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REVIEW

Hospital management of adults with severe acute respiratory syndrome (SARS) if SARS re-emerges—updated 10 February 2004

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KEYWORDS

SARS; Case definitions; UK guidelines

Summary Severe Acute Respiratory Syndrome (SARS) is a potentially severe and highly infectious disease to which healthcare workers involved in the management of cases are particularly vulnerable. These guidelines briefly summarise optimal and safe practice for clinicians involved in the emergency care of patients with probable or confirmed SARS.

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Introduction

During 2003 Severe Acute Respiratory Syndrome caused by a novel coronavirus (SARS-CoV) emerged as an infectious disease with a significant in-hospital mortality and posed a considerable occupational risk for healthcare workers.¹⁻⁵ The initial SARS outbreak ended in July 2003 when the World Health Organisation (WHO) announced that all known person-to-person transmission of SARS-CoV had ceased. At the time of preparation of these guidelines, there have been a further two laboratory-acquired cases of SARS and further community-acquired cases. These cases emphasise the potential for SARS to re-emerge and spread unpredictably. These guidelines document the hospital management of adults with probable or confirmed SARS. They are meant only as a brief summary for clinicians. These guidelines do not cover the

management in the community of a person under investigation (PUI) (see Case Definitions).

Guidelines for the management of paediatrics cases have not yet been developed.

As more information about SARS becomes available, guidance will be appropriately updated. Please consult the latest guidance available on the websites of the British Thoracic Society (<http://www.brit-thoracic.org.uk/>) and Health Protection Agency (http://www.hpa.org.uk/infections/topics_az/SARS/menu.htm).

UK SARS case definitions if SARS re-emerges

The following case definitions (see Tables 1-4) are designed for use during an outbreak of SARS, once the re-emergence of SARS has been verified by the World Health Organisation (WHO).

It is anticipated that patients with SARS will have a respiratory illness severe enough to warrant hospital admission. Management of such cases is covered in Sections 2-4. A person with a mild

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Table 1 Case definition for a probable case of SARS

An individual with a respiratory illness requiring hospitalisation on clinical grounds and characterised by:

Fever of $>38^{\circ}\text{C}$

AND

cough or breathing difficulty

AND

Radiographic evidence consistent with SARS, i.e.:
Radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS)

OR

Autopsy findings consistent with the pathology of pneumonia or RDS without an identifiable cause

AND a potential epidemiological link—i.e.: In the 10 days before the onset of illness:

a history of travel to an area classified by WHO as having recent local transmission (<http://www.who.int/csr/sars/areas/en/>)

OR

a history of exposure to laboratories or institutes which have retained SARS virus isolates and/or diagnostic specimens from SARS patients

OR

Close contact^a with a probable or confirmed SARS case

AND No alternate diagnosis to fully explain their illness

^a Close contact means healthcare worker or persons having cared for, lived with or had face-to-face (within 1 m) contact with, or having had direct contact with respiratory secretions and/or body fluids of a person with SARS.

respiratory illness and a potential epidemiological link to SARS should be defined as a PUI (see Table 4) and should be assessed in primary care and reviewed within 72 h.

Table 2 Case definition for a confirmed case of SARS

An individual with symptoms and signs that are clinically suggestive of SARS

AND

with laboratory evidence of SARS-CoV infection based on one or more of the following:

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

- At least two different clinical specimens (eg respiratory and stool) OR

- The same clinical specimen collected on two or more occasions during the course of the illness 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

- Four-fold or greater rise in antibody titre between the acute and convalescent phase sera tested in parallel

(c) Virus isolation

- Isolation in cell culture of SARS-CoV from any specimen; plus PCR confirmation using a validated method

Table 3 Case definition for a discarded case

A case is discarded when

- an alternative laboratory diagnosis^a is made which can fully explain the illness

OR

- the patient has a negative convalescent serology result (Note: a negative PCR result does not result in the declassification of a probable case)

^a Identification of another pathogen does not necessarily exclude the diagnosis of SARS.

A PUI does not require routine hospitalisation nor do they require a chest radiograph (CXR) or laboratory investigation for SARS CoV as part of their assessment. A PUI should only be hospitalised if his or her condition deteriorates. The management of such patients is covered in Section 5. If these patients are subsequently found to have radiographic evidence consistent with SARS, they should be reclassified as a 'probable SARS' case unless an alternative diagnosis is made.

A PUI should be reported to local Health Protection Units but does not need to be reported to CDSC Colindale.

Please discuss the classification of SARS patients with the Health Protection Agency's Communicable Disease Surveillance Centre (CDSC) Duty doctor (Tel.: 0208-200-6868) and complete a standard SARS report form and fax to your local Consultant in Communicable Disease Control (CCDC) and CDSC (details at: http://www.hpa.org.uk/infections/topics_az/SARS/forms.htm).

Table 4 Case definition for a person under investigation

A person with

EITHER

Fever of $>38^{\circ}\text{C}$ **OR** cough **OR** breathing difficulty

AND in the 10 days before the onset of illness,

Close contact^a with a probable or confirmed SARS case

OR

Fever of $>38^{\circ}\text{C}$

AND

cough or breathing difficulty

AND in the 10 days before the onset of illness,

a history of travel to an area classified by WHO as having recent local transmission (<http://www.who.int/csr/sars/areas/en/>)

OR

a history of exposure to laboratories or institutes which have retained SARS virus isolates and/or diagnostic specimens from SARS patients

^a As per footnote to Table 1.

Adult presenting to hospital with probable SARS

Patients are likely to present initially with a clinical picture of pneumonia which may be consistent with SARS. Therefore, other causes of pneumonia should be considered. Confirmation that a patient has SARS may occur following further investigation.

Infection control issues

Detailed guidance regarding the infection control issues during hospital management of a patient, or patients, presenting with SARS can be found at the HPA website: http://www.hpa.org.uk/infections/topics_az/SARS/hops_infect_cont.htm.

Briefly, the key recommendations are:

- Give the patient a surgical mask to wear continuously (unless requiring face mask for oxygen).
- Admit the patient to a negative pressure isolation room. If none available, use a single-room.
- Consider transfer to a designated centre with negative pressure facilities as appropriate.
- Ensure healthcare workers adhere to local SARS infection control measures: minimum requirement—gown, gloves, goggles or visors, masks (respirators) conforming to at least EN149:2001 FFP3 and strict hand-washing.⁶ For further details see http://www.hpa.org.uk/infections/topics_az/SARS/hosp_infect_cont.htm and <http://www.esccmid.org>.
- Detailed guidance on the use of masks (respirators) is available at: http://www.hpa.org.uk/infections/topics_az/SARS/maskFAQs.htm.

Ensure other infection control procedures are in place.

- Inform hospital infection control representative, CCDC regional designated SARS Infectious Diseases Unit and CDSC Duty Doctor (available on 0208 200 6868). Maintain a list of all staff that have contact with the patient.
- All staff should be vigilant for symptoms of SARS in the 10 days following exposure to a case and should not come to work if they have a fever. Further advice should be sought from the hospital infection control team and occupational health.
- Visitors should be restricted and may only include next of kin/legal guardian.

General management

The median time from exposure to fever is 5 days (2-10 days range). Patients generally have initial symptoms of fever, chills, rigors, myalgia and other features of a flu-like illness. Some patients have experienced diarrhoea.^{7,8} Respiratory symptoms begin approximately 3 days after the onset of these symptoms, mainly cough and dyspnoea. For a full description of the clinical features of large series of patients, consult Peiris et al. (Hong Kong),^{2,7} Lee et al. (Hong Kong)⁹ and Booth et al. (Toronto).¹ Rash, lymphadenopathy and central nervous system features suggest a diagnosis of SARS is less likely.

Recommendation

Confirm the travel history and/or history of contact with a patient with SARS. Explore other possible causes of pneumonia.

Assess pneumonia disease severity according to the BTS guidelines on the management of community acquired pneumonia (CAP) in adults (<http://www.brit-thoracic.org.uk/guide/guidelines.html>).¹⁰ In addition, determine whether the patient has any medical history of illness associated with a more severe outcome of SARS, i.e. diabetes and cardiovascular disease.¹

Obtain investigations as listed below (observe high risk infection control measures for all samples).

Laboratory testing for SARS

For full details, please see the HPA website at http://www.hpa.org.uk/infections/topics_az/SARS/micro.htm. Only send specimens once CDSC have been informed of a case via their standard report form. Please observe strict infection control procedures. All specimens should be double bagged and labelled as a biohazard.

Microbiology

- Expectorated sputum (if available)
- Urine (20-30 ml)
- Stool
- EDTA blood (20 ml for PCR)
- Acute serology (20 ml of clotted blood)

Do not obtain a nasopharyngeal aspirate as this is likely to generate aerosols.

Other tests

- (a) Chest X-ray
- (b) Pulse oximetry
- (c) Blood gases if oxygen saturation < 92% on air
- (d) Full blood count, urea, creatinine, electrolytes, liver function tests, lactate dehydrogenase, creatinine kinase and C-reactive protein.
- (e) Other samples for diagnostic testing as appropriate (remember there are much commoner causes of CAP than SARS).

Specific management of a patient with probable or confirmed SARS

Admit the patient to a designated isolation unit (see Section 2.1). Manage as for severe CAP according to BTS guidelines.¹⁰ Administer fluids and oxygen as required. Commence intravenous co-amoxiclav 1.2 g tds or cefuroxime 1.5 g tds plus erythromycin 500 mg qds or clarithromycin 500 mg bd. Please refer to the BTS guidelines for alternative recommended regimens.

Oxygen therapy

Oxygen supplementation should be administered according to standard/local guidelines. However, in order to reduce the risk of aerosol generation and hence spread of infection, high flow oxygen is not recommended, i.e. avoid oxygen flow rates of > 6 l/min. It should be possible to provide 30-40% oxygen supplementation using a standard low flow oxygen system and an air-entrainer together with a Ventimask.

Respiratory support and procedures

Procedures and practices that promote the generation of aerosols (Table 5) should be avoided wherever possible to reduce the risk of infection to healthcare workers.^{11,12} If such procedures need to be performed, e.g. tracheal intubation, it is advised that experienced operators only should

Table 5 Procedures that might promote the generation of aerosols (non-exhaustive list)

- Use of high flow oxygen (> 6 L/min)
- Use of nebulisers
- Chest physiotherapy
- Continuous positive airways pressure (CPAP)
- Non-invasive ventilation (NIV)
- Bronchoscopy
- Tracheal intubation
- Suctioning
- Humidification

undertake these procedures. These should, where possible, be planned and controlled. These procedures should ideally be undertaken in a negative pressure room. Only a minimum number of staff should be present and all must wear gowns, gloves, goggles/visors and respirators as described under infection control issues (see Section 2.1). Entry and exit from the room should be minimised during the procedure. The use of powered air purifying respirators (PAPRs) during aerosol generating procedures is not recommended. This is because there are concerns over the removal, disposal, cleaning and decontamination of this equipment, which may increase the potential risk of self-contamination and at this time there is inadequate evidence to determine whether PAPRs further reduce the transmission of SARS. If PAPRs are used, staff must be properly trained in their safe use.

Critical care

In studies from Canada and Singapore, approximately 20% of patients with suspected or probable SARS, according to the prevailing WHO case definition from March to June 2003, required ICU admission.^{3,4} Of these patients, 66-76% required mechanical ventilation. Average length of ICU stay was 10 days.

Recommendation

Preplanning and early consultation with local critical care providers is recommended.¹³ Patients who are likely to require intubation, should be identified early and the procedure should be undertaken electively. In order to avoid the use of CPAP or NIV, early intubation and invasive positive pressure ventilation (IPPV) may be required in some patients with impending respiratory failure.

The following issues need to be carefully considered:

- (a) Need for early intubation of patients with impending respiratory failure with avoidance of use of CPAP or NIV.
- (b) Adequacy of infection control policies (including training). See http://www.hpa.org.uk/infections/topics_az/SARS/hosp_infect_cont.htm.
- (c) Use of a negative pressure isolation room for intubation and subsequent IPPV. Transfer to designated centres with appropriate facilities may be necessary.

Further guidance for the management of critically ill patients is being developed.

Potential additional treatments for SARS

Steroids

The use of high-dose steroids has been anecdotally reported to contribute to decrease in fever and need for oxygen supplementation.¹⁴ A study from Guangzhou, China has suggested that the early administration of high-dose steroids together with CPAP ventilation is associated with a lower mortality.¹⁵ However, these findings are not based on adequately controlled data and there remain concerns regarding the use of high-dose steroids. The use of CPAP is certainly no longer recommended (see Section 2.5.2). In a retrospective analysis of Hong Kong patients who had received ribavirin in combination with different steroid regimens, patients who received initial high dose pulsed methylprednisolone intravenously had less oxygen requirement, better radiological improvement and less likelihood to require rescue pulse steroid use than patients who received non-pulse steroid therapy. However, the overall mortality rate, and requirement for mechanical ventilation or admission to the intensive care unit was the same for both regimens.¹⁶

Recommendation

The current recommendation is to consider moderate doses of steroid (prednisolone 30–40 mg/day or iv equivalent) in severely ill patients with SARS with increasing oxygen requirements who have a PaO₂ < 10 kPa or O₂ sats < 90% on air.

Ribavirin

Currently there is no convincing evidence that ribavirin alters clinical outcome. In laboratory studies, no in vitro activity against SARS-associated coronavirus (SARS-CoV) has been consistently demonstrated either. In addition, use of ribavirin is associated with significant toxicity including haemolysis (in ~76%) and decrease in haemoglobin of 2 g/dl or more (in ~49%).¹

Recommendation

The routine use of ribavirin in patients with SARS is not recommended.

Interferon

The antiviral activity of interferons against SARS coronavirus has been measured in vitro and interferon beta appears to be particularly active.¹⁷ The World Health Organisation is currently coordinating plans for clinical trials of interferons in the event of re-emergence of the disease.

Recommendation

None can be given at this time.

Management of the close contacts of a probable or confirmed SARS case

Generate a list of all close contacts. This should be initiated by the attending physician at the time of first contact with the patient. The local hospital infection control and Occupational Health teams may need to be involved if any healthcare workers are identified as close contacts. Record the date on which all close contacts last had contact with the case and inform them about SARS. Inform the local CCDC/Health Protection team of any contacts and their details to ensure follow-up.

Contacts of a probable SARS case

These contacts may continue with everyday activities, as long as they remain well. The local Health Protection Team will contact them on a regular basis to review their health.

Contacts of a confirmed SARS case

These contacts should be isolated at home. Please refer to the Health Protection Agency's guidelines on voluntary home isolation at http://www.hpa.org.uk/infections/topics_az/SARS/homeiso.htm.

If a contact becomes unwell within 10 days of their contact with a probable or confirmed SARS case they should phone a doctor urgently. For more information please refer to: http://www.hpa.org.uk/infections/topics_az/SARS/Guidelines.htm.

Discharge from hospital and follow up of a probable or confirmed SARS case

Guidelines for the safe discharge of patients recovering from SARS have been published by WHO. Please refer to the WHO website at <http://www.who.int/csr/sars/discharge/en/>.

Briefly, the following criteria should be considered before discharge:

- (a) Afebrile for 48 h
- (b) Resolving cough
- (c) Laboratory tests, if previously abnormal, returning to normal
- (d) Chest X-ray improved.

On discharge from hospital

Patients should monitor and record their temperature twice daily. If they have an elevated temperature of 38 °C or above on two consecutive occasions

they should inform (by telephone) the healthcare facility from which they were discharged.

Patients should remain at home for 7 days after discharge, keeping contact with others at a minimum. This is to reduce the risk of transmission until more is known regarding the potential for continued carriage in convalescent cases.

Additional home confinement may need to be considered, particularly in patients who are immunosuppressed. Inform the local Health Protection Team/CCDC regarding the hospital discharge of patients to ensure follow-up in the community.

Surveillance follow-up

A standard follow-up form should be completed and faxed to the local CCDC and CDSC on day 2, day 10, and/or once the patient is asymptomatic. Forms are available from http://www.hpa.org.uk/infections/topics_az/SARS/forms.htm. Follow-up post-discharge will be the responsibility of the local infection control team.

Convalescent serology should be obtained at 21 days after the date of disease onset.

Management of a person under investigation (PUI) who requires hospital admission but has a normal chest radiograph

PUIs who have symptoms and signs consistent with a lower respiratory tract infection (LRTI) but have a normal CXR do not fulfil the SARS case definition (see Table 1). Patients should be discharged and followed up in primary care unless their symptoms or social circumstances warrant continued hospital care.

Up to 30% of patients with probable SARS may initially present with normal chest radiographs. Therefore, PUIs who need ongoing hospitalisation require careful medical review in the first 48 h following admission.

Recommendation

Infection control measures as for patients with probable SARS should apply (see Section 2.1) until it is clinically clear that the PUI does not have probable SARS. Such patients should be treated as for non-pneumonic LRTI.

If the patient improves with treatment in the first 48 h following admission, the likelihood of SARS is small. Infection control measures may be relaxed

and the patient discharged if this is clinically appropriate.

If the patient does not improve with initial treatment (either no change or deteriorates), a repeat CXR should be obtained. An abnormal CXR with changes consistent with SARS would require the patient to be re-classified as having Probable SARS and be managed accordingly (see Section 2). If the repeat CXR remains normal, the patient remains a PUI. Further repeat CXRs may be required at 1-2 days intervals depending on clinical circumstances.

A PUI should be reported to the local Health Protection Unit but does not need to be reported to CDSC Colindale.

Appendix A

These guidelines were produced as a joint initiative between the British Thoracic Society, the British Infection Society and the Health Protection Agency.

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