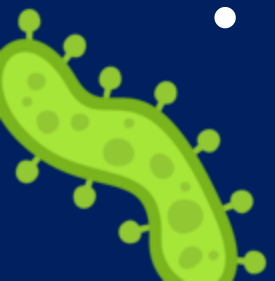
UWTASP tele-antimicrobial stewardship program | echo

July 16th, 2024

- Announcements:
  - Blood culture bottle shortage
  - CSiM annual evaluation
- John Lynch: *Bacterial Decolonization*
- Facility Question: Island Hospital

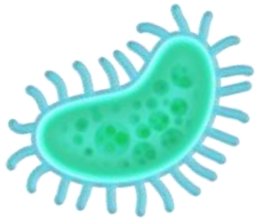


Project ECHO

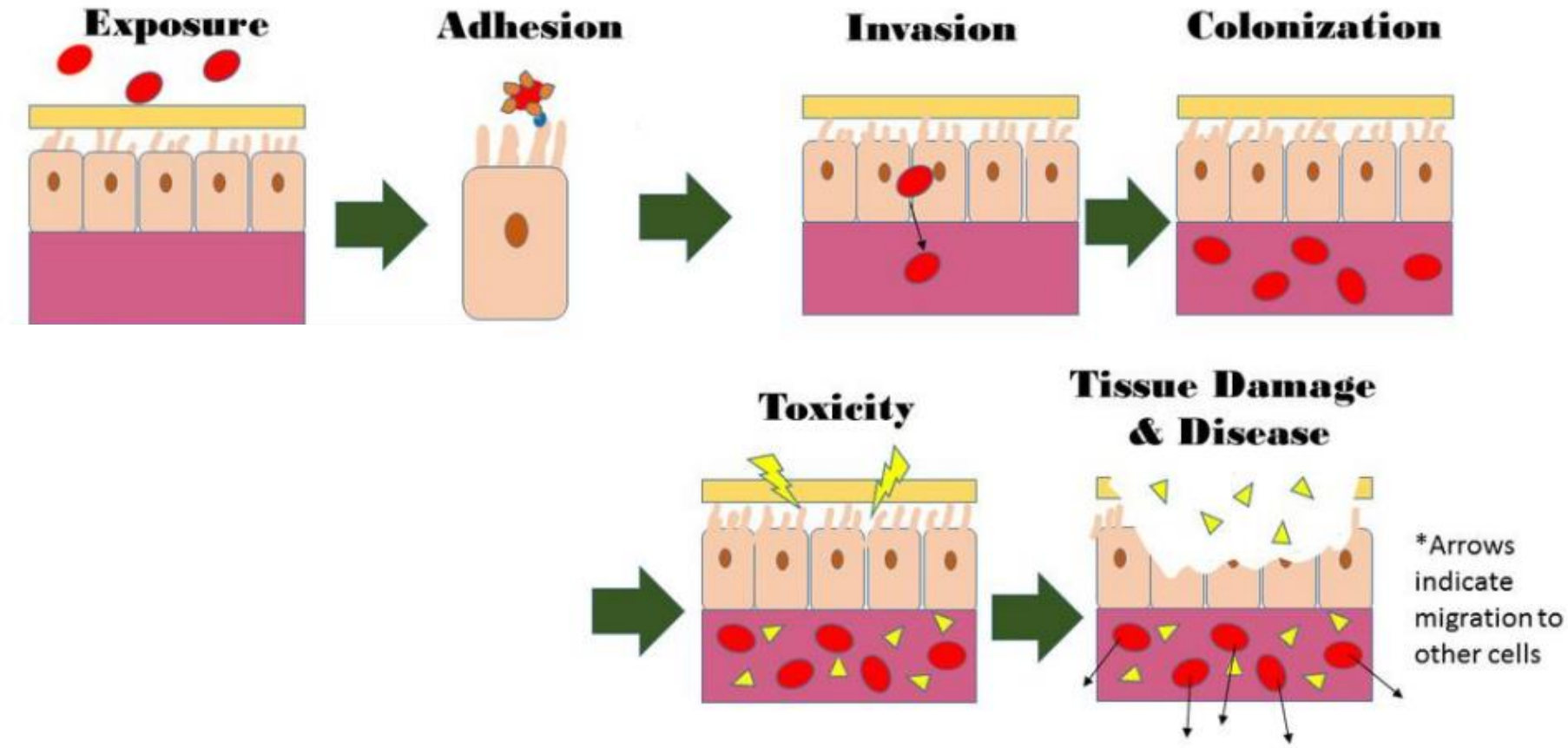
Some Terms

Table. Key definitions used to describe decolonization and pathogen reduction to prevent antimicrobial resistance and healthcare-associated infections

Term	Definition
Colonization	Harboring living, actively dividing, and stable bacterial cell populations that do not cause symptoms of disease or infection.
Decolonization	Removing or reducing the burden of a pathogen, either temporarily or permanently.
Pathogen reduction	Substantial reduction of colonizing pathogen load, inclusive of, but not solely related to, decolonization, and more focused over a short period of increased infection or transmission risk.
Cross-transmission	Transmission of bacterial infection and antimicrobial resistance.
Opportunistic pathogen	Disease-causing microbes that can invade the body and cause disease under conditions of weakened immune defense.
Pathobiont	Opportunistic pathogenic bacteria that can emerge from the human microbiota to cause disease when its microbial ecology is disturbed.
Pathotype	A group of bacteria within the same species that can attack a host in different ways.



Mangalea MR, Halpin AL, Haile M, Elkins CA, McDonald LC. Decolonization and Pathogen Reduction Approaches to Prevent Antimicrobial Resistance and Healthcare-Associated Infections. Emerg Infect Dis. 2024 Jun;30(6):1069-1076. doi: 10.3201/eid3006.231338. PMID: 38781679; PMCID: PMC11138981.



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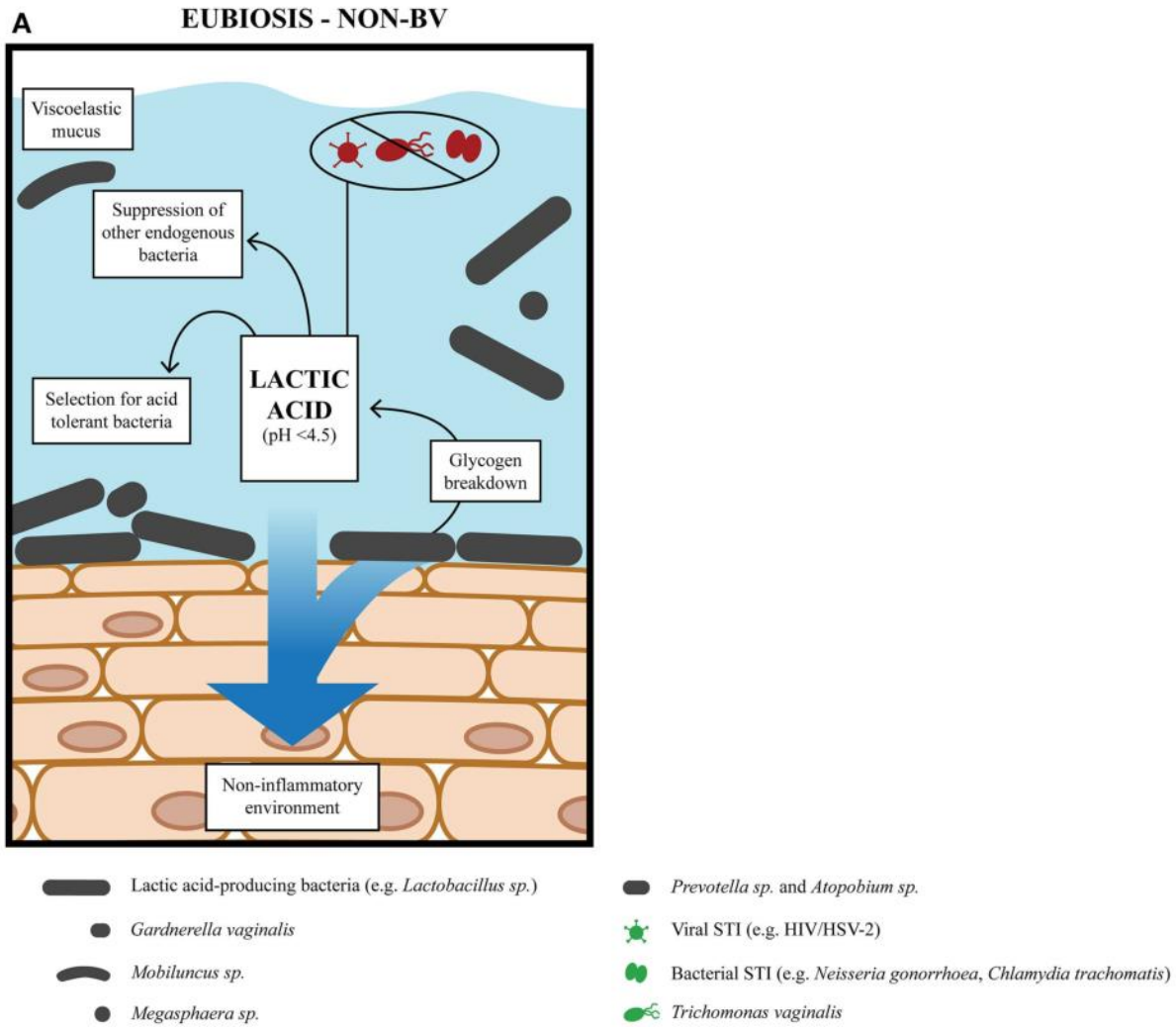
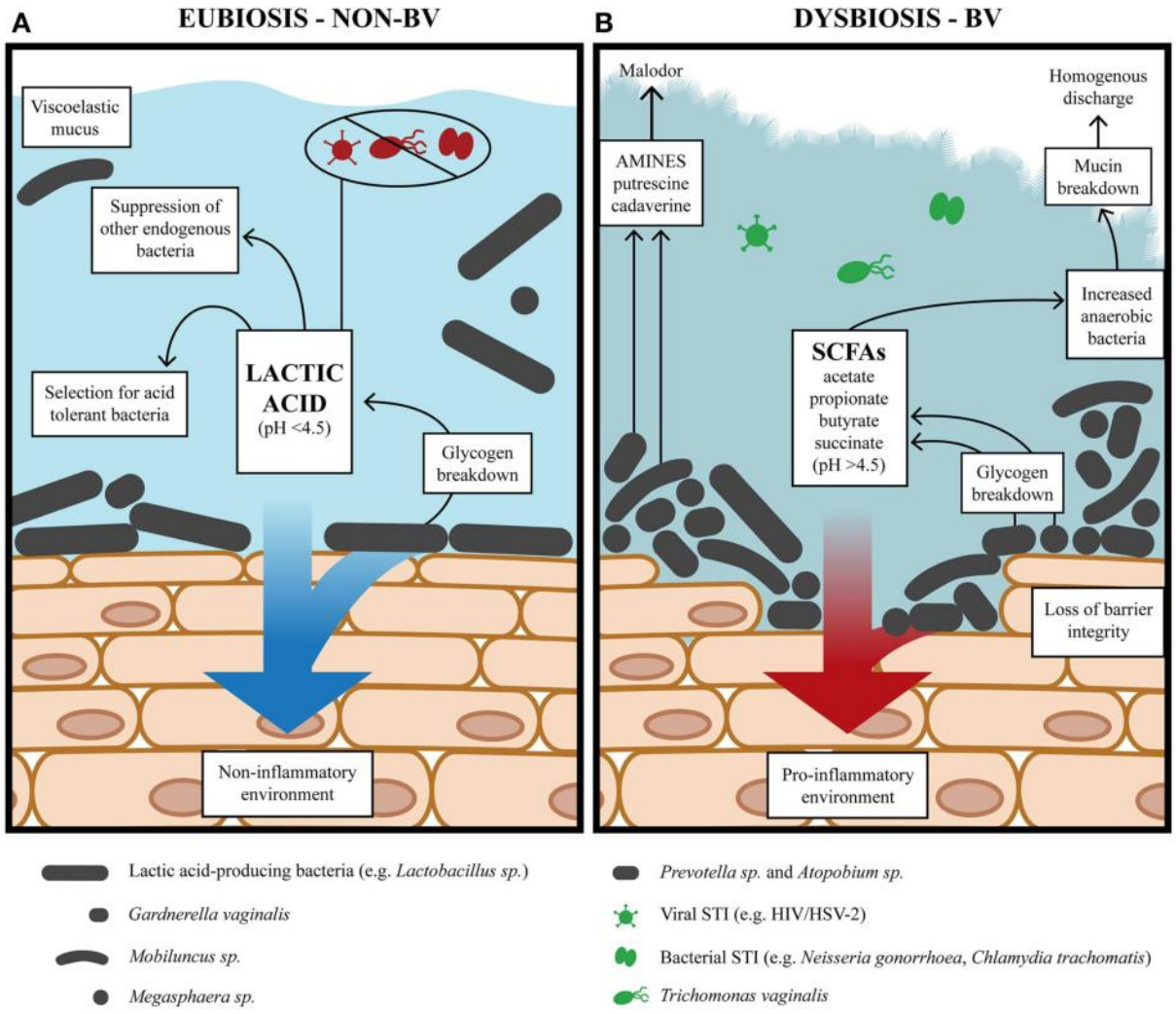


Aldunate, Front Physiol, 2015



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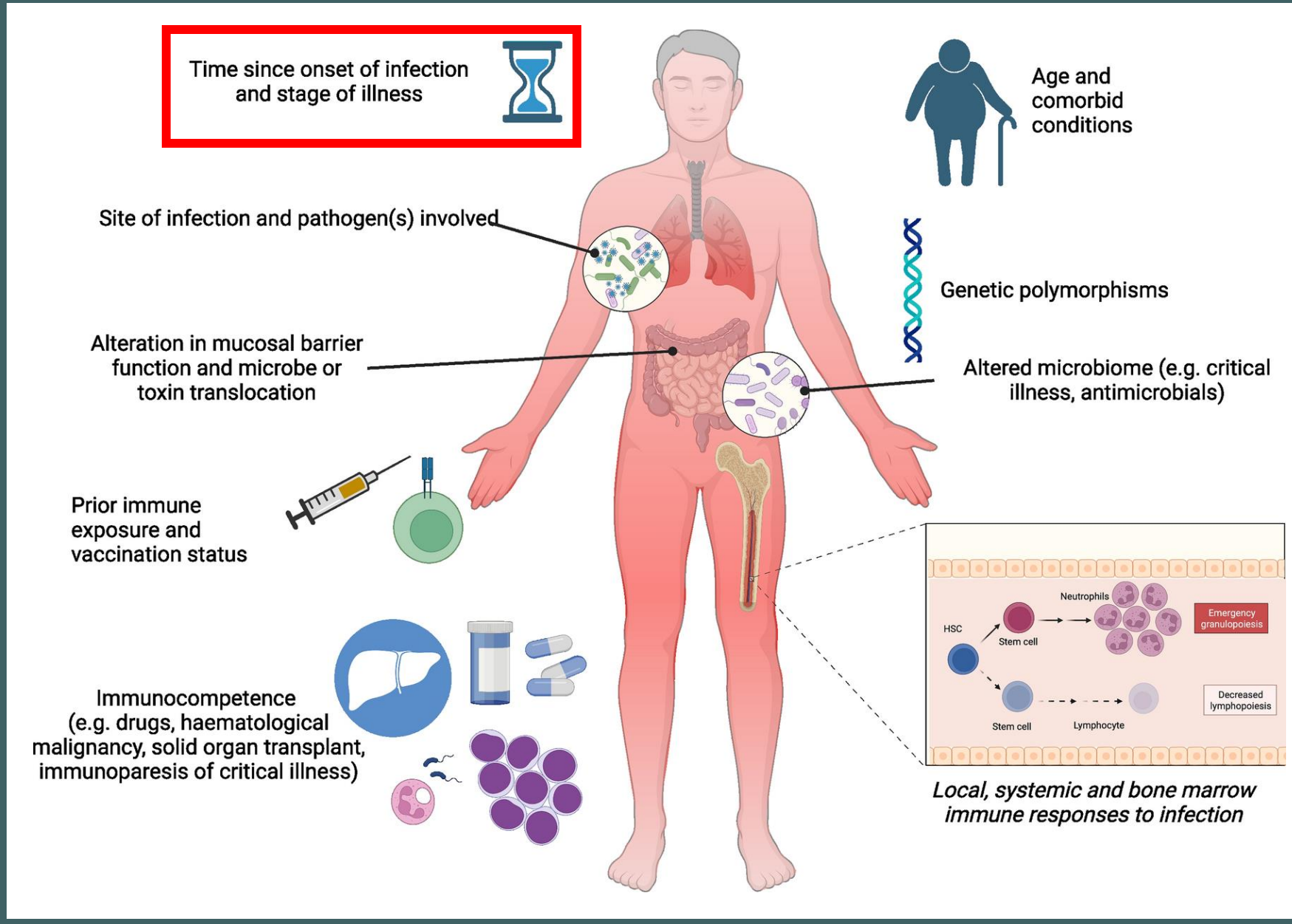


Local, systemic and bone marrow immune responses to infection

Table 2 Potential influence of a novel host-response marker

Host response / Microbiology	Sensitive and specific novel host marker(s) of infection positive	Novel host marker negative but clinical/ radiological suspicion of infection	Low clinical suspicion and no markers elevated
Obligate pathogen at high growth	**Infection** *Organism confirmed* Targeted antimicrobials	**Possible infection** High risk* - targeted antimicrobials Low risk - watch and wait	**Colonisation** No antimicrobial indicated (unless eradication considered)
Obligate pathogen at sub-threshold growth *OR* Non-pathogenic organism	**Infection** *Organism uncertain* Broad antimicrobials	**Colonisation** Watch and wait	**Colonisation** No antimicrobial indicated
Negative microbiology	**Infection** *Organism uncertain* Broad antimicrobials	**Unlikely infection or colonisation** Watch and wait High threshold antimicrobials	**No evidence** of infection or colonisation

INCREASED INFECTION RATES IN HEAVY NASAL CARRIERS OF COAGULASE-POSITIVE STAPHYLOCOCCI

ARTHUR WHITE[1]

Department of Medicine, University of Louisville, Louisville, Kentucky, and Department of Medicine, Medical College of Georgia, Augusta, Georgia

Antimicrob Agents Chemother, 30 (1963), pp. 667-670

TABLE 1. *Postoperative infection rates in nasal carriers of different numbers of coagulase-positive staphylococci**

No. of nasal staphylococci	No. of patients	Infection rate
		%
0	345	8
10^1 to 10^3	14	7
10^3 to 10^5	28	11
10^5 to 10^6	26	19
$>10^6$	38	29

*Total number of patients was 451; mean infection rate was 11.

ORIGINAL ARTICLE

Nasal Carriage as a Source of *Staphylococcus aureus* Bacteremia

The NEW ENGLAND JOURNAL of MEDICINE

Authors: Christof von Eiff, M.D., Karsten Becker, M.D., Konstanze Machka, M.Sc., Holger Stammer, M.Sc., and Georg Peters, M.D.* Author Info & Affiliations

Published January 4, 2001 | N Engl J Med 2001;344:11-16 | DOI: 10.1056/NEJM200101043440102 | VOL. 344 NO. 1

METHODS

In a multicenter study, swabs for culture were obtained from the anterior nares of 219 patients with S. *aureus* bacteremia. A total of 723 isolates were collected and genotyped. In a second study, 1640 S. *aureus* isolates from nasal swabs from 1278 patients were collected over a period of five years and then compared with isolates from the blood of patients who subsequently had S. *aureus* bacteremia.

RESULTS

In the multicenter study of S. *aureus* bacteremia, the blood isolates were identical to those from the anterior nares in 180 of 219 patients (82.2 percent). In the second study, 14 of 1278 patients who had nasal colonization with S. *aureus* subsequently had S. *aureus* bacteremia. In 12 of these 14 patients (86 percent), the isolates obtained from the nares were clonally identical to the isolates obtained from blood 1 day to 14 months later.

CONCLUSIONS

A substantial proportion of cases of S. *aureus* bacteremia appear to be of endogenous origin since they originate from colonies in the nasal mucosa. These results provide support for strategies to prevent systemic S. *aureus* infections by eliminating nasal carriage of S. *aureus*.

Research Letters

Risk and outcome of nosocomial *Staphylococcus aureus* bacteraemia in nasal carriers versus non-carriers

The Lancet
Volume 364, Issue 9435, 21–27 August 2004, Pages 703-705

Heiman FL Wertheim MD [a], Margreet C Vos MD [a], Alewijn Ott MD [a], Prof Alex van Belkum PhD [a], Prof Andreas Voss MD [b], Jan AJW Kluytmans MD [c], Peter HJ van Keulen MD [c], Prof Christina MJE Vandenbroucke-Grauls MD [d], Marlene HM Meester ICP [d], Henri A Verbrugh MD [a]

Table 1. Relative risk of nosocomial S *aureus* bacteraemia by nasal carrier status

	Nosocomial S aureus bacteraemia		
	yes	No	Relative risk (95%CI)
S aureus carrier	40* (1·2%)	3380 (98·8%)	3·0 (2·0–4·7)
Non-carrier	41 (0·4%)	10547 (99·6%)	1·0

*

Nasal and subsequent bacteraemic S aureus isolates were clonally related in 80%of patients, measured by pulsed-.eld gel electrophoresis.

CLINICAL MICROBIOLOGY REVIEWS, July 1997, p. 505–520
0893-8512/97/$04.00+0

Nasal Carriage of *Staphylococcus aureus*: Epidemiology, Underlying Mechanisms, and Associated Risks

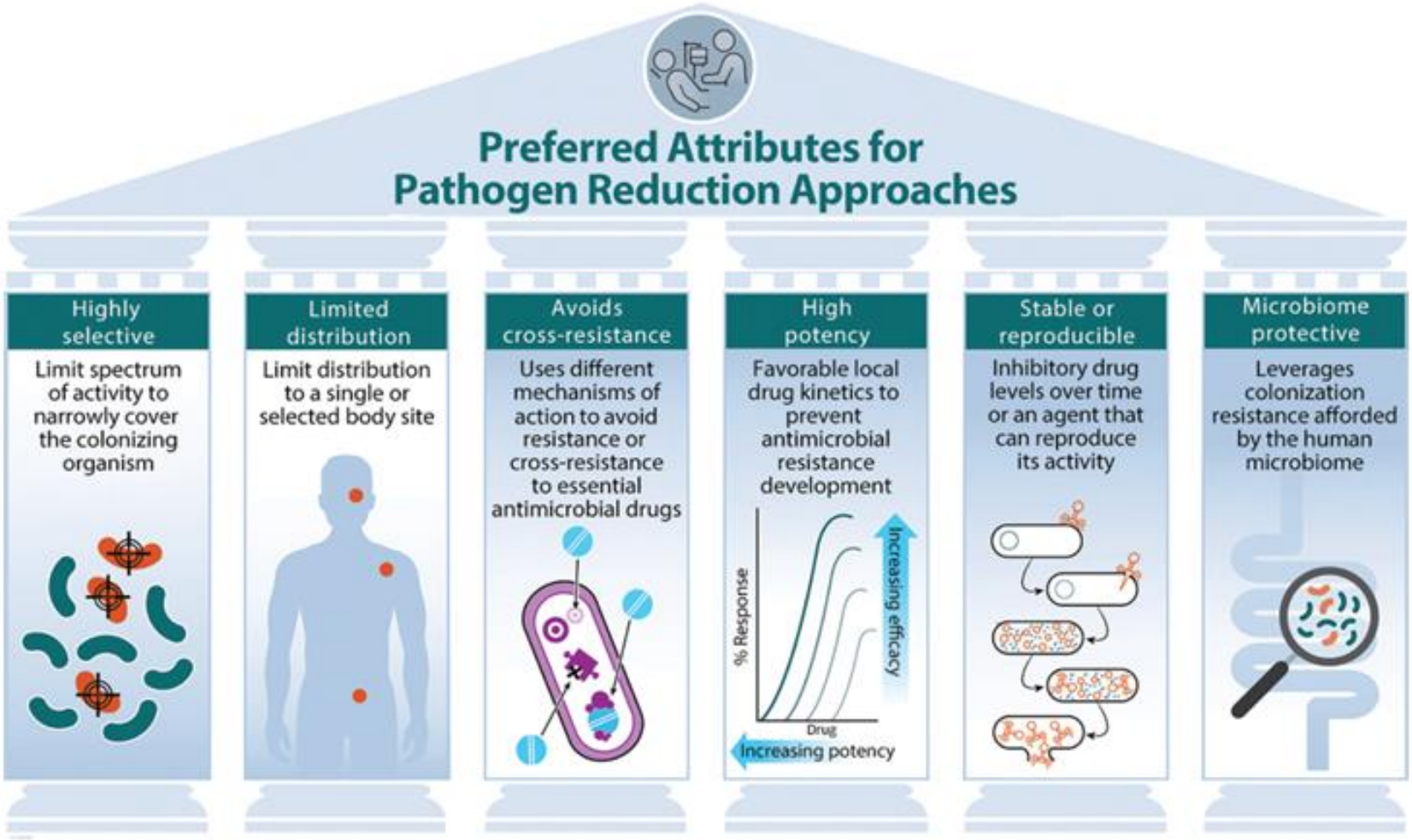
JAN KLUYTMANS,[1]* ALEX VAN BELKUM,[2] AND HENRI VERBRUGH[2]

Ignatius Hospital Breda, Breda,[1] and University Hospital Rotterdam, Rotterdam,[2] The Netherlands

TABLE 3. Nasal carriage of *S. aureus* as a risk factor in surgical patients

Reference		No. of patients	*S. aureus* carriage-rate (%)	No. of infections/no. of patients		Relative risk	95% confidence interval	% of identical types in carriers
No.	Yr			Carriers	Noncarriers			
32	1959	348	30	15/104	5/244	7.0	2.6–18.9	100
206	1959	125	34	16/43	9/82	3.4	1.6–7.0	91.7
210	1959	1,319	52	47/687	13/632	3.3	1.8–6.1	59.6
153	1960	3,056	27	73/821	158/2,235	1.3	1.0–1.6	42.9
72	1961	413	46	15/190	4/223	4.4	1.5–13.0	ND[a]
110	1961	187	40	12/74	11/113	1.7	0.8–3.6	ND
11	1963	520	85	24/442	6/78	0.7	0.3–1.7	58
		2,480	55	30/1,371	25/1,119	1.0	0.6–1.7	30
73	1963	100	68	6/68	2/32	1.4	0.3–6.6	50
78	1963	330	17	6/57	12/273	2.4	0.9–6.1	33.3
85	1963	430	42	57/181	15/249	5.2	3.1–18.9	94.7
207	1963	451	23	20/106	28/345	2.3	1.4–4.0	ND
			9 L[b]	4/42	28/345	1.2	0.4–3.2	
			6 M	5/26	28/345	2.4	1.0–5.6	
			8	11/38	28/345	3.6	1.9–6.6	
104	1967	146	46	25/67	16/79	1.8	1.1–3.2	ND
28	1969	269	36	16/96	16/173	1.8	0.9–3.4	100
			11 L	2/29	16/173	0.7	0.2–3.1	
			12 M	3/31	16/173	1.0	0.3–3.4	
			13 H	11/36	16/173	3.3	1.7–6.5	
27	1970	2,260	48	104/1,093	28/1,167	4.0	2.6–6.0	ND
			15 H	65/336	28/1,167	8.1	5.3–12.3	
124	1993	306	15	8/47	4/259	9.4	2.9–30.2	91
89	1995	1,980	13	21/264	19/1,716	7.2	3.9–13.2	100
162	1996	1,049	24	15/248	8/801	6.1	2.6–14.1	87
92	1996	255	27	6/69	2/186	8.1	1.7–39.1	ND
			9 L	0/23	2/186	NA[c]		
			18 H	6/46	2/186	12.1	2.5–65.4	

Pathogen Reduction Approaches



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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 13, 2013 VOL. 368 NO. 24

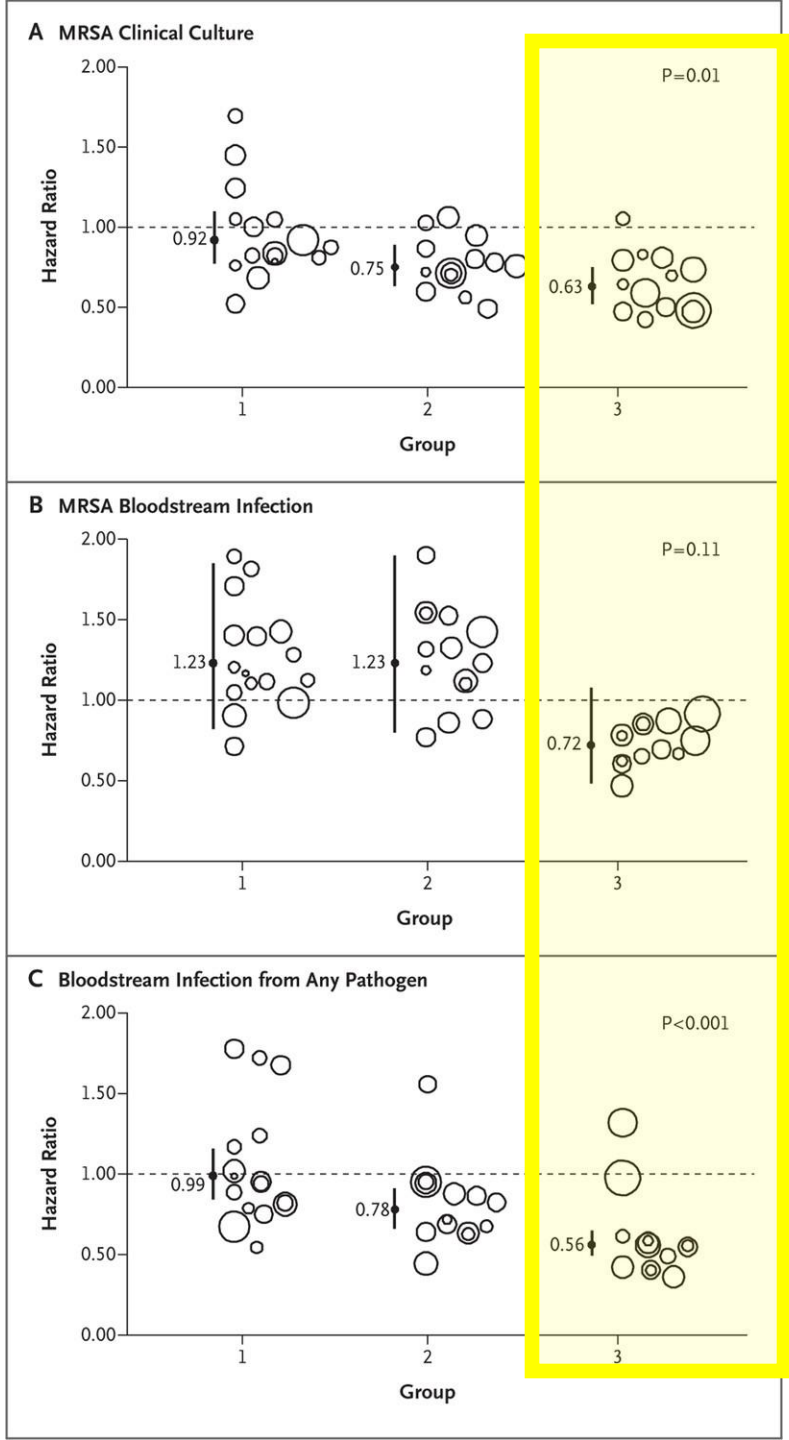
Targeted versus Universal Decolonization to Prevent ICU Infection

Susan S. Huang, M.D., M.P.H., Edward Septimus, M.D., Ken Kleinman, Sc.D., Julia Moody, M.S., Jason Hickok, M.B.A., R.N., Taliser R. Avery, M.S., Julie Lankiewicz, M.P.H., Adrijana Gombosev, B.S., Leah Terpstra, B.A., Fallon Hartford, M.S., Mary K. Hayden, M.D., John A. Jernigan, M.D., Robert A. Weinstein, M.D., Victoria J. Fraser, M.D., Katherine Haffenreffer, B.S., Eric Cui, B.S., Rebecca E. Kaganov, B.A., Karen Lolans, B.S., Jonathan B. Perlin, M.D., Ph.D., and Richard Platt, M.D., for the CDC Prevention Epicenters Program and the AHRQ DECIDE Network and Healthcare-Associated Infections Program*

The three strategy groups were defined as follows. In group 1 (screening and isolation), bilateral screening of the nares for MRSA was performed on ICU admission, and contact precautions were implemented for patients with a history of MRSA colonization or infection and for those who had any positive MRSA test. This was the previous standard of care in all hospitals. The MRSA screening program for patients in the ICU, who are a group at high risk for infection, began in 2007 at HCA hospitals.[16] More than 90% of the patients admitted to the ICU underwent screening, and contact precautions were implemented for carriers of MRSA and other multidrug-resistant pathogens.

In group 2 (targeted decolonization), MRSA screening and contact precautions were similar to those in group 1. Patients known to have MRSA colonization or infection underwent a 5-day decolonization regimen consisting of twice-daily intranasal mupirocin and daily bathing with chlorhexidine-impregnated cloths.

In group 3 (universal decolonization), there was no screening for MRSA on admission to the ICU. Contact precautions were similar to those in group 1. All patients received twice-daily intranasal mupirocin for 5 days, plus daily bathing with chlorhexidine-impregnated cloths for the entire ICU stay.



JAMA | Original Investigation

Reducing Hospitalizations and Multidrug-Resistant Organisms via Regional Decolonization in Hospitals and Nursing Homes

Gabrielle M. Gussin, MS; James A. McKinnell, MD; Raveena D. Singh, MA; Loren G. Miller, MD, MPH; Ken Kleinman, ScD; Raheeb Saavedra, AS; Thomas Tjoa, MPH, MS; Shruti K. Gohil, MD, MPH; Tabitha D. Catuna, MPH; Lauren T. Heim, MPH; Justin Chang, MD; Marlene Estevez, BA; Jiayi He, MS; Kathleen O'Donnell, MPH; Matthew Zahn, MD; Eunjung Lee, MD, PhD; Chase Berman, BS; Jenny Nguyen, BA; Shalini Agrawal, BS; Isabel Ashbaugh, MSc; Christine Nedelcu, BS; Philip A. Robinson, MD; Steven Tam, MD; Steven Park, MD, PhD; Kaye D. Evans, BA, MT; Julie A. Shimabukuro, BS; Bruce Y. Lee, MD, MBA; Emily Fonda, MD, MMM; John A. Jernigan, MD, MS; Rachel B. Slayton, PhD, MPH; Nimalie D. Stone, MD, MS; Lynn Janssen, MS; Robert A. Weinstein, MD; Mary K. Hayden, MD; Michael Y. Lin, MD, MPH; Ellena M. Peterson, PhD; Cassiana E. Bittencourt, MD; Susan S. Huang, MD, MPH; for the CDC Safety and Healthcare Epidemiology Prevention Research Development (SHEPheRD) Program

May 14, 2024 Volume 331, Number 18

The intervention involved universal decolonization in NHs and LTACHs using 2% leave-on chlorhexidine-impregnated cloths for bed bathing and 4% rinse-off chlorhexidine liquid for showering on admission and routinely thereafter. Additionally, all residents (from NHs) or patients (from LTACHs) received twice-daily nasal iodophor (10% povidone-iodine) for 5 days on admission and then Monday through Friday, every other week. Hospitals received refresher training for ongoing universal chlorhexidine bathing in intensive care units (ICUs) and adopted targeted decolonization for all non-ICU patients in contact precautions (CP). Targeted decolonization involved 5 days of chlorhexidine baths and twice daily nasal iodophor. Both participating and nonparticipating facilities maintained their usual bathing frequency. In both groups, residents in NHs generally received a bath or shower 3 times per week, while patients in LTACHs or hospitals were generally offered a daily bath or shower.

Participating facilities were provided coaching calls, in-person training, and a toolkit of protocols, educational materials, checklists, and assessment forms[17] (eAppendix 1 in Supplement 1). Adherence was assessed twice monthly using treatment administration records, bathing logs, and discussions with staff, patients, and residents. Project staff reviewed adherence data with nursing leadership, and refresher training was provided as needed. Participating facilities were given a standardized form for adverse events and encouraged to report events.

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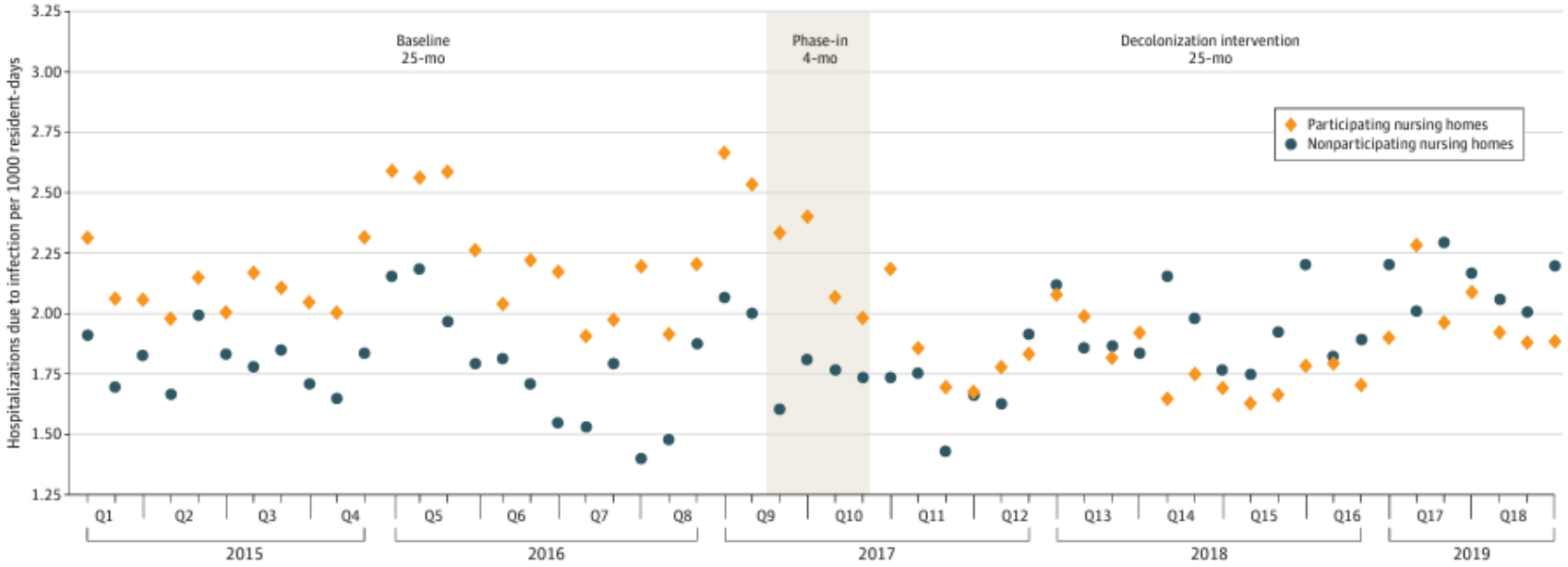
May 14, 2024 Volume 331, Number 18

Figure 5. Monthly Infection-Related Hospitalization Rates Among Nursing Homes Residents in Participating (Decolonization) vs Nonparticipating Nursing Homes



	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Q15	Q16	Q17	Q18
Participating nursing homes																		
No. events	354	342	349	387	406	349	334	379	394	347	293	320	309	287	281	300	345	322
At-risk person-years	424	436	432	438	429	425	432	438	426	437	440	442	426	442	434	436	430	448
Nonparticipating nursing homes																		
No. events	717	739	720	768	787	680	638	730	704	698	640	746	711	774	766	773	822	807
At-risk person-years	1020	1049	1052	1061	1036	1047	1057	1048	1020	1042	1033	1027	999	1026	1017	1014	990	1006

October 10, 2023

JAMA | Original Investigation

Nasal Iodophor Antiseptic vs Nasal Mupirocin Antibiotic in the Setting of Chlorhexidine Bathing to Prevent Infections in Adult ICUs

A Randomized Clinical Trial

Susan S. Huang, MD, MPH[1]; Edward J. Septimus, MD[2,3]; Ken Kleinman, ScD[4]; et al

IMPORTANCE Universal nasal mupirocin plus chlorhexidine gluconate (CHG) bathing in intensive care units (ICUs) prevents methicillin-resistant *Staphylococcus aureus* (MRSA) infections and all-cause bloodstream infections. Antibiotic resistance to mupirocin has raised questions about whether an antiseptic could be advantageous for ICU decolonization.

OBJECTIVE To compare the effectiveness of iodophor vs mupirocin for universal ICU nasal decolonization in combination with CHG bathing.

DESIGN, SETTING, AND PARTICIPANTS Two-group noninferiority, pragmatic, cluster-randomized trial conducted in US community hospitals, all of which used mupirocin-CHG for universal decolonization in ICUs at baseline. Adult ICU patients in 137 randomized hospitals during baseline (May 1, 2015-April 30, 2017) and intervention (November 1, 2017-April 30, 2019) were included.

INTERVENTION Universal decolonization involving switching to iodophor-CHG (intervention) or continuing mupirocin-CHG (baseline).

October 10, 2023

JAMA | Original Investigation

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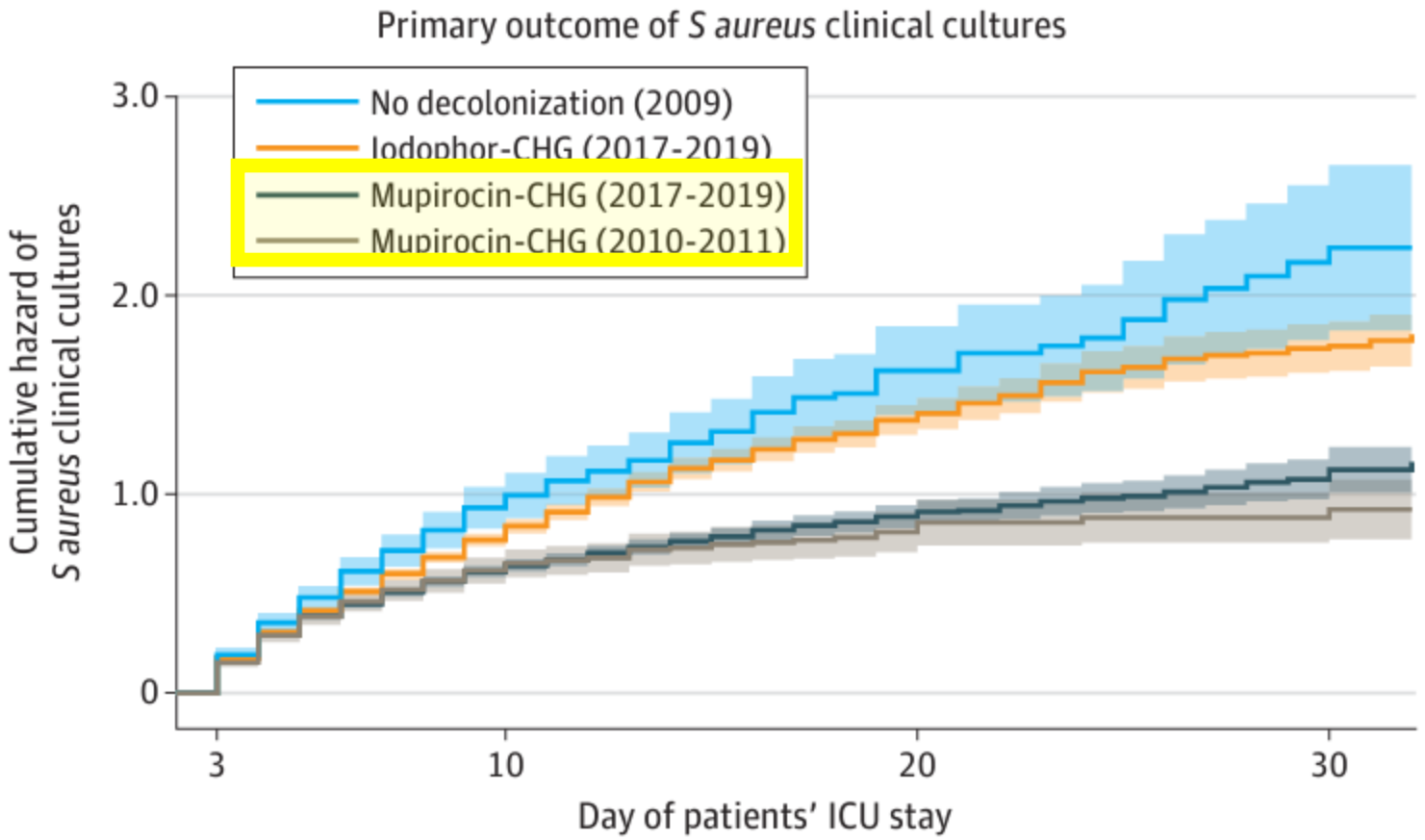
A Randomized Clinical Trial

Susan S. Huang, MD, MPH[1]; Edward J. Septimus, MD[2,3]; Ken Kleinman, ScD[4]; et al

CONCLUSIONS AND RELEVANCE Nasal iodophor antiseptic did not meet criteria to be considered noninferior to nasal mupirocin antibiotic for the outcome of *S aureus* clinical cultures in adult ICU patients in the context of daily CHG bathing. In addition, the results were consistent with nasal iodophor being inferior to nasal mupirocin.



Major Article

Nasal decolonization: What antimicrobials and antiseptics are most effective before surgery and in the ICU

Matthew Smith MD, MPH [a b], Loreen Herwaldt MD [a c]

American Journal of Infection Control
Volume 51, Issue 11, Supplement, November 2023, Pages A64-A71

Highlights

- Intranasal mupirocin is effective pre-operatively for orthopedic and cardiac procedures.
- Mupirocin is effective for nasal decolonization in the intensive care unit setting.
- Intranasal povidone-iodine is most effective for pre-operative nasal decolonization.
- Other decolonization agents lack sufficient data for widespread use.
- Additional research on decolonizing agents is still needed.

Major Article

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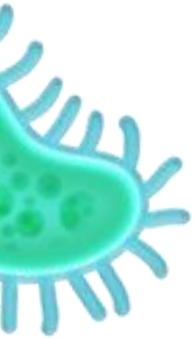
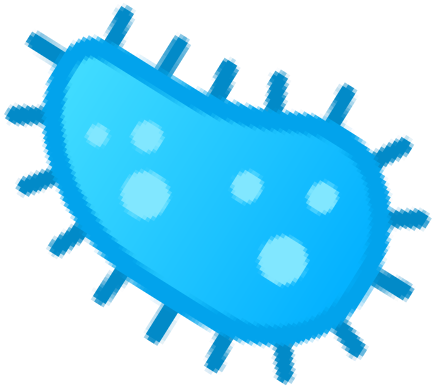
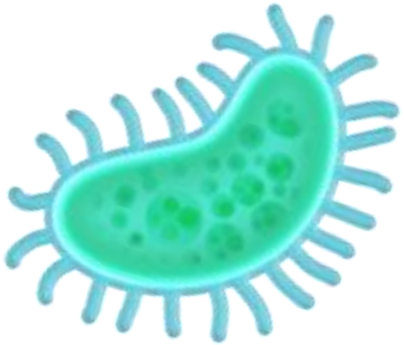


Table 1. Comparison of mupirocin and povidone-iodine

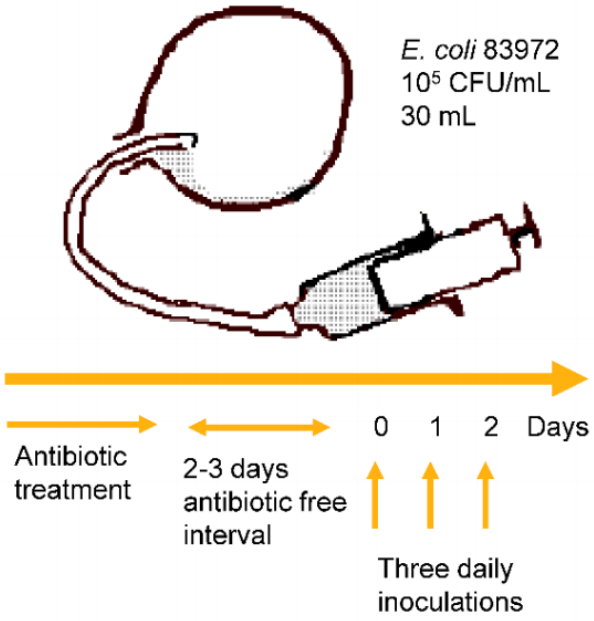
	Mupirocin	Povidone-iodine (PI)
Duration of efficacy	Short/medium-term decolonization (days to months)	Transient suppression of bacteria (hours)
Best studied pre-operative use	2% ointment applied to nares 2x daily for five days before orthopedic surgery (best data) and cardiac surgery (modest data)	1-2 applications of 10% PI solution to nares 1-3 hours before orthopedic surgery
Best studied ICU use	2% ointment applied to nares 2x daily as part of targeted or universal decolonization strategy	Insufficient data supporting use in ICU setting
Pros	Abundant data demonstrating efficacy	Can be given immediately prior to surgery, improving adherence Slightly better tolerated than mupirocin
Cons	Multi-step protocols lead to low adherence Cannot be completed before urgent or emergent procedures Widespread use has been associated with resistance	Effect is transient Less effective in the ICU* setting than mupirocin Published studies in surgical populations are all single-center



Thank you!

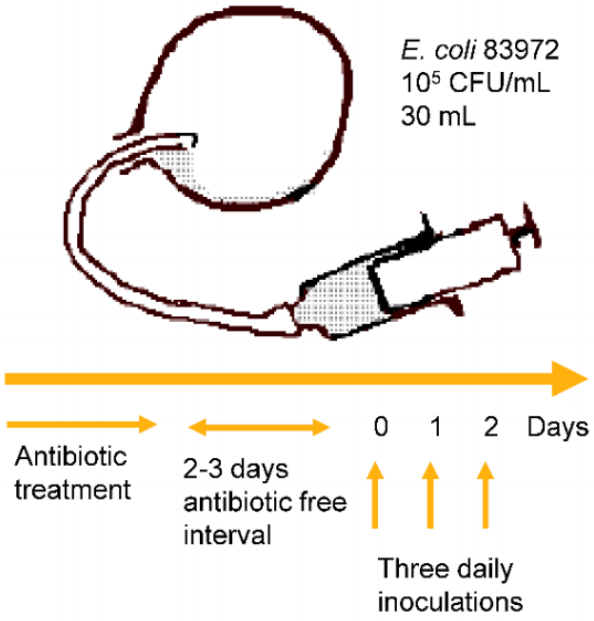


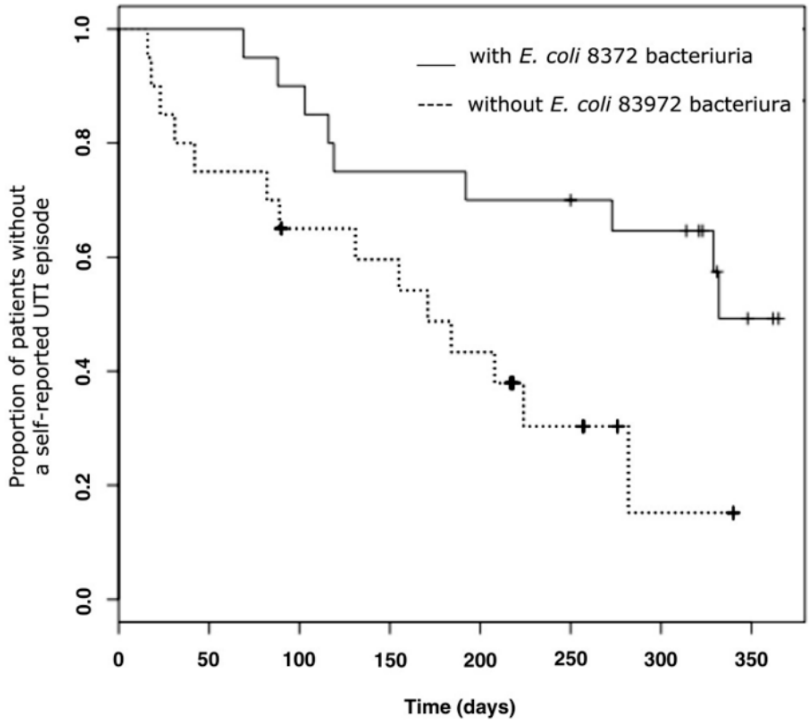
ASB as Prevention



Wullt, B. & Svanborg, C. Deliberate Establishment of Asymptomatic Bacteriuria-A Novel Strategy to Prevent Recurrent UTI. *Pathogens* **5**, (2016).

ASB as Prevention





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Intensive Care Med
https://doi.org/10.1007/s00134-023-07108-6

NARRATIVE REVIEW

Differentiating infection, colonisation, and sterile inflammation in critical illness: the emerging role of host-response profiling

Mark Jeffrey[1,2], Kerina J. Denny[3,4], Jeffrey Lipman[5,6,7] and Andrew Conway Morris[1,2,8*]

Abstract

Infection results when a pathogen produces host tissue damage and elicits an immune response. Critically ill patients experience immune activation secondary to both sterile and infectious insults, with overlapping clinical phenotypes and underlying immunological mechanisms. Patients also undergo a shift in microbiota with the emergence of pathogen-dominant microbiomes. Whilst the combination of inflammation and microbial shift has long challenged intensivists in the identification of true infection, the advent of highly sensitive molecular diagnostics has further confounded the diagnostic dilemma as the number of microbial detections increases. Given the key role of the host immune response in the development and definition of infection, profiling the host response offers the potential to help unravel the conundrum of distinguishing colonisation and sterile inflammation from true infection. This narrative review provides an overview of current approaches to distinguishing colonisation from infection using routinely available techniques and proposes matrices to support decision-making in this setting. In searching for new tools to better discriminate these states, the review turns to the understanding of the underlying pathobiology of the host response to infection. It then reviews the techniques available to assess this response in a clinically applicable context. It will cover techniques including profiling of transcriptome, protein expression, and immune functional assays, detailing the current state of knowledge in diagnostics along with the challenges and opportunities. The ultimate infection diagnostic tool will likely combine an assessment of both host immune response and sensitive pathogen detection to improve patient management and facilitate antimicrobial stewardship.

Keywords: Infection, Colonisation, Host-response, Antimicrobial stewardship, Rapid diagnostics

Introduction

Infection develops when a microorganism enters a space intolerant of that microorganism, overgrows, or releases toxins that damage the host and provoke an inflammatory response, that if severe enough results in organ failure (sepsis). The macroscopic, cellular, and biochemical features of infection overlap with inflammation from sterile tissue damage. The majority of critically ill patients manifest features of systemic inflammation irrespective of their admitting problem [1]. Critically ill patients rapidly develop dysbiosis, with emergence of pathogen-dominant microbiomes in mucosal organs even in the absence of frank infection. Thus, distinguishing colonisation from infection in the critically ill is challenging.

The advent of highly sensitive molecular pathogen detection shows promise in improving antimicrobial prescribing [2, 3]; however, these techniques may exacerbate the problem of unnecessarily treating colonisation, as organisms can be identified in almost all mucosal organ

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https://doi.org/10.1007/s00134-023-07108-6

Take home message

Infection can be difficult to distinguish from colonisation and sterile inflammation, with only the former requiring antimicrobial therapy. The rise of highly sensitive microbial diagnostics is likely to exacerbate this problem. The key role of the host immune response in defining infection makes it an attractive target to discriminate infection from colonisation, and thereby maximise benefits and minimise harms from antimicrobials. This article describes current approaches to distinguishing colonisation from infection, the underlying immunopathology of infection and summarises the current and future diagnostic tools.