KY Antimicrobial Stewardship Innovation Consortium

Clinical Practice Review

KY-MRSA: A Comprehensive Review of Methicillin-resistant *Staphylococcus aureus* PCR Nasal Screening Practices across Nine Institutions in Kentucky

On behalf of the Kentucky Antimicrobial Stewardship Innovation Consortium (KASIC)

Nasal methicillin-resistant *Staphylococcus aureus* (MRSA) polymerase chain reaction (PCR) is commonly used as a stewardship effort to de-escalate anti-MRSA antibiotic by many health systems. The KASIC Advisory Board members in Kentucky provide their nasal MRSA PCR screening protocols and guidelines which may offer other stewardship programs a framework to customize their own protocols and guidelines.

Introduction

The Centers for Disease Control and Prevention (CDC) considers methicillin-resistant *Staphylococcus aureus* (MRSA) as a serious threat because it can cause difficult-to-treat infections with high mortality.[1] Current pneumonia guidelines recommend empiric MRSA coverage for community-acquired pneumonia (CAP) in patients with risk factors (prior respiratory isolation or recent hospitalization receiving parenteral antibiotics), hospital-acquired (HAP)/ventilator-associated pneumonia (VAP) in patients treating in units where >10-20% of *S. aureus* isolates are methicillin resistant which essentially means all patients receive empiric anti-MRSA in practice.[2,3] Anti-MRSA activity is also recommended empirically in purulent skin soft tissue infection, bone and joint infection, central nervous system infection, and surgical prophylaxis in patients colonized with MRSA.[4,5,6,7] While this empirical approach helps cover for potential invasive MRSA infection, prolonged MRSA coverage can lead to unnecessary exposure, higher risk for developing resistance such as vancomycin-resistant *Enterococcus* (VRE), adverse reactions, longer hospital stays, and higher treatment costs.[8] Therefore, finding reliable diagnostic methods to safely discontinue anti-MRSA therapy is essential in antimicrobial stewardship programs.

S. aureus often colonizes in the human nares, and its colonization frequently precedes the onset of clinical infection.[8] There are two types of nasal MRSA swabs used in clinical practice to detect MRSA colonization: culture and polymerase chain reaction (PCR).[8] The advantage of nasal MRSA PCR is its faster turnaround time and its higher sensitivity compared to nasal MRSA culture, but comes at an increase cost.[8] Recent literature has shown that nasal MRSA PCR can be utilized as an antimicrobial stewardship tool to de-escalate anti-MRSA therapy in pneumonia with limited studies suggested its role for non-pneumonia indications.[8] Although some institutions have shared their nasal MRSA PCR protocol and experience, no study has provided a comprehensive review of MRSA PCR nasal screens practice across multiple sites.[9,10] This gap in information creates challenges for new stewardship programs to develop practical nasal MRSA PCR protocols/guidelines as staffing and clinical practice models vary between different types of institutions (academic medical centers vs community hospitals; large health-system vs small hospitals). This study aims to summarize and emphasize the similarities and differences in nasal MRSA PCR practices among various institutions in Kentucky.

Methods

The Kentucky Antimicrobial Stewardship Innovation Consortium (KASIC) was established in 2022 with a goal of promoting optimal antimicrobial use across the state. KASIC included an Advisory Board, consisting of 26 pharmacists who practice in established antimicrobial stewardship program, and a network of antimicrobial stewardship leads at all adult hospitals and long-term care facilities throughout Kentucky. KASIC asked the Advisory Board members to share their nasal MRSA PCR swab protocols and guidelines. Protocol was defined as a policy allowing pharmacists to order a diagnostic test if a patient meets pre-determined criteria without an order from a provider. Guideline was generally considered a recommendation but did not grant pharmacist autonomy to place an order per protocol. These documents were subsequently evaluated and analyzed to identify the similarities and differences in how various institutions in Kentucky used nasal MRSA PCRs.

Results

Nine of ten institutions (90%) represented by the Advisory Board responded to KASIC's request to share their nasal MRSA PCR practice. Among those, 7/9 (77.8%) were adult community health-systems with licensed beds ranged from approximately 200 to 2300, 1/9 (11.1%) was an adult academic health-system with > 1,300 beds, and 1/9 (11.1%) was an academic health-system comprised of adult hospitals with total beds > 1,000 and a 205-bed pediatric hospital.

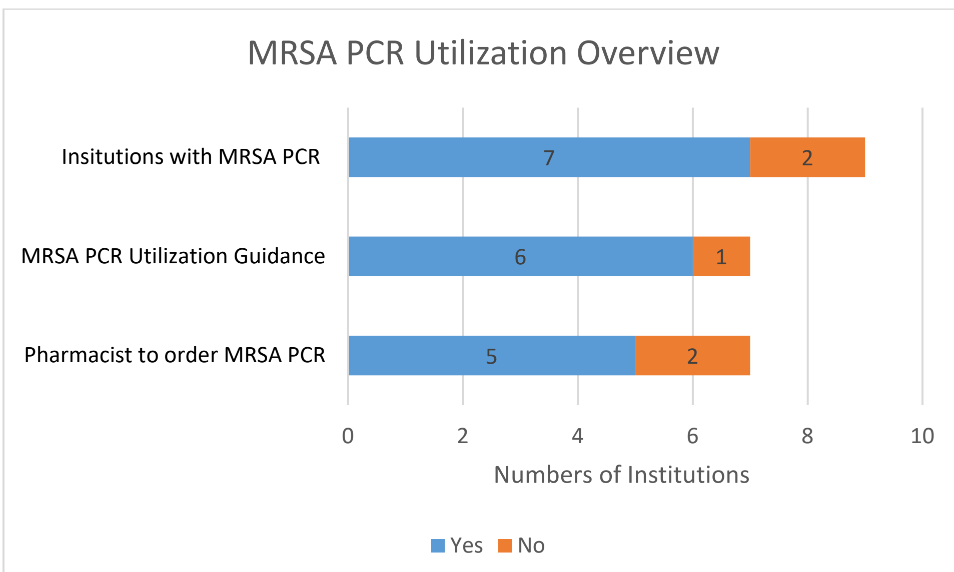

Figure 1. Number of institutions with MRSA PCR utilization

Most institutions employing MRSA PCR nasal swabs established either protocols (5/7; 71.4%) or guideline (1/7; 14.3%) to ensure appropriate use. One institution, without an official policy, noted their pulmonologist would use MRSA PCR nasal screen as needed. All six institutions with established guidelines/protocols endorsed the use of nasal MRSA PCR for pneumonia, with 3/6 (50%) using it for non-pneumonia indications in addition to pneumonia. Among the five institutions with MRSA PCR protocols, 3/5 (60%) allowed pharmacists to order a MRSA PCR upon initiation of IV vancomycin or linezolid for pneumonia. 1/5 (20%) enabled pharmacists to order a MRSA PCR no later than 48 hours after MRSA therapy initiated for all indications except central nervous system (CNS), and 1/5 (20%) endorsed pharmacists to order a MRSA PCR within 72 hours of anti-MRSA therapy initiation for certain indications (pneumonia, bone and joint, skin soft tissue infection, and intra-abdominal infection) provided no presence of abscess. Notably, no institutions permitted pharmacists to discontinue anti-MRSA therapy per protocol based on a negative MRSA nasal PCR result**.** There was one healthcare system established nasal MRSA PCR guidelines for both adult and pediatric patients. In adults, a nasal MRSA PCR was recommended for HAP/VAP. For pediatric patients, this institution suggested using nasal MRSA PCR for complicated CAP (parapneumonic effusion or empyema), preseptal and orbital cellulitis.

Diagnostic Stewardship Practice

Inquiries were made regarding diagnostic stewardship efforts of MRSA PCRs. Several institutions provided guidance for MRSA PCR nasal screen based on a patient's recent MRSA colonization/de-colonization status. Two institutions specifically excluded patients from pharmacist MRSA PCR protocols if patients have existing nasal MRSA PCR result within last 7 days and/or positive MRSA cultures within last 7-14 days. Another healthcare system recommended utilizing available MRSA screen result if obtained within a week prior to pneumonia diagnosis and advised against using MRSA PCR nasal screen in patients having nasal MRSA de-colonization within last 30 days. The abbreviated protocols/guidelines can be found in the Appendix.

Discussion

This review identifies that the majority of institutions employing MRSA PCR nasal screens have established protocols allowing pharmacists to order the test without an order from a provider. MRSA PCR nasal screens were used universally by these institutions to guide pneumonia therapy. Compelling evidence supporting the use of MRSA PCR in pneumonia drives its widespread adoption in Kentucky hospitals' policies. The performance of MRSA nasal swabs to predict MRSA pneumonia was reviewed in a meta-analysis of 22 studies (11 with PCR, 4 utilizes nasal MRSA cultures, one has both PCR and cultures, and 6 do not specify MRSA screen method) reported a pooled sensitivity of 70.9%, specificity of 90.3%, positive predictive value (PPV) of 44.8%, and negative predictive value (NPV) of 96.5% for all pneumonia.[11] In this analysis, nasal MRSA culture and PCR swabs had higher sensitivities in CAP compared to VAP (85% vs 40.3%).[11] PPV of MRSA swab remained low regardless the type of pneumonia but has high NPV for both CAP and VAP (98.1% and 94.8% respectively).[11] Due to low PPV and high NPV of nasal MRSA swabs (culture and PCR) across different types of pneumonia, nasal MRSA PCR is valuable when negative for de-escalating therapy in pneumonia but less helpful when the result is positive. Although KASIC did not request the Advisory Board to share data on impact of MRSA PCR protocols at their institutions, as it was outside the scope of this manuscript, other stewardship programs have reported a reduction in vancomycin duration after implementing pharmacist-led MRSA PCR nasal screening protocols.[9,10] Additionally, in a retrospective cohort study at Stanford HealthCare, no difference in clinical outcomes including hospital length of stays (LOS), ICU LOS, and in-hospital mortality was found despite shortened vancomycin duration in post-MRSA PCR protocol period.[9] Similar outcomes were observed in a prospective study at Barnes Jewish Hospital, which used MRSA nasal culture to de-escalate empiric anti-MRSA therapy for critically ill patients with suspected pneumonia.[12]

Despite the extensive evidence supporting the use of MRSA PCR for pneumonia, the evidence for nasal MRSA PCR in patients who developed complications from pneumonia (parapneumonic effusion, lung empyema, or lung abscess) remains limited. A retrospective cohort study at St's Mary Medical Center in Wyoming evaluated the performance of nasal MRSA PCR in 93 patients with lung empyema and 46 patients with lung abscess.[13] This study found 80% sensitivity, 84% specificity, 42% PPV, and 97% NPV for empyema and 0% sensitivity, 90% specificity, 0% PPV, and 90% NPV for lung abscess.[13] No studies examined nasal MRSA in adult patients with parapneumonic effusion. The use of nasal MRSA PCR to rule out clinical MRSA infection in adult patients with complicated lung infections warrants caution. In Kentucky, one institution specifically had presence of abscess as an exclusion criterion in their nasal MRSA PCR pharmacist protocol.

Unlike pneumonia, only a few institutions in Kentucky have adopted MRSA PCR for non-pneumonia indications, partly due to limited data.[8] Among non-pneumonia indications, the data is most consistent for intra-abdominal infection with a few retrospective cohort studies reported NPV of 98%.[8] The performance of MRSA PCR for SSTI is more heterogeneous depending on its location (non-extremity vs extremity), presence of ulcers, and presence of prosthetic implant.[8] There were no independent studies assessing performance of nasal MRSA PCR in urinary tract infection (UTI).[8] It should be noted that MRSA is extremely uncommon cause for UTI, and thus the use of MRSA nasal PCR is likely low benefit.[8] No study investigated the performance of MRSA nasal PCR in central nervous system infections (CNS).[8] Given high mortality risk of CNS infections and the use of anti-MRSA agent to target other non-MRSA pathogens (such as drug-resistant *Streptococcus pneumoniae*), the use of nasal MRSA PCR could not be recommended at this time.[8] This also aligned with practice in Kentucky, as no institutions endorsed MRSA PCR nasal screen to guide therapy for CNS indications.

An important aspect of MRSA PCR protocol/guidance was determining the utility of MRSA PCR in patients receiving anti-MRSA therapies or MRSA de-colonization. Only two institutions in Kentucky limited the ordering of MRSA PCR to within 48-72 hours of initiation of anti-MRSA antibiotics whereas another institution suggested avoid using MRSA PCR nasal screen in patients undergoing de-colonization within last 30 days. This was in part due to scarce data examining durability of MRSA PCR positivity while patients on active MRSA antibiotics or undergo de-colonization. A study conducted at Upstate University Hospital demonstrated that a positive nasal MRSA PCR typically persisted after 48-96 hours of continuous systemic anti-MRSA antibiotics.[14] On the other hand, a retrospective observational cohort study showed reduced NPV of MRSA PCR nasal screen for pulmonary infections after mupirocin administration.[15] Decisions to order MRSA PCR nasal screen routinely in patients receiving anti-MRSA therapies and/or MRSA de-colonization should be carefully evaluated to avoid unnecessary laboratory expenditures.

Another aspect in MRSA PCR protocol/guideline to deliberate is the necessity of repeating MRSA PCR nasal screening. Two institutions excluded patients who had previous MRSA PCR result and MRSA in respiratory cultures within 7-14 days from their pharmacist MRSA PCR protocols. A study comprising of 736 patients from a community health-system examined NPV of nasal MRSA PCR based on the time between nasal PCR and respiratory samples. NPV of nasal MRSA PCR screen remained high regardless of the time elapsed between nasal MRSA PCR and respiratory culture collection.[16] The NPVs were 93.8% in $\leq$ 24 hours group (n=316), 98.6% in 25 to 48 hours group (n=80), 95.7% in 49 hours to 7 days group (n=190), 92.9% in 8-14 days group (n=99), and 95.5% in > 14 days group (n=51).[16] Another study in Utah found conversion rate from negative MRSA PCR nasal swab to positive within 14 days was rare (0.9%).[17] These data suggest that repeating nasal MRSA PCR within 14 days of a prior test might not be necessary, and may serve as an additional factor to consider when developing MRSA PCR nasal screen protocol/guideline.[16,17]

The use of nasal MRSA PCR has become a widely adopted tool in antimicrobial stewardship, and guidelines and protocols are critical factors in its successful integration. Allowing all pharmacists—not just those in stewardship roles—to order MRSA nasal PCR can streamline the process and ensure quicker results. While no institutions in Kentucky currently permit pharmacists to discontinue anti-MRSA therapy based on a negative nasal MRSA screen without discussion with provider, it would be beneficial to consider protocols in the future that enable pharmacists to do so for specific indications, such as pneumonia. This potentially can facilitate more timely clinical interventions.

Conclusion

This study represents the first statewide review of MRSA PCR nasal screen practice revealing variations across multiple institutions. It can serve as a resource for stewardship programs by providing a range of approaches and allowing them to adapt elements that align with their local needs and operational feasibility into their nasal MRSA PCR protocol/guideline.

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Appendix

PROTOCOL 1

SCOPE: Inpatient Care

PURPOSE: The purpose of this policy is to allow the pharmacist to order a methicillin resistant Staphylococcus aureus (MRSA) nares polymerase chain reaction (PCR) as part of a System-wide antimicrobial stewardship initiative to reduce antibiotic use and adverse effects in patients started on therapy.

DEPARTMENTS AFFECTED: Pharmacy

POLICY: Pharmacists may order an MRSA nares PCR on adult patients within 48 hours of the start of antibiotics when a provider has ordered vancomycin, linezolid, or any other agent for the purposes of treating MRSA. This policy applies to antibiotics started for all antibiotic indications, excluding central nervous system (CNS) infections and surgical prophylaxis.

PROCEDURE:

A. When a provider orders an anti-MRSA agent for the purpose of treating MRSA, the pharmacist may order an MRSA nares PCR on adult patients, preferably within 24 hours, but no later than 48 hours beyond the start of anti-MRSA therapy as part of a diagnostic workup to help rule out MRSA as the potential infectious cause, excluding CNS infections.

B. The pharmacist will assess the results and discuss with the team. If the MRSA nares PCR is negative, the pharmacist will then discuss the results, clinical situation, and potential antibiotic de-escalation with the provider

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PROTOCOL 2

POLICY: Appropriate cultures of blood (2 sets), sputum, urine, wounds, and normally sterile bodily fluids should be obtained BEFORE the institution of antimicrobial therapy. If order received for restricted antibiotic without order for appropriate cultures, the clinical pharmacist processing the order may enter an order to obtain the appropriate cultures but should not cause an excessive delay (>1 hour to initiation of antimicrobial agent), (i.e. blood cultures should be ordered "stat"). Other diagnostic tests may be ordered by a pharmacist to assist with opportunities for antimicrobial de-escalation (e.g. procalcitonin, urine antigens, etc.).

PROCEDURE: Pharmacists will order MRSA nasal swab when vancomycin or linezolid is ordered with clinical indication of pneumonia.

PROTOCOL 3

POLICY: Pharmacists may order an MRSA PCR swabs on patients when provider consult pharmacy for vancomycin or linezolid for pneumonia.

PROTOCOL 4

PURPOSE: To outline the responsibilities of clinical pharmacists when consulted to dose vancomycin for pneumonia.

POLICY:

Responsible Persons: All Clinical Pharmacy Staff

GUIDELINES:

1. Providers are required to enter indications for antimicrobials per hospital policy.
2. When consulted to dose vancomycin specifically for pneumonia in adult patients only, clinical pharmacists should follow the outlined procedures
3. Exclusions:
    a. Patients with an existing nasal MRSA PCR swab within the last 7 days
    b. Confirmed MRSA in respiratory or nasal culture within the last 14 days

PROCEDURE:

1. When consulted to dose vancomycin for pneumonia, pharmacists should order a nasal MRSA PCR swab. Orders should be entered under the consulting provider and signed as "Per Pharmacy Consult (No Cosign Required)."
    a. See Guidelines, Sec. 3 for exclusions
2. Negative results should be relayed to attending provider by a clinical pharmacist within 24 hours of final result.

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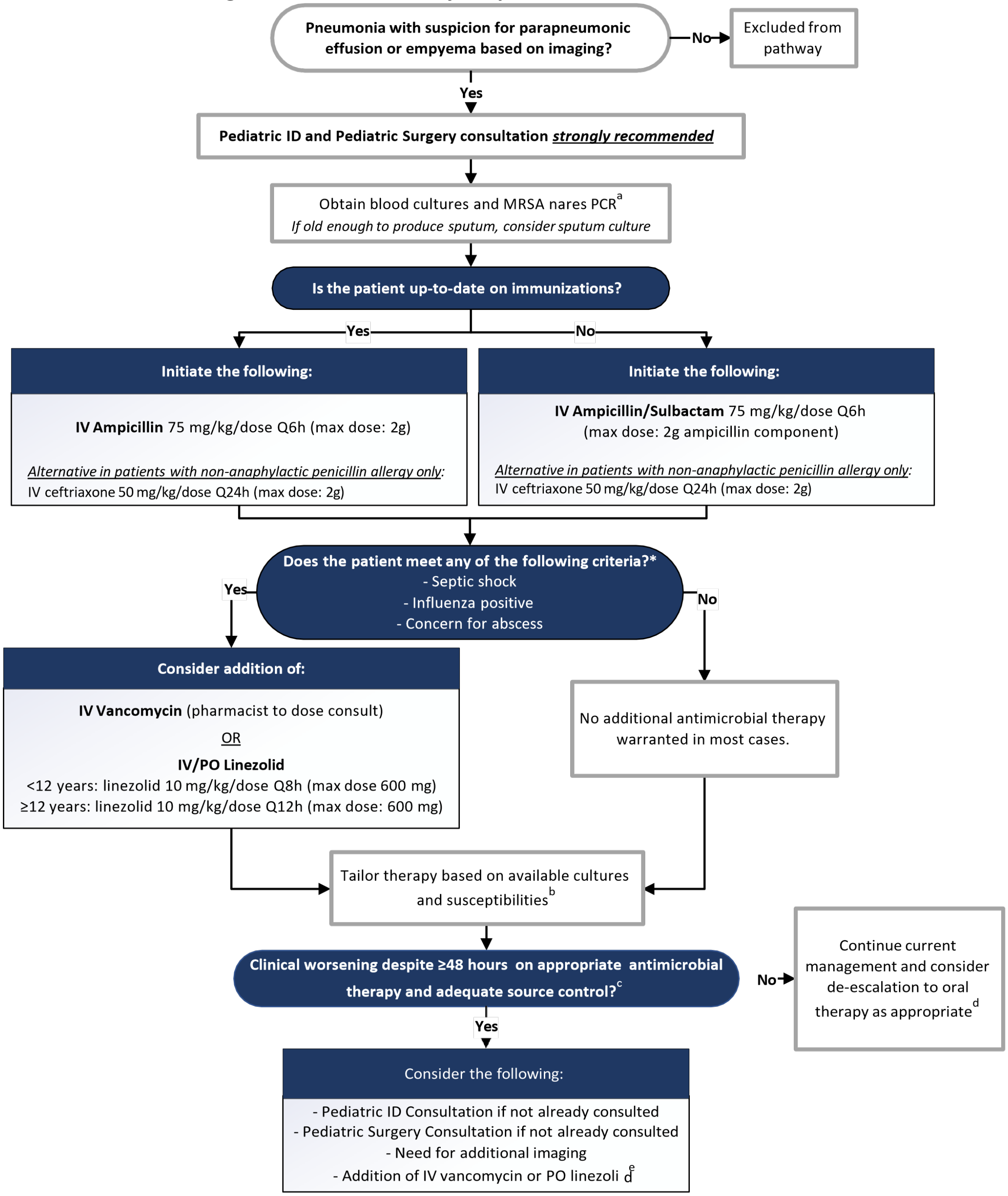
GUIDELINE 1

Guideline for the Management of Community-Acquired Pneumonia in Pediatrics



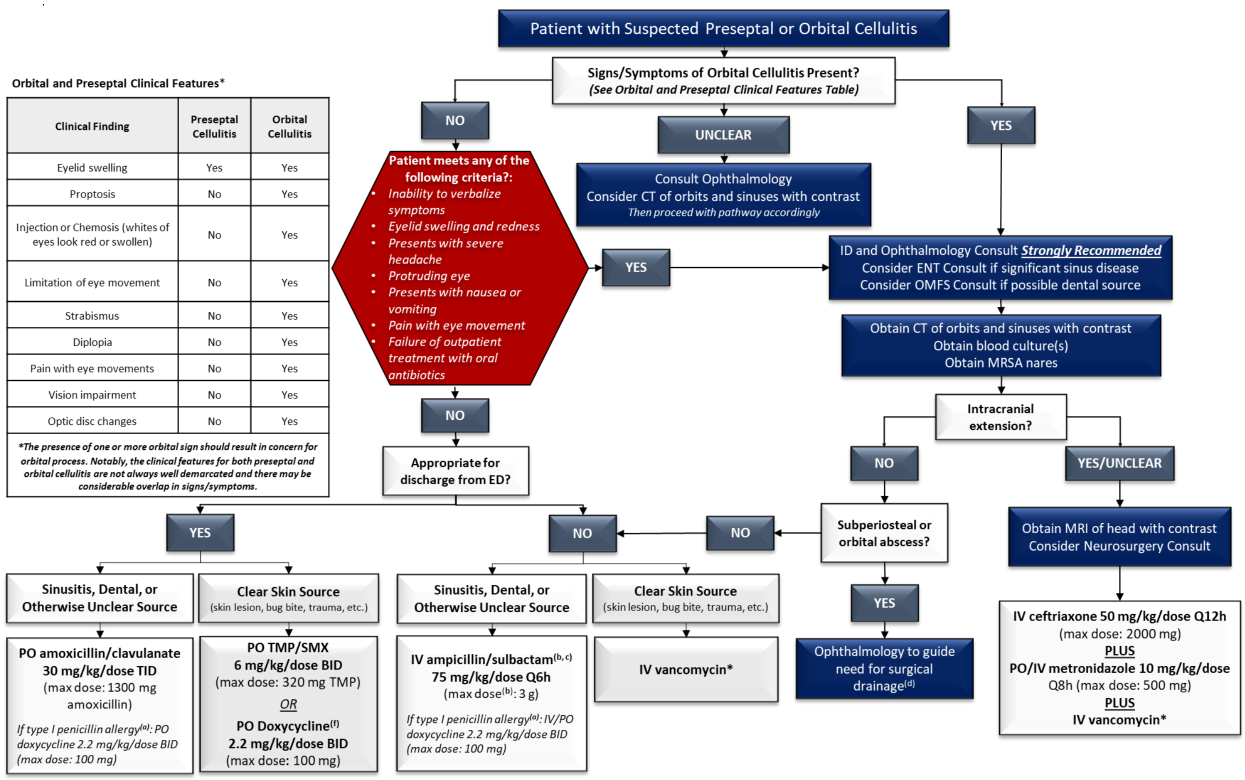
a: MRSA nares PCR has very high negative predictive value and may be utilized to guide discontinuation of MRSA therapy. This diagnostic does ***not*** have high positive predictive value. **b:** This algorithm is intended to provide guidance on appropriate *empiric* therapy. Therapy should be tailored based on final cultures and susceptibilities. **c:** Adequate source control defined as surgical or procedural drainage of effusions. **d:** Transition from IV to PO may be considered following chest tube removal in patients clinically improving and able to tolerate oral therapy. Oral transition to amoxicillin is recommended, even when treated empirically with IV ceftriaxone. **e:** The addition of IV vancomycin or linezolid may be considered to provide coverage of MRSA in patients with continued worsening following >48 hours of appropriately selected and dosed antibiotics when all of the following criteria have been met: (1) adequate source control has been assured, (2) cultures are unavailable, and (3) MRSA nares PCR positive.

Management of Pediatric Patients with Suspected Preseptal or Orbital Cellulitis

Orbital and Preseptal Clinical Features*

Clinical Finding	Preseptal Cellulitis	Orbital Cellulitis
Eyelid swelling	Yes	Yes
Proptosis	No	Yes
Injection or Chemosis (whites of eyes look red or swollen)	No	Yes
Limitation of eye movement	No	Yes
Strabismus	No	Yes
Diplopia	No	Yes
Pain with eye movements	No	Yes
Vision impairment	No	Yes
Optic disc changes	No	Yes

The presence of one or more orbital sign should result in concern for orbital process. Notably, the clinical features for both preseptal and orbital cellulitis are not always well demarcated and there may be considerable overlap in signs/symptoms.



GUIDELINE 2

Nosocomial Pneumonia Guideline

MRSA Nasal Screening

- MRSA PCR-based nares screening should be utilized in patients with HAP and VAP to assist in the de-escalation of MRSA targeted antibiotics (for example, linezolid or vancomycin).
  - Background: MRSA is a common colonizer of the nares. In a 2018 meta-analysis, the negative predictive value (NPV) for MRSA pneumonias was found to be 96.5%.[4] Clinical outcomes, including mortality rates, have been noted to be similar among patients with therapy de-escalations derived from MRSA nasal screens.[4] The evidence is strongest in patients with HAP, where the evidence in VAP remains less clear as MRSA can be introduced by an alternative route (artificial airway). Screening is still recommended in VAP as NPV has been reported to be 94.8%; however, it is important to take an individualized approach when considering de-escalating in this population (consider hemodynamic stability, history of MRSA infection etc.).[4]
  - Considerations
    - PCR-based screening is preferred. Culture-based screens are performed in the ICUs on a weekly basis and may be used if available.
    - MRSA screen results can be utilized if known within a week prior to pneumonia diagnosis.[5]
    - MRSA nares screens do not have high positive predictive value in the diagnosis of MRSA pneumonia and should only be used as a marker for de-escalation.[1]
      - If MRSA nares PCR is positive, follow respiratory culture for de-escalation
    - Screening should not be used for therapy decisions in patients with recent (within 30 days) nasal MRSA decolonization. This occurs in pediatric and adult patients with a foley catheter, central line, or history of MRSA, as well as all ICU patients.
    - Nasal screening *may* occur after initiation of therapy as parenteral antimicrobials are ineffective at clearing nasal colonization and MRSA persists in the respiratory tracts for the first few days of therapy.[6]