Methicillin-resistant *Staphylococcus aureus*: Challenges and Risks

*Experts discuss MRSA and how it affects patients in your practice.*
In Part 1, we explore:
- the history and evolution of MRSA
- the types of MRSA infection
- transmission of MRSA
- control of MRSA via education and hygiene
- infection surveillance programs
- treatment of MRSA

In Part 2, we discuss:
- exposure to MRSA in practice
- the responsibility of each practice to prevent MRSA
- MRSA as it relates to contact lens patients, compliance challenges and solution performance

Jimmy D. Barlett, OD, DOS, ScD
Dr. Barlett received his doctorate in optometry in 1974 from Southern College of Optometry. After serving as Chief of the Optometry Service at the Tampa V.A. Hospital and Assistant Professor in the Department of Ophthalmology of the University of South Florida College of Medicine, he assumed his present position at the School of Optometry, University of Alabama at Birmingham in 1977. Dr. Barlett is Chairman of the Department of Optometry, Professor of Optometry in the School of Optometry and Professor of Pharmacology in the Department of Pharmacology and Toxicology at the University of Alabama School of Medicine. Dr. Barlett has served as Editor-in-Chief of the Journal of the American Optometric Association, Co-editor of Clinical Ocular Pharmacology, and serves on the editorial advisory boards for Ophthalmic Drug Facts and Journal of Ocular Pharmacology and Therapeutics. Dr. Barlett has been engaged as a consultant and has been a member of the advisory boards of Alcon, Allergan, Bausch + Lomb and Vistakon.

Chris Snyder, OD, MS, FAAO
Dr. Snyder earned a doctorate in optometry, a graduate degree and a residency certificate in contact lens practice from The Ohio State University. He served as an optometrist in the U.S. Navy and was a Professor of Optometry at the University of Alabama at Birmingham (UAB) School of Optometry for more than 24 years where he served as the Director and Chief of the Cornea and Contact Lens Service of UAB EyeCare and practiced optometry in the faculty practice. He has served as a Contributing Editor for Contact Lens Spectrum, as Co-editor of the International Contact Lens Clinic Journal and is the U.S. Regional Editor of the U.K.-based (British Contact Lens Association) indexed journal Contact Lens and Anterior Eye. Dr. Snyder is Director of Professional Relations for Bausch + Lomb U.S. Vision Care and continues an active relationship with UAB as an adjunct professor.

Ron Melton, OD, FAAO
Dr. Melton has lectured nationally and internationally on ocular disease and pharmacology at more than 300 continuing medical education meetings. He sits on the editorial boards of Optometric Physician and Primary Care Optometry News and is a contributing editor to Clinical and Refractive Optometry. Dr. Melton has authored or co-authored more than 100 papers on optometry and is the co-author of the annual “Clinical Guide to Ophthalmic Drugs,” published by Review of Optometry. He has acted as an investigator in more than 50 clinical research trials. Dr. Melton has been engaged as a consultant for Bausch + Lomb, ICARE, Pfizer and RPS and has been a member of advisory panels for Bausch + Lomb, Pfizer and RPS.

Randall Thomas, OD, MPH, FAAO
Dr. Thomas has lectured nationally and internationally on ocular disease and pharmacology at more than 300 continuing medical education meetings. He sits on the editorial boards of Optometric Physician and Primary Care Optometry News and is a contributing editor to Clinical and Refractive Optometry. Dr. Thomas has authored or co-authored more than 100 papers on optometry and is the co-author of the annual “Clinical Guide to Ophthalmic Drugs,” published by Review of Optometry. He is on the hospital staff at Northeast Medical Center, where he serves as the Ophthalmic Consultant to the Diabetes Management Committee, and actively teaches on the Cabarrus Family Medicine Residency Faculty. Dr. Thomas has been engaged as a consultant for Bausch + Lomb, ICARE, Pfizer and RPS and has been a member of advisory panels for Bausch + Lomb, Pfizer and RPS.

Authors were compensated for their contributions to this project.
Infection by methicillin-resistant *Staphylococcus aureus* (MRSA) is a growing concern that presents implications for both systemic and ophthalmic health. Eyecare and healthcare providers should be familiar with the clinical characteristics of a MRSA infection and with the treatment and management protocols for MRSA. They should be familiar with infection prevention control measures for clinical practice and they should know how to decrease the potential for MRSA infection in their patients through appropriate recommendations and counseling.

*Staphylococcus aureus*, often referred to simply as “staph,” is a common bacterium that’s colonized on human skin and in the noses of 25% to 30% of the population of healthy people. It can affect individuals of any age. Individuals are said to be “colonized” when bacteria are present, but not harming the host or causing symptoms. Staph is the most common cause of localized skin infections, such as folliculitis, furuncles (boils), pimples and impetigo. Moreover, the endo- and exotoxins from staph on the eyelids can cause inflammatory conditions such as staphylococcal blepharitis, phlyctenular conjunctivitis and infiltrative keratitis. Staph can be a serious pathogen, particularly when associated with a wound to the skin, surgical or otherwise, or in an immunocompromised patient. Most life-threatening staph infections are acquired in a healthcare setting, such as a hospital or nursing home. Colonizing staph can cause serious conditions such as abscesses, osteomyelitis, staphylococcal pneumonia, septicemia, toxic shock syndrome and endocarditis. Around and in the eye, infection by *Staphylococcus aureus* can be the cause of preseptal and orbital cellulitis, lid abscess, conjunctivitis, corneal ulcers, endophthalmitis and blebitis.

**TREATMENT WITH ANTIBIOTICS**

- **MSSA**
  *Staphylococcus aureus* was generally susceptible to the beta-lactam antibiotics when they were introduced in the early 1940s. Beta-lactams are the most widely-used group of antibiotics and they include penicillin, penicillin’s synthetic derivatives (methicillin, oxacillin, nafcillin, cloxacillin, dicloxacillin and flucloxacinil) and the cephalosporins (cephalexin, cefadroxil, cefazolin, and others).

- **VSSA**
  Vancomycin is a glycopeptide antibiotic that inhibits cell wall synthesis in Gram-positive bacteria. *Staphylococcus aureus* microorganisms that are susceptible to vancomycin are referred to as vancomycin-susceptible *Staphylococcus aureus* (VSSA). Vancomycin is often effective in treating Gram-positive bacteria that are unresponsive to beta-lactams. Vancomycin will not pass across the gastrointestinal mucosa and therefore must be administered intravenously for systemic therapy, requiring in-patient care.

**DEVELOPMENT OF RESISTANCE TO ANTIBIOTICS**

- **MRSA**
  In 1944, *Staphylococcus aureus* was found to demonstrate some resistance to penicillin, likely in response to the wide usage of beta-lactam drugs, making it the first known bacterium to acquire antibiotic resistance. Resistance to penicillin became widespread during the 1950s, and increasing resistance to the semisynthetic penicillinase-resistant antimicrobial agents (such as methicillin, oxacillin, nafcillin) followed in the 1960s.

The resistance to these semisynthetic penicillins had become so prevalent by the 1990s that they could no longer be used as first-line empirical therapy for serious staphylococcal infections. Methicillin-resistant *Staphylococcus aureus* (MRSA) is the name given to *Staphylococcus aureus* microorganisms that have become resistant to penicillin and its synthetic derivatives.
While vancomycin has been considered the drug of choice after treatment failure with other antibiotics, bacterial resistance to vancomycin has also developed during the past 20 years. Vancomycin-resistant *Staphylococcus aureus* (VRSA) is the name given to *Staphylococcus aureus* microorganisms that have become resistant to vancomycin.

**TYPES OF MRSA**

MRSA disease has become a major public health problem. Before the 1980s, MRSA was primarily considered to be a nosocomial infection — one that is acquired in a hospital or healthcare setting (such as nursing homes); not present or incubating prior to the patient being admitted to the health care facility, but occurring within 72 hours after admittance to the facility. Nosocomial MRSA infections are referred to as “Health Care-Associated Methicillin Resistant *Staphylococcus aureus*” (HA-MRSA) infections to distinguish them from MRSA infections acquired in the general community outside of the healthcare setting. These staph infections occur most frequently among persons who have a weakened immune system and include surgical wound infections, urinary tract infections, bloodstream infections and pneumonia. Approximately 20% of bloodstream infections in the hospital setting are caused by *S. aureus* and the proportion of hospital-onset *S. aureus* infections that were methicillin-resistant reached 64.4% in U.S. intensive care units in 2003. Standardized mortality rate (in-hospital deaths) was 6.3 per 100,000.

Approximately 1% of the population is colonized with MRSA. Kleven and colleagues reported that invasive MRSA infection is a major public health problem primarily related to health care but no longer confined to healthcare settings. Non-nosocomial MRSA infections are referred to as Community-Associated Methicillin Resistant *Staphylococcus aureus* (CA-MRSA) infections. Individuals with these infections have neither been recently hospitalized (within the prior year) nor had a medical procedure (such as dialysis, surgery, catheterization). CA-MRSA infections typically manifest as skin infections such as pimples, abscesses and boils, and other pus-filled lesions.

Since 1981, CA-MRSA has become the most frequent cause of skin and soft tissue infections presenting to emergency departments in the United States and the prevalence of CA-MRSA is rapidly increasing. Naseri and colleagues reported a significant increase in the prevalence of CA-MRSA head and neck infections in the pediatric population from 2001 through 2006. Blomquist reviewed the records of culture-positive MRSA patients in an urban public health care system (2000-2004) to identify patients with ocular, orbital and ocular adnexal infection. He found that the most common manifestation of ophthalmic MRSA infection was preseptal cellulitis and/or lid abscess, followed by conjunctivitis. Sight-threatening infections also occurred, including corneal ulcers, endophthalmitis, orbital cellulitis and blebitis.

The distinction between HA-MRSA and CA-MRSA is based upon genetic studies that show that isolates causing HA- and CA-MRSA infections are different species, meaning CA-MRSA organisms aren’t HA-MRSA organisms that have simply moved into the general community. Differences in virulence factors between HA-MRSA and CA-MRSA organisms may allow the community strains to spread more easily or to cause more skin disease compared with the traditional hospital-based MRSA strains. HA-MRSA is typically a multidrug-resistant organism, while CA-MRSA isolates are usually susceptible to most nonbeta-lactam antimicrobial agents.

**TRANSMISSION AND CONTROL**

Clinicians should be familiar with infection prevention control measures for clinical practice, must routinely use measures to prevent the transmission of MRSA, and know how to decrease the potential for MRSA infection through appropriate recommendations and patient counseling.

**HA-MRSA**

The most important reservoirs of MRSA in hospitals are infected or colonized patients. Hospital personnel are most commonly identified as the transmission link between patients, mainly via their hands, which may become contaminated by contact with colonized or infected patients, colonized or infected body sites of the personnel themselves, or from contact with devices, items or environmental surfaces contaminated with body fluids containing MRSA. HA-MRSA isolates can

---

**Footnotes**

a HA-MRSA: health care-associated MRSA is sometimes referred to as health care-acquired MRSA.

b CA-MRSA: community-associated MRSA is sometimes referred to as community-acquired MRSA.
survive on a variety of inanimate surfaces, sometimes for weeks.15

Infection control is the key to limiting or eradicating MRSA and other health care-associated infectious pathogens in hospitals. Control measures include aggressive hand hygiene programs, interventions to reduce catheter-related bloodstream infections, ventilator-associated pneumonia, and surgical site infections; and chlorhexidine bathing of ICU patients.16-19 Additional information on infection control in healthcare settings is available from the CDC.20

• CA-MRSA

Factors known to increase the risk of spreading CA-MRSA skin and soft tissue infections include close skin-to-skin contact, openings in the skin such as cuts or abrasions, poor hygiene, crowded living conditions and contaminated items and surfaces.1 The presence of CA-MRSA isolates on items such as clothing, towels and athletic equipment may contribute to outbreaks. Settings, circumstances and activities that provide close contact conditions include households, schools, day care facilities, dormitories, military barracks, correctional facilities, athletics (particularly contact sports) and IV drug use. Groups in the population that tend to have a higher incidence of CA-MRSA infections include Native Americans, Pacific Islanders and men who have sex with men.15 CA-MRSA disease can even be shared between pets and human handlers, as demonstrated in cases where the pets (dogs, cats, livestock and birds) have been identified as the MRSA carriers.21,22

Advice for prevention of CA-MRSA transmission includes the consistent practice of appropriate personal hygiene, avoidance of an unclean/unsanitary environment and use of barriers to bacterial transmission.

Basic prevention advice for all individuals should include the following recommendations16,23:

- Practice good personal hygiene:
  - Keep hands clean by washing with soap and water regularly or by using an alcohol-based hand sanitizer.
  - Don’t share personal items that come into direct contact with bare skin, such as towels and razors.
  - Avoid contact with other people’s wounds or bandages.
  - Keep skin abrasions and cuts covered to prevent them from becoming infected (always use clean, dry bandages until healed).

- Keep high-touch surfaces clean:
  - High-touch surfaces (that are frequently in contact with hands) should be kept clean, and all surfaces that might come into direct contact with people’s skin should be cleaned routinely.

- Practice healthy hygiene in exercise and sports:
  - Barrier-like clothing or a towel should be used between skin and equipment, such as weight-training benches.
  - Showering should be done immediately after participating in activities with frequent skin-to-skin contact, such as exercise and sports.

Basic infection control recommendations for clinicians includes using standard precautions24,25:

- Perform hand hygiene (proper hand-washing or using alcohol-based hand gel):
  - after touching blood, body fluids, secretions, excretions and contaminated items, even when gloves are worn
  - between patients
  - when moving from a contaminated body site to a clean site on the same patient

- Wear gloves when managing wounds
- Wear gown and mask/eye protection or face shield for procedures that are likely to generate splashes or sprays of blood, body fluids, secretions or excretions
■ Clean shared equipment between uses
■ Avoid overcrowding and separate infected patients
■ Clean surfaces of exam rooms with commercial disinfectant or a 1:100 solution of diluted bleach (1 tablespoon bleach in 1 quart water)

Additional information about CA-MRSA for both clinicians and the public is available from the CDC.10,26

INFECTION SURVEILLANCE PROGRAMS

The CDC plays a large role in MRSA surveillance by monitoring the incidence of health care-associated infections, the associated risk factors and pathogens by gathering data through the National Healthcare Safety Network (NHSN),27 a voluntary reporting system shared by all U.S. hospitals, long-term care facilities, other healthcare organizations and the CDC. The CDC also participates in MRSA prevention, epidemiologic and laboratory research, and outbreak and laboratory support.27

Another useful program is The Surveillance Network (TSN), which was established in 1994 as an electronic repository of infectious organisms, specimen sources and antimicrobial susceptibility data.28 TSN monitors the patterns of antimicrobial susceptibility of pathogens, such as MRSA, in infections requiring diagnostic testing. While most TSN data are from systemic infections, data from cultured ocular infections have also been captured, demonstrating an increase in the rate of ocular MRSA infections of 12.1% over a 5-year period (from 29.5% in 2000 to 41.6% in 2005) (Figure 1).28 Asbell and colleagues concluded that MRSA isolates soon may become the dominant phenotype in serious ocular S. aureus infections.28

TSN data also showed that MRSA in ocular infections could be classified as multidrug resistant, including all the fluoroquinolones tested, and that trimethoprim was the most effective agent against MRSA.28

Shortly after the TSN program was launched, the “Tracking Resistance in the U.S. Today” (TRUST) program was initiated in 1996 to assess pathogen susceptibility to fluoroquinolones and other antimicrobials when levofloxacin was first introduced for systemic use.29 The ongoing program allows for monitoring of trends in antibiotic resistance with nationwide susceptibility data. The TRUST program, however, did not systematically track in vitro susceptibility in ocular isolates. To fill this gap, Ocular TRUST began in 2005 as a longitudinal nationwide susceptibility surveillance program, tracking antimicrobial susceptibility patterns of common ocular pathogens. Ocular isolates are tested against a panel of antimicrobials representing six pharmacologic classes: fluoroquinolones (ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin); dihydrofolate reductase inhibitors (trimethoprim); macrolides (azithromycin); aminoglycosides (tobramycin); polypep-

---

**Figure 2. Results for Staphylococcus aureus in vitro susceptibility from Ocular TRUST 3: Ongoing Longitudinal Surveillance of Antimicrobial Susceptibility in Ocular Isolates**

![Graph showing in vitro susceptibility results for methicillin-susceptible and resistant S. aureus isolates.](image-url)

tides (polymyxin B); and beta-lactams (penicillin). Among the results from the third year of Ocular TRUST (Figure 2):

- Most antimicrobials, except penicillin and polymyxin B, continue to be highly active against MSSA (azithromycin shows only moderate activity).
- With the exception of trimethoprim and tobramycin, less than one-third of MRSA strains are susceptible to ophthalmic antimicrobials.
- Susceptibility profiles of the fluoroquinolones remain weak for MRSA.

**TREATMENT OF MRSA**

Clinicians should be aware of the currently recommended therapeutic regimens that incorporate new knowledge regarding the most effective antibiotics administered systemically or topically for both HA-MRSA and CA-MRSA.

**HA-MRSA**

Since HA-MRSA strains are multidrug-resistant organisms (MDRO), final therapy should be guided by results of susceptibility testing from cultures obtained before the initiation of empirical therapy. For initial empirical antibiotic therapy for HA-MRSA, Grayson has suggested vancomycin, linezolid, daptomycin or rifampin plus trimethoprim–sulfamethoxazole. Treatment for severe infection (where the patient appears toxic, vital signs are unstable and a sepsis-syndrome is present) would include the following:

- Intravenous therapy for MRSA is preferred; vancomycin remains a first-line therapy (although, owing to concerns about possible development of vancomycin-resistant bacteria, its use is restricted in most hospitals, and requires approval of the Infectious Disease Unit).
- Final therapy based on results of culture and susceptibility testing
- Consult with infectious disease and critical care specialist

**CA-MRSA**

CA-MRSA infections often begin as skin or soft tissue lesions, such as a boil or abscess and/or cellulitis, with patients frequently reporting a lesion that is red, swollen and painful. CA-MRSA should be suspected particularly if a patient reports, or presents with, a wound resembling a spider bite, since MRSA strains can cause painful lesions in the absence of previous skin trauma.

---

**Systemic antibiotics of interest in the treatment of S. aureus and MRSA infections**

- Trimethoprim-sulfamethoxazole (co-trimoxazole), as a sulfonamide antibacterial combination, is effective against MRSA because it synergistically inhibits successive steps in the folate synthesis pathway, starving the bacteria of the folic acid that is necessary for DNA replication and transcription.
- Clindamycin (a lincosamide antibiotic) can be effective against MRSA infections because it reduces the production of staph exotoxins and may also induce changes in the surface structure of bacteria that make them more sensitive to immune system attack (opsonization and phagocytosis).
- Doxycycline, as a semi-synthetic tetracycline, is effective against MRSA infections primarily through inhibition of bacterial protein synthesis leading to bacteriostasis.
- Daptomycin, a cyclic lipopeptide, acts on the bacterial cytoplasmic membrane and is bactericidal against most Gram-positive bacteria, including Staphylococcus aureus.
- Linezolid, an oxazolidinone, is active against almost all CA-MRSA isolates and group A streptococci. High cost, lack of routine availability, hematologic side effects, and the potential for resistance among Staphylococcus aureus strains are relative contraindications for usage.
- Rifampin is highly active against susceptible community-associated MRSA isolates but it must be used in combination with trimethoprim-sulfamethoxazole or doxycycline due to high frequency of resistance when rifampin is used alone.
- Fluoroquinolones interrupt bacterial replication by binding to both deoxyribonucleic acid (DNA) gyrase and topoisomerase IV. They should not be used to treat skin and soft-tissue infections caused by CA-MRSA since Staphylococcus aureus resistance develops readily and is already widely prevalent.
- Augmentin (GlaxoSmithKline) — a combination of amoxicillin, a beta-lactam antibiotic, and clavulanic acid, a beta-lactamase inhibitor — addresses bacterial resistance to beta-lactam with the clavulanic acid antagonizing the beta-lactamase enzyme, binding irreversibly to it and allowing the amoxicillin to attack bacterial cell wall synthesis. Augmentin is effective in treating MSSA infection, but is not effective against MRSA.
Moran and colleagues\textsuperscript{11} reported that while more than 80\% of patients with skin and soft-tissue infections associated with MRSA received empirical antimicrobial therapy for their infections, 57\% of those patients were infected with a MRSA isolate that was resistant to the agent prescribed. Susceptibility testing of MRSA isolates in this study revealed that 100\% were susceptible to trimethoprim-sulfamethoxazole, 95\% to clindamycin, 92\% to tetracycline, and 60\% to fluoroquinolones. Similar to their findings regarding susceptibility to trimethoprim-sulfamethoxazole, Asbell\textsuperscript{28} reported that trimethoprim is the most effective topically applied antibiotic against ocular MRSA infection.

In treating nonpurulent cellulitis, as in preseptal cellulitis, there is a chance that the infection involves group A streptococcus,\textsuperscript{31} which is mostly resistant to trimethoprim–sulfamethoxazole.\textsuperscript{11} For coverage of streptococcal infection, clindamycin or a combination of a beta-lactam plus trimethoprim–sulfamethoxazole may be preferable.\textsuperscript{11} Trimethoprim–sulfamethoxazole and tetracyclines are reasonable choices for cases where CA-MRSA infection is either confirmed or strongly suggested by the presence of purulent material.\textsuperscript{13}

Asbell\textsuperscript{28} suggested that a clinician would be prudent to consider the possibility of methicillin or multidrug resistance with any \textit{Staphylococcus aureus} ocular infection, even in the absence of recognized risk factors, because of recent increases in the prevalence of MRSA and the inability of clinical or epidemiological risk factors to reliably distinguish between CA-MRSA and MSSA.\textsuperscript{12} Ideally, cultures should be obtained for suspected MRSA infections, with the susceptibility profile of the organism(s) ultimately guiding the antibiotic treatment.\textsuperscript{11,24}

The following is a treatment summary for initial empirical antibiotic therapy.

- For MSSA, penicillinase-resistant penicillin or a first-generation cephalosporin should be used.\textsuperscript{25} (Note that the penicillins are more effective than vancomycin in treating MSSA.)
- For MRSA:
  - Generally:
    - avoid beta-lactam antibiotics (e.g., no penicillins or cephalosporins) for MRSA
  - Based on HA- or CA-MRSA:
    - HA-MRSA:
      - Vancomycin\textsuperscript{25}; alternatives to vancomycin, particularly to manage VRSA, include linezolid, dapto-mycin, trimethoprim, or rifampin plus trimethoprim–sulfamethoxazole.\textsuperscript{6,25,28} Asbell\textsuperscript{28} has reported that trimethoprim can be as effective as vancomycin in both systemic and ocular MRSA infections
    - CA-MRSA:
      - Systemically:
        - trimethoprim–sulfamethoxazole, clindamycin, or a long-acting tetracycline such as doxycycline\textsuperscript{6,25}
        - CA-MRSA can cause severe and sometimes fatal invasive disease.\textsuperscript{2,31} When a CA-MRSA infection is severe, it should be treated in the same manner as previously described for severe HA-MRSA infection.
      - Ophthalmically:
        - while fluoroquinolones are commonly used to treat ocular surface infections, alternatives should be considered.\textsuperscript{29} Trimethoprim has been reported to be the most effective topically applied antibiotic that is active against MRSA.\textsuperscript{28,30}

CONTROLLING MRSA

The increasing prevalence of MRSA has resulted in a paradigm shift to include this group of organisms in the differential diagnosis of numerous diseases, including those that affect the ocular tissues. The spread of MRSA can be controlled through appropriate steps by individuals, and clinicians must routinely use measures to prevent transmission of these organisms. To treat MRSA infection, clinicians should be aware of the currently recommended therapeutic regimens that incorporate new knowledge regarding the most effective systemic and topical antibiotics for HA-MRSA and CA-MRSA. CLS


Gram-positive bacterial pathogens (particularly *Staphylococcus aureus* and *epidermidis*) are the most common causes of ocular infections. An evolving aspect of patient protection and safety centers on the increasing prevalence of infections from methicillin-resistant *Staphylococcus aureus* (“MRSA”) and, accordingly, we addressed clinical aspects of MRSA infection and treatment in our 2009 Clinical Guide to Ophthalmic Drugs. This article allows us to take a broader look at MRSA as it relates to eyecare practitioners, their clinical practices and patients.

There are two general types of MRSA, primarily differentiated by genotypic and environmental features: Healthcare-Associated MRSA (HA-MRSA) and Community-Associated MRSA (CA-MRSA). HA-MRSA is contracted in a healthcare setting, such as a hospital or nursing home, and usually by people who are in poor health or are immunocompromised. HA-MRSA organism virulence and susceptibility to antibiotics is somewhat different than CA-MRSA, which is contracted in the general community, has more genetic variants, is susceptible to various antibiotics (whereas HA-MRSA tends to be multidrug resistant), spreads more easily — causing more skin disease than HA-MRSA, and can be associated with severe pneumonia in children.

We routinely read the scientific literature so our clinical practices are evidence-based and aligned with current knowledge and thinking in eye and healthcare. A recent article by Blomquist reviewed the medical records of documented cases of MRSA ophthalmic and adnexal infections in an urban area over a 2-year period. Blomquist reported that CA-MRSA infections were most commonly preseptal cellulitis and/or lid abscess, with the second-most common being conjunctivitis. Corneal ulcers, endophthalmitis and orbital cellulitis also were documented. Overall, his results were in agreement with those of other recent studies, which indicate the prevalence of CA-MRSA is rapidly increasing.

**MRSA TREATMENT OVERVIEW**

We offer a brief reminder of a reasonable treatment approach for the more common ophthalmic/adnexal MRSA infections that were reported in the Blomquist study. When preseptal cellulitis and/or lid abscess conditions present, trimethoprim is an excellent, broad-spectrum bacteriostatic antibiotic that is particularly effective against *Staphylococcus aureus* and MRSA. Systemically, trimethoprim combined with sulfamethoxazole — historically marketed as Bactrim (AR Scientific) or Septra (Monarch Pharmaceuticals) — is a drug of choice when treating systemic soft tissue infections caused by MRSA pathogens.

For conjunctivitis caused by MRSA, topical trimethoprim solution is highly effective and available generically in combination with polymyxin B (originally known by the brand name Polymyxin [Allergan]). Because this combination drug is particularly effective against *Streptococcus pneumoniae* and *Haemophilus influenzae*, two common pathogens in the pediatric...
population, this is the drug of choice for children with bacterial conjunctivitis.

With a corneal ulcer, if the lesion is clearly infectious, an excellent initial approach is to prescribe a fluoroquinolone every hour while awake and Polysporin ointment at bedtime. If there’s no response or a suboptimal response, polymyxin B sulfate and trimethoprim may be used hourly, because if the ulcer is caused by a MRSA bacterium, the fluoroquinolone may be suboptimal but the trimethoprim should aid in the eradication of any resistant bacteria.

EXPOSURE TO MRSA AND OUR RESPONSIBILITIES IN PRACTICE

What is your daily exposure to MRSA? For every 100 patients you see, 25-30 will have Staphylococcus aureus colonized in their nostrils and 1 in 100 will be colonized with MRSA.1 The colonized individuals are not necessarily infected but rather are carriers, ready to transmit the organisms to others (or to perhaps infect themselves). Hand-washing is extremely important to prevent microorganism transmission and infection.

To supplement correct and frequent hand-washing, an alcohol-based hand sanitizer should be readily available in various locations throughout your office. Beyond aggressive hand-washing, using barriers to transmission, such as gloves and bandages, may help prevent and/or control the transmission of MRSA. It is critical to routinely disinfect instruments, counter tops and other high-touch areas. A commercial disinfectant or a 1:100 solution of diluted bleach (1 tablespoon bleach in 1 quart water) can be used to disinfect counter tops and other surfaces. In short, it is appropriate to have a protocol for infection control in place in any healthcare practice, with regular training and updates for all practice personnel.

You should educate patients on how to minimize transmission of infections. Advise them to practice good personal hygiene and remind them of these simple steps to help stop the spread of germs and infection:

- Keep hands clean by using soap and water or an alcohol-based hand sanitizer
- Don’t share personal items that come into direct contact with bare skin, such as towels and razors
- Keep high-touch surfaces clean
- Use barrier-like clothing or a towel between skin and shared exercise/fitness equipment
- Shower immediately after participating in exercise or sports activities that involve skin-to-skin contact.

MRSA AND THE CONTACT LENS PATIENT: COMPLIANCE AND SOLUTION PERFORMANCE

There are approximately 38 million contact lens wearers in the United States.4 Ocular exposure to CA-MRSA may be higher in contact lens wearers because many patients place worn lenses that could be contaminated on their eyes and they frequently touch their eyelids. As such, it is very important to remind them about the proper use of contact lens care products and clean hands to minimize the microbial exposure to the eye and adnexa. It is a well established fact, however, that patients commonly fail to heed proper “wear and care” guidelines. Examples of common noncompliance include:

- Handling lenses under nonhygienic conditions
- Not properly washing hands
- Not properly following lens rub or no-rub cleaning protocols (we encourage all of our patients to rub their lenses upon removal each evening)
- Using a dirty lens case
- Not using enough solution in the lens case

<table>
<thead>
<tr>
<th>BRAND</th>
<th>MANUFACTURER</th>
<th>DISINFECTING AGENT(S)</th>
<th>REQUIRED SOAK TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotrue</td>
<td>Bausch + Lomb</td>
<td>PHMB and polyquaternium</td>
<td>4 hours</td>
</tr>
<tr>
<td>renu fresh</td>
<td>Bausch + Lomb</td>
<td>PHMB</td>
<td>4 hours</td>
</tr>
<tr>
<td>renu sensitive</td>
<td>Bausch + Lomb</td>
<td>PHMB</td>
<td>4 hours</td>
</tr>
<tr>
<td>AQuify</td>
<td>CIBA Vision</td>
<td>PHMB</td>
<td>4 hours</td>
</tr>
<tr>
<td>COMPLETE Easy Rub</td>
<td>Abbott Medical Optics</td>
<td>PHMB</td>
<td>6 hours</td>
</tr>
<tr>
<td>OPTI-FREE Express</td>
<td>Alcon Laboratories</td>
<td>POLYQUAD and ALDOX</td>
<td>6 hours</td>
</tr>
<tr>
<td>OPTI-FREE RepleniSH</td>
<td>Alcon Laboratories</td>
<td>POLYQUAD and ALDOX</td>
<td>6 hours</td>
</tr>
<tr>
<td>Clear Care</td>
<td>CIBA Vision</td>
<td>HYDROGEN PEROXIDE</td>
<td>6 hours</td>
</tr>
</tbody>
</table>

Table 1: Today’s MPS products and a hydrogen peroxide product.
Topping off used solution in the lens case with fresh solution

A number of studies have shown that the overall rate of noncompliance with contact lens care varied from 50% to 99%, despite many of the lens wearers believing they were compliant. Yung evaluated compliance levels in experienced contact lens wearers and reported all subjects showed some degree of noncompliance in the care of their contact lenses or lens care accessories, with a majority (60%) noncompliant with at least six of a total of 15 lens care procedures. Patient compliance with contact lens care depends, in part, on patients following the recommended minimum soak time. Yung also found that 12% of subjects did not soak their lenses for the minimum indicated disinfection time or longer.

Even with the ease-of-use that multipurpose solutions provide, eyecare practitioners can expect that most patients will not use a solution properly and consistently. All eyecare practitioners should use easy-to-understand, clinically relevant guidelines to give each contact lens patient as a take-home handout. These materials should stress meticulous hygiene, including hand-washing; adherence to prescribed lens-wearing and replacement schedules; following directions on lens care packaging for processing of the lenses upon removal, whether indicated for a lens rubbing or no-rub regimen; use of fresh solution each evening with specific avoidance of “topping off” behavior; and at least quarterly replacement of the contact lens case. (A downloadable copy of “What You Need to Know about Contact Lens Hygiene and Compliance” is available on the American Optometric Association’s website.)

The elimination of microorganisms from lens surfaces is an essential component of proper contact lens care to minimize the potential for adverse events, such as bacterial, fungal or protozoal keratitis. Because of the association between these events and inadequate hygienic practices and noncompliance with lens care regimens (such as cleaning, rinsing and disinfecting), multipurpose solutions (MPS) with high disinfection levels are desirable. A variety of today’s MPS products are listed in Table 1.

An appropriate way to assess the performance of leading MPS products is to use well-accepted laboratory testing procedures and protocols. The U.S. Food and Drug Administration (FDA) and International Standards Organization (ISO) require evaluation of stand-alone biocidal efficacy, using a standard set of five microorganisms. The required panel of microorganisms is intended to represent the diverse microbial challenge that one might encounter:

- Two Gram-negative bacteria (Pseudomonas aeruginosa and Serratia marcescens)
■ One Gram-positive bacterium (*Staphylococcus aureus*)
■ Two fungal microorganisms (the mold *Fusarium solani* and yeast *Candida albicans*)

This standardized testing uses microbial strains from the American Type Culture Collection (ATCC), applying the stand-alone primary criteria for effective disinfection, which is a reduction in the number of bacteria by a minimum of 3 logs (99.9%) and a reduction of mold and yeast by a minimum of 1 log (90%) within the recommended disinfection time. These criteria must be fully met for a lens care product to be approved for marketing in the United States. Stand-alone biocidal test results show that each of the MPS products pass FDA/ISO standards for log reduction and that differences in disinfection performance exist between the products (Figure 1).

During a meeting of the Ophthalmic Devices Panel of the FDA in June 2008, recommendations were made for preclinical testing of contact lens products, including more rigorous and standardized “real-world” scenarios that more accurately replicate conditions and environments of consumers. (We aren’t aware of any new official testing requirements that have been implemented as of the date of this publication.) Assessing biocidal effectiveness of lens care solutions against microorganisms collected from clinically worn lenses and used lens cases is one example of what is called a “real world” scenario. Microorganisms recovered from clinical circumstances are referred to as clinical isolates and represent a variety of microbial strains from the community.

Isolating and testing microorganisms from common environmental/community sources may provide both broader and deeper insights into the biocidal profiles of various lens care products than what is gained from testing against the standard ATCC challenge organisms. It is important to note that employing such test protocols against clinical isolates is not required for marketing approval. Only the required standards establish efficacy and safety of lens care products. Tests against clinical isolates, even though they use the identical protocols applied to testing of standard microorganisms, simply indicate differences in disinfection performance profiles of care products.

MRSA is not included by the standards organizations (ISO and FDA) as one of the lens care solution test panel microorganisms, yet, as we’ve discussed, MRSA is an increasingly prevalent organism in the community. Testing of the biocidal efficacy of today’s leading multipurpose solutions (MPS) and a hydrogen peroxide disinfection solution has revealed notable differences in disinfection performance among the solutions against ocular clinical

---

![Figure 2](image_url)

**Staphylococcus aureus**

(n=10 clinical isolates, tested 3 times each)

<table>
<thead>
<tr>
<th>Solutions</th>
<th>Log Reductions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotrue</td>
<td>0.0</td>
</tr>
<tr>
<td>ReNu Fresh</td>
<td>1.0</td>
</tr>
<tr>
<td>ReNu Sensitive</td>
<td>1.5</td>
</tr>
<tr>
<td>OPTI-FREE RepleniSH</td>
<td>2.0</td>
</tr>
<tr>
<td>OPTI-FREE Express</td>
<td>2.5</td>
</tr>
<tr>
<td>Aquity</td>
<td>3.0</td>
</tr>
<tr>
<td>COMPLETE Easy Rub</td>
<td>3.5</td>
</tr>
<tr>
<td>Clear Care</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Results of in vitro study following FDA/ISO stand-alone procedure for disinfection products. Log reduction values at a minimum 5-minute soak time with organic soil. Each point represents test results for an individual clinical isolate. 10 isolates were tested 3 times each. Shaded line depicts mean log reduction, measured after manufacturer’s recommended disinfection time (60 minutes) of the 3 runs for all of the 10 isolates.

* Test performed not required by FDA/ISO standards.

---

Figure 2. Contact lens care product performance against *Staphylococcus aureus* clinical isolates. N = 10 clinical isolates, tested 3 times each.
isolates of \textit{Staphylococcus aureus} (Figure 2) and methicillin-resistant \textit{Staphylococcus aureus} (Figure 3). Data points at or above the horizontal 3 log reduction line meet the stated stand-alone efficacy requirement established for the standard ATCC challenge organisms.

Yet another difference between how lens care products disinfect is their rate of disinfection. Recalling that 12% of patients did not soak their lenses for the minimum indicated disinfection time or longer, a good clinical question might be “how do MPS perform with respect to disinfection efficacy if patients don’t follow the manufacturer’s minimum soak time instructions?”

From the results of a study that examined the stand-alone disinfection efficacy of five different MPS products at 10, 20 and 30 minutes against various pathogens, we gain insights into how the disinfecting profiles may differ between leading care products in this simulated situation of noncompliant behavior for the time periods evaluated. But first, an important caveat to the reader: just like testing of MPS against clinical isolates, the rate of disinfection efficacy is not required for product marketing approval.

It is important to note that the study cited here was neither intended to show nor meant to suggest that any MPS be used for less than its labeled, recommended disinfection soak time.

Two of the MPS lens care solutions (reNu fresh, formerly ReNu MultiPlus [Bausch + Lomb] and AQuify [Ciba Vision]) showed significantly higher rates of disinfection at 30 minutes against \textit{Staphylococcus aureus} (ATCC 6538). The minimum soak time for several lens care products to achieve adequate disinfection is 6 hours (minimum), while others require only a 4-hour minimum soak (Table 1), even against MRSA (Figure 3).

**ENCOURAGING COMPLIANCE, PROTECTING PATIENTS**

We’ve offered a brief overview of MRSA and its infection control and treatment in the eyecare practice. Gram-positive bacterial pathogens, particularly staphylococcal species, are some of the most common causes of ocular infections. The prevalence of CA-MRSA is rapidly rising. It is well known that compliance with the steps in proper contact lens care and wearing hygiene, even with the ease of use with MPS, is generally quite low. With questionable compliance, recommending a contact lens solution for your patients that provides strong disinfection (> 3 log reduction) against clinical isolates (even though not specifically required by official ISO/FDA lens care performance standards) of \textit{Staphylococcus aureus}, and particularly against MRSA, may be in the best interest of your patients and your practice.
Specific References


General References

- Donshik PC, Ehlers WH, Anderson LD, Suchecki JK. Strategies to better engage, educate, and empower patient compliance and safe lens wear: compliance: what we know, what we do not know, and what we need to know. Eye Contact Lens. 2007;33:430-433.