Information for staff on Enterovirus D68 (EV-D68)

The purpose of this information is to provide an aide-memoire for clinical staff and Infection Prevention and Control Teams (IPCT) who may be involved in the outbreak prevention and management of Enterovirus D68.

All staff should be familiar with Standard Infection Control Precautions (SICPs) and Transmission Based Precautions (TBPs).

The following advice is supplementary and provides details of specific actions necessary to detect, prevent and manage Enterovirus D68 outbreaks.

Background

Enterovirus D68 (EV-D68) is a non-polio enterovirus. The virus was first identified in 1962; however, until recently the number of identified cases has been low. A large upsurge in cases occurred in the USA and Canada in 2014;[1] since 2014 outbreaks have been reported in North and South America, Europe, Asia and Australia and EV-D68 surveillance studies have found the virus in circulation on most continents.[2-4] EV-D68 has been found previously in Scotland[2] and in 2016 five cases of acute flaccid myelitis (AFM) in children were associated with the virus. There is no vaccine or specific (antiviral) treatment for EV-D68.[1]

What are the symptoms of Enterovirus D68?

EV-D68 can cause mild to severe respiratory illness, infection may also be asymptomatic.[1] Symptoms may include sore throat, rhinorrhea, sneezing, cough and body/muscle aches;[1;5-9] the most commonly reported symptoms associated with severe illness are cough, wheezing and breathing difficulties,[4;5;10-21] fever may be present but this is not a consistent symptom in the literature. In addition, EV-D68 has been associated with neurological symptoms such as aseptic meningitis, acute flaccid myelitis (AFM), and potentially Guillain-Barré syndrome (GBS) in adults.[2;7;11;22-31] Although rare, EV-D68 associated deaths have been reported.[2]

Who is most at risk from Enterovirus D68?

EV-D68 mainly affects children, teenagers and immunocompromised adults.[1-3;8;22;32] Although EV-D68 does also infect healthy adults, they are more likely to have mild or asymptomatic infections.[1;3] Children with a history of asthma or wheezing appear to be particularly at risk of severe respiratory illness caused by EV-D68,[4;10;14-17;20;33] however, EV-D68 may also cause wheezing in previously healthy children.[1] A higher male to female ratio has been reported but this is inconsistent, possibly due to the small number of cases in most studies.[6;7;11;13;17;20;21;27;29;34]

When are Enterovirus D68 outbreaks most likely?

EV-D68 infections (and therefore outbreaks) can happen at any time of year; however, infections are more common in summer and autumn.[1] In the literature there is a clear seasonal trend with infection rates peaking occurring between September and October.[2]

How is Enterovirus D68 transmitted?

EV-D68 is spread via infectious respiratory secretions, such as saliva, nasal mucus and sputum.[1;35] Virus has also been detected in both cerebrospinal fluid[36] (CSF) and faeces[7] of infected patients but this is not consistent among cases.

Are there any specific infection control precautions for Enterovirus D68?

If EV-D68 is suspected or confirmed, contact and droplet precautions should be implemented in addition to SICPs.[37] If performing aerosol generating procedures (AGPs), HCWs must use airborne precautions including the wearing of facial and respiratory PPE.[37] EV-D68 has been found in the CSF of some infected patients with AFM; although there is no evidence of transmission by this route if lumbar puncture is required HCWs must wear appropriate PPE as per SICPs (i.e. disposable gown, gloves, surgical mask and eye protection).[37]

Suspected or confirmed cases should be placed in a single room en-suite with a clinical wash hand basin.[16;37] If multiple patient cases of the same infection are confirmed or if single rooms are unavailable, cohorting of patients may be appropriate.[37] The restriction of visitors should be considered, particularly children[16] or immunocompromised adults.

EV-D68 is a non-enveloped virus and is therefore less susceptible to disinfectants and antimicrobial agents including alcohol-based hand rub.[38] Hand hygiene should be performed according to the '5 moments' using non-antimicrobial liquid soap and water, unless performing a clean/aseptic procedure (moment 2) in which case antimicrobial liquid soap or ABHR must be used.[37] A chlorine releasing agent at 1000 ppm available chlorine should be used for all routine cleaning of the patient's environment and during terminal cleaning.[37]

Duration of isolation

There is limited evidence available on duration of isolation, EV-D68 persistence up to 22 days has been noted in immunocompromised patients in one study[11] and was a feature of the five recent cases of AFM in Scotland. Patient(s) should remain in isolation/cohort whilst they remain symptomatic and/or are considered infectious and the door must remain closed. Before discontinuing isolation; individual patient risk factors should be considered and the clinical judgement of those involved in the patient's management should be sought.[37]

When should clinicians suspect Enterovirus D68 cases or outbreaks?

It is assumed that as an increase in cases presenting with AFM has been seen in East Scotland it is possible that enterovirus D68 is circulating more widely nationally. In cases of severe respiratory disease or in cases which present with muscle weakness or symptoms suggestive of AFM or GBS take a respiratory sample for respiratory pathogen PCR which includes rhino-/-enterovirus molecular detection. If this is detected initially, EV-D68 should be considered as a potential cause of the disease

Respiratory specimens offer the best prospect of detection of with nasopharyngeal or lower respiratory specimens preferred to throat swabs.[7] Stool/rectal swab or CSF samples can also be submitted as well particularly as they may be important for differential diagnosis. Local enterovirus/ rhinovirus PCR positive specimens can be further tested for typing (Edinburgh) or PCR testing for EV-D68 alone (Edinburgh or Glasgow).

It also recommended that hospitals should be alert to the possibility of nosocomial infections, particularly in immunocompromised patients.[35]

References

(1) Centres for Disease Prevention and Control. Enterovirus D68. 2016 http://www.cdc.gov/non-polio-enterovirus/hcp/ev-d68-hcp.html

(2) Poelman R, Schuffenecker I, Van Leer-Buter C, Josset L, Niesters HG, Lina B, et al. European surveillance for enterovirus D68 during the emerging North-American outbreak in 2014. Journal of Clinical Virology 2015 Oct;71:1-9.

(3) Holm-Hansen CC, Midgley SE, Fischer TK. Global emergence of enterovirus D68: A systematic review. The Lancet Infectious Diseases 2016;16(5):01.

(4) Vazquez-Perez JA, Ramirez-Gonzalez JE, Moreno-Valencia Y, Hernandez-Hernandez VA, Romero-Espinoza JAI, Castillejos-Lopez M, et al. EV-D68 infection in children with asthma exacerbation and pneumonia in Mexico City during 2014 autumn. Influenza and other Respiratory Viruses 2016;10(3):01.

(5) Machin N, Whitfield T, Mutton K, Hesketh L, Guiver M, Turner A. A prospective study of enterovirus D68 in a regional UK center. Future Virology11(8):August.

(6) Reiche J, Bottcher S, Diedrich S, Buchholz U, Buda S, Haas W, et al. Low-level circulation of enterovirus D68-associated acute respiratory infections, Germany, 2014. Emerging Infectious Diseases 2015;21(5):2015.

(7) Williams CJ, Thomas RH, Pickersgill TP, Lyons M, Lowe G, Stiff RE, et al. Cluster of atypical adult Guillain-Barre syndrome temporally associated with neurological illness due to EV-D68 in children, South Wales, United Kingdom, October 2015 to January 2016. Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin21(4):2016.

(8) Waghmare A, Pergam SA, Jerome KR, Englund JA, Boeckh M, Kuypers J. Clinical disease due to enterovirus D68 in adult hematologic malignancy patients and hematopoietic cell transplant recipients. Blood 2015;125(11):12.

(9) Meijer A, Benschop KS, Donker GA, van der Avoort HG. Continued seasonal circulation of enterovirus D68 in the Netherlands, 2011-2014. Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2014;19(42):2014.

(10) Midgley CM, Jackson MA, Selvarangan R, Turabelidze G, Obringer E, Johnson D, et al. Severe respiratory illness associated with enterovirus D68 - Missouri and Illinois, 2014. MMWR Morbidity and mortality weekly report 2014;63(36):12.

(11) Levy A, Roberts J, Lang J, Tempone S, Kesson A, Dofai A, et al. Enterovirus D68 disease and molecular epidemiology in Australia. Journal of Clinical Virology 2015;69(pp 117-121):01.

(12) Calvo C, Cuevas MT, Pozo F, Garcia-Garcia ML, Molinero M, Calderon A, et al. Respiratory infections by enterovirus D68 in outpatients and inpatients Spanish children. Pediatric Infectious Disease Journal 2016;35(1):01.

(13) Peci A, Winter AL, Warshawsky B, Booth TF, Eshaghi A, Li A, et al. Epidemiology of Enterovirus D68 in Ontario. PLoS ONE [Electronic Resource] 2015;10(11):e0142841.

(14) Xiao Q, Ren L, Zheng S, Wang L, Xie X, Deng Y, et al. Prevalence and molecular characterizations of enterovirus D68 among children with acute respiratory infection in China between 2012 and 2014. Scientific Reports 2015;5:16639.

(15) Martin G, Li R, Cook VE, Carwana M, Tilley P, Sauve L, et al. Respiratory Presentation of Pediatric Patients in the 2014 Enterovirus D68 Outbreak. Canadian Respiratory Journal 2016;2016(no pagination):8302179.

(16) Schuster JE, Newland JG. Management of the 2014 Enterovirus 68 Outbreak at a Pediatric Tertiary Care Center. Clinical Therapeutics 2015;37(11):01.

(17) Schuster JE, Miller JO, Selvarangan R, Weddle G, Thompson MT, Hassan F, et al. Severe enterovirus 68 respiratory illness in children requiring intensive care management. Journal of Clinical Virology 2015;70(pp 77-82):01.

(18) Drews SJ, Simmonds K, Usman HR, Yee K, Fathima S, Tipples G, et al. Characterization of enterovirus activity, including that of enterovirus D68, in pediatric patients in Alberta, Canada, in 2014. Journal of Clinical Microbiology 2015;53(3):01.

(19) Poelman R, Scholvinck EH, Borger R, Niesters HGM, Van Leer-Buter C. The emergence of enterovirus D68 in a Dutch University Medical Center and the necessity for routinely screening for respiratory viruses. Journal of Clinical Virology 2015;62(pp 1-5):01.

(20) Moyer K, Wang H, Salamon D, Leber A, Mejias A. Enterovirus D68 in hospitalized children: Sequence variation, viral loads and clinical outcomes. PLoS ONE11(11):e0167111.

(21) Lam H-Y, Wong ATC, Tsao Y-C, Tang BSF. Prevalence and phylogenetic characterization of human enterovirus D68 among children with respiratory infection in Hong Kong. Diagnostic Microbiology and Infectious Disease85(2):01.

(22) Wali RK, Lee AH, Kam JC, Jonsson J, Thatcher A, Poretz D, et al. Acute neurological illness in a kidney transplant recipient following infection with enterovirus-D68: An emerging infection? American Journal of Transplantation 2015;15(12):December.

(23) Esposito S, Lunghi G, Zampiero A, Tagliabue C, Orlandi A, Torresani E, et al. Enterovirus-D68 in the Cerebrospinal Fluid of Two Children with Aseptic Meningitis. Pediatric Infectious Disease Journal 2016;35(5):01.

(24) Schuffenecker I, Mirand A, Josset L, Henquell C, Hecquet D, Pilorge L, et al. Epidemiological and clinical characteristics of patients infected with enterovirus D68, France, July to December 2014. Eurosurveillance 2016;21(19):12.

(25) Pfeiffer HC, Bragstad K, Skram MK, Dahl H, Knudsen PK, Chawla MS, et al. Two cases of acute severe flaccid myelitis associated with enterovirus D68 infection in children, Norway, autumn 2014. Eurosurveillance 2015;20(10):21062.

(26) Messacar K, Schreiner TL, Van HK, Yang M, Glaser CA, Tyler KL, et al. Acute flaccid myelitis: A clinical review of US cases 2012-2015. Annals of Neurology 2016;80(3):01.

(27) Skowronski DM, Chambers C, Sabaiduc S, Murti M, Gustafson R, Pollock S, et al. Systematic community- and hospital-based surveillance for enterovirus-D68 in three Canadian provinces, August to December 2014. Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2015;20(43):2015.

(28) Lang M, Mirand A, Savy N, Henquell C, Maridet S, Perignon R, et al. Acute flaccid paralysis following enterovirus D68 associated pneumonia, France, 2014. Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2014;19(44):2014.

(29) Aliabadi N, Messacar K, Pastula DM, Robinson CC, Leshem E, Sejvar JJ, et al. Enterovirus D68 infection in children with acute flaccid Myelitis, Colorado, USA, 2014. Emerging Infectious Diseases 2016;22(8):August.

(30) Crone M, Tellier R, Wei X-C, Kuhn S, Vanderkooi OG, Kim J, et al. Polio-Like Illness Associated with Outbreak of Upper Respiratory Tract Infection in Children. Journal of Child Neurology 2016;31(4):01.

(31) Greninger AL, Naccache SN, Messacar K, Clayton A, Yu G, Somasekar S, et al. A novel outbreak enterovirus D68 strain associated with acute flaccid myelitis cases in the USA (2012-14): A retrospective cohort study. The Lancet Infectious Diseases 2015;15(6):01.

(32) Marjolein Knoes, Elisabeth H.Schölvinck, Randy Poelman, Sylvia Smit, Clementien L.Vermont, Hubert G.M.Niesters, and Coretta C.Van Leer-Buter. Upsurge of Enterovirus D68, the Netherlands, 2016. Ahead of print release. 2016 http://wwwnc.cdc.gov/eid/article/23/1/16-1313_article

(33) Bragstad K, Jakobsen K, Rojahn AE, Skram MK, Vainio K, Holberg-Petersen M, et al. High frequency of enterovirus D68 in children hospitalised with respiratory illness in Norway, autumn 2014. Influenza and other Respiratory Viruses 2015;9(2):01.

(34) Bottcher S, Prifert C, Weissbrich B, Adams O, Aldabbagh S, Eis-Hubinger AM, et al. Detection of enterovirus D68 in patients hospitalised in three tertiary university hospitals in Germany, 2013 to 2014. Eurosurveillance 2016;21(19):12.

(35) European Centre for Disease Prevention and Control. Rapid risk assessment. Enterovirus 68 detected in the USA, Canada and Europe. Second update. 25-11-2014.

(36) Messacar K, Schreiner TL, Van HK, Yang M, Glaser CA, Tyler KL, et al. Acute flaccid myelitis: A clinical review of US cases 2012-2015. Annals of Neurology80(3):01.

(37) Health Protection Scotland. National Infection Prevention and Control Manual. 2016 http://www.nipcm.hps.scot.nhs.uk/

(38) Centres for Disease Prevention and Control. Enterovirus D86 for Healthcare Professionals. 2016 http://www.cdc.gov/non-polio-enterovirus/hcp/ev-d68-hcp.html