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## Healthcare-Associated Infections (HAIs): Guide to HAI Terminology

This document is intended to help provide definitions of terms commonly used in discussing multi-drug resistant organisms (MDROs), primarily within the context of healthcare facilities.

### *Multi-drug resistant organisms*

Multidrug-resistant organisms are bacteria and other microorganisms that have developed resistance to antimicrobial drugs.<sup>1</sup> Examples include:

- MRSA - methicillin/oxacillin-resistant *Staphylococcus aureus*
- VRE - vancomycin-resistant *Enterococcus*.
- C-Diff - *Clostridium difficile*

### Key pathogens

#### *Clostridium difficile*

*Clostridium difficile* is a bacterium that causes diarrhea and more serious intestinal conditions such as colitis.<sup>2</sup> Over the past two years, several U.S. states have reported increased rates of *C. difficile*-associated disease, noting more severe disease and an associated increase in mortality.<sup>3</sup> This may be caused by changes in antibiotic use, changes in infection prevention and control practices, or the emergence of a new strain of *C. difficile*-associated disease with increased virulence and/or antimicrobial resistance.<sup>4</sup>

The usual treatment for *C. difficile*-associated disease includes, when possible, stopping antibiotics being given for other purposes and/or treatment with metronidazole or vancomycin.<sup>5</sup> Depending upon the severity of the *C. difficile*-associated disease, metronidazole is likely to be the appropriate first-line therapy for most cases.

Infection prevention and control measures should include: hand hygiene<sup>6</sup> practices effective against *C. difficile* spores; contact precautions; and environmental cleaning and sterilization.<sup>7</sup>

#### **MRSA**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of staph that is resistant to certain antibiotics.<sup>8</sup> These include methicillin and other more common antibiotics such as oxacillin, penicillin and amoxicillin. MRSA causes infections typically resulting in extended hospital stays, associated excess healthcare costs and carries a high mortality rate.<sup>9</sup> MRSA first appeared in the late 1970s and currently accounts for 40-50 percent of staph strains isolated from United States hospitals.<sup>10</sup> Limited treatment options include vancomycin, considered to be the drug of "last resort" when other antibiotics fail.

MRSA differs from non-resistant staph by having a gene known as *mecA*. This allows production of a protein (penicillin binding protein (PBP) 2a) that effectively inactivates antibiotics related to penicillin.<sup>11</sup> As a result, MRSA is resistant to the entire class of beta-lactam antibiotics, including penicillins and cephalosporins, and often to many other antibiotics.

- **CA-MRSA**

Community-associated MRSA (CA-MRSA) infections are acquired by people who have not been hospitalized or had a medical procedure (such as dialysis, surgery, catheter insertion) within the past year.<sup>12</sup> These infections usually appear as skin infections, such as pimples and boils, in otherwise healthy people.

The differences between the healthcare-associated (HA) and community-associated strains of MRSA can be demonstrated on a genetic level.<sup>13</sup> The genes that cause methicillin resistance in CA-MRSA strains differ from those conferring resistance in HA strains. For example, virtually all CA-MRSA strains (and no HA strains) contain genes that allow production of the toxin Panton-Valentine leukocidin (PVL), which causes tissue destruction.

- **HA-MRSA**

Healthcare-associated MRSA, also known as nosocomial MRSA, is a new infection that a patient acquires while under the care of a healthcare institution. This type of infection poses a major threat to patients admitted to many hospitals.<sup>14</sup> In 1980, the MRSA accounted for only 2 percent of all *S. aureus* HAIs reported in the United States to the CDC through its National Nosocomial Infections Surveillance system (NNIS).<sup>15</sup> Today, MRSA accounts for over 60 percent of *S. aureus* infections in the United States, creating a serious healthcare issue.

## **MSSA**

Methicillin-sensitive or methicillin-susceptible *Staphylococcus aureus* refers to strains of the bacterium that are not resistant to methicillin.<sup>16</sup>

## **PVL**

Panton-Valentine leukocidin (PVL) is a toxin that causes white blood cell destruction and death of tissues (necrosis).<sup>17,18</sup> It was first described in 1932 by Panton and Valentine. PVL is mostly associated with CA-MRSA, particularly in skin and soft tissue infections, and less often to pneumoniae and bacteremia; it is carried by up to 2 percent of clinical isolates of *Staphylococcus aureus*.<sup>19,20</sup>

## **SCC *mec***

The genetic basis of MRSA's methicillin resistance is the presence of *mecA*, a gene coding for a penicillin binding protein. This gene is found on a mobile genetic element called SCC-*mec* (staphylococcal cassette chromosome *mec*).<sup>21</sup>

## ***Staph infection***

*Staphylococcus aureus*, often referred to simply as “staph”, is a bacterium found on the skin and inside the noses of healthy people.<sup>22,23</sup> This is one of the most common causes of skin infections in the United States, many of which are minor (pimples, boils and other skin conditions). Staph is also a significantly problematic healthcare-associated pathogen causing infections including septicemia, pneumonia, wound sepsis, septic arthritis, osteomyelitis, and postsurgical toxic shock syndrome.<sup>24</sup> Some infections, such as bacteremia, may have death rates as high as 40 percent.

### ***USA300***

First observed in 2000, USA300 is the most common clone (or strain) of staph causing CA-MRSA in the U.S.;<sup>25</sup> this clone is not associated with HA-MRSA. USA300 is a very stable strain resistant to treatment with penicillin, oxacillin and erythromycin and is variably resistant to the antibiotic tetracycline.<sup>26</sup>

### ***USA400***

Another clone that is linked to CA-MRSA in the United States is USA400. Prior to the emergence of the USA 300/400 strains, most patients with CA-MRSA infections had identifiable risk factors, including recent hospitalization or nursing home residence, invasive/percutaneous procedure, and/or chronic dialysis therapy. However, initial reports suggest that patients with USA300/400 strains have not had these risk factors; risk factors for infection with these strains remain poorly defined.

### ***VISA/VRSA***

The term vancomycin-resistant *Staphylococcus aureus* (VRSA) describes strains of this bacterium that are resistant to doses of the antibiotic vancomycin at or above 32 micrograms per milliliter.<sup>27</sup> Strains of staph that are killed by doses of vancomycin less than or equal to 4 micrograms per milliliter are considered susceptible to the antibiotic, while strains that require vancomycin doses of 8 to 16 micrograms per milliliter to kill them are considered to have intermediate levels of resistance (vancomycin-intermediate *Staphylococcus aureus* (VISA)).

Since glycopeptides, particularly vancomycin, have been mainstays of therapy for MRSA, the emergence of resistance to these agents is of great concern.<sup>28</sup> Reduced vancomycin susceptibility increases the chance that some strains of MRSA may become fully resistant to all currently available antibiotics.<sup>29</sup>

VISA and VRSA infections have been rare.<sup>30</sup> To date, there have been sixteen cases of infection caused by VISA and six cases of infection caused by VRSA have been reported in the United States. Cases of VISA have also been reported in France, Japan and Hong Kong.<sup>31,32,33</sup> People who developed VISA and VRSA infections had several underlying health conditions (such as diabetes and kidney disease), previous MRSA infections, underwent catheterization, recent hospitalizations, or recent exposure to vancomycin and other antibiotics.<sup>34</sup> To date, all VISA and VRSA isolates have been susceptible to several FDA-approved drugs.<sup>35</sup>

### ***VRE***

First reported in 1989, Vancomycin-resistant *Enterococcus* (VRE) is an antibiotic-resistant form of a type of a bacterium that is normally present in human intestines and in the female genital tract, and is often found in

the environment.<sup>36</sup> Enterococci are a leading cause of healthcare-associated bacteremia, surgical wound infections and urinary tract infections. They are becoming resistant to many, and sometimes all, standard therapies.<sup>37</sup> Data reported to CDC in 2004 showed that VRE caused about one-third of infections in intensive care units.

Most VRE infections occur in hospitals and are usually transmitted by direct contact with stool, urine or blood containing the bacterium.<sup>38</sup> They can also be spread indirectly via the hands of healthcare providers or on contaminated environmental surfaces. The following populations are at an increased risk of becoming infected with VRE:<sup>39</sup>

- People who have been previously treated with vancomycin and combinations of other antibiotics such as penicillin and gentamicin.
- Those who are hospitalized, particularly when they receive antibiotic treatment for long periods.
- Individuals with weakened immune systems, such as patients in Intensive Care Units, or in cancer or transplant wards.
- Patients who have undergone surgical procedures such as abdominal or chest surgery.
- Those with medical devices that stay in for some time, such as urinary catheters or central intravenous catheters.

Most VRE infections can be treated with antibiotics other than vancomycin.<sup>40</sup> The treatment of VRE is determined by laboratory testing to determine which antibiotics are effective. People who are colonized (bacteria are present, but have no symptoms of an infection) with VRE do not usually need treatment.

## Recognition

### *Carrier*

A person who harbors a specific pathogenic organism, has no discernible signs and symptoms, and is potentially capable of spreading the organism to others.<sup>41</sup>

### *Colonization*

The organism is present in or on the body but is not causing illness.<sup>42</sup>

### *Colonization and infection: risk factors*

Risk factors for both colonization and infection include:<sup>43</sup>

- Severity of illness
- Previous exposure to antimicrobial agents
- Underlying diseases or conditions, particularly chronic renal disease, insulin-dependent diabetes, peripheral vascular disease, dermatitis or skin lesions
- Invasive procedures, such as dialysis, presence of invasive devices, urinary catheterization
- Repeated contact with the healthcare system
- Previous colonization by a multidrug-resistant organism (MDRO)
- Advanced age

For MRSA, the proportion of colonized patients who become infected varies from 5 to 60 percent, depending on the study population and strain of MRSA.<sup>44</sup> The risk of colonization leading to infection is increased if the skin is broken.

### ***Contamination***

The presence of microorganisms on inanimate objects.<sup>45</sup>

### ***HAI***

A healthcare-associated infection (HAI) is a new infection that a patient acquires while under the care of a healthcare institution. It may also be referred to as a nosocomial infection.

The urinary tract is the most common site for HAIs, accounting for more than 40 percent of the total reported by acute-care hospitals and affecting an estimated 600,000 patients per year (1979).<sup>46</sup> Pneumonia is the second most common HAI, accounting for approximately 15 percent of all HAIs and 27 percent and 24 percent of all infections acquired in the medical intensive-care unit (ICU) and coronary care unit, respectively.<sup>47</sup> Surgical site infections (SSIs) are the third most frequently reported HAI, accounting for 14 to 16 percent of all HAIs among hospitalized patients (based on 1993 NNIS system reports).<sup>48</sup> Catheter-related bloodstream infections are another significant category of HAIs.<sup>49</sup>

### ***Infection***

The organism is present and causing illness.<sup>50</sup>

### ***Outbreak***

A sudden increase in the number of individuals who contract a specific infectious disease in a population, putting others at risk.<sup>51</sup>

### ***Pathogen***

A disease-producing agent.<sup>52</sup>

### ***Prevalence***

In the context of MRSA, prevalence refers to how frequently the bacterium occurs in the population, as well as to the proportion of *Staphylococcus aureus* strains that show methicillin resistance. For example, in the United States, MRSA accounted for only 2 percent of all *S. aureus* HAIs reported in 1980 to the CDC through its NNIS hospitals. Today, MRSA accounts for over 60 percent of *S. aureus* infections, creating a serious healthcare issue.<sup>53</sup> Some 25 to 30 percent of the United States population is colonized with staph, and about 1 percent is colonized with MRSA.<sup>54</sup> Surveillance studies indicate that some 7 percent of patients admitted to the hospital are carriers of MRSA.<sup>55</sup>

### **Source**

The location or object from which a pathogen is immediately transmitted to a host.<sup>56</sup>

### **Staph infections: risk factors**

The body's defenses must be weakened or breached before *Staphylococcus aureus* can cause disease.<sup>57</sup> The bacterium enters the body through wounds such as burns, deep cuts or surgical incisions. People whose immune systems are weakened from other illnesses, such as hospital patients with influenza, leukemia, skin disorders or diabetes, or patients recovering from kidney transplants, are particularly vulnerable. Patients receiving radiation or chemotherapy are also more susceptible to staph infections.

### **Toxin**

A microbial product or component that at low concentrations can injure a cell or organism.<sup>58</sup>

### **Virulence**

The degree or intensity of pathogenicity of an organism as indicated by mortality rate from the related disease and/or ability to invade tissues and cause disease.<sup>59</sup>

## **Detection**

### **Active surveillance**

Surveillance is ongoing monitoring using methods distinguished by their practicability, uniformity and rapidity.<sup>60</sup> It aims to detect changes in trends or distribution of infections, so that investigative or control measures can be started. Active surveillance is systematic and involves review of each case within a defined time frame; it includes routine patient screening for pathogens of concern and involves a multidisciplinary approach for the management and control of healthcare-associated infections. Ideally, it prevents single clones of infectious microbes from spreading within a population and thereby minimizes the number of persons affected.<sup>61</sup>

### **Active surveillance testing**

Active surveillance testing involves taking patient specimens upon admission to the hospital to test for MRSA. This action may be repeated at specified intervals and upon discharge or transfer to another ward. Prompt identification of MRSA enables healthcare providers to initiate appropriate interventions aimed at preventing MRSA-associated infections.

### **BD GeneOhm™ MRSA Assay**

A rapid, real-time molecular test for the detection of MRSA directly from a single nasal swab specimen. The test provides an innovative, accurate, and rapid format to detect MRSA carriage. Using polymerase chain reaction (PCR) technology, it can detect MRSA in less than two hours directly from the patient specimen. The test works by detecting a unique molecular sequence that confers a double specificity: one half of this sequence is the unique *Staphylococcus aureus* chromosome, and the second half is the *SCCmec* cassette, the genetic element that confers methicillin resistance.

## ***Culture***

A microbiological (or microbial) culture is a method of growing a microbial organism to determine what it is, its abundance in the sample being tested, or both.<sup>62</sup> One of the primary diagnostic methods of microbiology, it is often used as a tool to determine the cause of infectious disease by letting the agent multiply (or reproduce) in predetermined media in the laboratory. The most common method of microbiological culture uses Petri dishes with a layer of agar-based growth medium to grow bacterial cultures. This is generally done inside of an incubator.

The sample taken from the patient – for example, a nasal swab – is commonly referred to as a “culture specimen” or “culture,” even though it may subsequently be used for a molecular test rather than being grown in a Petri dish.

## ***Gram stain***

A differential staining procedure that allows categorization of bacteria into two groups, Gram-positive (such as staph and enterococci) and Gram-negative (such as *Salmonella* and *E. coli*) based on their ability to retain crystal violet when decolorized with an organic solvent such as ethanol.<sup>63</sup>

## ***Nasal swab***

A test performed by swabbing the nostrils that is sent for culture to determine the presence of MRSA.<sup>64</sup> A positive nasal swab indicates exposure, not infection.

*Staphylococcus aureus* is carried in the nostrils or on the skin of about 30 percent of the population.<sup>65</sup> This increases to about 50 percent in healthcare workers or hospital in-patients. Nasal carriage is considered a source of subsequent infection in healthcare settings.<sup>66</sup>

## ***Sensitivity***

In screening for an infection such as MRSA, the sensitivity of the test is the proportion of people with MRSA who are correctly identified by a screening test.<sup>67</sup>

## ***Specificity***

The proportion of people without an infection who are correctly identified by a test. The specificity is the number of true negative results divided by the sum of the numbers of true negative plus false positive results.<sup>68</sup>

## ***Universal surveillance***

Universal surveillance, also known as all-admissions surveillance, introduces the testing of all admitted patients, not just “high-risk” patients. This approach has been shown to be far more effective than passive or targeted active surveillance when monitoring for MRSA.<sup>69</sup>

## Intervention

### *Antibiotic*

A microbial product, or its derivative, that kills or inhibits the growth of susceptible microorganisms.<sup>70</sup>

### *Antibiotic resistance*

Antibiotic resistance describes the condition of bacteria whose growth and reproduction is unaffected by particular antibiotics.<sup>71</sup> Bacteria have a variety of mechanisms for evading the toxic effects of antibiotics. In some cases, the bacterial cell membranes are altered so that an antibiotic cannot enter the cell. In others, resistant bacteria actively pump the antibiotic out of the cell as soon as it enters. Still other resistant bacteria make an enzyme that degrades an antibiotic as soon as it enters the cell.

### *Antimicrobial agent*

A substance that kills or inhibits the growth of microorganisms.<sup>72</sup>

### *Decolonization*

Removal of organisms at body site(s), through use of topical and/or other treatment with antimicrobial agents.<sup>73</sup>

### *Disinfection*

A process that eliminates many or all microorganisms except spores.<sup>74</sup>

### *Contact precautions*

Contact precautions are designed to help prevent transmission of infections from individuals known to be colonized or infected. They include:<sup>75</sup>

- Placing a patient with MRSA in a private room.
- Wearing gloves (clean nonsterile gloves are adequate) when entering the room, removing gloves before leaving the patient's room, and washing hands immediately with an antimicrobial agent.
- Wearing a gown when entering the room if substantial contact with the patient or environmental surfaces is expected, then removing it before leaving the room.
- Limiting movement of the patient from the room to essential purposes only.
- Ensuring that patient-care items, equipment and surfaces receive daily cleaning.
- When possible, dedicating the use of noncritical patient-care equipment and items to a single patient (or group of patients infected or colonized with MRSA). If use of common equipment is unavoidable, it should be cleaned and disinfected.

### *Infection prevention and control*

Infection prevention and control practices aim to keep patients and healthcare workers in healthcare settings protected from infectious diseases.<sup>76</sup>

## *Methicillin*

Methicillin is a narrow-spectrum beta-lactam antibiotic that was previously used to treat staph infections.<sup>77</sup> It is no longer in clinical use, having been largely replaced by flucloxacillin and dicloxacillin. However, the term methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be used to describe staph strains that are resistant to penicillins.

## *"Search and destroy"*

This approach to MRSA control is used successfully in some northern European countries, including the Netherlands, Finland and Denmark, to keep MRSA at low levels.<sup>78 79 80</sup> It involves active surveillance screening and isolating high-risk patients upon hospital admission, as well as strictly enforced contact precautions for patients who test positive for MRSA. Judicious use of broad-spectrum antibiotics is also emphasized.<sup>81</sup>

An example of a "search and destroy" program is one led by Dr. Margreet Vos, head of infection control at Erasmus University Medical Center (Rotterdam, the Netherlands).<sup>82</sup> This 1,200 bed university hospital offers all general medical specialties and transplant programs and is a leader in developing effective MRSA control strategies.<sup>83</sup> An outbreak of MRSA in 2002 was successfully controlled using "search and destroy," which involves the early detection and containment of infection among patients, healthcare workers and the healthcare environment."

## *Transmission*

The process by which infectious micro-organisms such as MRSA and VRE move from colonized or infected people to non-infected individuals. Transmission of infection in a hospital requires at least three elements: a source of infecting microorganisms, a susceptible host and a means of transmission.<sup>84</sup>

- ***Transmission: how it occurs***

The main transmission of MRSA is through direct contact via the transiently contaminated hands of healthcare workers, although airborne and environmental transmission also occurs.<sup>85</sup> Since staph can survive dry conditions, it can remain viable for long periods of time on dust particles, clothing, furniture or hospital equipment.<sup>86</sup> Staph is able to grow with or without oxygen, and it can survive the aerobic conditions of the skin or nasal passages, waiting for an opportunity to invade deeper tissues. Once inside the body, staph can produce powerful toxins that destroy and disrupt tissues. Staph can also resist immune system cells that engulf and destroy invading bacteria.

A high percentage of hospital workers are passive carriers of staph, harboring it on their skin and in their upper respiratory tracts without showing any symptoms.

CDC's recommendations for preventing transmission of MRSA and VRE in hospitals consist of the standard precautions needed for all patient care.<sup>87</sup> These include hand washing, gloving, masking, gowning, appropriate device handling, and appropriate handling of laundry.<sup>88</sup> CDC also recommends contact precautions when the facility considers a multidrug-resistant organism to be of special clinical and epidemiologic significance.<sup>89</sup>

Recommendations for preventing MRSA and VRE in hospitals include:

- Obtain stool cultures or rectal swab cultures of roommates of patients newly found to be infected or colonized with VRE, and also obtain nasal swabs for MRSA colonization

- Adopt a policy for deciding when patients can be removed from isolation, such as upon receiving VRE-negative results on at least three consecutive occasions, one or more weeks apart.

### *Vancomycin*

A glycopeptide antibiotic used to treat Gram-positive bacteria such as staph. It has traditionally been reserved as a drug of "last resort."<sup>90</sup>

- <sup>1</sup> [http://www.cdc.gov/ncidod/dhqp/ar\\_multidrugFAQ.html](http://www.cdc.gov/ncidod/dhqp/ar_multidrugFAQ.html)
- <sup>2</sup> [http://www.cdc.gov/ncidod/dhqp/id\\_Cdiff.html](http://www.cdc.gov/ncidod/dhqp/id_Cdiff.html)
- <sup>3</sup> [http://www.cdc.gov/ncidod/dhqp/id\\_Cdiff.html](http://www.cdc.gov/ncidod/dhqp/id_Cdiff.html)
- <sup>4</sup> [http://www.cdc.gov/ncidod/dhqp/id\\_Cdiff.html](http://www.cdc.gov/ncidod/dhqp/id_Cdiff.html)
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- <sup>22</sup> [http://science.education.nih.gov/supplements/nih1/diseases/activities/activity5\\_vrsa-database.htm#2](http://science.education.nih.gov/supplements/nih1/diseases/activities/activity5_vrsa-database.htm#2)
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