WHAT THE NOSE KNOWS: MRSA NARES AS A TOOL FOR ANTIMICROBIAL PRESCRIBING IN DIABETIC FOOT INFECTIONS

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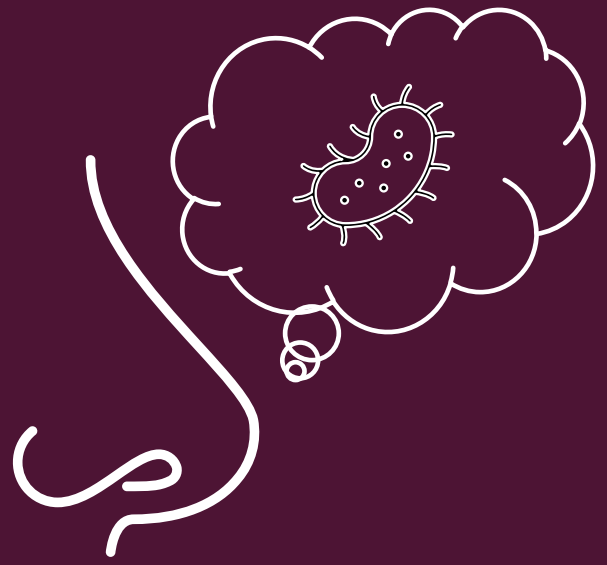


FINANCIAL DISCLOSURES

THE SPEAKER HAS NO FINANCIAL CONFLICTS OF INTEREST TO DISCLOSE

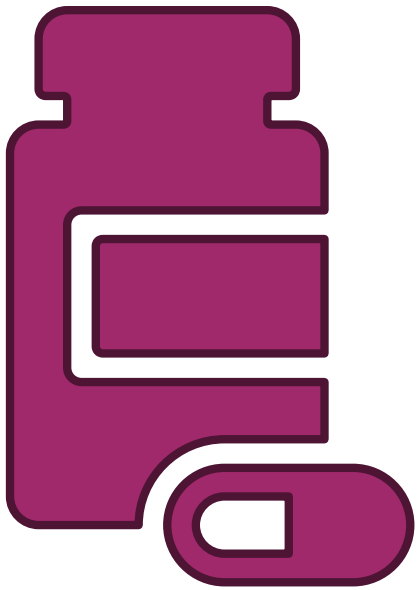
ABBREVIATIONS

DFI: Diabetic Foot Infection

NPV: Negative Predictive Value

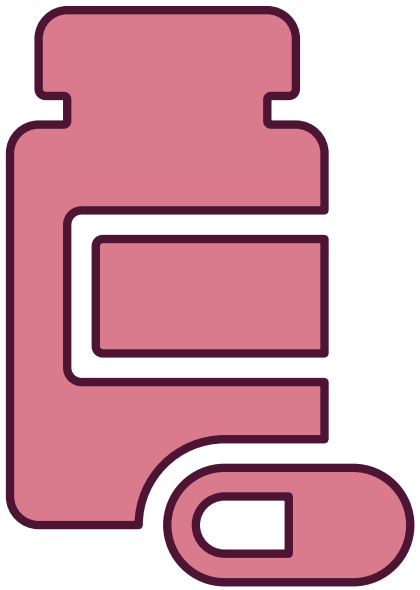
PPV: Positive Predictive Value

PHARMACIST LEARNING OBJECTIVES



- Identify the impact of MRSA in diabetic foot infections
- Analyze current literature for using MRSA nares to optimize antimicrobial therapy in diabetic foot infections
- Recommend empiric treatment regimens regarding MRSA in diabetic foot infections

TECHNICIAN LEARNING OBJECTIVES



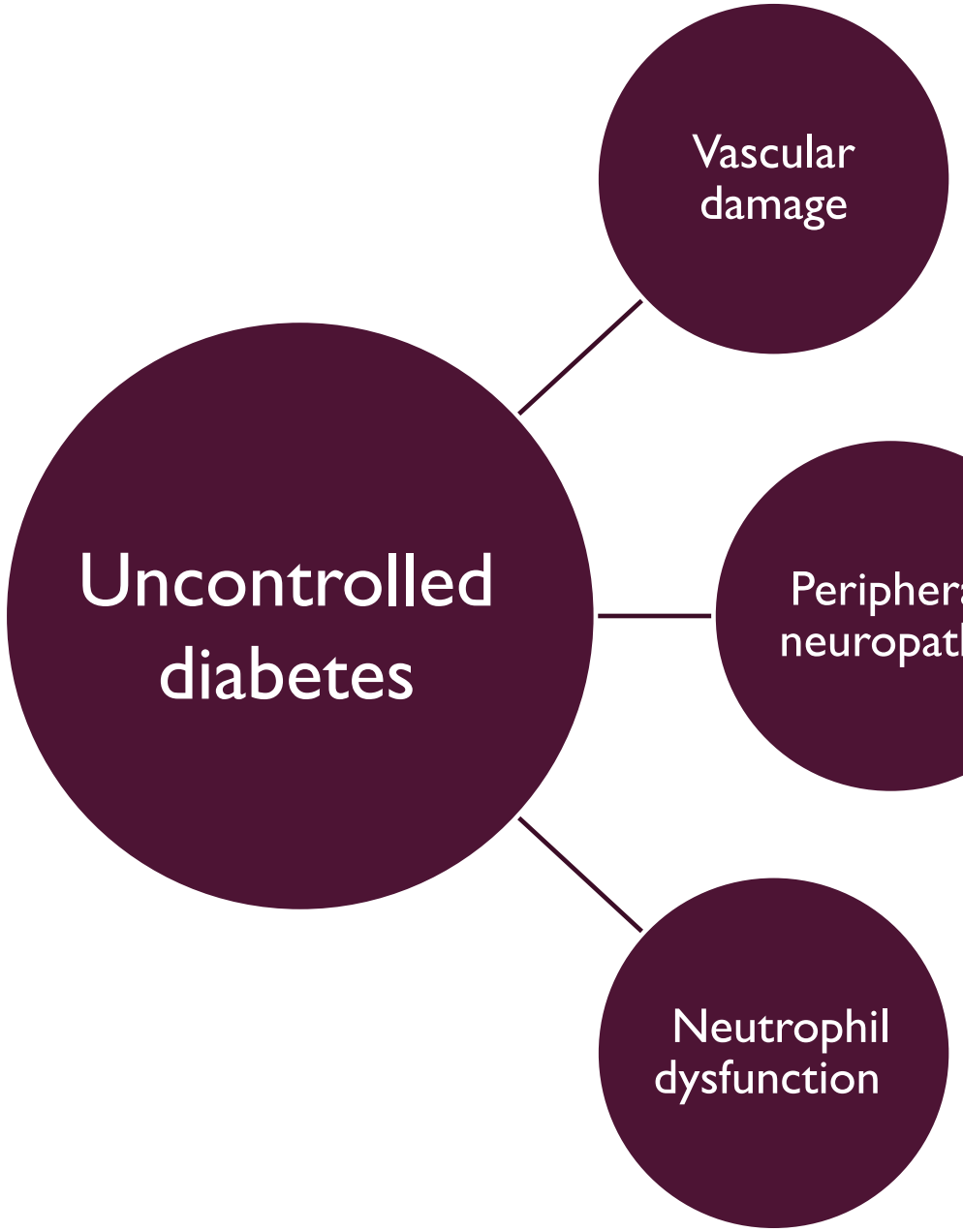
- Explain the role of the MRSA nasal screening test
- Analyze the use of MRSA nasal screening in respiratory infections
- Summarize recent literature on use for MRSA nares for diabetic foot infections

DIABETIC FOOT INFECTIONS

EPIDEMIOLOGY

- In 2021, 573 million adults aged 20-79 years were living with diabetes
- Frequently results in hospitalization and amputation
- 85% of amputations in diabetics are attributable to ulceration on the foot
  - Chronic infection and gangrene
- Average cost breakdown
  - Ulcer: $3,368
  - Minor amputation: $10,486
  - Major amputation: $30,131

Clinical Infectious Diseases,2023; ciad527;Ther Adv Endocrinol Metab. 2018 Jan; 9(1): 29–31, Int Wound J. 2021 Jun;18(3):375-386



- High blood sugar damages blood vessels (including in the foot)

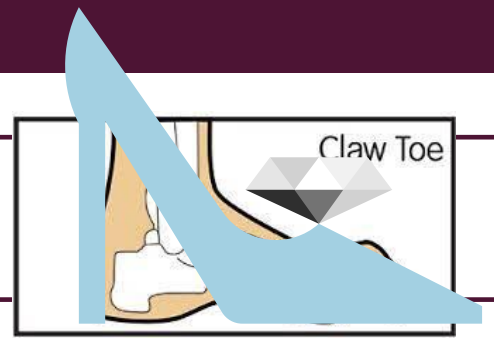
- Blood vessels that supply nerves are damaged
- Decreased sensation to pain/injury

- Decreased immune response

Clinical Infectious Diseases, 2023; ciad527, *Am Fam Physician.* 2008;78(1):71-79. Diabetes Metab Res Rev. 2020 Mar:36 Suppl 1:e3250

PROGRESSION OF INFECTION

- Impaired awareness of trauma
- Claw toe increases risk of trauma



- Tissue exposure to pathogens (superficial infection)
- Progression to deeper infection (tendon, muscle, joint, bone)
  - Impaired host defenses
- Inflammatory response increases pressure
  - Tissue necrosis

Clinical Infectious Diseases, 2023;, ciad527, *Am Fam Physician.* 2008;78(1):71-79. Diabetes Metab Res Rev. 2020 Mar:36 Suppl 1:e3250

PATHOPHYSIOLOGY

Risk factors

Deep wound that is long-standing, recurrent, or traumatic

Renal failure

Chronic hyperglycemia

Peripheral artery disease

Systemic symptoms

Fever

Chills

Marked leukocytosis

- **Uncommon**
- **Can indicate severe, limb/life-threatening infection**

Bone involvement

20-60% of infections

Correlates to severity of infection

Clinical Infectious Diseases, 2023;, ciad527, *Am Fam Physician.* 2008;78(1):71-79. Diabetes Metab Res Rev. 2020 Mar:36 Suppl 1:e3250

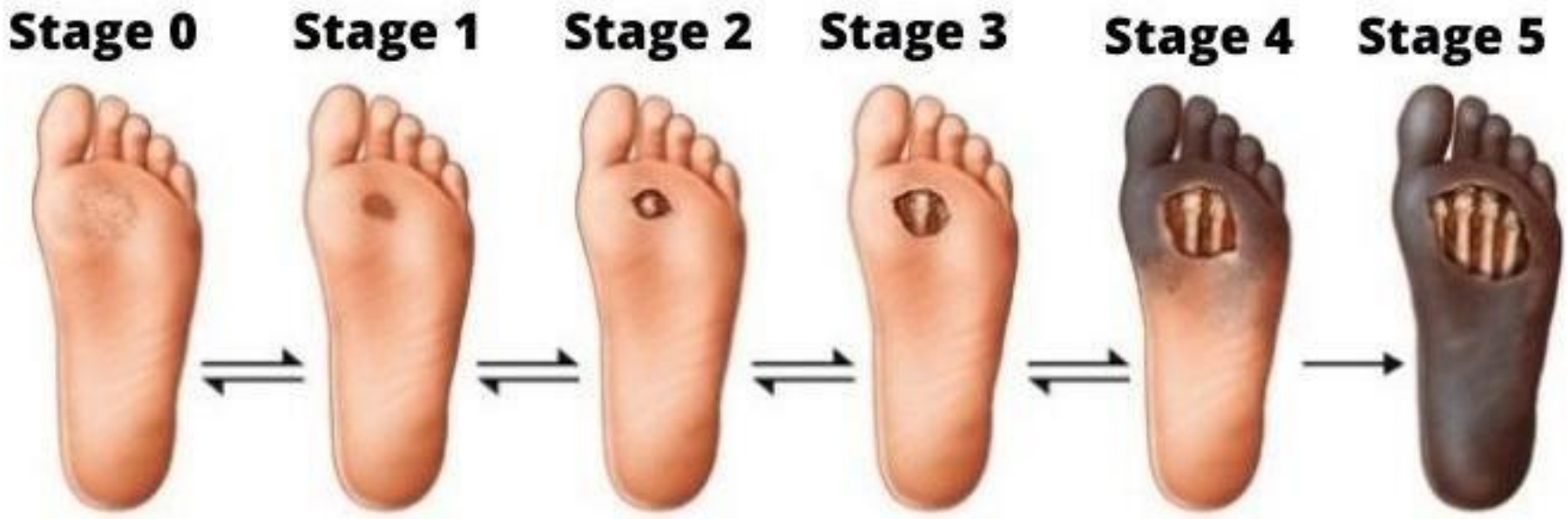
2023 IWGDF/IDSA CLASSIFICATION

IWGDF: International Working Group on the Diabetic Foot
IDSA: Infectious Diseases Society of America

Clinical Classification	IWGDF/IDSA Classification
No systemic or local symptoms or signs of infection	1 (Uninfected)
Infected: at least 2 of the following: • Local swelling or induration • Erythema >0.5 but <2 cm around the wound • Local tenderness or pain • Local increased warmth • Purulent discharge	2 (Mild) *no other cause of inflammatory response (trauma, gout, thrombosis, venous stasis)
Infection with no systemic manifestation • Erythema >2 cm from wound margin and/or • Tissue infected deeper than skin and subcutaneous tissues (tendon, muscle, or joint)	3 (Moderate)
Any foot infection with systemic manifestations (SIRS) • Temperature >38°C or <36°C • Heart rate >90 bpm • Respiratory rate >20 breaths/min • WBCs >12,000/mm^3	4 (Severe)
Infection involving bone	Add "O"

Clinical Infectious Diseases, 2023;, ciad527

WAGNER CLASSIFICATION OF DFI



https://ecampusontario.pressbooks.pub/casestudieshealthsciences/chapter/jacks-health-diabetic-foot-ulcers/

A1C CORRELATION TO DFI SEVERITY

Parameter	Wagner Classification				
Hgb A1C	**1**	**2**	**3**	**4**	**5**
6.5-7.5%	1	0	**4**	0	0
7.6-8.5%	0	6	**21**	7	0
8.6-9.5%	0	0	4	**18**	2
>9.5%	0	0	0	7	**18**

- A1C has a linear relationship with the Wagner Classification of DFI
  - Most patients with Grade 4 and 5 have a Hgb A1c >8.5% ($p<0.0001$)

Cureus. 2020 Jul; 12(7): e9199

PATHOGENS

Mild

Gram positive cocci

- Beta-hemolytic *Streptococcus*
- *Staphylococcus aureus*

Key point:
DFI are often POLYMICROBIAL but commonly include skin pathogens like *Streptococcus* and *Staphylococcus* species

Moderate-severe

Mix of gram positive, gram negative, and anaerobic species

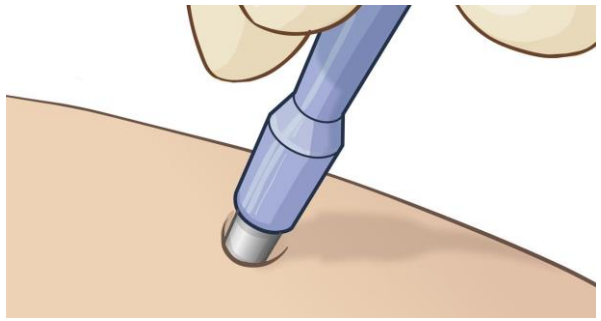
Anaerobes most common with foot ischemia or gangrene

Am Fam Physician. 2008;78(1):71-79

APPROPRIATE CULTURE

Soft-tissue Diabetic Foot Infection

- Aseptic collection of a tissue specimen from the wound for culture
  - Curettage or biopsy



Diabetic Foot Osteomyelitis

- Intra-operative or percutaneous bone cultures
- Low correlation between bone and soft-tissue culture results (<50%)
  - Highest correlation is with *S. aureus* (46.7%)
- Ongoing trial to determine if wound vs bone cultures affect treatment outcomes
  - BeBoP trial

Clinical Infectious Diseases, 2023;, ciad527, https://www.gynexcorporation.com/product/sims-uterine-curettes-size-00/,

COLONIZATION VS INFECTION

Colonization: presence of bacteria on the wound surface without evidence of invasion into host tissues

Infection: multiplication of organisms that induce an inflammatory response

Tissue damage

Masking by peripheral neuropathy, peripheral artery disease, or immune dysfunction

Clinical Infectious Diseases, 2023;, ciad527

KNOWLEDGE CHECK

Which of the following is not involved in the pathophysiology of diabetic foot infections?

A. Peripheral neuropathy

B. Diabetic retinopathy

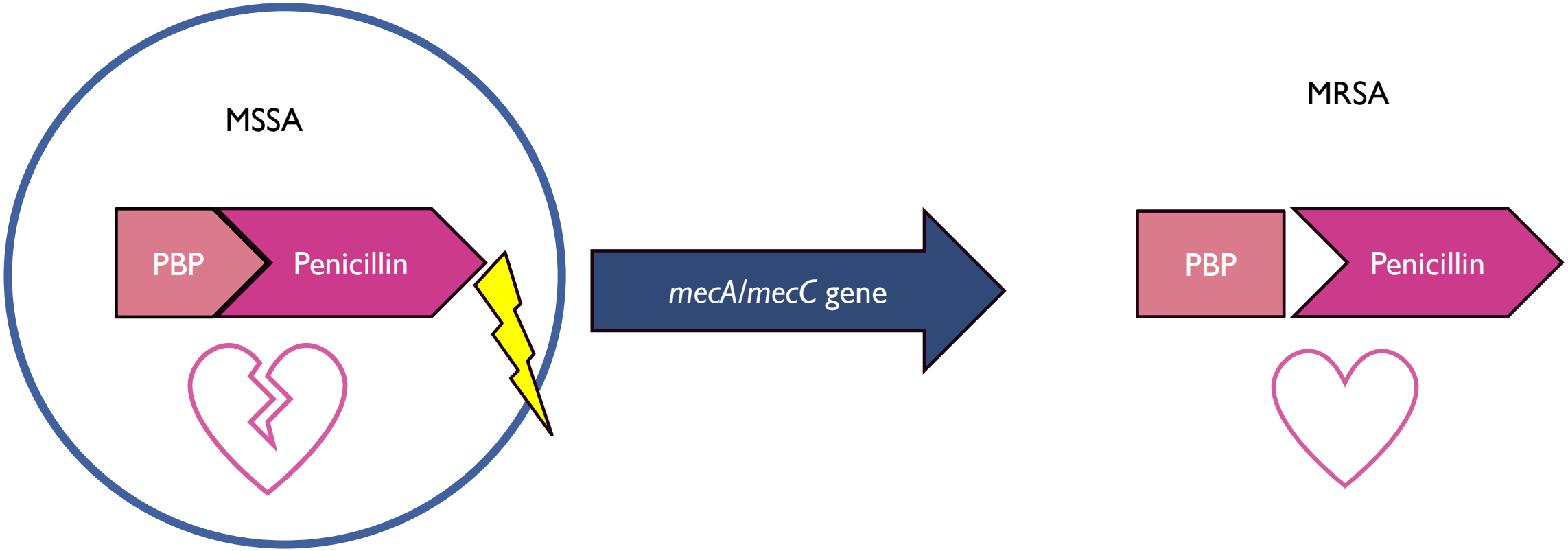
C. Diminished neutrophil function

D. Peripheral artery disease

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

MRSA

MRSA MECHANISM OF RESISTANCE



Annu Rev Biochem. 2015:84:577-601

MSSA TREATMENT OPTIONS FOR DFI

Drug	Toxicities and monitoring	Route	Dosing assuming normal renal function
Cephalexin	GI upset	PO	500 mg QID
Cefazolin		IV	1-2 g Q8H
Oxacillin		IV	1-2 g Q4H
Nafcillin		IV	1-2 g Q4H
Amoxicillin/clavulanate	Non-*C. difficile* associated diarrhea	PO	875 mg amoxicillin/125 mg clavulanate Q12H
Ampicillin/ sulbactam	Injection site pain	IV	3 g Q6H

Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; July 30, 2021.

MRSA TREATMENT OPTIONS FOR DFI

Drug	Toxicities and monitoring	Route	Dosing assuming normal renal function
Vancomycin	Nephrotoxicity and ototoxicity Requires daily therapeutic drug monitoring	IV	10-15 mg/kg Q8-12H, with adjustments based on trough levels
Daptomycin	Myopathy and rhabdomyolysis Requires weekly monitoring of creatinine kinase	IV	Superficial: 4-6 mg/kg Q24H Bone: 6-10 mg/kg Q24H
Linezolid	Myelosuppression Requires weekly monitoring of CBC	IV/PO	600 mg Q12H
Trimethoprim-sulfamethoxazole	Hyperkalemia, hyponatremia, hypoglycemia, acute kidney injury	PO	2 double strength (180 mg trimethoprim/800 mg sulfamethoxazole) tablets twice daily

Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; July 30, 2021.

MRSA TREATMENT OPTIONS FOR DFI

Drug	Toxicities and monitoring	Route	Dosing
Clindamycin	*C. difficile* infection	PO/IV	PO: 300-450 mg Q6-8H IV: 600 mg/day in 2-4 divided doses
Doxycycline	Photosensitivity, skin hyperpigmentation, and esophageal injury	PO/IV	PO/IV: 100 mg Q12H
Levofloxacin	Tendonitis/tendon rupture, peripheral neuropathy, CNS effects (neuroexcitation), exacerbation of myasthenia gravis QT prolongation	PO/IV	Mild-moderate: 500 mg PO Q24H Moderate-severe: 750 mg IV Q24H
Moxifloxacin		PO/IV	400 mg Q24H

Lexicomp Online, Pediatric and Neonatal Lexi-Drugs Online. Waltham, MA: UpToDate, Inc.; July 30, 2021.

KNOWLEDGE CHECK

How would you classify a patient presenting with a diabetic foot ulcer with penetration into the bone, fever of 39°C, and WBCs of 15,000 cells/mm^3?

A. Class 2
B. Class 3-O
C. Class 4
D. Class 4-O

GUIDELINE RECOMMENDATIONS FOR MRSA COVERAGE IN DFI

2012

High local prevalence

Cases of severe infection

2023

Mild

- History of MRSA infection
- History of MRSA colonization

Moderate-severe

- MRSA risk factors

Clinical Infectious Diseases, 2023;, ciad527

MRSA RISK FACTORS 2023

- Prolonged hospitalization
- Intensive care admission
- Recent hospitalization
- Recent antibiotic use
- HIV infection
- Hemodialysis
- Discharge with long-term central venous access
- Invasive procedures
- Admission to nursing home
- Presence of open wounds

Clinical Infectious Diseases, 2023;, ciad527

MRSA PREVALENCE

- Meta-analysis of ~11000 diabetic foot infections worldwide showed MRSA prevalence of 16.8%
- 1.8% of the population is colonized with MRSA
- MRSA accounts for 32-39% of all *S. aureus* infections at local hospital systems

Acta Diabetol. 2019 Aug;56(8):907-921, PLoS One. 2016; 11(8): e0161658 ; Int J Low Extrem Wounds. 2019 Sep;18(3):236-246 . J Antimicrob Chemother. 2018 Jun; 73(6): 1692–1699

GENDER AND MRSA DIABETIC FOOT INFECTIONS

Setting, year	Number of patients	Finding	P-value
Outpatient, specialized diabetic foot clinic, 2022	75	Male gender was an independent risk factor for MRSA DFI	0.029
Inpatient, 2010-2014	318	Male gender was an independent risk factor for MRSA DFI	0.0085
Inpatient in Nigeria, 2022	217	Male patients with diabetic foot ulcers were more infected with MRSA than females	<0.04

PLoS One. 2016; 11(8): e0161658. Int J Low Extrem Wounds. 2022 Apr 13. Diabetes Obes Int J 2022, 7(2): 000254.

NEED FOR BETTER DE-ESCALATION TOOLS IN DFI

Vancomycin overuse

- 15% of DFI patients had MRSA infection and 86% received MRSA-targeted therapy
- 78% of those patients received vancomycin

Vancomycin increases the risk for VRE bacteremia

- Higher risk with longer durations of therapy

Acta Diabetol. 2019 Aug;56(8):907-921, PLoS One. 2016; 11(8): e0161658 ; Int J Low Extrem Wounds. 2019 Sep;18(3):236-246 . J Antimicrob Chemother. 2018 Jun; 73(6): 1692–1699

MRSA NARES SCREENING

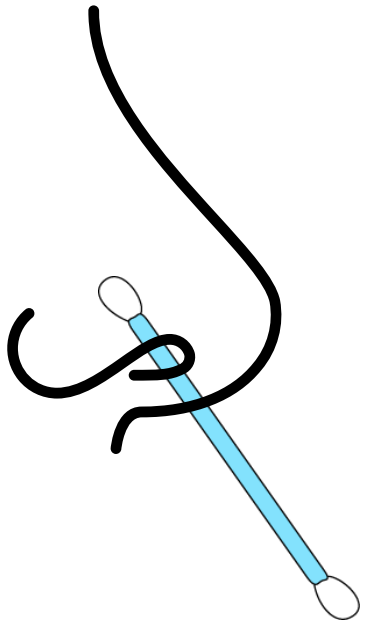
MRSA NARES SCREENING

Nasal swab to detect colonization of MRSA in the nasal cavity

Nares are most common site of colonization

Two modalities:

- CHROMagar™ culture
- Polymerase chain reaction (PCR)



BMJ Clin Evid. 2015; 2015: 0923

COMPARISON OF MRSA NASAL TEST MODALITIES

Test	PCR	CHROMagar™
Time to result	1-2 hours	18-48 hours
Mechanism	Polymerase chain reaction (PCR)	Agar that selects for MRSA
Sensitivity	91.9%	91.8%
Specificity	97.9%	97.2%
Price	$36/cassette	$6.70/plate

https://www.cepheid.com/en-US/tests/hai-other-infectious-diseases/xpert-mrsa-nxg.html, https://www.chromagar.com/en/product/chromagar-mrsa/

STATISTICS OVERVIEW

STATISTICS OVERVIEW

		Disease		
Test Result		**Sick**	**Healthy**	
	Positive	True positive	False positive	**PPV**
	Negative	False negative	True negative	**NPV**
		Sensitivity	**Specificity**	

POSITIVE PREDICTIVE VALUE

	Disease			
Test Result		**Sick**	**Healthy**	
	Positive	True positive	False positive	**PPV**
	Negative	False negative	True negative	**NPV**
		Sensitivity	**Specificity**	

$$= \frac{TP}{TP + FP}$$

NEGATIVE PREDICTIVE VALUE

		Disease		
		Sick	**Healthy**	
Test Result	**Positive**	True positive	False positive	**PPV**
	Negative	False negative	True negative	**NPV**
		Sensitivity	**Specificity**	

$$= \frac{TN}{TN + FN}$$

SENSITIVITY

	Disease			
		Sick	**Healthy**	
Test Result	**Positive**	True positive	False positive	**PPV**
	Negative	False negative	True negative	**NPV**
		Sensitivity	**Specificity**	

$$= \frac{TP}{TP + FN}$$

SPECIFICITY

		Disease		
Test Result		**Sick**	**Healthy**	
	Positive	True positive	False positive	**PPV**
	Negative	False negative	True negative	**NPV**
		Sensitivity	**Specificity**	

$$= \frac{TN}{FP + TN}$$

MRSA NARES AND PNEUMONIA

SUPPORTING EVIDENCE FOR MRSA NARES IN PNEUMONIA

Predictive Value of Methicillin-Resistant Staphylococcus aureus (MRSA) Nasal Swab PCR Assay for MRSA Pneumonia (2014)

Population	Intervention	Outcome	Conclusion
- Patients with confirmed pneumonia (CAP or HCAP) - Nasal swab MRSA PCR test - Bacterial culture (blood or respiratory)	Calculation of NPV, PPV, sensitivity, and specificity	- **NPV: 99.2%** - **PPV: 35.4%** - Sensitivity: 88% - Specificity: 90.1%	A negative MRSA nasal swab may be reasonably used to guide antibiotic de-escalation

Antimicrob Agents Chemother. 2014;58(2):859-64

SUPPORTING EVIDENCE FOR MRSA NARES IN PNEUMONIA

Nasal Methicillin-Resistant Staphylococcus aureus (MRSA) PCR Testing Reduces the Duration of MRSA-Targeted Therapy in Patients with Suspected MRSA Pneumonia (2018)

Population	Intervention	Outcome	Conclusion
Patients initiated on vancomycin or linezolid for suspected MRSA pneumonia	Retrospective review of pharmacist-ordered MRSA PCR testing on duration of MRSA-targeted antimicrobials	- Use of MRSA nasal PCR reduced MRSA-targeted antimicrobial duration by 46.6 hours ($p<0.0001$) - No significant differences in hospital LOS, days to clinical improvement, or hospital mortality	The MRSA nasal PCR test is a powerful antimicrobial stewardship tool and greatly reduces duration of MRSA-targeted therapy without negatively impacting clinical outcomes

Antimicrob Agents Chemother. 2017 Apr; 61(4): e02432-16

2019 PNEUMONIA GUIDELINES FOR USE OF MRSA NARES

Negative test

- MRSA coverage not needed

Positive test

- Initiate MRSA-targeted therapy
- Collect blood and sputum cultures
- If negative: de-escalate

Acta Diabetol. 2019 Aug;56(8):907-921, PLoS One. 2016; 11(8): e0161658 ; Int J Low Extrem Wounds. 2019 Sep;18(3):236-246 . J Antimicrob Chemother. 2018 Jun; 73(6): 1692–1699

KNOWLEDGE CHECK

Which statistical value helps us rule out MRSA infection when MRSA nares are negative?

A. Low PPV
B. Low NPV
C. High PPV
D. High NPV

NPV OF MRSA NARES IN OTHER INFECTIONS

MERGENHAGEN ET AL. 2020

Determining the Utility of Methicillin-Resistant *Staphylococcus aureus* Nares Screening in Antimicrobial Stewardship

Population	Intervention	Outcomes	Conclusion
Patients from VA medical centers nationwide	561, 325 clinical cultures isolated from various anatomical sites taken within 7 days of MRSA nasal swab (analyzed via PCR or culture)	- NPV o **Overall: 96.5%** o Bloodstream: 96.5% o IAI: 98.6% o Respiratory: 96.1% o **Wound: 93.1%** o Urinary: 99.1% - PPV o **Overall: 24.6%**	MRSA nares screening may be a powerful stewardship tool for de-escalation and avoidance of empirical anti-MRSA therapy

Clin Infect Dis. 2020 Aug 22;71(5):1142-1148

CLINICAL QUESTION: CAN MRSA NARES SCREENING BE USED AS A DE-ESCALATION TOOL FOR DIABETIC FOOT INFECTIONS?

UTILITY OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* NARES SCREENING FOR PATIENTS WITH A DIABETIC FOOT INFECTION

MERGENHAGEN ET AL.

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

Objective

- To determine the negative predictive value of MRSA nares screening in the determination of subsequent MRSA infection in patients with diabetic foot infection

Design

- Retrospective cohort across VA medical centers from 2007-2018

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

Inclusion criteria

- ≥18 years old
- MRSA nasal swab on admission or transfer to a VA **inpatient** facility
  - PCR or chromogenic agar
- ICD code for DFI
- Subsequent cultures

Exclusion criteria

- Outpatient

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

Included cultures

Obtained after, but within 7 days of MRSA nasal swab

Classification

Superficial: swab or other site not classified as "deep"

Deep: abscess, fluid, surgical, aspirate, or bone culture

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

Primary outcomes

- NPV
- PPV
- Sensitivity
- Specificity

Secondary analysis

- Deep vs superficial
- Geographic region
- Foot vs toe culture
- 2007-2012 vs 2013-2018

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

BASELINE CHARACTERISTICS

Characteristic	Result (n=8,163)
Age, mean (SD)	65.0 (9.2)
Men, %	98.9
Nasal Screening	
PCR	72.3%
Standard culture	27.7%
Positive screening result	17.8%
Pathogen in culture	
MRSA	7.5%
MSSA	24.8%
Coagulase negative *Staphylococcus spp.*	11.5%
Enterococcus spp.	14.7%
Escherichia spp.	4.9%
Klebsiella spp.	3.1%
Morganella spp.	2.5%
Proteus spp.	7.4%
Pseudomonas spp.	6.9%
Streptococcus spp.	5.1%

RESULTS

Screening Parameter	No of isolates	% sensitivity	% specificity	% PPV	% NPV
Whole cohort	8,163	50.2	89	48.7	**89.6**
Deep culture	5,499	48.8	89.2	48.7	**89.2**
Superficial culture	2,664	53.2	88.6	48.7	**90.3**
Northeast	1,190	53.4	89.6	53.7	**89.5**
South	2,727	50.4	87.4	46.4	**89.0**
Midwest	1,658	54.1	91.9	57.8	**90.8**
West	2,588	45.7	88.6	43.6	**89.4**
2007-2012	2,947	53.4	86.4	44.5	**90.1**
2013-2018	5,216	48.5	90.5	51.7	**89.3**
Culture from foot	5,563	51.2	88.2	47.4	**89.7**
Culture from toe	2,600	48.2	90.7	51.9	**89.4**
Duplicates removed	5,403	51.8	90.0	51.0	**90.3**

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

Strengths

- Large sample size across entire US
- Consistent NPV across subgroups
- MRSA swabs taken at admission

Limitations

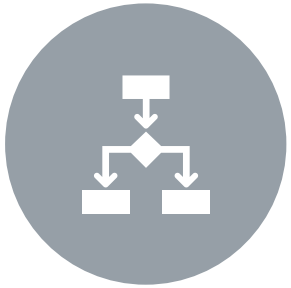
- No assessment of antibiotic exposure in relation to culture data
- Positive culture does not confirm infection
- Clinical status of patient was not assessed

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

CONCLUSIONS

Large multicenter trial with high negative predictive values of MRSA nares in relation to diabetic foot infections

VA population may lead to practitioner discomfort in generalization of results to other populations



No assessment of clinical outcomes on MRSA nares use

Reasonable subgroup analysis, with need for further evaluation of NPV compared to MRSA risk factors

Antimicrob Agents Chemother. 2020 Mar 24;64(4):e02213-19

CORRELATION BETWEEN PATIENTS WITH MRSA NARES COLONIZATION AND DIABETIC FOOT INFECTION

BRONDO ET AL.

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

Objective

- To evaluate the utility of MRSA nares to rule out MRSA in DFIs using **NPV**
- Secondary objectives:
  - Evaluate the **PPV, sensitivity, and specificity** of patients with positive MRSA nasal swabs and MRSA DFIs
- Characterize the **microbiology** of DFIs in the veteran population

Design

- Singe-site retrospective chart review from October 2013-October 2019

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

Inclusion criteria

- Age ≥18
- Admitted with a DFI
- MRSA nares test result
- Diabetic foot wound cultures (swab, wound, tissue, abscess, or bone)

Exclusion criteria

- Pregnancy
- History of MRSA infection within 1 year prior to index admission for DFI

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

MRSA nasal swab

Primarily analyzed via PCR

MRSA culture used if PCR unavailable

Culture data

Separated by location collected (bone, tissue, wound, abscess, or swab)

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

Primary outcome

- NPV

Secondary outcomes

- PPV
- Sensitivity
- Specificity

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

BASELINE CHARACTERISTICS

Characteristic	Result (n=200)
Age, mean (SD)	63 (10.5)
White	68%
African American	14.5%
Other race	17.5%
Culture type, n (%)	
Bone	127 (63.5)
Tissue	90 (45)
Wound	87 (43.5)
Abscess	29 (14.5)
Swab	10 (5.0)
Organisms grown, n (%)	
MSSA	56 (28)
MRSA	25 (12.5)
Other Gram +	34 (17.0)
Gram -	84 (42.0)
Anaerobes	22 (11.0)

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

RESULTS

Endpoint	Result
Negative predictive value	94%
Secondary endpoints	
Positive predictive value	58%
Sensitivity	56%
Specificity	94%

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

Strengths

- Higher MRSA prevalence
- Consistent NPV with Mergenhagen et al.

Limitations

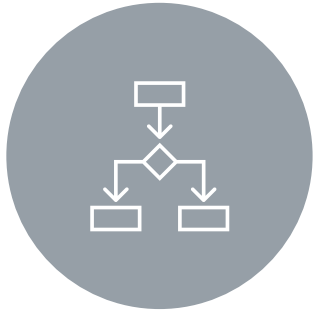
- No timeline association of MRSA nares and culture data
- Clinical status of patient was not assessed

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

CONCLUSION

Supplement to Mergenhagen et al. further replicating NPV of MRSA nares with diabetic foot infections

Local and recent data



No assessment of clinical outcomes

Small sample size limits reliability

Int J Low Extrem Wounds. 2022 Dec;21(4):502-505

CLINICAL UTILITY OF METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* NASAL PCR TO STREAMLINE ANTIMICROBIAL USE IN TREATMENT OF DIABETIC FOOT INFECTION WITH OR WITHOUT OSTEOMYELITIS

HARB ET AL.

BMC Infect Dis. 2023 May 5;23(1):297

Objective

- To evaluate the effect of MRSA nasal PCR testing on MRSA-targeted antibiotic use and **clinical** outcomes in patients with DFI

Design

- Single center retrospective quasi-experimental study

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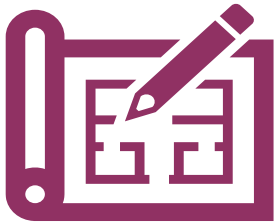
INTERVENTION



Protocol

Implemented December 2020

Local clinical pathway guiding de-escalation with MRSA nares

MRSA nares order added to vancomycin order set

Clinician and pharmacy specialist education

Groups

PRE-protocol (5/1/2019-4/30/2020)

POST-protocol (12/1/2020-11/30/2021)

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Inclusion criteria

- Age ≥18
- MRSA nasal PCR
- Culture data obtained from site of diabetic foot infection on same admission
  - Wound swab
  - Tissue
  - Abscess
  - Bone

Exclusion criteria

- History of MRSA infection within 1 year prior to index admission for DFI

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Primary outcome

- Median hours of empiric inpatient MRSA-targeted antibiotic therapy

Secondary outcomes

- Proportion of patients needing MRSA coverage added back for MRSA infection after de-escalation
- Hospital readmission
- Length of hospital stay
- Patient mortality
- Acute kidney injury

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STATISTICAL ANALYSIS

- A Wilcoxon Rank Sum test was used to assess the difference between the groups for the primary outcome.
- A sample size of 32 patients in total was estimated to meet 80% power for the primary outcome.
- For numerical secondary endpoints, Wilcoxon Rank Sum test was used to assess the difference between the groups.
- For categorical secondary endpoints, a chi-square or Fisher's Exact test was used to assess the difference between the groups.

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BASELINE CHARACTERISTICS

Characteristic	PRE (n=83)	POST (n=68)
Age, median [IQR]	66.8 [56.1-72.9]	63.7 [55.7-68.5]
Male (%)	97.6	97.1
A1c (mean)	8.3 ±2.2	8.5 ±1.9
Comorbid conditions, n (%)		
Peripheral vascular disease	27 (32.5)	22 (32.4)
Transplant	1 (1.2)	1 (1.5)
Malignancy	11 (13.2)	2 (2.9)
Osteomyelitis	36 (43.3)	36 (52.9)
Microbiologic culture, n (%)		
Swab	6 (7.2)	0
Wound	33 (39.7)	26 (38.2)
Tissue	42 (50.5)	44 (64.7)
Abscess	16 (19.2)	5 (7.4)
Bone	46 (55)	30 (44.1)
Organisms Isolated, n (%)		
MRSA	10 (12.0)	12 (17.6)
MSSA	18 (21.7)	26 (38.2)
Other Gram Positive	41 (49.3)	36 (52.9)
Gram negative	38 (45.8)	18 (26.4)
Anaerobes	14 (16.9)	8 (11.8)
Culture negative	13 (15.7)	9 (13.2)

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RESULTS

Outcome	PRE (n=83)	POST (n=68)	p-value
Primary endpoint: duration of empiric MRSA-targeted antibiotic therapy, hours, (median [IQR])	72 (27-120)	24 (12-72)	<0.01
Secondary endpoints			
MRSA coverage added back for MRSA, %	0	0	
Acute kidney injury, %	15.7	6.1	0.07
Length of stay, days (median [IQR])	8 (5-13)	9 (6.3-14)	0.32
In-hospital mortality, %	2.4	2.9	1.00
9-month readmission due to DFI, %	18.1	31.3	0.06

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RE-ADMISSIONS ASSESSMENT

Group	6-month	9-month	12-month
PRE (n=83)			
All-cause, n (%)	35 (42.2)	35 (42.2)	37 (44.6)
Due to DFI, n (%)	14 (16.8)	15 (18.1)	16 (19.3)
POST (n=68)			
All-cause, n (%)	31 (45.6)	34 (50)	36 (52.9)
Due to DFI, n (%)	19 (27.9)	21 (30.9)	22 (32.4)

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NEGATIVE PREDICTIVE VALUES

PRE

- 94%

POST

- 95%

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Strengths

- Assessed stewardship and clinical outcomes
- Consistent NPV with previous studies

Limitations

- Source control not assessed
- ED antibiotic exposure not assessed
- Antibiotics used between groups not specified

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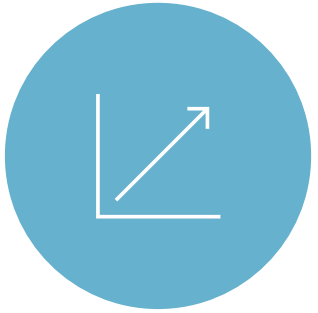
CONCLUSION

MRSA nares screening decreases length of MRSA-targeted antibiotic exposure

No statistically significant sacrifice of clinical outcomes

Further study in non-VA population is warranted with larger sample size



Further validation of high NPV

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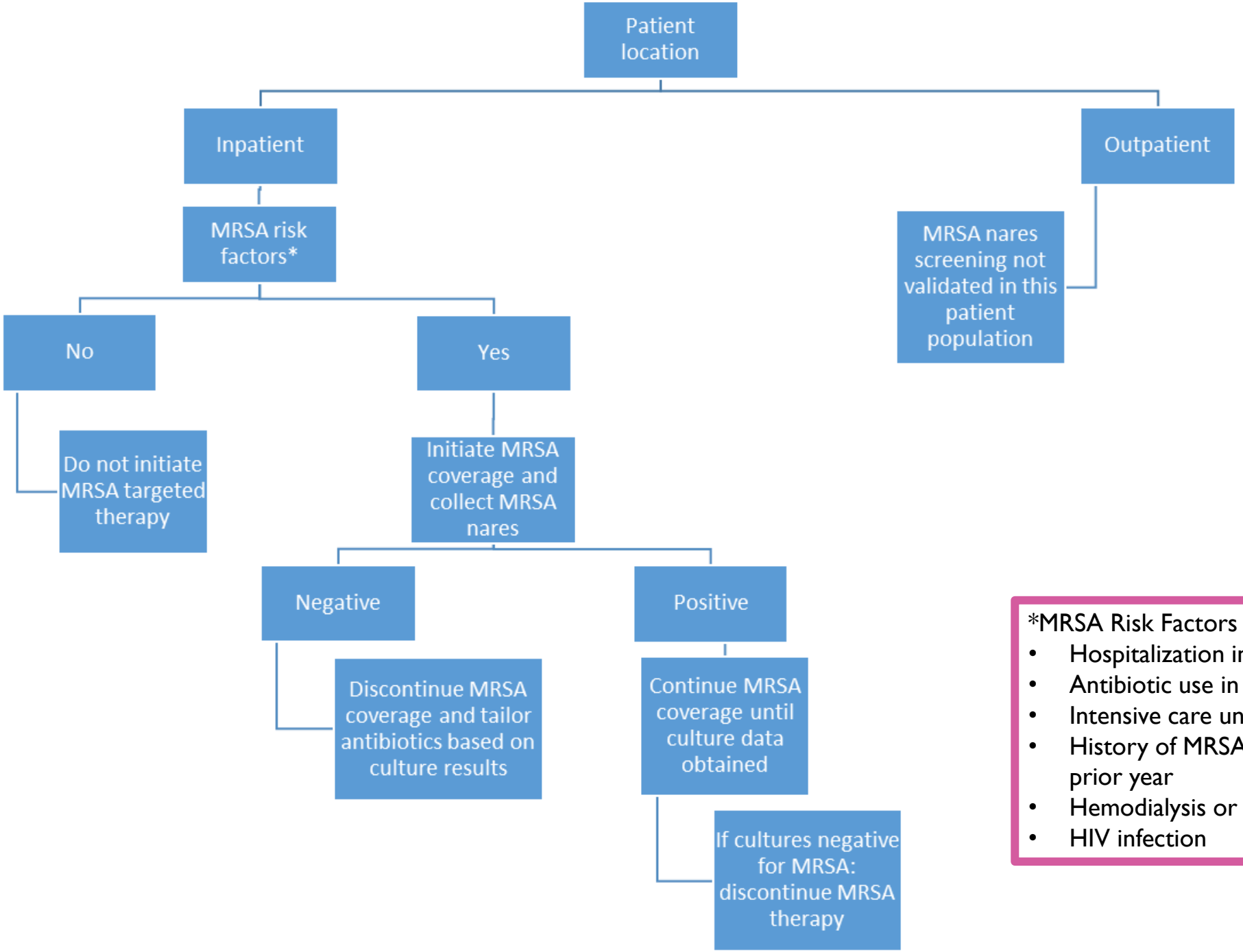
ALGORITHM



*MRSA Risk Factors

- Hospitalization in the last 90 days
- Antibiotic use in the last 90 days
- Intensive care unit admission
- History of MRSA infection within prior year
- Hemodialysis or central venous access
- HIV infection

POST-TEST QUESTIONS

POST TEST QUESTION #1

Based on current local data, what percentage of patients have diabetic foot infections that grow MRSA on culture?

A. 12-17%

B. 15-32%

C. 40-50%

D. 60-70%

POST TEST QUESTION #2

A 52 year old male is admitted to the podiatry service at your institution. He reports wearing a new pair of boots that caused a blister which has progressively worsened over the last 2 weeks. On exam, the wound is red and swollen, with invasion into the tendon, but without gangrene or ischemia. His vitals are normal and his WBC's are 13. His past medical history include T2DM, HTN, and HLD. His A1c on admission is 10.3 and he reports taking metformin 500 mg twice daily. He recently was hospitalized for diabetic ketoacidosis last month. **What is a reasonable empiric regimen to start in this patient?**

A. Piperacillin/tazobactam

B. Cephalexin

C. Vancomycin + ceftriaxone

D. Daptomycin

POST TEST QUESTION #3

A 52 year old male is admitted to the podiatry service at your institution. He reports wearing a new pair of boots that caused a blister which has progressively worsened over the last 2 weeks. On exam, the wound is red and swollen, with invasion into the tendon, but without gangrene or ischemia. His vitals are normal and his WBC's are 13. His past medical history include T2DM, HTN, and HLD. His A1c on admission is 10.3 and he reports taking metformin 500 mg twice daily. He recently was hospitalized for diabetic ketoacidosis last month. **Today is day 2 of hospitalization and he is scheduled for wound debridement tomorrow. His MRSA nares have resulted and are negative. His wound culture is still pending**. **The podiatry attending is hesitant to discontinue MRSA coverage. What could you say that might convince them to de-escalate?**

A. MRSA nares have a positive predictive value of 90-94%. It is unlikely that MRSA is a causative pathogen for this patient

B. MRSA nares have a negative predictive value of 90-94%. It is unlikely that MRSA is a causative pathogen for this patient

C. Negative MRSA nares tests mean the patient definitively does not have MRSA as a causative pathogen

POST TEST QUESTION #4

A 52 year old male is admitted to the podiatry service at your institution. He reports wearing a new pair of boots that caused a blister which has progressively worsened over the last 2 weeks. On exam, the wound is red and swollen, with invasion into the tendon, but without gangrene or ischemia. His vitals are normal and his WBC's are 13. His past medical history include T2DM, HTN, and HLD. His A1c on admission is 10.3 and he reports taking metformin 500 mg twice daily. He recently was hospitalized for diabetic ketoacidosis last month. **The attending accepts your recommendation to de-escalate. What is the empiric regimen you recommend?**

A. Vancomycin

B. Ceftriaxone

C. Aztreonam

D. Cefazolin + piperacillin-tazobactam

THANK YOU

Tina Beck, PharmD, MSCR, BCPS

- Mentor

Travis Carlson, PharmD, BCIDP

- Critiquer

CO-CURRICULAR CREDIT QR CODE

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- **Access code for February 9,2024:**
  - **Pharmacist: 322792**
  - **Technician: 728472**

  Deadline to obtain CE credit is March 22, 2024