Explaining Unexplained Infectious Deaths, Minnesota 2003-2007

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Background
In 1995, the Minnesota Department of Health (MDH) began participating in the CDC’s Emerging Infections Program (EIP) Unexplained Critical Illness and Death Project (UNEX). Since 2003, increased molecular and immunohistochemical (IHC) testing has enhanced diagnostic capacity.

Methods
A case was defined as a previously healthy person aged 6 months to 49 years with an illness suggestive of an infectious disease resulting in death, and no cause identified on clinical or routine post-mortem testing from 2003-2007. Cases were identified through infection control practitioners, physicians, medical examiners, and death certificates. Testing at MDH and CDC included microscopic pathology, culture, targeted PCR, 16S PCR, and IHC. Cases were classified as explained per UNEX protocol.

Results
Of 170 persons identified, 74 (44%) met the case definition. Syndromes included 26 respiratory, 15 cardiac, 9 neurologic, 6 gastrointestinal, 6 sudden death, 2 hepatic, and 1 other. Median age was 28 years; 49% were female. 56 (76%) had one or more specimens available for testing. 20 of 56 (36%) had an etiologic agent identified. Etiologic agents were more likely to be identified in patients < 5 years of age vs. > 5 years of age (88% vs. 21% p<.01). The proportion of cases explained by syndrome was similar. Pathogens explaining the death included Influenza and enterovirus in 3 each, S. aureus, adenovirus, pneumococcus and Fusobacterium sp in 2 each, and parainfluenza, N. meningitides, Legionella, echovirus, C. perfringens, and rotavirus in one each. Explained deaths increased from 10% in 2003 to 60% in 2007.

Conclusions
Enhanced laboratory capacity provided diagnoses in 36% of cases for which specimens were available. Many pathogens identified were of public health importance including 7 cases of vaccine preventable diseases. Enhanced surveillance and diagnostic capacity, as applied in the UNEX Project, is an increasingly powerful tool to explain causes of death not identified through routine testing.