Title

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What the Nose Knows – When Can a MRSA Nares Swab Guide Antibiotic Stewardship?

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Introduction:

Clinicians treating infections in the hospital often face uncertainty about when coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) is warranted. Though MRSA infections are associated with significant mortality,[1] anti-MRSA therapy in hospitalized patients is frequently excessive and suboptimal; prescribing patterns are often discordant with practice guidelines[2] or final culture results.[3] Strategies to rapidly de-escalate unnecessary MRSA coverage (often intravenous vancomycin) could minimize potential harms including antimicrobial resistance, nephrotoxicity, and increased pharmacy monitoring costs.[1]

The MRSA nares swab, whether PCR or culture-based, can rapidly identify whether patients are colonized with MRSA.[1] This information may support early tailoring of antibiotics, curbing overuse of vancomycin and other anti-MRSA agents. However, the utility of the nares swab depends on several factors, including MRSA prevalence, which varies with the type of infection, and also clinical features such as illness severity. Here we review how the swab may be used alongside disease prevalence and clinical factors to determine when MRSA coverage is needed for common inpatient infections.

Community Acquired Pneumonia (CAP):

The prevalence of MRSA in CAP is low, ranging from 7 to 13%.[4,5] Due to this low likelihood of disease, MRSA coverage is not routinely warranted in most

patients. The Infectious Diseases Society of America recommends empiric MRSA coverage only in certain at-risk patients, including those with prior detection of MRSA in respiratory cultures, or those who have severe disease and recent hospitalization with exposure to intravenous antibiotics.[6,5] In these more vulnerable patients where empiric MRSA coverage is reasonable, clinicians may use the MRSA nares swab to safely discontinue MRSA coverage if the test returns negative.

There is robust evidence to support using the nares swab in this manner. In a meta-analysis of over 5,000 patients, the swab's negative predictive value (NPV) exceeded 98%.[4] However, this excellent NPV is dependent on low MRSA prevalence, as the two are inversely correlated with one another.[1] MRSA prevalence in CAP from this meta-analysis was only 7 to 13%.[4] In settings with higher prevalence and/or clinical findings that raise suspicion for MRSA pneumonia (e.g., cavitary lung lesions), a negative swab result has diminished utility in excluding MRSA.[1,4]

Conversely, since a test's positive predictive value (PPV) directly correlates with disease prevalence, the swab's PPV in CAP is poor, ranging from 16% when MRSA prevalence is 3% to 4445% with a prevalence of 10%.[5,6] With this low PPV, clinicians should not use a positive swab result as the sole justification to add MRSA coverage to treat CAP in an otherwise hemodynamically stable patient without other risk factors for MRSA.

Skin and Soft Tissue Infections (SSTI):

Non-purulent SSTI (i.e., SSTI without abscesses, furuncles, or carbuncles), are caused by beta-hemolytic *Streptococcus* in over 90% of cases.[7] MRSA prevalence is sufficiently low in this setting, such that empiric treatment should target *Streptococcal* species in hemodynamically stable patients irrespective of the nares swab result. As such, we do not recommend sending a nares swab or starting empiric MRSA coverage in stable patients admitted with non-purulent cellulitis.

The nares swab should also not be used in purulent SSTI, where *S. aureus*, especially MRSA, is the predominant pathogen.[7] In one systematic review of skin abscesses, MRSA accounted for 49% of all cases.[8] With this high prevalence, the swab's NPV is poor, ranging from 65-76%, making a negative swab insufficient to justify withholding MRSA coverage.[1] The PPV in this scenario is as high as 94%.[1] However, finding purulence on exam already suggests a high likelihood of MRSA, and empiric treatment for MRSA should be initiated. A nasal swab is not indicated ~~since~~ as neither a positive nor a negative result ~~do not~~will add actionable information.

Diabetic Foot Infections:

Clinicians caring for patients with diabetic foot infections usually face complex antimicrobial decisions, especially in the absence of prior culture

data. Empiric MRSA coverage is often continued until definitive culture results come back.[9] The nares swab holds potential to guide initial therapy before these results become available. When local antibiograms suggest a low to moderate local MRSA prevalence (e.g. <15%), the swab maintains an excellent NPV, exceeding 90%.[9] In these settings, clinicians may discontinue MRSA coverage unless their patient is severely ill. This high NPV could be especially impactful in settings where a deep wound culture or bone biopsy cannot be easily arranged. However, as local MRSA prevalence increases, the swab's NPV decreases. Once local MRSA prevalence reaches 30% or higher, the swab's NPV is 80% at best.[9] With this much diagnostic uncertainty, clinicians should not rely solely on a negative result to guide antibiotic decisions, and instead should await results of deep tissue sampling.

Urinary Tract Infections (UTI):

MRSA prevalence in UTI is exceedingly low at only 0.5 to 1%.[10] Given this extremely low likelihood of disease, the nares swab should not be ordered as neither a negative nor positive result would change management. While a negative swab result theoretically rules out MRSA with a NPV of nearly 100%, it is largely irrelevant to clinical practice as empiric MRSA coverage is rarely chosen for UTI. Even when a nasal swab is positive, the post-test probability of MRSA UTI remains exceedingly low due to its baseline low prevalence.[1]

Conclusions:

Identification of MRSA colonization holds promise as a stewardship strategy to reduce morbidity and costs associated with overuse of vancomycin and other therapies directed against MRSA. Existing literature suggests that the swab is most useful in rapidly ruling out MRSA, allowing clinicians to discontinue MRSA coverage in areas of low to moderate MRSA prevalence (**Figure**).[1,4,9] Positive swab results are generally unhelpful and should not be used to justify changes in antimicrobial management. Importantly, clinicians must remember that the prevalence of MRSA in a particular infection is driven by the frequency of *S. aureus* infection at that anatomic site, which is relatively constant across institutions, and the proportion of *S. aureus* isolates which are MRSA (i.e., local prevalence), which varies across institutions and can be ascertained by review of local antibiograms. When ~~local MRSA prevalence~~pre-test probability of MRSA is exceedingly low or high, or when consequences of a missed MRSA infection are unacceptably high, clinicians should avoid using the nares swab altogether.

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Conflicts of Interest Disclosure:

Dr. Wu reports receiving personal fees from Glass Health and being an investor in Glass Health outside the submitted work.

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