

The Pros and Cons of Alternative Disinfection Technologies for Room Decontamination

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Conflict Of Interest Disclosure

- An inventor of AsepticSure[®]
- Chief Medical Officer of Medizone International Inc.
- Shareholder of Medizone International Inc

Objectives

- At the end of this presentation I hope you:
 - Will be able to describe the two types of UV lamp technologies, their characteristics and efficacy
 - Will be able to describe the basis for the hydrogen peroxide vapor and mist technologies and their efficacy
 - Will be able to describe how effective ozone based methods are as a space disinfection technology
 - Understand the synergy of combining ozone and hydrogen peroxide as a novel high level disinfection technology for health care spaces and other applications
 - Will know what to look for in *in vitro*, *in vivo* and clinical studies of the new technologies for room decontamination and disinfection

Agenda

- The characteristics of an ideal room disinfection system
- Quality of Evidence
- Ultraviolet light
- Hydrogen peroxide
- Ozone
- Ozone and Hydrogen Peroxide Synergy

What I Cannot Cover Today

- Formaldehyde fogging
- Aerosolization of surface cleaning agents
- Chlorine dioxide
- Detailed cost estimates of all technologies
- Most of the data presented is about bacteria and bacterial spores
 - With apologies to the viruses and fungi in the room!

The Problem

- Too many healthcare infections
- Needless suffering and mortality
- Despite innovations and best efforts
- Environment a major source and reservoir
- We need to find a transformational technology!
- Just cleaning where the “dots are” is not good enough!

Characteristics of the Ideal Room Disinfection System

- ✓ Highest possible kill of all relevant organisms especially *C. difficile* spores
- ✓ Fast
- ✓ Simple to perform
- ✓ Cost effective
- ✓ Can be safely deployed
- ✓ No environmental residues
- ✓ Reduces incidence of healthcare infections
- ✓ High quality supportive scientific evidence

Quality of Evidence Concerning H2O2, UV, O3

- Can be very mixed so read it critically
- Peer reviewed literature best
- *in vitro* studies
 - Using test chambers etc
 - Bacteria or other organisms on various materials
 - Steel discs/coupons
 - Fabric, carpet, plastics, various building finishes
 - Good controls with many replicates
 - Quantitative Carrier Tests (QCT) Protocol by Springthorpe and Sattar et al
 - Use of a soil load
 - Each organism brings unique challenges

in vivo Testing

- In hospital rooms, laboratories, various field locations
 - Random assignment of rooms/spaces
 - No overlap of methods, “wash out times”
 - Detailed surface culture protocol with large number of samples
 - Highly standardized, with different methods
 - Supplemented with microbe loaded coupons in standard locations in the room
 - Always use spores of spore forming pathogens
 - eg *C. difficile*, *Bacillus spp*, *Geobacillus spp.* etc.

Interpreting Results

- Want to see expression of data as log₁₀ kill (or log₁₀ survivor)
 - Kill = starting inoculum - survivors
 - Expressed as log₁₀ kill
 - Use geometric means for large number of samples
 - Need dozens of replicates under any one set of conditions especially for *in vitro* testing
- Surface swabs
 - Typically expressed as cfu/cm²
 - Typically see 10's to 100's cfu/cm²
 - Count specific pathogens
 - Or count all heterotrophic bacteria on the surface

Clinical Studies

- Before and after studies citing reductions in infections
 - Rates of HAI vary significantly over time
 - Be cautious in the interpretation of these results
- Prefer randomized and multicenter design ideally
 - Difficult to do and costly
 - Combined with surface cultures and loaded coupons and clinical outcomes to make a comprehensive evaluation

A Bit of Physics About UV Light

- Ultraviolet germicidal irradiation (UVGI)
- Wavelength shorter than that of visible light
 - UVA 400 nm to 315 nm
 - UVB 315 nm to 280 nm
 - UVC 280 nm to 200 nm
- The entire UV spectrum can kill or inactivate many different microorganisms
- UVC energy provides the most germicidal
- 265 nm optimum wavelength

Susceptibility to UV Light

- Susceptibility to UV irradiation varies by species
- Also upon other conditions:
 - Eg air, water, temperature, flow rates, etc
- Microbial susceptibility is very variable
- Design of UV light systems not that standardized
- No consensus guidelines for design

Susceptibility of Organisms to UVC

Organism Group	Member Group
Vegetative Bacteria	<i>Staphylococcus aureus</i>
	<i>Streptococcus progenies</i>
	<i>Escherichia coli</i>
	<i>Pseudomonas aeruginosa</i>
	<i>Serratia marcescens</i>
Mycobacteria	<i>Mycobacterium tuberculosis</i>
	<i>Mycobacterium bovis</i>
	<i>Mycobacterium leprae</i>
Bacterial Spores	<i>Bacillus anthracis</i>
	<i>Bacillus cereus</i>
	<i>Bacillus subtilis</i>
Fungal Spores	<i>Aspergillus versicolor</i>
	<i>Penicillium chrysogenum</i>
	<i>Stachybotrys chartarum</i>

From Martin SB et al . ASHRE Journal. August 2008

Mercury Vapor Lamps

- In mercury vapor lamps, the mercury vapor is excited to create UV-C
- Create UV at 253.7 nm.
- This is close to the average peak DNA absorbed at 260-265 nm.
- Mercury lamps produce continuous UV light

Xenon Vapor Lamps

- Pulsing a xenon UV lamp PX-UV
- Results in a flash of light with a broad spectrum from 200 nm to 320 nm
- Millisecond pulses
- More UV-C wavelengths are produced
- High intensity of the fast pulses may give PX-UV better disinfection efficacy?

Tru-D Unit by Lumalier



From ECRI Health Devices May 2011

Mercury UV System Tru-D

- An automated mobile UV-C unit
- Tru-D; by Lumalier
- Shown to produce a 3 log₁₀ kill of vegetative bacteria
 - MRSA, VRE, and *A. baumannii*
- 2.4-log₁₀ kill of *C. difficile* seeded onto Formica surfaces in experimentally contaminated patient room

Rutala WA, Gergen MF, Weber DJ. Room decontamination with UV radiation. *Infect Control Hosp Epidemiol* 2010;31:1025–1029.

Tru-D

- Tru-D, Lumalier studied in reducing environmental contamination with vegetative bacteria
- Measured using aerobic colony counts and *C. difficile* inoculated onto stainless steel carrier disks
 - Boyce JM et al. *Infect Control Hosp Epidemiol* 2011;32:737–742

Tru-D

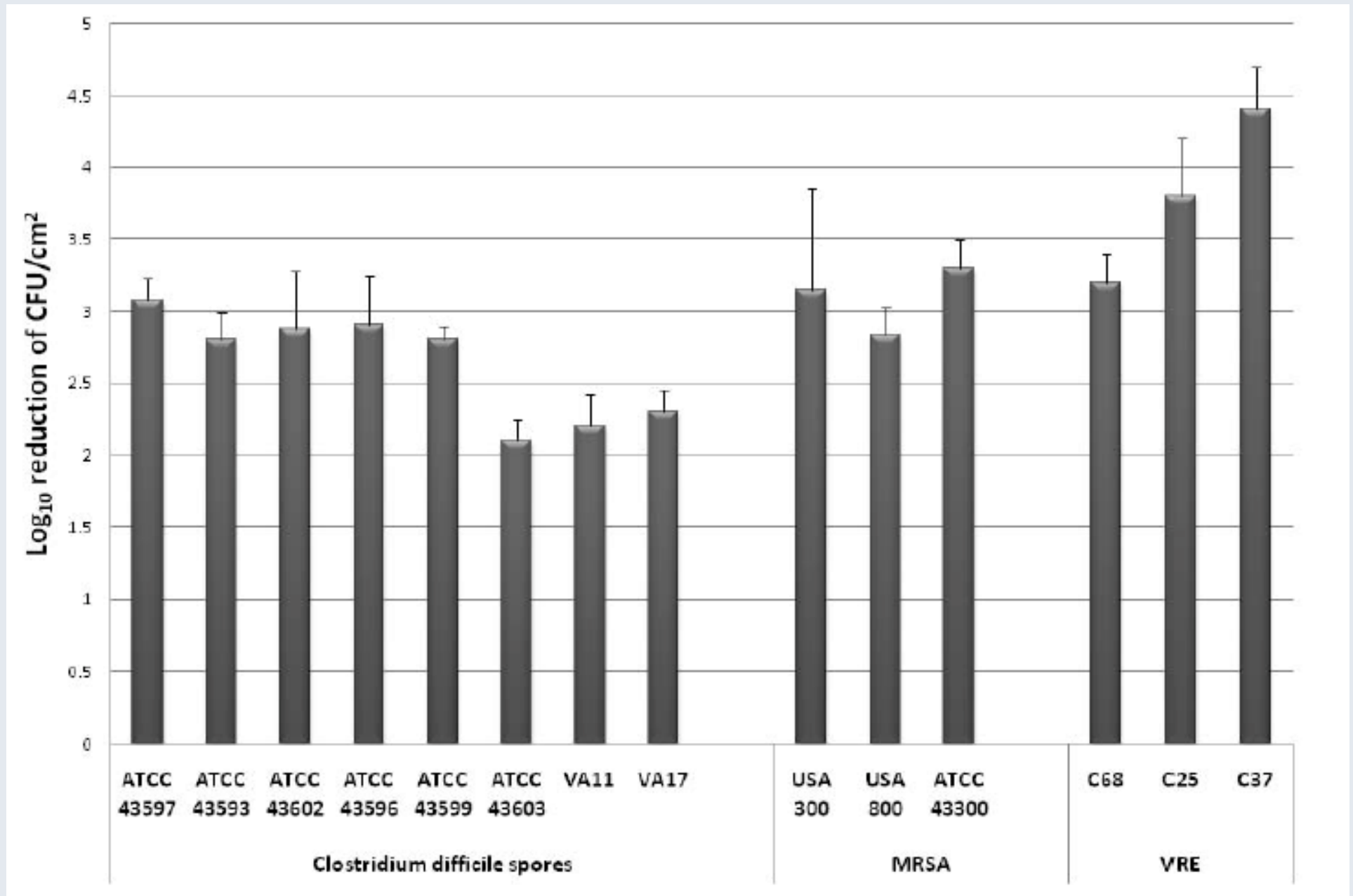
- Room decontamination with the Tru-D UV system
- Reductions in aerobic bacteria on 5 high-touch surfaces.
- Mean *C. difficile* log₁₀ reductions ranged from 1.8 to 2.9 when cycle times of 34.2–100.1 minutes were used.
- Surfaces in direct line of sight were significantly more likely to yield negative culture results after UV decontamination than before decontamination
 - Boyce JM et al. *Infect Control Hosp Epidemiol* 2011;32:737–742

Tru-D

- On inoculated surfaces
- Reflected dose of 22,000 $\mu\text{Ws}/\text{cm}^2$ for 45 minutes
- Kill of *C. difficile* spores and MRSA by $>2-3 \log_{10}$ colony forming units (CFU)/ cm^2
- Kill of VRE by $>3-4 \log_{10}$ CFU/ cm^2

- Same level of kill of MRSA and VRE was achieved in 20 minutes at a reflected dose of 12,000 $\mu\text{Ws}/\text{cm}^2$,
- But killing of *C. difficile* spores was reduced significantly.
 - Nerandzic MM. *BMC Infect Dis* 2010;10:197.

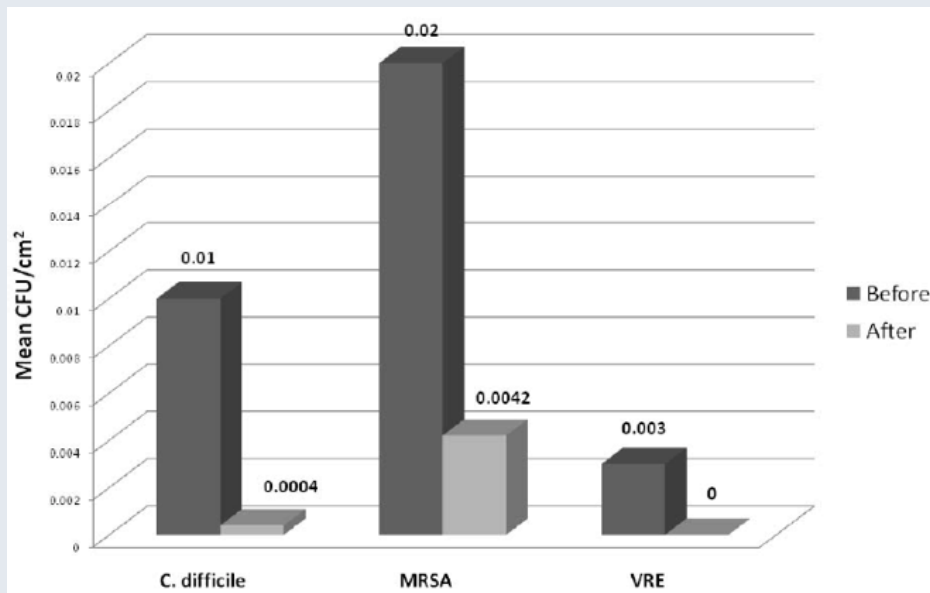
Tru-D Log10 Bacterial Kill



From Nerandzic MM et al. *BMC Infect Dis* 2010;10:197

Tru-D Surface Swabs

- High touch surfaces of a bathroom
 - 60,000 cm²
 - *C. difficile* spores
 - Before: 600 spores
 - After: 24 spores
 - MRSA bacteria
 - Before: 1,200
 - After: 240
 - VRE bacteria
 - Before: 180
 - After: 0



Xenex

Pulsed xenon UV light



From: www.xenex.com

XENEX *in vitro* Lab Study

Organism	Control (cfu)	Log10 Kill	
		480 sec (8 min)	720 sec (12 min)
MRSA	1.23×10^5	5.01	n/a
VRE	2.75×10^4	4.44	n/a
<i>C. difficile</i>	3.33×10^5	4.52	5.52

- ***C. difficile*** was 1 meter from lamp, MRSA and VRE 2 meters from lamp.
- ***C. difficile*** 9 samples, MRSA & VRE 4 samples.
- “The experiment was conducted at an independent microbial testing laboratory”
- Modified from: Stibich M. *Abstract presented at SHEA/Fifth Decennial Meeting 2010*

Xenex Study at MD Anderson

- January to March 2010 at MD Anderson Cancer Center, Houston Tx
- 12 rooms extensively surface cultured at discharge for VRE isolation
- Isolation clean with germicide x 30 mins.
- 3 x 4 min exposures to Xenex lamp
- Cultures taken before cleaning, after cleaning and using the Xenex lamp

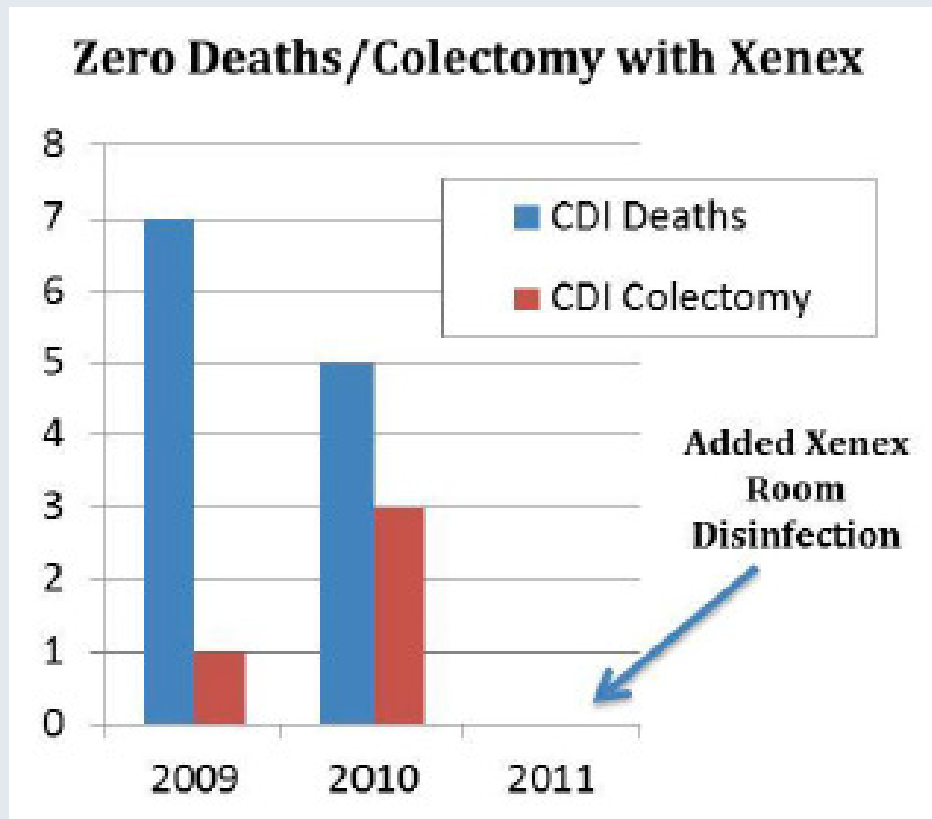
Stibich et al. Infect Control Hosp Epidemiol 2011;32(3)

XENEX

TABLE 2. Impact of Standard Cleaning and Pulsed-Xenon Ultraviolet (PX-UV) Disinfection on Room Bacterial Heterotrophic Plate Count (HPC)

Room status	No. of samples	HPC mean, CFU/cm ²	<i>z</i>	<i>P</i>
Comparison 1			2.638	.0083
Before cleaning	73	33.0		
After standard terminal cleaning	91	27.4		
Comparison 2			6.430	<.0001
Before cleaning	73	33.0		
After PX-UV treatment	75	1.2		
Comparison 3			4.309	<.0001
After standard terminal cleaning	91	27.4		
After PX-UV treatment	75	1.2		

Xenex Cooley Dickinson Hospital Study



- 140 bed acute hospital, Northampton MA
- January-September 2011 Xenex used
- Uncontrolled observational study
 - 2x7 min in room
 - 1x7 min in bathroom
- Pre-cleaned with chlorine bleach (SOP throughout)
- CDI Rates
 - 2009: not stated
 - 2010: 0.95/1000 PtDay
 - 2008-2010 Q1-3: 0.98/1000 PtDay
 - 2011 (Q1-3): 0.32/1000 PtDay

UV Light Summary

Property	UV-C Light	Xenon Pulse Light
Source	Mercury bulb	Xenon bulb
Exposure time	20-100 min	8-12 mins over 2-3 doses
Vegetative bacterial kill	3-4 log	4-5 log
C. difficile spore kill	2-3 log	4-5 log (limited data)
Risks	UV exposure	UV exposure
Toxicities/By Products	Mercury vapor	None
Controlled Clinical Trials	Yes	None yet
Costs	\$124,500 capital \$1,600 for lamps (9000 h)	?? Lamps x 3-4 months
Other	Line of sight effect	Scant data, line of sight effect

H2O2 Technologies

- Bioquell
 - 30% H2O2 solution
 - H2O2 vapor
- Glosair (ASP)
 - 5-6% H2O2 solution
 - ASP (J&J) acquired Sterinis in 2009
 - H2O2 mist/aerosol
- VHP (Steris)
 - 35% H2O2 solution
 - H2O2 vapor



Steris VHP 1000 ED System



From: www.steris.com

BioQuell Q-10



Glosair (ASP)

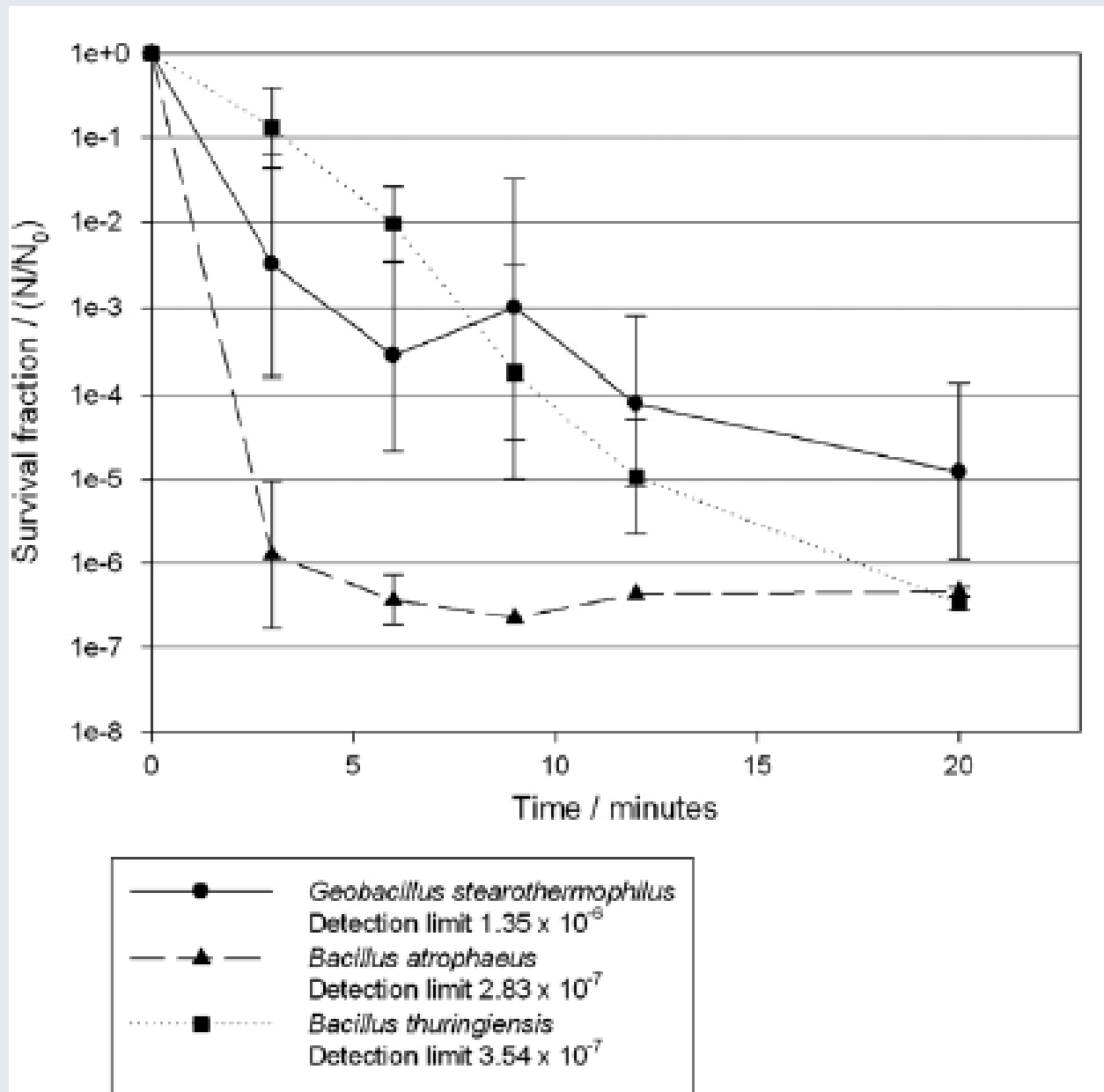
Glosair 600



Glosair 400



VHP (Steris) Against Aerobic Spores



Sealing Ducts in a Room



Jim Doyle in www.stltoday.com/business/article published August 15, 2010

Bioquell Efficacy for CDI

- HPV decontamination of 5 high-incidence CDI wards followed by hospital-wide decontamination of rooms vacated by patients with *C. difficile* infection (CDI)
- 25.6% of cultures from surfaces before HPV decontamination yielded *C. difficile*
- compared with 0 cultures of samples obtained after HPV decontamination ($P < .001$)

Bioquell and CDI Cont'd

- During 9 month intervention period
- On the 5 high incidence wards rates of CDI dropped from 2.28 vs 1.28 cases per 1,000 patient-days ($P < .047$)
- Hospital wide incidence fell from 1.89 vs 0.88 cases per 1,000 patient-days ($P < .047$) during the high incidence months pre and post intervention.

Bioquell and MRSA

- 74% of 359 swabs taken before cleaning yielded MRSA
- After cleaning, all areas remained contaminated, with 66% of 124 swabs yielding MRSA.
- After treatment of 6 rooms with HPV (Bioquell) only 1 of 85 (1.2%) swabs showed MRSA
 - note smaller sample size after exposure however
- 5 hour cycle time
- 500 ppm H₂O₂ (high)
 - French GL et al. Journal of Hospital Infection (2004) 57, 31–37

Sterinis Trial (becomes Glosair)

- Teaching hospital in Zonguldak, Turkey
- Steel discs inoculated and placed in many locations in patient rooms 53m³
- MRSA and *A. baumannii*
- Applied Sterinis HP Mist
- 2.5 hr cycles
 - Piskin N et al. Am J Infect Control. 2011 Nov;39(9):757-62

Table 4. Comparison of the activity of the DMHP system according to presence or absence of a barrier

	Reduction in initial contamination, Mean (\pm SD), log ₁₀ cfu		P value
	In absence of a barrier	In presence of a barrier	
Pure MRSA suspension carrying disks	4.70 \pm 0.0	3.52 \pm 1.82	.059
Pure Acinetobacter suspension carrying disks	4.67 \pm 0.0	3.79 \pm 1.35	.059
Serum containing MRSA suspension carrying disks	4.45 \pm 0.63	1.49 \pm 1.86	.003
Serum containing Acinetobacter suspension carrying disks	4.44 \pm 0.0	2.92 \pm 1.75	.01

SD, standard deviation.

H2O2 (Sterinis) vs Bleach

In vitro

TABLE 1. Comparison of the In Vitro Activity of Sodium Hypochlorite and Hydrogen Peroxide Against *Clostridium difficile* Spores, According to the Material Used as a Spore Carrier

Disinfection method	Reduction in initial contamination, mean (\pm SD), log ₁₀ cfu	
	Vinyl polychloride	Laminate
0.5% Sodium hypochlorite solution	4.18 \pm 0.33	4.47 \pm 0.32
Hydrogen peroxide-silver cation dry-mist	4.19 \pm 0.86	4.17 \pm 0.74

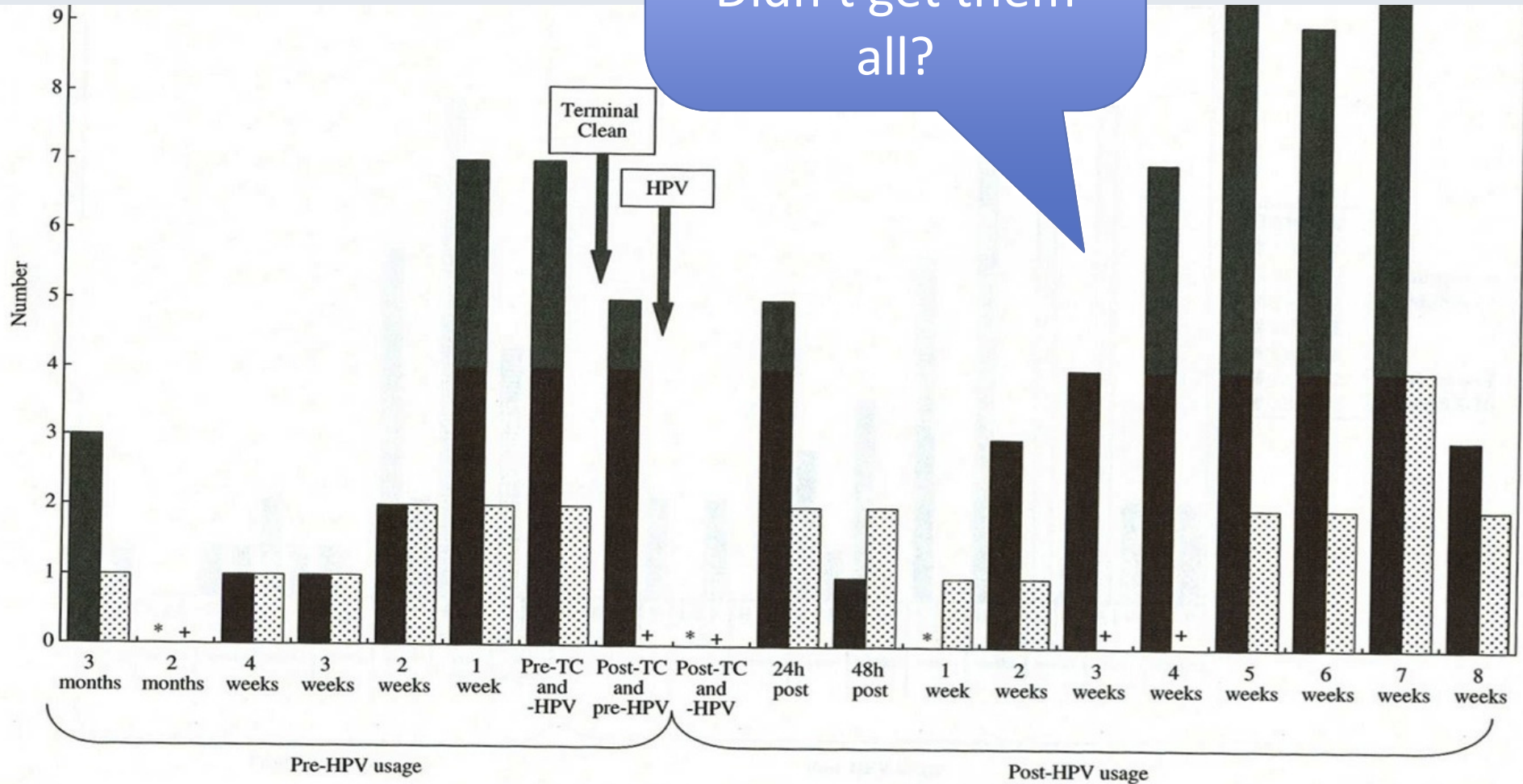
In vivo

- *C. difficile* terminal clean rooms
- 0.5% bleach x 10 min x 16 rooms
 - 24% to 12% room contamination reduction (50%)
- Sterinis x 1.5-2 hr x 15 rooms
 - 19% to 2% room contamination reduction (91%)

Tru-D vs Bioquell “Head to Head”

- 500 bed hospital
 - 15 patient rooms at random from 8 wards
- 5 high touch surfaces cultured for ACC
- Steel discs loaded with 10^6 *C. difficile* spores placed in 5 areas close to high touch surfaces
- BI's with 10^4 and 10^6 *G. stearoothermophilus*
- Results
 - HPV (Bioquell)
 - 93% ACC negative
 - 6 log₁₀ *C. difficile* kill
 - 99-100% BI's killed
 - 2.5-3 hr cycles
 - UV-C (TRU-D)
 - 52% ACC negative
 - <2 log₁₀ *C. difficile* kill
 - 0-22% % BI's killed
 - 0.6-1.7 hr cycles

Rapid MRSA regrowth after HPV.
Didn't get them all?



Comparison of H2O2 Systems

Parameter	Glosair (ASP)	VHP (Steris)	BioQuell
H2O2 %	5-6%	35%	35%
Dispersion	Dry Mist/Aerosol	Vapor	Vapor
Final Conc H2O2	50-80 ppm	~500 ppm	~500 ppm
Cycle Time	~2-3 hr	2-8 hrs	≥2 hr, up to 5 hr
<i>C. difficile</i> log10 kill	2-3 log	*NPD for <i>C. difficile</i> . 5-6 log for Bacillus	6 log for <i>C. difficile</i> . 6 log for Bacillus
Controlled Clinical Trials	Some small	?	Yes
Cost	\$65,000? \$50 per room	?	\$44,000 capital Cost per room?

*NPD= No Published Data

Ozone Actions

- The first ozone disinfection experiment was conducted in France in 1886
- de Meritens demonstrated that diluted ozonized air could sterilize polluted water
- Ozone gas (O₃) with a molecular weight of 48
- Highly reactive with a large excess of energy (~143 KJ/mol) and a high level of oxidizing power
- Marked tropism for extracting electrons from other molecules and simultaneously releasing one of its own oxygen atoms in the process.

Pure O3 as Antibacterial

Table 1. Bacterial susceptibility to ozone gas

	ATCC #	Log ₁₀ reduction in cfu's	
		Wet sample	Dry sample
Gram-positive bacteria			
<i>Bacillus cereus</i>	11778	> 3.1	> 3.1
<i>Bacillus spizizenii</i>	6633	> 3.2	> 3.2
<i>Clostridium difficile</i>	43593	> 4.0	> 4.0
MRSA	Clinical isolates	> 3.0	> 3.0
Methicillin-sensitive	Clinical isolates	> 2.5	> 2.5
<i>Staphylococcus aureus</i>			
<i>Propionibacterium acnes</i>	11827	≅ 4	≅ 4
<i>Streptococcus pyogenes</i>	12384	≅ 4	≅ 4
Gram-negative bacteria			
<i>Ainetobacter baumannii</i>	19606	≅ 4	≅ 4
<i>Enterococcus faecalis</i>	51299	> 3	> 3
<i>Escherichia coli</i>	25922	> 3.1	> 3.1
<i>Haemophilus influenzae</i>	19418	≅ 4	≅ 4
<i>Klebsiella pneumoniae</i>	10031	≅ 4	≅ 4
<i>Legionella pneumophila</i>	33152	≅ 4	≅ 4
<i>Pseudomonas aeruginosa</i>	27853	≅ 4	≅ 4
Acid-fast bacteria			
<i>Mycobacterium smegmatis</i>	14468	> 2.7	> 2.7

Ozone & Hydrogen Peroxide in Biological Systems

- Antibodies have been shown to have catalytic activity that produces **BOTH H₂O₂ AND O₃**
 - BUT the amount produced of each is so low that neither could kill any microorganism
- Trioxidane (H₂O₃) has been detected as the extremely reactive intermediary molecule of this reaction
- Trioxidane is lethal to organisms in minute amounts!

Nyffeler, Wentworth & Lerner et al. Angewandte Chemie
2004, from Scripps Research Institute and Oxford
University



What Can be Learned From Mother Nature!

- Medizone experiments that led to synergy
- Goals:
 - To study the antimicrobial effects of ozone gas **and** of hydrogen peroxide vapour
 - Against common **healthcare** and **food borne** pathogens
 - And to document the **synergy of ozone AND hydrogen peroxide** as rapid means to achieve a high level of disinfection in full sized rooms

Hydrogen Peroxide *OR* Ozone

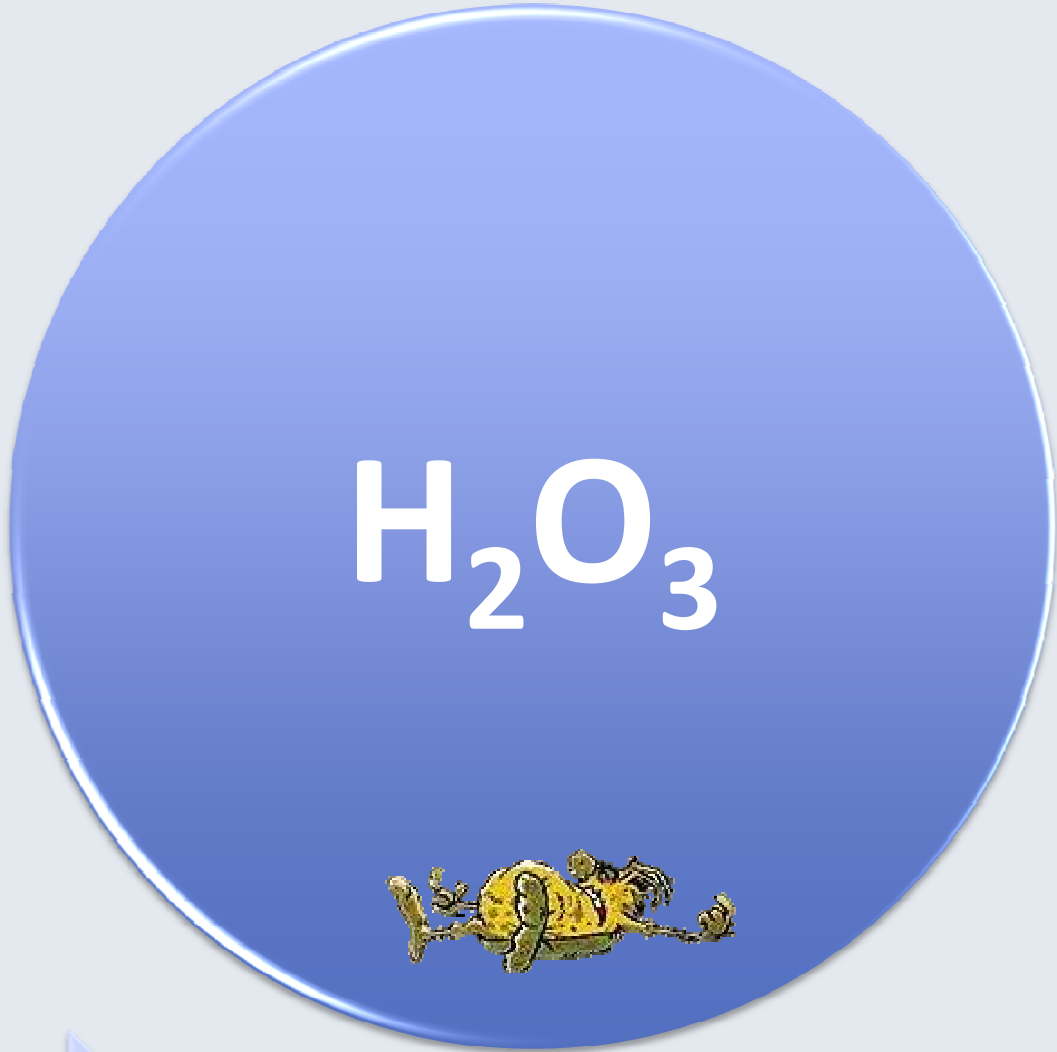
Hydrogen Peroxide

- Used alone at 1-3%
- Resulted in $< 1 \log_{10}$ bacterial kill with up to 60 minute exposures
- Certainly not sporocidal

Ozone

- Used alone at 30-200 PPM
- Resulted in $< 1 \log_{10}$ bacterial kill with up to 90 minutes exposures
- At 500-800 PPM for 90 mins see kill of $6 \log_{10}$

The Science of Synergy



No Kill



$>6 \log_{10}$ Kill

Our Microbiology Techniques



1 cm stainless steel disks as the bacteria & spore carriers



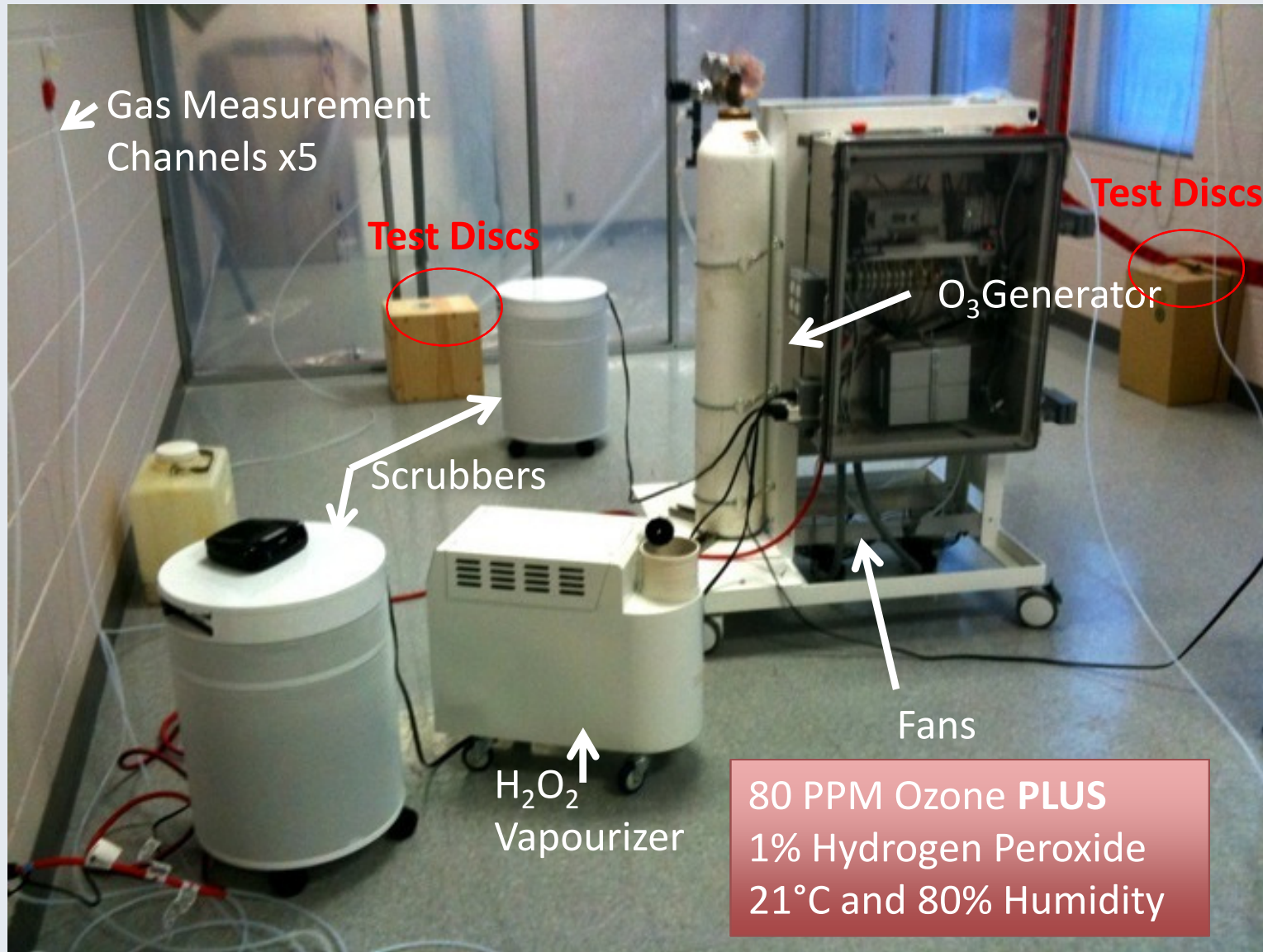
The quantitative carrier test (QCT-2) standard used or modified

In vitro Testing System

- Polycarbonate chamber
- Fully instrumented to measure conditions
- Computer controlled and recorded results
- Used MRSA as test organism initially to define optimal conditions



In vivo Testing System



Frankenstein and Woody



The Results

Organism	Ozone (PPM)	H2O2 (%)	Exposure (min)	Microbial Kill (Log₁₀)
MRSA	80	1	15	6.3
VRE	80	1	15	6.2
<i>E. coli</i>	80	1	15	6.5
<i>S. typhimurium</i>	80	1	15	6.1
<i>P. aeruginosa</i>	80	1	15	6.0
<i>L. monocytogenes</i>	80	1	15	6.3
<i>C. difficile</i> spores	80	1	15-30	6.1
<i>B. subtilis</i> spores	80	1	30	6.1
<i>Mycobacterium terrae</i>	80	1	30	6.2

Testing Materials

- AsepticSure system also effective on:
 - Stainless steel
 - Plastic from toilet seats
 - Laminate
 - Carpeting
 - Cotton or synthetic cloth
 - With and without organic soil load

Summary of AsepticSure

- **First ever** use of **ozone and hydrogen** peroxide for high level disinfection of clinical spaces and surfaces
- Capitalizes upon **HUGE synergy** between ozone and hydrogen peroxide producing **trioxidane**
- Very **fast**
- **Broad** spectrum
- Consistent **high level** disinfection ($6 \log_{10}$ =sterilization)
- **Penetrating** gas goes everywhere
- **Low doses** of ozone and hydrogen peroxide reduces costs, risks and damage to infrastructure
- Technology proven to be very **robust** and **reliable**
- Capital Cost~ \$95,000 + ~\$10-20 per room

Am J Inf Control 2011;39:873-9

Effectiveness of a novel ozone-based system for the rapid high-level disinfection of health care spaces and surfaces

Dick Zoutman, MD, FRCPC,^a Michael Shannon, MD, MSc,^{b,c} and Arkady Mandel, MD, PhD, DSc^c
Kingston and Ottawa, Ontario, Canada

Background: Vapor-based fumigant systems for disinfection of health care surfaces and spaces is an evolving technology. A new system (AsepticSure) uses an ozone-based process to create a highly reactive oxidative vapor with broad and high-level antimicrobial properties.

Methods: Ozone gas at 50-500 ppm was combined with 3% hydrogen peroxide vapor in a test chamber and upscaled in rooms measuring 82 m³ and 90 m³ in area. Test organisms included methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococcus, *Escherichia coli*, *Pseudomonas aeruginosa*, *Clostridium difficile*, and *Bacillus subtilis* spores dried onto steel discs or cotton gauze pads.

Results: The combination of 80-ppm ozone with 1% hydrogen peroxide vapor achieved a very high level of disinfection, with a ≥ 6 log₁₀ reduction in the bacteria and spores tested on steel discs and MRSA tested on cotton gauze during a 30- to 90-minute exposure. The entire system was scalable such that it achieved the same high level of disinfection in both the 81-m³ and 90-m³ rooms in 60-90 minutes.

Conclusion: The ozone hydrogen peroxide vapor system provides a very high level of disinfection of steel and gauze surfaces against health care-associated bacterial pathogens. The system is an advanced oxidative process providing a rapid and effective means of disinfecting health care surfaces and spaces.

Key Words: Ozonation; hydrogen peroxide; fumigation.

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AsepticSure



Bed Bugs!



AsepticSure and Bed Bugs

- Collaboration with Department of Entomology, Purdue University
- 100% kill of all stages of bed bugs including the very hard to kill eggs
- Higher concentration of ozone & H₂O₂ required (180 ppm and 3%)
- And longer exposure time of up to 24 hours.

Characteristics of the Ideal Room Disinfection System

- ✓ Highest possible kill of all relevant organisms especially *C. difficile* spores
- ✓ Fast
- ✓ Simple to perform
- ✓ Cost effective
- ✓ Can be safely deployed
- ✓ No environmental residues
- ✓ Reduces incidence of healthcare infections
- ✓ High quality supportive scientific evidence

The Final Result

