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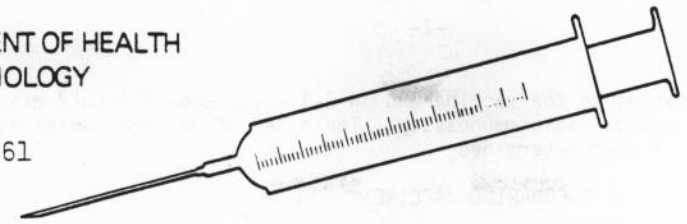

EPIDEMIOLOGY BULLETIN

James B. Kenley, M.D., Commissioner
Grayson B. Miller, Jr., M.D., Epidemiologist

EDITOR: Tom A. Sayvetz, M.D.

Recommendation of the Immunization Practices Advisory Committee (ACIP)

Pneumococcal Polysaccharide Vaccine

INTRODUCTION

Polyvalent polysaccharide vaccine against disease caused by Streptococcus pneumoniae (pneumococcus) was licensed in the United States in 1977. This statement includes a summary of current knowledge about the vaccine and a guide to its use in selected persons and groups.

VACCINE-PREVENTABLE PNEUMOCOCCAL DISEASE

Data on the precise occurrence of serious pneumococcal diseases in the United States are not available. Estimates come from limited surveys, research reports, and several community-based studies (Table 1).

Community studies indicate that pneumococcal pneumonia usually represents less than 25% of all cases of pneumonia. Yet, it remains an important problem, even in the antibiotic era, because of the substantial annual numbers of cases and deaths that occur.

Pneumococcal pneumonia occurs in all groups, although incidence increases with age over 40 years. Pneumococcal meningitis is seen primarily in young children, particularly those ≤2 years old. Mortality from pneumococcal disease is highest in patients who have bacteremia or meningitis, in patients with underlying medical conditions, and in older persons.

Patients with certain chronic conditions are clearly at increased risk of developing pneumococcal infection as well as experiencing more severe pneumococcal illness. These conditions include sickle cell anemia, multiple myeloma, cirrhosis, renal failure, splenic dysfunction, and having had a splenectomy or organ transplant. Other patients may be at greater risk of developing pneumococcal infection or having more severe illness as a result of being alcoholic or having diabetes mellitus, congestive heart failure, chronic pulmonary disease, or conditions associated with immunosuppression. Patients with cerebrospinal fluid leakage complicating skull fracture or neurosurgical procedure can have recurrent pneumococcal meningitis.

Surveillance of the antibiotic susceptibilities of recent S. pneumoniae isolates has not indicated any trend toward increased resistance to penicillin. From 1978 to 1980, less than 2% of clinically significant isolates of S. pneumoniae were relatively penicillin-resistant (MIC* 0.1-0.9 µg/ml). Penicillin remains the antimicrobial agent of choice for treatment of invasive pneumococcal disease.

PNEUMOCOCCAL POLYSACCHARIDE VACCINES

The pneumococcal vaccine licensed in 1977 for use in the United States contains purified capsular material of 14 types of S. pneumoniae (Danish types 1,2,3,4,6A,7F,8,9N,12F,14, 18C,19F,23F, and 25). When the vaccine is being prepared, polysaccharides are extracted separately and combined in a final product. Each dose of vaccine contains 50 µg of each polysaccharide. The 14 bacterial types represented in the vaccine are responsible for 68% of bacteremic pneumocccal disease in the United States (3). An additional 17% of bacteremic pneumococcal disease is due to serotypes immunologically related to types in the vaccine. Studies of the cross-reactivity of human antibodies against related types suggest that cross-protection may occur among some of these types (for example, 6A and 6B) (4).

*Minimal inhibitory concentration.

TABLE 1. Estimated occurrence of serious pneumococcal disease, United States

Pneumococcal disease	Estimated cases (thousands/yr)	Estimated incidence*	Case-fatality ratio (%)
Pneumonia	150-570	68-260	5-7
Meningitis (1)	2.6-6.2	1.2-2.8	32
Bacteremia (2)	16-55	7-25	20

*Per 100,000 population/yr.

Most healthy adults respond to the vaccine and in 2-3 weeks show a 2-fold rise in type-specific antibody, as measured by radioimmunoassay. The titer of antibody which is protective against each serotype has not been determined

EFFECTIVENESS OF PNEUMOCOCCAL POLYSACCHARIDE VACCINES

Several pneumococcal vaccines were developed and tested in the 1920's, 1930's, and 1940's. An unblinded trial of a trivalent vaccine was performed from 1937 to 1943 in an elderly institionalized population (5). Protection was demonstrated against pneumonia and bacteremia due both to pneumococcal types in the vaccine and to ones that were not in the vaccine. A tetravalent polysaccharide vaccine tested in 1944 in a young male military population with a high endemic rate of disease prevented pneumonia caused by types in the vaccine (6). Disease due to other types was not prevented. A combined pneumococcal polysaccharide vaccine was distributed in the United States from 1945 to 1947. However, when effective antibiotics became available, the vaccine was infrequently used, and the manufacturer voluntarily discontinued production.

In the 1970's, a 12-valent pneumococcal vaccine was field tested in South Africa in healthy, young, adult gold-miner recruits among whom there was a high annual incidence of pneumococcal pneumonia-200 cases/1,000 persons/year (7). This vaccine conferred type-specific protection, significantly reducing the frequency of pneumococcal pneumonia and general respiratory morbidity. When 14-valent vaccine was tested in a native population in New Guinea, where there was a large amount of acute and chronic respiratory disease, much of it caused by the pneumococcus, pneumonia morbidity and mortality was significantly reduced (8).

Two randomized, controlled trials of pneumococcal vaccine in older-age adults have been conducted in the United States (9). One was in outpatients over 45 years old and the other was in inpatients of a chronic-care psychiatric facility. In neither study was there any difference in the occurrence of respiratory morbidity and mortality between those vaccinated with a polyvalent pneumococcal vaccine and those given a placebo. In the first study, data suggested some vaccine protection against bacteremic pneumococcal disease, but the incidence of pneumococcal disease was low (less than 2.5/1,000 population/year) and may not have enabled a valid assessment of vaccine efficacy. In the other study, there were no fewer cases of radiologically diagnosed pneumonia among vaccinees than among controls.

The data from these 2 trials were analyzed using a case definition based on seroconversion to a vaccine serotype and radiographic documentation of pneumonia. With this case definition, vaccine efficacy of 80%-100% was calculated. However, because persons who have been vaccinated do not show an increase in antibody titer on revaccination, vaccinees may have been unable to seroconvert to a natural infection, making it difficult to document cases in vaccinees. The vaccine efficacy based on this case definition could therefore be overestimated.

There have been only a few studies of pneumococcal vaccine efficacy in children. The vaccine was generally found to be less antigenic for children <2 years old than for other vaccinees. However, in a small, nonrandomized study of children and young adults 2-25 years old who had sickle cell anemia or had had splencetomy, occurrence of bacteremic pneumococcal disease was found to be significantly reduced by immunization with an 8-valent vaccine (10).

A recent proposed method to evaluate protection with pneumococcal vaccine compares the distribution of serotypes of pneumococci isolated from the blood or cerebrospinal fluid of vaccinated and unvaccinated patients (11). When this method was used to compare 36 vaccinated patients >10 years old-unclassified with respect to underlying medical conditions-with about 10 times that many comparable unvaccinated controls, a vaccine efficacy rate of 49% was found (66%, if only patients with blood isolates were considered.) As more patients become available for evaluation, estimates for specific diagnostic categories can be made, and the broad confidence intervals now associated with the analysis, reduced.

The duration of protection induced by vaccination is unknown. Studies of persistence of elevated antibody titers are ongoing; currently available data show elevation of titers 3-5 years after immunization.

SIDE EFFECTS AND ADVERSE REACTIONS

About half of those given pneumococcal vaccine develop side effects such as erythema and mild pain at the site of injection. Severe adverse effects such as anaphylactoid reactions have been quite rare-about 5/million doses administered.

Severe local and systemic reactions have been common among adults given second doses (12). They are thought to result from localized antigen-antibody reactions involving antibody induced by previous vaccination. Whether prior infection with the S. pneumoniae types represented in the vaccine will result in comparable local reactions after vaccination is unknown. Several studies indicate that pneumococcal vaccine and influenza vaccine can be given at different sites at the same time without an increase in side effects (13), but it should be emphasized that pneumococcal vaccine should be given only once to adults. Data on revaccination of children are not yet sufficient to provide a basis for comment.

VACCINE USAGE

The currently available 14-valent pneumococcal vaccine (as well as the earlier pneumococcal vaccines) has been shown in selected populations to reduce by approximately 80% the incidence of pneumonia with bacteremia caused by S. pneumoniae types represented in the vaccines. In extrapolating this information for recommendations on vaccine use, it is important to recognize that data on effectiveness have come predominantly from studies in groups of adults who were at increased risk of disease but who were not chronically ill. Because age and some chronic illnesses apparently predispose individuals to more severe pneumococcal disease, it would be ideal if recommendations on immunization could be based on definitive clinical trials in groups of elderly patients and patients with chronic illnesses. While data on pneumococcal vaccine effectiveness in chronically ill persons and in others continue to accumulate, they are not yet sufficient for conclusive interpretations. Therefore, the Committee's recommendations that follow are derived from admittedly limited data.

1. On the basis of preliminary evidence, persons >2 years old who have splenic dysfunction or anatomic asplenia should benefit from immunization. Vaccine failures have been reported, perhaps due to impairment of antibody responsiveness, but vaccination is recommended for such patients because they are known to be at high risk of developing fatal bacteremia.

2. Adults and children >2 years old with chronic illnesses which are or appear to be associated with an increased risk of pneumococcal disease or its complications (see above) should be considered candidates for vaccination. Vaccine may be increasingly beneficial as these patients grow older because the elderly are at increased risk of dying from pneumococcal infections. Vaccine efficacy in these groups needs further evaluation and is currently under study.

3. There can be acute outbreaks or a high rate of endemic pneumococcal disease in some populations, such as in nursing homes and other institutions where there is increased risk that the disease will be severe. Under these conditions, vaccination of the entire closed population should be considered.

4. Localized outbreaks of pneumococcal disease caused by types represented in the vaccine can occur in the general population, albeit rarely. In such instances, selective immunization of those at high risk should be considered.

5. There are not yet sufficient data with which to formulate a recommendation on routine use of pneumococcal vaccine in immunization programs for the general population, including the elderly. This should not preclude health-care providers from giving vaccine to unimmunized healthy persons who in their judgment, might benefit.

PRECAUTIONS

The safety of pneumococcal vaccine in pregnant women has not been evaluated. It should not be given during pregnancy unless the risk of infection is substantially increased.

Because of a marked increase in adverse reactions with reinjection of pneumococcal vaccine, second or "booster" doses should not be given, at least at this time.

Complete records on vaccination can help to avoid repeat doses.

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MONTH: October

DISEASE	STATE					REGIONS				
	THIS MONTH	LAST MONTH	TOTAL TO DATE 1981	TOTAL TO DATE 1980	MEAN 5 YEAR TO DATE	THIS MONTH N.W.	N.	S.W.	C.	E.
CHICKENPOX	20	9	1630	376	800.0		3	8	3	6
MEASLES		2	9	338	1391.8					
MUMPS	3	4	125	68	126.8					3
PERTUSSIS	1	1	8	7	12.6		1			
RUBELLA	1	3	6	40	263.4			1		
MENINGITIS – ASEPTIC	56	49	240	161	148.8	8	5	25	12	6
BACTERIAL	18	9	181	147	113.8		7	6	1	4
ENCEPHALITIS – INFECTIOUS	4	3	36	30	24.4	1		1	1	1
POST-INFECTIOUS			3	5	7.2					
HEPATITIS A (INFECTIOUS)	13	23	179	263	253.8	1	3	3	1	5
B (SERUM)	64	53	452	438	301.2	4	20	8	19	13
SALMONELLOSIS	153	153	162	1090	807.0	20	26	14	62	31
SHIGELLOSIS	53	44	1138	119	118.8	5	4	21	23	
TUBERCULOSIS – PULMONARY	50	35	453	448						
EXTRA-PULMONARY	8	7	89	86						
SYPHILIS (PRIMARY & SECONDARY)	75	52	588	476	471.2	1	3	18	41	12
GONORRHEA	2170	1882	18,821	19,026	20,446.4					
ROCKY MOUNTAIN SPOTTED FEVER	4	7	103	91	107.6			2	2	
RABIES IN ANIMALS	22	23	116	21	22.4	12	9	1		
MENINGOCOCCAL INFECTIONS	10	4	87	50	50.6	1	1	1	3	4
INFLUENZA	12	23	4936	782	4594.8	4		4		4
MALARIA	5	4	29	57	25.4		4		1	
OTHER: Hepatitis Unspec.	17	15	157	134	148.2	1	8	1	1	6

COUNTIES REPORTING ANIMAL RABIES: Loudoun-7 rac.; 1 red fox; 1 bat; Fauquier-9 rac., 1 skunk; Shenandoah-1 rac.; Scott-1 skunk; Charlottesville-1 bat.

OCCUPATIONAL ILLNESSES: Occuaptional pneumonconioses-12, Occupational dermatoses-3, Occupational hearing loss-4; Asbestosis-9; Chemical inhalation syndrome-3.

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