## Frequently Asked Questions About MRSA PCR Nasal Screening

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1. What is the difference between the nasal culture and PCR? Why do we run both on some patients?

The MRSA nasal culture is currently being performed as a state-mandated screening for certain patients thought to be at high risk for MRSA colonization.<sup>1</sup> Aside from data collection for surveillance and reporting, however, little is done clinically with this screening data, as patients are only placed in contact isolation if they have an active MRSA infection. Thus, from an operational standpoint, a culture is performed as very high sensitivity and fast turn-around time are not necessary for those purposes. The MRSA nasal PCR is also a screening test for MRSA colonization in the nares, but this test will be used to identify pneumonia patients at low risk for having MRSA as the causative organism, as multiple studies have shown that the PCR has >98% negative predictive value in this population.<sup>2-4</sup> The PCR has been shown to have equal or higher sensitivity to the culture, most notably in patients who are currently on anti-MRSA antibiotics as the PCR can also detect DNA from non-viable organisms.<sup>5</sup> The PCR also can be performed in a matter of hours,<sup>6,7</sup> allowing for earlier discontinuation of anti-MRSA antibiotics in patients with a negative result compared to use of MRSA culture.<sup>8-10</sup>

Some patients will have both studies done as the MRSA culture for screening is performed at the time of admission or transfer in or out of the ICU by state law. The MRSA PCR can be performed at the same time as mandated screening if the patient has pneumonia as the cause for admission or transfer and is started on empiric vancomycin, as the PCR result will return much faster. The PCR can also be performed separately from the screening culture if the patient develops pneumonia in the hospital, even if they were screened with the MRSA culture earlier in the hospitalization, unless the culture was performed within the past 7 days and was positive.

2. What if the nasal PCR is performed days after vancomycin/linezolid has been on board? Can we reliably interpret the results?

The sensitivity of the PCR is likely reduced in this setting, though it is difficult to say by how much. Within the first 24-48 hours the reduction in sensitivity appears to be limited based on published literature;<sup>5</sup> however, beyond that timeframe, the sensitivity may be significantly reduced and the reliability of the test compromised, though recent studies suggest that systemic antibiotics alone do not eliminate upper respiratory colonization with *S. aureus* in ventilated patients.<sup>11-12</sup> If respiratory cultures were also obtained at the time antibiotics were started, it may be prudent to make the decision on descalation based on those culture results and the patient's clinical response rather than on the MRSA PCR result alone.

3. My patient started vancomycin and piperacillin/tazobactam for suspected pneumonia, has clinically improved, but the nasal MRSA PCR resulted positive. She wasn't able to provide sputum for a respiratory culture. Should I continue vancomycin?

The decision to de-escalate should be made clinically in this situation. The MRSA PCR is unhelpful in predicting the likelihood of MRSA pneumonia when positive due to the frequency of colonization of the upper airways with MRSA and the infrequency of true MRSA pneumonia.<sup>13,14</sup> The PCR only has a positive predictive value for MRSA pneumonia of around 30%,<sup>2-4</sup> meaning a patient with pneumonia and a positive PCR is still more likely to have a different causative organism rather than MRSA. Clinically, MRSA pneumonia tends to be aggressive with significant local tissue destruction, which typically allows for positive culture results, and patients are often quite ill and improve much more slowly.<sup>15</sup> So, in general, a patient who has improved quickly and was never making sputum is less likely to have had MRSA as a causative organism and vancomycin can likely be discontinued after 48 hours or so. The MRSA PCR is this case likely represents colonization.

4. My patient's nasal MRSA PCR is negative, but the patient was just started on pressors. Is it safe to de-escalate vancomycin? There are no respiratory cultures.

The MRSA nasal PCR is most helpful in patients with a highly suspected or definitive pneumonia as colonization in the nares is correlated with presence elsewhere in the respiratory tract. It is less helpful when there is no definitive source, as patients may be infected with MRSA due to colonization at sites other than the nares, such as at a central line insertion site. If a patient is critically ill, it also may be imprudent to de-escalate immediately even with a negative nasal PCR and a clear diagnosis of pneumonia as the consequences of a false negative may be too significant in clinically tenuous patients. In this setting, it may be reasonable to wait 24 hours to evaluate for clinical improvement or for additional culture results to guide de-escalation. That being said, de-escalation of vancomycin in response to a negative MRSA PCR has been studied in patients admitted to the ICU with nosocomial pneumonia and patients who were de-escalated had a shorter ICU length-of-stay despite similar SOFA scores in one study,<sup>9</sup> though this may have been due to bias based on severity of illness or clinical concern for MRSA pneumonia.

5. My patient has febrile neutropenia. We don't know the source so sent pan-cultures and a nasal MRSA PCR. The nasal PCR returned negative. Was this an appropriate use of the test and how do we use this result?

No literature supporting the use of MRSA nasal PCR to guide therapy in treatment of febrile neutropenia has been identified. In the absence of a clear site of infection, these patients are generally febrile due to gut translocation of gram-negative organisms, and gram-positive infections are more likely to be a result of central line infections rather than an entity such as MRSA pneumonia. It is not recommended that MRSA nasal PCRs be obtained in this patient population, and, if performed, there is no guidance available on how to effectively use this data to alter antimicrobial coverage. Current IDSA guidelines do not recommend use of vancomycin as part of initial therapy for uncomplicated febrile neutropenia, and de-escalation should be done in response to blood culture results and clinical status if vancomycin is used empirically.<sup>16</sup>

6. Any limitations in use of this test in lung transplant patients? Chest tube prophylaxis? Immunocompromised patients?

There is no reason to suspect that the test would not have similar performance characteristics in transplant and other immunocompromised patients as the detection of MRSA genetic material is not dependent on the immune status of the patient. However, it would be reasonable to base de-escalation on MRSA PCR result plus clinical improvement in these populations, especially if they are still early in their post-transplant course or highly immunosuppressed, given the serious consequences of a false negative result. When vancomycin is used for "chest tube prophylaxis," the goal is to prevent infection at the chest tube insertion site and in the pleural space, and the risk of MRSA colonization at these sites may not be modified significantly by the absence of MRSA in the nares. MRSA nasal PCR should not be performed if the only reason for vancomycin use is chest tube prophylaxis.

7. Can nasal MRSA colonization be used to rule in/out MRSA infection at other body sites?

MRSA colonization in the nares is associated with colonization elsewhere in the body,<sup>17</sup> but a negative result from the nares does not definitively rule out the presence of MRSA elsewhere.<sup>18,19</sup> It is not recommended that MRSA nasal PCR be obtained to assess the risk of MRSA as the causative organism in patients with suspected infections outside of the respiratory tract.

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