Group A *Streptococcus* Surveillance Report 2005

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 29.7 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 invasive GAS disease comprises the Tri-County (Clackamas, Multnomah, and Washington) Portland metropolitan area with a 2005 estimated population of 1,543,910. More information on the Oregon ABCs program is found at: http://oregon.gov/DHS/ph/acd/abc.shtml.

Methods

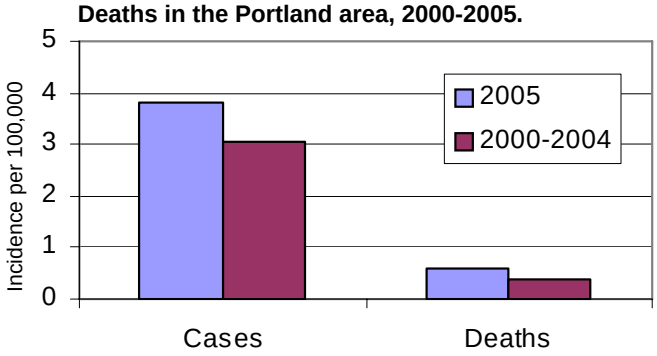
Invasive disease is defined as the isolation of GAS from a normally sterile body site or fluid or from a wound accompanied by necrotizing fasciitis or toxic shock syndrome in a Tri-County resident. Tri-County hospital laboratories submit GAS isolates to the Oregon State Public Health Laboratory, from where they are forwarded 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 2005, 59 cases of invasive GAS disease were reported in the Tri-County Portland area, corresponding to an incidence rate of 3.8/100,000 persons (Figure 1). This is slightly higher than the average annual incidence rate in the Portland area from 2000–2004 (3.1/100,000) and the 2005 national projection of invasive disease (3.5/100,000).[1] Of these cases, there were nine deaths, for an annual mortality rate due to invasive GAS disease of 0.6/100,000 (Figure 1). As with case incidence, this rate is higher than both the 2000–2004 Portland area (0.4/100,000) and the 2005 national projections (0.5/100,000).[1] The mean and median ages of death due to invasive GAS disease in 2005 were 71 and 82 years, respectively. The 2005 case fatality rate for invasive GAS disease in the Portland area was 15%, compared with 13% for the Portland area from 2000–2004 and the entire ABCs network in 2005.[1] Of 53 cases where sex was known, 53% were male. Race was recorded for only 30 cases; all of which were white.

Figure 1: Incidence of Invasive GAS Cases and Deaths in the Portland area, 2000-2005.



As seen in Figure 2, the incidence rate of invasive GAS disease in Multnomah County in 2005 (5.9/100,000) was higher than that reported from either Clackamas (2.2/100,000) or Washington (2.0/100,000) Counties. This is similar to the historical pattern throughout the Portland area from 2000-2004. While similar to the 5-year average in Clackamas and Washington Counties, the 2005 incidence rate in Multnomah County was higher. In 2005, the mortality rate due to GAS was highest in Clackamas County (0.8/100,000), followed by Multnomah (0.7/100,000), and Washington (0.2/100,000). The mortality rate from 2000-2004 was 0.5/100,000 for Clackamas and Multnomah Counties and 0.3/100,000 in Washington County.

Figure 2: Incidence of Invasive GAS Disease by County, 2000-2005.

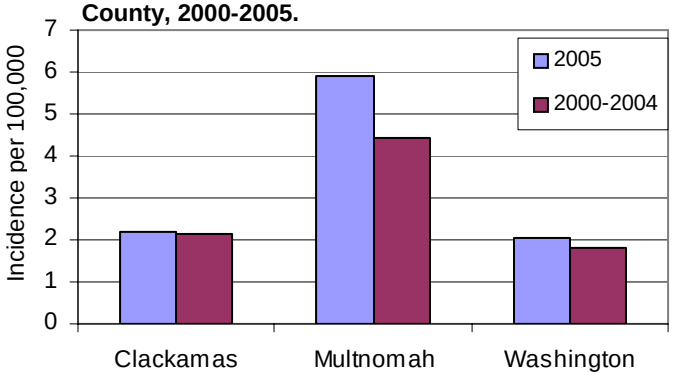
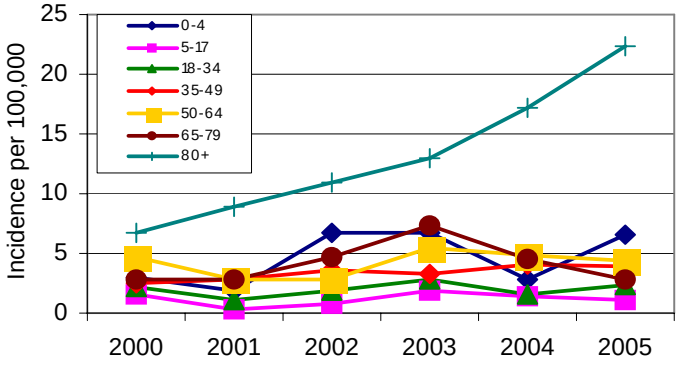


Figure 3: Incidence of Invasive GAS Disease in the Portland Area by Age, 2000-2005.



The burden of disease was highest in those ≥80 years of age (11 cases; incidence 22.5/100,000 persons), followed by those under four years of age (7 cases; case incidence of 6.6/100,000) (Figure 3). While the incidence among all other age groups was relatively constant over recent years, it has been rising steadily among persons ≥80 years of age—from 6.7/100,000 since 2000. Invasive GAS mortality was also highest in those ≥80 years of age. Five of the nine deaths in 2005 were among persons in this age group, for a mortality of 10.2/100,000 and a case fatality rate of 46%. This mortality is higher than that seen in the Portland area during 2000–2004 (3.5/100,000) and from all ABCs sites in 2005 (1.9/100,000).[1]

Clinical Manifestations

The top four clinical manifestations of invasive GAS disease reported in 2005, as seen in Table 1, include Primary Bacteremia, Cellulitis, Septic Arthritis, and Bacteremic Pneumonia. This is consistent with historical patterns. However, a statistically significant increase in reported bacteremia—and a concurrent decrease in cellulitis—has been occurring since 2000 (p=0.02 and p=0.0002, respectively); 2005 was the first year since reporting began in 1995 in which bacteremia was reported in more cases than was cellulitis.

Table 1: Percent of Invasive GAS cases reporting common clinical syndromes.†

Syndrome	2005	2000-2004
Primary Bacteremia	32	18
Cellulitis	22	43
Septic Arthritis	15	13
Pneumonia	9	17
Necrotizing Fasciitis	5	6
Sterile Abscess	3	7
Meningitis	2	2
Toxic Shock	0	4

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

The clinical syndromes of invasive GAS disease vary by age. Invasive GAS meningitis was reported significantly more frequently (p=0.0005)—and cellulitis significantly less (p=0.0021)—among children than among adults. Among all adults, septic arthritis and sterile abscess

infection were reported more frequently among those 18–64 years of age (p=0.02 and p=0.01, respectively), while pneumonia and bacteremia were reported more frequently among those ≥65 years of age (p=0.03 and p=0.02, respectively).

Pneumonia and bacteremia were also significantly associated with a fatal outcome among invasive GAS cases. Even after controlling for patient age, a fatal outcome was 5.1 times (95% confidence interval [CI] 2.4, 10.9) as likely among those with pneumonia and 5.0 times (95% CI (2.4, 10.3) as likely among those with bacteremia than among those with other clinical manifestations.

Underlying Conditions

Table 2 lists underlying conditions that are known risk factors for invasive GAS disease or were reported frequently among adult cases in the Portland area during 2000–2005. Asthma, injection drug use (IVDU) and penetrating trauma were significantly associated with cases among younger adults, while cardiovascular disease, chronic obstructive pulmonary disease (COPD), and diabetes were significantly associated with cases among older adults.

Table 2: Percent of Adult Invasive GAS Cases with Reported Underlying Conditions.

	18-64	65+	p-value
Asthma	**8**	**3**	**0.043**
Blunt Trauma	10	13	0.444
Burns	1	0	0.083
Cardiovascular Disease	**14**	**59**	**<0.0001**
COPD	**8**	**21**	**0.003**
Diabetes	**15**	**30**	**0.004**
Dialysis	8	7	0.885
Immunosuppression	7	9	0.535
IVDU	**26**	**0**	**<0.0001**
Penetrating Trauma	**8**	**1**	**0.0007**
Surgical Wound	3	4	0.647

Table 3 shows statistically significant associations of underlying conditions and death due to invasive GAS disease. Older age, immunosuppression, and cardiovascular disease were all significantly associated with a fatal outcome in univariate analysis. However, in a logistic regression model controlling for age, only immunosuppression was independently associated with death.

Table 3: Significant Associations between Underlying Conditions and Death.

Bivariate Analysis	OR	95% CI
Older Age	2.7	(1.5, 4.8)
Immunosuppression	3.0	(1.3, 7.0)
Cardiovascular Disease	1.9	(1.1, 3.5)

Logistic Regression	aOR	95% CI
Older Age	2.6	(1.5, 4.8)
Immunosuppression	3.0	(1.2, 7.1)

Two clinical syndromes were positively associated with underlying conditions. Cellulitis was associated with IVDU (p=0.014), while pneumonia was associated with immunosuppression (p=0.019), COPD (p=0.005), and cardiovascular disease (p=0.001). Cardiovascular disease and COPD seem to be stronger predictors of pneumonia, as the effect of age became non-significant in the respective bivariate models of age and COPD or cardiovascular disease.

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 2005, *emm* types were determined for 41 cases and 16 different *emm* types were reported. Since 2000, 34 *emm* types isolated from 251 cases have been reported for cases of invasive GAS disease in the Portland area. The five *emm* types seen most frequently, along with type 89 and selected significant associations, are presented in Table 4. Although among the most commonly reported *emm* types in 2005 (5 cases), type 89 had not been seen in Oregon before two cases with this type emerged in 2004.

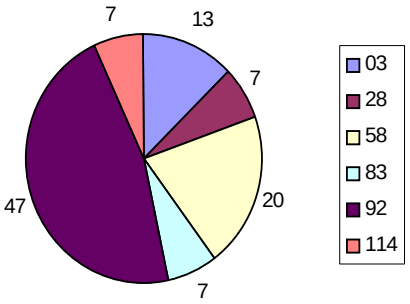
Table 4: Selected Demographic and Clinical Attributes of Invasive GAS Disease, by Isolate *emm* Type.

emm type	Number (%)	Fatal Outcome	Age 65+ Years	Bacteremia	Pneumonia
1	53 (19)	**3.6 (1.8, 7.4)**	1.1 (0.6, 2.1)	0.9 (0.4, 1.7)	**3.3 (1.7, 6.5)**
3	22 (8)	**6.0 (2.3, 15.2)**	1.8 (0.7, 4.4)	1.0 (0.4, 2.7)	**5.3 (2.2, 12.8)**
12	18 (6)	1.9 (0.5, 7.0)	2.0 (0.8, 5.1)	0.7 (0.2, 2.4)	1.4 (0.4, 5.2)
28	18 (6)	1.8 (0.6, 5.7)	**4.0 (1.8, 8.6)**	1.5 (0.6, 3.6)	2.2 (0.8, 5.9)
89	7 (2)	**5.4 (1.3, 22.8)**	**10.5 (2.6, 42.3)**	**6.8 (1.8, 25.0)**	1.1 (0.1, 8.7)
92	26 (9)	1.5 (0.4, 5.5)	0.8 (0.3, 2.3)	0.8 (0.3, 2.3)	1.1 (0.3, 4.1)

Antibiotic susceptibility

The antibiotic susceptibility profile of invasive GAS strains has been assessed at several points since the beginning of ABCs. Of 80 cases for which antibiotic susceptibility information is available since 2000, 100% are susceptible to penicillin, clindamycin, ampicillin, cefotaxime, cefuroxime, cefazolin, and vancomycin.

Figure 3: Percentage of erythromycin-resistant isolates, by *emm* type.



However, 15 of 80 (19%) invasive GAS cases are resistant to erythromycin, 5 of 80 (6%) display intermediate susceptibility, and the remaining 75% are fully susceptible. Erythromycin resistance is not associated with any particular clinical manifestation of invasive GAS disease or with a fatal outcome. Figure 3 shows the percentage of erythromycin-resistant isolates by *emm* type. Since 2000, *emm* type 92 has accounted for a disproportionate percentage of the erythromycin-resistant isolates—47%—compared with 9% of all isolates during this time period. Furthermore, while neither resistant isolates nor *emm* type 92 are associated with a particular clinical syndrome overall, *emm* type 92 isolates resistant to erythromycin are positively associated with bacteremia (p=0.047).

Discussion

Invasive GAS disease disproportionably affects the elderly in Oregon, a pattern seen nationally. Additionally, the profile of invasive disease differs across the age of the population. For instance, children are much more likely to experience GAS meningitis than are adults. Among young adults, invasive disease is more likely to manifest as a sterile abscess or septic arthritis and is more likely to be associated with penetrating trauma and injection drug use. 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]

An interesting finding of these analyses is the potentially changing epidemiology of invasive GAS epidemiology in Oregon, most notably the increase in disease among those ≥80 years of age and the changing clinical profile of disease. An increase in underlying conditions among the elderly that are known risk factors for invasive GAS disease and the emergence in this population of a new strain of GAS associated with bacteremia may help explain these trends. Also to be considered is whether these trends simply represent year-to-year variability. Continued surveillance in Oregon, analysis of the larger EIP Network dataset, and additional epidemiological research should help to shed light on this observation.

References:

1. Centers for Disease Control and Prevention. 2006. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Group A Streptococcus, 2005-*provisional.* Available at http://www.cdc.gov/ncidod/dbmd/abcs/survreports/gas05.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.