Prevention of Community-Acquired Pneumonia:
Influenza and Pneumococcal Vaccines

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Introduction

Influenza and pneumonia are major causes of suffering and death throughout the world. Despite the substantial impact of antimicrobial agents and modern medical care on mortality, pneumonia and influenza were the sixth leading cause of death in the United States at the end of the 20th century and the leading cause of infectious disease deaths (National Center for Health Statistics, 1998). From 1972 through 1992, influenza caused up to 11,800 excess pneumonia and influenza deaths (i.e., number of deaths above the expected baseline number of deaths) and up to 47,200 excess all-cause deaths during each influenza season in the United States alone (Simonsen et al., 1997). Streptococcus pneumoniae (the pneumococcus) is the most common cause of community-acquired pneumonia (Marrie, 1994; Marston et al., 1997). Roughly one in five older adults with pneumococcal bacteremia will die from the infection, and case fatality approaches 40% among persons aged ≥85 years (Plouffe et al., 1996). Moreover, the global emergence of drug-resistant strains of S. pneumoniae emphasizes the need for prevention of pneumococcal infections through immunization. Vaccination against influenza and pneumococcal infection are among only a small number of preventive health interventions for the elderly that have been shown to be cost-saving (Office of Technology Assessment, 1981; Sisk et al., 1997; Nichol et al., 1994,1998). Thus, influenza and pneumococcal vaccination may be the most effective methods for preventing community-acquired pneumonia from both a clinical and economic standpoint.

Vaccines are under investigation to prevent community-acquired lower respiratory tract infection caused by other agents including respiratory syncytial virus (RSV), parainfluenza virus, and Mycobacterium tuberculosis (Murphy et al., 1994; Jacobs et al., 1997; Dudas & Karron, 1998; Breiman et al., 1999). The focus of this chapter is the prevention of community-acquired pneumonia through the use of two currently available vaccines—inactivated influenza virus vaccines and pneumococcal polysaccharide vaccines—with an update on developmental vaccines against influenza and pneumococcal infections. Other chapters in this volume provide reviews of the epidemiology, clinical features, diagnosis, and treatment of influenza and pneumococcal pneumonia.
Influenza Vaccines

Development of Inactivated Vaccines

Early influenza vaccines, based on live viruses grown in mice lung suspension, were tested in the 1930s (Chenoweth et al., 1936). The discovery that influenza viruses could be propagated in large quantities in chicken embryos led to the development and testing of inactivated whole-cell vaccines in the 1940s (Francis et al., 1945). Early preparations often caused systemic and local reactions, due in part to contamination with bacterial endotoxins. The introduction of additional purification steps to remove nonviral contaminants substantially reduced side effects (Couch et al., 1997). Vaccines prepared by disruption of viral components with ethyl ether or detergents (split-virus vaccines) and vaccines composed of partially purified viral surface proteins (surface antigen vaccines) further reduced the incidence of localized and systemic reactions after influenza vaccination.

Trivalent whole-virus, split-virus, and surface antigen inactivated influenza vaccines are currently available in North America. These vaccines generally contain viral hemagglutinin (HA) and neuraminidase (NA) antigens to two strains of influenza A and one strain of influenza B and are standardized to contain 15 μg of each HA per 0.5-mL dose. Formulation of influenza vaccines needs to be reconsidered annually, and one or two vaccine strains are usually replaced each year because of antigenic drift. In this process, minor antigenic changes resulting from mutations in genes encoding for the HA and NA lead to the emergence of antigenic variants. Immunity afforded by vaccination or previous influenza infection is reduced depending on the degree of HA or NA antigenic change among circulating influenza virus strains. Vaccine effectiveness can be markedly reduced when antigens in the vaccine and in circulating influenza strains differ greatly. Episodic major changes in the antigens also occur due to antigenic shift; that is, the appearance in human populations of a new subtype of influenza A virus bearing a novel HA or HA and NA combination. Only influenza A viruses undergo antigenic shift, which can occur by the reassortment of genes between human and animal influenza A viruses. Such reassortment is facilitated by the segmented influenza virus genome. Alternatively, newly reassorted strains may be transmitted to humans directly from animals. Most of the human population will have little or no immunity to the new strains that result from an antigenic shift. A novel influenza virus strain that can infect humans and be transmitted from person to person will have the potential to spread rapidly, resulting in a global pandemic of influenza illness. Vaccine composition is reviewed annually on the basis of intensive global surveillance designed to assess the prevalence of viral subtypes in circulation and to detect the appearance of new strains (Cox et al., 1994).

Effects of Vaccination

Immune Responses

Prevention of influenza infection following vaccination requires production of antibodies to homologous HA in both serum and respiratory secretions (Couch et al., 1997). In addition, antibodies to HA and NA can ameliorate the clinical severity of influenza infection. Vaccine-induced T-cell cytotoxicity may also reduce the severity of illness and play a major role in recovery from infection. Healthy children and young adults develop high levels of antibody to HA after vaccination, but the elderly and persons with certain chronic medical conditions may develop lower postvaccination levels (Centers for Disease Control and Prevention [CDC], 1999; de Bruijn et al., 1999). Peak antibody concentrations occur within 1 to 2 weeks after vaccination (Gross et al., 1997). Antibody response is less brisk and results in lower peak antibody levels among immunologically naive persons, such as young children, who have never previously experienced influenza infection or vaccination (Kilbourne, 1994). Duration of protection appears to be related to antibody concentrations 1 month after vaccination (Clark et al., 1983), but it is assumed that immunity rarely persists for more than 1 year (Kilbourne, 1994).

Clinical Impact

Randomized Trials The elderly, the very young, pregnant women, and persons with certain chronic medical conditions are at greatest risk for