Enterovirus D68 and disease severity: more questions than answers

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The 2014 outbreak of enterovirus D68 associated with respiratory illness occurred in 2014. Possible risk factors for severe disease include history of atopy or asthma. Whether EV-D68 is truly more severe than other respiratory viruses remains to be determined. Enteroviruses can cause a range of symptoms, but association with neurologic complications is unproven.
have a family history of allergy, and a trend toward increased personal atopy that did not reach statistical significance was seen. Schuster and colleagues did document statistically significant increased odds of asthma or recurrent wheeze in patients admitted to intensive care with EV-D68. Therefore, although it is important to consider that history would have been dependent on parental self-report and provider documentation, it seems reasonable to hypothesize that EV-D68 may be a more virulent pathogen in patients with pre-existing atopic disease when compared with rhinoviruses and other enteroviruses.

Why were infants, children and teenagers predominantly affected in the EV-D68 outbreak? The likely explanation is that people in these age groups do not yet have immunity from previous exposure to these viruses. Illness is therefore more likely to develop after exposure in these patients than in their adult counterparts. With respect to the association between EV-D68 and asthma or atopy, questions arise relating to the immunologic basis of this association. In this regard, a possible explanation might lie in the relative balance of T helper cell (T₃) 1 to T₃2 in the patient, with the T₃2 profile more likely to be associated with asthma and atopy. A T₃2 profile is associated with less cell-mediated immune control and, theoretically, an increased susceptibility to infections in which cell-mediated immunity plays a role in controlling, notwithstanding the pivotal role that humoral immunity has in the defense against enteroviral infections.

Whether there are viral genetic factors that contributed to the 2014 outbreak is a question worthy of further study. Although EV-D68 is a member of the enterovirus D species, it has phenotypic characteristics that are more consistent with rhinoviruses. Whether the strains that were associated with the 2014 outbreak are characterized by special virulence factors that contribute to illness severity remains to be addressed.

Although beyond the scope of the accompanying article, the potential role of EV-D68 in neurologic complications deserves specific mention. Enteroviruses are known to be associated with neurologic manifestations including meningitis, encephalitis and acute flaccid paralysis. Shortly after EV-D68 was noted to be causing respiratory illness, an apparent increase in cases of acute flaccid paralysis was seen, which subsequently declined with the decrease in EV-D68 respiratory disease. This temporal relationship raised the question as to whether EV-D68 could be responsible for the cases of acute flaccid paralysis. The virus was found in respiratory specimens from some, but not all, children with acute flaccid paralysis. Thus, the role of EV-D68 in acute flaccid paralysis associated with the 2014 outbreak is yet to be determined. Indeed, some evidence suggests that enteroviruses other than EV-D68 may have contributed to the acute flaccid paralysis.

Further studies are needed to define whether EV-D68 is truly a more severe pathogen than other enteroviruses and rhinoviruses for all patients, or whether there are certain populations at increased risk of severe disease. Such research should also address whether there are factors that are related to viral or patient genetic variation that might be associated with disease severity.

References