Introduction

• Staphylococcus Aureus is a frequent colonizer of the skin and mucosa of humans and animals.
• It is present in the anterior nares of up to 30% of the healthy human population and can produce a wide variety of diseases.
• It has a unique ability to develop antibiotic resistance and this reflects an extraordinary capacity to adapt and survive in a great variety of environments.

• Molecular and genetic dissection of S. aureus has revealed a great number of surface adhesins, which mediate adherence to and colonization of target tissues, and secreted enzymes and toxins that are responsible for invasion and distant disease.
• S. aureus harbors a large number of mobile genetic elements from exogenous origin which contain specific determinants responsible for disease and antibiotic resistance.
Antibiotic Resistance

- In the 1940s, penicillin was introduced for the treatment of infection.
- In 1942, strains of *S. aureus* resistant to penicillin were detected in hospitals.
- By 1950, approximately 80% of hospital-acquired infections were PCN resistant.
- Shortly after the introduction of the β-lactamase-stable antibiotics (e.g., methicillin) in the early 1960s, the first reports of MRSA appeared.
- Methicillin resistance resulted from the production of an alternative penicillin-binding protein, PBPS2 encoded by the meca gene on the staphylococcal cassette chromosome mec (SCCmec), a mobile genetic element.
- Today, MRSA strains are found worldwide, and most are multi-drug resistant.
Methicillin-resistant Staphylococcus aureus (MRSA) has undergone rapid evolutionary changes and epidemiologic expansion to become a major cause of nosocomial and community-acquired infections worldwide.

- It continues to cause significant morbidity and mortality despite huge advances in medical care.
- MRSA strains account for 50% of all S. aureus strains causing clinical disease in many hospitals.
- MRSA infections kill 19,000 hospitalized American patients annually; this is similar to the number of deaths due to AIDS, tuberculosis, and viral hepatitis combined.

Infections can occur when there is a breach of the skin or mucosal barrier that allows the organism access to adjoining tissues or the bloodstream.

Risk for infection is increased by the presence of foreign materials.
• MRSA infections associated with high morbidity and mortality.
  • Mortality due to MRSA infection was greater than that due to methicillin susceptible S. aureus.


Cohen & Powderly: Infectious Diseases, 3rd ed, 2010

• Reasons for the increased mortality associated with MRSA infection are likely to be multifactorial and incompletely understood.

• Potential explanations include:
  1. Increased virulence of the pathogen
  2. Clinical differences between patients infected with MRSA and those infected with MSSA
  3. Decreased efficacy of MRSA therapy relative to MSSA therapy
  4. Delay in initiation of appropriate therapy.

CA versus HA MRSA

• Community-acquired MRSA is different from health care-acquired MRSA, from both epidemiologic and molecular points of view.
  • They likely represent different organisms that produce different clinical syndromes.
  • HCA-MRSA was associated with risk factors that included recent hospitalization or surgery, living in a nursing home, or carrying an indwelling catheter or device. It produced mostly hospital-related pneumonia and bacteremia.
  • CA-MRSA was not associated with any risk factors and produced primarily skin and soft tissue infections, and sometimes rapidly fatal necrotizing pneumonia, but also associated with other severe infections like necrotizing fasciitis, severe sepsis.
  • HCA-MRSA was multi-resistant whereas CA-MRSA was pauci-resistant.
CA-MRSA clones carry SCCmec subtypes IV and V and also the (lukSF-PV) genes, which encode Panton-Valentine leukocidin (PVL), a leukotoxin that may be associated with more severe disease presentations.

Most common CA-MRSA strains circulating in the USA are USA300 and USA400.

HA-MRSA isolates typically have SCCmec subtypes I–III and rarely carry the gene for PVL.

Some SCCmec types carry various additional genetic elements that can confer resistance to additional antibiotic classes and these are especially common in HA-MRSA.

Table 2. Epidemiologic risk factors for infection with community-associated methicillin-resistant Staphylococcus aureus (MRSA).

<table>
<thead>
<tr>
<th>Risk group or factor</th>
</tr>
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<tbody>
<tr>
<td>Children &lt;2 years old [46]</td>
</tr>
<tr>
<td>Athletes (mainly participants in contact sports) [47, 48]</td>
</tr>
<tr>
<td>Injection drug users [47]</td>
</tr>
<tr>
<td>Men who have sex with men [47, 48]</td>
</tr>
<tr>
<td>Military personnel [48]</td>
</tr>
<tr>
<td>Persons living in congregate facilities, residential homes, or shelters [47, 48]</td>
</tr>
<tr>
<td>Veterinarians, pet owners, and pig farmers [49, 50]</td>
</tr>
<tr>
<td>Adults aged &gt;65 years [14]</td>
</tr>
<tr>
<td>Blacks [14]</td>
</tr>
<tr>
<td>Recent influenza-like illness or severe pneumonia [32–34]</td>
</tr>
<tr>
<td>Concurrent skin and soft-tissue infection [46]</td>
</tr>
<tr>
<td>History of colonization or recent infection with a community-associated MRSA strain [46]</td>
</tr>
<tr>
<td>Known close contact (in the same household) with a person colonized and/or infected with MRSA [46]</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Commercially Available (CA) and Health Care-Associated (HA) Methicillin-Resistant Staphylococcus aureus (MRSA) isolates in the United States.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CA-MRSA</th>
<th>HA-MRSA</th>
</tr>
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<tbody>
<tr>
<td>Susceptibility* drug</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Usually susceptible</td>
<td>Frequently resistant</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Usually susceptible</td>
<td>Rarely resistant</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Usually susceptible</td>
<td>Frequently resistant</td>
</tr>
<tr>
<td>Erythromycin-resistant</td>
<td>Usually resistant</td>
<td>Usually resistant</td>
</tr>
<tr>
<td>Erythromycin-susceptible</td>
<td>Geographically variable, often resistant</td>
<td>Usually resistant</td>
</tr>
<tr>
<td>TMP-SMZ</td>
<td>Usually susceptible</td>
<td>Usually susceptible</td>
</tr>
<tr>
<td>SCC mec type</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Lineage</td>
<td>USA300, USA400</td>
<td>USA100, USA 200</td>
</tr>
<tr>
<td>Toxic-producing</td>
<td>None</td>
<td>Present</td>
</tr>
<tr>
<td>Panton-Valentine leukocidin-producing</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Prior health care exposure</td>
<td>Less frequent</td>
<td>Very common</td>
</tr>
</tbody>
</table>

Note: Adapted with permission from the CDC, CDC Laboratory Standards Institute. 2014. Another potential drug-resistant strain is MRSA, which results in various subtypes of MRSA, as represented in Table 3.


Antibiotics with MRSA activity

- Vancomycin
- Clindamycin
- TMP-SMX
- Rifampin
- Quinupristin-Dalfopristin
- Telavancin
- Ceftaroline
- Linezolid
- Daptomycin
- Tetracycline/Tigecycline
- Erythromycin-resistant

Antibiotics with MRSA activity

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Vancomycin

- **Vancomycin**: Is a glycopeptide and has been the mainstay of parenteral therapy for MRSA infections.
- **Mechanism of action**: Inhibits bacterial cell wall biosynthesis.
- **Distribution**: Following parenteral administration, it is widely distributed in body tissue and fluids.
- **Side Effects**:
  - Red man syndrome:
  - Renal function impairment
  - RARE
  - Neutropenia
  - Eosinophilia
  - Drug fever, allergic reactions w/ rash, IgA bullous dermatitis
  - Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)
  - Tissue irritation
  - Ototoxicity
  - Thrombocytopenia

Vancomycin Dosing/Monitoring

- **Vancomycin Dosing/Monitoring**: 15 mg/kg/dose every 8–12 h, not to exceed 2 g per dose, is recommended in patients with normal renal function.
- **Trough vancomycin concentrations**: Are the most accurate and practical method to guide vancomycin dosing.
- **Serum trough concentrations**: Should be obtained at steady state conditions, prior to the fourth or fifth dose.
- For serious infections, vancomycin trough concentrations of 15–20 ug/ml are recommended.
- Higher vancomycin doses and trough concentrations may be associated with increased nephrotoxicity and high-frequency hearing loss in older patients.
Vancomycin susceptibility testing
• MIC breakpoints were lowered by the CLSI in 2006:
  • VSSA MIC <2 ug/ml
  • VISA MIC 4–8 ug/ml
  • VRSA MIC >16 ug/ml
  • hVISA: strains are vancomycin sensitive by MIC testing but have a sub-population of cells that can grow at higher vancomycin concentrations.

• The high prevalence of MRSA in hospitals necessitated extensive use of vancomycin, which has been the ‘last resort’ antibiotic for MRSA infections for many years.
  • The first S. aureus strain with reduced vancomycin was isolated in Japan in 1997 (the Mu50 strain) and has now emerged among major hospital MRSA-lineages.
  • In 2005, 0.2% of 240 000 S. aureus isolates in the Surveillance Network data from US laboratories were vancomycin-intermediate S. aureus (VISA), defined by a minimum inhibitory concentration (MIC) of >2 and ≤8 mg/l.
  • Intermediate resistance to glycopeptides is associated with thickening of the bacterial cell wall.

Clindamycin
• MECHANISM OF Action: It is a lincosamide and inhibits protein synthesis by binding to 50S ribosomal subunits, interfering with transpeptidation and early chain termination
  • It has excellent tissue penetration, particularly in bone and abscesses, although penetration into the CSF is limited.
  • In vitro rates of susceptibility to clindamycin are higher among CA-MRSA than they are among HA-MRSA.
  • D test recommended for detection of inducible clindamycin resistance in erythromycin-resistant, clindamycin-susceptible isolates and is now readily available.
  • Diarrhea is the most common adverse effect and occurs in up to 20% of patients, and Clostridium difficile-associated disease may occur more frequently, compared with other oral agents.
Daptomycin

- **Mechanism Of action:** is a lipopeptide class antibiotic that disrupts cell membrane function via calcium-dependent binding, resulting in bactericidal activity in a concentration-dependent fashion.
- It is FDA-approved for adults with S. aureus bacteremia, right-sided infective endocarditis, and cSSTI.
- Daptomycin should not be used in patients with pneumonia because of inactivation by pulmonary surfactant, yet it can be used in septic pulmonary emboli.
- It is highly protein bound (91%) and renally excreted.
- Nonsusceptible isolates have emerged during therapy in association with treatment failure.
- Prior exposure to vancomycin and elevated vancomycin MICs have been associated with increases in daptomycin MICs, suggesting possible cross-resistance.

**Side Effects:** CPK elevation.
- Patients should be observed for development of muscle pain or weakness and have weekly CPK levels determined, with more frequent monitoring in those with renal insufficiency or who are receiving concomitant statin therapy.
- Daptomycin induced eosinophilic pneumonia have been described.

Linezolid

- **Linezolid:** is a synthetic oxazolidinone and inhibits initiation of protein synthesis at the 50S ribosome.
- It is FDA-approved for adults and children for the treatment of SSTI and nosocomial pneumonia due to MRSA.
- It has in vitro activity against VISA and VRSA.
- It has 100% oral bioavailability.
- Linezolid resistance is rare, although an outbreak of linezolid-resistant MRSA infection has been described.

**Side Effects:** hematologic toxicity, with thrombocytopenia occurring more frequently than anemia and neutropenia, peripheral and optic neuropathy, and lactic acidosis.
- Linezolid is a weak, nonselective, reversible inhibitor of monoamine oxidase and has been associated with serotonin syndrome in patients taking concurrent selective serotonin receptor inhibitors.
Linezolid and serotonergic drug interactions: a retrospective survey

- **Methods.** This study was a retrospective chart review of inpatients at the Mayo Clinic (Rochester, MN) with concomitant orders or therapy within 14 days for linezolid and an SSRI from 2000 to 2004.

- **Results:** 72 patients received linezolid and an SSRI or venlafaxine within 14 days of each other. 52 patients (72%) received concomitant therapy with linezolid and an SSRI or venlafaxine, and 20 patients (28%) did not receive concomitant therapy but received linezolid and an SSRI within a 14-day period.

- Overall, only 2 patients (3%) had a high probability of serotonin syndrome. In both patients with high probability, symptoms reversed rapidly on discontinuation of serotonergic therapy.

- **Conclusions.** If the clinical situation warrants use of linezolid in a patient receiving an SSRI, linezolid may be used concomitantly with SSRIs, without a 14-day washout period and with careful monitoring for signs and symptoms of serotonin syndrome. Serotonergic agents should be promptly discontinued if serotonin syndrome is suspected.

Rifampin

- Rifampin has bactericidal activity against S. aureus and achieves high intracellular levels, in addition to penetrating biofilms.

- Inhibits initiation of chain formation for RNA synthesis by inhibiting DNA-dependent RNA polymerase.

- Because of the rapid development of resistance, it should not be used as monotherapy but may be used in combination with another active antibiotic in selected scenarios.

- The role of rifampin as adjunctive therapy in MRSA infections has not been definitively established, and there is a lack of adequately powered, controlled clinical studies in the literature.

- SE: Orange discoloration of urine, tears, sweat, hepatotoxicity, drug interactions

Adjunctive Use of Rifampin for the Treatment of Staphylococcus aureus Infections: A Systematic Review of the Literature

- **Methods:** A systematic review of the literature to identify in vitro, animal, and human investigations that compared single antibiotics alone and in combination with rifampin therapy against S. aureus.

- **Results:** In vitro studies varied substantially and the effect of rifampin therapy was often inconsistent. It did not necessarily correlate with in vivo investigations, and findings seemed heavily dependent on the method used. Animal studies tended to show a microbiologic benefit of adjunctive rifampin use, particularly in osteomyelitis and infected foreign body infection models; however, many studies failed to show a benefit of adjunctive therapy.

- Few human studies have addressed the role of adjunctive rifampin therapy. Adjunctive therapy seems most promising for the treatment of osteomyelitis and prosthetic device-related infections, although studies were typically underpowered and benefits were not always seen.

Tetracyclines

- **Mechanism of Action:** Inhibit protein synthesis by mainly binding to 30S ribosomal subunit and blocking binding of aminoacyl transfer-RNA.

- Tetracyclines appear to be effective in the treatment of SSTI, but data are lacking to support their use in more-invasive infections

- SE: GI upset, staining of teeth in children, pancreatitis
Tigecycline

- **Tigecycline** is a glycyclcline, a derivative of the tetracyclines, and is FDA approved in adults for cSSTIs and intraabdominal infections.
- It has a large volume of distribution and achieves high concentrations in tissues and low concentrations in serum.
- For this reason, and because it exhibits bacteriostatic activity against MRSA, caution should be used in treating patients with bacteremia.
- The FDA recently issued a warning to consider alternative agents in patients with serious infections because of an increase in all-cause mortality noted across phase III/IV clinical trials.

**Mechanism Of action:** TMP act synergistically with SMX by interfering with folic acid production.
- Is not FDA-approved for the treatment of any staphylococcal infections.
- 95%–100% of CA-MRSA strains are susceptible in vitro and it has become an important option for the outpatient treatment of SSTI.
- SE: GI intolerance, rash, hyperkalemia, pseudo elevation of cr, BM suppression.

Telavancin

- Telavancin is a parenteral lipoglycopeptide that inhibits cell wall synthesis by binding to peptidoglycan chain precursors, causing cell membrane depolarization.
- It is bactericidal against MRSA, VISA, and VRSA.
- It is FDA-approved for cSSTI in adults.
- SE: taste disturbance, Redman syndrome, nephrotoxicity, QT prolongation.

Ceftaroline

- Is a cephalosporin
- FDA approved indication:
  - Complicated skin and skin structure infections (including cases caused by MRSA)
  - CAP (including cases caused by PCN-resistant *S. pneumoniae*)
Quinupristin-Dalfopristin

- Quinupristin-dalfopristin is a combination of 2 streptogramin antibiotics and inhibits protein synthesis.
- Each agent binds at a different site of bacterial 50S ribosomal subunit, resulting in interruption of protein synthesis.
- It is FDA-approved for cSSTI in adults and children >16 years of age.
- It has been used as salvage therapy for invasive MRSA infections in the setting of vancomycin treatment failure in adults and children.
- Toxicity, including arthralgias, myalgias, nausea, and infusion-related reactions, has limited its use.
- Must be infused by central venous line.

Management of MRSA infections

- SSTI
- Bacteremia/endocarditis
- Pneumonia
- Bone and joints
- CNS

SSTI

- For a cutaneous abscess, incision and drainage is the primary treatment.
- For simple abscesses or boils, incision and drainage alone is likely adequate.
- Purulent cellulitis: empirical therapy for CA-MRSA is recommended pending culture results.
- Nonpurulent cellulitis: empirical therapy for infection due to b-hemolytic streptococci is recommended.
- Empirical coverage for CA-MRSA is recommended in patients who do not respond to b-lactam therapy.

Conditions in which Antimicrobial Therapy is Recommended after Incision and Drainage of an Abscess due to Community-Associated Methicillin-Resistant Staphylococcus aureus

- Severe or extensive disease (eg, involving multiple sites of infection) or rapid progression in presence of associated cellulitis
- Signs and symptoms of systemic illness
- Associated comorbidities or immunosuppression (diabetes mellitus, human immunodeficiency virus infection/AIDS, neoplasm)
- Extremes of age
- Abscess in area difficult to drain completely (eg, face, hand, and genitalia)
- Associated septic phlebitis
- Lack of response to incision and drainage alone

Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. CID 2011:52
Complicated SSTI

- Defined as patients with deeper soft-tissue infections, surgical/traumatic wound infection, major abscesses, cellulitis, and infected ulcers and burns.
- Options include the following:
  - vancomycin, linezolid, daptomycin, telavancin, clindamycin.
- Duration: 7-14 days

Recurrent infections

- Preventive educational messages on personal hygiene and appropriate wound care are recommended for all patients with SSTI.
- Instructions should be provided to:
  - Keep draining wounds covered with clean, dry bandages
  - Maintain good personal hygiene with regular bathing and cleaning of hands with soap and water or an alcohol-based hand gel.
  - Avoid reusing or sharing personal items (e.g., disposable razors, linens, and towels)

MRSA Bacteremia and Endocarditis

- MRSA bacteremia and infective endocarditis are serious diseases associated with high morbidity, and mortality
- Mortality rates are 30%-37% for MRSA endocarditis.
- Careful history, physical examination and imaging are important to detect source and embolic or metastatic foci

Environmental hygiene measures should be considered in patients with recurrent SSTI in the household or community setting:

- Focus cleaning efforts on high-touch surfaces
- Commercially available cleaners or detergents appropriate for the surface being cleaned should be used according to label instructions for routine cleaning of surfaces.
Vancomycin is the mainstay of therapy for MRSA bacteremia and endocarditis.

The addition of gentamicin or rifampin to vancomycin is not recommended for bacteremia or native valve infective endocarditis.

Daptomycin is an alternative to vancomycin for adults in the treatment of MRSA bacteremia or endocarditis.

Some experts recommend higher doses of daptomycin doses (8–10 mg/kg)

Quinopristin-dalfopristin, linezolid, TMP-SMX, and telavancin are not recommended as first-line therapy for MRSA bacteremia.

Duration of treatment.

The recommended minimum duration of therapy for uncomplicated bacteremia is 2 weeks, as defined by:
1. exclusion of endocarditis
2. no implanted prostheses (e.g., prosthetic valves, cardiac devices, and arthroplasties)
3. follow up blood cultures drawn 2–4 days after the initial set that do not grow MRSA
4. defervescence within 72 h of therapy
5. no evidence of metastatic sites of infection

If the above criteria are not met, 4–6 weeks of therapy is recommended for complicated bacteremia depending on the extent of infection.

Echocardiography is recommended for all adult patients with bacteremia.

TEE is preferred over TTE because of its superiority, compared with TTE, for the detection of vegetations.

Additional blood cultures 2–4 days after initial positive cultures and as needed thereafter are recommended to document clearance of bacteremia.
• Evaluation for valve replacement surgery is recommended if:
  • Large vegetation (10 mm in diameter)
  • Occurrence of >1 embolic event during the first 2 weeks of therapy
  • Severe valvular insufficiency, valvular perforation or dehiscence
  • Decompensated heart failure
  • Perivalvular or myocardial abscess
  • New heart block
  • Persistent fevers or bacteremia are present.

Prosthetic valve
• IV vancomycin plus rifampin for at least 6 weeks plus gentamicin for 2 weeks.
• Early evaluation for valve replacement surgery is recommended.

• The recommendation to treat prosthetic valve MRSA endocarditis with vancomycin, gentamicin, and rifampin is based on small retrospective studies of methicillin-resistant coagulase-negative staphylococci and the 2005 American Heart Association (AHA) Infective Endocarditis Guidelines.

Persistent MRSA Bacteremia/Vancomycin failure
• Patient’s overall clinical response
• Vancomycin trough serum concentrations
• Results of susceptibility testing
• The presence of and ability to remove other foci of infection.

• The decision to modify therapy and the time frame at which this occurs may vary depending on the clinical scenario.

• Options:
  • High-dose daptomycin (10 mg/kg/ day), if the isolate is susceptible, in combination with another agent (e.g. gentamicin, rifampin, linezolid, TMP-SMX)

  • If reduced susceptibility to vancomycin and daptomycin are present, options may include the following: quinupristindalfopristin, TMP-SMX, linezolid or telavancin.

  • These options may be given as a single agent or in combination with other antibiotics.
**MRSA Pneumonia**

- MRSA has emerged as a cause of severe CAP, particularly in the context of a preceding or concurrent influenza-like illness.
- For hospitalized patients with severe community-acquired pneumonia defined by any one of the following:
  1. a requirement for ICU admission
  2. necrotizing or cavitary infiltrates
  3. Empyema

Empirical therapy for MRSA is recommended pending sputum and/or blood culture results.

- For HA-MRSA or CA-MRSA pneumonia, IV vancomycin or linezolid.
- Clindamycin if the strain is susceptible.
- Duration: 7-21 days
- High failure rates have been observed in the treatment of MRSA pneumonia which has been attributed to vancomycin's poor penetration into pulmonary tissue and lung epithelial lining fluid.
- On the other hand, in 2 prospective studies involving adult patients with nosocomial pneumonia, Linezolid and vancomycin were associated with comparable cure rates
- A randomized study of linezolid versus vancomycin for MRSA VAP also found no significant difference in early microbiologic response rates.
- Thus, it is unclear whether 1 drug is definitively superior to the other for treatment of MRSA VAP, and additional studies are ongoing.

**Osteomyelitis**

- MRSA bone and joint infections arise from hematogenous seeding, a contiguous focus of infection, or direct inoculation from trauma or a medical procedure
- Surgical debridement and drainage of associated soft tissue abscesses is the mainstay of therapy and should be performed whenever feasible.
- Antibiotics available for parenteral administration include Vancomycin and Daptomycin.
- Some antibiotic options with parenteral and oral routes of administration include the following: TMP-SMX, linezolid, clindamycin.
- Some experts recommend the addition of rifampin to the antibiotic chosen above.
- A minimum 8-week course is recommended
- Some experts suggest an additional 1-3 months of oral agent chosen according to susceptibility for chronic infection or if debridement is not performed.
Septic arthritis

• Drainage or debridement of the joint space should always be performed.

• A 3-4-week course of therapy is recommended.

Device-related osteoarticular infections

• For early-onset (<2 months after surgery) prosthetic joint infections involving a stable implant with short duration (<3 weeks) of symptoms and debridement (but device retention), initiate parenteral therapy plus rifampin for 2 weeks followed by rifampin plus an oral agent for 3 or 6 months for hips and knees, respectively.

• Prompt debridement with device removal whenever feasible is recommended for unstable implants, late-onset infections, or in those with long duration (>3 weeks) of symptoms.

MRSA CNS Infections

• CNS infections caused by MRSA occur as a complication of a neurosurgical procedure, in association with a contiguous focus of infection, or hematogenously as a complication of bacteremia or infective endocarditis.

• Treatment is difficult because of the critical location of these infections and the blood brain barrier, which limits penetration of systemically administered antibiotics to the site of infection.

• No prospective randomized trials on the treatment of MRSA infections of the CNS.

• Vancomycin has been the drug of choice, but outcomes have been very poor when it has been used as monotherapy.

• Some recommend addition of Rifampin despite a paucity of clinical data demonstrating benefit of the combination.
• Intraventricular vancomycin or daptomycin may be considered in patients who have ventricular access or who do not respond to systemic antimicrobial.

• Several case reports describe the successful use of linezolid, TMP-SMX, and daptomycin for the treatment of MRSA CNS infections, but additional research is needed to define their role in the management of such infections.

Meningitis
• Meningitis: Vancomycin for 2 weeks is recommended
• Some experts recommend the addition of rifampin.
• Alternatives include the following: linezolid or TMP-SMX
• For CNS shunt infection, shunt removal is recommended and it should not be replaced until CSF cultures are repeatedly negative.

Brain abscess, subdural empyema, spinal epidural abscess
• Incision and drainage is recommended
• Vancomycin for 4–6 weeks is recommended
• Rifampin?
• Alternatives: ??

Prevention of MRSA
• Hand and environmental hygiene
• Active surveillance cultures: controversial, expensive, complex
• Decolonization: decolonization strategies to prevent MRSA are usually not recommended and should be considered only for selected patient populations.
References


References cont’d


- Cohen & Powderly: Infectious Diseases, 3rd ed, 2010
- Mandell, Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th ed, 2009
- John Hopkins antibiotic guide.

Thank You

Questions???