaving 15 min at 121°C	**~5.5**
Klenzyme + autoclaving	**~6.5**
Enzyme Cleaner 2 + autoclaving	**~3.0**

Not all enzymatic & alkaline cleaners perform in the same way

***Alkaline* Methods**	***„Log“ Reduction***
Hamo50 (1%, 65°C; 10 min.)	**~3**
Hamo50 (1%, 70°C; 10 min.)	**~6.5**
CIP150 (1,6%, 43°C; 15 min.)	**>7**
Hamo100	
(1%, 65°C; 10 min.)	**>7**
(0,8%; 43°C; 7,7 min.)	**>7**
(0,8%; 43°C; 7,7 min.); Plastic wires	**>7**

Detergent formulations are critical for prion inactivation & removal

Two in one Detergent

- Outstanding Cleaner
- Removes and Inactivates Prions

Key product components

- Potassium Hydroxide (KOH)
- Surfactants
- Chelating Agents

Key product components

Why Potassium Hydroxide (KOH) over Sodium Hydroxide (NaOH)?

- Both increase the solubility of soils
- Potassium ions and salts are more soluble in water than Sodium ions and salts
- No need to neutralize with acid

- **Better Rinsing Ability!**

Key product components

- **Surfactants- Surface Active Agent**
  - Penetrate soil and surface irregularities
  - Ability to displace particles

No Surfactants | **Surfactant A** | **Surfactant B**

Key product components

Chelating Agents

- Sequester hard water ions
- Keeps them in a suspension
- Prevents them re-depositing on surface

Prion Decontamination Cycle

- **Manual Soak with HAMO100 PID**
  - Fill basin with water to a temp of 43°C (keep warm)
  - Add **0.8%** Hamo 100 PID
  - Submerge instruments in water (5cm above instruments)
  - Typical soak time = **7.5 min**
  - Rinse and then pass through normal process

Prion Decontamination Cycle

- **HAMO 100 PID usage in washer/disinfector**

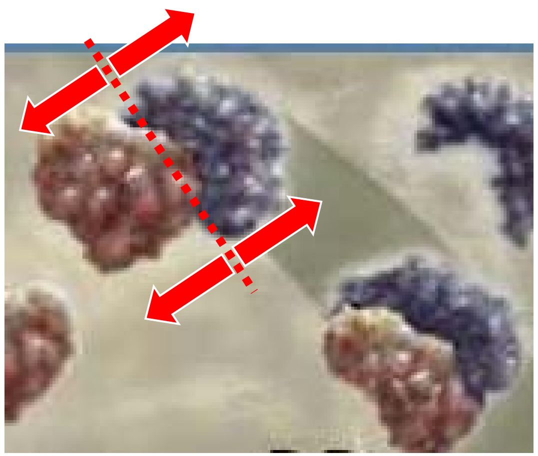
Phase	Temp	Time	Concentration	Comment
Pre- Wash	≤ 43 °C	1 – 2.5 min	0.2%	Dosed pre-wash can be used when instruments have been allowed to dry
Wash	≥ 43 °C	4 – 7.5 min	0.2 – 0.8%	Concentration depends on water quality

How does the formulation act

- **Removes** prions & bioburden from surfaces
- Keeps them **suspended**
- **Inactivates** through **hydrolysis** & allows suspended residues to be **freely rinsed** without re-adhering to the surface
- **Substrate Compatibility** (Instrument materials)

Hydrolysis as inactivating mechanism

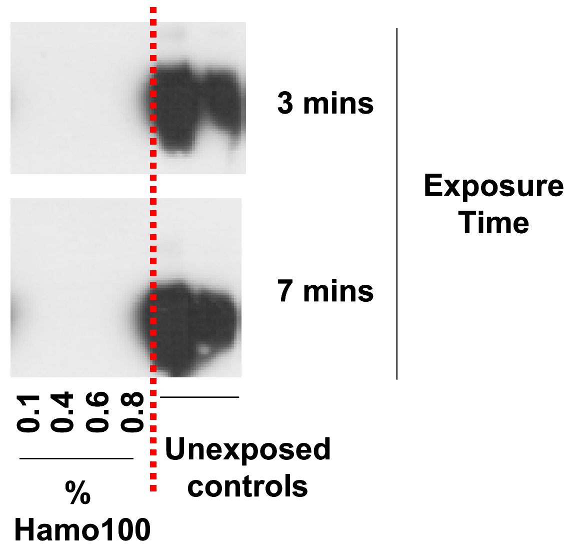
- Breaks down the peptide bonds through the introduction of water between the atoms of the bond, thus inactivating the infectivity of the prion

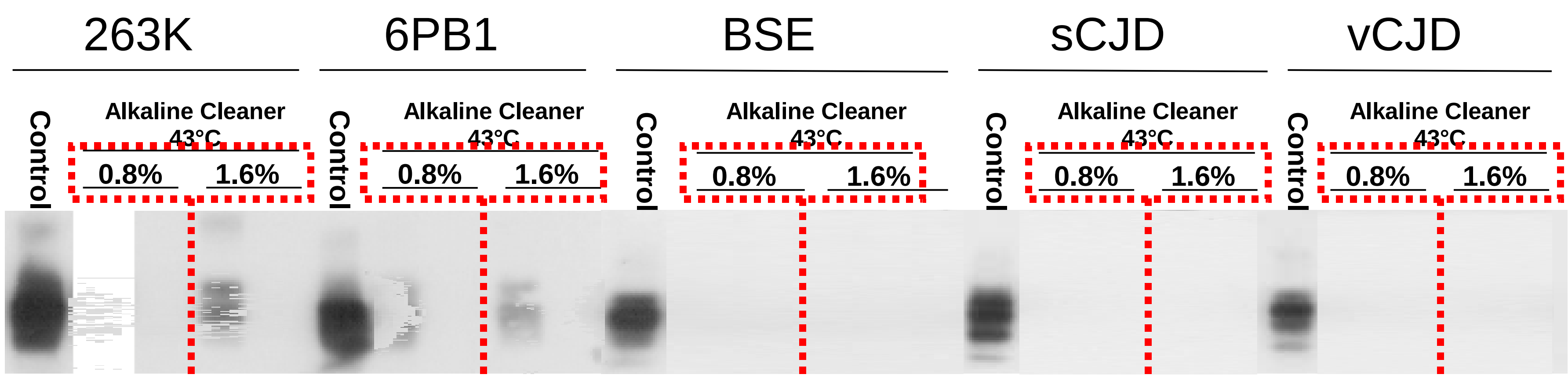


Degradation with Hamo 100

- >6 log reduction in prion titers against multiple strains of prions including CJD & vCJD
- Total cleaning of ISOEN15883 part 5 test soils incl. Edinburgh & blood soils

Degradation with Hamo 100





Conclusion

- Prions can be transmitted on device surfaces
- Methods have been developed to verify the effectiveness of decontamination methods
- Cleaning alone can be effective
  - Choice of cleaner and process is important
- Disinfection and sterilisation can be effective
  - Choice of biocide and process is important
  - New methods of prion decontamination have been identified

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