Alert, verification and public health management of SARS in the post-outbreak period

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1.Rationale for continued vigilance for SARS

First recognized as a global threat in mid-March 2003, Severe Acute Respiratory Syndrome (SARS) was successfully contained in less than four months. On 5 July 2003, WHO reported that the last human chain of transmission of SARS had been broken.

While much has been learned about this syndrome since March 2003, including its causation by a new coronavirus (SARS-CoV), our knowledge about the epidemiology and ecology of SARS coronavirus infection and of this disease remains limited. Resurgence of SARS remains a distinct possibility and does not allow for complacency.

In the post-outbreak period, all countries must remain vigilant for the recurrence of SARS and maintain their capacity to detect and respond to the re-emergence of SARS should it occur. The WHO case definitions during the outbreak period relied heavily on epidemiological criteria to increase the specificity of syndromic clinical criteria for atypical pneumonia or respiratory distress syndrome (RDS). However, epidemiological links to cases of SARS and areas reporting recent local transmission are no longer of use in helping to define incident cases. Furthermore, the non-specific clinical features of SARS, the lack of a current rapid diagnostic test that can reliably detect SARS-CoV in the first few days of illness, and the seasonal occurrence of other respiratory diseases, including influenza, may confound any surveillance for SARS or demand a level of quality and intensity which few health care system worldwide can sustain. Even with the most sophisticated surveillance systems, the first case of SARS in the post-outbreak period may escape early detection.

This document describes a SARS alert mechanism for the post-outbreak period. It provides guidance for managing a SARS "alert" through to laboratory confirmation or exclusion of persons under investigation as SARS cases. The document does not address complex surveillance issues or case categorization for SARS.

It also provides guidance to clinicans on the clinical presentation, laboratory and radiological findings to assist in diagnosis of SARS and in decisions to implement transmission-based infection control.

For additional information on the previous SARS outbreak, please also refer to SARS: breaking the chains of transmission

2. Risk assessment

Ideally, each Member State should determine the intensity of its surveillance for SARS in the post-outbreak period on the basis of a risk assessment. WHO has defined three major areas that take into account the experience during the recent outbreak of SARS and the potential for resurgence:

Potential zone of re-emergence of SARS-CoV

- Identified as source(s) of the previous outbreak in November 2002 or areas with an increased likelihood of animal to human transmission of SARS-CoV infection.

Nodal areas

- Sustained local transmission experienced during the previous outbreak or entry of large numbers of persons from the potential zone of re-emergence of SARS-CoV.

Low risk areas

- Never reported cases, reported only imported cases or experienced only limited local transmission during the previous outbreak.

Thus, WHO recommends a staged approach to surveillance:

Potential zone of re-emergence of SARS

- SARS Alert **AND**
- enhanced surveillance for SARS**AND**
- special studies for SARS-CoV infections in animal and human populations

Nodal areas

- SARS Alert **AND**
- enhanced surveillance for SARS

Low risk areas

- Surveillance for clusters of "alert" cases among health care workers, other hospital staff, patients and visitors in the same health care unit (see section 3 – The SARS Alert)

3. The SARS Alert

The SARS Alert is an operational definition to ensure that appropriate infection control and public health measures are implemented until SARS has been ruled out as a cause of the atypical pneumonia or RDS.

3.1 Objectives of the SARS Alert

- Provide early warning of the potential recurrence of SARS to:
  - rapidly implement appropriate infection control measures
  - expedite diagnosis
  - activate the public health response
- Raise a global alert if indicated

Definition of a SARS Alert

Two or more health care workers in the same health care unit fulfilling the clinical case definition of SARS (see section 3.3) and with onset of illness in the same 10-day period.

OR

Hospital acquired illness in three or more persons (health care workers and/or other hospital staff and/or patients and/or visitors) in the same health care unit fulfilling the clinical case definition of SARS (see section 3.3) and with onset of illness in the same 10-day period.

A jurisdiction may chose, based on its experience, to increase the minimum number of "alert" cases defining a cluster. The definition of the health care unit in which the cluster occurs will depend on the local situation. Unit size may range from an entire health care facility if small, to a single department or ward of a large tertiary hospital.

3.2 Case description of SARS

See Annex 1 Clinical description of SARS. The case description provides details of the clinical evolution of SARS and radiological and laboratory findings to assist clinicians with its diagnosis. It provides information on the spectrum of the disease, including atypical presentations.

3.3 Case Definitions

Clinical case definition of SARS
The following clinical case definition has been developed for public health purposes.

A person with a history of:

Fever (≥ 38°C)

AND One or more symptoms of lower respiratory tract illness (cough, difficulty breathing, shortness of breath)

AND

Radiographic evidence of lung infiltrates consistent with pneumonia or RDS **OR** autopsy findings consistent with the pathology of pneumonia or RDS without an identifiable cause.

AND
No alternative diagnosis can fully explain the illness.

Laboratory case definition of SARS

A person with symptoms and signs that are clinically suggestive of SARS **AND** with positive laboratory findings for SARS-CoV based on one or more of the following diagnostic criteria:

a) PCR positive for SARS-CoV
PCR positive using a validated method from:

- At least two different clinical specimens (eg nasopharyngeal and stool) **OR**
- The same clinical specimen collected on two or more occasions during the course of the illness (eg sequential nasopharyngeal aspirates) **OR**
- Two different assays or repeat PCR using a new RNA extract from the original clinical sample on each occasion of testing.

b) Seroconversion by ELISA or IFA

- Negative antibody test on acute serum followed by positive antibody test on convalescent phase serum tested in parallel **OR**
- Fourfold or greater rise in antibody titre between acute and convalescent phase sera tested in parallel

c) Virus isolation

- Isolation in cell culture of SARS-CoV from any specimen **AND** PCR confirmation using a validated method.

Testing should only be undertaken in a national or regional reference laboratory as per WHO recommendations (Use of laboratory methods for SARS diagnosis). WHO will assist resource poor countries to confirm their first cases of SARS through laboratory collaboration.

3.4 Public health management of a SARS Alert

When a SARS Alert is raised:
1. Patient(s) should be immediately isolated and transmission-based precautions instituted, if not already in place (see clinical management guidelines)

2. The diagnosis should be expedited (see Annex 2 Guidance regarding the diagnosis of SARS in the post-outbreak period – A concern for all health care workers). WHO will assist in the investigation of SARS alerts as appropriate, including the facilitation of access to laboratory services (see Annex 3 WHO Focal Points for SARS).

3. Contacts of persons under investigation for SARS should be traced and quarantined **until SARS has been ruled out as the cause of the illness** .

3.1 A contact is a person who is at greater risk of developing SARS because of exposure to a SARS case. Risky exposures include having cared for, lived with, or having had direct contact with the respiratory secretions, body fluids and/or excretions (e.g. faeces) of cases of SARS.

3.2 Individuals with risky exposures to a person or persons in a SARS alert cluster should be managed as contacts until SARS has been ruled out as the cause of the illness.

3.3 Contact within the health care setting should be managed in the following way:

- Inpatient contacts should be isolated or cohorted away from unexposed patients and transmission-based precautions instituted. They should be placed on fever surveillance.

- Exposed staff should be placed on active fever surveillance, and either cohorted to care for exposed patients (as above) or placed on home quarantine depending on local circumstances.

3.4 Community contacts should be:

- Given information on the clinical picture, transmission, etc. of SARS
- Placed under active surveillance for 10 days and voluntary home quarantine recommended
- Visited or telephoned daily by a member of the public health care team
- Temperature recorded daily.
- If the contact develops disease symptoms, they should be investigated locally at an appropriate health care facility.
- The most consistent first symptom that is likely to appear is fever.

3.5 National public health authorities should report every laboratory confirmed case of SARS to WHO (see below).

International reporting of SARS

A new outbreak of SARS is defined as the occurrence of one or more clinically compatible, laboratory-confirmed cases of SARS in any country based on definitive laboratory investigations. The reappearance of SARS in the human population would be considered a global public health emergency.

For the purposes of the international reporting of SARS in the post-outbreak period, Member States are requested to inform WHO of laboratory-confirmed cases only.

Laboratory confirmed cases of SARS could be detected through a SARS alert verification process but also as sporadic case(s) of acute respiratory illness on which SARS-CoV testing was undertaken (i.e. fulfil the case definition described in section 3.3). Reporting to WHO should include both of these scenarios but should **exclude** asymptomatic persons with a positive laboratory test or symptomatic persons without laboratory confirmation. No nil reporting is required.

WHO requests that Members States immediately inform the focal points at Regional Offices or Headquarters of every person meeting the laboratory-confirmed case definition of SARS (see Annex 3 WHO Focal Points for SARS). This will allow WHO to assess the need for a global alert and re-institute global surveillance for SARS on the basis of that notification as appropriate.

The development of new case definitions applicable to the new situation, surveillance standards and a step-down strategy may be required once laboratory-confirmed cases have been reported.

In the event of an international traveller being investigated for SARS, all Member States involved in international contact tracing around the case(s) should communicate directly with each other during the investigation. WHO should be informed only when the incident is laboratory confirmed.

WHO will continue to identify and verify rumours of events of international public health concern, including rumours about SARS, through its usual well-established mechanisms.

Indicators of the quality of the SARS alert mechanism

WHO recommends that national public health authorities monitor the quality of the SARS alert mechanism, e.g. by establishing indicators based on:

- the number of alerts expected and reported by health facilities over time
- the time taken to implement transmission-based precautions and expedite diagnosis
- the time taken to alert local public health authorities, national public health authorities
- the time taken to complete contact tracing and quarantine contacts.

This list is not meant to be exhaustive but rather a suggested approach to monitoring the alert mechanism.

4. Enhanced surveillance and special studies for SARS-CoV infections in animal and human populations

Jurisdictions in nodal areas and areas of potential re-emergence have maintained heightened SARS surveillance established during the outbreak period, and continue doing so for the foreseeable future. WHO will encourage these jurisdictions to make available to the global community the details of these surveillance activities and will offer its assistance in summarizing and updating available information on its web site.

Depending on risk assessment and available resources, nodal areas and areas of potential re-emergence may include one or more of the following activities:

- Surveillance for atypical pneumonia in settings such as nursing homes, rehabilitation units, community health care centres and in private practice (see Annex, Guidance regarding the diagnosis of SARS in the post-outbreak period - A concern for all health care workers)
- Surveillance of persons discharged from hospital with a diagnosis of unspecified atypical pneumonia
- Surveillance for absenteeism among health care workers
- Laboratory-based surveillance of SARS-CoV infection
- Surveillance for requests for laboratory testing of respiratory pathogens or SARS-CoV
- Surveillance for unexplained deaths following an acute respiratory illness
- Serological surveillance of high risk populations (health care workers, animal handlers, market vendors, hunters, etc)
- Community-based serological surveys to monitor changes in the seroprevalence of SARS-CoV infection
- Serosurveys among animal populations.

This list is not meant to be exhaustive but rather a suggested approach to enhanced surveillance.

Annex 1 Clinical case description of SARS

Aetiology

Severe acute respiratory syndrome (SARS) is a disease caused by SARS coronavirus (SARS-CoV).

Epidemiology

Nosocomial transmission of SARS CoV has been a striking feature of the SARS outbreak. The majority of the cases are adults. Children are rarely affected.

The mean incubation period is 5 days with the range of 2-10 days although there are isolated reports of longer incubation periods. There have been no reports of transmission occurring before the onset of symptoms.

Natural history of the disease

Week 1 of illness

Patients initially develop influenza-like prodromal symptoms. Presenting symptoms include fever, malaise, myalgia, headache, and rigors. No individual symptom or cluster of symptoms has proven specific. Although history of fever is the most frequently reported symptom, it may be absent on initial measurement.

Week 2 of illness

Cough (initially dry), dyspnoea and diarrhoea may be present in the first week but more commonly reported in the second week of illness. Severe cases develop rapidly progressing respiratory distress and oxygen desaturation with about 20% requiring intensive care. Up to 70% of the patients develop diarrhoea which has been described as large volume and watery without blood or mucus. Transmission occurs mainly during the second week of illness.

Clinical outcomes

Based on an analysis of data from Canada, China, Hong Kong SAR, Singapore, Viet Nam and the United States the case fatality ratio (CFR) of SARS is estimated to range from 0% to more than 50% depending on the age group affected, with an overall CFR estimate of approximately 11% (see Update 49 - SARS case fatality ratio, incubation period). Higher mortality has also been associated with male sex and presence of co-morbidity in various studies.

Elderly and paediatric cases and SARS in pregnancy

Atypical presentations such as afebrile illness or concurrent bacterial sepsis/pneumonia have been highlighted as a particular problem in the elderly. Underlying chronic conditions and their more frequent use of health facilities have both contributed to initially unrecognized nosocomial transmission events.

SARS occurred less frequently and was observed to be a milder illness in the paediatric population.

Known cases of SARS in pregnancy have suggested an increase in fetal loss in early pregnancy and maternal mortality in later pregnancy.

Radiological findings

Early chest radiograph or CT changes are observed in most of the patients as early as days 3-4 of illness in spite of the absence of respiratory signs. These typically show patchy consolidation starting with a unilateral peripheral lesion which progress to multiple lesions or ground glass appearance. Some lesions follow a shifting pattern. Features during the later stages have sometimes included

spontaneous pneumothorax, pneumomediastinum, sub-pleural fibrosis and/or cystic changes.

Haematological and biochemical findings

There are no haematological or biochemical parameters specific for SARS; however, studies have consistently highlighted the following:

Haematological findings

Lymphopenia is common on presentation and progresses during the course of the illness. Sometimes thrombocytopenia and prolonged APTT are observed.

Biochemical findings

LDH is frequently high and some reports have suggested association with poor prognosis. ALT, AST and CPK elevation are less frequently reported. Abnormal serum electrolytes have also been reported on presentation or during hospitalization including hyponatraemia, hypokalaemia, hypomagnesaemia and hypocalcaemia.

Annex 2 Guidance regarding the diagnosis of SARS in the post-outbreak period – A concern for all health care workers (HCW's)

Making a diagnosis of SARS sufficiently early in the disease to implement effective infection control and public health measures will prove a challenge that requires all HCWs to always incorporate risk-based infection control measures in care provision. This will only occur within a culture that treats infection prevention and control as everyone's responsibility. All HCWs should be encouraged to consider the possibility of SARS in a patient under their care. If there are features suggestive of SARS then any concerns should be raised promptly and trigger risk-based infection control measures. There must be monitoring and feedback on this process.

The non-specific nature of the presentation of SARS could lead to concern being raised in a vast number of patients who will ultimately prove to have another diagnosis. In practice, concern about the possibility of SARS may often be expressed at the stage where atypical pneumonia is suspected.

This process should not rely wholly on clinicians but should be responsive to the concerns raised by other HCWs.

Concern of SARS raised by clinicians

For clinicians the process of diagnosis from initial concern to confirmation or exclusion of a SARS diagnosis (see case description) is usually an incremental one following sequential information gathering from various sources that include:

- clinical history
- clinical examination
- bedside monitoring
- radiology investigations
- haematology investigations
- biochemistry investigations
- microbiology and virology investigations
- response to treatment
- epidemiological information obtained from the individual, the health facility or the community.

Concern about SARS raised by other health professionals

Concerns regarding SARS may be raised by any HCW. All HCW's need to ensure they are fully aware of what constitutes a clinical concern about SARS and how, in the course of their duties they could be involved in the presentation, investigation or treatment of an unrecognized SARS case.

They should be encouraged to raise concerns with both the clinicians and infection control team who should provide monitoring and feedback on the process.

Some examples are given:

- infection control staff e.g. noting an increase in hospital acquired pneumonias
- nursing staff e.g. noting a pattern of deterioration in a patient suggestive of SARS
- staff involved in care of the elderly e.g. noting an increase in severe illness
- occupational health staff e.g. noting staff sickness compatible with atypical pneumonia
- physiotherapists e.g. noting a pattern of atypical pneumonia
- radiographers e.g. noting a pattern of atypical pneumonia
- radiologists e.g. noting a pattern of atypical pneumonia
- haematologists e.g. noting a profile suggestive of atypical pneumonia
- biochemists e.g. noting a profile suggestive of atypical pneumonia
- microbiologists e.g. noting an increase in undiagnosed pneumonias

- virologists e.g. noting an increase in requests for respiratory serology
- pharmacists e.g. noting an increase in prescribing for pneumonia

Atypical pneumonia

Common bacteria, such as *Streptococcus pneumoniae* and *Haemophilus influenzae* cause so-called "typical pneumonia". Cases of typical pneumonia present with fever, respiratory symptoms (cough, which is usually early in the illness and often productive, shortness of breath etc.), elevated white cell count and well-defined changes on the chest radiograph. They tend to respond to antibiotic therapy for community acquired pneumonia.

In contrast, "atypical pneumonia" is defined as pneumonia or lower respiratory tract infection with an atypical presentation often with a gradual onset of symptoms such as non-productive, dry cough, a variable white blood cell count and the chest radiograph changes. These include patchy, poorly defined changes, which may be often more severe than the clinical picture would suggest. The causative agents include, *Mycoplasma pneumoniae, Chlamydia spp., Legionella pneumophila, Coxiella burnetii.*

Diagnosis of atypical pneumonia is in itself challenging but will be assisted by careful clinical assessment (including non-respiratory symptoms), and given the likely absence of auscultatory signs, accurate measurement of respiratory rate and oxygen saturation (where available) becomes even more important. Chest radiography is of great use in achieving diagnosis and should be considered even in the absence of respiratory signs.

Features of SARS that may commonly help with clinical diagnosis

SARS	Example	Caution
Clinical history	Sudden onset of flu-like prodrome, dry cough, non –respiratory symptoms e.g. diarrhoea common	Take a travel history, history of hospitalisation and history of contact with healthcare facility. The absence of such a history should not automatically exclude diagnosis of SARS.
Clinical examination	Does not correlate with chest radiology changes	Lack of respiratory signs particularly in groups such as the elderly
Bedside monitoring	Hypoxia	Temperature may not be elevated on admission, respiratory rate should be documented
Haematology investigations	Low lymphocyte count	
Biochemistry investigations	Raised LDH	Check profile for electrolytes and liver function
Radiology investigations	CXR changes poorly defined, patchy, progressive changes	May present as a lobar pneumonia, pneumothorax and pneumomediastinum may occur
Microbiology investigations	Investigate for community, and hospital acquired pneumonias including atypical pneumonias	Concurrent infections may occur
Virology investigations	Investigate for other causes of atypical pneumonia	Interpret SARS test results with caution
Treatment	As yet there is not proven treatment for SARS, supportive measures are recommended	Lack of response to treatment with standard antibiotics for community acquired pneumonia including atypical pneumonia may be indicative of SARS

Annex 3 WHO Focal Points for SARS

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