

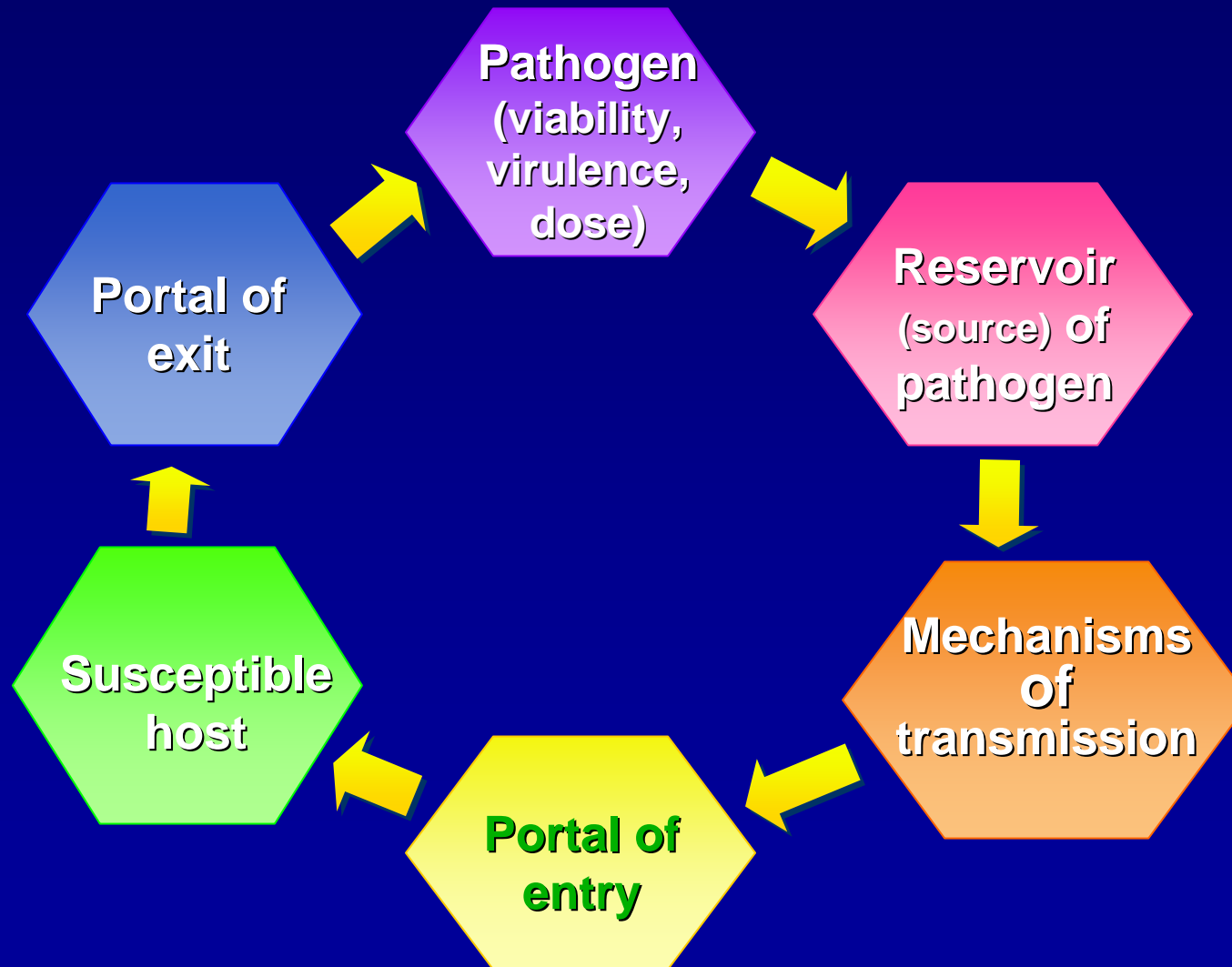
# Decontamination of emerging resistant pathogens



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- **Introduction**
- **Purpose of decontamination**
- **Special infectious agents**
  - **Bioterrorism, *Bacillus anthracis***
  - **Antibiotic-Resistant organisms and emerging pathogens, *Clostridium difficile***
  - **TSE agents (prions)**
- **Conclusion**

# « Chain of infection »



# Environmentally mediated infection transmission

- **Directly or indirectly**
  - **From environmental sources**
    - **Air**
    - **Contaminated fomites**
    - **Medical/laboratory instruments**
    - **Aerosols**
- **To patients in hospital**
- **To laboratory/hospital staff**

# Environmentally mediated infection transmission

- **In the laboratory setting**
  - **Relatively rare events**
    - High concentrations of pathogens: common
    - Conventional cleaning procedures
      - Reduction of environmental microbial contamination
      - Frequent use of sterilization (as steam autoclaving)
      - Usually unnecessary overkilling and expense
  - **Need for a rational basis for decontamination**
    - Spill control plan
    - Housekeeping procedures
    - Space decontamination requirements and procedures

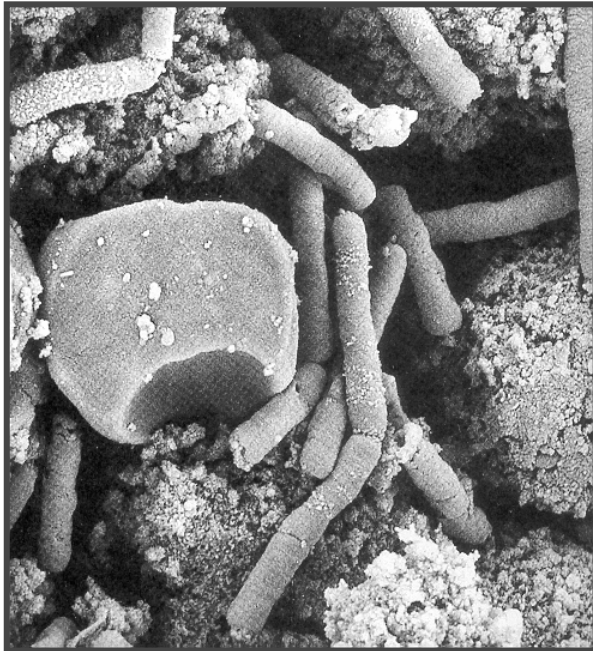
# In the microbiology laboratory

## Purpose of decontamination

- **To protect**
  - the laboratory worker
  - those who enter the lab
  - those who handle laboratory products away from the lab
  - the environment
- **To render safe to handle**
  - An area, a device, an item or material
- **To reduce the level of microbial contamination**
  - To eliminate the risk of transmission of infection

# Special infectious agents

## *Bacillus anthracis*



- **Bioterrorism, December 2001, USA**
  - 22 confirmed cases of anthrax
  - Press and general public
    - Fear and misunderstanding of the principles of sterilization and decontamination

**Do weapons of biological warfare have « Herculean properties » ?**  
**Are new or modified disinfection/sterilization procedures needed to kill them?**

# ***Bacillus anthracis***

- **Conventional disinfection and sterilization procedures**
  - More than adequate to kill *B.anthraxis*
  - Quick killing results
  - No need to extend sterilizing cycles
- **Normal infection control precautions**
  - Adequate to care for « anthrax » patients
    - Do not have spores in biological specimens but vegetative cells
- **Government building or post office**
  - Same principles of decontamination
  - Application of germicidal agents more difficult (physical logistics)



# Bioterrorism agents

- **Anthrax is unique**
  - **A bacterial spore, more resistant**
  
- **All other potential weapons for biological warfare**
  - **Vegetative bacteria or viruses**
  - **Susceptible to common array of chemical germicides**

# Antibiotic-resistant organisms & emerging pathogens

- **Background**
  - **Outbreaks of disease**
    - Newly discovered microorganisms
    - Microorganisms with acquired resistance to antimicrobial agents
  - **Disease control strategies**
    - « as if » agents extraordinary R to commonly used sterilization/disinfection procedures

**SARS-associated coronavirus, HIV, Hepatitis B, Ebola virus, multi-R M.tuberculosis, Vancomycin-R enterococci and MRSA**

# Antibiotic-resistant organisms

- **Methicillin Resistant *Staphylococcus aureus* (MRSA)**
  - Usually highly R to antibiotics
  - Spread worldwide
  - No increased R to disinfectants commonly used in hospitals
  
- **Antibiotic-resistant Gram negative bacilli**
  - *P.aeruginosa*, *Klebsiella* and *Enterobacter spp*, *Serratia marcescens* and *Acinobacter spp*
  - Infection problems
  - Little evidence of increased R to disinfectants commonly used in hospitals

# Antibiotic-resistant organisms & emerging pathogens

## No relationship between

- Ability to cause serious and fatal infections
- Resistance to antimicrobial agents used for therapy

And

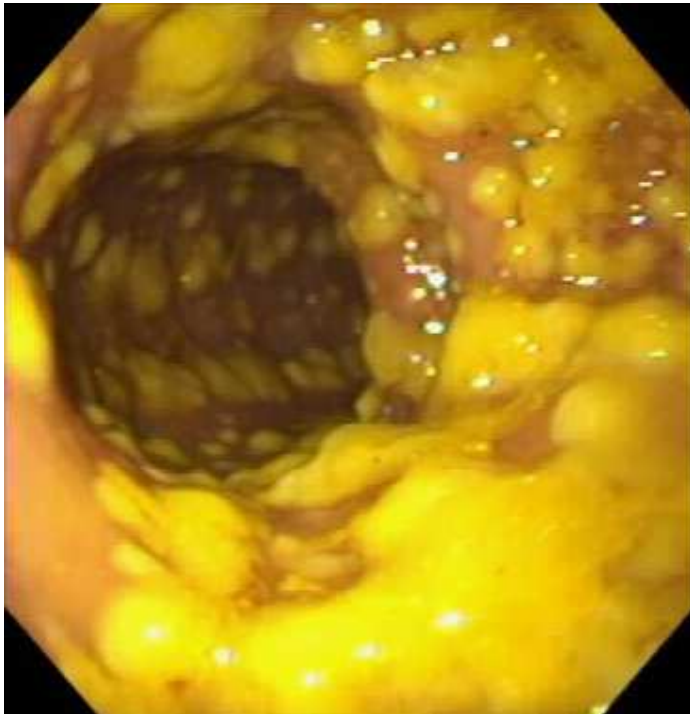
- Innate resistance to chemical germicides or sterilization

No need to change current protocols

major exceptions to the rule

- *Clostridium difficile*
- Prions

# ***Clostridium difficile***



Endoscopic visualization of pseudomembranous colitis, Pseudomembranes are visible as raised yellow plaques (2-10 mm) scattered over the colorectal mucosa.

- ***C.difficile*-associated diarrhea and pseudomembranous colitis**
  - Recent increase of incidence
  - Recent, increase of severity
  
- **2003, emergence of a more virulent strain**
  - Ribotype O27
  - High level of toxins
  - From North America to Europe
  - Increase of morbidity
  - Increase of mortality (4 to >13%)
  - Increase length of hospitalization
  - In hospitals, in nursing homes

# Outbreaks of *C. difficile* associated disease

***Clostridium difficile*-associated diarrhea in a region of Quebec from 1991 to 2003: a **changing pattern of disease severity****

Jacques Pépin, Louis Valquette, Marie-Eve Alary et al, CMAJ 2004 171: 27-9

**A large outbreak of *Clostridium difficile*-associated disease with an **unexpected proportion of deaths and colectomies** at a teaching hospital following increased fluoroquinolone use.**

CA Muto et al, Infect Control Hosp Epidemiol, 2005

# *Clostridium difficile*

- **A spore forming bacteria**
- **Can be part of the normal intestinal flora**
- **Transmission**
  - **Direct or indirect contact between 2 patients**
    - **!!! Indirect contact !!!**
      - Hands of medical/nursing staff
      - Via environment (floor, furnitures, bathroom, toilets, ...)
      - Via contaminated material (thermometers, bedpan, bell, ..)
  - **Feco-oral route**

# *Clostridium difficile*

- **Primary reservoir**
  - The symptomatic patient
    - $10^7$  -  $10^9$  cfu of *C.difficile* /gr of stool
    - Within 24 hours, environment massively contaminated
- **Secondary reservoir**
  - The environment
- **Spores**
  - Survival for several weeks
  - Highly R to heat, dehydration
  - **HIGHLY R to chemical disinfection**



# Prevention of *C. difficile* associated disease

## Belgian guidelines for control and prevention of *C.difficile* associated diseases in hospital and nursing homes

Superior health Council of Belgium Draft of CSS n°8365, submitted in 2007

### To prevent horizontal transmission

- **General precautions**
  - Hand hygiene, hydro-alcoholic solution (+/- washing with soap)
- **Additional precautions if Cd disease**
  - Individual room
  - Gloves for patient care and contact with his environment followed by soap washing+ hydroalcoholic solution
- **Additional precautions if uncontrolled outbreak of Cd disease**
  - Gloves for every patient care (in the ward) and contact with his environment followed by soap washing+ hydroalcoholic solution

# Prevention of *C. difficile* associated disease

## Belgian guidelines for control and prevention of *C.difficile* associated diseases in hospital and nursing homes

### Cleaning and disinfection of environment

- **Chemical disinfectants**
  - Activity of bleach and some chlorinated compounds
    - $\geq 1000$  to 5000 ppm of Chlorine
      - Bleach
      - Tablets of sodium dichloroisocyanurate (NaDCC)
  - Some non-chlorinated hospital disinfectants favor sporulation
  - Practical recommendations for preparation of solutions
  - H<sub>2</sub>O<sub>2</sub> spray: sporicidal activity to confirm for room disinfection
- **Recommendations**
  - Environment (see next slide)
  - Linen, cloth
  - Crockery, dishes

# Prevention of *C. difficile* associated disease

	NO OUTBREAK	OUTBREAK PERIOD
<b>Daily cleaning and disinfection</b>		
Floor	<b>Detergent</b>	<b>Sodium hypochlorite 1000/5000 ppm 1x/day</b>
Surfaces		
Bathroom toilet		
Material	-	-
<b>Final cleaning</b>		
Floor	<b>Sodium hypochlorite 1000/5000 ppm</b>	<b>Sodium hypochlorite 1000/5000 ppm</b>
Surfaces		
Bathroom toilet		
Material	<b>Thermodisinfection or Sodium hypochlorite 1000/5000 ppm</b>	
<b>Utility sale</b>		
	<b>Sodium hypochlorite 1000/5000 ppm 1x/day if ...</b>	<b>Sodium hypochlorite 1000/5000 ppm 1x/day</b>

# Transmissible spongiform Encephalopathy agents (Prions)

- **Prions**
  - Proteinaceous infectious particles
  - No nucleic acids
  - Abnormal pathogenic isoform of a normal cellular protein
    - The PrP or prion protein
    - Designated PrP<sup>Sc</sup> (Sc for scrapie)
- **Scrapie**
  - Prototypic prion disease
- **Other prion diseases**
  - Transmissible Spongiform Encephalopathies (TSEs)
    - Neurodegenerative diseases of humans and animals
    - Fatal issue, no cure
- **Prion diseases**
  - Infectious, inherited and sporadic illnesses

# Transmissible spongiform Encephalopathy agents (Prions)

Past decade

- **Heightened concerns about safety issues**
  - **Potential transmission of scrapie**
    - Through contaminated foodstuffs
  - **1991, BSE epidemic in the United Kingdom**
  - **More recently, link between BSE and the new variant of CJD**
- **Profound reassessment of public health policy**
  - **Worldwide**
  - **Prion-associated risks to the human population**
  - **Recommendations influenced by the invariably fatal outcome of CJD infection**
    - To sort out the truth from the myth
    - To sort out the legitimate from the unreasonable
    - To provide rationale for actions to be implemented

# Creutzfeldt-Jakob disease CJD

- **Familial CJD**
  - Inherited
- **Sporadic CJD**
  - Spontaneous conversion of PrP
- **Iatrogenic CJD**
  - < prion contaminated products derived from human tissues
    - Dura mater grafts
    - Pituitary-extracted human growth hormone
  - < surgical instruments or medical devices exposed to contaminated tissues
- **Variant CJD**
  - Link between BSE and new variant of CJD (vCJD)
  - BSE < consumption of contaminated foodstuffs

# Care of patients with human prion disease

- **No evidence for contact or aerosol transmission from one human to another**
  - Standard precautions for HIV, hepatitis = adequate
  - However infectious under particular circumstances
    - Cannibalism in New Guinea (Kuru)
    - Iatrogenic CJD
    - Two recent incidents of transfusion related to vCJD
- **Surgical procedures, including brain biopsy**
  - Should be minimized in suspected/confirmed CJD
  - Transmission not documented through contact
    - with blood, CSF, intact skin or mucous membranes
  - Recommendations for sterilization of instruments

# Inactivation of prions

## Extreme resistance to conventional procedures

**Need to combine  $\geq 2$  methods** to enhance level of « sterility »  
assurance

### Recommended methods (WHO)

- Steam autoclaving at 134°C - 18 min, or 6 successive cycles of 3 min
- Soaked in sodium hypochlorite (NaOCl) 20,000 ppm, for 1 h at room T°
- Soaked in 2 N sodium hydroxyde solution (NaOH), for 1 h at room T°



# Inactivation of prions

## More or less active

- **Soaked in formic acid 96 % for 1 h,**
- **Soaked in sodium sodiumdodecylsulfate (SDS) 10% for 30 min**
- **Soaked in 4 M guanidine thiocyanate for at least 1 h or a night**

## To be used in very specific settings

**eg, SDS combined with autoclaving for 15 min: complete inactivation of vCJD bound to stainless steel wires  
= basis of a non-corrosive treatment**

# Inactivation of prions

## Inactive methods !

- **Dry heat**
- **Steam autoclaving at 121°C for 15 min or 134°C for 3 min (1 cycle)**
- **Ethylène oxyde sterilization**
- **Disinfectants like**
  - **Glutaraldéhyde**
  - **Formalin (Anatomo pathologic preparation still infectious)**
  - **Phenols, alcohols, peracetic acid, H<sub>2</sub>O<sub>2</sub>, etc**
  - **Radiations (UV,  $\gamma$ ,  $\beta$ ), microwaves**

# Inactivation of prions

## Promising methods under investigation

- **Ozone**
- **Gaz plasma sterilization with H<sub>2</sub>O<sub>2</sub> alone or in combination with a disinfecting procedure (Sterrad)**
- **Peracetic acid (Steris)**

## Recommendations for the prevention of transmission of TSE (CJD) in hospital settings

May 2006

### Practical approach for different situations

- Definitions of cases
- Staff
- Environment
- Surgical rooms
- Autopsy room
- Biopsy, endoscopy
- Accidental exposure
- Sterilization department
- Dental procedures
- Laboratory measures

- **Existing knowledge still incomplete**
- **Extreme resistance to conventional inactivation procedures**
- **Uncomfort for recommendations**
  - **Highly conservative precautionary measures**
- **For a long time, lack of sensitive tests to detect prions**
- **From epidemiological data, worldwide**
  - **Classical CJD prions**
    - **Not transmitted from human-to-human through blood or derivatives**
  - **vCJD**
    - **Situation substantially different**
    - **Under continuing review**