HOSPITAL PHYSICIAN®

INFECTIOUS DISEASES BOARD REVIEW MANUAL

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Influenza Virus Infection

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I. INTRODUCTION

Influenza is an acute, self-limited febrile respiratory illness caused by infection with influenza type A or B virus. Epidemics of influenza occur nearly every winter in temperate climates and are responsible for approximately 20,000 deaths per year in the United States. Influenza viruses can also cause global epidemics of disease, known as *pandemics*, during which rates of morbidity and mortality from influenza-related complications increase markedly. The greatest pandemic occurred in 1918–1919, when 21 million deaths were recorded worldwide, 549,000 of which were in the United States.

Influenza viruses cause disease in all age groups.[1] Rates of infection are highest among children, but rates of serious morbidity and mortality are highest among persons older than 65 years and those with medical conditions, particularly underlying cardiopulmonary disease, that place them at high risk for lower respiratory complications.[2] Influenza viruses A and B account for more than 50% of community-acquired viral pneumonias.[3]

Although management strategies have primarily focused on prevention of influenza, options for antiviral therapy have recently been expanded.

II. EPIDEMIOLOGY

HISTORY

Interpretations of accounts of epidemics support the existence of influenza as a widespread communicable disease back at least to the 12th century, and possibly back to 430 BC. Four pandemics swept the world in the 20th century: the Spanish or swine influenza (H1N1) of 1918, Asian influenza (H2N2) of 1957, Hong Kong influenza (H3N2) of 1968, and the Russian influenza (H1N1) of 1977.

ANTIGENIC VARIATION

The genetics of the influenza virus is a fascinating study of the ways that nature can create new varieties of an organism. Two genes are of major importance in the disease. Each encodes a protein, hemagglutinin (H) or neuraminidase (N), that exists on the surface of the virus. While these molecules each function in the life cycle of the virus, they also serve as the major sites of attachment for protective antibodies that confer immunity.

Antibody specificity studies have led to the convention of naming influenza strains according to variations in the hemagglutinin and neuraminidase molecules by numbering each significant change as it is discovered. There are 13 subtypes of hemagglutinin, but only subtypes H1, H2, and H3 have been identified among the strains that have attacked humans in the 20th century. The rest appear to be specific for other animals as widespread as ducks and whales.[4] Neuraminidase occurs in 9 subtypes, although only subtypes N1 and N2 are normally identified in human infections.

For the most part, each strain of influenza is limited to a specific animal host. It appears that avian strains seldom jump directly to human hosts. However, the pig is capable of being host of both human and avian strains, and likely serves as a mixing bowl for reassortment of the influenza genes between human and nonhuman viruses. China, where influenza can be isolated year round and where swine, birds, and humans often live under the same roof, appears to be the source of influenza outbreaks.[1]

Genetic reassortment allows influenza to periodically sweep the world.[5] During episodes of multiple infection, a new virus that has the characteristics of both infecting strains may be created. This new strain will be antigenically different from any previous strain and may become pandemic in a population with little or no immunity (**Figure 1**). Such a major change, involving acquisition of entirely new gene segments or marked alterations in amino acid sequences of hemagglutinin or neuraminidase, is termed *antigenic shift*.[6] In the nomenclature of influenza, these shifts are designated with changes in the number of the H and/or N code. During the 20th century, such shifts occurred several times. When the Asian influenza appeared in 1957, it was discovered to have undergone a shift in both the hemagglutinin and neuraminidase molecules and was designated as an H2N2 strain as compared to the previously common strain, H1N1.[7]

Minor changes in the antigenic structure of the hemagglutinin and neuraminidase molecules occur continuously. The effects of these minor changes are cumulative and appear to be selected for by increasing