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Haemophilus b Conjugate Vaccines

Recommendations of the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service*

These recommendations include information on use of two vaccines recently licensed for use with infants: Haemophilus *b Conjugate Vaccine (Diphtheria CRM197 Protein Conjugate) (HbOC), manufactured by Praxis Biologics, Inc., and* Haemophilus *b Conjugate Vaccine (Meningococcal Protein Conjugate) (PRP-OMP), manufactured by Merck Sharp and Dohme, newly licensed for use with infants. This statement expands on earlier product-specific recommendations made in the November 1990 and January 1991 issues of the* Virginia Epidemiology Bulletin *and also updates recommendations for use of these and other* Haemophilus *b conjugate vaccines with older children and adults.*

Introduction

Haemophilus influenzae type b (Hib) is the leading cause of invasive bacterial disease among children in the United States. Before effective vaccines were introduced, one in 200 children developed invasive Hib disease by the age of 5 years. Sixty percent of these children had meningitis; 3%-6% died. Permanent sequelae, ranging from mild hearing loss to mental retardation, affect 20%-30% of all survivors of meningitis. Ninety-five percent of the cases of invasive *H. influenzae* disease among children less than 5 years of age are caused by organisms with the type b polysaccharide capsule. Approximately two-thirds of all cases of Hib disease affect infants and children <15 months of age, a group for which a vaccine has not previously been available.[1]

Three *Haemophilus* b conjugate vaccines are currently licensed for administration to children 15 months of age or older in the United States. Recently, the Food and Drug Administration approved the use of HbOC (October 4, 1990) and PRP-OMP (December 13, 1990) for routine administration to infants beginning at 2 months of age. This statement a) summarizes available information about *Haemophilus* b conjugate vaccines, b) offers guidelines for use of HbOC and PRP-OMP for infants for prevention of Hib disease, and c) advises how to use conjugate vaccines for older children. It should be noted that HbOC and PRP-OMP have different schedules for administration, which are discussed below.

Immunology of Hib

The polyribosylribitol phosphate (PRP) capsule of Hib is a major virulence factor for the organism. Antibody to PRP is the primary contributor to serum bactericidal activity, and increasing levels of antibody are associated with decreasing risk of invasive Hib disease. The human immune response to PRP resembles the murine response to T-cell independent antigens: B cells provide the primary response without a contribution from T-helper cells. In contrast to T-cell dependent antigens, T-cell independent antigens are characterized by a) induction of a poor antibody response in <18-month-old in-

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Table 1. Characteristics of *Haemophilus* b Conjugate Vaccines

Vaccine (producer)	Polysaccharide	Protein carrier	Linkage
HbOC, HibTITER™ (Lederle-Praxis)	small	CRM_{197} mutant *Corynebacterium diphtheriae* protein	no spacer
PRP-OMP, PedvaxHIB™ (Merck Sharp and Dohme)	medium	*Neisseria meningitidis* outer membrane protein complex	spacer
PRP-D, ProHIBIT™ (Connaught Laboratories)	medium	diphtheria toxoid	spacer

fants and children, b) a variable and quantitatively smaller antibody response than that seen with T-cell dependent antigens, c) production of a higher proportion of immunoglobulin M (IgM), and d) inability to induce a booster response.

Polysaccharide vaccines

Vaccines derived from PRP alone (polysaccharide vaccines) were developed in the 1970s. After demonstration of safety, immunogenicity, and induction of serum bactericidal activity, an efficacy of 90% (95% confidence interval [CI] = 50%-95%) was shown for one dose of vaccine given to children 18-71 months old in a large trial in Finland. However, the vaccine was ineffective for infants 3-17 months of age.[2] Beginning in 1985, several PRP vaccines were licensed for use in the United States for children 18 months of age or older, and a series of post-licensure case-control studies demonstrated variable efficacy. Four of five studies showed efficacy in the range of 41%-88%, and one study showed no efficacy.[3]

Conjugate vaccines

Covalent linkage (conjugation) of PRP with T-cell dependent protein antigens was evaluated in an attempt to overcome the T-cell independent characteristics of PRP. At present three different *Haemophilus* b conjugate vaccines are licensed for use with older children—HbOC, PRP-OMP, and *Haemophilus* b conjugate vaccine (Diphtheria Toxoid Conjugate, Connaught Laboratories, Inc.) (PRP-D). As noted above, two of these vaccines, HbOC and PRP-OMP, have recently been licensed for use with 2-month-olds. The conjugate vaccines differ by protein carrier, polysaccharide size, and method of chemical conjugation, including use of a spacer (a linking moiety) between the PRP and protein carrier (Table 1).[4]

Immunogenicity

Immunogenicity studies of each of the three conjugate vaccines have been performed among 2- to 6-month-old children. Comparisons of these individual evaluations are difficult, however, because assays for antibody to PRP are not standardized and study designs differ. Recent studies among Alaskan Native infants and infants in California, however, suggest that the three conjugate vaccines induce markedly different immunologic responses (Table 2).[5,6] The immunogenicity of HbOC among non-Alaskan Natives was not evaluated in these studies. A separate study in which HbOC was administered to infants and children in New York State and Pennsylvania showed higher immunogenicity than that reported for Alaskan natives; however, the assays were performed in different laboratories. Studies comparing administration of the three vaccines

to 2- to 6-month-old infants in Nashville also demonstrated substantial differences in immunologic responses.[7] The precise level of antibody required for protection, particularly in the presence of immunologic memory stimulated by conjugate vaccines, is not known; however, geometric mean titers of 1 ug/mL are considered to be indicative of long-term protection.[8]

Similar comparative data for the different conjugate vaccines among 7- to 14-month-old children are not available. However, among 432 children who received two doses of HbOC, with the initial dose given at 7-14 months of age, more than 99% achieved serum antibody levels >1 ug/mL (Praxis Biologics, Inc., unpublished data). In a separate study among 94 children who received two doses of PRP-OMP, with the initial dose given at 7-11 months of age, 94% achieved serum antibody levels >1 ug/mL.[9]

Efficacy

Results of efficacy trials among infants are available for the three conjugate vaccines. The first efficacy trial of an Hib conjugate vaccine among infants was completed in Finland using the PRP-D vaccine. In a systematic, unblinded trial involving 60,000 infants (30,000 of whom received the vaccine at 3, 4, and 6 months of age), the point estimate of efficacy was 87% (95% CI = 50%-96%).[10] In a randomized, double-blind, placebo-controlled study of 2,102 Alaskan Natives, however, the point estimate of efficacy was 35% (95% CI = [-57%]-73%).[11] Immunogenicity of the vaccine was limited in both trials. In the Finnish trial, <40% of infants had attained an antibody level of >1 ug/mL 1 month after receiving the third of three doses (geometric mean titer (GMT) = 0.42 ug/mL). In Alaska, infants with a similar vaccination schedule had lower mean titers (GMT = 0.2 ug/mL) 3 months after receiving the third dose. A subsequent immunogenicity study documented antibody responses that were similar to those in the Alaskan and Finnish efficacy trials (Table 2).

The reason for the observed differences in efficacy estimates between Alaskan Native and Finnish infants is unclear. These populations have been observed to have differences in age distribution of Hib disease as

well as differences in other risk factors. For example, in Finland 28% of the reported cases of Hib disease among <5-year-old children occur before the children are 1 year of age; this percentage is 64% for Alaskan Natives and 54% for the United States population.[12]

A recent study of HbOC vaccine was conducted among 60,000 infants who were enrolled in the Northern California Kaiser Permanente Health Plan and who were vaccinated at 2, 4, and 6 months of age. Approximately one-half of these infants received HbOC vaccine. Twelve of the unvaccinated children and none of the children who had received a full series of vaccine (i.e., three doses) subsequently had Hib disease, an efficacy of 100% (lower 95% CI = 68%). Three children who had received one dose of the vaccine and none of the children who had received two doses had Hib disease.[13] Although children were not randomly assigned to vaccine and comparison groups, analysis of the results suggests that the observed efficacy was not due to lack of comparability between the two groups.

A randomized, placebo-controlled, double-blind trial of PRP-OMP vaccine was performed among Navajo infants vaccinated at 2 and 4 months of age. Vaccine efficacy was evaluated for 3,486 infants who completed the primary two-dose regimen. Fourteen cases of invasive Hib disease occurred in the placebo group compared with one case in the vaccine group, an efficacy of 93% (95% CI = 45%-99%) (M. Santosham, personal communication). Among infants who received only one dose of vaccine or placebo, eight cases of Hib disease occurred in the placebo group, compared with none in the vaccine group (p=0.008).

Recommendations for vaccine use

1. On the basis of the above considerations, the ACIP recommends that all children receive one of the conjugate vaccines licensed for infant use (HbOC or PRP-OMP), beginning routinely at 2 months of age (Table 3). Administration of the vaccine series may be initiated as early as age 6 weeks.

2. If HbOC is to be used, previously unvaccinated infants 2-6 months of age should receive three doses given at least 2 months apart. Unvaccinated infants 7-11 months of age should receive two doses of HbOC, given at least 2 months apart, before they are 15 months old (Table 4). Unvaccinated children 12-14 months of age should receive a single dose of vaccine before they are 15 months of age. An additional dose of HbOC should be given to all children at 15 months of age, or as soon as possible thereafter, at an interval not less than 2 months after the previous dose. The other two conjugate vaccines licensed for use at 15 months of age may be used for this dose, but there are no data demonstrating that a booster response will occur. An interval as short as 1 month between doses is acceptable but not optimal.

3. If PRP-OMP is to be used, previously unvaccinated infants 2-6 months of age should receive two doses 2 months apart and a booster dose at 12 months of age. Children 7-11 months of age not previously vaccinated should receive two doses 2 months apart and a booster dose at 15 months of age (or as soon as possible thereafter), not less than 2 months after the previous dose. Children 12-14 months of age not previously vaccinated should receive a single dose and a booster dose at 15 months of age (or as soon as possible thereafter), not less than 2 months after the previous dose. The other two conjugate vaccines licensed for use at 15 months of age may be used for this dose, but there are no data demonstrating that a booster response will occur. An interval as short as 1 month between doses is acceptable but not optimal.

4. Unvaccinated children 15-59 months of age may be given any one of the three conjugate vaccines licensed for this age group.

5. Ideally, the same conjugate vaccine should be used throughout the entire vaccination series (according to the schedule outlined in Table 4). No data exist regarding the interchangeability of different conjugate vaccines with respect to safety, immunogenicity, or efficacy. However, situations will arise in which the vaccine provider does not know which type of Hib conjugate vaccine the

Table 2. Immunogenicity of Three *Haemophilus* b Conjugate Vaccines in Infants

Age (months)/ vaccine dose*	PRP-D		PRP-OMP		HbOC	
	Alaska	California	Alaska	California	Alaska	New York†
2/Pre	0.06 (4%)§	0.04 (3%)	0.16 (14%)	0.09 (6%)	0.15 (6%)	0.20 (12%)
4/Post1	0.04 (2%)	0.03 (0%)	1.37 (57%)	2.15 (73%)	0.07 (0%)	0.30 (15%)
6/Post2	0.06 (11%)	0.14 (25%)	2.71 (79%)	3.76 (92%)	0.59 (43%)	5.11 (84%)
7/Post3	0.55 (43%)	0.46 (37%)	–	–	13.72 (94%)	16.84 (98%)
9-12/ Post-2 or -3	0.20 (20%)	0.13 (22%)	0.53 (29%)	0.98 (52%)	3.70 (81%)	7.41 (94%)
15-18/ Post-2 or -3	0.04 (0%)	–	0.21 (16%)	–	1.94 (71%)	

*PRP-D, HbOC given as three doses at 2, 4, and 6 months; PRP-OMP given at 2 and 4 months. Pre = blood drawn before any vaccine is administered; Post 1 = blood drawn after one dose of vaccine; Post 2 = blood drawn after two doses of vaccine; Post 3 = blood drawn after three doses of vaccine.

†Assays for this study were performed in different laboratories from others in this table. Due to interlaboratory variability, definitive comparisons between this group of vaccines and others in this table cannot be made based on these data.

§Anti-PRP antibody geometric mean titer expressed in micrograms per microliter (%>1 μg/mL).

Table 3. ACIP-recommended *Haemophilus influenzae* type b (Hib) Routine Vaccination Schedule

Vaccine	2 months	4 months	6 months	12 months	15 months
HbOC	dose 1	dose 2	dose 3		booster
PRP-OMP	dose 1	dose 2		booster	

child to be vaccinated had previously received. Under these circumstances, it is prudent for vaccine providers to ensure that at a minimum an infant 2-6 months of age receives a primary series of three doses of conjugate vaccine. These recommendations may change as data become available regarding the response to different conjugate vaccines in a primary series.

6. Children <24 months of age who have had invasive Hib disease should still receive vaccine, since many children of that age fail to develop adequate immunity following natural disease. The vaccine series can be initiated (or continued) at the time of hospital discharge.

7. Chemoprophylaxis of household or day-care classroom contacts of children with Hib disease should be directed at both vaccinated and unvaccinated contacts because immune individuals may asymptomatically carry and transmit the organism. Because of the time required to generate an immunologic response, vaccination following exposure should not be used to prevent secondary cases. However, the ACIP strongly supports extensive use of the Hib vaccine for infants attending day-care facilities; that action should substantially decrease the occurrence of primary cases of Hib disease in day-care facilities. If every child in a household or day-care classroom has been fully vaccinated, chemoprophylaxis is unnecessary.

8. Conjugate vaccine may be given simultaneously with diphtheria and tetanus toxoids and pertussis vaccine adsorbed (DTP); combined measles, mumps, rubella vaccine (MMR); oral poliovirus vaccine (OPV); or inactivated poliovirus vaccine (IPV). Any of the vaccines may be injected in the thigh, and two injections may be given in the same deltoid. All licensed conjugate vaccines should be administered by the intramuscular route. There are no known contraindications to simultaneous administration of any Hib conjugate vaccine with either pneumococcal or meningococcal vaccine.

9. No efficacy data are available on which to base a recommendation concerning use of the vaccine for older children and adults with the chronic conditions associated with an increased risk of Hib disease. Studies suggest, however, good immunogenicity in patients with sickle cell disease,[15] leukemia,[16] patients who have had splenectomies[17] or who have HIV infection,[18,19] and administering vaccine to these patients is not contraindicated.

Side Effects and Adverse Reactions

Reported reactions to the three conjugate vaccines have been mild among both infants and children. In one study, approximately 300 1- to 6-month-old infants who received HbOC vaccine (without simultaneous administration of DTP) were evaluated; within 24 hours of injection, no serious side effects were noted. Following the third dose, 2.2% were noted to have a temperature >38.3 C, 2.2% had localized redness, 1.1% had swelling, and <1% had warmth.[14] Adverse events following the first and second doses were less frequent.

Serious adverse reactions to PRP-OMP also have been rare. Among 4,459 healthy Navajo infants 6-12 weeks of age, no differences were reported in the type and frequency of serious adverse events among those who received PRP-OMP and those who received placebo. Of the infants in the group who were 2-14 months of age, 3%-4.3% had a temperature >38.3 C within 48 hours of receiving a second dose of vaccine, 0.7%-1.2% had erythema of >2.5 cm in diameter, and 0.9%-3.7% had swelling and induration of >2.5 cm in diameter. Adverse events following the first dose were less frequent.

Precautions and Contraindications

Conjugate vaccines that contain either diphtheria toxoid or protein should not be considered as an immunizing agent against diphtheria; no changes in the schedule for administering DTP are recommended. A conjugate vaccine that contains meningococcal protein should not be considered as an immunizing agent against meningococcal disease.

References

1. Broome CV. Epidemiology of *Haemophilus influenzae* type b infections in the United States. Pediatr Infect Dis J 1987;6:779-82.

2. Peltola H, Kayhty H, Sivonen A, Makela PH. *Haemophilus influenzae* type b capsular polysaccharide vaccine in children: a double-blind field study of 100,000 vaccinees 3 months to 5 years of age in Finland. Pediatrics 1977;60:730-7.

3. Ward JI, Broome CV, Harrison LH, Shinefield HR, Black SB. *Haemophilus influ-*

Table 4. Detailed Vaccination Schedule for *Haemophilus* b Conjugate Vaccines

Vaccine	Age at 1st dose (months)	Primary series	Booster
HbOC (Lederle-Praxis)	2-6	3 doses, 2 mo. apart	15 mo.*
	7-11	2 doses, 2 mo. apart	15 mo.*
	12-14	1 dose	15 mo.*
	15-59	1 dose	–
PRP-OMP (Merck Sharp and Dohme)	2-6	2 doses, 2 mo. apart	12 mo.*
	7-11	2 doses, 2 mo. apart	15 mo.*
	12-14	1 dose	15 mo.*
	15-59	1 dose	–
PRP-D (Connaught)	15-59	1 dose	–

*At least 2 months after previous dose.

enzae type b vaccines: lessons for the future. Pediatrics 1988;81:886-93.

4. Wenger JD, Ward JI, Broome CV. Prevention of *Haemophilus influenzae* type b disease: vaccines and passive prophylaxis. In: Remington JS, Swartz MN, eds. Current clinical topics in infectious diseases. Boston: Blackwell Scientific Publications, 1989:306-39.

5. Ward JI, Berkowitz C, Burkart K, Brenneman G, Pescetti J, Marcy M. Comparative immunogenicity of *H. influenzae* type b (Hib) conjugate vaccines (PRP-D/PRP-OMP) in infants months of age. In: Program and Abstracts of the Twenty-Eighth Interscience Conference of Antimicrobial Agents and Chemotherapy, Los Angeles, California, Oct.23-26, 1988.

6. Wainwright RB, Letson GW, Chiu CY, Bulkow LR, Burkart K, Ward JI. Immunogenicity of three *Haemophilus influenzae* type b Hib conjugate vaccines in Alaska USA native infants. In: Joint Meeting of the American Pediatric Society and the Society for Pediatric Research, Anaheim, California, May 7-10, 1990.

7. Decker MD, Edwards KM, Bradley R, Palmer P. Four conjugate *Haemophilus* b vaccines in infants: a comparative trial. In: Program and Abstracts of the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, Georgia, Oct. 21-24, 1990.

8. Peltola H, Kayhty H, Virtanen M, Makela PH. Prevention of *Haemophilus influenzae* type b bacteremic infections with the capsular polysaccharide vaccine. N Engl J Med 1984;310:1561-6.

9. Ahonkhai VI, Lukacs LJ, Jonas LC, et al. *Haemophilus influenzae* type b conjugate vaccine (Meningococcal Protein Conjugate)(PedvaxHIB™): Clinical evaluation. Pediatrics 1990;85(4Pt2):676-81.

10. Eskola J, Peltola H, Takala AK, et al. Efficacy of *Haemophilus influenzae* type b polysaccharide-diphtheria toxoid conjugate vaccine in infancy. N Engl J Med 1987;317:717-22.

11. Ward J, Brenneman G, Letson GW, Heyward WL, Alaska *H. influenzae* Vaccine Study Group. Limited efficacy of a *Haemophilus influenzae* type b conjugate vaccine in Alaska Native infants. N Engl J Med 1990;323:1393-401.

12. Ward JI, Lum MK, Hall DB, Silimperi DR, Bender TR. Invasive *Haemophilus influenzae* type b disease in Alaska: background epidemiology for a vaccine efficacy trial. J Infect Dis 1986;153:17-26.

13. Black SB, Shinefield RA, Hiatt B, Fireman B, Polen M, Lampert D. Efficacy of HbOC conjugate *Haemophilus influenzae* type b vaccine in a study population of 48,000 infants. In: Program and Abstracts of the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, Georgia, Oct. 21-24, 1990.

14. Madore DV, Johnson CL, Phipps DC, et al. Safety and immunologic response to *Haemophilus influenzae* type b Oligosaccharide CRM_{197} conjugate vaccine in 1-to 6-month-old infants. Pediatrics 1990;85:331-7.

15. Frank AL, Labotka RJ, Rao S, et al. *Haemophilus influenzae* type b immunization of children with sickle cell diseases. Pediatrics 1988;82:571-5.

16. Feldman S, Gigliotti F, Shenep JL, Roberson PK, Lott L. Risk of *Haemophilus influenzae* type b disease in children with cancer and response of immunocompromised leukemic children to a conjugate vaccine. J Infect Dis 1990;161:926-31.

17. Jakacki R, Luery N, McVerry P, Lange B. *Haemophilus influenzae* diphtheria protein conjugate immunization after therapy in splenectomized patients with Hodgkin Disease. Ann Intern Med 1990;112:143-4.

18. Steinhoff MC, Auerbach BS, Nelson K, et al. Effect of protein conjugation on immune response of HIV-infected adults to *H. influenzae* type b (Hib) polysaccharide (PS) vaccine. In: Program and Abstracts of the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, Georgia, Oct. 21-24, 1990.

19. Janoff EN, Worel S, Douglas JM, et al. Natural immunity and response to conjugate vaccine for *Haemophilus influenzae* type b in men with HIV. In: Program and Abstracts of the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, Georgia, Oct. 21-24, 1990.

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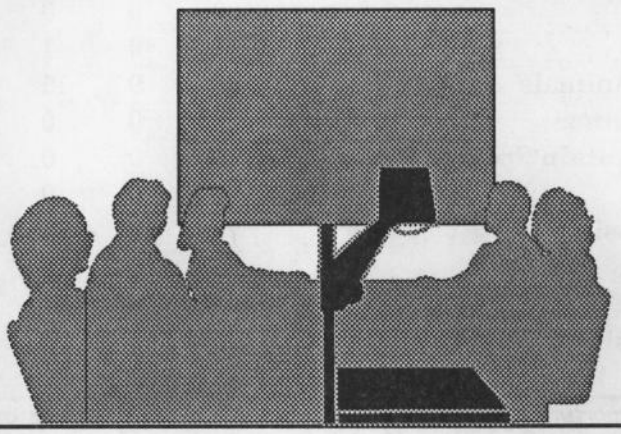

Notice

APIC-Va Educational Conference

The Virginia Chapter of the Association for Practitioners in Infection Control (APIC) is pleased to announce their 17th annual educational conference:

Date: September 25-27, 1991

Place: Best Western Patrick Henry Inn, Williamsburg, Virginia

Theme: "A Revolutionary Experience"

Contact: Mary Ann Robinson, RN, Eastern State Hospital, Drawer A, Williamsburg, Virginia 23187-3701
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Cases of Selected Notifiable Diseases, Virginia, April 1 through April 30, 1991.

Disease	Total Cases Reported This Month						Total Cases Reported to Date in Virginia		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	56	4	11	7	11	23	236	205	121
Campylobacter	40	10	10	8	8	4	114	141	126
Gonorrhea	1192	-	-	-	-	-	5409	6128	5414
Hepatitis A	17	1	10	0	1	5	64	84	86
Hepatitis B	12	1	2	1	6	2	78	78	107
Hepatitis NANB	3	0	1	1	0	1	9	12	18
Influenza	6	1	0	3	2	0	597	759	1991
Kawasaki Syndrome	4	1	1	1	0	1	14	7	7
Legionellosis	1	0	0	0	0	1	4	6	3
Lyme Disease	3	0	1	1	0	1	10	9	3
Measles	6	1	1	0	3	1	20	27	20
Meningitis, Aseptic	16	2	4	2	4	4	66	62	50
Meningitis, Bacterial*	10	1	2	4	1	2	48	59	71
Meningococcal Infections	2	0	1	0	0	1	13	22	29
Mumps	0	0	0	0	0	0	19	29	25
Pertussis	1	0	1	0	0	0	5	8	12
Rabies in Animals	38	9	16	5	5	3	87	60	99
Reye Syndrome	0	0	0	0	0	0	1	0	
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	
Rubella	0	0	0	0	0	0	0	0	
Salmonellosis	79	12	25	12	14	16	287	292	299
Shigellosis	50	5	3	35	7	0	119	51	83
Syphilis ~	109	6	21	16	26	40	376	281	175
Tuberculosis	23	0	9	2	5	7	99	104	119

Localities Reporting Animal Rabies: Albemarle 1 skunk; Appomatox 1 raccoon; Augusta 1 raccoon; Botetourt 2 skunks; Craig 1 Bobcat; Fairfax 5 raccoons; Faquier 2 foxes, 1 skunk; Frederick 1 skunk; Gloucester 2 raccoons; James City 1 raccoon; Loudoun 1 fox, 8 raccoons; Lunenburg 1 raccoon; Madison 1 raccoon; Prince William 1 dog, 1 raccoon; Rockingham 1 skunk; Shenandoah 1 skunk; Surry 1 raccoon; Sussex 2 raccoons, 1 skunk; Washington 1 skunk.

Occupational Illnesses: Asbestosis 6; Carbon Monoxide Exposure 1; Carpal Tunnel Syndrome 69; Coal Workers' Pneumoconiosis 64; Dermatitis 1; Hearing Loss 10; Mesothelioma 1; Propane Gas Exposure 1; Repetitive Motion Disorder 9.

~Total now includes military cases to make the data consistent with reports of the other diseases.
*other than meningococcal

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