Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surveillance Report 2009

Oregon Active Bacterial Core Surveillance (ABCs)

Office of Disease Prevention & Epidemiology
Oregon Health Authority

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Background

The Active Bacterial Core surveillance (ABCs) program is a core component of the Emerging Infections Program (EIP) Network sponsored by the Centers for Disease Control and Prevention (CDC). The purpose of the ABCs program 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), *Streptococcus pneumoniae*, and methicillin-resistant *Staphylococcus aureus* (MRSA). The entire EIP Network for invasive MRSA represents over 19 million persons in 10 surveillance areas around the United States. More information on the EIP/ABCs Network is found at: http://www.cdc.gov/abcs/index.html.

In Oregon, the surveillance area for invasive MRSA comprises the tri-county (Clackamas, Multnomah, and Washington) Portland metropolitan area, with a 2009 estimated population of 1,631,665.[*] More information on the Oregon ABCs program is found at: http://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/Pages/abc.aspx.

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 voluntarily submit all sterile site MRSA isolates to the Oregon State Public Health Laboratory (OSPHL). A subset is sent to CDC 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, underlying illnesses or conditions, healthcare-associated risk factors, and illness outcome.

Cases of invasive disease are classified into one of three epidemiologic classifications based on the presence or absence of established healthcare risk factors and time of culture collection in relation to hospital admission, as indicated in the medical record.

- Healthcare-onset (HO-) MRSA infections are those in which the initial culture was collected >2 days after hospital admission.

[*] Source: Portland State University Population Research Center (http://www.pdx.edu/prc/)

[†] MRSA *infection* is the invasion of bacteria in the tissues of the host leading to clinical signs and symptoms of illness or infection whereas *colonization* refers to the presence of bacteria but without tissue damage and signs of illness or infection. Colonized patients are also known as asymptomatic carriers.

- Healthcare-associated, community-onset (HACO-) MRSA infections are those in which the initial culture was collected ≤2 days after hospital admission or evaluation, and the medical chart indicates one or more of the following risk factors:
    - A history of hospitalization, surgery, dialysis, or residence in a long term care facility in the previous year, or
    - Presence of a central vascular catheter ≤2 calendar days prior to collection of initial culture.
- Community-associated (CA-) MRSA infections are those in which none of the previously mentioned criteria are met.

Additional technical information on surveillance methodology, including data elements collected, healthcare risk factors, clinical manifestations, and underlying diseases and conditions can be found at the CDC EIP/ABCs Network website listed above.

Surveillance Results

Descriptive Epidemiology

In 2009, we identified 245 cases of invasive MRSA disease for an overall incidence of 15.0/100,000 persons (Figure 1). Of these, 49 (20%) were recurrent cases, reported in those with a previous invasive MRSA infection. A recurrent case must have a specimen isolated greater than 30 days after any previous initial MRSA culture. Since the beginning of surveillance in 2004, when 405 cases were reported (26.6/100,000), the incidence of invasive MRSA disease has decreased 44 percent. The highest incidence of invasive MRSA disease occurred among residents of Multnomah county (19.2/100,000); followed by residents in Clackamas (12.1/100,000) and Washington (9.5/100,000) counties.

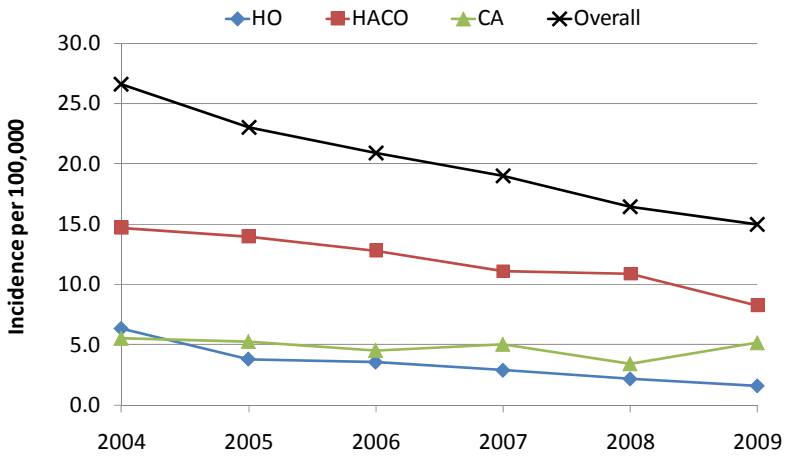
Thirty-seven cases were fatal, for mortality and case fatality rates of 2.3/100,000 and 15%, respectively. The case fatality rate has not changed since 2004. The mean and median ages of death due to invasive MRSA infection were 70 and 73 years, respectively, with a range of 38 to 93 years. Risk of death was associated with increasing age (p=0.0003). Among those who died, 62% were 65 and older, and 95% were 50 and older. There were no deaths among those younger than 35 years of age.

The mean and median ages of cases reported in 2009 were 59 and 60 years, respectively (range: 0-97 years). Fifty-five percent of all reported cases were male. Race was reported for 142 cases; of these, 82% were white, 10% were black, and 8% were of another race.

Epidemiologic Classifications

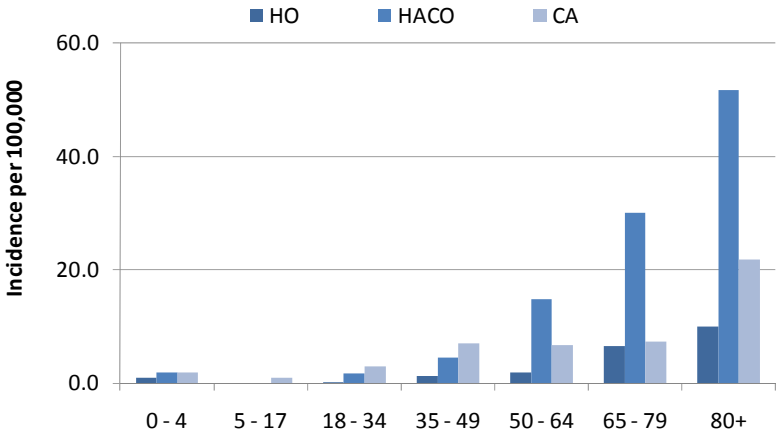
Of the 245 total cases reported, 26 (11%) were HO (1.6/100,000); 135 (55%) were HACO (8.3/100,000); and 84 (34%) were CA (5.2/100,000). Since 2004, the incidence of HO has decreased 75 percent, that of HACO has decreased 44 percent and that of CA has decreased 7 percent (Figure 1). HO cases have comprised a *decreasing* proportion of all MRSA cases, from 24 percent in 2004 to 11 percent in 2009 (test for trend, $p<0.0001$), while CA cases have comprised an *increasing* proportion of all MRSA cases, from 21 percent in 2004 to 34 percent in 2009 ($p=0.0022$). The proportion of HACO cases have not changed significantly over time.

Figure 1: Incidence of Invasive MRSA Cases in Tri-county Area



Epidemiologic classification of cases as HO, HACO, or CA-MRSA was associated with age (Figure 2). The mean and median ages for CA infections (51 and 49, respectively) were significantly lower than those seen for HACO (63 for each) and for HO infections (63 and 66, respectively). Classification was not associated with sex or race.

Figure 2: Incidence of Invasive MRSA by Infection Type and Age 2009



Mortality was highest among HACO cases (1.3/100,000), followed by CA (0.6/100,000) and HO (0.4/100,000); case fatality was highest among HO (27%), followed by HACO (16%) and CA (11% each). After adjusting for age, the odds of death were almost two times *higher* (OR 1.9; 95% CI [1.3, 3.0]) for HO cases than CA cases.

Clinical Manifestations

The most common clinical manifestations of invasive MRSA infections reported in 2009 are displayed in Table 1. The profiles for these syndromes are not significantly different from those reported during 2004-2008 with the exception of arthritis, endocarditis and pneumonia. CA cases were more likely to manifest as an abscess from a normally sterile site (OR 3.4; CI 1.4, 8.2) than cases with healthcare associated risk factors (HO and HACO cases). Other syndromes were reported similarly across infection types.

Table 1: Common Clinical Manifestations of Invasive MRSA Cases[†] by Epidemiologic Classification, 2009

Underlying Condition	HO n=26 n (%)	HACO n=135 n (%)	CA n=84 n (%)	Total n=245 n (%)
Bacteremia	21 (81)	119 (88)	68 (81)	208 (85)
Pneumonia*	5 (19)	29 (21)	20 (24)	54 (22)
Cellulitis	0 (0)	16 (12)	15 (18)	31 (13)
Osteomyelitis	0 (0)	19 (14)	8 (10)	27 (11)
Abscess	0 (0)	9 (7)	14 (17)	23 (9)
Urinary Tract Infection	2 (8)	7 (5)	4 (5)	13 (5)
Empyema	1 (4)	1 (1)	8 (10)	10 (4)
Bursitis	0 (0)	2 (1)	3 (4)	5 (2)
Meningitis	0 (0)	0 (0)	3 (4)	3 (1)
Peritonitis	1 (4)	1 (1)	0 (0)	2 (1)
Arthritis	0 (0)	0 (0)	0 (0)	0 (0)
Endocarditis	0 (0)	0 (0)	0 (0)	0 (0)
None	0 (0)	2 (1)	7 (8)	9 (4)

[†] Some cases report more than 1 syndrome.

* Only those cases of pneumonia with a sterile site isolate are included. Sputum or endotracheal aspirates are not considered sterile sites.

Underlying Conditions

Almost all (96%) invasive MRSA cases were in individuals reporting one or more underlying diseases or conditions (Table 2). Cases with healthcare-associated risk factors (including HO and HACO) were *more* likely to report diabetes (OR 2.4; CI 1.3, 4.3), renal failure (OR 4.2; CI 2.0, 8.4), cardiovascular disease or congestive heart failure (CVD/CHF) (OR 4.7; CI 2.3, 9.6), chronic obstructive pulmonary disease (COPD) (OR 3.0; CI 1.2, 7.5), obesity (OR 3.0; CI 1.2, 7.5), peripheral vascular disease (PVD) (OR 4.1; CI 1.2, 14.0), and immunosuppressive therapy (OR 3.0; CI 1.2, 7.5), and *less* likely to report intravenous drug use (IVDU) (OR 0.3; CI 0.1, 0.8) and smoking (OR 0.5; CI 0.3, 0.9) than CA cases.

After controlling for age and infection type, none of the underlying conditions were associated with fatal outcome.

Table 2: Common Underlying Conditions Reported Among Invasive MRSA Cases[†] by Epidemiologic Classification, 2009

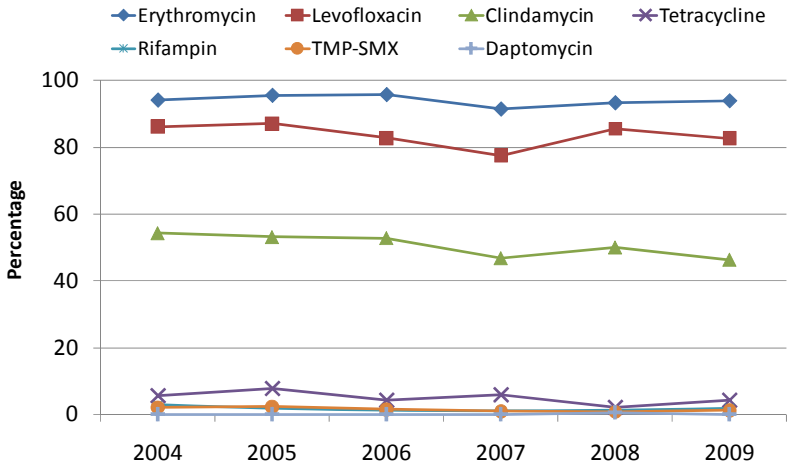
Underlying Condition	HO n=26 n (%)	HACO n=135 n (%)	CA n=84 n (%)	Total n=245 n (%)
Diabetes	5 (19)	69 (51)	22 (26)	96 (39)
Cardiovascular Disease	10 (38)	57 (42)	11 (13)	78 (32)
Renal Failure	11 (42)	51 (38)	11 (13)	73 (30)
Smoking	3 (12)	24 (18)	24 (29)	51 (21)
Chronic obstructive pulmonary disease	4 (15)	26 (19)	6 (7)	36 (15)
Immunosuppressive Therapy	4 (15)	26 (19)	6 (7)	36 (15)
Obesity	4 (15)	26 (19)	6 (7)	36 (15)
Solid Organ Malignancy	5 (19)	16 (12)	6 (7)	27 (11)
Peripheral Vascular Disease	1 (4)	20 (15)	3 (4)	24 (10)
Stroke/CVA	1 (4)	16 (12)	7 (8)	24 (10)
Intravenous Drug Use	0 (0)	8 (6)	12 (14)	20 (8)
Alcohol Abuse	2 (8)	6 (4)	10 (12)	18 (7)
Cirrhosis	1 (4)	11 (8)	2 (2)	14 (6)
Asthma	2 (8)	8 (6)	3 (4)	13 (5)
None	0 (0)	2 (1)	7 (8)	9 (4)

[†] Some cases report more than 1 syndrome.

Antibiotic Susceptibilities

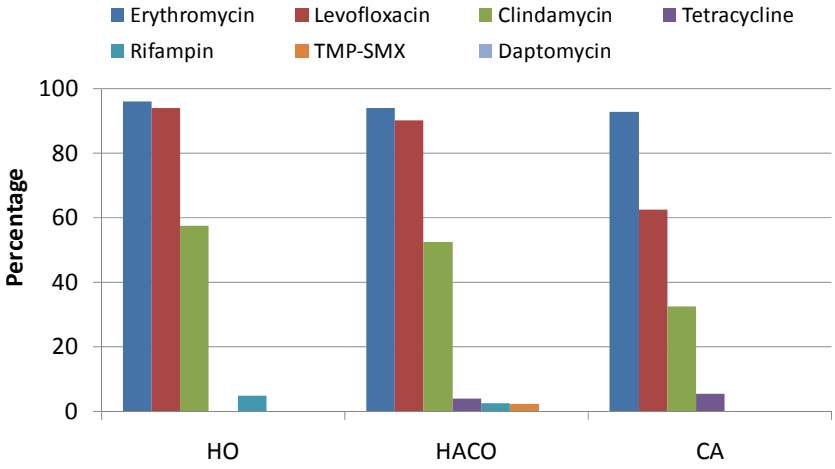
By definition, all MRSA isolates are resistant to β-lactam antibiotics, including penicillin and methicillin. Additionally, among isolates tested, a proportion displayed intermediate/full resistance or decreased susceptibility to several commonly assayed antibiotics in 2009, including: erythromycin (94%, n=244), levofloxacin (83%, n=138), clindamycin (46%, n=242), tetracycline (4%, n=215), rifampin (2%, n=206), and trimethoprim-sulfa (1%, n=244). Since 2004, the percentages of invasive MRSA isolates with decreased susceptibility to these select antibiotics have remained relatively stable (Figure 3). No isolates during this time period have displayed decreased susceptibility to daptomycin, linezolid or vancomycin. Resistance to antibiotics was not associated with a fatal disease outcome.

Figure 3: Percentage of Invasive MRSA Isolates with Decreased Susceptibility (Intermediate or Full Resistance) to Select Antibiotics



In 2009, HO and HACO cases, combined, were six times more likely to display decreased susceptibility to levofloxacin (95% CI 2.3, 15.2) and almost 2.5 times more likely to display decreased susceptibility to clindamycin (95% CI 1.4, 4.1) than community-associated cases (Figure 4). Other differences were not statistically significant or were unable to be tested due to insufficient sample size.

Figure 4: Percentage of Invasive MRSA Isolates with Decreased Susceptibility (Intermediate or Full Resistance) to Select Antibiotics by Infection Type, 2009

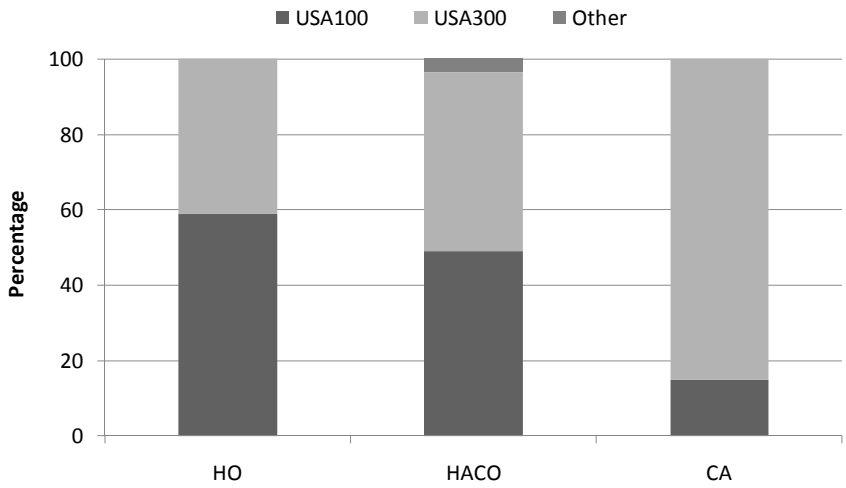


Strain Typing

In 2009, strain typing results by pulsed-field gel electrophoresis (PFGE) were available for a subset of invasive MRSA cases (135/245 (55%)). Of the 135 isolates, 54 (40%) were USA100, 78 (58%) were USA300, and 3 (2%) were other types (i.e. USA200, 500, 800)**.** USA100, USA200, and USA500 are predominantly from healthcare-associated infections and are considered to be of healthcare origin, while USA300, USA400, USA1000, and USA1100 are obtained primarily from community infections and are considered to be of community origin.[1]

Figure 5 displays the percentage of cases of isolates determined to be USA100, USA300, and other strain type, by epidemiologically classified infection type.

Figure 5: Percentage of Isolates Typed as USA100, USA300, and Other by Infection Type, 2009



Among cases for which PFGE results were available, bacteremia was by far the most common clinical manifestation among those with USA100 (94%) and USA300 (94%). All other clinical syndromes were present in fewer than 20 percent of the cases. Among cases with USA100, cardiovascular disease (46%), diabetes (46%), and renal failure (37%) were the most common underlying conditions. Among those with USA300 type, diabetes (35%), smoking (30%), cardiovascular disease (28%), and renal failure (28%) were the most common underlying conditions.

Expanded HACO Analysis

Table 3: Distribution of Healthcare Risk Factors Among HACO

Risk Factor	2004-2008 n=994 n (%)	2009 n=135 n (%)
Hospitalization[2]	850 (86)	122 (90)
Surgery[2]	639 (64)	76 (57)
LTCF Residence[2]	389 (39)	52 (39)
Dialysis[2]	212 (21)	24 (18)
Central Venous Catheter[1]	224 (23)	28 (21)

[1] In place ≤2 calendar days prior to initial culture
[2] Within year before date of initial culture

The distribution of healthcare risk factors among HACO cases is shown in Table 3. HACO infections are those in which the initial MRSA culture was collected ≤2 days after hospital admission or evaluation, and the medical chart indicates a history of hospitalization, surgery[*], residence in a long term care facility, dialysis in the previous year, or the presence of a central vascular catheter[†] ≤2 calendar days prior to collection of initial culture. Among HACO cases in 2009, 37 (27%) had one healthcare risk factor; 44 (33%) had two; 40 (30%) had three; 11 (8%) had four; 3 (2%) had five. The proportion of cases with multiple reported risk factors has remained stable since 2004.

Since 2004, we identified 270 patients with invasive MRSA who underwent dialysis within the year before their initial culture date. Of these individuals, 65 percent were male, 85 percent were hospitalized, 13 percent had a fatal outcome, 87 percent were classified as having a HACO infection, and 60 percent of 111 cases with known PFGE pattern were considered to be of healthcare origin. The mean and median ages were 61 and 60 years, respectively (range: 14-90 years).

Discussion

Six full years of surveillance have allowed for a better characterization of the epidemiology of invasive MRSA disease in the Portland tri-county metropolitan area. Over this time, the incidence of invasive MRSA disease has decreased substantially, with the greatest decrease seen among HO cases.

Results from 2009 are consistent with previous years, in that invasive MRSA disease—including community associated cases—manifests largely in those with an underlying condition or behavior that is related to their infection. Almost all cases in those with healthcare-defining risk factors were in those with underlying chronic diseases, such as diabetes, cardiovascular disease, renal failure, etc., that require frequent encounters with the healthcare system or invasive medical procedures. Invasive MRSA cases generally increase with age and occur primarily among those 65 and older.

[*] The definition of this variable changed in 2009. *Old definition*: Surgery within year before index culture date. *New definition*: Surgery within year before initial culture date.
[†] The definition of this variable changed in 2009. *Old definition*: Central vascular catheter in place at time of admission/evaluation. *New definition*: Central vascular catheter in place at any time in the 2 calendar days prior to initial culture.

The more frequent susceptibility of CA-MRSA isolates to clindamycin is consistent with the fact that a greater proportion of these are USA300 PFGE type, which usually carries fewer resistance genes than healthcare associated PFGE types. Clindamycin is not generally used as primary therapy for invasive MRSA disease. Intermediate or full resistance to vancomycin has not been detected among invasive MRSA isolates in Oregon, based on accepted breakpoint minimum inhibitory concentration (MIC) values. There are numerous reports in the medical literature of possible decreasing effectiveness of vancomycin due to small but significant increases in resistance of MRSA to this drug, reflected in slowly rising MIC values. However, since methods for determining MICs may vary between laboratories, and isolates are generally reported as either "susceptible" or not, the extent vancomycin MICs have been increasing over time among MRSA isolates in Oregon is unclear. Additional characterization of the MRSA isolates is required to answer this question.

The use of molecular strain type information has demonstrated an increase in the traditional community-associated USA300 strain among cases classified epidemiologically as healthcare-associated. This finding raises two possibilities: The frequency of transmission of USA300 strains within the healthcare setting could be increasing (an observation supported in recently-published literature); or cases may be misclassified as healthcare-associated, due to the presence of the established "risk factors", when colonization or infection was actually acquired in the community.[2,3] Although both factors likely play some role, further investigation will be needed to better understand the dynamics of MRSA transmission between healthcare and community settings.

References

1. Centers for Disease Control and Prevention. Invasive Methicillin-Resistant *Staphylococcus aureus* Infections Among Dialysis Patients – United States, 2005. MMWR 2007;56:09. Available via the Internet: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5609a3.htm. Accessed 14 Jul 2011.
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3. Boyce JM. Community-associated Methicillin-Resistant *Staphylococcus aureus* as a cause of healthcare-associated infection. *Clin Infect Dis*. 2008;46:795-8.