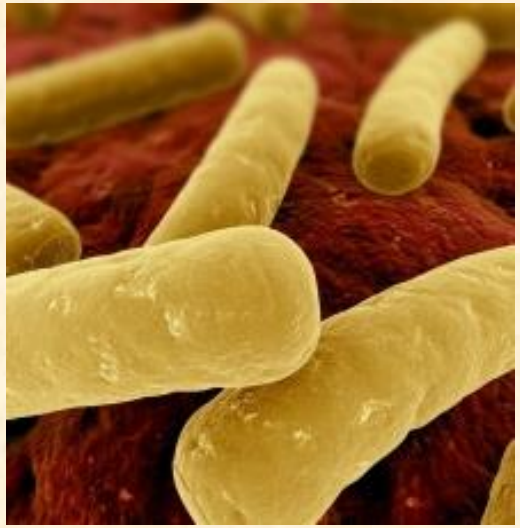
C. Diff and the vectors of Cross-Contamination

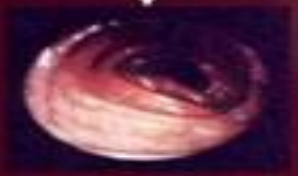


Dr. Helene Paxton

What is *C. difficile?*

Clostridium difficile

- Anaerobic spore-forming bacillus
- *Clostridium difficile*-associated diarrhea (CDAD)
- Pseudomembranous colitis, toxic megacolon, sepsis, and death
- Fecal-oral transmission through contaminated environment and hands of healthcare personnel
- Antimicrobial exposure is major risk factor for disease
  - Acquisition and growth of *C. difficile*
  - Suppression of normal flora of the colon
- Clindamycin, penicillins, and cephalosporins

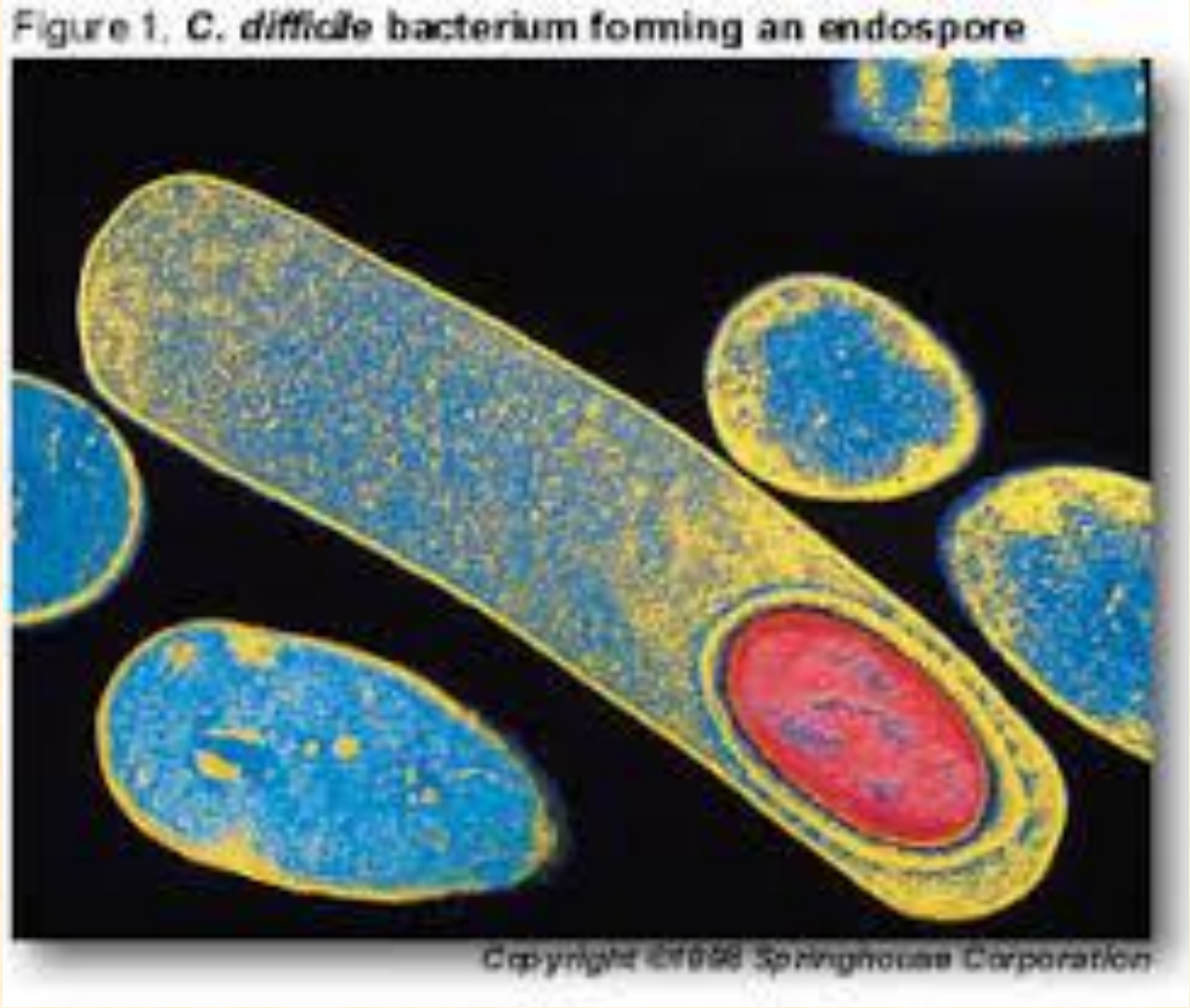


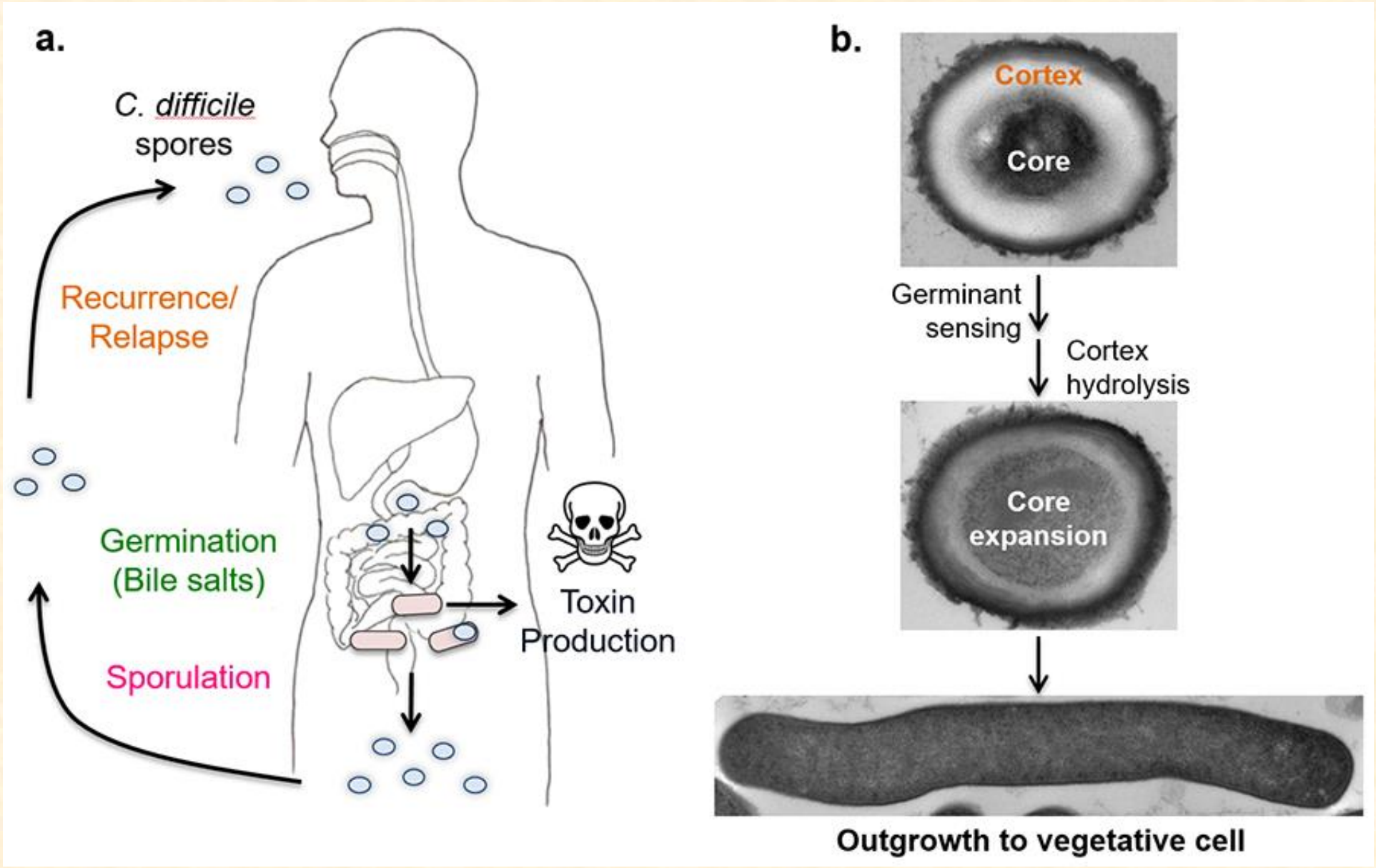
Healthy colon

Pseudo-membranous colitis

Clostridium Spore is Hardy!!

Figure 1. ***C. difficile*** **bacterium forming an endospore**



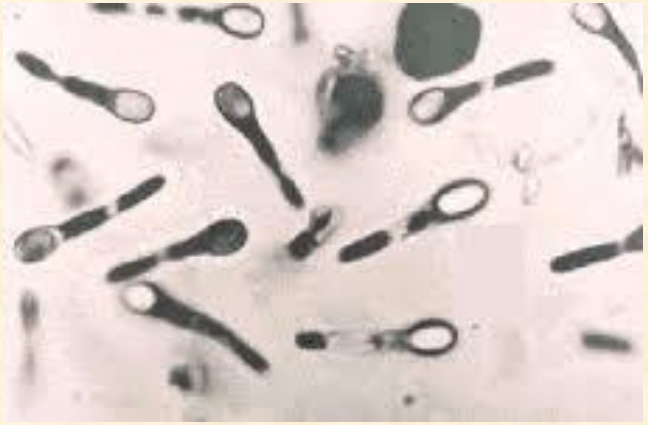

a.
C. difficile
spores
Recurrence/
Relapse
Germination
(Bile salts)
Sporulation
Toxin
Production
b.
Cortex
Core
Germinant
sensing
Cortex
hydrolysis
Core
expansion
Outgrowth to vegetative cell

Asymptomatic *C. diff* Carriers

60% of stool carriers in one study also had it on their skin and their surrounding environment

- Spores on the skin of these carriers were easily transferred to others

- Non-poopers are important sources of potential infection to others- everyone should wash with soap and water!



Incidence of *C. difficile* Infection (CDI)

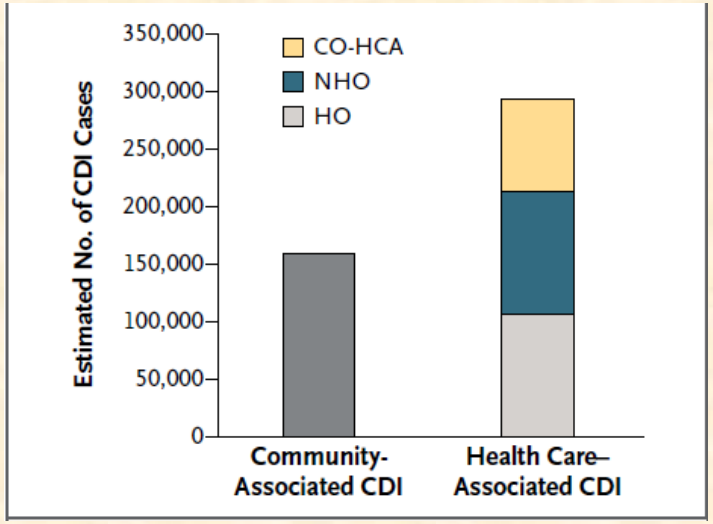
- Important healthcare-associated infection and growing health care problem.
- Estimated at 6.5 cases per 10,000 patient days in hospital.
- About 250,000 hospitalizations were associated with CDI in 2005.
- Elderly people in hospitals account for the majority of severe morbidity and mortality.
- Residents of long-term care facilities are also at higher risk.
- Incidence rates may increase by four or five-fold during outbreaks.
- Incidence and severity may be increasing due to the emergence of a hypervirulent strain of *C. difficile*.
- AHRQ

C.difficile: Impact

Point Prevalence:

CDC Funded Study[1]

1. 450,000 annual *C. difficile* infections
2. 29,000 attributable deaths annually
3. $1B in excess costs annually
4. 35%(159,700) attributed to community



Trend:

10 year retrospective US patient discharge chart review[2]

1. The incidence of CDI among hospitalized adults in the United States nearly doubled from 2001-2010.
2. Little evidence of improvement in patient mortality or hospital LOS

1)Lessa et al, NEJM, 372:825-834, 2015

2) **Reveles, K. R., Lee, G. C., Boyd, N. K., & Frei, C. R. (2014). The rise in Clostridium difficile infection incidence among hospitalized adults in the United States: 2001-2010. *AJIC: American Journal of Infection Control*, *10*(42), 1028-1032**

Chlorox slide

C. Difficile Lab Diagnosis Challenges

Diagnostic Test	Description	Advantages/Disadvantages
Cell cytotoxin assay	• Fecal samples are plated on human fibroblasts • If toxin B is present, this results in cell death	• Time consuming, laborious, and expensive • Lacks sensitivity • No longer considered gold standard
Enzyme immunoassay	• Immunoassay directed towards both toxins A and B	• Widely used • Rapid and easy to perform • Lacks sensitivity
Glutamate dehydrogenase test (GDH)	• Relies on the presence of GDH antigen, which is produced by all isolates of *C. difficile*	• Excellent negative predictive value • Positive test necessitates second confirmatory test to assess whether toxin is present
Nucleic acid amplification of toxin A or B gene	• Real-time polymerase chain reaction of toxin A or B gene	• Highly sensitive and specific • Expensive, limited availability

1. **No single commercial test can be used as a stand-alone test for diagnosing CDI.**
2. **Therefore, the use of a two-step algorithm is recommended.**
3. **PCR has a false positive rate greater than 47% for actual clinical disease**

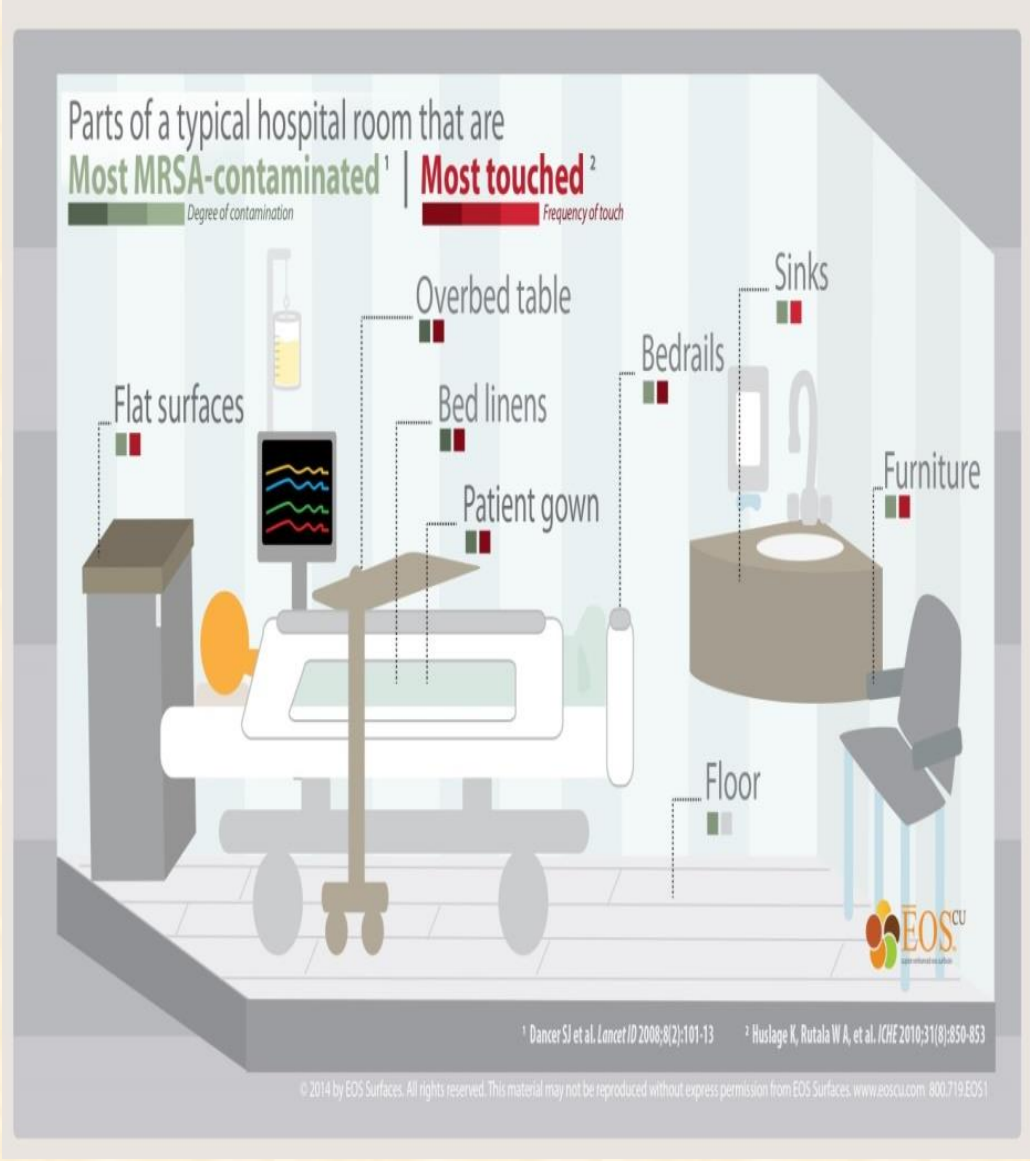
Crobach MJ, Dekkers OM, Wilcox MH, Kuijper EJ. European Society of Clinical Microbiology and Infectious Diseases (ESCMID): data review and recommendations for diagnosing Clostridium difficile-infection (CDI). Clin Microbiol Infect 2009;15:1053-66.

So what do we do??

Environmental Services Cleaning……

High Touch Areas

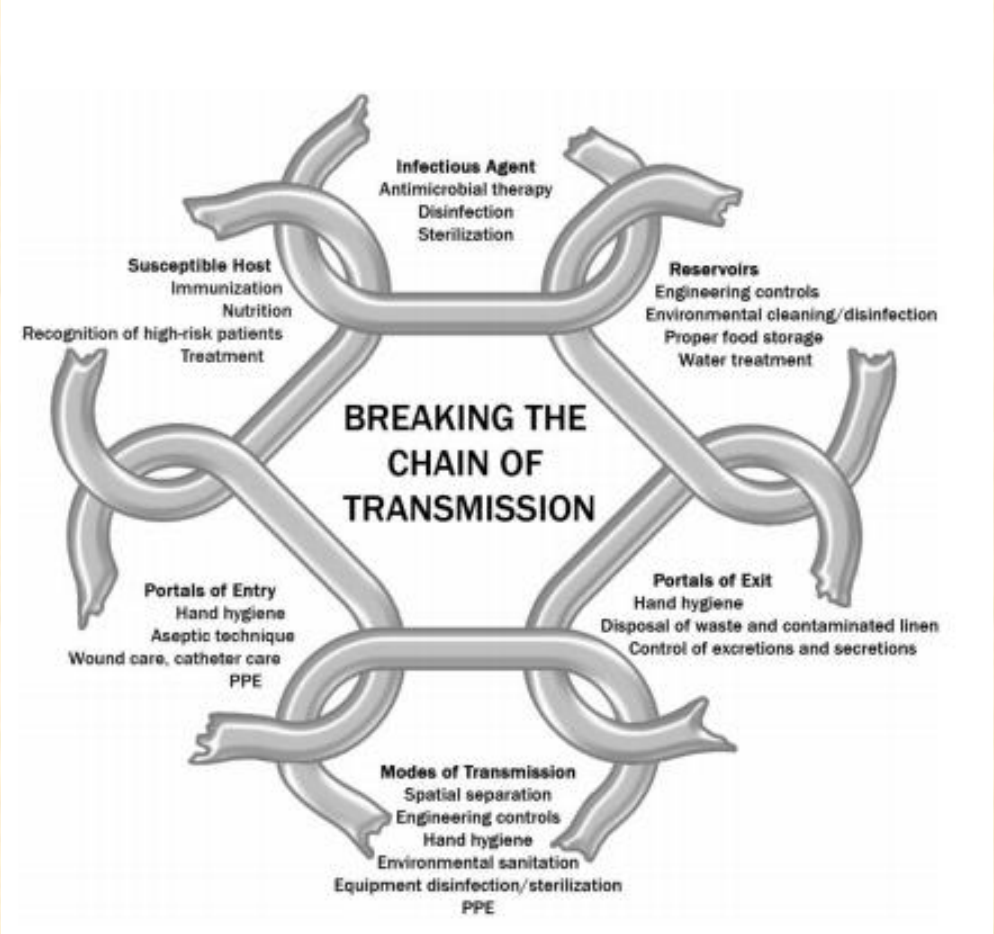
- High touch surfaces are those that have frequent contact with hands.
- High touch surfaces in care areas require more frequent cleaning and disinfection than minimal contact surfaces.
- Cleaning and disinfection is usually done at least daily and more frequently if the risk of environmental contamination is higher (e.g., intensive care units).
- Notice floors are not considered high touch in this graphic???



Goal must be to reduce bioburden!

Process of CDI Disease Transmission: Chain of Infection

1. *Hand hygiene*
2. *Contact precautions*
3. *Identification of cases*
4. *Appropriate use of antibiotics*
5. *Environmental disinfection*



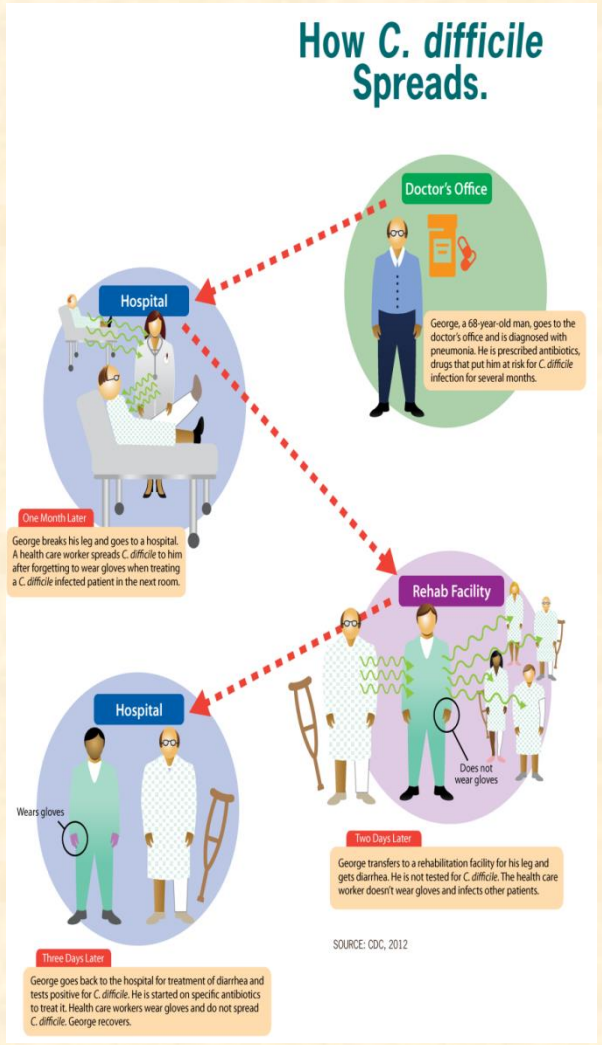
1)Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. Annex C – Testing, Surveillance and Management of Clostridium difficile. Annexed to: Routine Practices and Additional Precautions in All Health Care Settings. Toronto, ON: Queen's Printer for Ontario; 2013. –Source of Chain of Infection Image

Chlorox slide

Environmental Services Cleaning

A recent study by Sitzlar, et al. (2013) suggested that effective cleaning coupled with staff supervision is a powerful method in decreasing the potential for *C. difficile* infections (CDI) transmission in hospitals.

EVS staff is critical in a healthcare facility yet are often left out of infection control training. They are often the lowest pay grade with the highest turnover rate.



Cleaning Opportunities

1. C.difficile was recovered on 49% of sites in rooms occupied by patients with CDI and on 29% of sites in rooms occupied by asymptomatic carriers.[1,2]

2. Computer touch screens can be potential reservoirs of opportunistic pathogens in hospitals cleaning instructions such as Mild Soap , Lint free cloth and water current increase risk of infection transmission[4]

3. Non Sporicidal agents have been shown to promote sporulation of hyper virulent strains like NAP1[2]

4. Published literature has shown that as levels of environmental contamination increase, so does the prevalence of *C. difficile* hand carriage among health care workers[3]

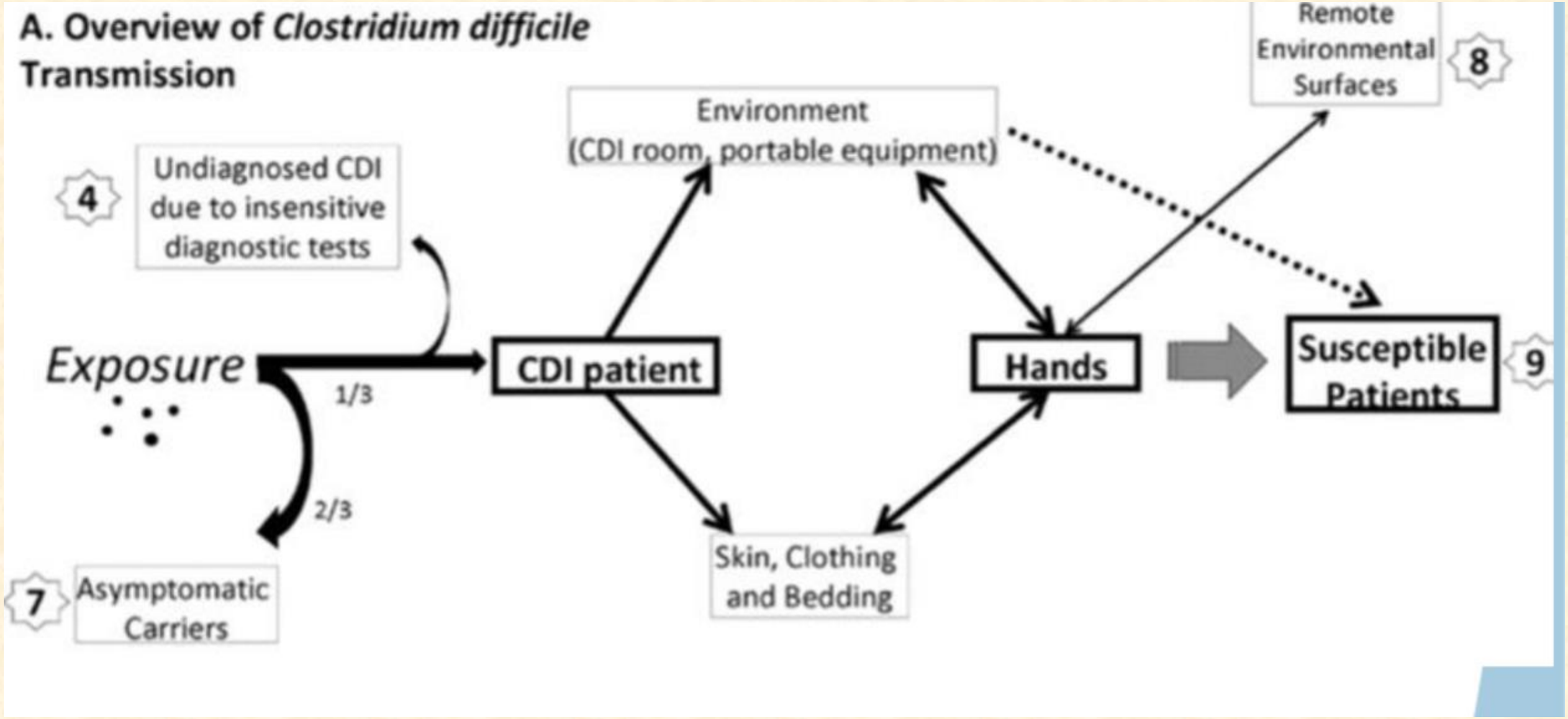
1. Guerreiro, Isabelle et al Using expert process to ombat *Clostridium difficile* infections American Journal of Infection Control , Volume 0 , Issue 0

2. Wilcox MH, Fawley WN. Hospital disinfectants and spore formation by Clostridium difficile. Lancet 2000;356:1324

3. Underwood S, Stephenson K, Fawley WN, et al. Program and abstracts of the 45th Annual Interscience Conference on Antimicrobials and Chemotherapy (Washington, DC). 2005. Effects of hospital cleaning agents on spore formation by North American and UK outbreak *Clostridium difficile* (CD) strains [abstract LB-28-2005].

4. Hirsch, Elizabeth B., et al. "Surface microbiology of the iPad tablet computer and the potential to serve as a fomite in both inpatient practice settings as well as outside of the hospital environment." *PloS one* 9.10 (2014): e111250.

5. Chlorox


A. Overview of Clostridium difficile
Transmission
Remote Environmental Surfaces
8
Environment (CDI room, portable equipment)
4
Undiagnosed CDI due to insensitive diagnostic tests
Exposure
1/3
2/3
CDI patient
Hands
Susceptible Patients
9
Skin, Clothing and Bedding
7
Asymptomatic Carriers

Limitations of Research on CDI Prevention

- Studies mainly evaluated effectiveness of CDI prevention during an epidemic or in a hyperendemic environment.
- Studies did not evaluate the sustainability of the interventions beyond the study period.
- The potential negative impact these interventions would have on the institutional environment other than cost was not evaluated in these studies but may include:

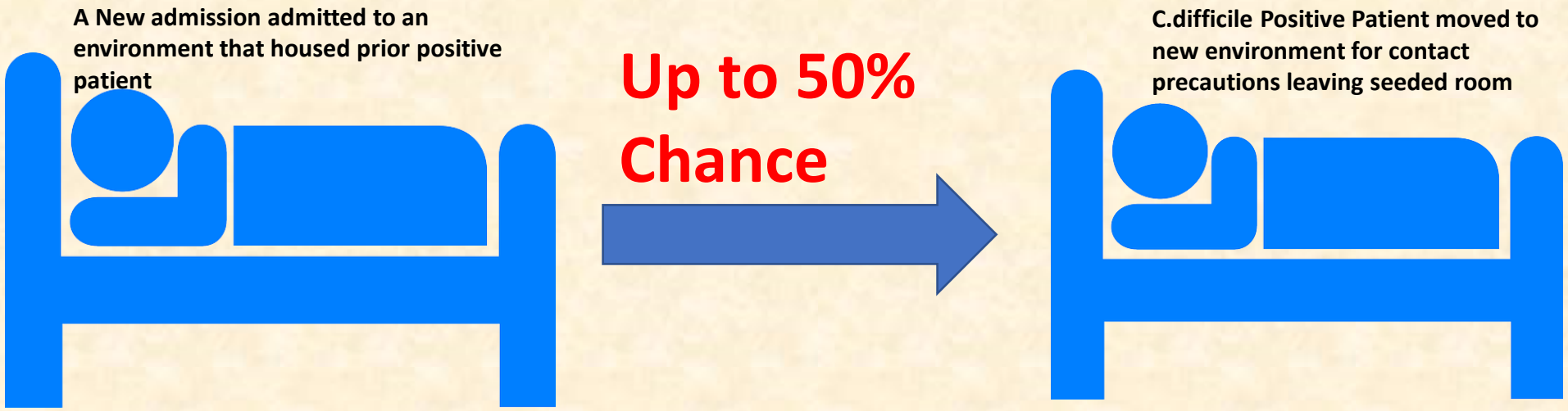
- AHRQ

Negative Impact:

- Time needed to perform disinfection;
- Possible harm to surfaces or equipment from harsh decontamination chemicals;
- Failure of vapor disinfection systems; Failure of UV robots
- Exposure of patients and personnel to toxic chemicals;
- Rates of recontamination after hand washing that results from touching equipment or surfaces in patient rooms contaminated with *C. difficile* spores, which may persist on some surfaces for up to 5 months;
- The reduction in direct patient-care contact due to isolation.

- AHRQ data

Prior Room Occupancy



1. **A meta-analysis of the combined data from included studies overwhelmingly indicated an increased risk of acquisition when put in a room that previously housed a patient with *C.difficile*[1].**
2. **Current environmental cleaning practices fail to reduce the risk of acquisition as spores can be airborne up to 48hrs after discharge of *C.difficile* Patient[1].**
3. **Receipt of antibiotics by prior bed occupants was associated with increased risk for CDI in subsequent patients. Antibiotics can directly affect risk for CDI in patients who do not themselves receive antibiotics[2].**

1. Mitchell BG, Dancer SJ, Anderson A, Dehn E. Risk of organism acquisition from prior room occupants: a systematic review and meta-analysis. J Hosp Infect 2015;91:211–217.
2. Freedberg DE, Salmasian H, Cohen B, Abrams JA, Larson EL. Receipt of Antibiotics in Hospitalized Patients and Risk for Clostridium difficile Infection in Subsequent Patients Who Occupy the Same Bed. JAMA Intern Med. Published online October 10, 2016. doi:10.1001/jamainternmed.2016.6193

Tenacity Of C.difficile

Increase in Resistance

Bacterial spores:
- *Clostridium difficile*
- *Bacillus atrophaeus*

Mycobacteria:
- *Mycobacterium tuberculosis*

Nonlipid or small viruses:
- *Rhinovirus*
- *Influenza Virus*

Fungi:
- *Aspergillum spp.*
- *Candida spp.*

Vegetative bacteria:
- *Staphylococci spp.*
- *Streptococci spp.*
- *Escherichia coli*

Lipid or medium-sized viruses:
- *Hepatitis B Virus (HBV)*
- *Hepatitis C Virus (HCV)*
- *Human Immunodeficiency Virus (HIV)*
- *Herpes Simplex Virus Types 1 (HSV 1)*
- *Herpes Simplex Virus Types 2 (HSV 2)*

Table 1: Persistence of clinically relevant bacteria on dry inanimate surfaces.

Type of bacterium	Duration of persistence (range)
Acinetobacter spp.	3 days to 5 months
Bordetella pertussis	3 – 5 days
Campylobacter jejuni	up to 6 days
Clostridium difficile (spores)	5 months
Chlamydia pneumoniae, C. trachomatis	≤ 30 hours
Chlamydia psittaci	15 days
Corynebacterium diphtheriae	7 days – 6 months
Corynebacterium pseudotuberculosis	1–8 days
Escherichia coli	1.5 hours – 16 months
Enterococcus spp. including VRE and VSE	5 days – 4 months
Haemophilus influenzae	12 days
Helicobacter pylori	≤ 90 minutes
Klebsiella spp.	2 hours to > 30 months
Listeria spp.	1 day – months
Mycobacterium bovis	> 2 months
Mycobacterium tuberculosis	1 day – 4 months
Neisseria gonorrhoeae	1 – 3 days
Proteus vulgaris	1 – 2 days
Pseudomonas aeruginosa	6 hours – 16 months; on dry floor: 5 weeks
Salmonella typhi	6 hours – 4 weeks
Salmonella typhimurium	10 days – 4.2 years
Salmonella spp.	1 day
Serratia marcescens	3 days – 2 months; on dry floor: 5 weeks
Shigella spp.	2 days – 5 months
Staphylococcus aureus, including MRSA	7 days – 7 months
Streptococcus pneumoniae	1 – 20 days
Streptococcus pyogenes	3 days – 6.5 months
Vibrio cholerae	1 – 7 days

What about Residual Pathogens?

- Since the effective dose of a pathogen varies,

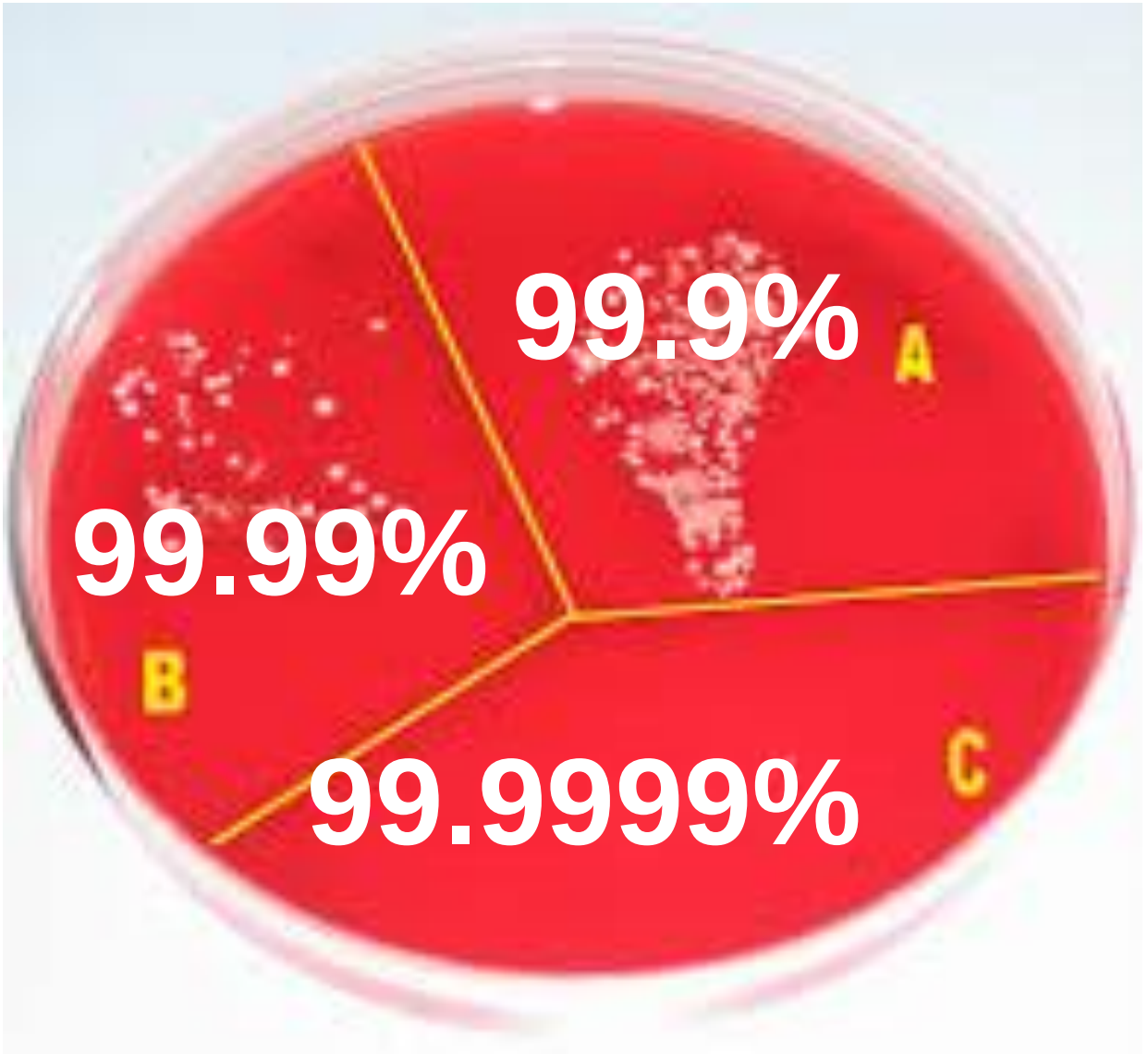
  Does leaving 1 or 100 or 1000 organisms

  on a field matter?
- What methods a necessary to assure there are no organisms left?
- **Data suggest that some organisms will require at least two passes to lower the residual numbers.[1]**

1. Tuladahar, E et al. Appl. Environ. Microbiol, Nov. 2012;78:21 (7769-7775)

Does Log kill Make a difference?

- Do users really understand the difference?



Automated Methods

“No-Touch” Technologies

- Room Foggers
- Electrostatic Systems
- Ultraviolet Machines

Application Modalities: Is there a difference?

Foggers vs. Electrostatic methods:

BioMist

- **Isopropyl alcohol 55-65%**
- Other ingredients 35-45%

AltaPure

- **Hydrogen Peroxide 22%**
- Peracetic Acid 4.5 %
- Inert Ingredients 73.5%

Electrostatic Methods Are Not Validated As To Their Delivery by the EPA…

- Liquid being dispersed is validated as a liquid, not as a fog/mist.

- There is no data supporting the dispersal/application methods.

- **What is the rate of delivery? What is the effective dwell time, etc.?**

- **How do we know if there is effective kill?**

Let's look at some of the labels….

STERAMIST™ BINARY IONIZATION TECHNOLOGY	bioquell	Sanosil®	STERIS®	ALTAPURE
	*7.8% H_2O_2 ionized	*30% H_2O_2	*5% H_2O_2 & Silver	*35% H_2O_2	*22% H_2O_2 Peracetic Acid 4.5 %
	Non Corrosive Converts to Oxygen, and Water (humidity)	Highly Corrosive Dangerous off-gassing	Moderately Corrosive however Leaves Silver Cations in the environment, Oxygen, and Water	Highly Corrosive Dangerous off-gassing	Highly Corrosive Dangerous off-gassing Vinegar smell

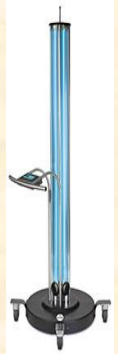
*Ingredients taken from EPA label

Application Modalities:
UVC

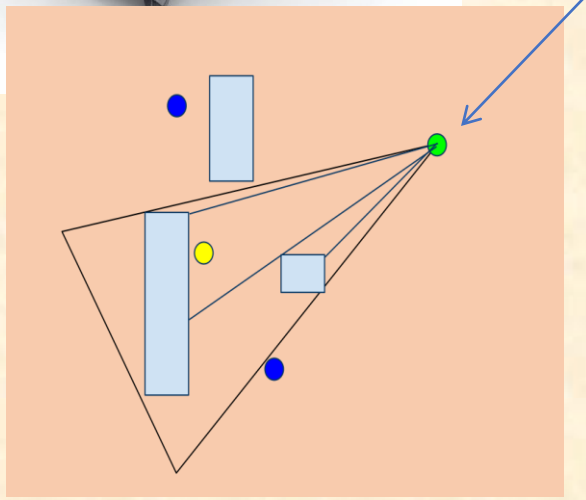
- XENEX
- STERIS-PATHOGEN UV DEFENSE SYSTEM
- SURFACIDE-HELIOS SYSTEM
- LUMALIER TRU-D
  SMART UVC SYSTEM
- AMERICAN AIR - ARTZ MOBILE ROOM UVC
- CLOROX
- OPTIMUM-UV SYSTEM
- UV-C TECHNOLOGIES IRS 3200M








Ultraviolet Disinfection Systems: Requirements



Ultra Violet

- Room must be vacated and disinfected (terminal clean).
- Furniture must be moved away from walls to prevent shadowing.
- Long room turn-around time for kill.
- Direct line of sight necessary.
- Relative Log kill effectiveness is not validated by EPA
- Pulse or direct wave
- Correct wave length emissiom

Issues with Hands Free Technologies…

- They vary in their approaches to disinfection leading to confusion as to the real effectiveness. 3 log. 4 log. 6 log ?
- Many of the technologies are not validated for efficacy by the EPA including UV-C and the liquid-wipe disinfectants which are sprayed through a variety of systems.
- Large sums of monies are often spent without knowing the “true” effectiveness of the application. Studies for many systems are anecdotal and appear to be effective but are not well controlled.
- Labeling claims are confusing and the end-used does not know how these were determined.

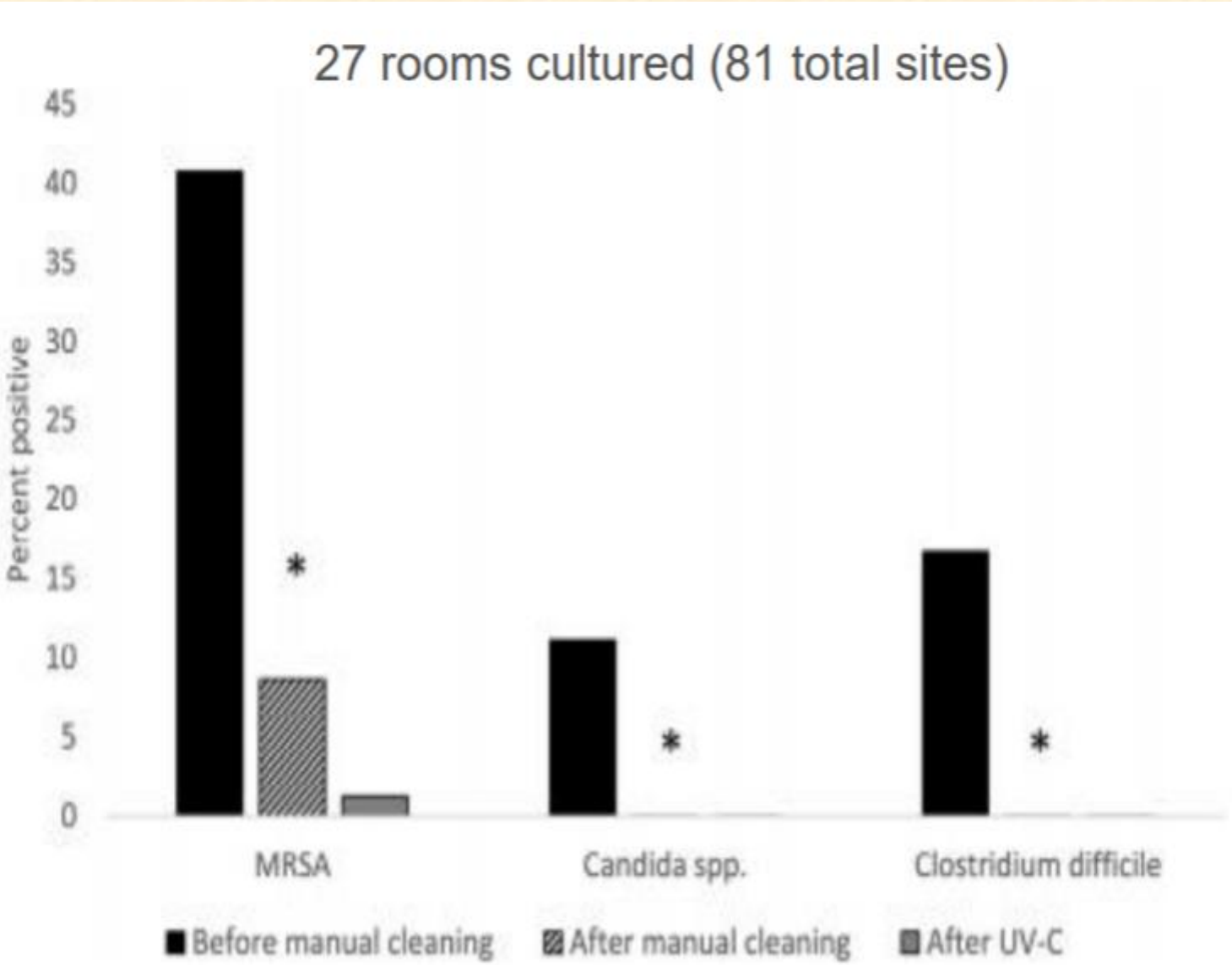


Fig 1. Percentage of positive cultures (number of sites positive/number of sites cultured) for MRSA, *Candida* spp, and *Clostridium difficile* from hospital room floors before postdischarge cleaning, after postdischarge cleaning by environmental services personnel, and after operation of an UVC device for 5 minutes. *MRSA*, methicillin-resistant *Staphylococcus aureus*; *UV-C*, ultraviolet C. *$P < .01$

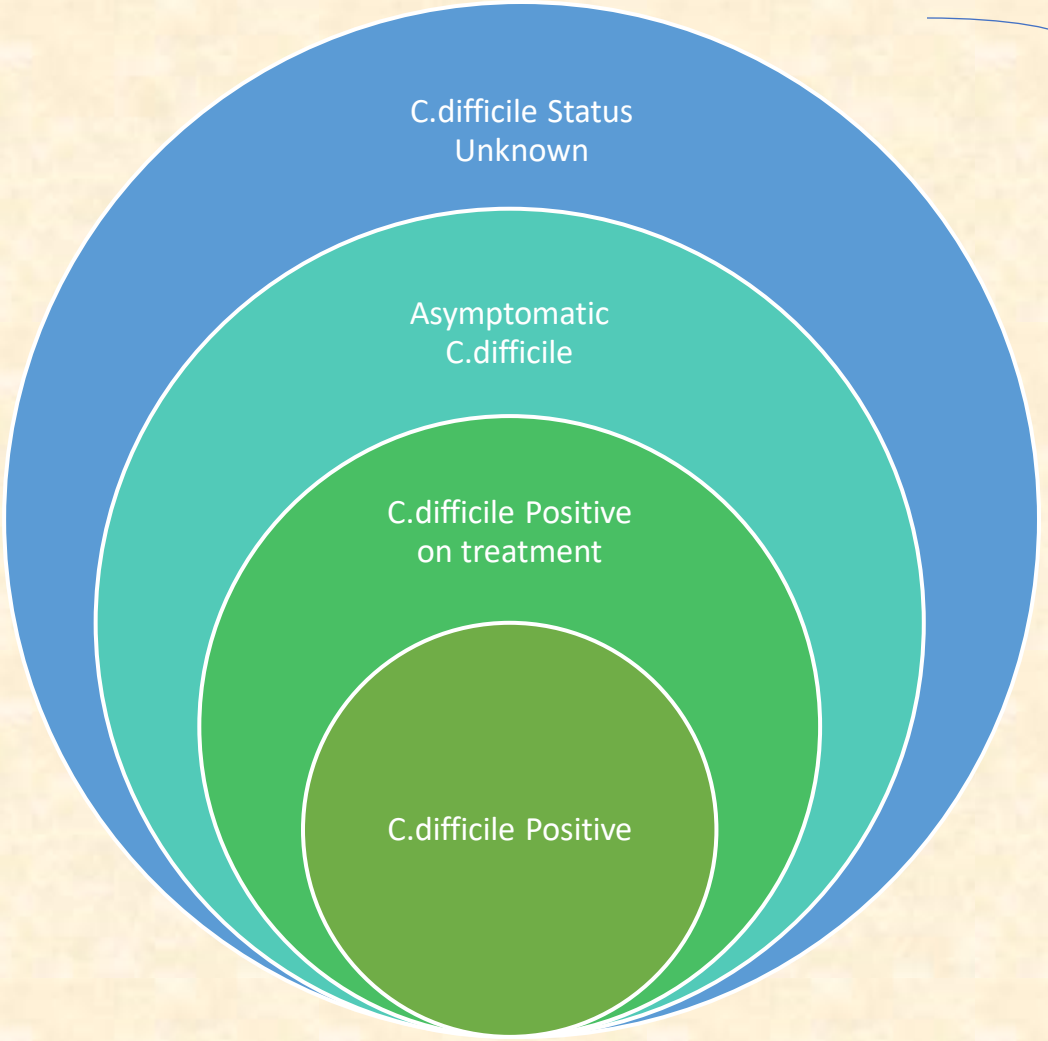
All Hospital Disinfectants must be EPA Registered

All disinfectants and pesticides marketed for use in United States must meet safety requirements as described in OCSPP 810.2200, (*1) Applicability.*

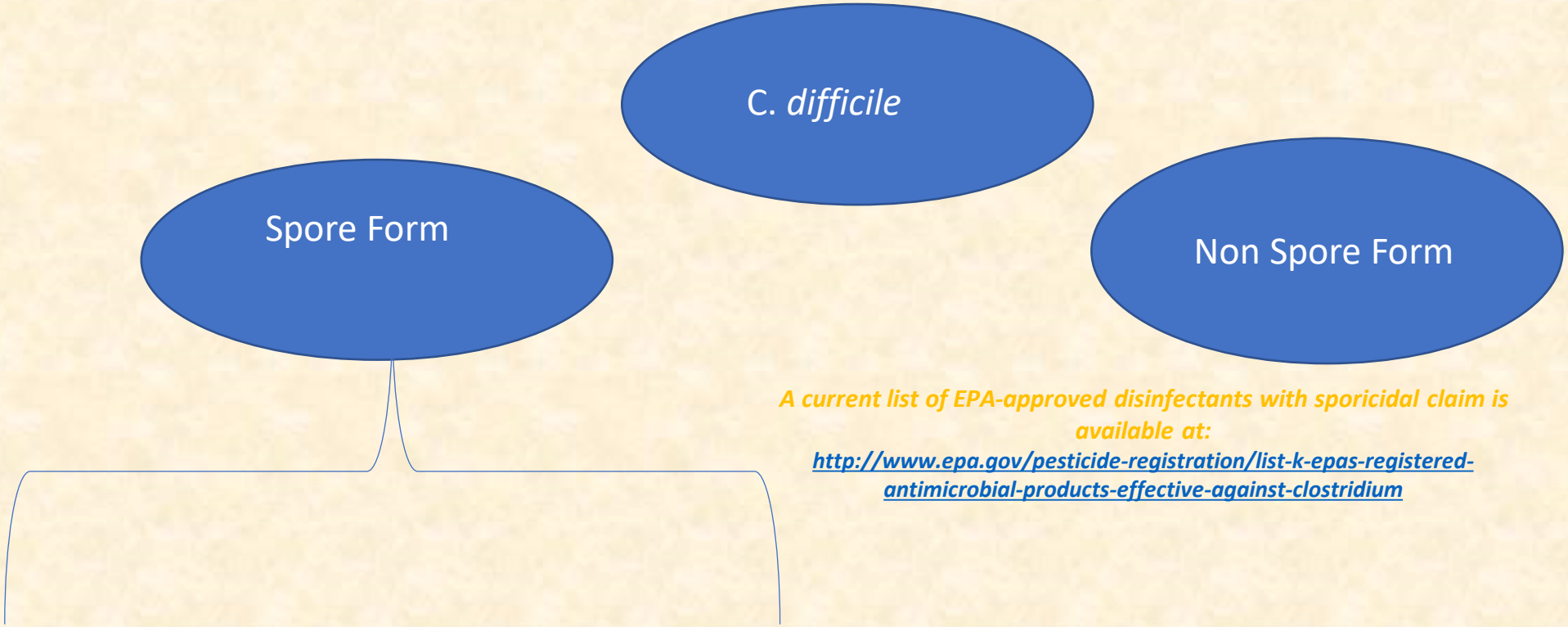
This guideline describes test methods that EPA believes will generally satisfy testing requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136, et seq.) and the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. 346a).

It addresses testing to demonstrate the effectiveness of antimicrobial pesticides bearing claims as disinfectants, fungicides, virucides, and tuberculocides. (EPA 712-C-07-074)

In Conclusion: Use Sporicidal Disinfectants on all Cases



Disinfection and C. *difficile*



A current list of EPA-approved disinfectants with sporicidal claim is available at:
http://www.epa.gov/pesticide-registration/list-k-epas-registered-antimicrobial-products-effective-against-clostridium

E.P.A Registered Sporicide

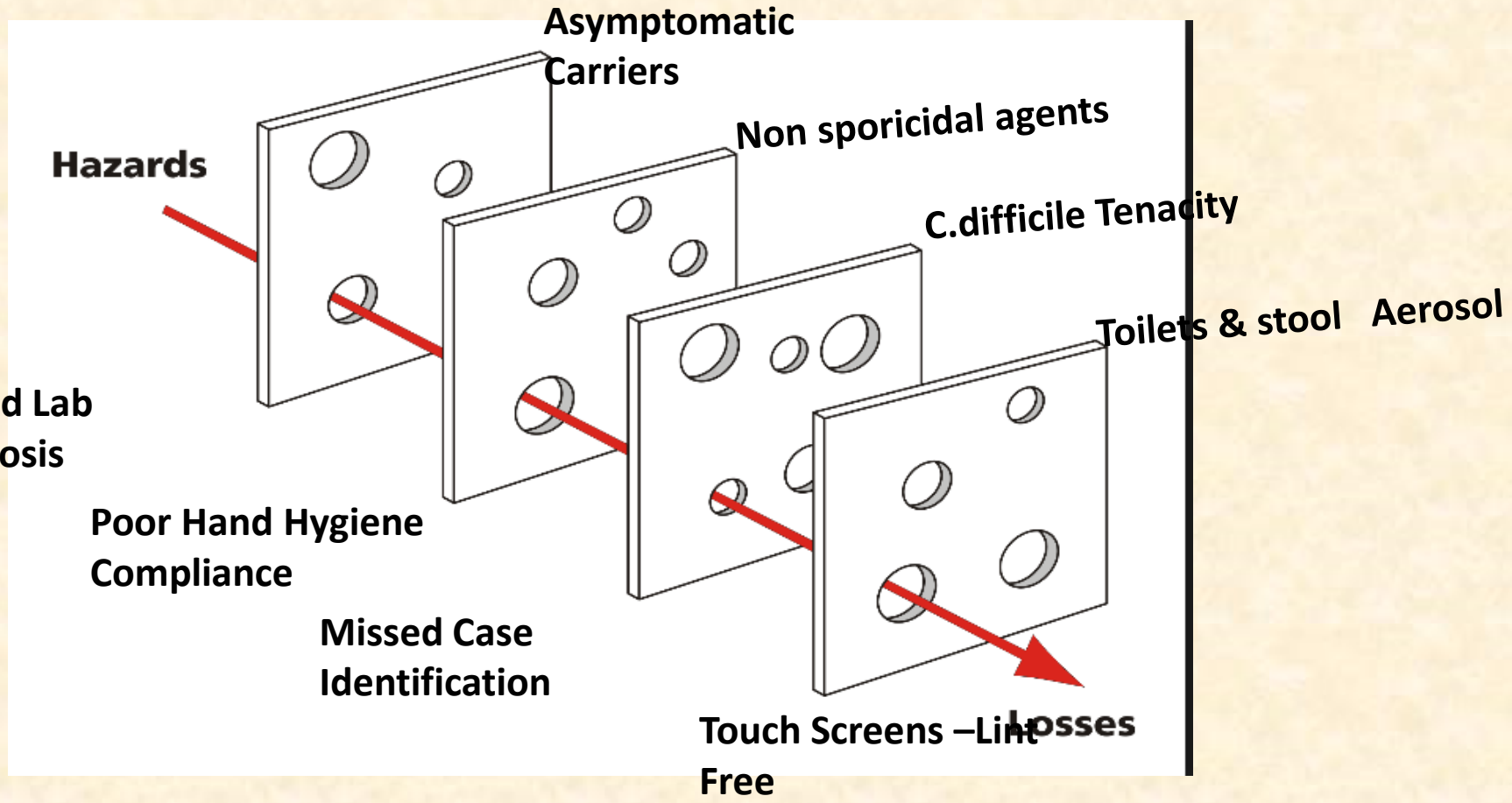
1. **Sodium Hypochlorite**
2. **Peracetic/Hydrogen Peroxide Combination**

Non-Touch: Not EPA

1. **Ultraviolet Light Devices**
2. **Fogging Systems**
3. **Spray Systems**

Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. Annex C – Testing, Surveillance and Management of Clostridium difficile. Annexed to: Routine Practices and Additional Precautions in All Health Care Settings. Toronto, ON: Queen's Printer for Ontario; 2013

Recap of Challenges in Inpatient



Successful translation of evidence-based practice guidelines requires that the "work system" as well as the behavioral patterns of the providers are addressed [1]

1. Hebden, J. N., & Murphy, C. (2013). Minimizing ambiguity to promote the translation of evidence-based practice guidelines to reduce health care-associated infections. *AJIC: American Journal of Infection Control, 41*(1), 75-76. doi:10.1016/j.ajic.2012.09.002 Chlorox

New Technologies …..

- UVC systems have not performed EPA validation or GLP studies.
- Other aerosolized and or vaporized technologies have not demonstrated this combination of performance to the EPA as a fog or mist.
- Some technologies have a HAZMAT potential and environmental damage issues.
- We as users need to ask for data to support the use of hands free systems!

In conclusion...There's lots to think about

- We need to assess our current technologies….
- Do they meet our needs?
- How do we add hands free new technologies in a safe and effective manner?
- We need to define our measures of success with regards to HAI and antibiotic usage for our institutions.
- **We need to emphasize mechanisms of prevention and prevent infections! We need to reduce antimicrobial usage.**


QUESTIONS