Infection Control for MRSA

Infection commonly occurs under compromised host and wound conditions. Wound infection extends inflammatory response, delays collagen synthesis, retards epithelialization, and results in increased tissue destruction. Chronic wounds are commonly contaminated with one of several flora – *enterococcus, staphylococcus, bacillus* and occasionally gram-negative organisms.[1] Infection is defined as invasion of a micro-organism into tissue and, numerically, totals at least 10^{4-5} (depending on the specific laboratory).

Resistance is of major concern to health care providers and is of two types: acquired and absolute. Most articles and references discuss "acquired relative" resistance. However, it is important to note the definition of "relative": the gradual increase in the minimal inhibitory concentration (MIC_{90}) occurring in susceptible organisms over time. With relative resistance, the antibiotic is still effective against the organism. Most resistance encountered in clinical care is of this type. Absolute resistance occurs with a previously sensitive organism becoming no long sensitive to an antibiotic regardless of dosage. Acquired absolute resistance is the most serious problem encountered in critical care practice.[5]

Of particular concern to wound patients are the two conditions of Methicillin-resistant staphylococcus aureus (MRSA) and more recent development of Vancomycin-resistent enterococcus (VRE). The presence of staph aureus on the skin is a given for as many as 20% - 50% of patients. Given the opportunity of a skin break, staph aureus quickly invades and results in a blatant infection.

Since the 1940s, science has developed medical treatments –including penicillin – to treat infections. Unfortunately the strain soon developed enzymes (penicillinase) that inactivated certain antibiotics – including ampicillin, etc. Methicillin, semisynthetic penicillin, is the first semi-synthetic penicillin found to be effective against the penicillinase-resistant strains. However, within the first decade of its use in the late '60s and early '70s, an outbreak of methicillin-resistant staph aureus occurred. Currently such outbreaks account for 20%-25% of *S.aureou* isolates. [2] Outbreaks occurred in both acute and long-term facilities, the latter hosting a higher prevalence of MRSA than acute-care hospitals. In some persons the strains mutate and develop a greater dilemma of developing resistance to other antibiotics. Mulligan reports that many contemporary strains of MRSA are resistant to multiple classes of antimicrobial agents. Aminoglycoside resistance is usually due to presence of a bifunctional aminoglycoside-modifying enzyme.

Most persons attribute over-usage to the causation of resistance. Yet, Cunha disagrees and cites the common usage of drugs such as ampicillin, tobramycin, and doxycycline and other. Though third generation cephalosporins receive the blame for resistance problems within an institution, Cunha further differentiates the lack of problems with most agents in this drug class. He identifies the association of resistance of organisms to ceftazidime – a proof that resistance relates more to a specific antibiotic than to a class of drugs.[5]

The problem

There are two mechanisms that are responsible for the resistance to B-lactam antimicrobial agents. The first is the production of B lactamases that destroy the drugs, a factor that led to the development of B-lactamase-resistant antistaphylococcal penicillins such as methicillin.

Secondly, *Staph aureus* produces enzymes (penicillin-binding proteins – PBS) that can be interfered with by antibiotics to prevent cell wall synthesis and cause organism death. There

must be a high affinity between the drugs and the bacterial PBPs for the drug to effective.[6] Unfortunately, MRSA strains have developed alterations to one of these PBPs that prevents binding with certain antibiotics.[4] Given the multiplicity of antibiotics included in this group, the strain has also acquired a pseudo-title of "multiple resistant *Staph aureus.*"

A commensal of the colon, Staph aureus colonizes the nares in 30% percent of the population, the perineum in half that number. Transmission is usually by hand-contact. Hospital workers, physicians, intravenous drug abusers, patients undergoing dialysis as well as those with dermatological disease or with diabetes mellitus are often carriers.[6]

The significance in wound care is an essential consideration. With slough and necrotic tissue present in many wounds, the environment of such wounds provides a primary opportunity for MRSA – and again leads to the difficulty of controlling the problem. MRSA colonization precedes infection. Therefore the main treatment is one of offense: treat colonization; use antiseptic and antimicrobial agents.

Treatment of the Individual Patient

Treatment for the individual patient is often intravenous vancomycin. Since Rifampin is effective in combination with other antibiotics, it can be highly effective with vancomycin when vancomycin alone is ineffective. ***But*** the combination of two agents can also create an antagonistic effect even when the organism is susceptible to each. Gentamycin and vancomycin together can be effective; however, ototoxicity and nephrotoxicity require careful monitoring with this combination therapy. Other individual classes of drugs or agents have some success *in vitro* but have also resulted in some resistance leading to recommendations for combination therapy or limited use to prevent advancing of resistance.

Recently, the advent of greater dilemmas has struck with the knowledge that MRSA is impacting health care workers and has the potential for any individual to acquire gene-conferring vancomycin resistance from vancomycin-resistant enterococci (vancomycin resistant staphylococcus aureus). With vancomycin commonly being the favored drug to treat MRSA, such developments create a severe and critical problem!

Topical treatment of MRSA includes antimicrobial therapy with (Mupirocin) Bactroban being a favored agent. Thus, it is wise to use mupirocin judiciously in other wounds to prevent a resistance to this antimicrobial as well. Given, the multiple transfers and activities for patients among hospital or facility units, universal precautions are imperative to prevent cross-contamination.

MRSA outbreak

Mode of transmission for MRSA is admission of an infected or colonized patient or, less often, through the transmission by an infected or colonized hospital worker.[6] Wenzell's self-appointed consensus panel defines "outbreak" as an increase in the rate of MRSA cases or a clustering of new cases due to the transmission of a single microbial strain in a health care institution.[2] The panel further carefully and precisely defines various terms:

> "Case" includes both newly infected and colonized patients;
> "Infected" requires meeting of CDC criteria for infection with a positive MRSA culture;
> Identification of a "Colonized" patient may occur through routine cultures or through one conducted for point prevalence purpose. Previously acquired MRSA infections and continued colonization cases upon readmission are not included in the definition of new cases relative to an outbreak.

"Nosocomial" includes detection of MRSA in patients after 72 hours of hospital admission. Should a patient be colonized or infected on admission and is also known to have had a previous admission within 4 weeks are defined as having a nosocomial acquisition versus a community acquisition.
"Clustering" is the occurrence of at least two cases closely related by time, location, or other epidemiological inclusions. Universal precautions are imperative to prevent cross-contamination. [2]

The panel defines two methods of establishing an increase in the case rate – the *statistical approach* and the *experiential approach*, a more practical technique. The experiential approach provides for an increase over the threshold or in the absolute number of cases. The MRSA baseline data for an institution or the average baseline data compiled from similarly sized facilities serves as the definition of threshold baseline. Thus, given collection of data for at least 1 year, a 25% increase over baseline represents an [illegible] outbreak. [2] See Table 1 below:

Threshold rates for identifying high rates of MRSA transmissions[2]

Hospital beds	Number of new nosocomial cases per 100 admissions	Number of new nosocomial cases per 100 patient-days
<200	0.13	0.25
200-499	0.25	0.3
500+	0.5	0.6

The absolute number may vary dependent upon the type of unit, i.e. one serving high-risk patients may have zero-tolerance relative to outbreak definition. Consequently, even the development of one MRSA case is an outbreak. Other units, not having a zero tolerance or serving high-risk patients, can incur three nosocomial cases within the same unit within one month. The panel verifies that experiential criteria do not apply to units where MRSA is endemic. [2]

Techniques for Management of Outbreaks

An occurrence of MRSA outbreak initiates a series of events by facility personnel – an interdisciplinary process. With the first phase possibly in place, that of compilation of line lists and notification of unit personnel to intensify their universal precautions procedures, the facility moves into phase II, hypothesizing a source of outbreak by confirming any clusters and identifying a common source. In this phase microbiology should save organisms and experts review the antibiograms to determine relationship, if any, of the isolates. It is of course imperative that the team notify management of the outbreak and current action steps; reinforcement of compliance with universal precautions is essential during this and all phases.

Phase III marks the beginning of case-control. All persons (patients, personnel, known visitors) undergo sampling of suspicious lesions (boils, dermatitis, etc). In some cases staff may obtain cultures from multiple body sites (wounds, ostomy, dermatitis, umbilical cords). Simultaneously the facility monitors case rates in other patient care units or areas; this surveillance must include a comparison of rates occurring over the previous 3+ months. It can be prudent to treat high-risk patients with mupirocin calcium applications.

Phase IV marks the affirmation of the hypothesis. Continued microbiology testing continues, as do the efforts to practice infection control. The panel further recommends that the severity

and extent of the outbreak may warrant prophlylaxtic mupirocin calcium and nasal decolonization while awaiting completion of typing.[2]

Recurrence of the above protocol creates the need for the facility to determine presence of a single strain as well as enforce infection control measures and explore potential colonized patients or environmental reservoirs. Where these measures fail, the facility team can again initiate the algorithm at phase I with emphasis to each step. [2]

Management of Outbreaks

Simply put, infections, i.e. MRSA, cost money. With measures as inexpensive and simplistic as good hand-washing techniques being effective in infection control, designated personnel within facilities must be responsible for reviewing and implementing this and other strategies to preventing subsequent transient contamination of health care workers' hands, a primary mode of MRSA transfer. Other techniques, proven by double blind, placebo-controlled studies, include the use of a 5-day course of mupirocin calcium treatments to the anterior nares twice daily. Result showed elimination of *s. aureus* nasal carriage in 91% of health care workers 48-96 hours after treatment completion. A significant portion (74%) continued to have negative cultures weeks later. However, mupirocin use also reduced hand carriage and may also be useful in prophylactic treatment of high-risk patients during phase III. [2]

Combination oral (trimethoprin-sulfamethoxazole, rifampin) /topical therapy (mupirocin calcium) significantly reduced nasal carriage but achieved lower rates (66% - 81%) with extranasal sites. Failures in patients receiving combination therapy were largely due to Rifampin resistance. [6] Strains that have developed a mupirocin resistance are rare and respond well to a 2% mupirocin preparation. This finding does not connote endorsement of topical antibiotics as a substitute for systemic antibiotic therapy of that antibiotic as a technique to minimize resistance development. Note too that mupirocin application to sites other than the nares is difficult and ineffective. [2]

Concern in Wound Care

As stated above, transmission of MRSA is through nares and breaks in integumentary systems, i.e. wounds. Treatment in wound care is changing with the discouragement of topical antiseptics. Again, Bactroban is widely effective with once or twice daily use to colonized or infected wounds for 5 –14 days (unless indicated otherwise clinically). **But**, Cunford reiterates the caution from the above paragraph in that Bactroban usage is contraindicated in open wounds without MRSA since this usage may lead to further resistance. Rather, she recommends antibacterial agents such as chlorhexidine, iodine-based products, nitrofurazone, and silver sulphadiazine as acceptable alternatives. [4]

Other precautions that may have been previously instituted by facilities include:

- Hand washing by *all* persons having patient contact between patient encounters
- Use of disposable gloves for care and dressing of all wounds
- Wearing of gloves for all wound care; discarding *before* leaving patient care room/area. Follow with hand washing.
- Wearing of gowns with risk of exposure to draining wounds or danger of soiling clothes
- Sterilization of instruments between patient usage
- Cleansing of scissors between patient usage
- Wearing of masks if aerosolization or splashing of MRSA organisms can occur, e.g. with wound irrigation.

- Cleansing of patient care area per hospital protocol after usage (including out-patient) by MRSA patient
- Non-entry of patient chart into patient care area
- Flag the chart for notification upon readmission
- Notify other health care providers or sites of transfer of patient status[6]

Affect for health care workers

Mclaughlin et al cite the issue of the high colonization rate among health-care workers and the need for precautionary measures to decrease the incidence of MRSA among this group. However, the risk of health care workers who undergo surgery themselves create a greater risk for themselves and the employing facility.[3] Therefore, each facility must develop and adopt its policy regarding the isolation and/or restriction of facility personnel during decolonization phases. Some sites have opted for a short (2-3 day) medical leave for the employee who is a carrier and is undergoing treatment. While factors such as extent of outbreak, method of transmission, etc. may affect this decision, consideration for the employee surgical patient may warrant pre-operative nasal cultures with appropriate intervention for those with positive results.

Summary

MRSA is often due to the colonized patient leading to infection. Treatment must be aggressive with intravenous or oral antibiotic therapy. Treatment for the colonized patient includes topical therapy to the nares. Special precautions are essential for the wound care patient to prevent cross-contamination.