

CHG: Facts & More

Matthew M. Cooper, MD MBA FACS
Global Senior Medical Director &
Director, Patient Safety COE

April 2019



3M Science.
Applied to Life.™

Protecting Patients Against Microbial Contamination

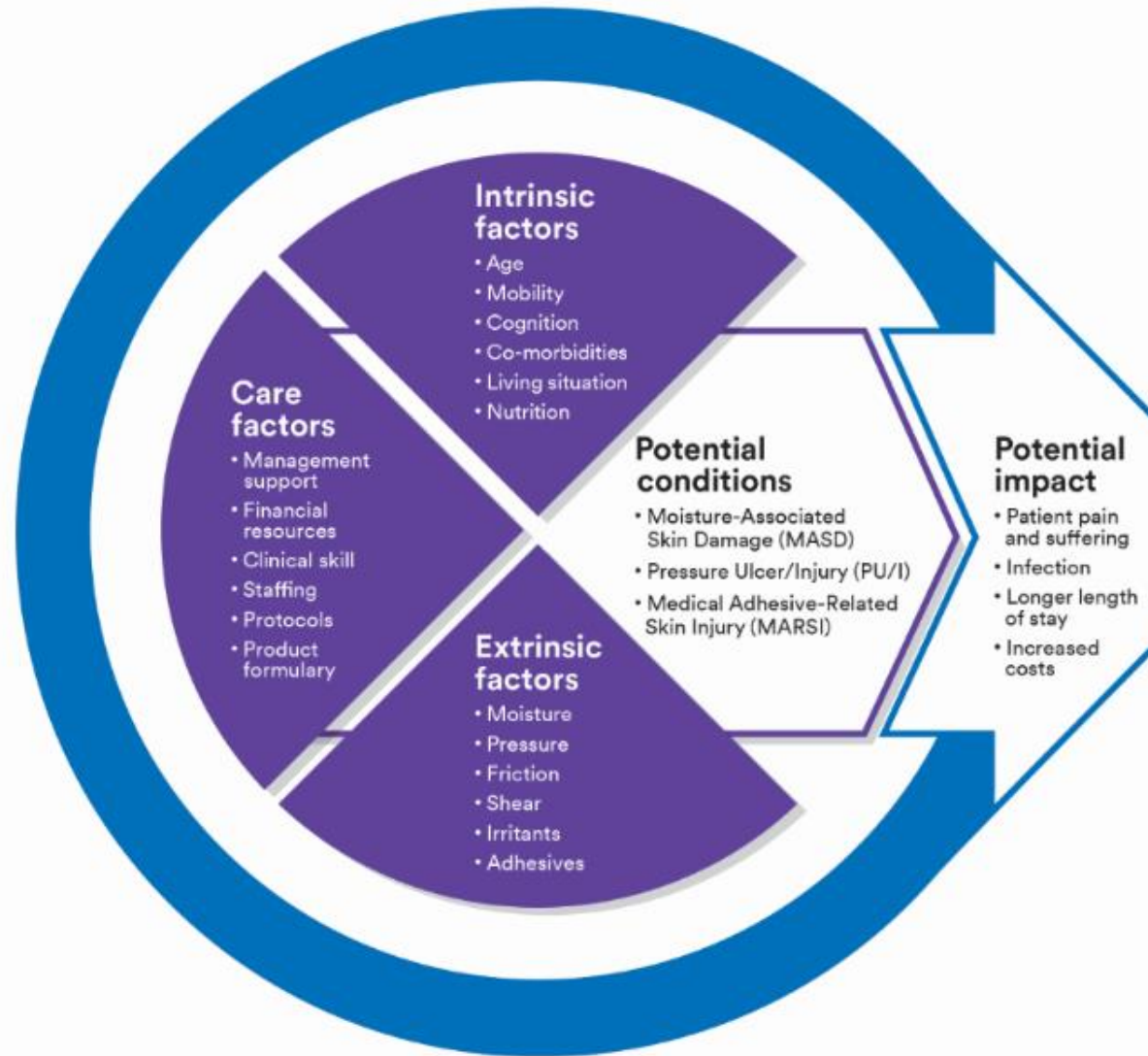
Surgical Skin Antiseptics and
Antimicrobial Incise Drapes

A close-up photograph of aged, wrinkled skin. The skin is a warm, brownish-orange color with deep, prominent wrinkles and creases. The texture is rough and uneven. Overlaid on the left side of the image is the text "Think skin first." in a black, sans-serif font.

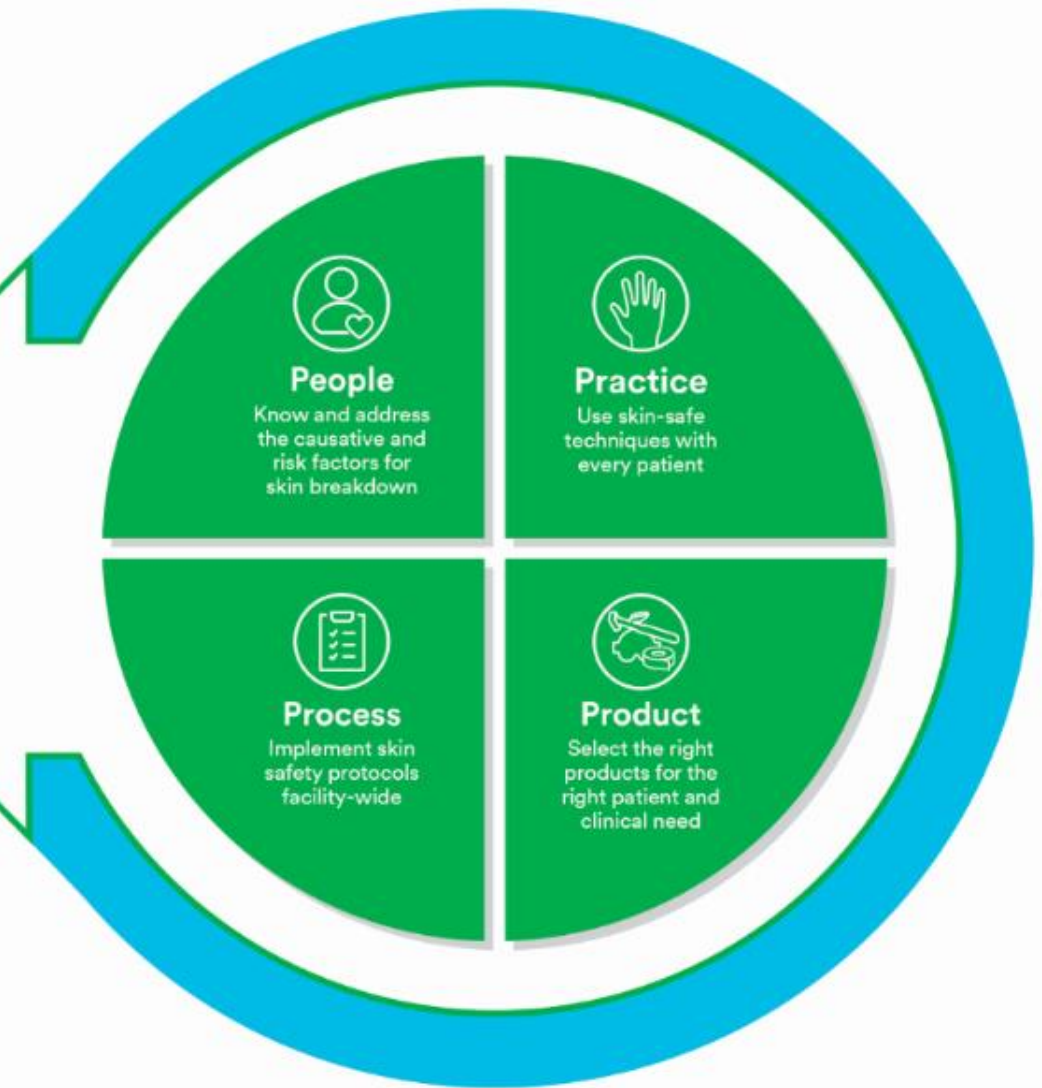
Think skin first.

Think skin deeper.

Multiple factors impacting skin damage*



Four factors that impact outcomes



*Adapted from: 1) Campbell, Skin Safety Model; and 2) Medical Adhesives and Patient Safety: State of the Science

A Comprehensive Framework for Infection Prevention & Management



- Develop highly trained teams (and continue education)
- Drive change facility-wide with standards and process
- Select proven technologies

Chlorhexidine

- A critical component, life-saver, in the prevention, control and management of infection
- Returning to previous practices ill-advised
 - Hospital acquired infections
 - Multi-drug resistant organisms

Helping you Meet the National Standards and Guidelines

Healthcare associated infections such as bloodstream or surgical site infections can result from organisms that are found on a patient's skin. Effective reduction of the bacterial load on skin through the use of topical antiseptics is therefore a critical infection prevention measure that should be performed prior to invasive procedures that puncture the skin.^{1,2,3}

Chlorhexidine has a broad spectrum of activity, particularly against gram-negative bacteria.⁴ One of the most important attributes of CHG is its persistence. It has strong affinity for the skin, remaining chemically active for at least 6 hours. Indeed, it probably has the best persistent effect of any agent currently on the market.⁵

National Standards and Guidelines for Intravascular Access Devices

Published evidence based guidelines and practice standards recommend the use of chlorhexidine gluconate (CHG) skin antiseptics.

NSQHS: STANDARD 3⁷
(Refer to NHMRC 2010)

“Alcohol-based preparations that have 70% isopropyl alcohol v/v and at least 0.5% chlorhexidine are recommended for procedures penetrating skin (including subcutaneous infusions).”

Intravenous Nursing NZ 2012⁸

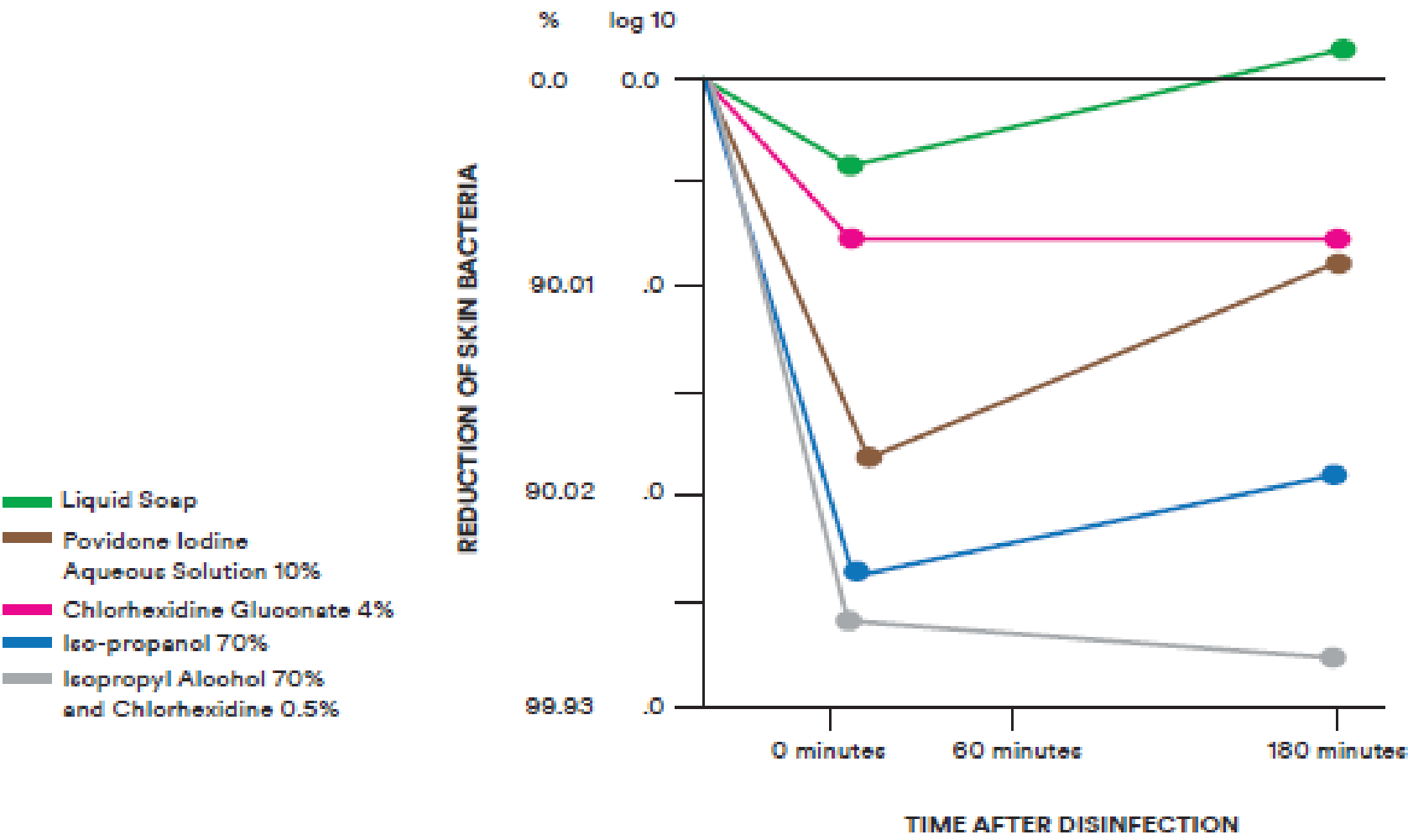
“use of >0.5% chlorhexidine gluconate and 70% alcohol as a skin antiseptic”

NICE Guidelines 2012⁹

“Decontaminate the skin at the insertion site with chlorhexidine gluconate in 70% alcohol before inserting a peripheral vascular access devices or a peripherally inserted central catheter.”

Chlorhexidine & Alcohol

Efficacy of Antiseptics⁶



Chlorhexidine & Alcohol

3M™ SoluPrep™ Antiseptic Solutions

2% w/v Chlorhexidine Gluconate and 70% v/v Isopropyl Alcohol:

- Fast initial kill with residual activity for up to 24 hours⁴
- Effective against most gram-positive and gram-negative bacteria, some fungi and viruses^{7,8}
- Hypoallergenic, poorly absorbed through skin⁷

CHG and alcohol is a highly effective combination for skin prep before surgery.^{1,7,9}

When antiseptics are compared for persistence and quick kill, a CHG and alcohol prep performs well compared with povidone iodine and alcohol, or any active alone.¹

Active	Quick Kill	Persistence
CHG + alcohol	Excellent 	Excellent 
Povidone-iodine + alcohol	Excellent 	Moderate 
CHG	Moderate 	Excellent 
Povidone-iodine	Moderate 	Moderate 
Alcohol	Excellent 	None 

Start with the proper prep

There are many antiseptic choices, but not all preps perform the same. Selecting the proper skin prep will reduce a patient's bacterial load throughout the perioperative process, providing both immediate and lasting protection.

Use CHG + alcohol

Guidelines issued by the World Health Organization (WHO) recommend using an alcohol-based antiseptic solution with chlorhexidine gluconate (CHG) for surgical site skin preparation.¹

CHG and alcohol is a highly effective combination for skin prep before surgery.^{2,3}



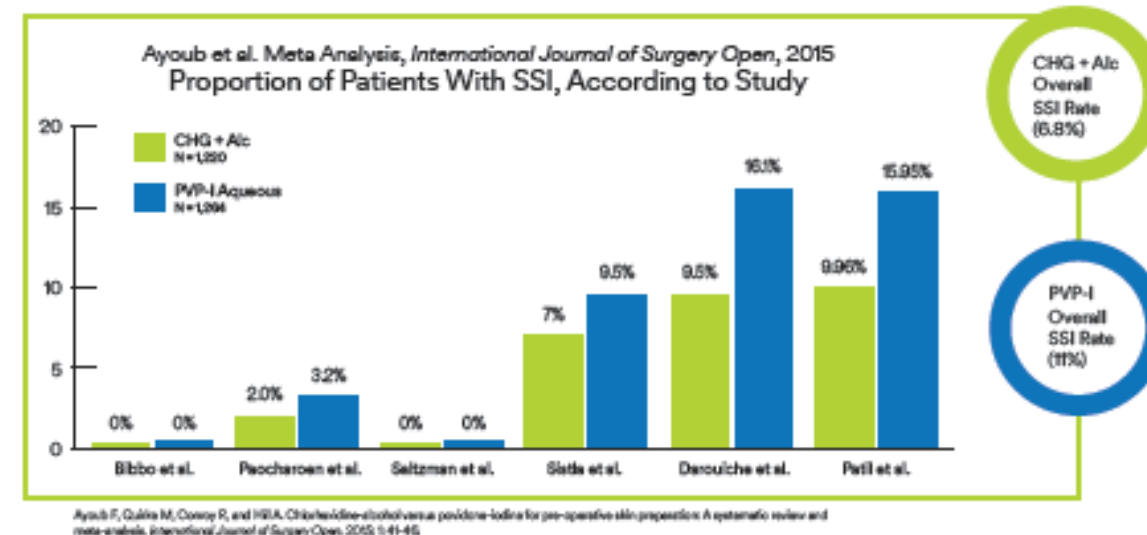
Efficacy of antiseptics

When antiseptics are compared for persistence and quick kill, a CHG and alcohol prep performs well compared with povidone iodine and alcohol, or any active alone.²

ACTIVE	QUICK KILL	PERSISTENCE
CHG + alcohol	Excellent	Excellent
Povidone-iodine + alcohol	Excellent	Moderate
CHG	Moderate	Excellent
Povidone-iodine	Moderate	Moderate
Alcohol	Excellent	None

CHG + alcohol more effective than PVP-I

Preoperative surgical skin preparation with chlorhexidine gluconate and alcohol is more effective than povidone-iodine aqueous in preventing SSI across clean and clean-contaminated surgery.⁴



CHG associated with lower risk of SSI and cost

Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection. *Infect Control Hosp Epidemiol.* 2010; (12):1219-29

Objective

Compare use of chlorhexidine with use of iodine for preoperative skin antisepsis with respect to effectiveness in preventing surgical site infections (SSIs) and cost.

Methodology

Systematic search for studies with keywords “systematic review,” “meta-analysis,” and “randomized controlled trial [RCT]”, interventions (“iodine,” “iodophor,” and “chlorhexidine”), and outcomes (“surgical wound infection” and “cellulitis”). Articles selected for inclusion met the following criteria: (1) systematic reviews, meta-analyses, or RCTs; (2) in the English language; (3) compared preoperative chlorhexidine versus iodine skin antisepsis; (4) evaluated adult surgical patients; and (5) assessed for at least one of the outcomes of interest (ie, SSI (primary) and positive skin culture result post-prep (secondary)). Initially, 1,508 studies were identified, 18 articles underwent review of the full text, and 9 RCTs representing 3,614 patients were included in the meta-analysis.



Findings

Moderate-quality of evidence supports the use of chlorhexidine over iodine for preoperative skin antisepsis to prevent SSI. Additionally, there is moderate quality evidence that use of chlorhexidine is associated with fewer positive skin culture results after application. There was a 36% reduction in the number of SSIs among patients who received preoperative skin antisepsis with chlorhexidine, compared with those who received iodine. A cost-benefit model baseline scenario, demonstrated that switching from iodine to chlorhexidine resulted in a net cost savings of \$16–\$26 per surgical case and \$349,904–\$568,594 per year for the Hospital of the University of Pennsylvania.

Summary 2

CHG & IPA preoperative skin prep is superior to PVP-I Aqueous in preventing SSI

Darouiche RO, Wall MJ, Jr., Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical site antisepsis. *New England Journal of Medicine* 2010; 362(1):18-26.

Objective

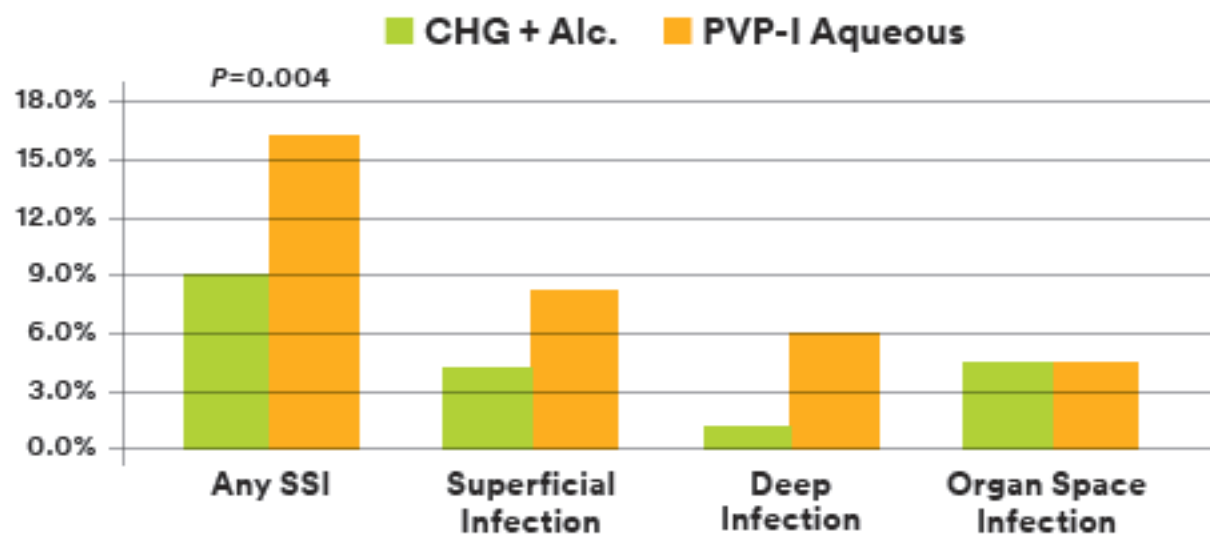
Determine whether optimization of preoperative skin antisepsis will decrease postoperative infections. Authors hypothesized that preoperative skin cleansing with chlorhexidine–alcohol is more protective against infection than is povidone–iodine aqueous solution.

Methodology

Adults undergoing clean- contaminated surgery in six hospitals were randomly assigned to preoperative skin preparation with either chlorhexidine–alcohol scrub or povidone–iodine scrub and paint. The primary outcome was any surgical-site infection within 30 days after surgery.

Findings

Preoperative skin preparation with chlorhexidine–alcohol is superior to skin preparation with povidone–iodine aqueous solution in preventing surgical-site infection after clean contaminated surgery.



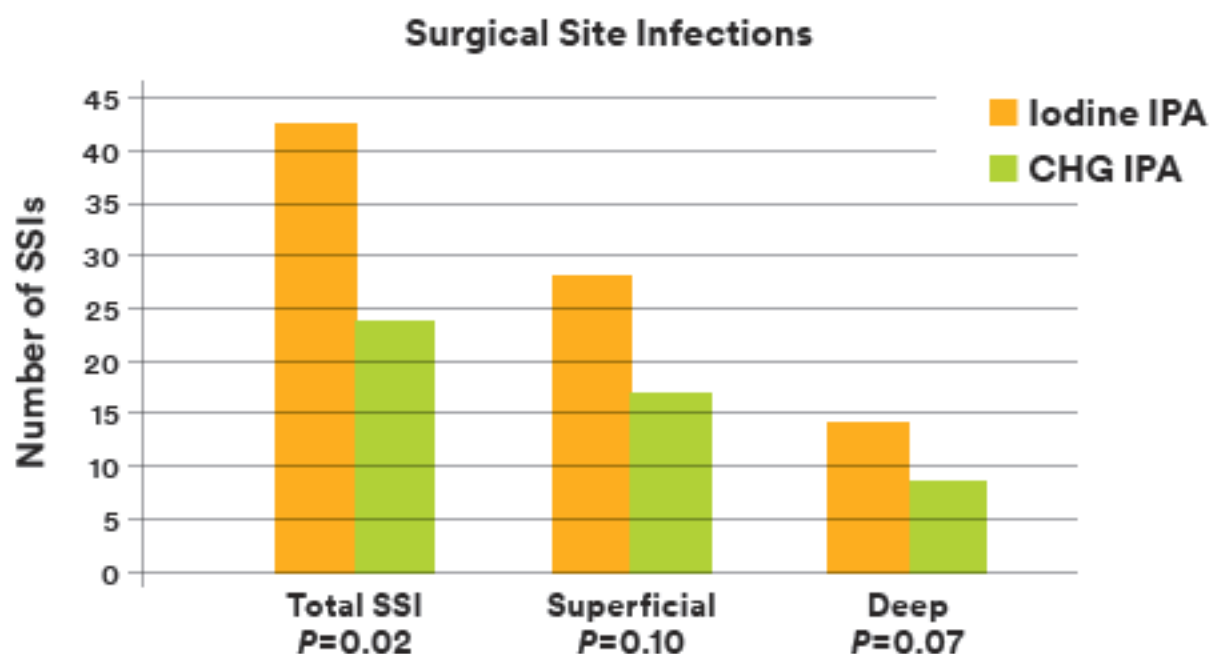
Summary 3

CHG and alcohol more effective in reducing SSI than povidone iodine and alcohol in cesarean delivery

Tuuli MG, Liu J, Stout MJ, et al. A Randomized Trial Comparing Skin Antiseptic Agents at Cesarean Delivery. *New England Journal of Medicine*. 2016; 374(7): 647–655.

Objective

Determine whether evidence supports a specific choice of antiseptic agent for use in cesarean delivery, which is the most common major surgical procedure among women in the United States.



Methodology

In this single-center, randomized, controlled trial, patients undergoing cesarean delivery were randomly assigned to skin preparation with either chlorhexidine–alcohol or iodine–alcohol. The primary outcome was superficial or deep surgical-site infection within 30 days after cesarean delivery on the basis of definitions from the Centers for Disease Control and Prevention.

Findings

The use of chlorhexidine–alcohol for preoperative skin antisepsis resulted in a significantly lower risk of surgical-site infection after cesarean delivery than did the use of iodine–alcohol. (Funded by the National Institutes of Health and Washington University School of Medicine in St. Louis.)

2% Chlorhexidine gluconate bathing reduces healthcare acquired infections

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Daily Chlorhexidine Bathing on Hospital-Acquired Infection

Michael W. Climo, M.D., Deborah S. Yokoe, M.D., M.P.H., David K. Warren, M.D., Trish M. Perl, M.D., Maureen Bolon, M.D., Loreen A. Herwaldt, M.D., Robert A. Weinstein, M.D., Kent A. Sepkowitz, M.D., John A. Jernigan, M.D., Kakotan Sanogo, M.S., and Edward S. Wong, M.D.

New Engl J Med (2013) 386: 533-542

The overall rate of hospital-acquired bloodstream infections was 4.78 cases per 1000 patient-days with chlorhexidine bathing versus 6.60 cases per 1000 patient-days with nonantimicrobial washcloths (P = 0.007), a 28% lower rate with chlorhexidine-impregnated washcloths.

Event	Measure : CHG	Measure : Control	P value
Number of central catheter associated bloodstream infections	21	43	0.004
Incidence rate (#/1000 catheter days)	1.55	3.30	

Chlorhexidine & Alcohol more effective than PVP-I Aqueous

Ayoub F, Quirke M, Conroy R, and Hill A. Chlorhexidine-alcohol versus povidone-iodine for pre-operative skin preparation: A systematic review and meta-analysis. *International Journal of Surgery Open*.2015; 1: 41-46.

Objective

To determine whether chlorhexidine–alcohol or povidone-iodine is the preferred preoperative skin preparation for reducing surgical site infections (SSIs) in clean, clean-contaminated and contaminated surgery.

Methodology

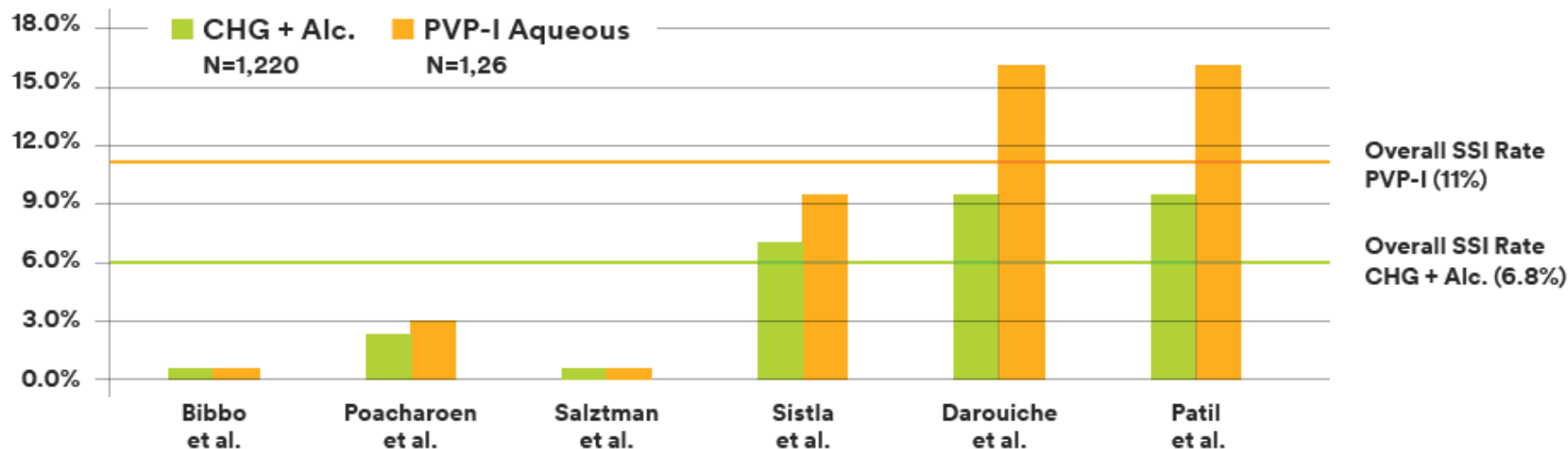
A systematic review of randomized trials was undertaken according to PRISMA guidelines to compare chlorhexidine with isopropyl alcohol against povidone-iodine in preventing surgical site infections in patients undergoing clean, clean-contaminated, and contaminated surgery. Inclusion criteria included all randomized controlled trials that reported the rate of postoperative SSI in patients who have undergone

clean, clean contaminated, and contaminated surgery to any part of the body. Exclusion criteria: non-randomized trials, studies with incomplete method selection, studies that did not compare chlorhexidine-alcohol versus povidone-iodine, studies that did not measure SSI, duplicate publications and narrative reviews. Six studies were identified for inclusion in the analysis.

Findings

Preoperative skin preps with chlorhexidine and alcohol are more effective than povidone-iodine in preventing SSI across clean and clean-contaminated surgeries.

Proportion of patients with SSI, according to study

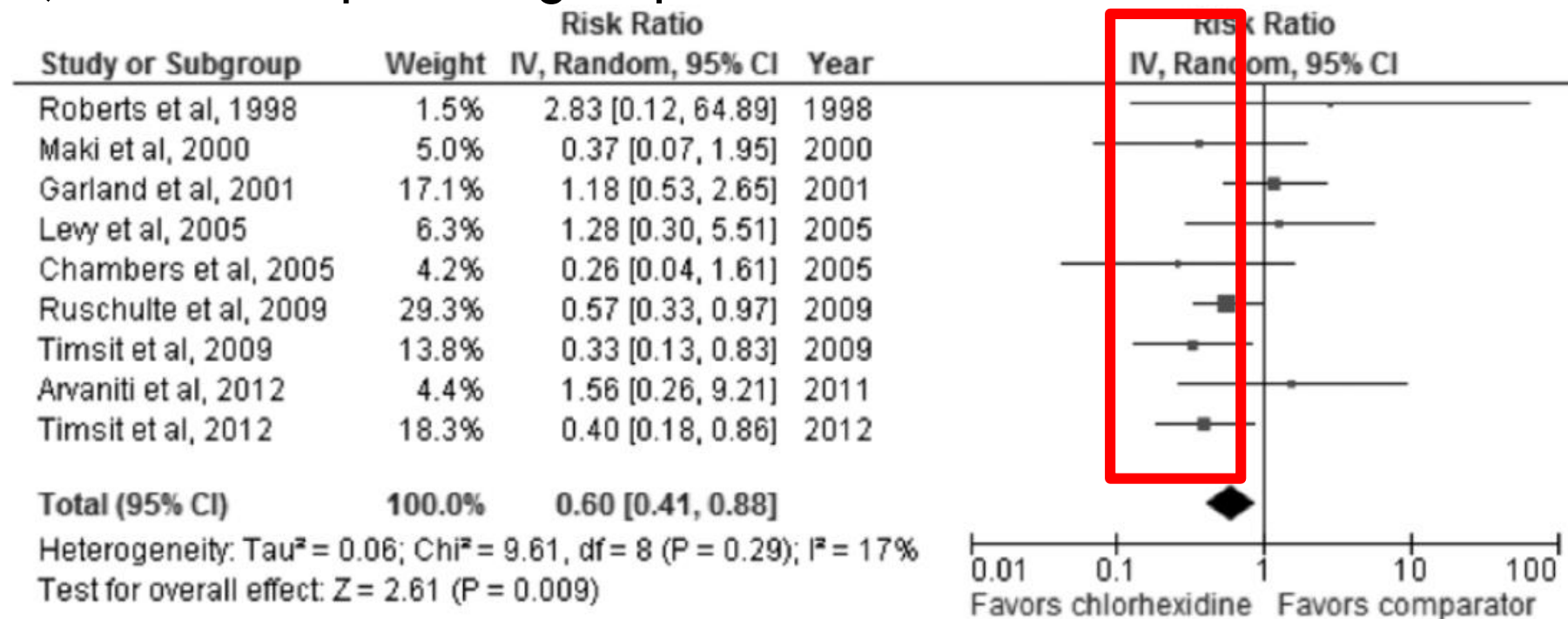


Chlorhexidine gluconate containing dressings reduce infection risk by ~50%

Safdar N, O'Horo JC, Ghufuran A., Bearden, A. Didier MA, Chateau D, Maki DG. Chlorhexidine-impregnated dressing for prevention of catheter-related bloodstream infection: A meta-analysis. *Critical Care Medicine* (2014) 42: 1703-1713.

Prevalence of CRBSI:

64 of 5,639 patients (1.1%) in the CHG group
120 of 5,608 (2.1%) in the comparator group.



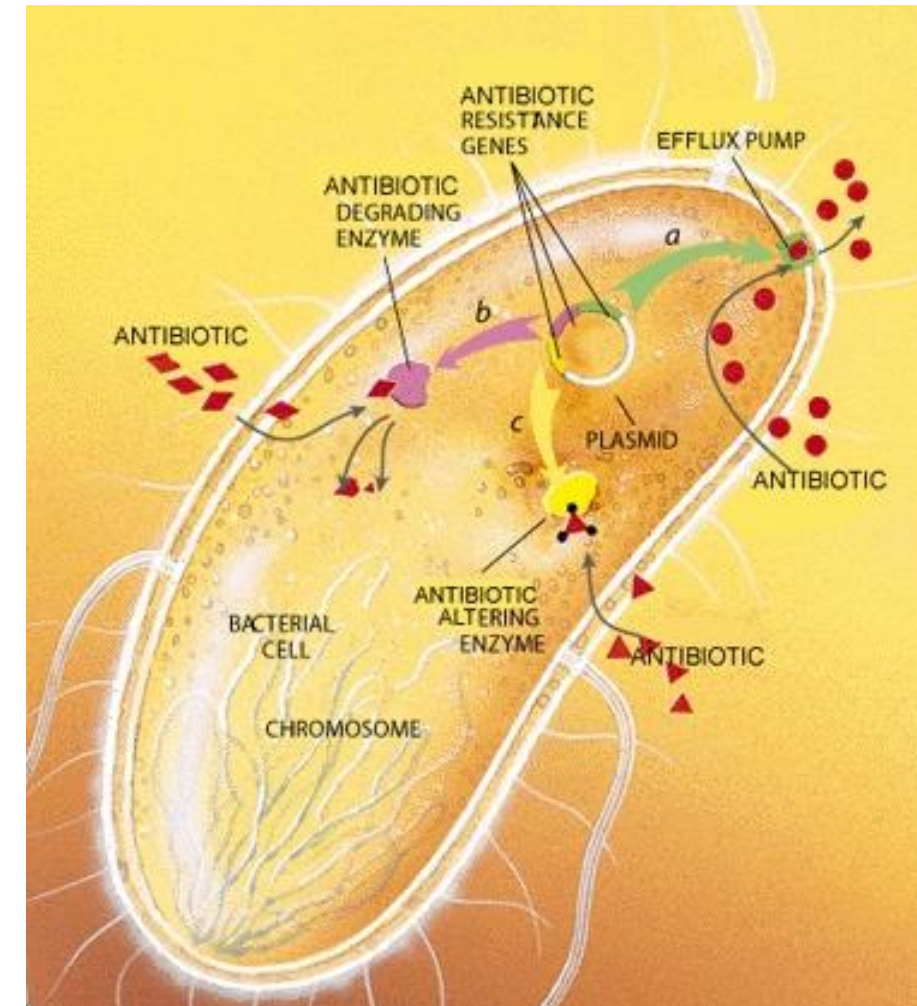
The CHG-impregnated dressing: **RR of 0.52** (95% CI, 0.43–0.64; $p < 0.001$)

Chlorhexidine can induce resistance to colistin

Mechanisms of Increased Resistance to Chlorhexidine and Cross-Resistance to Colistin following Exposure of *Klebsiella pneumoniae* Clinical Isolates to Chlorhexidine

Matthew E. Wand, Lucy J. Bock, Laura C. Bonney, J. Mark Sutton

January **2017** Volume 61 Issue 1 e01162-16
Antimicrobial Agents and Chemotherapy



Major article

Clinical evaluation of a chlorhexidine intravascular catheter gel dressing on short-term central venous catheters



Tarja J. Karpanen PhD^a, Anna L. Casey PhD^a, Tony Whitehouse FRCA^b,
Peter Nightingale PhD^c, Ira Das FRCPath^a, Thomas S.J. Elliott DSc^{d,*}

^aDepartment of Clinical Microbiology, University Hospitals Birmingham National Health Service (NHS) Foundation Trust, Birmingham, UK

^bDepartment of Anaesthetics and Intensive Care, University Hospitals Birmingham National Health Service (NHS) Foundation Trust, Birmingham, UK

^cWolfson Computer Laboratory, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

^dCorporate Division, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Key Words:

Catheter-related infection

Central venous catheter

Chlorhexidine

Sutures

Critical care patient

Intravascular dressing

Background: A major source of microbial colonization of short-term central venous catheters (CVC) is the patients' endogenous skin microorganisms located at the CVC insertion site. The aim of this study was to determine if a transparent film dressing incorporating a 2% (weight/weight) chlorhexidine gluconate (CHG) gel decreases CVC and insertion site microbial colonization compared with a nonantimicrobial dressing in adult patients in critical care.

Methods: On CVC removal, samples for microbiological investigation were taken from both the skin surrounding the CVC insertion site and also from sutures securing the CVC. The sutures and intradermal and tip sections of the CVC were also collected for microbiological investigation. Microorganisms recovered from the samples were subsequently tested for susceptibility to CHG.

Results: There was a significant reduction in the number of microorganisms recovered from the CVC insertion site, suture site, sutures, and catheter surface in the CHG dressing group (n = 136) compared with the nonantimicrobial dressing group (n = 137). There was no significant difference in susceptibility to CHG between the microorganisms isolated from the CHG and standard dressing study patients.

Conclusion: A film dressing incorporating a CHG gel pad significantly reduced the number of microorganisms at the CVC insertion and suture sites with concomitant reduced catheter colonization.

Copyright © 2016 by the Association for Professionals in Infection Control and Epidemiology, Inc.

Published by Elsevier Inc. All rights reserved.

Use of CHG gel pad does NOT lead to resistance

T.J. Karpanen et al. / American Journal of Infection Control 44 (2016) 54-60

Table 5

Median MIC of chlorhexidine gluconate (µg/mL) against microorganisms isolated from the CVC site (including skin around the CVC insertion site and suture securement sites, suture material, and catheter segments) compared with the control skin site (corresponding to the contralateral site to where the CVC was inserted)

Type of microorganism and sample site	Standard dressing group		CHG dressing group		P value*
	Median MIC (range)	(n)	Median MIC (range)	(n)	
GPC					
CVC site	4.0 (0.25-32.0)	(32)	4.0 (0.25-16.0)	(29)	.78
Control	4.0 (0.5-64.0)	(31)	4.0 (0.125-32.0)	(26)	.37
P value*	.513		.939		
GPR					
CVC site	2.0 (0.5-32.0)	(7)	4.0 (0.5-8.0)	(4)	.78
Control	0.75 (0.25-32.0)	(6)	4.0 (1.0-8.0)	(4)	.17
P value*	.198		> .999		
GN					
CVC site	4.0 (0.5-128.0)	(9)	32.0 (2.0-64.0)	(6)	.10
Control	4.0 (0.5-128.0)	(8)	32.0 (8.0-64.0)	(6)	.12
P value*	.440		.936		
Yeast					
CVC site	24.0 (16.0-32.0)	(3)	4.0 (4.0)	(1)	NA
Control	2.0 (2.0)	(1)	16.0 (16.0)	(1)	NA
P value*	NA		NA		

Gram Positive
Cocci

Gram Positive
Rods

Gram negatives

Yeast

Microbial susceptibility to chlorhexidine

There were no significant differences in microbial susceptibility to CHG between the 2 study groups (Table 5). There was also no significant differences in the median minimum inhibitory concentration of the microorganisms isolated from the CVC site (including CVC insertion site, sutures site, suture material, and catheter segments) in both patient groups compared with the corresponding contralateral control sites (Table 5).

CVC, central venous catheter; GN, gram-negative bacteria; GPC, gram-positive cocci; GPR, gram-positive rods; MIC, minimum inhibitory concentration; (n), number of patients with the microorganism tested for the MIC (when >1 same type of microorganism from the same patient was included in the MIC assay, the median MIC for each type of microorganism was used for the statistical analysis); NA, not applicable (unable to analyze because of too few results).

*Mann-Whitney test.

Chlorhexidine & “Resistance”

- Not “Resistance” as per antibiotics
- Biocide vs. Antibiotic (Think:)tissue levels)
- MIC is not MBC
 - Even with increased MIC, MBC not necessarily changed
 - No standardized definition of biocide resistance
 - No standard to assess clinical significance/correlate with therapeutic failure
- Bacterial populations are changing
 - Increase in qac A/B in Staph
 - Other genetic phenotypic changes noted
 - Correlation with “Resistance” inconsistent
- Mechanisms
 - Efflux pumps (e.g., SmvA in *K. pneumoniae*)
 - Other intracytoplasmic actions

Chlorhexidine & “Resistance” - 2

- Mechanisms (cont.)
 - Need for greater understanding of how mechanisms are changing the susceptibility of disease causing bacteria to biocides and antibiotics
 - Acquired (horizontal) and vertical (genetic) communication
 - Plasmid, chromosomal mutations, etc.
- Other agents
 - Octenidine – changes in bacterial populations and current measures reported
 - “Adaptation” = “Resistance”
- Identified Research Gaps
 - Relationship of genetics phenotypic markers to decreases in susceptibility
 - How to best utilize biocides given these considerations
 - Role of chlorhexidine in biofilm formation – if any

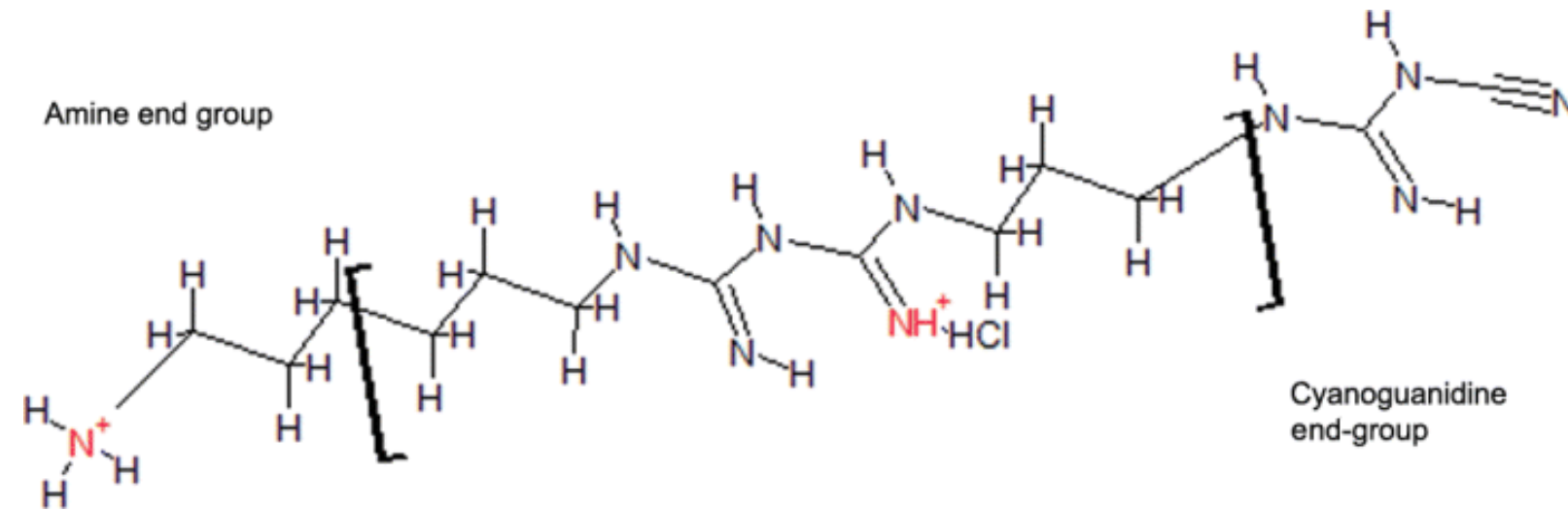
Chlorhexidine & Octenidine & PHMB

- Commonalities: cationic; variously lipophilic +/- hydrophobic
- Similar mechanisms of action: disruption of cell wall & cytoplasmic membrane
 - PHMB – chromosomal condensation
- Criticality of exposed concentrations in terms of “Resistance”
- Octenidine
 - Effective at lower concentrations
 - Sensitization, skin sensitivity and bullous reactions reported
 - Local irritation, aseptic necrosis, chronic inflammation
 - Reported cytotoxicity in wound applications
 - Has fueled Adaptation (=“Resistance”)
 - “Must be used correctly”
 - GMP issues

Chlorhexidine & Octenidine & PHMB - 2

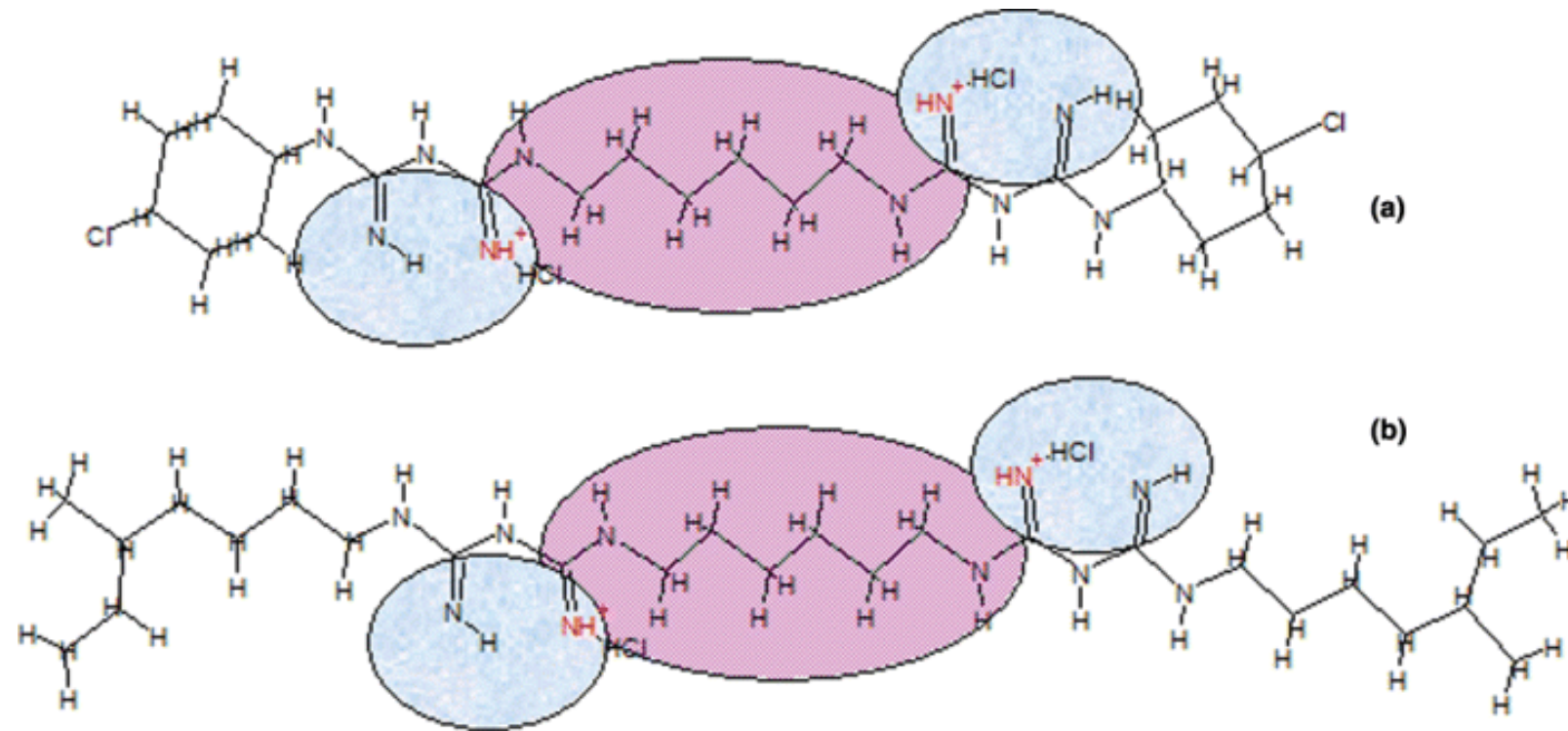
- PHMB
 - Strong antimicrobial effect
 - Chlorhexidine developed when unable to rationalize/standardize PHMB – i.e. difficulty in stabilization of formulations for clinical use
 - GMP issues
 - Anaphylaxis reported
 - Classified as low grade carcinogen in U.K.

Cationic antiseptics: diversity of action under a common epithet



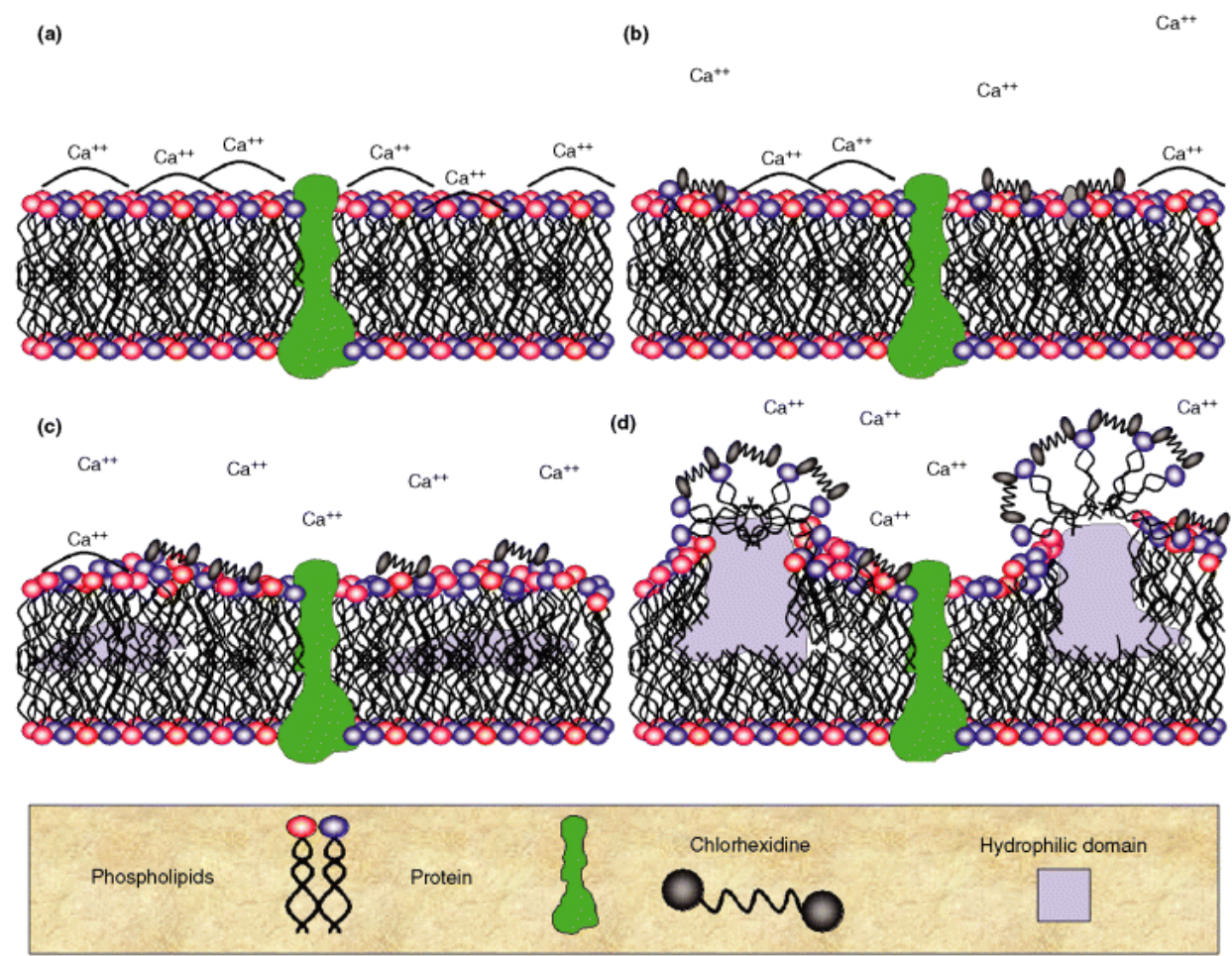
Generalize structure for polyhexamethylene biguanide (PHMB*)

*Classified as low grade carcinogen in UK



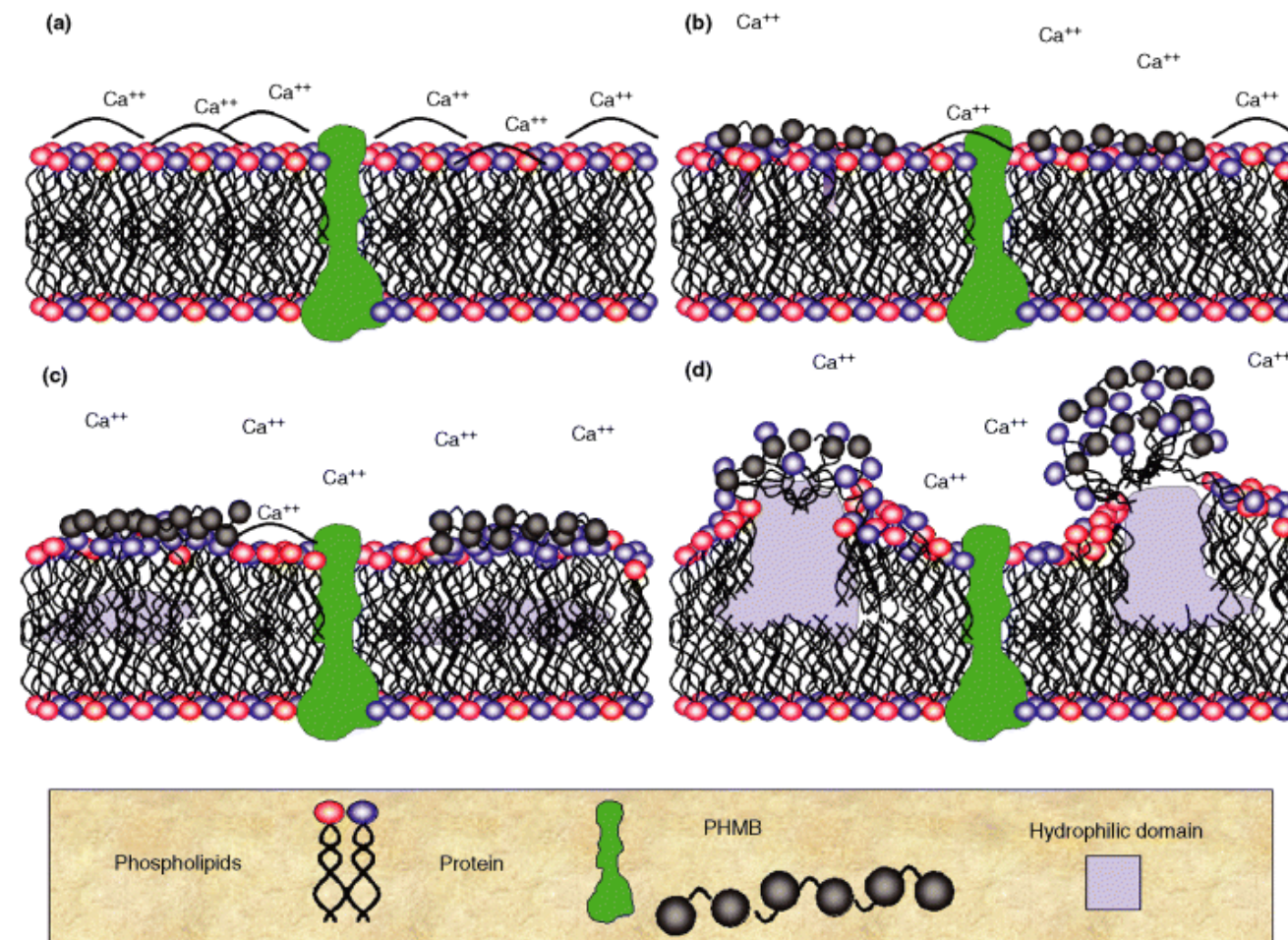
Chemical structures of bisbiguanides chlorhexidine (a) and alexidine (b)

Cationic antiseptics: diversity of action under a common epithet



Representation of interaction of chlorhexidine with bacterial cytoplasmic membrane

Cationic antiseptics: diversity of action under a common epithet



Representation of mechanism of action of PHMB with bacterial cytoplasmic membrane

Chlorhexidine Summary

- A stalwart of the modern prevention, control and management of infection
- “Resistance” to chlorhexidine is not the same as for antibiotics
 - Laboratory measures vs. clinical significance
- Potentially competitive biocides have similar mechanisms of action, sensitization, skin reactions, and impact on bacterial populations
- Gaps in knowledge exist

Chlorhexidine Summary - 2

- Exposure to non-lethal concentrations of biocides (all) may contribute to development of decreased susceptibility
 - Concentration and Contact Time critical
- “Better stewardship, regulation, and restriction of biocidal active ingredients in non-health care settings would limit exposure to antiseptics and may decrease selection of bacteria with reduced susceptibility to these agents.” (Harbath et al 2014)

3M Science. Applied to Life.™

3M Technology Advancing Every Company

3M Products Enhancing Every Home

3M Innovation Improving Every Life

Thank you!