RAPID RISK ASSESSMENT

Update: Severe respiratory disease associated with a novel coronavirus

26 November 2012

Main conclusions

- In September 2012, a group of novel coronaviruses were identified in two patients presenting with a severe acute respiratory illness. Both had a travel history to the Kingdom of Saudi Arabia (KSA) or Qatar. These novel coronaviruses are genetically different from the virus that in 2003 caused the SARS outbreaks (SARS-CoV).
- Since June 2012 and up to 25 November 2012, a total of six confirmed cases of infection with the novel coronavirus (of whom two died) have been reported to WHO, meeting the requirements of its case definitions. Severe respiratory disease was the common factor in all of these. Two of the cases were diagnosed after being transferred to Europe for further medical care.
- All six confirmed cases reside or travelled to KSA or Qatar. Two confirmed cases in KSA are from the same family household. A further person in this household is under investigation for infection with the novel coronavirus.
- The source and possible routes of transmission of the virus remain unknown. Investigations have yet to identify the source or route of infection and infectiousness. At this stage, the detection of a household cluster does not provide conclusive evidence for or against limited person-to-person transmission. It is possible that enhanced surveillance in KSA, Qatar and elsewhere will detect additional sporadic cases and clusters.
- Initial laboratory analyses in Europe of the first of these viruses (known as hCoV-EMC) suggest that it may be able to infect a range of mammalian cells including human cells making human-to-human transmission theoretically possible.
- Healthcare workers should be made aware of the possibility of attending to patients matching the characteristics of patients requiring investigation as per WHO case-definition; however, the geographical area should be extended from KSA and Qatar to include the whole of the Middle East. Healthcare workers caring for patients under investigation should exercise stringent infection control measures following national or international guidance. Testing for the novel coronaviruses should be considered in patients potentially undergoing medical evacuation for acute respiratory distress syndrome (ARDS) prior to their transfer. Healthcare workers caring for confirmed cases and close contacts of confirmed cases should be monitored for symptoms.
- Patients returning from the Middle East with unexplained pneumonia or ARDS, i.e. where full diagnostic workup for respiratory pathogens (bacterial and viral) is negative, should be considered for investigation and tested for novel coronavirus by EU national reference and research laboratories capable of such testing.
- Any probable or confirmed case being diagnosed in the EU/EEA should be reported to national authorities, through the Early Warning Response System (EWRS) and to WHO under the International Health Regulations (2005) (most easily via the option to report to IHR through EWRS to avoid double report entry).

Public health issue

What are the public health risk implications of the detection of further novel coronavirus cases identified in, or coming from, the Kingdom of Saudi Arabia (KSA) and Qatar?

Source and date of request

ECDC internal decision, 23 November 2012.

ECDC internal response team

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External experts consulted

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Disease background information

A description of the disease background to this virus is included in the Rapid Risk Assessment of 24 September 2012. One of the viruses has subsequently been sequenced and is closely related to some of the bat coronaviruses. The viruses are genetically distinct from the coronavirus which caused the SARS outbreaks world-wide in 2003. Further analysis of virus tropism in European laboratories has indicated that one of the viruses can infect a variety of cell lines (including human cells), although the significance of this has yet to become clear.

Case definition

The international case definition for cases infected with the novel coronavirus is available from the WHO website. It is currently under review and may be updated as more information becomes available.

Event information

Two cases have been described in the Rapid Risk Assessment of 24 September 2012 and a third case was described in an ECDC epidemiological update on 6 November.

On 23 November 2012, the Robert Koch Institute in Germany reported in EWRS and through a press release a newly identified case of novel coronavirus infection in a patient originating from Qatar (case 4). The patient was initially treated in a hospital in Qatar after symptom onset in October and later transferred to Germany for further medical care. Samples taken mid-October in Qatar tested positive for the novel coronavirus on 20 November in the UK Health Protection Agency.

On 23 November 2012, WHO provided information under the International Health Regulations about this case from Qatar treated in Germany and two other confirmed cases (cases 5 and 6, in KSA), one of whom died. These two cases in KSA are part of cluster in a family household involving two additional non-confirmed cases: one, for whom the laboratory results are pending, died, and one, for whom the lab results were negative, recovered.

Thus, as of 25 November, six confirmed cases of novel coronavirus have been reported since identification of this novel virus in September 2012. Two of the six confirmed cases (both from KSA) have died.

All cases identified so far are associated with travel to or residence in KSA (four cases) or Qatar (two cases). The reservoir and route of transmission of novel coronavirus remains unknown, and a possibility of limited person-to-person transmission among the family cluster in KSA cannot be excluded. There is indication that some cases had a history of visits to farms prior to illness, but no details are available concerning the kind of farms or related animal contact. Additional information on the field investigations is awaited from the national authorities.

Active case finding by the UK Health Protection Agency (HPA) and follow-up of contacts of the second case, including healthcare workers in the UK, identified no subsequent probable or confirmed cases in the UK to date. Investigations by German authorities have not identified any illness among medical staff in Germany caring for the fourth case, and follow-up investigations are continuing.

Threat assessment for the EU

Six confirmed cases of novel coronavirus infection have been confirmed as of 25 November.

All six confirmed cases visited, or resided in, Saudi Arabia or Qatar when falling ill, between June and November 2012. Two of the cases were treated in the United Kingdom and Germany after medical evacuation, but so far, despite intensive surveillance, there are no indications of transmission of the virus within the EU. To date, there is very limited information about potential exposures and knowledge about reservoir. Genome sequencing studies suggest the virus is closely related to some of the bat coronaviruses that are distant from SARS-CoV. Further studies suggest the viruses are capable of infecting a range of cells including human cell lines [9]. However the significance of this for human infection and human-to-human transmission is as yet unclear.

The identification of two and possibly three cases within one family household may indicate the possibility of person-to-person transmission, even though this could also be explained by exposure to a common (continuous) source. Further epidemiological investigations are needed to assess the risk of transmission.

Family members of patients or healthcare staff treating persons from the Middle East with severe acute respiratory infections may be exposed and at risk of infection with the novel coronavirus, unless personal protective measures are applied. However, it is possible that these rare infections are more widespread in their distribution, and WHO has now signalled that it wishes to broaden the scope of its case finding. Seroepidemiological studies are needed to investigate the possibility of milder and asymptomatic infections.

Basic epidemiological knowledge about this disease is still not known, such as its geographical distribution, incubation period, infectiousness, reservoirs, routes of transmission, and duration of viral shedding from infected human cases. However, these infections from a probable zoonotic or environmental source remain rare. The fact that there have not been any expanding clusters of cases indicates that currently the risk for EU citizens to acquire these infections has not increased and remains very low, based on the current information.

Two of the six confirmed cases were diagnosed in the EU after they were medically transferred to hospitals in the EU. Therefore, there is a possibility of additional cases in the future among patients presenting with ARDS and being medically transferred to hospitals in the EU and elsewhere. Equally, there is the possibility of cases developing in persons who recently returned from the Middle East*. However, the risk of further sustained transmission in the EU currently remains very low.

Conclusions

All cases share a history of residence in, or travel to, KSA or Qatar. The detection of a household cluster does not provide at this stage conclusive evidence for or against limited person-to-person transmission. It is possible that enhanced surveillance in the Middle East and worldwide will detect additional sporadic cases or clusters. It is possible that such cases have been occurring sporadically for some time but have been unrecognised among other severe respiratory infections.

In the absence of evidence of sustained person-to-person transmission outside of household settings, the current facts still point towards a hypothesis of a zoonotic or environmental source with occasional transmission to exposed humans.

WHO does not advise any travel or trade restrictions at this point for the Kingdom of Saudi Arabia or Qatar.

Recommendations

Healthcare workers should be made aware of the possibility of attending to patients matching the characteristics of patients requiring investigation as per WHO case-definition; however, the geographical area should be extended from KSA and Qatar to include the whole of the Middle East. Such cases should be investigated rapidly and managed as recommended by WHO or in national guidance documents.

Healthcare workers caring for patients under investigation should exercise stringent infection control measures following national or international guidance. Similarly, health professionals engaged in medical evacuation of patients presenting with ARDS should be particularly vigilant, especially with patients originating from the Middle East.

Testing for the novel coronaviruses should be considered in patients undergoing medical evacuation for ARDS prior to their transfer out of the Middle East. All hospitals and private healthcare facilities should test for the novel coronaviruses patients presenting with ARDS and medically evacuated from Middle East to their facility upon admission, unless these patients have already undergone testing prior to the evacuation and results are pending.

* http://ec.europa.eu/translation/english/guidelines/documents/styleguide_english_dgt_en.pdf

When medical evacuation is planned, any testing for novel coronavirus, whether already carried out or planned, should be communicated to the recipient hospital.

Healthcare workers caring for confirmed cases should be monitored for early symptoms of infection. This includes healthcare workers who provided direct clinical or personal care or performed examination of the cases while they were symptomatic. Close contacts of confirmed cases must be monitored for symptoms as well.

Patients returning from Middle East with unexplained pneumonia or ARDS, and where a full diagnostic workup for respiratory pathogens is negative, should be considered for further investigation and testing for novel coronavirus in the EU national reference and research laboratories capable of such testing.

WHO recommends that the testing of patients with unexplained pneumonia should be considered, even in the absence of travel or other associations with the two affected countries (KSA and Qatar). ECDC is now considering the implications of this recommendation in light of the potential burden of testing, EU Member State capacity for such testing, and the possibility of false positive results. ECDC will be discussing the possibility of developing more precise recommendations as to the patient target groups for such testing with EU Member States and with WHO and will report on this in the next version of this rapid risk assessment. Indeed, the burden for EU Member States of testing cases as indicated in the above-mentioned recommendation, although hard to estimate precisely, is probably high. The annual incidence of ARDS was estimated in several studies between 13–59/100 000 inhabitants/year, with 20% with unknown risk factors [10,12]. The annual incidence of community-acquired pneumonia (CAP) in the community is estimated to be 5–11 per 1000 adult population. Between 22% and 42% of adults with CAP are admitted to hospital. In about 30–45% (up to 90%) of CAP no aetiology is found [12,13] which would roughly translate into 750 000 patients with CAP with unknown aetiology in the EU annually, even when taking the lower bounds of the estimates into account. ECDC will also work with the EU Member States to map their capacity in terms of reference virology laboratories capable of testing for the novel coronavirus with a specific RT-PCR/sequencing assay.

ECDC agrees with WHO and at this point does not advise any travel or trade restrictions for the Kingdom of Saudi Arabia or Qatar.

WHO and ECDC re-emphasise the importance of rapidly reporting to authorities and timely thorough investigation of any clusters of severe acute respiratory infections in the community or in healthcare workers, regardless of where in the world they occur.

Any probable or confirmed case being diagnosed in the EU/EEA area should be reported to national authorities, through the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (2005) (ideally via the option to report to IHR through EWRS to avoid double reporting). Patients still under investigation do not need to be reported internationally before confirmation. Countries may consult with WHO under Article 8 of the IHR. However, notification at state and national level needs to follow national legislation or guidance to allow the implementation of infection control measures, initiation of outbreak investigation and epidemiological monitoring.

Sensitive and specific RT-PCR assays have been developed for the novel coronaviruses that target the regions upstream of the E gene (the upE target; recommended for screening) and open reading frame 1b (ORF1b; recommended for confirmation). A protocol and positive control material for the upE target can be obtained from the Institute of Virology, Bonn (see http://www.virology-bonn.de/index.php?id=40). More information has been published in Eurosurveillance by Bermingham et al. [14] and Corman et al. [5]. The information is also available on the ENIVD website. In the present context, pan coronavirus tests should be avoided and specific hCoV-EMC testing, and if possible sequencing, is recommended.

References

1. ProMedmail. Novel coronavirus – Saudi Arabia (15): new case (third). 4 November 2012 [cited 2012 25/11/2012]. Available from: http://www.promedmail.org/direct.php?id=20121104.1391285.
2. Promedmail. Novel coronavirus – Saudi Arabia (17): 4th case, request for information. 21 November 2012 [25/11/2012]. Available from: http://www.promedmail.org/direct.php?id=20121121.1418018.
3. UK Health Protection Agency. Genetic sequence information for scientists about the novel coronavirus 2012. [25/11/2012]. Available from: http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/NovelCoronavirus2012/respPartialgeneticsequenceofnovelcoronavirus/.
4. Robert Koch Institute. Case of novel Corona virus in Germany 23 November 2012. 23 November 2012 [25/11/2012]. Available from: http://www.rki.de/EN/Home/CornoaVirus.html.
5. Corman VM et al. Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. Euro Surveill. 2012;17(39):pii=20285. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=.
6. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 2012 8 November;367(19):1814-20.

7. van Boheemen S, de Graaf M, Lauber C, Bestebroer TM, Raj VS, Zaki AM, et al. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. mBio. 2012;3(6):e00473-12. Available from: http://mbio.asm.org/content/3/6/e-12.
8. US Centers for Disease Control and Prevention. How to investigate unexplained respiratory disease outbreaks. 2012 [25/11/2012]; Available from: http://emergency.cdc.gov/urdo/outbreak.asp.
9. Christian Drosten, personal communication, 26 Nov 2012.
10. Lewandowski. The epidemiology of ARDS. Minerva Anestesiol 2006;72:473-7.
11. E-medicine: http://emedicine.medscape.com/article/165139-overview#aw2aab6b2b3
12. British Thoracic Society. Community Acquired Pneumonia in Adults Guideline Group. Guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax. October 2009;64 (Supplement III):16-21. Avalailable at: http://www.brit-thoracic.org.uk/Portals/0/Clinical%0Information/Pneumonia/Guidelines/CAPGuideline-full.pdf [accessed 5/11/2012].
13. Bartlett JG. Review. Clin Infect Dis 2011;52(Suppl 4):S296-304. PMID: 214602889. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21460288 [Accessed 25/11/2012].
14. Bermingham A, Chand M, Brown C, Aarons E, Tong C, Langrish C, et al. Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012. Euro Surveill. 2012;17(40):pii=20290. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20290

Sources of additional information

European Network for Imported Viral Diseases: http://www.enivd.de/index.htm
WHO SARS collaborative laboratories: http://www.who.int/csr/sars/networkshome/en/index.html
WHO Novel Coronavirus 2012: Interim Recommendations for Laboratory Biorisk Management: http://www.who.int/csr/disease/coronavirus_infections/Biosafety_InterimRecommendations_NovelCoronavirus2012_31Oct12.pdf
WHO Guidance on infection control, December 2003: http://www.smp-council.org.hk/mlt/english/mlt_message_infection_e.pdf