Committee: Infectious Disease

Title: Influenza-Associated Pediatric Mortality

Statement of the Problem:
In 2004, CSTE adopted influenza-associated pediatric mortality reporting with a provision for review in three years. It is critical to maintain national surveillance for pediatric mortality as a core component of national influenza surveillance. An average of approximately 36,000 deaths in the U.S. are attributable to influenza annually. While a majority of these deaths occur among the elderly, reports of pediatric influenza-related deaths were prominent during the 2003-04 season. More complete data are needed to define the burden of severe influenza in children and to develop appropriate strategies for prevention of influenza-associated mortality among them.

Statement of the desired action(s) to be taken:
Influenza-associated pediatric death should be maintained on the national reportable disease list and placed under surveillance through the National Notifiable Diseases Surveillance System (NNDSS).

Goals of Surveillance:
1. Monitor and describe the incidence, distribution, and basic epidemiologic characteristics of deaths among children related to influenza virus infection.
2. Provide data to guide future influenza immunization policy.
3. Rapidly recognize influenza seasons in which the impact of influenza appears to be unusually severe among children.

Methods for Surveillance:
Deaths in children associated with laboratory-confirmed influenza reported by clinicians, laboratories, vital statistics registrars, and medical examiners will be collected by state health departments and reported each week throughout the year to CDC through the National Notifiable Diseases Surveillance System (NNDSS). Core data will be published in the NNDSS MMWR provisional tables and the MMWR Annual Summary of Notifiable Diseases, United States, while additional clinical, epidemiologic, and virologic data will be presented in separate reports. Reporting will occur through the usual NNDSS compliant mechanisms.

Case Definition:
An influenza-associated death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory or rapid diagnostic test. There should be no period of complete recovery between the illness and death. Influenza-associated deaths in all persons aged <18 years should be reported.

A death should not be reported if:
1. There is no laboratory confirmation of influenza virus infection.
2. The influenza illness is followed by full recovery to baseline health status prior to death.
3. The death occurs in a person 18 years or older.
4. After review and consultation there is an alternative agreed upon cause of death.

Laboratory criteria for diagnosis:
Laboratory testing for influenza virus infection may be done on pre- or post-mortem clinical specimens, and include identification of influenza A or B virus infections by a positive result by at least one of the following:
* Influenza virus isolation in tissue cell culture from respiratory specimens
* Reverse-transcriptase polymerase chain reaction (RT-PCR) testing of respiratory specimens
* Immunofluorescent antibody staining (direct or indirect) of respiratory specimens
* Rapid influenza diagnostic testing of respiratory specimens
* Immunohistochemical (IHC) staining for influenza viral antigens in respiratory tract tissue from autopsy specimens
* Four-fold rise in influenza hemagglutination inhibition (HI) antibody titer in paired acute and convalescent sera*

Serologic testing for influenza is available in a limited number of laboratories, and should only be considered as evidence of recent infection if a four-fold rise in influenza (HI) antibody titer is demonstrated in paired sera. Single serum samples are not interpretable.

**Case Classification:**
Confirmed - A death meeting the clinical case definition that is laboratory confirmed.

Laboratory or rapid diagnostic test confirmation is required as part of the case definition; therefore, all reported deaths will be classified as confirmed.

**Period of Surveillance:**
Reporting anticipated to continue throughout the year. States may begin participating as soon as this condition is made notifiable in their state.

**Background and Justification:**
Influenza in children can present with fever, respiratory, and/or gastrointestinal symptoms. Serious complications of influenza in children include pneumonia, respiratory failure, non-respiratory conditions such as shock and encephalopathy, and exacerbations of underlying chronic illness. Death associated with influenza can be directly related to the primary viral infection, or can result from a secondary complication. In certain cases, the progression from onset of illness to death can occur rapidly.

An average of approximately 36,000 deaths in the U.S. are attributable to influenza annually. Deaths in children comprise a small percentage of all influenza-associated deaths, and estimates of pediatric influenza mortality are therefore much less precise than those for adults. Limited studies indicate, however, that young children are at increased risk for hospitalization related to influenza.

During the fall of 2003, there were several widely publicized reports of influenza-associated deaths in children. These accounts generated concern that children were disproportionately affected by influenza during the current season. In December 2003, CDC requested that states voluntarily report influenza-associated deaths in children <18 years of age during the 2003-04 season. During October 11, 2003 - March 22, 2004, CDC received a total of 142 reports of pediatric fatalities associated with laboratory-confirmed influenza. Whether this represented an increase over baseline was unclear, since comparative data did not exist. In addition, a heightened awareness of severe complications and deaths associated with influenza and the increased availability of testing may have contributed to the identification of more influenza-associated fatalities.

Further, of these reported deaths, a significant number were 2 years of age or older and had no medical conditions recognized as high risk for influenza-related complications. Thus, these children were not among any groups currently targeted for influenza vaccination. Additional information is needed to further characterize those children at increased risk of influenza-related complications and deaths and to reassess current vaccination recommendations based on such information. This information could influence influenza vaccine policy by identifying specific pediatric groups at high risk for influenza-associated death or by providing data to support the expansion of pediatric age groups for targeted influenza vaccination.
Surveillance of influenza-associated pediatric deaths will serve to complement the current national influenza surveillance strategies. By including this element in the national reporting system, basic population-based epidemiologic characteristics, such as incidence, age and geographic distribution can be determined.

The collection of selected clinical information could potentially describe uncommon or previously unrecognized presentations, possible risk factors, and the impact of influenza vaccination. Linkage of mortality data with virologic and other laboratory data may provide information on strain virulence and abnormal host responses, and may guide vaccine strain selection.

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