



RAPID RISK ASSESSMENT

Update: Severe respiratory disease associated with a novel coronavirus

7 December 2012

Main conclusions and recommendations

- As of 4 December 2012, nine laboratory-confirmed cases of severe pneumonia caused by the novel coronavirus have been reported to WHO. Five of the nine cases were fatal. Onset of disease was from April to October 2012; all cases were resident in Saudi Arabia, Qatar or Jordan during the presumed 10 days incubation period.
- Two retrospectively tested and confirmed cases in Jordan in April 2012 have increased the geographical area in which transmission has occurred. The two fatal cases were part of a cluster of 11 patients with respiratory symptoms linked to a hospital, but the limited information available about this outbreak does not allow for an assessment of whether any human-to-human transmission occurred or whether the cases in this cluster had the same cause.
- Healthcare workers should be alerted to the possibility of attending to patients who meet the WHO case definition. Such cases should be investigated rapidly and managed according to WHO recommendations or national guidance documents.
- The new WHO recommendations for the investigation of patients favour the investigation of patients returning from the Arabian Peninsula or its neighbouring countries, but do not exclude the testing of patients with unexplained pneumonia in the absence such travel.
- Healthcare workers caring for patients under investigation should exercise stringent infection control measures as indicated by national or international guidance. Similarly, health professionals engaged in the medical evacuation of patients presenting with acute respiratory distress syndrome (ARDS) should be particularly vigilant, especially if patients originate from the Arabian Peninsula or its neighbouring countries.
- Testing for the novel coronaviruses should be considered in patients undergoing medical evacuation for ARDS prior to their transfer out of the Arabian Peninsula or its neighbouring countries. All public and private hospitals and private healthcare facilities should test patients on admission for the novel coronaviruses if they present with ARDS and have been medically evacuated from the Arabian Peninsula or its neighbouring countries. Referring providers should inform the recipient hospital if testing for novel coronavirus has been performed.
- 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.

Main conclusions and recommendations (continued)

- Any probable or confirmed case diagnosed in the EU/EEA should be reported to national authorities through the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (2005). Reporting through EWRS allows for an automatic IHR notification and avoids double reporting. Patients still under investigation do not need to be reported internationally before confirmation. However, notification at state and national levels needs to follow national legislation or guidance to allow the implementation of infection control measures, initiation of outbreak investigation, and epidemiological monitoring.
- A specific serological test and seroepidemiological studies are needed to investigate the occurrence of mild and asymptomatic infections.
- ECDC endorses WHO's travel advice and does not advise any travel or trade restrictions for Saudi Arabia or Qatar.
- WHO and ECDC re-emphasise the importance of timely and thorough investigations; this includes the reporting of any clusters of severe acute respiratory infections in the community or in healthcare workers, regardless of where in the world they occur.

Public health issue

This is the second update of the Rapid Risk Assessment on severe respiratory disease associated with a novel coronavirus. It was produced in view of two recent developments:

- The retrospective diagnosis of novel coronavirus infections in two fatal cases of severe pneumonia in April 2012 in Jordan. The two cases were part of a cluster of 11 cases of pneumonia linked in time and space to a hospital in Jordan in April 2012.
- The publication of the results of an ECDC survey of European laboratories on diagnostic capacities for novel coronavirus in Europe.

Source and date of request

ECDC internal decision, 30 November 2012.

ECDC internal response team

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Disease background information

The first known infection with novel coronavirus was reported in a 60-year-old Saudi male who died from severe pneumonia complicated by renal failure in Jeddah on 24 June 2012. The genome of the new coronavirus was sequenced at Erasmus University in Rotterdam, Netherlands, and is now in the public domain. In September 2012, a second case, a 49-year-old male Qatar resident, presented with symptoms similar to the first case. After the patient was referred to London for specialist care, a coronavirus could be isolated which was genetically almost identical to the one isolated from the first case. In November 2012, an additional five cases with similar symptomatology were diagnosed in Saudi Arabia and Qatar. The second Qatari case had onset of symptoms in October and was referred to Germany for medical care. Samples taken in mid-October in Qatar tested positive for novel coronavirus in a UK Health Protection Agency laboratory on 20 November. Virus RNA was also detected by the Robert Koch Institute (RKI) in a bronchoalveolar lavage sample taken on 25 October. Samples taken on 23 November 2012 – after the patient had recovered – tested negative with the same method, indicating that viral shedding had stopped. More information on the case treated in Germany is available on the RKI homepage at http://www.rki.de/EN/Home/Corona_Virus.html.

The novel virus is distinctly different from the coronavirus which caused the SARS outbreaks in 2003 and genetically related to bat coronaviruses. No animal reservoir or mode of zoonotic transmission has yet been identified for the novel coronavirus. Analysis of virus tropism indicates that the virus can infect a variety of cell lines, including human cells. For more information about the clinical case presentations, diagnostic procedures and virus genetics, please refer to the [Rapid Risk Assessment](#) of 24 September 2012 and the following Eurosurveillance articles:

- 'Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction' (available from: <http://www.eurosurveillance.org>)
- 'Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012' (available from: <http://www.eurosurveillance.org>)

As of 4 December 2012, there are a total of nine confirmed novel coronavirus cases in three countries. All infections appear to have been locally acquired in either Jordan, Qatar or Saudi Arabia. The two first reported cases are described in ECDC's Rapid Risk Assessment of [24 September 2012](#); the third case is described in an ECDC epidemiological update dated [6 November 2012](#); three further cases are featured in the update of the Rapid Risk Assessment of [26 November 2012](#); the latest three cases are described in an ECDC epidemiological update published on [30 November 2012](#).

All confirmed patients presented with pneumonia but a significant proportion also developed renal failure during the course of the illness. In two instances, infections occurred in clusters, one involving three cases in a family in Riyadh, Saudi Arabia, and one involving two laboratory-confirmed cases among healthcare workers with respiratory symptoms in a hospital near Amman, Jordan.

Table. Confirmed cases of novel coronavirus infection, April to 5 December 2012, in temporal order of symptom onset

	Onset	Age (years)	Sex	Probable place of infection	Date reported	Source	Outcome
1	April 2012	45	F	Jordan**	30/11/12	WHO/IHR	Dead
2	April 2012	25	M	Jordan**	30/11/12	WHO/IHR	Dead
3	13/06/12	60	M	Saudi Arabia	20/09/12	Saudi Arabia/ProMed	Dead
4	03/09/12	49	M	Qatar/Saudi Arabia***	22/09/12	HPA/WHO	Alive
5	NK	NK	NK	Saudi Arabia	04/11/12	Saudi Arabia/ SMJ/ProMed	Alive
6	12/10/12	45	M	Qatar****	23/11/12	RKI / WHO	Alive
7	NK	NK	M	Saudi Arabia*	19/11/12-23/11/12	Saudi Arabia/ ProMed /WHO	Alive
8	28/10/12	NK	M	Saudi Arabia*	23/11/12	WHO	Dead
9	Oct 2012	NK	M	Saudi Arabia*	28/11/12	WHO	Dead

* Part of family cluster

** Healthcare worker and part of outbreak linked to hospital

*** Patient transferred to UK

**** Patient transferred to Germany

NK: not known

Update on event information

The most significant recent epidemiological development is the retrospective identification of novel coronavirus in preserved biological samples from two fatal cases of severe pneumonia in Jordan in April 2012. The two cases were part of a cluster of eleven cases with respiratory symptoms linked in time and space to a hospital near Amman, Jordan. Eight of the cases in the cluster were healthcare workers. The two confirmed cases were reported on 30 November 2012 through the Event Information Site for International Health Regulation Focal Points and in a WHO press statement. A cluster of this size, especially when involving healthcare workers, raises questions about the possibility of human-to-human transmission. It is important to note, however, that there are reports that some or all of the nine non-fatal cases in the cluster were also tested for novel coronavirus, yet epidemiological information about this remains limited.

ECDC, jointly with WHO, has mapped the capacity of virology reference laboratories in EU/EEA Member States with regard to the novel coronavirus (RT-PCR/sequencing assay). So far, approximately 250 people have been tested for the novel coronavirus in the EU since the first case was reported. Except for the two confirmed cases, which were referred to the UK and Germany, none of the tests were positive. The results of this survey were published in Eurosurveillance on [6 December 2012](#).

Case definition

On 3 December, WHO published the revised '[Interim surveillance recommendations for human infection with novel coronavirus](#)', which include a definition for 'patient under investigation': a confirmed case is a case in which novel coronavirus has been identified in a biological sample from the patient.

Threat assessment for the EU

The retrospective identification of novel coronavirus infection in two fatal cases in Jordan has increased the geographical area in which transmission has been confirmed and also raised questions about possible nosocomial and human-to-human transmission. A total of 11 cases with respiratory symptoms was recorded in that cluster, but only the two fatal cases have tested positive for novel coronavirus. However, the currently available information about the cluster is very limited and does not allow confirmation or exclusion of human-to-human transmission. It is not known whether the nine non-fatal cases were of the same severity, whether they were investigated for novel coronavirus, or if there are preserved biological samples from the time of illness which could be tested. A serological test for novel coronavirus is being developed, and without such a test it is not possible to test for past disease.

Despite intensive surveillance among contacts of the two cases treated in Germany and the United Kingdom as well as among healthcare workers, there are no indications of secondary or nosocomial transmission. The risk of nosocomial transmission should be re-assessed when more information becomes available on the Jordan cluster.

The absence of expanding clusters of cases indicates that the risk of infection remains very low, although some human-to-human transmission is thought possible in the Jordan cluster.

So far, epidemiological information available about the disease caused by the novel coronavirus is very limited and many uncertainties remain, for example incubation period, infectiousness, reservoirs, routes of transmission, geographical distribution, and duration of viral shedding from infected human cases.

Two of the nine confirmed cases were diagnosed after the patients were transferred for tertiary care in the United Kingdom and Germany. Patients presenting with ARDS in and around the Arabian Peninsula will continue to be referred to hospitals in the EU for further care. Clinicians – particularly intensive-care physicians – should actively investigate epidemiological links and maintain a low threshold for testing for novel coronavirus in patients coming from this region.

The diagnostic capacity for novel coronavirus appears to be adequate in the EU. The virus genome is in the public domain and mechanisms for sharing samples and diagnostic methods between countries and laboratories are in place. Protocols can be obtained from the [Institute of Virology](#) at the University of Bonn, Germany; more information on this topic is available in articles by Bermingham et al. [15] and Corman et al. [7] and from the ENIVD website.

Family members of patients or healthcare workers treating persons from the Arabian Peninsula with severe acute respiratory infections may be at risk of infection with the novel coronavirus unless personal protective measures are applied. It is possible that novel coronavirus infections are more widespread than indicated by the low number of confirmed infections. WHO has signalled that it intends to broaden the scope of case-finding by including clusters of severe acute respiratory infection (SARI) of unknown aetiology, with a special focus on clusters of SARI among healthcare workers.

Conclusions

All cases identified so far were reported from the Arabian Peninsula: Saudi Arabia (5), Qatar (2) and Jordan (2). The virus reservoir and route of transmission remain unknown. In two instances the cases were clustered: in a family in Riyadh (three cases) and in an outbreak of respiratory disease among healthcare workers in Jordan (two cases). Investigations have so far failed to find any conclusive evidence of human-to-human or nosocomial transmission.

The broad geographical distribution, the long intervals between cases and clusters, and the absence of evidence for mild or asymptomatic human infections which could maintain a chain of transmission between outbreaks, point to intermittent zoonotic transmission or an environmental source. Zoonotic transmission does not exclude human-to-human transmission from an index case, but there is no evidence to date that this has occurred. The cluster in Jordan raises the question whether human-to-human transmission may be possible. However, the amount of information available from Jordan and WHO is insufficient to further assess this possibility. The outbreak involved 11 cases with respiratory symptoms, but only the two fatal cases were retrospectively tested and confirmed. It is possible that some or all of the non-fatal cases were caused by another infective agent.

Europe's capacity for the investigation and laboratory confirmation of the novel coronavirus infection is adequate.

It is possible that enhanced surveillance in the Arabian Peninsula and worldwide will detect additional sporadic cases or clusters in future.

Recommendations

Healthcare workers should be alerted to the possibility of attending to patients who meet specific [characteristics](#) which would require an investigation as per [WHO case definition](#). Such cases should be investigated rapidly and managed as recommended by WHO or in national guidance documents.

EU Member States should consider novel coronavirus in patients with severe respiratory disease of unknown origin returning from countries in the Middle East in addition to those in the Arabian Peninsula, including: Jordan, Kuwait, Qatar, Saudi Arabia, Bahrain, Iran, Iraq, the United Arab Emirates, Oman, Yemen, Syria, Lebanon, Occupied Palestinian territories and Israel.

The new WHO recommendations for the investigation of patients favour the investigation of patients whom return from the Arabian Peninsula and its neighbouring countries, but do not exclude the testing of patients with unexplained pneumonia in the absence such travel. The possibility of co-infection and colonisation should also be considered; identification of a possible causative agent should not exclude testing for novel coronavirus.

Healthcare workers caring for patients under investigation should exercise stringent infection control measures and adhere to national or [international guidance](#). Similarly, health professionals engaged in medical evacuation of patients presenting with ARDS should be particularly vigilant, especially if patients originate from the Arabian Peninsula or its neighbouring countries as defined above.

Testing for the novel coronaviruses should be considered in patients undergoing medical evacuation for ARDS prior to their transfer out of the Arabian Peninsula or its neighbouring countries. All public and private hospitals and private healthcare facilities should test patients on admission for the novel coronaviruses if they present with ARDS and have been medically evacuated from the Arabian Peninsula or its neighbouring countries. Referring providers should inform the recipient hospital if testing for novel coronavirus has been performed.

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.

Any probable or confirmed case diagnosed in the EU/EEA should be reported to national authorities; confirmed cases should be reported via the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (2005). Countries may consult with WHO under Article 8 of the IHR. However, notification at state and national levels needs to follow national legislation or guidance to allow for the implementation of infection control measures, initiation of outbreak investigation, and epidemiological monitoring.

A specific serological test and seroepidemiological studies are needed to investigate the occurrence of mild and asymptomatic infections.

ECDC agrees with WHO on the point of travel to affected areas and does not advise any travel or trade restrictions for Saudi Arabia, Qatar or Jordan.

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

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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 Interim Guidelines on Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care, 2007: http://www.who.int/csr/resources/publications/swineflu/WHO_CDS_EPR_2007_6/en/index.html