



## RAPID RISK ASSESSMENT

# Meningitis outbreak, Suceava county, Romania

June 2012

22 June 2012

## Main conclusions and recommendations

There is no indication that similar outbreaks of aseptic meningitis are occurring in countries neighbouring Romania. However, as enteroviruses (EV) outbreaks are common during the summer months it is possible that such outbreaks will occur in neighbouring countries, independently from the current outbreak in Romania.

- Public health authorities throughout European Union (EU) Member States and neighbouring countries should consider maintaining surveillance for aseptic meningitis in the coming summer and autumn months for this reason.
- Sanitation and personal hygiene are the most important and effective preventive measures.
- For bordering countries, follow up actions may include:
  - increasing and enhancing surveillance for aseptic meningitis
  - increasing awareness among clinicians for the summer and autumn months and the detection of EV infections, including the need to take samples (stool and cerebrospinal-fluid) in order to exclude polioviruses and other strains of EV that might lead to more severe clinical disease
  - communication campaigns to the general public to enforce personal hygiene measures.
- Public health control measures have been implemented by Romania to limit the spread and monitor the development of the outbreak. Information on the current situation was shared with other European Union Member States and public health international organisations in the European region through the appropriate channels.

## Source and date of request

Directorate-General for Health and Consumers – 20 June 2012

1. What are the potential risk factors for further spread of the outbreak?
2. What are the potential implications for bordering countries (including non EU countries)?
3. What possible options exist for outbreak control?

## Public health issue

Outbreak of aseptic meningitis in Suceava city, Romania, suspected to be due to non-polio type enterovirus.

## Consulted experts

National Centre for Surveillance and Control Communicable Disease (Romania): Adriana Pistol, Anca Sirbu, Florin Popovici.

## Disease background information

Enteroviruses (EV) are RNA viruses belonging to the Picornaviridae family and are classified in five human pathogenic species including polioviruses (type 1–3) and human enteroviruses A, B, C and D. More than 100 serotypes are described. Vaccination against polioviruses was implemented in the 1950's and the European region is declared polio-free by the World Health Organization (WHO). Other enteroviruses continue to circulate throughout the world.

Over 75% of individuals infected with enteroviruses will have an asymptomatic infection or have non-specific symptoms, such as fever. However, enteroviruses may cause a wide spectrum of symptoms including mild upper respiratory illness, rash, blisters, fever, aseptic meningitis, encephalitis, acute flaccid paralysis and neonatal sepsis-like disease [1–3]. Enteroviruses are today the most common cause of viral meningitis in both paediatric and adult populations. This disease is characterised by sudden onset fever with signs and symptoms of meningeal involvement, such as nausea, vomiting, photophobia, neck stiffness and altered mental status. Symptoms commonly resolve within a month and complications are rarely observed, but may include headache, difficulties to concentrate, reduced stress tolerance and fatigue. Enteroviruses meningitis may affect all age groups. No antiviral treatment or vaccine is available.

Enteroviruses infections appear more commonly during summer and autumn months in temperate climates but may occur and may be identified all year round. Faecal-oral transmission and spread by contact with respiratory or blister secretions (person-to-person, fomites, and possibly particle aerosol) are considered the most important modes of transmission [1]. Faecal contamination of recreational or drinking water may occur. Transmission within households has been well studied and young susceptible children often spread the disease to older family members.

Enteroviruses infections are not notifiable in the EU except as part of syndromic surveillance available in many countries for viral meningoencephalitis.

Enteroviruses meningitis is confirmed by either virus isolation or polymerase chain reaction (PCR) using cerebrospinal fluid (CSF). Serological confirmation and a four-fold rise in the level of antibodies between acute and convalescent sera is a diagnostic complement should no virus be identified in CSF [3–4]. Diagnostic testing for non-polio enteroviruses is commonly performed in laboratories also able to diagnose/exclude polioviruses. Patients with EV meningitis are commonly asked to supply faecal sample for further typing of the enterovirus, with the major goal to exclude poliovirus.

Enteroviruses are:

- relatively resistant to many common laboratory disinfectants, including 70% ethanol, isopropanol, dilute Lysol, and quaternary ammonium compounds
- relatively thermostable (most are inactivated at 42C, but some need higher temperatures)
- sensitive to ultraviolet inactivation [5].

Preventive measures include general precautionary hygienic measures such as frequent hand washing and providing clean recreational and drinking water [6]. The cleaning of contaminated surfaces and soiled articles first with soap and water, and then disinfecting them with a dilute solution of chlorine-containing bleach can be a very effective way to inactivate the virus, especially in institutional settings such as child care centres [7]. However, since most EV infected individuals are asymptomatic, it is difficult to prevent further spread of the virus.

Recent large scale outbreaks of viral meningitis in Romania and the European region have been reported:

- An outbreak was reported in the southern part of Romania in 2007 with 1 098 cases reported, presenting with meningitis and other clinical forms. It affected mainly children and occurred in the summer period [6].

- An outbreak of viral meningitis with 5 000 non-fatal cases occurred between July and September 1999 [8]:
  - The aetiological agents identified in this outbreak belonged to three different echovirus serotypes: 4, 7 and 30.
  - A case-control study was initiated at the time in four of the affected counties to identify risk factors for illness:
    - Factors associated with illness were contact with a body of water (i.e. swimming, bathing, and working), contact with a confirmed case of viral meningitis, contact with a person displaying meningeal signs or symptoms, male sex, and lack of organised household garbage disposal.
    - No association was found between illness and other possible risk factors such as household size, source of drinking water or type of toilet facilities. In response to this outbreak, the Ministry of Health initiated control measures that included a vigorous, nationwide education campaign that emphasised preventive measures. These measures included short-term closing of schools in the most affected counties, improved hygiene practices, and avoiding public swimming areas.
- Recent large scale outbreaks of relevance for this rapid risk assessment in the EU region have been reported from Latvia (2006 and 2010), Serbia (2010), Greece (2007), Spain (2007) and France (2005) [9–17].

## Event background information

**Surveillance of aseptic meningitis in Romania:** In Romania, surveillance of aseptic meningitis is based on mandatory clinical (syndromic approach) and laboratory investigation. Suceava county is known to have non-polio enteroviruses circulation during the summer periods. The most recent outbreak occurred in 1999.

**Geographical origin of cases:** Suceava district, Romania (northern Romania).

**Latest update:** 21 June 2012.

**Source:** Early warning response system and personal communication, A. Pistol, A. Sirbu, Fl. Popovici from the National Centre for Surveillance and Control Communicable Disease, Romania.

Between 28 May and 21 June, 62 cases have been reported in Suceava city (n=47) and district (n=15). Fifty-three cases presented with aseptic meningitis and nine with other clinical forms (gastrointestinal disorders, angina). No complications were reported.

Of the 48 cases with aseptic meningitis for which detailed information is available, the epidemiological and microbiological information is as follows:

1. Eighteen cases are related to an outbreak in a Kindergarten in Suceava city:
  - onset of disease was between 28 May and 11 June 2012
  - the median age is 5.2
  - the clinical presentation of disease has been mild
  - laboratory results indicate at this moment as aetiology a non-polio enterovirus (final results still pending)
2. Thirteen cases are secondary family and neighbourhood contacts to primary cases of the Kindergarten:
  - identified through enhanced epidemiological and clinical surveillance activities in Suceava city;
  - the median age is 6.8 years;
  - none of the adult family contacts of the 18 primary and 13 secondary have travelled abroad during the maximum one month incubation period.
3. Since 11 June 2012, eight cases in Suceava city and nine in Suceava district are considered sporadic:
  - the mean age of these cases is 8.3 years;

Eight cases have been reported in the bordering county of Botosani, seven in the town of Botosani and one in the county of Botosani. No severe case has been reported and the mean age of the affected is ten years. This is in line with the expected number of cases and close monitoring of the epidemiological situation is ongoing. Available information to date does not indicate a link between the outbreak in Suceava and cases reported in Botosani. Ongoing virological and epidemiological information may clarify the link between the two separate events.

Current control measures implemented by the local health authorities include:

- enhancement of clinical and epidemiological surveillance in communities, schools and kindergarten since onset of the initial outbreak;
- closure for seven days of the schools and kindergartens where cases were registered, for cleaning and disinfection with pupils being on summer leave from 22 June 2012
- renewed recommendations for the general population to follow personal hygiene recommendations (especially hand hygiene) and to avoid swimming in microbiologically uncontrolled waters

# ECDC threat assessment for the EU

## 1. What are the potential risk factors for further spread of the outbreak?

Outbreaks of non-polio EV are more common during summer and autumn. The timing and occurrence of the event in Suceava city in the kindergarten is therefore neither unexpected nor unusual. As the majority of non-polio EV infections are asymptomatic, reported cases of infection might only represent a small proportion of infected persons in a community and outbreaks may therefore be unnoticed. The main risk factors for further spread of this outbreak from Suceava city will be dependent on ensuring high standards of personal hygiene among cases and their close contacts and in the general population. Enteroviruses are easily transmitted through person-to-person contact (faecal-oral and respiratory routes) and transmission through water with faecal contamination has also been suggested [1]. Patients who have recovered clinically from EV infection may continue to excrete the virus for up to several weeks in their stool [1].

For this reason, high standards of personal hygiene should be maintained in all close contacts of identified cases even after symptoms have subsided. The current outbreak suggests that the highest proportion of affected persons is among young children. However, all age groups are susceptible for infection and therefore, new cases in other age groups cannot be excluded in the near future. Some strains of EV may be more neurotropic or prone to cardiac complications. Even though the strain/strains of EV in this outbreak are currently not characterised, the clinical presentation of illness is mild or medium which suggests that more pathogenic strains of EV are presently not circulating.

## 2. What are the potential implications for bordering countries (including non EU countries)?

At present, the outbreak is limited to primary and secondary cases in Suceava city linked to a kindergarten. Epidemiological links for additional cases in Suceava city and county and neighbouring Botasani county have not yet been established, nor have microbiological investigations indicated that they are due to the same EV. However, an increase in the number of cases and a shift of infection from younger to older age groups cannot be excluded in the future. Such a shift in age group would potentially increase the risk for further spread beyond Suceava (as adults are more likely to travel). In addition, the closure of schools, the start of summer holidays and expected travelling of individuals may present opportunity for wider spread of the infection.

There is no indication that similar outbreaks of aseptic meningitis are occurring in countries neighbouring Romania. However, as EV outbreaks are common during the summer months it is possible that such outbreaks will occur in neighbouring countries, independently from the current outbreak in Romania. Public health authorities throughout European Union (EU) and neighbouring countries should consider maintaining surveillance for aseptic meningitis in the coming summer and autumn months.

## 3. What possible options exist for outbreak control?

Sanitation and personal hygiene are the most important and effective preventive measures. These measures include hand washing, especially after going to the toilet or changing babies' nappies. Contaminated surfaces and soiled clothing should be disinfected. Romanian public health authorities have implemented kindergarten and school closures one week prior to the official summer holidays in order to reduce close contact with potentially infected children.

For countries bordering Romania, follow up actions may include:

- increasing and enhancing surveillance for aseptic meningitis
- increasing awareness among clinicians for the summer and autumn months and the detection of EV infections, including the need to take samples (stool and cerebrospinal-fluid) in order to exclude polioviruses and other strains of EV that might lead to more severe clinical disease
- communication campaigns to the general public to enforce personal hygiene measures

## Conclusions

In conclusion, ECDC currently considers the aseptic meningitis outbreak reported to be associated to a kindergarten in Suceava city, northern Romania, not to be an unexpected event. However, an increase in the number of cases and a shift of infection from younger to older age groups in the affected area cannot be excluded in the future. Public health control measures have been implemented by Romania to limit the spread and monitor the development of the outbreak. Information on the current situation was shared with other European Union member states and public health international organisations in the European region through the appropriate channels. Public health authorities throughout the EU and neighbouring countries are thereby encouraged to monitor aseptic meningitis in the coming summer and autumn months.

## References

1. Heymann DL. Control of Communicable Diseases Manual. 18th ed. American Public Health Association; 2004.
2. Palacios G, Oberste MS. Enteroviruses as agents of emerging infectious diseases. *J Neurovirol.* 2005. Oct;11(5):424–33.
3. Ramers C, Billman G, Hartin M, Ho S, Sawyer MH. Impact of a diagnostic cerebrospinal fluid enterovirus polymerase chain reaction test on patient management. *JAMA.* 2000 May 24–31;283(20):2680–5.
4. Dierssen U, Rehren F, Henke-Gendo C, Harste G, Heim A. Rapid routine detection of enterovirus RNA in cerebrospinal fluid by a one-step real-time RT-PCR assay. *J Clin Virol.* 2008 May;42(1):58–64.
5. Enteroviruses: polioviruses, coxsackieviruses, echoviruses and newer enteroviruses, Fields Virology, Fifth Edition, Editors-in-chief DM Knipe & PM Howley
6. Popescu C, Arama V, Bacruban R, Streinu-Cercel A, Hristea A, Abagiu A, et al. Outbreak of viral meningitis in Romania: cases managed in a national institute of infectious diseases. 2007. Available at <http://www.blackwellpublishing.com/eccmid18/abstract.asp?id=70084> (accessed 21 June 2012)
7. Centers for Disease Control and Prevention (CDC). Non-Polio Enterovirus Infections. Available at [http://www.cdc.gov/ncidod/dvrd/revb/enterovirus/non-polio\\_entero.htm](http://www.cdc.gov/ncidod/dvrd/revb/enterovirus/non-polio_entero.htm)
8. Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep. 2000. Jul 28;49(29):669–71. Outbreak of aseptic meningitis associated with multiple enterovirus serotypes-Romania, 1999.
9. Perevoščikovs J, Briļa A, Firstova L, Komarova T, Lucenko I, Osmjana J, et al. Ongoing outbreak of aseptic meningitis in south-eastern Latvia, June–August 2010. *Euro Surveill.* 2010;15(32):pii=19639. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19639>
10. Perevoščikovs J, Lucenko I, Nikiforova R. Outbreak of enteroviral meningitis in Latvia, August–October 2006. *Euro Surveill.* 2006;11(40):pii=3060. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3060>
11. Ćosić G, Đurić P, Milošević V, Đekić J, Čanak G, Turkulov V. Ongoing outbreak of aseptic meningitis associated with echovirus type 30 in the City of Novi Sad, Autonomous Province of Vojvodina, Serbia, June–July 2010. *Euro Surveill.* 2010;15(32):pii=19638. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19638>
12. Antona D, Chomel JJ, Enterovirus Surveillance Laboratory Network. Increase in viral meningitis cases reported in France, summer 2005. *Euro Surveill.* 2005;10(36):pii=2787. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=2787>
13. Logotheti M, Pogka V, Horefti E, Papadacos K, Giannaki M, Pangalis A, et al. *Clin Virol.* 2009 Nov;46(3):270–4. Epub 2009 Aug 20. Laboratory investigation and phylogenetic analysis of enteroviruses involved in an aseptic meningitis outbreak in Greece during the summer of 2007.
14. Juliá ML, Colomina J, Domínguez V, Orta N, Guerrero A. Meningitis outbreak caused by Echovirus serotype 30 in the Valencian Community. *Enferm Infecc Microbiol Clin.* 2009 May;27(5):263–8.
15. Ortner B, Huang CW, Schmid D, Mutz I, Wewalka G, Allerberger F, et al. Epidemiology of enterovirus types causing neurological disease in Austria 1999–2007: detection of clusters of echovirus 30 and enterovirus 71 and analysis of prevalent genotypes. *J Med Virol.* 2009 Feb;81(2):317–24.
16. Brunel D, Lévêque N, Jacques J, Renois F, Motte J, Andréoletti L. Clinical and virological features of an aseptic meningitis outbreak in North-Eastern France, 2005. *J Clin Virol.* 2008 Jun;42(2):225–8. Epub 2008 Mar 20.
17. Faustini A, Fano V, Muscillo M, Zaniratti S, La Rosa G, Tribuzi L, et al. An outbreak of aseptic meningitis due to echovirus 30 associated with attending school and swimming in pools. *Int J Infect Dis.* 2006 Jul;10(4):291–7. Epub 2006 Feb 3.