Neisseria meningitidis Surveillance Report 2015

Oregon Active Bacterial Core Surveillance (ABCs)

Center for Public Health Practice
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), and *Streptococcus pneumoniae.* The entire EIP Network for invasive *N. meningitidis* disease represents almost 43 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 *N. meningitidis* disease comprises the entire state, with a 2015 estimated population of 4,013,845.* More information on the Oregon ABCs program is found at: http://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/EmergingInfections/Pages/ActiveBacterialCoreSurveillance.aspx.

Methods

Invasive meningococcal disease (IMD) is defined as the isolation of *N. meningitidis* from a normally sterile body site in a resident of Oregon. Since IMD is reportable in Oregon, hospital laboratories submit sterile site *N. meningitidis* microbiology isolates to the Oregon State Public Health Laboratory for serogrouping as well as submitting demographic data electronically via Electronic Laboratory Reporting (ELR). Isolates are forwarded to a CDC laboratory for further testing. Additional cases are identified through regular laboratory record reviews. Health record reviews of each case provide standardized reports of demographic characteristics, clinical syndrome manifestations, underlying illnesses or conditions, and illness outcome.

Surveillance Results

Descriptive Epidemiology

In 2015, 27 cases of IMD were reported in Oregon, corresponding to an incidence rate of 0.67 per 100,000 persons. This is 20% higher than the average annual incidence rate in Oregon from 2010-2014 (0.56/100,000). This is likely explained by a meningococcal serogroup B outbreak at a large public university in Oregon in 2015. Six Oregon undergraduates were diagnosed with serogroup B meningococcemia. Their isolates all matched by pulse-field gel electrophoresis (PFGE) and whole genome sequencing (WGS). There was one death associated with the outbreak. IMD incidence in Oregon was significantly higher than both the most recent national estimate (0.14/100,000) and the Healthy People 2020 goal for IMD

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

(0.30/100,000) in 2014 and 2015.[1] Oregon's historically high rate of meningococcal disease was driven by a localized epidemic of serogroup B IMD that began in the early nineties and peaked in 1994 (3.4/100,000).[2] The incidence of serogroup B IMD has since then declined steadily, accounting for only twenty percent of our cases in 2014. Due largely to the 2015 outbreak, fifty-two percent of cases in 2015 were due to serogroup B The estimated incidence of serogroup B disease is 0.04 per 100,000 cases for all ABCs areas excluding Oregon, 99 percent lower than the Oregon-specific rate for serogroup B IMD (0.35 per 100,000).[1]

There were sixIMD deaths in 2015, for an annual mortality rate of 0. 15/100,000 (Figure 1). This is 190% higher than the average annual mortality rate in Oregon of 0.05/100,000 from 2010-2014, and 647% higher than the national projections (0.02/100,000).[1]

The 2015 case fatality rate (22.2%) for IMD in Oregon was 136%higher than the 9.4% percent reported for Oregon from 2010-2014 and 33% higher than the national projections (17%).[1]

Forty-one percent of cases were female. Race and ethnicity were obtained on 89% of cases; 71%were white. Four percent were Hispanic or Latino.

As depicted in Figure 2, the burden of IMD is typically highest in the very young (those 0-4 years of age). We observe a second peak in incidence in young adults. Among those 65 and older, 2015 IMD incidence (0.91/100,000) and mortality (0..46/100,000) were higher than the respective 5-year averages (0.70/100,000 and 0.04/100,000) with a 1000% increase in mortality among those over 65..

Figure 1: Incidence and Mortality Rates of IMD Cases in Oregon

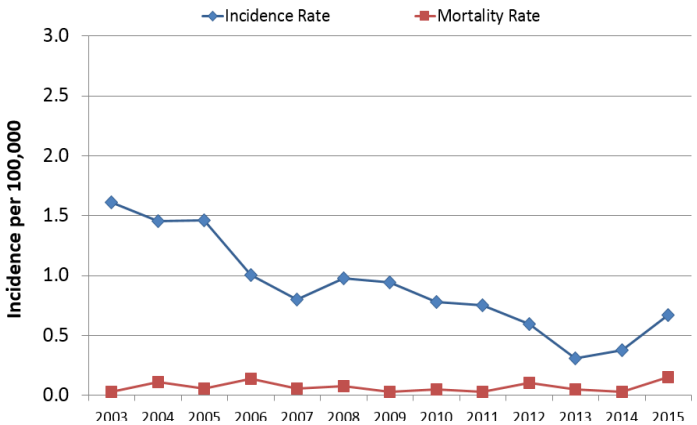
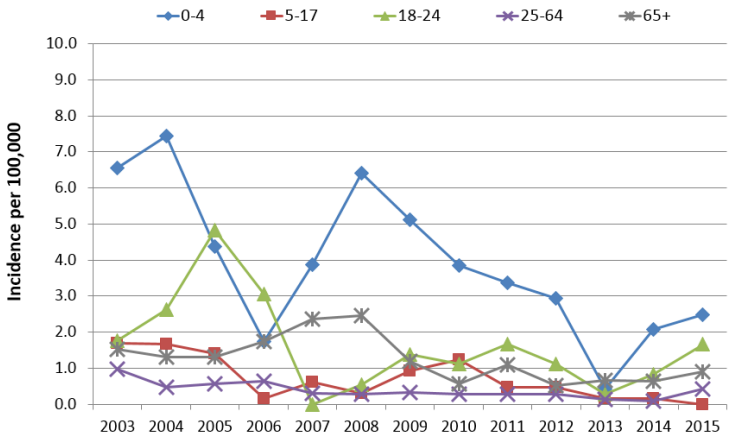


Figure 2: Incidence of IMD Cases in Oregon by Age



Clinical Manifestations

As is typical, the top clinical manifestation of invasive meningococcal disease in 2015 was meningitis (Table 1). No clinical syndrome was associated with an increased risk of a fatal outcome.

Table 1: Percent of IMD Cases† Reporting Common Clinical Syndromes

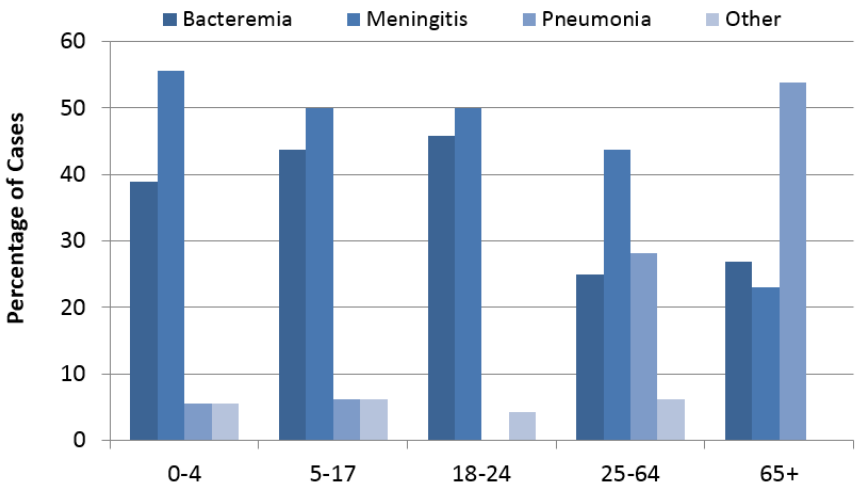
Syndrome	2015	2010-2014
Bacteremia	26	38
Meningitis	48	44
Pneumonia	26	18
Other††	0	6

† Some cases report more than 1 syndrome.

†† Other syndrome includes cellulitis, endometritis, epiglottitis, peritonitis, septic abortion, septic arthritis, and sterile abscess.

The clinical presentation of IMD varies according to age (Figure 3). From 2010-2015, meningitis was most common among those aged <65 years, and pneumonia was most common among those 65 and over. The association between age and clinical manifestation is statistically significant, with meningitis decreasing with increasing age (p=0.0044), and pneumonia increasing (p<0.0001) with increasing age.

Figure 3: Clinical Manifestation of IMD in Oregon by Age 2010-2015



Underlying Conditions

Table 2 lists underlying conditions that are known risk factors for invasive meningococcal disease or were noted frequently among adult IMD cases in Oregon from 2010-2015. During this time period, forty-five percent of all cases had no underlying conditions noted in the medical record, although this is not uniform across the age spectrum: 79 percent of children less than 18 years of age had no underlying conditions versus 24 percent of adults (p<0.0001).

Table 2: Underlying Conditions Reported Among Adult IMD Cases

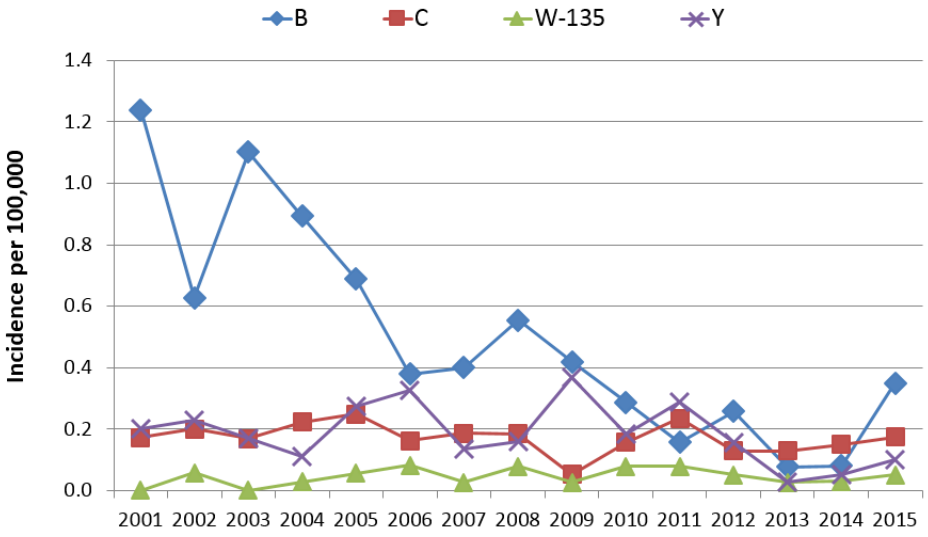
Underlying Condition	2015 (n=21 N (%)	2010-2014 (n=61) N (%)
Asthma	3 (14)	8 (13)
Cancer	0	2 (3)
Cardiovascular disease	4 (19)	9 (15)
COPD	2 (9)	12 (20)
Diabetes	2 (9)	11 (18)
Immunosuppression	0	5 (8)
Obesity	2 (9)	5 (8)
Smoking	2 (9)	17 (28)
None	8 (38)	12 (20)

Underlying conditions were further analyzed with regard to fatal outcome and clinical manifestation of IMD. After adjusting for age, none of the underlying conditions were significantly associated with a fatal outcome. COPD (p=0.0019) and smoking (p=0.02) were significantly associated with pneumonia after controlling for age. No underlying conditions were related to bacteremia or meningitis.

Serogroup Analysis

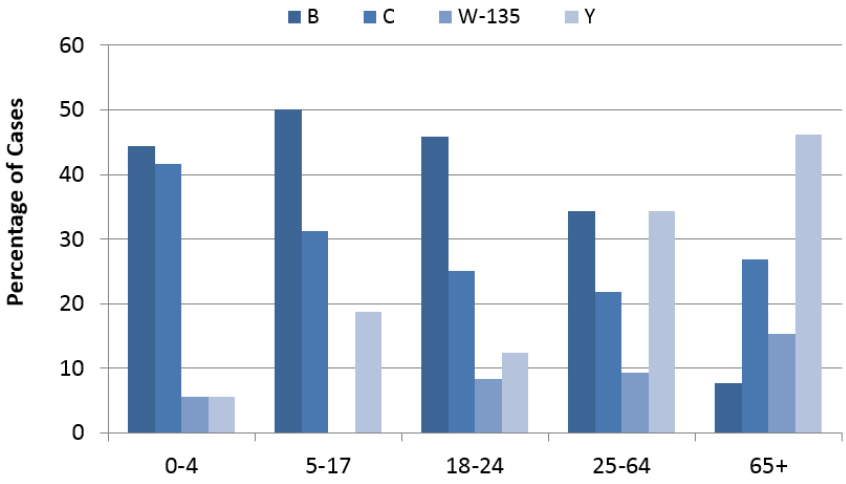
In 2015, the serogroups of *N. meningitidis* causing invasive disease were determined for all cases (n=27). Of these, serogroup B comprised 52 percent; serogroup C, 26 percent; serogroup W-135, 7 percent; and serogroup Y, 15 percent. Historically in Oregon, serogroup B has been the predominant serogroup causing IMD.

Figure 4: Serogroup of *N. meningitidis* Causing Invasive Disease in Oregon, 2001-2015



Changes in serogroup distribution since 2001 can be observed in Figure 4. A statistically significant decreasing trend in the proportion of cases due to serogroup B ($p<0.001$) and an increasing trend in the proportion of cases due to serogroups C, W-135 and Y ($p=0.0003$, $p<0.0001$ and $p<0.0001$, respectively) have been observed.

Figure 5: Serogroup of N. meningitidis Causing Invasive Disease in Oregon by Age Group, 2010-2015



During the six-year period from 2010-2015, serogroup B was the most commonly identified serogroup among those 5-17 years of age (50%), Serogroup C was most common among those aged 0-4 years (42%), followed by serogoup Y in those aged 25-64 (34%), and lastly serogroup W-135 among those 65 and older.

After controlling for age, no serogroup was significantly associated with a fatal outcome or any clinical manifestation.

Antimicrobial Susceptibility

Although clinically significant antimicrobial resistance (AMR) in *N. meningitidis* has historically been low[3], the detection of ciprofloxacin-resistant *N. meningitidis* in the US[4] has led to routine antimicrobial susceptibility testing of ABCs isolates submitted to the CDC Meningitis Laboratory.

Antimicrobial results from CDC were available for 89 isolates cultured in 2008, 2010, and 2011 (Table 3). The majority of these isolates were susceptible to the antibiotics tested. However, a subset of isolates exhibited intermediate antibiotic resistance to ampicillin, penicillin and rifampin and resistance to ciprofloxacin. Although the proportion of isolates with some level of resistance to penicillin has increased over time, the association cannot be statistically tested due to insufficient sample size.

Table 3: Antimicrobial Susceptibility of IMD Isolates†

Antibiotic	2008 N=37 (100% of isolates tested)			2010 N=25 (83% of isolates tested)			2011 N=27 (93% of isolates tested)		
	S	I	R	S	I	R	S	I	R
Ampicillin	NT	NT	NT	84	16		96	4	
Azithromycin	100			100			100		
Cefotaxime	NT	NT	NT	100			100		
Ceftriaxone	100			100			100		
Chloramphenicol	NT	NT	NT	100			100		
Ciprofloxacin	100			100			96		4
Meropenem	NT	NT	NT	100			100		
Penicillin	92	8		88	12		81	19	
Rifampin	97	3		100			100		

† Abbreviations: NT=not tested; S=susceptible; I=intermediate resistance; R=full resistance

Discussion

Oregon's highest recorded rate of meningococcal disease – 3.4 cases per 100,000 in 1994 – was driven by a clonal epidemic of serogroup B disease that began in 1993 and lasted for several years. In 2015, 27 cases of IMD were reported in the state, corresponding to an incidence rate of 0.67 cases per 100,000. This increase in cases is due to an outbreak of serogroup B meningococcal disease at a large public university in Oregon. Prior to 2015, there was an 89 percent decrease in incidence of serogroup B diease since the peak in 1994. As serogroup B disease continues to decrease, the profile of IMD serogroup distribution is becoming more similar to the national profile.

For updated meningococcal disease vaccination recommendations, visit:
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6003a3.htm

References

1. Centers for Disease Control and Prevention. 2014. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *Neisseria meningitidis*, 2014. Available via the Internet: http://www.cdc.gov/abcs/reports-findings/survreports/mening14.pdf. Accessed 25 Aug 2016.
2. Diermayer M, Hedberg K, Hoesly F, et al. Epidemic Serogroup B Meningococcal Disease in Oregon: The Evolving Epidemiology of the ET-5 Strain. *JAMA*. 1999;281:1493-7.
3. Rosenstein NE, Stocker SA, Popovic T, Tenover FC, Perkins BA. Antimicrobial resistance of *Neisseria meningitidis* in the United States, 1997. The Active Bacterial Core Surveillance (ABCs) Team. Clin Infect Dis 2000 Jan;30(1):212-3.
4. Wu HM, Harcourt BH, Hatcher CP, et al. Emergence of ciprofloxacin-resistant *Neisseria meningitidis* in North America. N Engl J Med 2009 Feb 26;360(9):886-92.