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Georgia Epidemiology Report

Haemophilus influenzae Disease in Georgia

Introduction

Haemophilus influenzae is a small, pleomorphic gram-negative bacterium that is highly adapted to its human host and does not survive for long in the environment. Most strains of *H. influenzae* are opportunistic pathogens, i.e. they live in the human respiratory tract without causing invasive disease unless other factors such as viral infections, chronic lung disease, or a compromised immune system create the opportunity. *H. influenzae* type B (Hib), although now rare because it is vaccine-preventable, is one type of the pathogen that is highly virulent and noted for causing devastating disease in healthy young children. The effect of the Hib vaccine has been a major public health success story. This report describes the history of ongoing surveillance, and for emerging issues in *H. influenzae* disease in Georgia.

Serotypes of *H. influenzae*

Serotyping of *H. influenzae* is based on the presence of a polysaccharide (polyribosyl-ribitol phosphate) capsule surrounding the organism—6 types (a, b, c, d, e, and f) have been identified. Although the capsule is considered to be a primary virulence factor, most invasive *H. influenzae* disease is now caused by non-encapsulated (non-typeable) *H. influenzae* organisms. Non-typeable *H. influenzae* commonly colonize the upper airway, where they often cause ear infections in children, and the lower respiratory tract of adults with chronic obstructive pulmonary disease, where they can cause bronchitis and pneumonia, and may invade the bloodstream.

Manifestations of Hib Disease

Hib is a uniquely virulent serotype of *H. influenzae*. Invasive Hib disease may manifest as meningitis, pneumonia, bacteremia, mastoiditis, arthritis, epiglottitis or periorbital cellulitis. Other less common manifestations include endocarditis and osteomyelitis. A characteristic feature of Hib disease is age-dependent susceptibility; before the availability of the Hib conjugate vaccine, Hib disease was most common in children under age 5 years (2). In the post-vaccine era (i.e. since the late 1980s), unvaccinated young children are at risk for developing Hib disease as they are not fully immune. Approximately, 3% to 6% of invasive Hib cases are fatal. Of surviving patients, up to 20% have permanent hearing loss or other long-term sequelae (3).

H. influenzae infections can be diagnosed by isolating the bacteria from a normally sterile body site (blood, cerebrospinal fluid, pleural fluid, etc.) using chocolate agar media.

Impact of Hib Vaccines

Until the introduction and routine use of Hib vaccines, Hib was the leading cause of bacterial meningitis in infants and children in the U.S., with annual incidence of 40 to100 cases per 100,000 children, resulting in death or permanently disability for approximately 6,000 children per year.

The Hib polysaccharide vaccine became available for toddlers in 1985 for children aged 18 months and older in the U.S., pioneering a gradual decline in Hib disease (3). Routine use of Hib conjugate vaccines began in 1991 for infants aged 2 months, and the impact was immediate and profound (1). By 1993, the Centers for Disease Control and Prevention (CDC) reported a 95% reduction in Hib disease in the U.S., and the incidence has now decreased by 99% to a national rate less than 1 case per 100,000 children. Hib vaccines have saved thousands of lives and prevented more than 100,000 cases of deafness and severe mental retardation. In addition, the vaccine decreases the rate of Hib carriage among vaccinated children, thereby decreasing the chance that unvaccinated children will be exposed to Hib. While Hib disease has virtually disappeared in the U.S. and the developed world, the cost of the conjugate vaccine has limited its use in developing countries where the disease remains a major cause of morbidity and mortality (4).

Surveillance of *H. influenzae* Disease in the U.S. & Georgia

Invasive *H. influenzae* disease became nationally reportable in 1991, just after Hib conjugate vaccines became licensed and routinely recommended. While *H. influenzae* infections have been reportable since 1991 in Georgia, methods of surveillance have improved and expanded over time. From 1991 to 1996, active and audited surveillance was performed in the 8-county Atlanta metropolitan statistical area (MSA). Active surveillance

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expanded to the 20-county Atlanta MSA for 1997 through 1999 and statewide since 2000.

Figure 1 depicts the rate of *H. influenzae* disease reported in Georgia since 1991 and the projected national rate since 1997, which is based on active surveillance performed under the Active Bacterial Core Surveillance (ABCs) of the Emerging Infections Program.[1]

Hib Disease in the U.S. & Georgia

The estimated national incidence of Hib disease from 1997 to 2007 remained below or equal to 1.0 per 100,000 population in the ten states monitored by the ABCs (5, 6, 7, 8, 9, 10, 11, 12, 13, 14). Eighteen Hib cases were recognized in Georgia between 1998 and 2007. One case patient was younger than age 2 months, 13 case patients were older than age 5 years, and four case patients were age-eligible for vaccination. Of the four Hib case patients that were eligible for vaccination, 3 had not been vaccinated and the vaccination status of the remaining case patient was unknown.

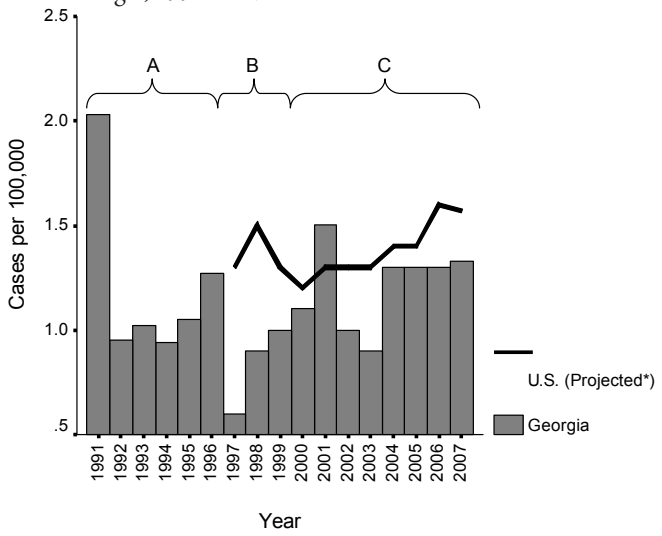
Hib disease is now rare, but continued surveillance for Hib disease is important to monitor effectiveness of current vaccines. However, monitoring *H. influenzae* serotypes in the current era requires sustained efforts to send isolates to the Georgia Public Health Laboratory for serotyping and serotype verification. Figure 2 illustrates how challenging complete serotype ascertainment has been. Between 2004 and 2007, roughly half of *H. influenzae* isolates in Georgia were not serotyped by the Georgia Public Health Laboratory. The highest rates of serotyping have been achieved under active statewide ABCs surveillance, a system that requires substantial public health resources. Efforts to encourage isolate submission are being redoubled at this time, in view of emerging events that further underscore the importance of serotyping.

Emerging Issues

Two emerging issues make serotyping of all *H. influenzae* isolates increasingly important: measuring the potential impact of Hib vaccine shortages, and monitoring the effectiveness of newer Hib vaccine formulations.

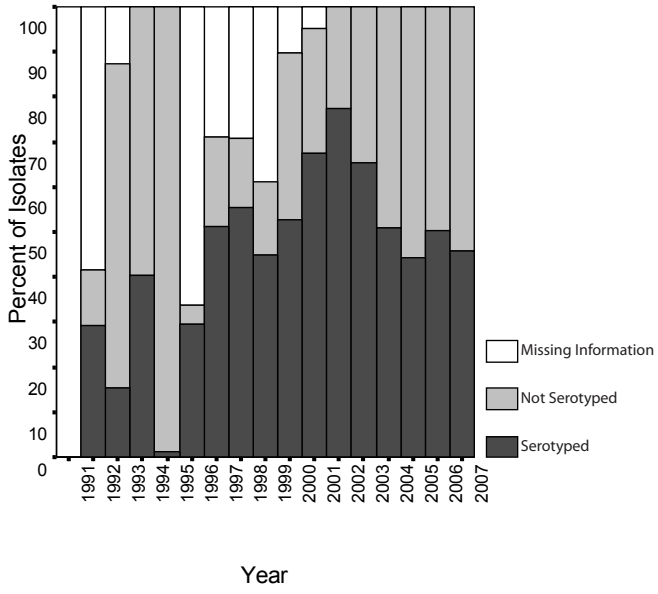
First, in late 2007, Merck & Co. voluntarily recalled over 1 million Hib vaccine doses because of concerns over potential

Figure 1: Incidence of Invasive *H. influenzae* (All Types), Georgia, 1991-2007



A –1991 to 1996, active surveillance in the 8-county Atlanta metropolitan statistical area (passive in the remainder of the state)
B – 1997 to 1999, active surveillance in the 20-county Atlanta metropolitan statistical area (passive in the remainder of the state)
C – 2000 to 2007, statewide active surveillance.
*U.S. Rate projected by ABCs (EIP) Active Surveillance (References 5-14).

Figure 2: Percent of *H. influenzae* Isolates Serotyped, Georgia, 1991-2007



[1]The Active Bacterial Core surveillance (ABCs), which is a core component of the CDC-sponsored Emerging Infections Program (EIP) and collaboration between 10 state health departments and universities across the country established in 1995, collects comprehensive data on H. influenzae and other emerging pathogens. This program aims to establish risk factors for disease, track disease trends, monitor efficacy of vaccines, and assess the effectiveness of prevention policies; based on data collected from nationally representative surveillance areas with over 35,500,000 persons.

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product contamination, resulting in a vaccine shortage. The recall involved two of Merck's Hib-containing vaccine products: a monovalent Hib conjugate vaccine (PedvaxHIB), and a combination Hib/hepatitis B vaccine (COMVAX). Merck suspended production of the two vaccines at that time and projected that distribution of these products would not resume until the fourth quarter of 2008.

As a result, the Advisory Committee on Immunization Practices (ACIP) recommended that health care providers temporarily defer administration of the Hib vaccine booster dose normally given at age 12-15 months, except for children in specific groups at higher risk. These groups include children with sickle cell disease, leukemia and malignant neoplasms, HIV and certain other immuno-compromising conditions, asplenia, as well as American Indian and Alaska Native children (15). Providers are receiving limited allocations of vaccine, and conceivably, some children might also be missing doses in the primary series, normally given at ages 2, 4, and 6 months of age.

It is important to know whether additional cases of Hib might result from the disrupted vaccine supply.

Second, on June 23, 2008, the U.S. Food and Drug Administration (FDA) licensed a new 5-component Hib-containing vaccine for the first time. The vaccine, called Pentacel®, contains Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccines, and is made by Sanofi Pasteur. The Pentacel® vaccine is approved for use in infants and children 6 weeks through 4 years of age (prior to fifth birthday) as a four-dose series at 2, 4, 6 and 15 to 18 months of age. Uptake of the new vaccine could be considerable, because of current shortages of other vaccine formulations and as a means to reduce the number of required injections during early childhood. As a newer vaccine formulation, it is important to monitor for vaccine effectiveness and post-licensure safety.

Request for *H. influenzae* Isolates

To accurately document the number of Hib cases occurring in Georgia and to monitor effects of Hib vaccine shortages and newer formulations, it is important to determine serotypes in all cases of invasive *H. influenzae* disease. Public Health strongly encourages hospitals and laboratories across the state to submit all isolates of invasive *H. influenzae* to the Georgia Public Health Laboratory for serotype information.

This article was written by Snehal R. Patel, M.P.H., and Kate E. Arnold, M.D.

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Reported Cases of Selected Notifiable Diseases in Georgia, Profile* for May 2008

Selected Notifiable Diseases	Total Reported for May 2008	Previous 3 Months Total Ending in May			Previous 12 Months Total Ending in May		
	2008	2006	2007	2008	2006	2007	2008
Campylobacteriosis	67	145	161	153	623	588	695
Chlamydia trachomatis	32	10214	11047	2934	36728	41758	33927
Cryptosporidiosis	16	36	37	69	183	272	269
E. coli O157:H7	2	9	2	5	36	37	46
Giardiasis	49	139	139	127	699	683	673
Gonorrhea	13	4864	4489	1042	17825	19706	13961
Haemophilus influenzae (invasive)	6	34	40	30	114	124	134
Hepatitis A (acute)	5	15	21	13	105	68	56
Hepatitis B (acute)	17	57	31	31	180	177	151
Legionellosis	2	6	12	8	35	49	37
Lyme Disease	4	0	2	6	6	9	15
Meningococcal Disease (invasive)	1	8	3	6	19	18	25
Mumps	1	1	0	2	2	3	2
Pertussis	0	3	3	3	38	28	15
Rubella	0	0	0	0	0	0	0
Salmonellosis	176	262	296	377	1944	1940	2046
Shigellosis	176	221	489	402	830	1701	1577
Syphilis - Primary	7	38	26	22	139	108	98
Syphilis - Secondary	31	88	130	124	487	530	605
Syphilis - Early Latent	18	98	115	76	401	420	388
Syphilis - Other**	68	270	310	253	1004	1071	1141
Syphilis - Congenital	1	3	3	2	7	9	10
Tuberculosis	57	136	134	138	516	516	475

* The cumulative numbers in the above table reflect the date the disease was first diagnosed rather than the date the report was received at the state office, and therefore are subject to change over time due to late reporting. The 3 month delay in the disease profile for a given month is designed to minimize any changes that may occur. This method of summarizing data is expected to provide a better overall measure of disease trends and patterns in Georgia.

** Other syphilis includes latent (unknown duration), late latent, late with symptomatic manifestations, and neurosyphilis.

AIDS Profile Update

Report Period	Disease Classification	Total Cases Reported*			Percent Female	Risk Group Distribution %						Race Distribution %			
		<13yrs	>=13yrs	Total		MSM	IDU	MSM&IDU	HS	Unknown	Perinatal	White	Black	Hispanic	Other
Latest 12 Months	HIV, non-AIDS	24	2,780	2,804	28	25	2	1	5	66	1	17	76	4	3
7/07-6/08	AIDS	8	1,933	1,941	28	28	3	1	8	59	<1	18	76	5	<1
Five Years Ago:**	HIV, non-AIDS	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7/03-6/04	AIDS	8	1,843	1,851	28	35	7	2	16	38	<1	20	74	5	<1
Cumulative:	HIV, non-AIDS	220	11,886	12,106	32	27	6	2	10	52	2	21	73	4	2
07/81-6/08	AIDS	241	32,761	33,002	20	43	14	5	14	23	1	30	66	3	1

Yrs - Age at diagnosis in years **MSM - Men having sex with men** **IDU - Injection drug users** **HS - Heterosexual**

* Case totals are accumulated by date of report to the Epidemiology Section ** Due to a change in the surveillance system, case counts may be artificially low during this time period
***HIV, non-AIDS was not collected until 12/31/2003