Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surveillance Report 2006

Oregon Active Bacterial Core Surveillance (ABCs)
Office of Disease Prevention & Epidemiology
Oregon Department of Human Services
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Background

Active Bacterial Core surveillance (ABCs) is a core component of the Emerging Infections Program (EIP) Network sponsored by the Centers for Disease Control and Prevention (CDC). The purpose of ABCs is to determine the incidence and epidemiologic characteristics of invasive disease due to *Haemophilus influenzae*, *Neisseria meningitidis*, group A *Streptococcus* (GAS), group B *Streptococcus* (GBS), and methicillin-resistant *Staphylococcus aureus* (MRSA). The entire EIP Network represents 39.5 million persons in 10 surveillance areas around the United States. More information on the EIP/ABCs Network is found at: http://www.cdc.gov/ncidod/dbmd/abcs.

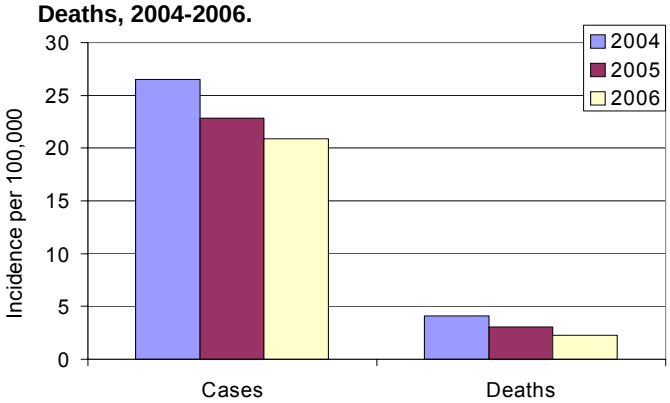
In Oregon, the surveillance area for MRSA comprises the Tri-County (Clackamas, Multnomah, and Washington) Portland metropolitan area with a 2006 estimated population of 1,569,170. More information on the Oregon ABCs program is found at: http://oregon.gov/DHS/ph/acd/abc.shtml.

Methods

An invasive MRSA infection is defined as the isolation of MRSA from a normally sterile body site in a Tri-County resident. Tri-County hospital laboratories submit MRSA isolates to the Oregon State Public Health Laboratory for strain typing (i.e. USA100, USA300, etc.) and forwarding to a CDC laboratory for further characterization and antimicrobial susceptibility testing. Additional cases are identified through regular laboratory record reviews. Health record reviews of each case allow standardized reports of demographic characteristics, clinical syndrome manifestations, underlying conditions, and illness outcome.

Cases are classified based on the presence of established healthcare risk factors and time of culture collection in relation to hospital admission. Healthcare-onset (HO-) MRSA infections are those in which the initial culture was collected >48 hours after hospital admission; Healthcare-associated, community-onset (HACO-MRSA) cases are those in which the initial culture was collected ≤48 hours after hospital admission or evaluation and the medical chart indicates one or more of the following risk factors: previous MRSA colonization or infection, presence of an invasive device or catheter at the time of admission or evaluation, or hospitalization, surgery, dialysis, or resident of a long-term care facility (LTCF) within the year preceding the index culture date; and community-associated (CA-MRSA) cases are those in which the initial culture was collected ≤48 hours after hospital admission or evaluation and none of above risk factors are noted in the medical record.

Figure 1: Incidence of Invasive MRSA Cases and Deaths, 2004-2006.



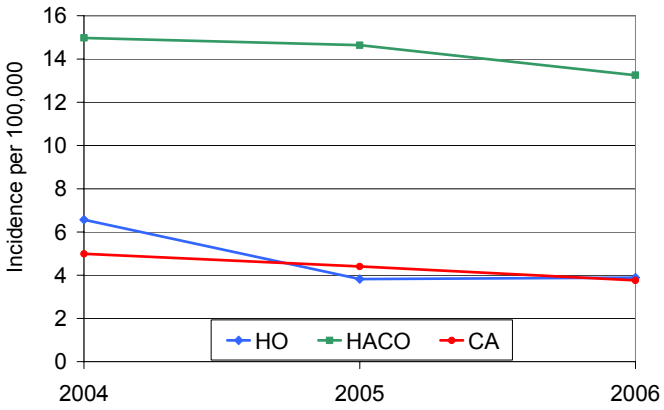
Surveillance Results

Descriptive Epidemiology

In 2006, we identified 328 cases of invasive MRSA disease for an overall incidence of 21/100,000 persons. This represents a decrease from 404 cases (27/100,000 persons) and 353 cases (23/100,000) reported in 2004 and 2005, respectively, with a 21% decrease in incidence since 2004 (Figure 1). Almost two-thirds (63%) of cases reported in 2006 were male. The mean and median ages of cases reported in 2006 were 56.7 and 57.0 years, respectively, with a range of 0 to 94 years of age. Of the 64% of cases for which race was reported, 86% were white, 11% were black, and 3% were of another race. The highest incidence of invasive MRSA disease in 2006 occurred in Multnomah (29/100,000); followed by Clackamas (18/100,000) and Washington (12/100,000) Counties. Of the 328 cases, 50 (15%) were recurrent invasive MRSA cases, reported in those with a previous invasive MRSA infection.

Mortality due to invasive MRSA infection also decreased over the three years, from 62 deaths reported in 2004 (4/100,000) to 36 reported in 2006 (2/100,000). Case fatality decreased from 15% in 2004 to 11% in 2006. The mean and median ages of death due to invasive MRSA infection were 67 and 72 years, respectively, with a range of 35 to 92 years.

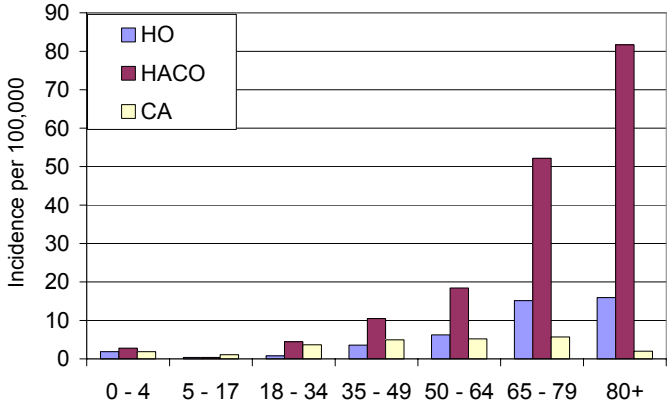
Figure 2: Incidence of Invasive MRSA Cases, by Infection Type, 2004-2006.



Infection Types

The incidences of all types of invasive MRSA infection have decreased over the previous three years (figure 2). The 41% decrease in HO incidence from 6.6/100,000 in 2004 to 3.9/100,000 in 2006 was the most dramatic, although the latter rate was similar to the 3.8/100,000 reported in 2005; CA incidence decreased 25% from 5.0/100,000 in 2004 to 3.8/100,000 in 2006; and HACO decreased 11%, from 15.0/100,000 in 2004 to 13.3/100,000 in 2006. HACO cases comprised 63% of cases in 2006, followed by HO (19%), and CA (18%). While racial and sex characteristics and geographic distribution of disease incidences were similar to the overall pattern, a difference in age by infection type was seen (figure 3). The mean and median ages for CA (43 and 44, respectively) were lower than those seen for HO (58 and 59, respectively) or HACO (60 and 63, respectively). Additionally, while the incidence of CA is relatively constant among adults, healthcare-associated MRSA incidence increases with increasing age, particularly among HACO cases.

Figure 3: Incidence of Invasive MRSA, by Infection Type and Age, 2006.



While mortality was highest with HACO (1.3/100,000), followed by HO (0.6/100,000) and CA (0.4/100,000), the case fatality rate was highest among HO (16%), followed by HACO and CA (10%). However, there was no significant association between death and infection type.

Clinical Manifestations

Commonly reported clinical manifestations of invasive MRSA infections are provided in Table 1. Healthcare-associated MRSA infections (including HO and HACO) are more likely to manifest as bacteremia, and less likely to manifest as cellulitis, internal abscess, and endocarditis than CA. Pneumonia, septic arthritis, osteomyelitis, and urinary tract infections (UTI) are similar across the infection types. A fatal outcome is five times more likely with bacteremia, and three times more likely with pneumonia, than other clinical manifestations. This effect is independent of age and infection type.

Table 1: Common clinical manifestations of invasive MRSA cases, by infection type, 2006.[†]

	HO	HACO	CA	Total
Bacteremia	47 (77)	173 (83)	41 (69)	261 (80)
Pneumonia	7 (11)	24 (12)	8 (14)	39 (12)
Cellulitis	2 (3)	25 (12)	12 (20)	39 (12)
Septic Arthritis	6 (10)	24 (12)	4 (7)	34 (10)
Osteomyelitis	9 (15)	20 (10)	5 (8)	34 (10)
Abscess	2 (3)	14 (7)	12 (20)	28 (9)
Endocarditis	1 (2)	13 (6)	12 (20)	26 (8)
UTI	2 (3)	20 (10)	3 (5)	25 (8)

[†] Some cases report >1 syndrome; not all syndromes shown.

Table 2: Common underlying conditions reported among invasive MRSA cases, by infection type, 2006.[†]

	HO N (%)	HACO N (%)	CA N (%)	Total N (%)
Diabetes	25 (41)	91 (44)	9 (15)	125 (38)
CVD/CHF	18 (30)	81 (39)	5 (8)	104 (32)
Smoking	12 (20)	47 (23)	27 (46)	86 (26)
Renal Failure	11 (18)	56 (27)	1 (2)	68 (21)
Immunosuppressive Therapy	14 (23)	44 (21)	5 (8)	63 (19)
IVDU	5 (8)	25 (12)	24 (41)	54 (16)
COPD	5 (8)	36 (17)	3 (5)	44 (13)
Obesity	10 (16)	32 (15)	2 (3)	44 (13)
Solid Organ Malignancy	14 (23)	24 (12)	1 (2)	39 (12)
Stroke	6 (10)	33 (16)	1 (2)	40 (12)
Asthma	3 (5)	16 (8)	5 (8)	24 (7)
None	4 (7)	4 (2)	11 (19)	19 (6)

[†] Some cases report >1 condition; not all conditions shown.

Underlying Conditions

Almost all (95%) of invasive MRSA cases were in individuals reporting one or more underlying condition (Table 2). Healthcare-associated MRSA cases (HO and HACO) were more likely to report diabetes, cardiovascular disease or congestive heart failure (CVD/CHF), renal failure, immunosuppressive therapy, chronic obstructive pulmonary disease (COPD), obesity solid organ malignancy, and stroke; CA cases were more likely to report smoking or intravenous drug use (IVDU) and were more likely not to have any underlying condition reported. Although smoking and IVDU were highly correlative, smoking was independently associated with CA disease, upon multivariate analysis.

Table 3: Odds ratios of significant univariate associations between common underlying conditions and clinical manifestation of invasive MRSA disease, 2006.

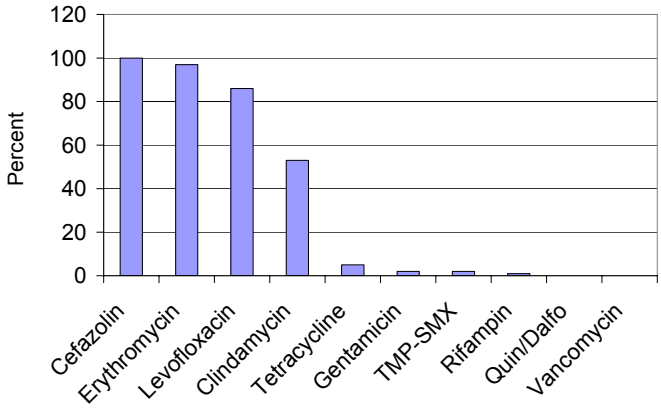
	Bacteremia	Pneumonia	Cellulitis	Osteo.	Abscess	Endocarditis	UTI
Diabetes	1.9 1.0, 3.4						
Smoking			2.5 1.2, 4.9	3.3 1.6, 6.7			
Renal Failure	2.6 1.1, 6.0						
IVDU			2.6 1.2, 5.6	3.3 1.5, 7.1	5.5 2.4, 12.3	20.7 8.1, 52.8	
COPD		2.6 1.2, 5.8					
Solid Organ Malignancy							4.1 1.6, 10.3
Asthma		2.7 1.0, 7.4					

Death due to invasive MRSA infection was significantly more likely to occur among those reporting solid organ malignancy, COPD, cirrhosis, and immunosuppressive therapy. However, after controlling for age, only cirrhosis and immunosuppressive therapy remained independently associated with death. The presence of reported underlying conditions is related to the clinical profile of invasive MRSA disease (Table 3).

Antibiotic Susceptibilities

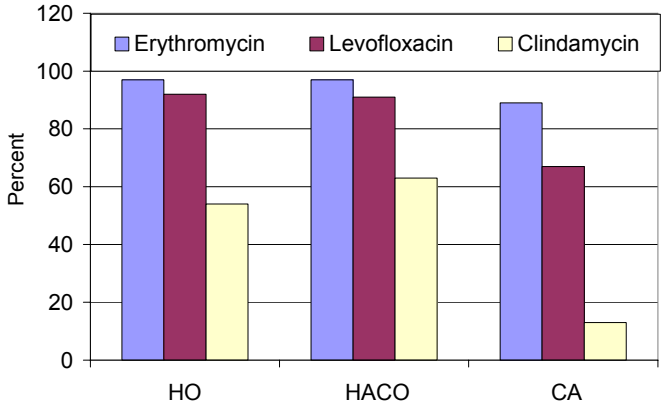
By definition, all MRSA isolates are resistant to β-lactam antibiotics, including penicillin and methicillin. Additionally, isolates display a varying susceptibility profile to commonly assayed antibiotics, from 100% of isolates demonstrating resistance to cefazolin to 100% demonstrating susceptibility to quinupristin/dalfopristin and vancomycin (Figure 4). There has been no change in the percentage of isolates with decreased susceptibility (either intermediate or full resistance, based on breakpoints) to any antibiotics over the past three years. Decreased susceptibility to antibiotics was not associated with death.

Figure 4: Percentage of invasive MRSA isolates with intermediate or full resistance to select antibiotics, 2006.



For three antibiotics, susceptibility varied significantly by infection type, with healthcare-associated cases (including HO and HACO) reporting a higher percentage of isolates with decreased susceptibility than CA cases (Figure 5). For instance, healthcare-associated MRSA cases were four, five, and 11 times more likely to be due to isolates with decreased susceptibility to erythromycin, levofloxacin, and clindamycin than CA cases.

Figure 5: Percentage of invasive MRSA isolates with intermediate or full resistance to select antibiotics, by infection type, 2006.



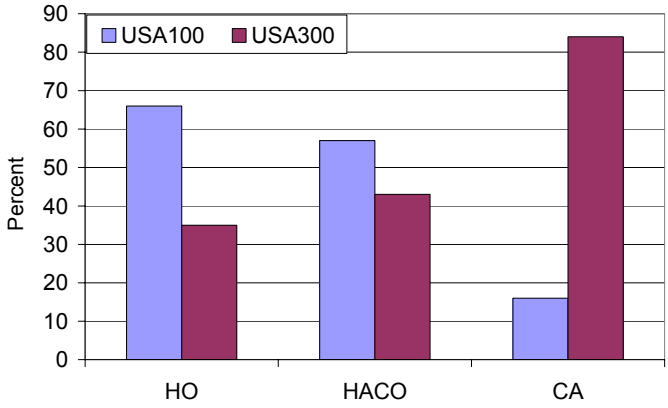
Strain Typing

Strain typing, by pulsed-field gel electrophoresis (PFGE), was completed for a subset of invasive MRSA cases. PFGE results are available for 188/353 (53%) cases reported in 2005 and 153/328 (47%) of cases reported in 2006, with results for twenty-six 2006 cases still pending.

Overall, 160 (47%) of isolates were typed as USA100, 156 (46%) were USA300, and 25 (7%) were another type. Of the 316 isolates determined to be either USA100 (51%) or USA300 (49%), there was no difference between the strains in the percentage of cases with a fatal outcome.

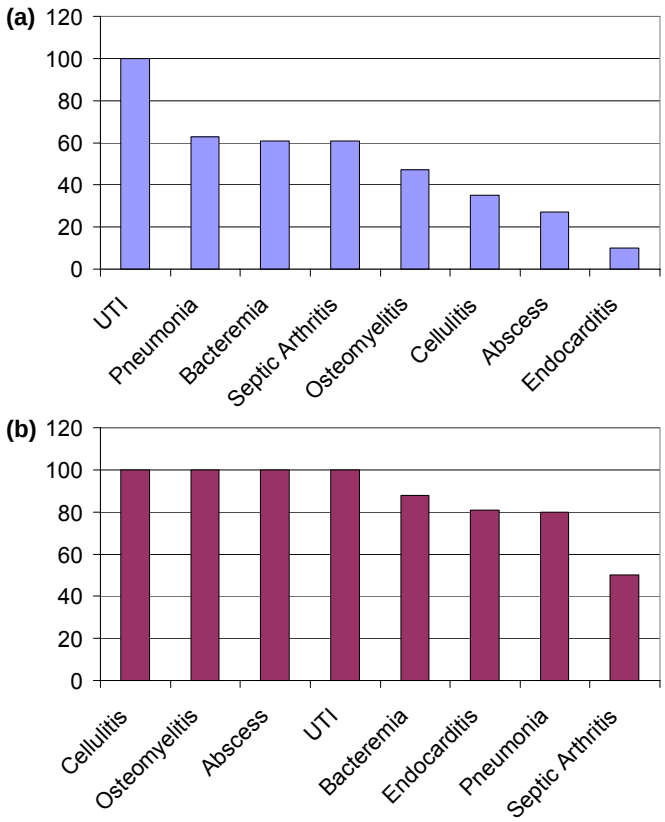
Figure 6 displays the percentage of cases of isolates determined to be USA100 or USA300, by epidemiologically classified infection type. While healthcare-associated cases are predominantly type USA100 (66% for HO and 57% for HACO), 84% of CA cases are USA300. As with infection type, strain type is significantly associated with age, as the mean and median ages of cases due to USA100 (66 and 68 years, respectively) were higher than those due to USA300 (49 and 48, respectively). However, the difference in age between strain types was not only present when looking at the type of infection. Among all healthcare-associated cases, including HO and HACO, the mean and median ages of USA100 strains (66 and 68 years, respectively) were higher than those due to USA300 (51 and 49, respectively).

Figure 6: Percentage of isolates typed as USA100 and USA300, by infection type, 2005-2006.



The clinical manifestation of disease is also dependent upon strain type. Roughly half of bacteremia (52%) and pneumonia (53%) cases were caused by USA100, as were 90% of urinary tract infection, 60% of arthritis, 37% of osteomyelitis, 24% of cellulitis 16% of internal abscess, and 15% of endocarditis cases. The situation becomes more complex, however, when considering both PFGE-determined strain type and epidemiologically-assessed healthcare-associated risk factors (Figure 7). While 100% of healthcare-associated urinary tract infections were due to USA100 strains, only 10% of healthcare-associated endocarditis cases were due to this strain. In every category except for septic arthritis (for which there were only two CA reports – 1 each due to USA100 and USA300), the percentage of CA cases due to USA300 was higher than the percentage of healthcare-associated cases due to USA100.

Figure 7: Percentage of (a) HO and HACO isolates typed as USA100 and (b) CA isolates typed as USA300, by infection type, 2005-2006.



Strain type also differed by underlying condition. USA100 was identified in a higher percentage of cases with the following underlying conditions reported: Solid Organ Malignancy (78%), Renal Failure (74%), CVA (74%), Immunosuppressive Therapy (72%), CVD/CHF (64%), Diabetes (58%), COPD (57%), and Obesity (56%). In contrast, USA300 comprised a higher proportion of cases reporting IVDU (96%), Smoking (73%) or no reported underlying risk factors (88%).

As with clinical manifestation, there was an association between PFGE-determined strain type and epidemiologically-classified healthcare risk factors for COPD, diabetes, CHD/CHF, and CVA, such that healthcare-associated cases tended to be USA100 and CA cases tended to be USA300. A few exceptions include underlying conditions for which a higher proportion of CA cases were USA100: renal failure (100%) and immunosuppressive therapy (67%), and conditions for which a higher proportion of healthcare-associated cases were USA300: IVDU (97%), asthma (59%), smoking (69%), and no reported risk factors (80%).

Discussion

Three full years of surveillance have allowed for a better characterization of the epidemiology of invasive MRSA disease in the Portland Tri-County metropolitan area. Most importantly, the incidence of invasive MRSA infection has decreased, most dramatically among HO cases. The extent to which changes in hospital infection control strategies are responsible for this decrease is currently being investigated. That decreases have also been seen among HACO and CA cases is welcome news, although the cause of this decrease is not yet known.

Also evident from these results is the extent to which invasive MRSA disease manifests in those with an underlying condition or behavior. Almost all healthcare-associated cases (97%) were in those with an underlying condition, most commonly one or more chronic diseases. Among CA cases, invasive MRSA disproportionably affects those reporting IVDU. Based on unpublished estimates of the number of persons who inject drugs, the risk of invasive MRSA disease in this population is 1 in 300 to 1 in 2,600. In contrast, the risk of invasive MRSA disease among those without established health care risk factors who do not inject drugs is estimated to be 1 in 35,000. Looking at disease manifestation along with underlying conditions, several patterns emerge: bacteremia commonly occurs in those with systemic conditions, such as diabetes and renal failure; pneumonia is associated with conditions of the lung, such as COPD and asthma; and behavioral conditions (IVDU in particular) were related to localized invasive infections, such as cellulitis, osteomyelitis, internal abscess, and endocarditis.

The addition of molecular strain type information has provided an interesting insight into the profile of invasive MRSA disease, especially in light of the epidemiologically-based classification. USA100 has been considered the 'healthcare-associated strain' and USA300 has been considered the 'community-associated strain'. While the association between infection type and strain type held in our analyses, in general, we did find a relatively high (41%) proportion of healthcare-associated cases due to the community-associated, USA300 strain. These results could be consistent with two possibilities. First, USA300 could increasingly be transmitted within the healthcare setting, an observation supported in recently-published literature.[1,2] Second, cases may be misclassified as healthcare-associated, due to the presence of the established 'risk factors', when they were actually acquired in the community. That certain disease manifestations (such as endocarditis, osteomyelitis, and cellulitis) are associated with underlying conditions thought to play a role in infection (i.e. IVDU) and USA300 strain type, regardless of epidemiological classification, seems to support this theory. It is likely that both factors may be playing a role and further molecular and epidemiological characterization of cases will increase our knowledge of the profile of invasive MRSA disease.

References:

1. Popovich KJ, Weinstein RA, Bota B. Are community-associated Methicillin-Resistant *Staphylococcus aureus* (MRSA) strains replacing traditional nosocomial MRSA strains? *Clin Infect Dis*. 2008;46:787-94.
2. Boyce JM. Community-associated Methicillin-Resistant *Staphylococcus aureus* as a cause of health care-associated infection. *Clin Infect Dis*. 2008;46:795-8.