



COMMUNICABLE DISEASE THREATS REPORT

CDTR Week 30, 19-25 July 2015

All users

This weekly bulletin provides updates on threats monitored by ECDC.

I. Executive summary EU Threats

New! Fatal case of anthrax following animal exposure – Bulgaria

Opening date: 22 July 2015 Latest update: 23 July 2015

On 18 July 2015, the Bulgarian Ministry of Health reported a fatal case of *B. Anthracis* in a man who handled contaminated meat whilst unprotected.

West Nile virus - Multistate (Europe) - Monitoring season 2015

Opening date: 2 June 2015 Latest update: 16 July 2015

West Nile fever (WNF) is a mosquito-borne disease which causes severe neurological symptoms in a small proportion of infected people. During the June-to-November transmission season, ECDC monitors the situation in EU Member States and neighbouring countries in order to inform blood safety authorities of WNF-affected areas and identify significant changes in the epidemiology of the disease.

→Update of the week

During the past week, no new cases were reported in the EU. In neighbouring countries, Israel reported two cases diagnosed in June, one in the Northern district and one in the Haifa district. Israel also reported that mosquitoes positive for the virus have been detected in Mai in the south of the country.

Cluster of Schistosoma haematobium - Corsica, France - 2014

Opening date: 8 May 2014 Latest update: 23 July 2015

In July 2015, a study of travellers returning from Corsica reported one case of *Schistosoma haematobium* presenting with eggs in the urine and one with two positive serological tests that they classified as confirmed, six cases with one positive serological test classified as probable and three cases with borderline positive serological results classified as suspected. One confirmed and two probable cases declared exposure in Cavu River in 2013, and one confirmed case reported exposure in the Cavu River in 2011 and 2014, but not in 2013.

→Update of the week

ECDC will publish an updated rapid risk assessment on 24 July 2015.

Monitoring environmental suitability of Vibrio growth in the Baltic Sea – Summer 2015

Opening date: 6 July 2015 Latest update: 23 July 2015

ECDC has developed a model to map the environmental suitability for Vibrio growth in the Baltic Sea (ECDC E3 Geoportal).

→Update of the week

This week, the environmental conditions in the southern part of the Baltic Sea, particularly around Kiel and Szczecin, are considered suitable for *Vibrio* growth at a very low to low level.

Non EU Threats

Middle East respiratory syndrome – coronavirus (MERS CoV) – Multistate

Opening date: 24 September 2012 Latest update: 23 July 2015

Since April 2012 and as of 23 July 2015, 1 395 cases of MERS-CoV have been reported by local health authorities worldwide, including 540 deaths. The source of the virus remains unknown but the pattern of transmission and virological studies point towards dromedary camels in the Middle East being a reservoir from which humans sporadically become infected through zoonotic transmission. Human-to-human transmission is amplified among household contacts and in healthcare settings.

→Update of the week

South Korea has not reported any new cases since 4 July. The number of cases remains at 186, including one case who travelled to China, and the number of deaths at 36.

Since 16 July 2015, Saudi Arabia has reported three new cases and four deaths in previously reported cases.

ECDC published an epidemiological update on 22 July 2015.

Ebola Virus Disease Epidemic - West Africa - 2014 - 2015

Opening date: 22 March 2014 Latest update: 23 July 2015

An epidemic of Ebola virus disease (EVD) has been ongoing in West Africa since December 2013, mainly affecting Guinea, Liberia and Sierra Leone. On 8 August 2014, WHO declared the Ebola epidemic in West Africa a Public Health Emergency of International Concern (PHEIC).

→Update of the week

As of 19 July 2015, WHO has reported 27 741 cases of Ebola virus disease related to the outbreak in West Africa, including 11 284 deaths.

According to the latest <u>WHO situation report</u> published on 22 July 2015, 26 confirmed cases of EVD were reported in the week up to 19 July: 22 in Guinea and 4 in Sierra Leone. For the second consecutive week, most cases were reported from Conakry and Freetown, the capitals of Guinea and Sierra Leone, respectively. All but two of the cases reported by WHO in the week up to 19 July were either registered contacts of a previous case or have an established epidemiological link to a known chain of transmission. Two cases, both from Guinea, have been identified as EVD-positive only after post-mortem testing.

Poliomyelitis - Multistate (world) - Monitoring global outbreaks

Opening date: 8 September 2005 Latest update: 23 July 2015

Global public health efforts are ongoing to eradicate polio, a crippling and potentially fatal disease, by immunising every child until all transmission of the virus stopped and the world becomes polio-free. Polio was declared a Public Health Emergency of International Concern (PHEIC) on 5 May 2014 due to concerns regarding the increased circulation and international spread of wild poliovirus during 2014. On 6 May 2015, the Temporary Recommendations in relation to PHEIC were extended for another three months.

→Update of the week

During the past week, no new cases of wild poliovirus type 1 (WPV1) and vaccine-derived poliovirus (cVDPV) were reported to WHO.

II. Detailed reports

New! Fatal case of anthrax following animal exposure – Bulgaria

Opening date: 22 July 2015 Latest update: 23 July 2015

Epidemiological summary

On 18 July 2015, <u>Bulgaria</u> reported a fatal case of *B. Anthracis* in a man who handled contaminated meat whilst unprotected. The patient owned and bred domestic animals (sheep and cows) in a village west of Varna city. On 7 July, he, with two friends, slaughtered a sick cow without informing the regional veterinary services. The meat was illegally butchered and sausages prepared. The sausages were eaten by their relatives. Three days later, the man fell ill with fever consistent with toxic infectious syndrome while displaying wounds on both hands.

The Regional Health Inspectorate in Varna has identified 26 people who were in contact with the ill cow or who handled or consumed the meat. All contacts have been prescribed antibiotic prophylaxis and are currently under medical observation. Local health authorities have taken the relevant action and public health control measures have been implemented.

ECDC assessment

Sporadic cases following the handling of contaminated meat without protection is not unexpected. Local health authorities in Bulgaria have taken the relevant action and implemented the appropriate public health measures. ECDC does not consider there to be any remaining risk for the EU with regards to this case.

West Nile virus - Multistate (Europe) - Monitoring season 2015

Opening date: 2 June 2015 Latest update: 16 July 2015

Epidemiological summary

As of 23 July 2015, one case of West Nile fever has been reported in the EU and two cases in neighbouring countries since the beginning of the 2015 transmission season.

Web sources: ECDC West Nile fever | ECDC West Nile fever risk assessment tool | ECDC West Nile fever maps | WHO fact sheet |

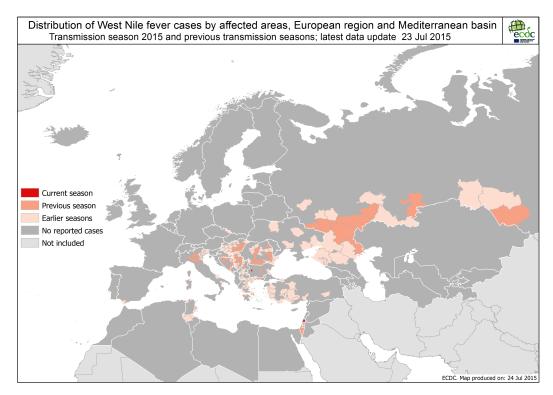
ECDC assessment

West Nile fever in humans is a notifiable disease in the EU. The implementation of control measures is considered important for ensuring blood safety by the national health authorities when human cases of West Nile fever occur. According to the <u>EU Blood Directive</u>, efforts should be made to defer blood donations from affected areas with ongoing virus transmission unless donations are tested using individual NAT.

Actions

ECDC produces weekly West Nile fever (WNF) maps during the transmission season (June to November) to inform blood safety authorities of WNF affected areas.

Source: ECDC



Cluster of Schistosoma haematobium - Corsica, France - 2014

Opening date: 8 May 2014 Latest update: 23 July 2015

Epidemiological summary

In April 2014, a cluster of *Schistosoma haematobium* infections was detected, linked to exposure in 2013 at Cavu, a natural freshwater swimming area in southern Corsica, France.

As of 14 April 2015, no cases were identified with exposure in 2014. None of 3 534 *Bulinus* snails in the Cavu River tested in summer 2014 were found to be infected. In addition, *Bulinus* snails were found in five bathing sites in three rivers (two sites in the Solenzara River, two sites in the Osu River and one site in the Tarcu River) of the 38 investigated sites in 19 rivers. None were found positive to *Schistosoma* spp. The swimming ban in the Cavu River was lifted on 4 June 2015.

Following a national screening campaign in France, 110 additional schistosomiasis cases were described (as of 25 March 2015) in residents of Corsica and visitors from other parts of France, over a two-year time span. The majority of these cases were recorded in children and teenagers. Epidemiological investigations are ongoing.

A <u>study</u> among 43 Italian travellers seeking medical screening after learning of the risk of acquiring schistosomiasis after freshwater exposure in Corsica was published in July 2015. The study classified five cases as confirmed on the basis of one positive western blot test, four of which were asymptomatic, and classified two as probable and eight as possible. Two cases reported exposure to the Cavu River in 2013, one in 2014 and one in 2011. Eight of these 15 cases reported an exposure to the Cavu River in 2013.

In addition, a <u>study</u> published in July 2015 by a travel medicine network detected 11 cases among travellers returning from Corsica. None reported exposure to freshwater in schistosomiasis endemic areas.

Web sources: ECDC 2014 RRA | French regional authorities statement | WHO factsheet

ECDC assessment

The risk for the occurrence of the parasitic cycle in other areas of Europe is dependent upon the presence of receptive areas where the intermediate host is present in suitable environmental conditions, the introduction of the parasite and exposure of humans.

Suitable environmental conditions for the development of *S. haematobium* in the freshwater snail are likely found during the summer months in Mediterranean areas, coinciding with the high attendance period for recreational activities involving exposure

to river water.

The introduction of the parasite into receptive areas may be associated with travellers who have acquired the infection while in endemic areas, such as tourists, armed forces personnel returning from deployments or immigrants from endemic areas. Recurrent seasonal foci of transmission of S. haematobium or S. haematobium/S. bovis could occur through the persistence of the parasite in intermediate hosts throughout the winter, or the reintroduction in receptive areas from an individual infected either abroad or locally in a previous season. In addition, there is a theoretical possibility that the hybrid parasite S. haematobium/S. bovis identified in Corsica could be reintroduced from an animal reservoir, although ongoing investigations have not yet substantiated this hypothesis.

Web Sources: ECDC RRA 2014 | Emerging Infectious Diseases article

Monitoring environmental suitability of Vibrio growth in the Baltic Sea – **Summer 2015**

Opening date: 6 July 2015 Latest update: 23 July 2015

Epidemiological summary

In late June 2015, the Vibrio suitability tool on the ECDC E3 Geoportal helped ECDC to ascertain favourable environmental factors for Vibrio growth.

On 3 July 2015, ECDC launched an Urgent Inquiry (UI) in EPIS-FWD after detecting elevated sea surface temperatures (according to the National Oceanic and Atmospheric Administration, NOAA) in the Baltic Sea (as of 2 July 2015).

ECDC assessment

Elevated sea surface temperatures in marine environments with low salt content provide ideal environmental growth conditions for certain Vibrio species. These conditions can be found during the summer months in estuaries and enclosed water bodies with moderate salinity. In contrast, open ocean environments do not offer appropriate growth conditions for these bacteria due to the high salt content, low temperatures, and limited nutrient content. These Vibrio species can cause vibriosis infections, particularly V. parahaemolyticus, V. vulnificus and non-toxigenic V. cholerae.

Vibriosis in humans caused by these species in the Baltic region have occurred in the past during hot summer months, particularly when the sea surface temperature has been elevated. The most common clinical manifestations are gastroenteritis (with nausea, vomiting, and diarrhoea), wound infections (exposure of a cut, wound, or abrasion to contaminated seawater), primary septicaemia, and otitis externa (swimmer's ear). Risk factors for illness include consumption of shellfish, particularly raw oysters, and contact with natural bodies of water, especially marine or estuarine waters.

Actions

ECDC launched an UI in EPIS-FWD to inform the FWD network about the elevated surface water temperatures measured in the Baltic Sea which create a favourable environment for the growth of *Vibrio* bacteria. ECDC will monitor this threat on a weekly basis during the summer of 2015 and report on increased environmental suitability for growth of Vibrio bacteria.

The Vibrio suitability tool is available on the ECDC E3 Geoportal. Please note that this model has been calibrated to the Baltic region in northern Europe and might not be compatible with other regional settings prior to validation.

Middle East respiratory syndrome – coronavirus (MERS CoV) – Multistate

Opening date: 24 September 2012 Latest update: 23 July 2015

Epidemiological summary

The last case from South Korea was reported on 4 July 2015. Transmission can be considered to have ended when no new cases are detected for a period of 28 days (two times the maximum 14-day incubation period) after the last case being treated has tested negative two times (with a minimum of 24 hours between the two tests) or the case has died.

Between April 2012 and 23 July 2015, 1 395 cases of MERS-CoV have been reported by local health authorities worldwide, including 540 deaths.

The distribution is as follows: Confirmed cases and deaths by region:

Middle East

Saudi Arabia: 1 051 cases/464 deaths United Arab Emirates: 81 cases/11 deaths

Oatar: 13 cases/5 deaths Jordan: 19 cases/6 deaths Oman: 6 cases/3 deaths Kuwait: 3 cases/1 death Egypt: 1 case/0 deaths Yemen: 1 case/1 death Lebanon: 1 case/0 deaths Iran: 6 cases/2 deaths

Europe

Turkev: 1 case/1 death UK: 4 cases/3 deaths Germany: 3 cases/2 deaths France: 2 cases/1 death Italy: 1 case/0 deaths Greece: 1 case/1 death Netherlands: 2 cases/0 deaths Austria: 1 case/0 deaths

Africa

Tunisia: 3 cases/1 death Algeria: 2 cases/1 death

Asia

Malaysia: 1 case/1 death Philippines: 3 cases/0 deaths South Korea: 185 cases/36 deaths

China: 1 case/0 deaths Thailand: 1 case/ 0 deaths

Americas

United States of America: 2 cases/0 deaths

Web sources: ECDC's latest rapid risk assessment | ECDC novel coronavirus webpage | WHO | WHO MERS updates | WHO travel health update | WHO Euro MERS updates | CDC MERS | Saudi Arabia MoH | ECDC factsheet for professionals

ECDC assessment

According to ECDC experts, the MERS-CoV outbreak poses a low risk to the EU. Efforts to contain the nosocomial clusters in the affected countries are vital to prevent wider transmission. Although sustained human-to-human community transmission is unlikely, secondary transmission to unprotected close contacts, especially in healthcare settings, remains possible, as documented in South Korea.

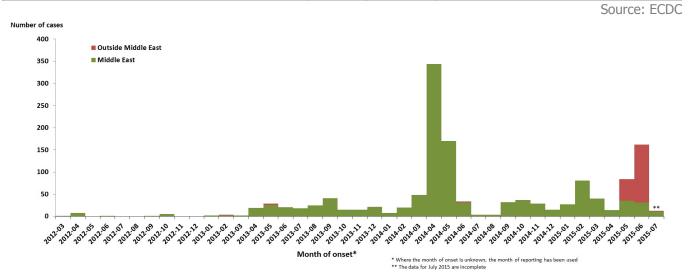
Countries should advise travellers returning from all countries affected by MERS to seek medical attention if they develop a respiratory illness with fever and cough during the two weeks after their return and to disclose their recent travel history to the healthcare provider. The travellers, especially with pre-existing medical conditions, should be reminded of the importance of good hand and food hygiene, and to avoid contact with sick people. In addition, travellers to the Arabian Peninsula should avoid close contact with camels, visiting farms and consuming unpasteurised camel milk, urine or improperly cooked meat.

Actions

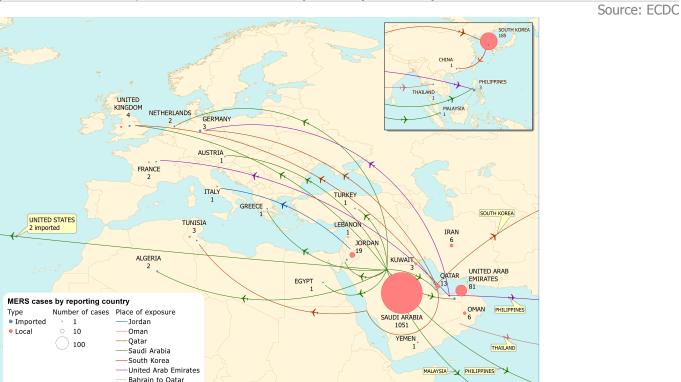
ECDC published an epidemiological update on 22 July 2015.

ECDC published a rapid risk assessment on 1 July 2015.

Distribution of confirmed cases of MERS-CoV by first available date and place of probable infection, March 2012 - 23 July 2015 (n=1 395)

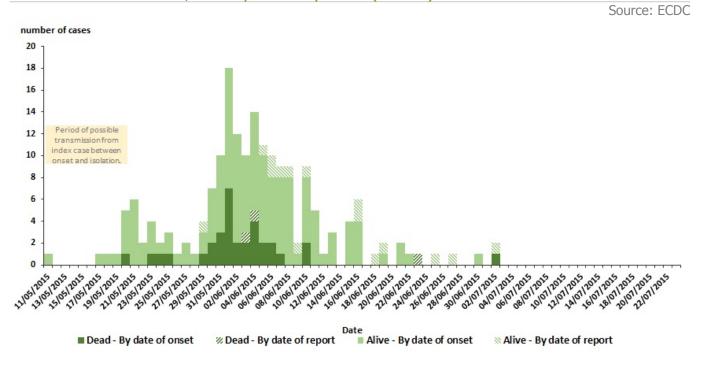


Distribution of confirmed cases of MERS-CoV by first available date and place of probable infection, March 2012 - 23 July 2015 (n=1 395)



Distribution of confirmed cases of MERS-CoV by first available date and by status in South Korea and China, 11 May - 23 July 2015 (n=186)

ECDC. Numbers in the map indicate the total number of local and imported MERS cases. Map produced on: 23 Jul 2015



Ebola Virus Disease Epidemic - West Africa - 2014 - 2015

Opening date: 22 March 2014 Latest update: 23 July 2015

Epidemiological summary

Distribution of cases as of 19 July 2015:

Countries with intense transmission:

- Guinea: 3 783 cases of which 3 322 are confirmed and 2 512 deaths.
- Sierra Leone: 13 250 cases of which 8 692 are confirmed and 3 949 deaths.
- **Liberia:** 10 666 cases as of 9 May 2015, when Liberia was declared Ebola-free. Since then, as of 15 July, 6 cases and 2 deaths have been reported.

Countries that have reported an initial case or localised transmission:

• Nigeria, Senegal, the USA, Spain, Mali, the UK and Italy.

Situation in West African countries

In **Guinea**, WHO reported 22 new confirmed cases in the week up to 19 July, compared to 13 during the previous week. Transmission was centred in three prefectures: Conakry (n=13), Forecariah (n=7) and Coyah (n=2). The prefecture of Coyah has not reported confirmed cases since April 2015. Two cases registered in Conakry are healthcare workers. Overall, 21 (95%) of 22 cases in Guinea were registered contacts: the highest reported proportion since the onset of the outbreak. Only one case in Forecariah arose from an unknown chain of transmission.

In **Sierra Leone**, WHO reported 4 new confirmed cases in the week up to 19 July, compared with 14 during the previous week. Transmission was centred in two prefectures: Western Area Urban, which includes the capital Freetown (n=2) and Port Loko (n=2). One of the cases registered in Freetown is a healthcare worker. The second case was found with advanced disease (symptoms including vomiting and diarrhoea) and the case is not a registered contact of any known chain of transmission. Contact tracing has been complicated by the fact that the case has no fixed address and was infectious for an unknown period prior to identification.

In **Liberia**, no new cases were reported from WHO. As of 21 July, 56 contacts associated with the chain of transmission are under follow-up. Eighteen contacts have completed the 21-day follow up period. If there are no further cases all contacts will have completed follow-up on 2 August.

Situation among healthcare workers

Two new infections in healthcare workers were reported from Guinea and one from Sierra Leone in the week up to 19 July. There have been 879 confirmed infections in healthcare workers reported from Guinea, Liberia and Sierra Leone since the start of the outbreak, with 510 reported deaths.

Outside of the three most affected countries, 2 Ebola-infected healthcare workers were reported in Mali, 11 in Nigeria, 1 in Spain (infected while caring for an evacuated EVD patient), 2 in the UK (both infected in Sierra Leone), 6 in the USA (2 infected in Sierra Leone, 2 in Liberia, and 2 infected while caring for a confirmed case in Texas) and 1 in Italy (infected in Sierra Leone).

Medical evacuations and repatriations from EVD-affected countries

Since the beginning of the epidemic and as of 24 July 2015, 65 individuals have been evacuated or repatriated worldwide from the EVD-affected countries. Of these, 38 individuals have been evacuated or repatriated to Europe. Thirteen were medical evacuations of confirmed EVD-infected patients to: Germany (3), Spain (2), France (2), UK (2), Norway (1), Italy (1), Netherlands (1) and Switzerland (1). Twenty-five asymptomatic persons have been repatriated to Europe as a result of exposure to Ebola in West Africa: UK (13), Denmark (4), Sweden (3), Netherlands (2), Germany (1), Spain (1) and Switzerland (1). Twenty-seven persons have been evacuated to the United States.

No new medical evacuations have taken place since 18 March 2015.

Other news

On 20 July, WHO declared **Italy** free of EVD transmission after the completion of 42 days without a case since the country's first and only case of EVD to date was confirmed EVD-negative and discharged from hospital.

Images

- Epicurve 1: the epicurve shows the confirmed cases in the three most affected countries.
- Epicurve 2: the epicurve shows the confirmed cases in Guinea, Sierra Leone and Liberia.
- Map: this map is based on country situation reports and shows only confirmed cases of EVD in the past six weeks.

Web sources: ECDC Ebola page | ECDC Ebola and Marburg fact sheet | WHO situation summary | WHO Roadmap | WHO Ebola

Factsheet | CDC | Liberian media

ECDC assessment

This is the largest ever documented epidemic of EVD, both in terms of numbers and geographical spread. The epidemic of EVD increases the likelihood that EU residents and travellers to the EVD-affected countries will be exposed to infected or ill persons. The risk of infection for residents and visitors in the affected countries through exposure in the community is considered low if they adhere to the recommended precautions. Residents and visitors to the affected areas run a risk of exposure to EVD in healthcare facilities.

The risk of importing EVD into the EU and the risk of transmission within the EU following an importation remains low or very low as a result of the range of risk reduction measures that have been put in place by the Member States and by the affected countries in West Africa. However, continued vigilance is essential. If a symptomatic case of EVD presents in an EU Member State, secondary transmission to caregivers in the family and in healthcare facilities cannot be excluded.

According to WHO, for the second consecutive week, more than half of all cases were reported from the capitals of Guinea and Sierra Leone, Conakry and Freetown. There are indications of a continuation of the improvements in contact tracing and case investigation seen in recent weeks. Most of the newly detected cases are part of known transmission chains.

Actions

As of 24 July 2015, ECDC has deployed 89 experts (on a rotating basis) from within and outside the EU in response to the Ebola outbreak. This includes an ECDC-mobilised contingent of experts to Guinea. Furthermore, additional experts are already confirmed for deployment to Guinea over the next few months.

ECDC is looking for additional French-speaking experts with field epidemiology experience from EU Member States to join the ECDC-coordinated contingent in response to the Ebola outbreak in Guinea. For further information, please contact Alice Friaux at alice.friaux@ecdc.europa.eu with copy to support@ecdc.europa.eu.

An epidemiological update is published weekly on the EVD ECDC page.

ECDC updated the list of affected countries and regions on its <u>website</u> to include the newly affected county of Margibi, Liberia. ECDC updated the event background on its <u>website</u> to report the newly reported cases in Liberia.

The latest (12th) update of the rapid risk assessment was published on 1 July 2015.

On 22 January 2014, ECDC published <u>Infection prevention and control measures for Ebola virus disease. Management of healthcare workers returning from Ebola-affected areas.</u>

On 4 December 2014, EFSA and ECDC published a <u>Scientific report assessing Risk related to household pets in contact with Ebola cases in humans.</u>

On 29 October 2014, ECDC published a training tool on the <u>safe use of PPE</u> and <u>options for preparing for gatherings in the EU</u>. On 23 October 2014, ECDC published <u>Public health management of persons having had contact with Ebola virus disease cases in the EU.</u>

On 22 October 2014, ECDC published <u>Assessing and planning medical evacuation flights to Europe for patients with Ebola virus</u> <u>disease and people exposed to Ebola virus</u>.

On 13 October 2014, ECDC published <u>Infection prevention and control measures for Ebola virus disease: Entry and exit screening measures</u>.

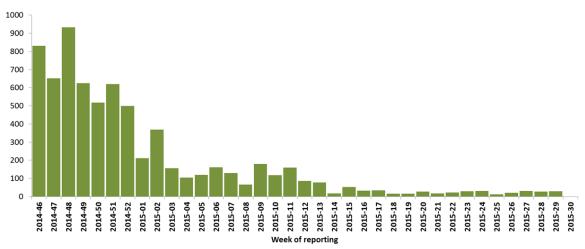
On 6 October 2014, ECDC published <u>risk of transmission of Ebola virus via donated blood and other substances of human origin in</u> the EU.

On 22 September 2014, ECDC published <u>assessment and planning for medical evacuation by air to the EU of patients with Ebola virus disease and people exposed to Ebola virus</u>.

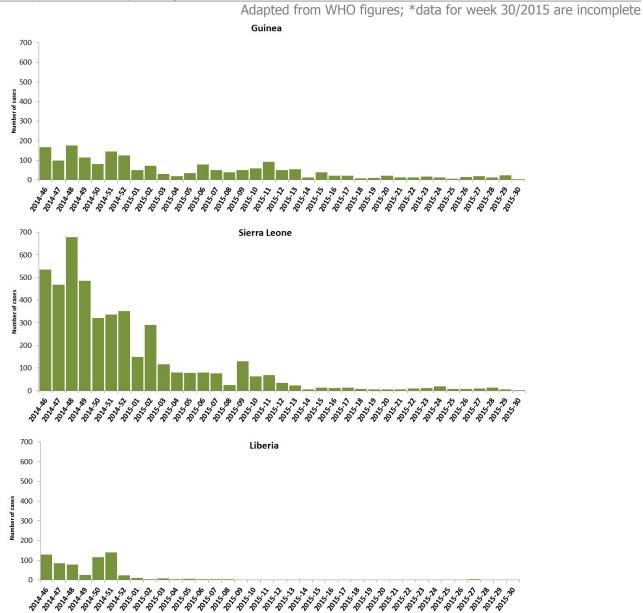
On 10 September 2014, ECDC published an EU case definition.

Distribution of confirmed cases of EVD by week of reporting in Guinea, Sierra Leone and Liberia (weeks 46/2014 to 30/2015)

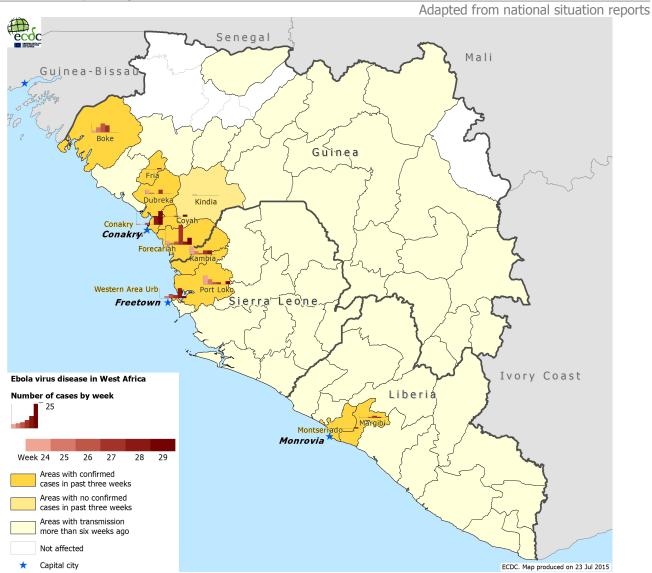
Adapted from WHO figures; *data for week 30/2015 are incomplete



Distribution of confirmed cases of EVD by week of reporting in Guinea and Sierra Leone (weeks 46/2014 to 30/2015)



Distribution of confirmed cases of EVD by week of reporting in Guinea and Sierra Leone (as of week 29/2015)



Poliomyelitis - Multistate (world) - Monitoring global outbreaks

Opening date: 8 September 2005 Latest update: 23 July 2015

Epidemiological summary

Worldwide in 2015, 33 wild poliovirus type 1 (WPV1) cases have been reported to WHO so far, compared with 128 for the same period in 2014. Since the beginning of the year, two countries have reported cases: Pakistan (28 cases) and Afghanistan (5 cases).

In 2015, nine cases (eight in Madagascar and one in Nigeria) of circulating vaccine-derived poliovirus (cVDPV) have been reported to WHO so far, compared with 26 for the same period in 2014. The cases in Madagascar are genetically linked to a case reported in September 2014, indicating prolonged and widespread circulation of the virus.

Web sources: Polio Eradication: weekly update | MedISys Poliomyelitis | ECDC Poliomyelitis factsheet | Temporary Recommendations to Reduce International Spread of Poliovirus | Statement on the 4th IHR Emergency Committee meeting regarding the international spread of wild poliovirus

ECDC assessment

Europe is polio-free. The last locally acquired wild-polio cases within the current EU borders were reported from Bulgaria in 2001. The most recent outbreak in the WHO European Region was in Tajikistan in 2010, when importation of WPV1 from Pakistan resulted in 460 cases.

The confirmed circulation of wild poliovirus in several countries and the documented exportation of wild poliovirus to other countries support the fact that there is a potential risk of wild poliovirus being re-introduced to the EU/EEA. The highest risk of large poliomyelitis outbreaks occurs in areas with clusters of unvaccinated populations and in people living in poor sanitary conditions, or a combination of both.

References: ECDC latest RRA | Rapid Risk Assessment on suspected polio cases in Syria and the risk to the EU/EEA | Wild-type poliovirus 1 transmission in Israel - what is the risk to the EU/EEA? |

Actions

ECDC monitors reports of polio cases worldwide through epidemic intelligence in order to highlight polio eradication efforts and identify events that increase the risk of wild poliovirus being re-introduced into the EU. Following the declaration of polio as a PHEIC, ECDC updated its <u>risk assessment</u>. ECDC has also prepared a background document with travel recommendations for the EU.

The Communicable Disease Threat Report may include unconfirmed information which may later prove to be unsubstantiated.