

SEVERE ACUTE RESPIRATORY INFECTIONS ASSOCIATED WITH A NOVEL CORONAVIRUS, EMC 2012

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Introduction

In the last few months the World Health Organisation has alerted countries to several reports of a new coronavirus associated with severe respiratory disease

in patients with an epidemiological link to the Arabian Peninsula.¹ Coronaviruses are a large family of viruses, some of which may cause respiratory infections in humans and animals. Such respiratory infections may

range from mild respiratory illness (such as the common cold) but can also include more serious disease. The new coronavirus, human coronavirus-Erasmus Medical Centre 2012 (EMC-2012), was first identified in September 2012 from a patient in Saudi Arabia who died from a severe respiratory infection in June 2012.¹ The novel coronavirus has thus far only been identified in a small

number of cases of acute, serious respiratory illness who presented with fever, cough, shortness of breath and breathing difficulties. To date, WHO has been informed of a total of 17 confirmed cases of human infection with the novel coronavirus, including eleven deaths globally.² These cases are summarized in table 1.

Table 1. Confirmed cases by country of human infection with novel coronavirus, EMC-2012.

Country	# of cases	# cases with travel history	Place Diagnosed	# of deaths	Risk factors
Saudi Arabia	9	Not applicable	Saudi Arabia	6	
Qatar	2	Not applicable	1 United Kingdom 1 Germany	1	
Jordan	2	Not applicable	Jordan	2	
United Kingdom	3	1 (Saudi Arabia and Pakistan)	United Kingdom	2	Underlying malignant condition
United Arab Emirates	1	Not applicable	Germany	1	

The aim of this article is to provide information concerning currently available data on this virus to healthcare providers in South Africa.

Clinical presentation

Patients have generally presented with pneumonia, although a significant proportion have also experienced renal failure. With the exception of one case from the UK cluster, all confirmed cases presented with severe respiratory illness.²

Transmission

Based on the small number of cases reported so far, there is limited information on mode of transmission, source of the virus, its geographic extent and the spectrum of illness. Genetic sequencing to date suggests that the virus is closely related to coronavi-

ruses detected in bats.³

Infections occurred in clusters in three instances. The first cluster of two fatal cases from Jordan occurred in April 2012. Stored samples from these two cases tested positive retrospectively for the novel coronavirus. These were part of a hospital cluster of 11 cases (2 confirmed and 9 probable cases), 8 of whom were health workers. The second cluster occurred in October 2012 in a family from Saudi Arabia with three confirmed cases and one probable case. Two of them died. The most recent cluster occurred in the UK in February 2013. In this cluster three family members presented with laboratory confirmed novel coronavirus infection. Two of them reported no recent travel history outside of the UK suggesting that transmission had occurred in the UK. One family member had travelled to the Middle East and

Pakistan and was ill on his return. One case with an underlying pre-existing medical condition that might have increased susceptibility to infection died.⁴

Recent information from the UK family cluster suggests that human-to-human transmission does occur and it may have occurred in two instances in the Middle East. The mode of human-to human transmission is unknown but may involve different routes of transmission such as droplet and contact transmission.²

Who should be tested for novel coronavirus?

WHO recommends that testing for the new coronavirus should be considered in patients with unexplained pneumonias, or in patients with unexplained, severe, progressive or complicated respiratory illness who are not responding to treatment. Any clusters of severe acute respiratory illness (SARI) or SARI in health care workers should be thoroughly investigated, regardless of where in the world they occur.²

A prioritisation process should ensure that testing for the novel coronavirus is undertaken only when there is clinical or epidemiological link to a patient or region with laboratory confirmed case/s. This serves to avoid the inappropriate use of scarce resources, the generation of false positives and the risk of overwhelming the health system. If clinicians are not sure whether a patient meets the criteria for testing, the Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD), National Health Laboratory Service, can be contacted through the NICD Hotline: 0828839920. Additional information on laboratory testing and contact details can be accessed from the NICD website

([www.nicd.ac.za: About us – Our Centres – Respiratory Disease and Meningitis](http://www.nicd.ac.za>About-us-Our-Centres-Respiratory-Disease-and-Meningitis)).⁴

WHO Case definition as of 3 December 2012⁵

Patients under investigation

A person with acute respiratory infection, which may include history of fever or measured fever ($\geq 38^{\circ}\text{C}$) and cough,

AND

Suspicion of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome), based on clinical or radiological evidence of consolidation,

AND

Residence in or history of travel to the Arabian Peninsula or neighbouring countries within 10 days prior to onset of illness,

AND

Not already explained by any other infection or aetiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines. It is not necessary to wait for all test results for other pathogens before testing for novel coronavirus.

Probable Case

A person with an acute respiratory infection* with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome, (ARDS)),

AND

no possibility of laboratory confirmation for novel coronavirus either because the patient or samples are not available for testing,

AND

close contact** with a laboratory-confirmed case.

* This may include but is not limited to cases with a history of fever or measured fever.

** Close contact includes:

anyone who provided care for the patient, including a health care worker or family member, or who had other

similarly close physical contact;
anyone who stayed at the same place (e.g. lived with, visited) as a probable or confirmed case while the case was symptomatic.

Confirmed Case

A person with a laboratory confirmation of infection with the novel coronavirus
(http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/index.html).

Contacts

Individuals with acute respiratory illness of any degree of severity who, within 10 days before onset of illness, were in close physical contact with a confirmed or probable case of novel coronavirus infection, while the case was ill.

Any person who has had close contact with a probable or confirmed case while the probable or confirmed case was ill should be carefully monitored for the appearance of respiratory symptoms. If symptoms develop within the first 10 days following contact, the individual should be considered a “patient under investigation”, regardless of the severity of illness, and investigated accordingly.

Clusters

Any cluster of severe acute respiratory infection, particularly clusters of patients requiring intensive care, without regard to place of residence or a history of travel,

AND

Not already explained by any other infection or aetiology, including all clinically indicated tests for

community-acquired pneumonia according to local management guidelines.

Health care workers

Health care workers with pneumonia, who have been caring for patients with severe acute respiratory infections, particularly patients requiring intensive care, without regard to place of residence or history of travel, AND

Not already explained by any other infection or aetiology, including all clinically indicated tests for community-acquired pneumonia according to local management guidelines.

Specimen collection and transport

Based on current but limited information, lower respiratory specimens (naturally produced sputum, broncho-alveolar lavage, tracheal aspirates, and tissue from biopsy/autopsy from lung) appear to have the highest titre. Upper respiratory specimens (nasopharyngeal aspirate, combined nose/throat swab, nasopharyngeal swab) are also recommended (table 2).⁵ Paired serum samples should also be collected and stored. Respiratory virus diagnosis depends on the collection of high-quality specimens, their rapid transport to a laboratory and appropriate storage before laboratory testing. Virus is best detected in specimens containing infected cells and secretions. Specimens should be collected as soon as possible, preferably during the first 72 hours after onset of disease. However, specimens will still be processed if collected up to 7 days after the onset of symptoms.⁵

Table 2. Coronavirus specimen collection, packaging and transport.

Specimen type	Transport medium	Transport to laboratory	Dangerous goods shipping category	Comment
Naturally produced sputum*	no	On ice. If a delay in testing of > 24 hours consider freezing with dry ice	Biological substance, Category B	The preferred sample but need to ensure the material is from the lower respiratory tract.
Bronchoalveolar lavage	no	On ice. If a delay in testing of > 24 hours consider freezing with dry ice	As above	There may be some dilution of virus but still a worthwhile specimen.
Tracheal aspirate	no	On ice. If a delay in testing of > 24 hours consider freezing with dry ice	As above	
Nasopharyngeal aspirate	no	On ice. If a delay in testing of > 24 hours consider freezing with dry ice	As above	
Combined nose/throat swab	Virus transport medium	On ice.	As above	Virus has been detected in this type of specimen
Nasopharyngeal swab	Virus transport medium	On ice.	As above	
Tissue from biopsy or autopsy including from lung	Virus transport medium or saline	On ice. If a delay in testing of > 24 hours consider freezing with dry ice	As above	
Serum for serology or virus detection: always collect paired samples if possible. Acute – first week of illness Convalescent -3 to 4 weeks later	no	On ice or frozen	As above	
Whole blood	EDTA anticoagulant	On ice	As above	For virus detection, particularly in the first week of illness

* The collection of induced sputum samples may pose an additional infection risk for health care workers.

Source: Interim surveillance recommendations for human infection with novel coronavirus, 3 December 2012⁵

Laboratory test methods and algorithm

All suspected cases should be referred to the CRDM which is a WHO reference laboratory for the testing of novel coronavirus in Africa. A number of reverse transcription polymerase chain reaction RT-PCR assays that are specific for the novel coronavirus have been developed and published.⁵ The assay for the E protein

gene target (UpE) is considered highly sensitive, and has been implemented at the NICD. A second confirmation PCR on the open reading frame 1b (ORF1b) will be performed on all UpE positive specimens and a pan-Coronavirus PCR will be run on all specimens.

The following criteria are used to laboratory confirm a case:

- Positive PCR assay for at least two different specific targets in the novel coronavirus genome; or
- One positive PCR assay for a specific target in the novel coronavirus genome and an additional different PCR product sequenced.⁵

Patients meeting the case definition should also undergo routinely available laboratory investigations for common aetiologies of community acquired pneumonia. The CRDM is able to test for: Para-Influenza viruses 1-3, influenza A virus, influenza B virus, respiratory syncytial virus, enterovirus, rhinovirus, human metapneumovirus, adenovirus, human bocavirus, human coronaviruses 229E, OC43, NL63 and HKU1, by real-time PCR. These tests will be run in parallel with the novel coronavirus specific PCR on all suspected cases.

Infection control

It is advised by WHO that standard and droplet precautions should be applied to all patients with confirmed and suspected coronavirus infection. Airborne

precautions should be added when performing aerosol generating procedures.⁶ Additional information on infection control can be accessed from the WHO website.⁷

Surveillance for novel coronavirus implemented at NICD

Private and public health care professionals are invited to submit cases of severe acute respiratory infections, meeting the case definition of unexplained pneumonia or a travel history to the Arabian Peninsula, for investigation of the novel coronavirus.

Advice on travel

The WHO does not recommend that any travel or trade restrictions be applied. In addition, no screening at points of entry should be enforced.⁵

Updated information

The situation with regards to this virus is rapidly evolving as new cases are detected and reported. For updated information please consult the NICD webpage at www.nicd.ac.za or World Health Organisation at www.who.int/csr/disease/coronavirus_infections.

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