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The Importance of Targeting Intraoperative Transmission of Bacteria with Antibiotic Resistance and Strain Characteristics

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Abstract

Background: Evidence-based intraoperative infection control measures can reduce *Staphylococcus aureus* transmission and infections. We aimed to determine whether transmitted *S. aureus* isolates were associated with increased risk of multidrug resistance and associated traits.

Methods: *S. aureus* isolates obtained from intraoperative environmental, patient skin, and provider hand reservoirs among 274 operating room case pairs (1st and 2nd case of the day) across 3 major academic medical centers from March 2009 to February 2010 underwent systematic-phenotypic-genomic analysis to identify clonal transmission events. The association of clonal *S. aureus* transmission with multidrug resistance and resistance traits was investigated. Transmission dynamics were characterized.

Results: Transmitted isolates (N=58) were associated with increased risk of multi-drug antibiotic resistance [33% (19/58) transmitted vs. 19% (12/115) other isolates, risk ratio 3.14, 99% CI 1.34–7.38, P=0.0006]. Transmission was associated with a significant increase in resistance traits including mecA [40% transmitted isolates vs. 17% other isolates, risk ratio 2.28, P=0.0026] and ant (6)-Ia [26% transmitted isolates vs. 9% other isolates, risk ratio 2.97, P=0.0050]. Provider hands were a frequent reservoir of origin, between-case a common mode of transmission, and patient skin and provider hands frequent transmission locations for multidrug resistant pathogens.

Conclusions: Intraoperative *S. aureus* transmission was associated with multidrug resistance and resistance traits. Proven infection control measures should be leveraged to target intraoperative transmission of multidrug resistant pathogens.

Keywords

Intraoperative period and pathogen transmission; surgical site infection; antibiotic resistance; antibiotic stewardship; infection control

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Details of Author Contributions

Randy Loftus helped design the study, conduct the study, analyze the data, and write the manuscript. Franklin Dexter helped analyze the data and write the manuscript. Jeremiah Brown helped write the manuscript.

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Introduction

Innovative solutions are needed to address the global problem of increasing antibiotic resistance.[1] *Staphylococcus aureus* is a leading cause of surgical site infections (SSIs) and has acquired resistance and virulence traits that make infections more difficult to treat when they develop. [2–7] SSIs are a major health issue affecting 2–5% of patients undergoing surgery,[8] prolonging hospital duration and increasing mortality and hospital readmission rates,[9,10] increasing the risk of intensive care unit admission by 2/3,[11] and generating substantial increases in direct and indirect healthcare costs.[9,11]

SSI pathophysiology involves: 1) the transfer of one or more pathogens, *S. aureus* the number one cause, from a nonsterile to a sterile site and 2) host immunosuppression derived from advanced age, underlying comorbidities, surgical inflammation, and general anesthesia.[12,13] The impact of pathogen transfer and prophylactic antibiotic resistance [14,15] on SSI development highlights the importance of preventing transmission in the first place[2,16,17] to augment host optimization strategies such as antibiotic selection and timing of administration, temperature management, glucose control.[18–20]

An evidence-based, multifaceted solution involving optimized provider hand hygiene, environmental cleaning, vascular care, and patient decolonization improvement strategies can generate substantial reductions in *S. aureus* transmission and SSIs.[21] Implementation effectiveness and feasibility of the approach have been confirmed in multiple randomized trials across several centers.[21–24]

In this study, we sought to determine whether transmitted intraoperative *S. aureus* isolates from a previous cohort study[6] were associated with increased risk of multidrug resistance (primary aim) and antibiotic resistance traits (secondary aim). If so, greater focus on prevention of intraoperative *S. aureus* transmission could be used to target bacterial resistance among surgical patients.

Methods

Overview:

In a prospective observational study performed from March 2009 to February 2010, two hundred and seventy-four operating room case pairs (2 sequential surgical cases in the same operating room environment) were randomly selected via use of a computer-generated list for observation at the University of Iowa (103 pairs), Dartmouth-Hitchcock Medical Center (99 pairs), and UMass Memorial Hospital (72 pairs).[6] For each working day (Monday-Friday) of the study period, operating rooms involving care of adult patients undergoing general anesthesia requiring placement of an intravenous catheter were considered eligible for enrollment. The University of Iowa declared that this study did not meet the definition of human subject's research with analysis limited to de-identified data.

Baseline Infection Control Practices:

Infection control practices at the time of bacterial collection included routine and terminal environmental cleaning with quaternary ammonium compounds ± surface disinfection

wipes. All providers had access to alcohol dispensers located on the wall and/or anesthesia carts.[6] Gloves were immediately available for use.[6]

Sample collection procedures: (Fig. 1)

Provider hand sampling: A modified glove juice technique was utilized to sample provider (providers who interacted with the anesthesia work area including anesthesia attending physicians, anesthesia resident physicians, Certified-Registered Nurse Anesthetists [CRNAs], break providers, and/or clinical anesthesia technologists) hands before, during (after induction of anesthesia but prior to emergence), and after patient care.[6, 25,26]

Patient sampling: The patient nasopharynx[27] and axilla[28] were sampled after induction of anesthesia and patient stabilization because those skin sites are strongly associated with postoperative SSIs.[21,29] A sterile nasopharyngeal swab (ESwab, Copan Diagnostic Inc., Corona, CA) was moistened with sterile transport medium and inserted gently into either the internal surface of each nasopharynx bilaterally or the midpoint of the axilla bilaterally and rotated 360° ten times to obtain a culture.

Environmental sampling: The adjustable pressure-limiting valve and agent dial of the anesthesia machine were sampled. These sites are associated with an increase in the probability of bacterial contamination of patient intravenous stopcock sets, high-risk transmission events directly linked to postoperative infection and repeatedly associated with increased patient mortality.[6] Sites were sampled at baseline, after active decontamination (ten minutes of air drying according to protocol) by study investigators at case 1 start using Dimension III (Sturtevant, WI, USA), and after routine decontamination (same disinfectant without mandated air drying time) at case 2 start by environmental cleaning personnel. Sites were sampled again at case 1 and case 2 end without prior surface disinfection. Sterile polyester fiber-tipped applicator swabs moistened with sterile transport medium (ESwab, Copan Diagnostic Inc., Corona, CA) were rolled several times over the selected areas to obtain cultures.

Sample transport conditions: All culturing was performed at Dartmouth-Hitchcock Medical Center. Samples shipped from the University of Iowa and UMass Memorial Hospital were placed under similar environmental conditions (ambient temperature) during the 12 hours required for shipping. Samples collected on the same day at Dartmouth-Hitchcock Medical Center did not require shipping, but they were kept at ambient temperature to mimic the environment of those samples being shipped. No samples for a given study day were incubated until all samples for that day from all research sites were present at Dartmouth-Hitchcock Medical Center.[6]

Microbial culture conditions: Each swab was inoculated onto a sheep's blood agar plate using a zigzag pattern and swab rotation. Each plate was incubated for 48 hours at 35°C.[30]

Isolate analysis: Temporal association (same day of surgery, same operating room, same sampling period), analytical profile indexing (a standardized protocol for identification of Gram-negative and Gram-positive bacteria that yields a unique number for database cross

referencing), Kirby-Bauer antibiotic susceptibility testing involving commonly employed prophylactic antibiotics),[30] multi-locus sequence typing (identifying isolate sequence type via whole cell genome analysis), and single nucleotide variant (SNV) analysis (comparing isolate nucleotides to a reference sequence) were used to compare two or more isolates obtained from distinct reservoirs within an observational unit.[31–33] Clonally related isolates were defined as epidemiologically related isolates (temporal association with analytical profile indexing and antibiotic susceptibility testing match) with >99.99% agreement in SNV analysis. Greater than 99.99% agreement in SNVs corresponded to 77±36 SNVs for clonally related isolates, while isolates of the same multi-locus sequence type had 1270 ± 340 SNVs.[29]

Surgical site infection: All patient medical records were screened for evidence of elevated white blood cell count, fever, antimicrobial order, office note documentation of infection, and culture acquisition. Patients with at least 1 of the 5 criteria underwent full chart review to identify surgical site infections according to National Healthcare Safety Network definitions of SSI.[6, 21,22]

Outcome variables and variables definition:

Primary:

Clonal transmission: Defined by the isolation of ≥ 2 isolates from ≥ 2 distinct measured reservoirs that were identical by class of pathogen, analytical profile indexing, antibiotic susceptibility, and had fewer than 77±36 SNVs or the presence of an isolate in a measured reservoir at case end that was not present at case start. [21,22, 29]

Multidrug resistance: Defined by resistance to ≥ 4 commonly employed antibiotics in the perioperative arena: methicillin, ampicillin, ceftazidime, cefuroxime, ciprofloxacin, clindamycin, gentamicin, meropenem, penicillin, piperacillin-tazobactam, sulfamethoxazole-trimethoprim, linezolid, and/or tetracycline.[34]

Secondary:

Resistance traits: Genes associated with beta-lactam resistance (e.g., spc, mecA, blaZ), macrolide resistance (e.g., aadD, ermA, ermC, mphC, inuA, msrA), aminoglycoside resistance (e.g., aph3III, aac6-aph2, ant(6)-1a), tetracycline resistance (e.g., tetM and tetK), and fluoroquinolone resistance (e.g., norA) were identified with the microbial genetics module.[31–34] The module was used to detect known resistance traits within analyzed sequence read maps.

Exploratory:

Transmission Dynamics: Primary reservoir(s) of origin, transmission locations, modes of transmission, portals of entry (stopcock), and strain characteristics (sequence type and link to infection) for *S. aureus* isolates. Clonally related isolates were aligned according to acquisition timing within an observational unit to identify a transmission pathway.

The reservoir of origin was identified according to the following logic, and subsequent reservoirs were identified as transmission locations (i.e., 1st patient to 2nd patient of the day in the same operating room):

Provider *origin* of within case contamination was confirmed if the transmitted isolate was clonally related to an isolate from the hands of one or more anesthesia providers sampled upon room entry before patient care, while provider origin of between case transmission was confirmed if one or more isolates from provider hands in case 1 were clonally related to one or more isolates in case 2 without potential alternative sources of transmission from case 2 reservoirs.

Environmental *origin* of within case contamination was confirmed if the transmitted isolate was clonally related to an isolate from the environment sampled at baseline or at case end but not isolated either from the hands of providers or from the patient at case start. Environmental origin of between-case transmission was confirmed if one or more environmental isolates from case 1 were clonally related to one or more isolates in case 2 without potential alternative sources of transmission from case 2 reservoirs.

Patient *origin* of within case contamination was confirmed if the transmitted isolate was clonally related to an isolate from the patient sampled at case start but was not isolated either from the hands of providers at case start (as patient samples were obtained after induction of anesthesia) or from baseline environmental samples. Patient origin of between case transmission was confirmed if one or more patient isolates from case 1 were clonally related to one or more isolates in case 2, without potential alternative sources of transmission from case 2 reservoirs.

The within-case *mode* of transmission was confirmed if the origin and transmission location(s) for a clonal series were confined to a single case in an observational unit. The between-case mode of transmission was confirmed if the clonal series spanned both cases in an observational unit.

Intravascular device (stopcock) involvement (*portal of entry*) was defined by contamination of the internal lumen of a patient intravenous stopcock set in one or both cases, as all patients received fresh stopcock sets for the study, which have been shown to be invariably culture negative upon removal from packaging.

The association of *S. aureus* sequence type with multidrug resistance was assessed. Patient *S. aureus* cultures obtained for infectious workup were compared to transmitted isolates to identify clonal transmission.[6,7,21,22,29]

Statistics:

Our primary aim was to test the association of clonal transmission with multidrug resistance. Fisher's exact test was used to compare the proportion of transmitted isolates with multidrug resistance vs. all other isolates that were without evidence of transmission. We tested for an association of the following procedural demographic variables with clonal transmission using Fisher's exact test; none were associated (P>0.10) (Table 1): age, sex, ASA physical status classification, Study on the Efficacy of Nosocomial Infection control (SENIC),[35] case

duration, count of patient comorbidities, patient origin, patient discharge location, dirty or infected site, and general abdominal surgery.

For our secondary aim, the Fisher's exact test was used to test the association of clonal transmission with each of 16 resistant traits (Table 2). The Wilcoxon rank-sum test was also used to compare the number of different resistance traits among transmitted isolates as compared to all other isolates. Similarly, we tested the association of *S. aureus* MLST 5 with commonly employed prophylactic antibiotic resistance, including to the antibiotic given to the individual patient prior to surgery. Simple descriptive statistics were used to characterize the epidemiology of transmission of multidrug resistant *S. aureus* isolates (Table 3), including those isolates and associated resistance traits linked by genome analysis to SSI development (Table 4).

As a sensitivity analysis, we tested for stability over time of the association of transmission with prophylactic antibiotic resistance for 2018/19 *S. aureus* isolates. Unlike for the data otherwise used throughout the paper, transmission for this limited isolate subset was determined by at least 2 *S aureus* isolates obtained from at least 2 distinct, temporally associated reservoirs and/or the isolation of at least 1 pathogen from a reservoir at case end that was not present at case start.[21] Homogeneity of odds ratio of stratified 2 × 2 tables was calculated by exact test and pooled relative risk was calculated with exact confidence interval using Fisher's method (StatXact-12, Cytel, Cambridge, MA).

Due to the multiple comparisons, $P < 0.01$ was considered statistically significant, and we reported 99% confidence intervals. Calculations were performed using Stata 17.0 (StataCorp, College Station, TX).

Power Analysis

This study was designed and performed for the different purpose of detecting a rate of between case stopcock bacterial transmission events of 5% with an alternative rate of 1%. Approximately 400 patients (200 pairs) were needed to be powered at 0.9 with a type 1 error rate of 0.05.[6] All *S. aureus* isolates from that study were included in this paper.

Results:

Fifty-eight clonal *S. aureus* transmission events were identified among 274 case-pair observational units. Baseline patient and procedural characteristics stratified by clonal transmission are shown in Table 1. Clonal transmission of *S. aureus* was associated with increased risk of multidrug resistance [33% (19/58) transmitted vs. 19% (12/115) of isolates that were not transmitted, risk ratio 3.14, 99% CI 1.34–7.38, P=0.0006].

S. aureus transmission was associated with a significant increase in resistance traits including mecA (beta-lactam resistance) [40% (23/58) transmitted vs. 17% (20/115) isolates that were not transmitted, risk ratio 2.28, P=0.0026] and ant (6)-1a (aminoglycoside resistance) [26% (15/58) transmitted vs. 9% (10/115) isolates that were not transmitted, risk ratio 2.97, P=0.0050] (Table 2). Clonally transmitted isolates may have been associated with increased acquisition (a higher number) of resistance traits (a median of 4 different

resistance traits for transmitted isolates [25th 2, 75th 6] vs. a median of 3 different resistance traits for non-transmitted isolates [25th 2, 75th 5], P=0.021).

S. aureus multilocus sequence type 5 (MLST 5) was associated with resistance to methicillin, ampicillin, cefazolin, cefepime, ceftazidime, cefuroxime, meropenem, piperacillin-tazobactam, penicillin, ciprofloxacin, and clindamycin (Risk ratio 3.30, 99% CI 1.55–7.03, P=0.0012). MLST 5 was associated with resistance to the antibiotic the individual patient was given before surgery (prophylactic) (risk ratio 2.98, 99% CI 1.18–7.47, P=0.0061).

The epidemiology of transmission of multidrug resistant isolates is shown in Table 3. Provider hands were a frequent reservoir of origin, between-case a common mode of transmission, and patient skin sites and provider hands frequent locations for within and between-case transmission events. There were 13 *S. aureus* isolates linked by genome analysis to six patient cultures obtained for infectious disease workup (Table 4). Intraoperative transmission of *S. aureus* causing infection was confirmed by whole cell genome analysis in 83% (5/6) of cases, and MLST 5 transmission causing infection was confirmed in 20% (1/5). Confirmed patient to environmental transmission of resistance traits linked to infection included spc, ant(6)-1a, mecA, blaZ, ermA, mphC, and msrA.

Assessing stability over time, for 2009/2010, *S. aureus* were resistant to the prophylactic antibiotic for 22% (18/83) of transmitted isolates versus 8% (5/59) not transmitted, estimated risk ratio 2.56. For 2018/2019, resistance was 15% (11/71) for transmitted versus 1% (2/163) not transmitted, estimated risk 12.63. Assuming homogeneity (P=0.098), the pooled risk ratio was 5.15 (99% CI 1.92–39.2), P < 0.0001.

Discussion:

Prevention of intraoperative *S. aureus* transmission is an important target for prevention of SSIs.[7, 21,22] In this study, we show that transmitted *S. aureus* isolates were associated with increased risk of multidrug resistance and resistance traits. These findings suggest that optimization of basic intraoperative infection control measures that reduce transmission and prevent infections before they develop may also be useful for reducing the spread of antibiotic resistance and associated resistant traits among surgical patients. [1, 2]

The association of transmission with resistance is likely due to acquisition of virulence factors that enhance transmission, such as increased strength of biofilm formation and desiccation tolerance, and resistance traits.[7,29] As shown in this study, *S. aureus* MLST 5, a hyper transmissible strain characteristic associated with increased strength of biofilm formation and desiccation tolerance,[29] also is associated with prophylactic antibiotic resistance and linked by whole cell genome analysis to SSI development when transmission involved resistance to the prophylactic antibiotic employed. This is an alarming finding given multiple routes by which anesthesia work area transmission events can lead to infection development including aerosolization of particles, direct contamination of the wound, intravenous injection, or intraoperative patient skin contamination and postoperative contiguous spread. [12] As shown in this study, within-case transmission events involving

multidrug resistant pathogens to patient skin sites occurred frequently. There is an urgent need to employ an evidence-based, multifaceted approach proven to generate substantial reductions in anesthesia work area *S. aureus* transmission and SSIs (Fig. 2).[1,2]

We utilized whole cell genome analysis to map the spread of resistance traits among anesthesia work area reservoirs. We confirmed intraoperative patient-to-patient and patient-to-environment transmission of mecA, a mechanism for beta lactam resistance that was directly linked to postoperative infection development. Thus, advanced molecular techniques, while vastly underestimating the true magnitude of the problem, confirm that further improvement in basic preventive measures such as environmental cleaning and preoperative patient decolonization are indicated to improve perioperative patient safety. Importantly, preventable spread of bacterial resistance traits linked to infection is a likely rationale for the increase in methicillin-resistant *S. aureus* infections associated with a lapse in basic infection preventive measures in the acute COVID-19 era. [36]

Potential Limitations: Isolates utilized for this study were obtained in 2009–2010. However, we confirmed stability of the association of transmission and prophylactic antibiotic resistance for 2018/19 *S. aureus* isolates. If there were a trend, it would be an increased risk ratio (i.e., strengthening of association). Thus, archival pathogens can be utilized to generate results that guide clinical care and further research. Pathogen resistance and virulence can vary by hospital. We addressed this potential limitation with the multicenter analysis to provide generalizability. Seasonal variation can impact pathogen exposure.[37] The 1-year study duration accounts for seasonal variation and change in personnel. Other pathogens besides *S. aureus* can be resistant to antibiotics and cause infection. We focused the analysis on *S. aureus* because this is one of 6 pathogens associated with increased global mortality,[1,2] and *S. aureus* transmission is associated with surgical site infection development at the patient level,[21] is a proven marker for compliance with behavioral infection control measures,[38] and when attenuated, infections fall.[21,22] Finally, evidence-based interventions proven to reduce *S. aureus* have also been shown to reduce other gram-negative and gram-positive bacterial pathogens[21–24] and more recently, SARS-CoV-2.[39, 40]

In conclusion, *S. aureus* isolates in the intraoperative arena with multidrug resistance and resistance traits had increased risk of transmission. We have confirmed intraoperative patient-to-patient transmission of multidrug resistant pathogens and resistance traits leading to infection along with patient transfer of resistance traits to the surrounding environment. Infection control measures proven to reduce *S. aureus* transmission and SSIs should be used to address the intraoperative spread of antibiotic resistant strains and strain characteristics among surgical patients.

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Declaration of Interests:

• Randy W. Loftus reported research funding from Georgia-Pacific Manufacturing, Sage Medical Inc., B. Braun, Draeger, and Kenall, has one or more patents pending, and is a partner of RDB Bioinformatics, LLC, and 1055 N 115th St #301, Omaha, NE 68154, a company that owns OR PathTrac, and has spoken at educational meetings sponsored by Kenall (AORN) and B. Braun (APIC).

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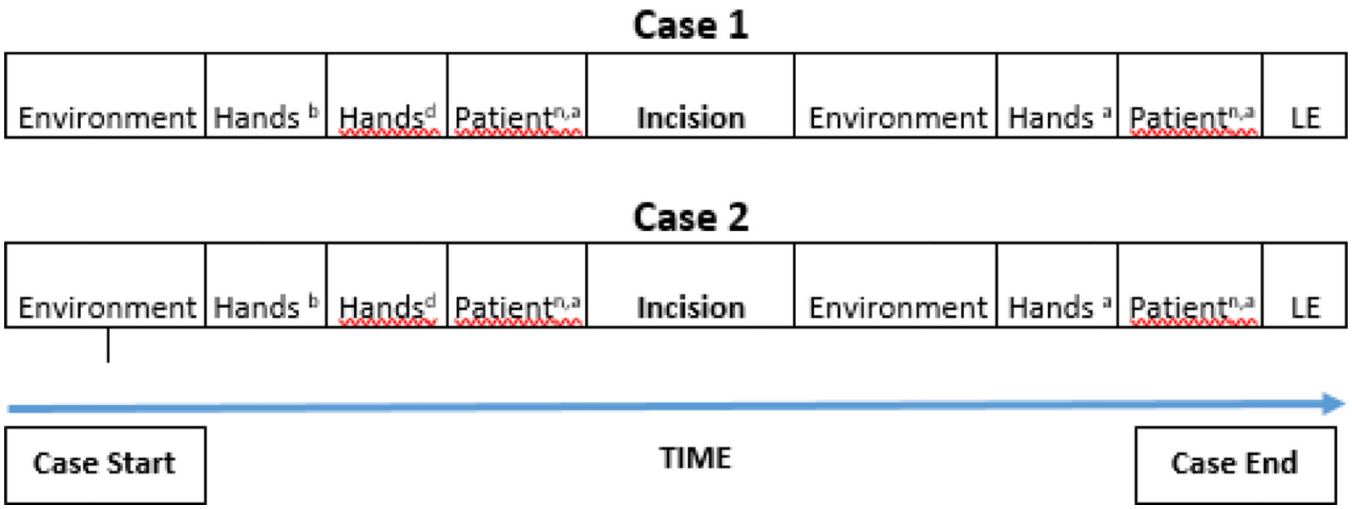

Fig. 1.

Shown is the sample collection sequence, obtained before and after the surgical incision. Sample collection began with case 1 and was followed by case two in the same operating room, a case-pair. The included the adjustable pressure-limiting valve and agent dial of the anesthesia machine. Provider hands included anesthesia attending and resident physicians, Certified-Registered Nurse Anesthetists, break providers, and clinical anesthesia technologists. Patient nares and axilla were sampled.

a=hands before, d=hands during, a = hands after. LE=the internal lumen of the patient intravenous stopcock set, sampled only once at the end of each case of the pair. patient nares = n, patient axilla = a

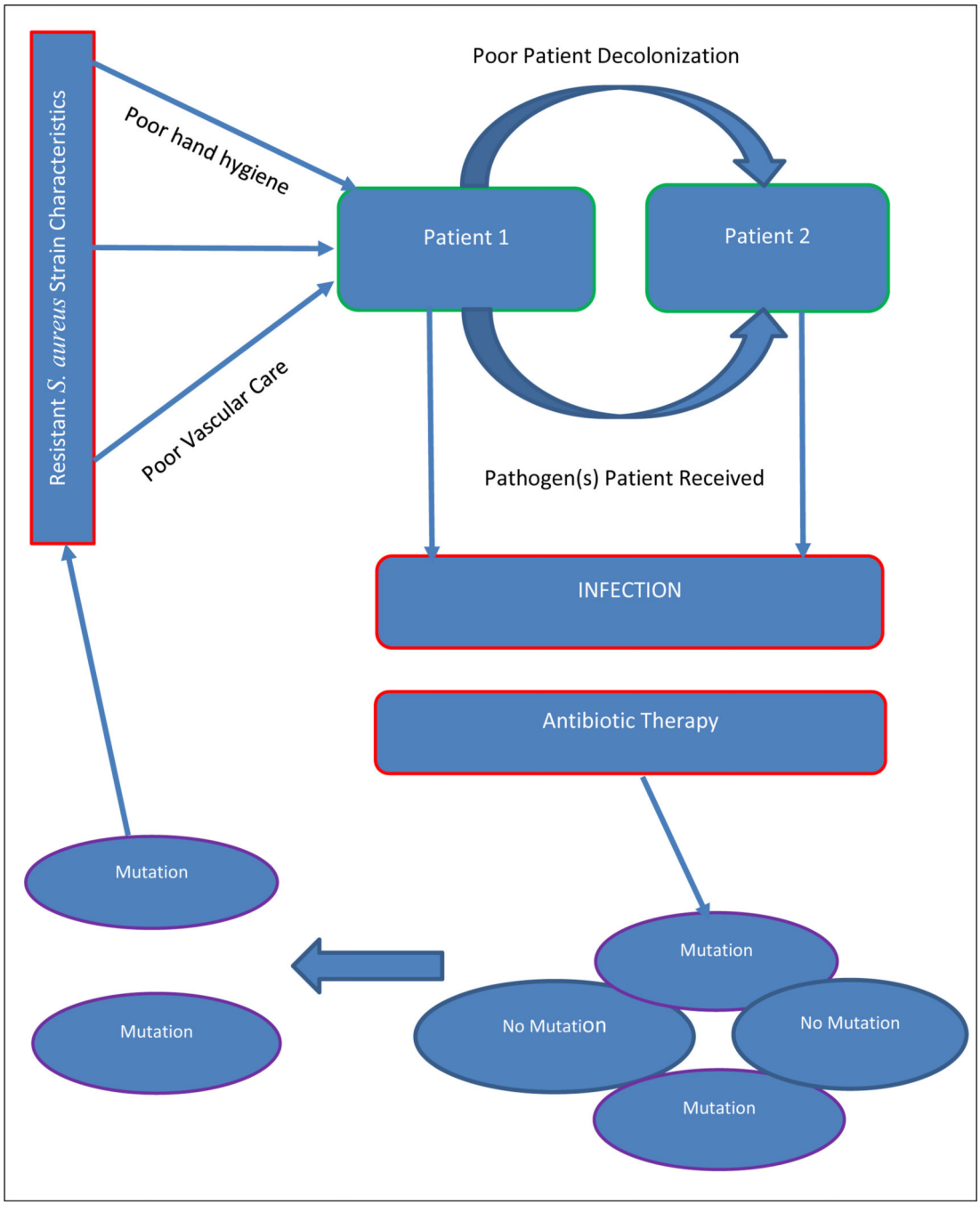

Fig. 2.

Shown is the impact of within and between-case *S. aureus* transmission. Failure in basic preventive measures resulting in transmission and infection can result in antibiotic use which can in turn drive selection of mutations and perpetuate transmission of resistant strain characteristics.

Table 1:

Baseline Patient and Procedural Demographics Stratified by Genomic Transmission

	Genomic Transmission (N = 58)	No Transmission (N = 115)	P-Value
Age Years Mean (SD)	54 (13)	51 (15)	0.11
Male N (%)	23 (40)	53 (46)	0.52
ASA > 2 N(%)	23 (40)	29 (25)	0.06
SENIC > 2 N(%)	2 ()	2 (2)	0.60
Comorbidity > 2 N (%)	13 (22)	19 (16)	0.41
Dirty or Infected	6 (10)	9 (7)	0.58
Anesthesia Duration > 2 Hours N (%)	29 (50)	44 (38)	0.15
Urgent N (%)	6 (10)	10 (9)	0.79
Inpatient preoperatively, N (%)	8 (14)	16 (14)	0.99
Inpatient postoperatively, N (%)	33 (57)	60 (52)	0.63
Hospital			0.18
1	23 (40)	41 (36)	
2	16 (28)	21 (18)	
3	19 (33)	53 (46)	
Specialty			
Orthopedics	15 (26)	24 (21)	0.10
General abdominal	7 (12)	31 (27)	
Otolaryngology	7 (12)	17 (15)	
Other	29 (50)	43 (37)	

The age in years was compared using Wilcoxon-Mann-Whitney test. The other variables were compared using Fisher's exact test.

ASA = American Society of Anesthesiologists (ASA) Health Classification

SENIC = Study on the Efficacy of Nosocomial Infection control (SENIC) [38] score (an index predicting the probability of postoperative HAI development for a given patient)

Table 2:

Resistance Traits Stratified by Genomic Transmission

	Genomic Transmission (N = 58)	No Genomic Transmission (N = 115)	Risk Ratio	99% CI	P-Value
mecA N (%)	23 (39.66)	20 (17.39)	2.28	1.17–4.45	0.0026
ant(6)-Ia N (%)	15 (25.86)	10 (8.69)	2.97	1.13–7.82	0.0050
msr (A) N (%)	28 (48.28)	35 (30.43)	1.59	0.96–2.63	0.029
norA N (%)	0 (0)	9 (7.83)	0	N/A	0.030
aph(3')-III N (%)	14 (24.14)	15 (13.04)	1.85	0.78–4.38	0.084
aadD N (%)	15 (25.86)	17 (14.78)	1.75	0.78–3.94	0.10
spc N (%)	39 (67.24)	63 (54.78)	1.23	0.89–1.69	0.14
aac(6')-aph(2") N (%)	0 (0)	4 (3.48)	0	N/A	0.30
mphC N (%)	17 (29.31)	27 (23.48)	1.25	0.63–2.47	0.46
erm A N (%)	32 (55.17)	70 (60.87)	0.91	0.63–1.30	0.51
tet (K) N (%)	0 (0)	2 (1.74)	0	N/A	0.55
tet (M) N (%)	2 (3.45)	2 (1.74)	1.98	0.16–25.2	0.60
erm C N (%)	6 (10.34)	14 (12.17)	0.85	0.26–2.78	0.81
blaZ N (%)	50 (86.21)	97 (84.35)	1.02	0.86–1.21	0.82
InuA N (%)	1 (1.72)	2 (1.74)	0.99	0.04–22.62	0.99
dfrG N (%)	0 (0)	1 (0.87)	0	N/A	1

CI = Confidence Interval

Listed P-values are two-sided, Fisher's exact test. The two highlighted rows are statistically significant.

Aminoglycoside resistance: spc, addD, aph(3")-III, aac(6')-aph(2"), ant(6)-1a

Methicillin resistance: mecA and blaZ

Macrolide resistance: erm(A), erm(C), mph(C), Inu(A), and msr(A)

Tetracycline resistance: tet(M) and tet(k)

Sulfamethoxazole-trimethoprim resistance: dfrG

Fluoroquinolone resistance: norA

Table 3:

The Epidemiology of Transmission of 31 Multidrug Resistant *Staphylococcus aureus* isolates.

Reservoir of Origin (N=31)	
Provider hand N(%)	14 (45)
Patient skin N(%)	10 (32)
Environment N(%)	3 (10)
Unknown N(%)	4 (13)
Mode of Source Transmission (N=31)	
Within-case N(%)	5(16)
Between-case N(%)	9(29)
Unknown N(%)	17(55)
Transmission Event Mode (N=31)	
Within-case N(%)	9(29)
Between-case N(%)	5(16)
Unknown N(%)	17(55)
Transmission Location Within (N=9)	
Provider hand N(%)	2(22)
Patient skin N(%)	5(56)
Environment N(%)	2(22)
Transmission Location Between (N=5)	
Provider hand N(%)	2(40)
Patient skin N(%)	1(20)
Environment N(%)	2(40)

Table 4:

Genomic Transmission Stories Involving Infection

Patient infection culture case 1[#]	**Environment at end case 2**[^]				
Patient nares[*] start case 2[*,#]	Patient 2 infection culture				
Patient axilla start case 1	Provider hands during care	Patient infection culture case 1	Patient axilla start case 2	Environment end case 2[&]	Internal lumen intravascular catheter end case 2
Patient nares start case 2	Patient 2 infection culture				
Patient nares start case 2	Patient 2 infection culture				
Patient axilla and nose at start case 1[%#]	Patient 1 infection culture	Patient nares start case 2	Environment end case 2		

[*] Multilocus Sequence Type 5,

[#] Resistant to ≥ 4 antibiotics,

[^] spc, aph(3')-III, ant(6)-1a, mecA, blaZ, ermA, mphC, msrA transmitted from the patient,

[&] ermC transmitted from the patient,

[%] spc, blaZ, ermA, mphC transmitted from the patient to the environment.