Group A *Streptococcus* Surveillance Report 2008

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 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 represents over 38 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 GAS disease comprises the tri-county (Clackamas, Multnomah, and Washington) Portland metropolitan area with a 2008 estimated population of 1,614,465. More information on the Oregon ABCs program is found at: http://oregon.gov/DHS/ph/acd/abc.shtml.

Methods

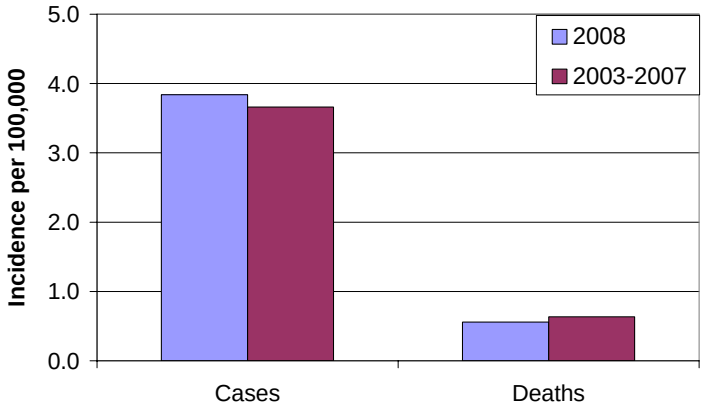
Invasive GAS disease (IGAS) is defined as the isolation of GAS from a normally sterile body site or fluid, or from a wound accompanied by necrotizing fasciitis or toxic shock syndrome in a tri-county resident. Tri-county hospital laboratories submit GAS isolates to the Oregon State Public Health Laboratory, which forwards them to CDC for typing. 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.

Surveillance Results

Descriptive Epidemiology

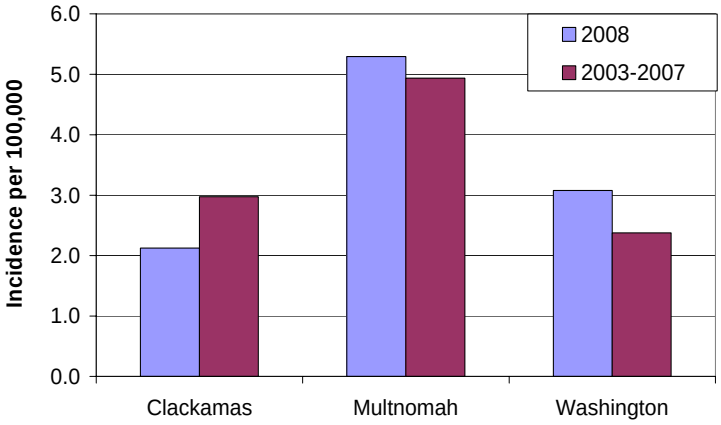
In 2008, 62 invasive GAS cases were reported in the tri-county Portland area, for an incidence rate of 3.8/100,000 persons (Figure 1). This is comparable to the 2008 national projection of invasive disease (3.8/100,000) and the average annual incidence rate in the Portland area from 2003–2007 (3.7/100,000).[1] With 9 deaths reported, IGAS mortality in 2008 was 0.56/100,000 (Figure 1), 14 percent higher than the 2008 national projections (0.51/100,000) and 11 percent lower than the 2003–2007 Portland area average annual mortality rate (0.63/100,000).[1] The mean and median ages of IGAS cases were 53 and 57 years, respectively (range: 2-89), and those of IGAS deaths were 61 and 63 years, respectively (range: 31-84). The 2008 case fatality rate for IGAS in the Portland area was 15 percent, compared with 17 percent for the Portland area from 2003–2007 and 13 percent for the entire ABCs network in 2008.[1] Over sixty percent of cases were male; of

Figure 1: Incidence of Invasive GAS Cases and Deaths in the Portland area, 2003-2008.



24 cases where race was known, 21 (88%) were white, 2 (8%) were black, and 1 (4%) was Asian/Pacific Islander.

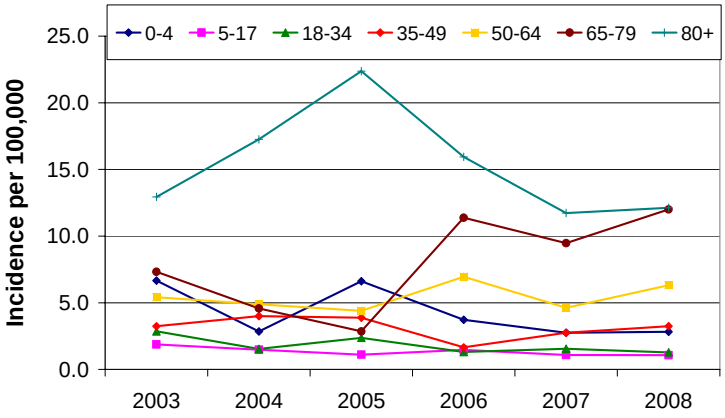
Figure 2: Incidence of Invasive GAS Disease by County, 2003-2008.



The 2008 incidence of IGAS was highest in Multnomah (5.3/100,000), followed by Washington (3.1/100,000), and Clackamas (2.1/100,000) counties (Figure 2). Compared with the previous five-year average, the 2008 incidence was 29 percent lower in Clackamas, 7 percent higher in Multnomah, and 29 percent higher in Washington counties. IGAS mortality was highest in Multnomah (0.98/100,000), followed by Clackamas (0.27/100,000) and Washington (0.19/100,000) counties. This contrasts with the five-year average, in which mortality has been highest in Clackamas county (0.83/100,000), followed by Multnomah (0.66/100,000) and Washington (0.45/100,000) counties.

The burden of disease was highest in those ≥80 years of age (6 cases; 12.1/100,000 persons), followed closely by those 65-79 years of age (14 cases; 12.0/100,000) (Figure 3). The incidence among those 5-49 has remained largely stable, within annual variation, over the past six years. Among those 80 and over, incidence has decreased 46 percent since peaking in 2005 and is 24 percent lower than the previous 5-year average incidence in this age group. Among those 65-79 years of age, incidence is 68 percent higher than the 2003–2007 five-year average incidence. It is yet unclear if this reflects an increasing trend or annual variation in occurrence. In 2008, the case fatality rate was highest among those over the age of 65 (20%). Increasing age is significantly related to fatal outcome from IGAS ($p<0.0001$).

Figure 3: Incidence of Invasive GAS Disease in the Portland Area by Age, 2003-2008.



Clinical Manifestations

Although there are annual fluctuations in rates of clinical manifestations of IGAS, the overall increases noted for certain syndromes since 2003 are not statistically significant (Table 1). In 2008, four cases of necrotizing fasciitis and five cases of toxic shock syndrome were reported, including one case who presented with both syndromes. Three of the five cases of toxic shock syndrome died. All three had underlying conditions.

Table 1: Percent of Invasive GAS Cases with Common Clinical Syndromes by Age Group, 2003-2008.[†]

	2008			2003-2007		
Syndrome	<18 years (N=6)	18-64 years (N=36)	65+ years (N=20)	<18 years (N=43)	18-64 years (N=163)	65+ years (N=77)
Cellulitis	17	42	30	16	37	36
Bacteremia	50	22	30	26	25	35
Pneumonia	17	22	30	16	11	18
Septic Arthritis	0	22	0	26	14	7
Abscess	0	6	15	5	6	1
Toxic Shock	0	8	10	0	6	1
Necrotizing Fasciitis	0	3	15	0	9	3
Meningitis	33	3	0	9	2	1

[†] Not mutually exclusive; some cases may report more than one syndrome. Not all syndromes reported are shown here.

Certain clinical syndromes of invasive GAS disease vary by age (Table 1). Among cases reported since 2003, cellulitis increased (p=0.0312) with increasing age, and septic arthritis (p=0.0012) and meningitis (p=0.0084) both decreased with increasing age. Additionally, among adults, only septic arthritis was noted significantly more frequently among those 18–64 years of age (p=0.0038) compared with older adults aged 65 and older.

Bacteremia, necrotizing fasciitis and pneumonia cases were significantly more likely - and cellulitis significantly less likely - to be associated with a fatal outcome among IGAS cases in bivariate analysis. After controlling for patient age, all four clinical syndromes remained significant. A fatal outcome was two times (95% confidence interval [CI] 1.1, 3.9) more likely among those with bacteremia, five times more likely among those with necrotizing fasciitis (CI 1.9, 13.7), two times more likely among those with pneumonia (CI 1.1, 4.4), and four times less likely among those with cellulitis (CI 1.9, 9.2) than among those with other clinical manifestations.

Underlying Conditions

In 2008, two children (33%) carried a diagnosis of asthma; one child (17%) had a history of penetrating and blunt trauma, and the remainder had no underlying conditions listed in their medical record. Among adults, the profile of underlying conditions reported in 2008 was similar to that reported from 2003-2007, with the exception of intravenous drug use (IDU) and obesity. IDU was reported less frequently in 2008 (p=0.0253), while obesity was reported more frequently in 2008 (p=0.0331). Younger adults were more likely to report IDU or no underlying conditions, while older adults were more likely to have cardiovascular disease, COPD, and diabetes (Table 2). All other

Table 2: Percent of Adult IGAS Cases with Underlying Conditions by Age Group, 2003-2008.[†]

Conditions	18-64 years (N=248)	65+ years (N=97)
Asthma	11	6
Blunt Trauma	13	14
Burns	2	2
Cardiovascular Disease	**9**	**48**
COPD	**4**	**20**
Diabetes	**15**	**30**
Dialysis	2	5
Immunosuppression	10	14
Intravenous Drug Use	**11**	**1**
Obesity	10	9
Penetrating Trauma	9	8
Surgical Wound	4	2
None	**35**	**8**

[†] Bold type indicates a significant difference (p<0.05).

underlying conditions were reported similarly among all adults. After controlling for age, only immunosuppression was significantly related to fatal outcome among cases (Odds Ratio [OR] 3.5, CI 1.7, 7.3).

In terms of clinical manifestation, after adjusting for age, pneumonia was associated with COPD (OR 2.6, CI 1.1, 6.4) and immunosuppression (OR 2.4, CI 1.1, 5.3); septic arthritis was associated with blunt trauma (OR 2.5, CI 1.1, 5.6); and necrotizing fasciitis was associated with blunt trauma (OR 4.8, CI 1.8, 12.3) and burns (OR 6.6, CI 1.2, 36.6).

Emm type Analysis

The surface M protein – a known virulence factor for disease – has been the basis for GAS strain typing for decades. Since 1995, CDC has determined the M protein type through sequencing the DNA of the corresponding gene (*emm*), providing an *emm* type.[2] In 2008, 17 *emm* types were determined for isolates from 56 cases (90%). The five most frequent *emm* types reported in 2008 were 1 (27%), 3 (13%), 12 (10%), 28 (6%), and 82 (6%). Since 2003, 38 *emm* types were determined for 345 isolates. The most frequent *emm* types seen over this time are presented in Table 3.

Table 3: Selected Demographic and Clinical Attributes of Invasive GAS Disease, by Isolate *emm* Type, 2003-2008.†

	Total (N=345)	Fatal (N=58)	Age 65+ (N=97)	Necrotizing Fasciitis (N=21)	Pneumonia (N=54)
emm type	N (%)	N (%)	N (%)	N (%)	N (%)
1	82 (24)	22 (38)	22 (23)	11 (52)	25 (46)
3	20 (6)	7 (12)	7 (7)	1 (5)	3 (6)
4	15 (4)	1 (2)	5 (5)	1 (5)	0 (0)
12	29 (8)	4 (7)	9 (9)	2 (10)	6 (11)
28	21 (6)	2 (3)	10 (10)	1 (5)	1 (2)
92	30 (9)	4 (7)	4 (4)	2 (10)	4 (7)

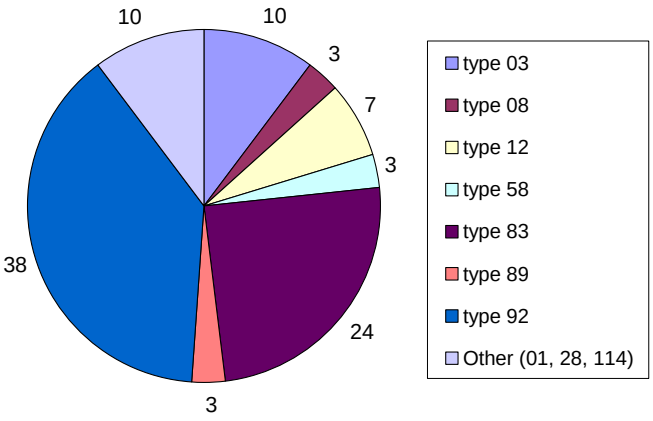
† Percentages are number of isolates with displayed *emm* type out of the total number of isolates in that category.

Emm types 1 and 3 are both significantly associated with a fatal outcome (OR 2.6, CI 1.3, 5.3 and OR 3.9, CI 1.4, 11.0, respectively); *emm* type 1 is also associated with necrotizing fasciitis (OR 7.5, CI 2.0, 27.7). *Emm* type 4 is associated with cellulitis (OR 5.1, CI 1.5, 16.7).

Antibiotic Susceptibility

The antibiotic susceptibility profile of invasive GAS strains has been assessed at several points since the beginning of ABCs, the most recent of which occurred in 2006. Antibiotic susceptibility results are available for 217 isolates obtained from 2003-2008. Of these, 100 percent were susceptible to penicillin, ampicillin, cefotaxime, and vancomycin. Thirty-four isolates (16%) exhibited some level of antibiotic resistance: five displayed intermediate resistance and 26 displayed full resistance to erythromycin alone; three were resistant to erythromycin and clindamycin.

Figure 4: Percentage of Erythromycin-Resistant Isolates by *emm* Type, 2003-2008 (N=29).



Note: Percentage total does not equal 100% due to rounding.

Erythromycin resistance is not associated with any particular clinical manifestation of invasive GAS disease or with a fatal outcome. Figure 4 shows the percentage of erythromycin-resistant isolates by *emm* type. Since 2003, *emm* type 92 has accounted for a disproportionate percentage of the erythromycin-resistant isolates—38 percent—compared with 9 percent of all isolates during this time period.

Discussion

Results of invasive GAS disease surveillance in Oregon in 2008 continue to portray a profile of disease similar to that seen nationally. IGAS disproportionably affects the elderly in Oregon. Additionally, certain clinical syndromes of invasive GAS disease differ across the age of the population. For instance, cellulitis increased with age, while septic arthritis and meningitis both decreased with age. Among young adults, invasive disease is more likely to be associated with injection drug use or no reported underlying condition. The elderly are more likely to have systemic disease associated with chronic underlying conditions that may affect immune function. Although it is not possible to assess risk factors for disease through surveillance alone, this association has been well documented.[3]

Monitoring trends in necrotizing fasciitis and toxic shock syndrome as well as potentially-preventable nosocomial infections (such as surgical wound infections) have been objectives of IGAS surveillance through the ABCs network. In general, most clinical manifestations have remained relatively stable over the past six years. Trends will continue to be monitored by the Oregon ABCs program.

References

1. Centers for Disease Control and Prevention. 2009. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Group A *Streptococcus*, 2008. Available at http://www.cdc.gov/abcs/reports-findings/survreports/gas08.pdf.
2. Beall B, Facklam RR, Thompson T. Sequencing *emm*-specific PCR products for routine and accurate typing of group A streptococci. *J Clin Microbiol* 1996;34:953-8.
3. Factor SH, Levine OS, Schwartz B, et al. Invasive Group A Streptococcal Disease: Risk Factors for Adults. *Emerg Infect Dis* 2003;8:970–7.