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 »

- Pathogen (viability, virulence, dose)
- Reservoir (source) of pathogen
- Mechanisms of transmission
- Portal of entry
- Susceptible host
- Portal of exit

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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

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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

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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?
Conventional disinfection and sterilization procedures
  - More than adequate to kill \textit{B. anthracis}
  - 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)
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
- Innate resistance to chemical germicides or sterilization

And

No need to change current protocols
- Major exceptions to the rule
  - Clostridium difficile
  - Prions
**Introduction**

- **Decontamination**
- **Special agents**
  - *C. difficile*
- **Conclusion**

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**Clostridium difficile**

- *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

Endoscopic visualization of pseudomembranous colitis,

Pseudomembranes are visible as raised yellow plaques (2-10 mm) scattered over the colorectal mucosa.
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


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
Introduction

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Special agents

C. difficile

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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
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
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

**Prevention of *C. difficile* associated disease**

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
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
    - ≥ 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
  - $H_2O_2$ spray: sporicidal activity to confirm for room disinfection

- **Recommendations**
  - Environment (see next slide)
  - Linen, cloth
  - Crockery, dishes
# Prevention of *C. difficile* associated disease

<table>
<thead>
<tr>
<th></th>
<th>NO OUTBREAK</th>
<th>OUTBREAK PERIOD</th>
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<td><strong>Daily cleaning and disinfection</strong></td>
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<td>Detergent</td>
<td>Sodium hypochlorite 1000/5000 ppm 1x/day</td>
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<tr>
<td>Surfaces</td>
<td></td>
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<tr>
<td>Bathroom toilet</td>
<td>Sodium hypochlorite 1000/5000 ppm 1x/day</td>
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<tr>
<td>Material</td>
<td>-</td>
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<td><strong>Final cleaning</strong></td>
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<tr>
<td>Floor</td>
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<td>Sodium hypochlorite 1000/5000 ppm</td>
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<td>Surfaces</td>
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<tr>
<td>Bathroom toilet</td>
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<tr>
<td>Material</td>
<td>Thermodisinfection or Sodium hypochlorite 1000/5000 ppm</td>
<td>Sodium hypochlorite 1000/5000 ppm 1x/day</td>
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<tr>
<td><strong>Utility sale</strong></td>
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<td>Sodium hypochlorite 1000/5000 ppm 1x/day if ...</td>
<td>Sodium hypochlorite 1000/5000 ppm 1x/day</td>
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**Introduction**

Decontamination

Special agents

*C. difficile*

Conclusion

- Sodium hypochlorite 1000/5000 ppm 1x/day
- Sodium hypochlorite 1000/5000 ppm
- Thermodisinfection or Sodium hypochlorite 1000/5000 ppm
- Sodium hypochlorite 1000/5000 ppm 1x/day
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\textsuperscript{Sc} (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)

- 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

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Past decade

pm-chulg - 11.12.07 - BBP
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 ≥ 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 dodecylsulfate (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, $H_2O_2$, etc
  - Radiations ($UV$, $\gamma$, $\beta$), microwaves
Promising methods under investigation

- Ozone
- Gaz plasma sterilization with $\text{H}_2\text{O}_2$ alone or in combination with a disinfecting procedure (Sterrad)
- Peracetic acid (Steris)
Practical approach for different situations

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

Conclusion

- 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