



The SARS coronavirus



Micro Morphs

A New Disease Called SARS

From the Center for Disease Control and Prevention website



NATIONAL MEDICAL LABORATORY WEEK 2003
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Laboratory Professionals: Exceptional People – Exceptional Work

The Centers for Disease Control and Prevention (CDC) is investigating a new disease called severe acute respiratory syndrome (SARS) that has recently been reported in Asia, North America, and Europe. As of April 13, about 190 cases of SARS had been reported in the United States. This fact sheet provides basic information about the disease and what is being done to combat its spread.

Symptoms of SARS

In general, SARS begins with a fever greater than 100.4°F (>38.0°C). Other symptoms may include headache, an overall feeling of discomfort, and body aches. Some people also experience mild respiratory symptoms. After 2 to 7 days, SARS patients may develop a dry cough and have trouble breathing.

How SARS spreads

The primary way that SARS appears to spread is by close person-to-person contact. Most cases of SARS have involved people who cared for or lived with someone with SARS, or had direct contact with infectious material (for example, respiratory secretions) from a person who has SARS. Potential ways in which SARS can be spread include touching the skin of other people or objects that are contaminated with infectious droplets and then touching your eye(s), nose, or mouth. This can happen when someone who is sick with SARS coughs or sneezes droplets onto themselves, other people, or nearby surfaces. It also is possible that SARS can be spread more broadly



through the air or by other ways that are currently not known.

Who is at risk for SARS

Cases of SARS continue to be reported mainly among people who have had direct close contact with an infected person, such as those sharing a household with a SARS patient and health-care workers who did not use infection control procedures while taking care of a SARS patient. In the United States, there is no indication of community spread at this time. CDC continues to monitor this situation very closely.

Cause of SARS

On 16 April 2003, the World Health Organization (WHO) gave definitive confirmation that a new pathogen, a member of the coronavirus family never previously seen in humans, is the cause of Severe Acute Respiratory Syndrome (SARS). Identification of the coronavirus means that scientists can now move towards developing treatments for SARS and successfully controlling this disease.

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SARS a new disease cont'd.....

Diagnosis/Evaluation

Initial diagnostic testing for suspected SARS patients should include chest radiograph, pulse oximetry, blood cultures, sputum Gram's stain and culture, and testing for viral respiratory pathogens, notably influenza A and B and respiratory syncytial virus. A specimen for Legionella and pneumococcal urinary antigen testing should also be considered. Clinicians should save any available clinical specimens (respiratory, blood, and serum) for additional testing until a specific diagnosis is made. Acute and convalescent (greater than 21 days after onset of symptoms) serum samples should be collected from each patient who meets the SARS case definition. Paired sera and other clinical specimens can be forwarded through State and local health departments for testing at CDC. Specific instructions for collecting specimens from suspected SARS patients are available.

Clinicians evaluating suspected cases should use standard precautions (e.g., hand hygiene) together with airborne (e.g., N-95 respirator) and contact (e.g., gowns and gloves) precautions (see the Updated Interim Domestic Infection Control Guidance in the Health Care and Community Setting for Patients with Suspected SARS). Until the mode of transmission has been defined more precisely, eye protection also should be worn for all patient contact. As more clinical and epidemiologic information becomes available, interim recommendations will be updated.

CDC RECOMMENDATIONS

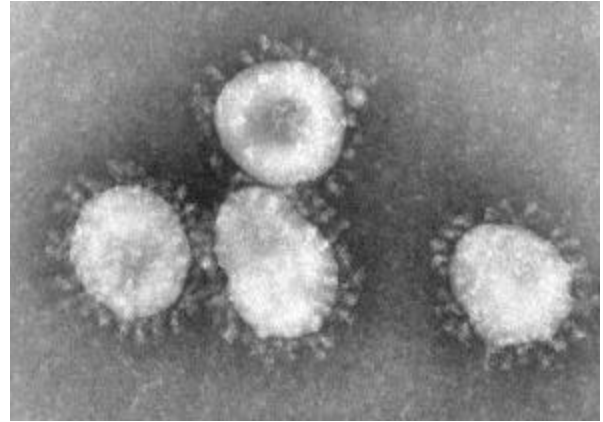
CDC has issued recommendations and guidelines for people who may be affected by this outbreak.

For individuals considering travel to affected parts of Asia:

CDC advises that people planning elective or nonessential travel to mainland China and Hong Kong, Singapore, and Hanoi, Vietnam may wish to postpone their trips until further notice. Visit the Travelers' Health web site for more information about CDC's advice to travelers.

For individuals who think they might have SARS:

People with symptoms of SARS (fever greater than 100.4°F [$>38.0^{\circ}\text{C}$] accompanied by a cough and/or difficulty breathing) should consult a health-care provider. To help the health-care provider make a diagnosis, tell them about any recent travel to places where SARS has been reported or whether there was contact with someone who had these symptoms



Coronaviruses are a group of viruses that have a halo or crown-like (corona) appearance when viewed under a microscope.

For health-care workers:

Transmission of SARS to health-care workers appears to have occurred after close contact with sick people before recommended infection control precautions were put into use. CDC has issued interim infection control recommendations for health-care settings see Interim Domestic Infection Control Guidance in the Health-Care and Community Setting for Patients with Suspected SARS page as well as for the management of exposures to SARS in health-care and other institutional settings, see Domestic Guidance for Management of Exposures to Severe Acute Respiratory Syndrome (SARS) for Healthcare and Other Institutional Settings.

For family members caring for someone with SARS:

CDC has developed [interim infection control recommendations for patients with suspected SARS](#) in the household. These basic precautions should be followed for 10 days after respiratory symptoms and fever are gone. During that time, SARS patients are asked to limit interactions outside the home (not go to work, school, or other public areas).

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SARS a new disease cont'd.....

What CDC is doing about SARS

CDC is working closely with the World Health Organization (WHO) and other partners in a global effort to address the SARS outbreak. For its part, CDC has taken the following actions:

- Activated its Emergency Operations Center to provide round-the-clock coordination and response.
- Committed more than 300 medical experts and support staff to work on the SARS response.
- Deployed medical officers, epidemiologists, and other specialists to assist with on-site investigations around the world.
- Provided ongoing assistance to state and local health departments in investigating possible cases of SARS in the United States.
- Conducted extensive laboratory testing of clinical specimens from SARS patients to identify the cause of the disease.
- Initiated a system for distributing health alert notices to travelers who may have been exposed to cases of SARS.



For more information, visit CDC's SARS Web site, or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY).
Source www.WHO.org

FDA Issues Guidance on Severe Acute Respiratory Syndrome to Further Safeguard the Blood Supply

T03-28
April 17, 2003 Media Inquiries: 301-827-6242
Consumer Inquiries: 888-INFO-FDA

FDA today issued guidance to the nation's blood establishments on measures for further safeguarding the blood supply against Severe Acute Respiratory Syndrome (SARS). FDA is taking this interim measure to assure the safety of the blood supply while more is learned about the disease. At this time, it is unknown whether SARS can be transmitted through blood. Current FDA regulations require that a donor be in good health at the time of donation. Standard procedures already in place should serve as an effective safeguard against donation by a potential donor with symptoms.

The new SARS guidance sets forth measures for temporarily deferring potential donors who may have been exposed recently to SARS or have experienced acute SARS. These measures include limited additional questioning of potential donors to help ascertain if they may be at elevated risk for SARS, due to recent travel to known high risk areas as defined by CDC or due to exposure to a person with SARS or suspected SARS.

In addition, the guidance calls for blood establishments to actively encourage those who have already donated to report any SARS-related exposure that occurred within 14 days before donation or SARS illness or treatment occurring within 28 days prior to their donation. Donors should also be encouraged to report SARS illness or treatment that occurs within 14 days after donation. Donated units identified as having come from potentially SARS-exposed or infected donors will be quarantined and indefinitely kept out of the general blood supply.

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Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Severe Acute Respiratory Syndrome (SARS)

From the Center for Disease Control and Prevention website

Background

The Centers for Disease Control and Prevention (CDC) and the World Health Organization have received reports of patients with Severe Acute Respiratory Syndrome (SARS) from various international and domestic sources. The cause of these illnesses is unknown and is being investigated, but current findings strongly suggest a viral etiology with a coronavirus as the leading candidate. The primary way that SARS appears to spread is by close person-to-person contact. Most cases of SARS have involved people who cared for or lived with someone with SARS, or had direct contact with infectious material (for example, respiratory secretions) from a person who has SARS. Potential ways in which SARS can be spread include touching the skin of other persons or objects that are contaminated with infectious droplets and then touching your eye, nose, or mouth. This can happen when someone who is sick with SARS coughs or sneezes droplets onto themselves, other persons, or nearby surfaces. It is also possible that SARS can be spread more broadly through the air or by other ways that are currently not known.

It is estimated that several thousand diagnostic specimens from patients with SARS have been processed in routine clinical laboratories throughout the world and to date there have been no reported clusters of SARS illness among laboratory workers. Nonetheless, until more information about the transmission of the SARS agent in the laboratory setting is known, reasonable precautions should be taken in handling these specimens. Effective and timely communication between clinical and laboratory staff is essential in minimizing the risk incurred in handling specimens from patients in whom SARS is suspected. Specimens from patients with suspected SARS should be labeled accordingly and the laboratory should be alerted to insure proper specimen handling. Listed below are interim biosafety guidelines for handling these specimens. A detailed description of recommended facilities, practices, and protective equipment for the various laboratory biosafety levels (BSLs) given below may be found in the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories manual (BMBL).

Blood and Urine Specimens

These specimens may be handled using Standard Precautions (previously Universal Precautions) in BSL-2 laboratories. Laboratory workers should wear protective equipment, including disposable gloves, laboratory coats, eye protection and a surgical mask, or face shield to provide a barrier to mucosal surface exposure.

Careful attention should be given to hand hygiene after removal of gloves and especially before touching the eyes or mucosal surfaces.

Any procedure with the potential to generate fine particulate aerosols (e.g. vortexing or sonication of specimens in an open tube) should be performed in a biological safety cabinet (BSC). The use of sealed centrifuge rotors or sample cups, if available, should be employed for centrifugation. Ideally, these rotors or cups should be unloaded in a BSC.

Procedures performed outside of a BSC should be performed in a manner that minimizes the risk of exposure to an inadvertent sample release.

Work surfaces and equipment should be decontaminated after specimens are processed. Standard decontamination agents that are effective against lipid-enveloped viruses should be sufficient.

If the safety equipment described above is not available, administrative measures and/or additional personal protective equipment may be employed to reduce risk. This should be done in the context of a careful risk assessment by the laboratory safety officer. For example, the workflow of the laboratory may be adjusted so that a minimum number of workers are present during centrifugation.

Consideration may be given to implementing respiratory protection for workers for use during centrifugation or other procedures with increased potential for inadvertent sample release. Acceptable methods of respiratory protection include a properly fit tested NIOSH approved filter respirator (N-95 or higher); or powered air-purifying respirators (PAPRs) equipped with high efficiency particulate air (HEPA) filters. Accurate fit testing is a key component of effective respirator use. Personnel who cannot wear fitted respirators because of facial hair or other fit-limitations should wear loose fitting hooded or helmeted PAPRs. Consideration may also be given to referral of specimens to a suitably equipped reference laboratory.

Other Specimens:

1. The following activities may be performed in BSL-2 facilities with standard BSL-2 work practices:
 - Pathologic examination and processing of formalin-fixed or otherwise inactivated tissues.
 - Molecular analysis of extracted nucleic acid preparations.
 - Electron microscopic studies with glutaraldehyde-fixed grids.
 - Routine examination of bacterial and mycotic cultures.
 - Routine staining and microscopic analysis of fixed smears.

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Laboratory Biosafety Guidelines cont'd...

Final packaging of specimens for transport to diagnostic laboratories for additional testing. Specimens should already be in a sealed, decontaminated primary container.

2. Activities involving manipulation of untreated specimens may be performed in BSL-2 facilities, but with more stringent BSL-3 work practices. Laboratory workers should wear protective equipment, including disposable gloves, solid front gowns with cuffed sleeves, and full face protection. Specimen manipulations should be carried out in a certified biological safety cabinet.

When a procedure or process cannot be conducted within a biological safety cabinet, then appropriate combinations of personal protective equipment (e.g., respirators, face shields) and physical containment devices (e.g., centrifuge safety cups or sealed rotors) must be used. Acceptable methods of respiratory protection include a properly fit tested NIOSH approved filter respirator (N-95 or higher); or powered air-purifying respirators (PAPRs) equipped with high efficiency particulate air (HEPA) filters. Accurate fit testing is a key component of effective respirator use. Personnel who cannot wear fitted respirators because of facial hair or other fit-limitations should wear loose fitting hooded or helmeted PAPRs.

Centrifugation should be carried out using sealed centrifuge cups or rotors that are unloaded in a biological safety cabinet.

Examples of these activities include:

- Aliquoting and/or diluting specimens
- Inoculation of bacterial or mycological culture media.
- Performing diagnostic tests that don't involve propagation of viral agents in vitro or in vivo.
- Nucleic acid extraction procedures involving untreated specimens

Preparation and chemical- or heat-fixing of smears for microscopic analysis.



Preparation and chemical- or heat-fixing of smears for microscopic analysis.

3. The following activities require BSL-3 facilities and BSL-3 work practices. When a procedure or process cannot be conducted within a biological safety cabinet, then appropriate combinations of personal protective equipment (e.g., respirators, face shields) and physical containment devices (e.g., centrifuge safety cups or sealed rotors) must be used.

Viral cell culture

Initial characterization of viral agents recovered in cultures of SARS specimens.

4. The following activities require Animal BSL-3 facilities and Animal BSL-3 work practices:

- Inoculation of animals for potential recovery of the agent from SARS samples.
- Protocols involving animal inoculation for characterization of putative SARS agents.

Packaging, shipping and transport of specimens from suspect and probable SARS cases must follow the current edition of the International Air Transport Association (IATA) Dangerous Goods Regulations and US DOT 49 CFR Parts 171-180. Step-by-step instructions on appropriate packaging and labeling can be viewed at this CDC website.

April 16, 2003, 10:30 AM ET

FDA Issues Guidance cont'd....

Under the guidance, potential donors who have recently been to areas of the world in which a relatively large number of cases of SARS have been reported (at present, People's Republic of China; Hanoi, Vietnam; and Singapore), but showing no symptoms of the disease, will be deferred from donating blood for 14 days after their return to the US from those endemic areas. Those who have suffered from an acute case of SARS, as evidenced by a combination of symptoms and travel history, will be deferred from donating until 28 days after their symptoms are resolved and any treatment is completed.

The agency recommends that blood establishments implement the guidance as soon as possible and no later than 30 days after its issuance.

Because the guidance only calls for a marginal increase in procedures already in effect to protect the blood supply against other diseases, it is expected to have a minimal effect on the number of available blood donors and on the quantity of the blood supply. Based on current travel estimates, it is believed that 0.1 percent to 0.2 percent of potential donors, and at most 0.4 percent, will be deferred as a result of the guidance at this time.

The guidance reflects consultation with the Centers for Disease Control and is intended as an interim measure to protect against the potential risk to the blood supply posed by SARS. At this time, there are no known cases of SARS transmission via blood products.



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However, detection of the genes of the possible causative virus in blood has been reported in a patient with SARS. Also, as in some other viral infections, persons with SARS could potentially have virus in their blood early in infection without any symptoms. Therefore, transfusion transmission of SARS may be possible.

FDA will continue to monitor this evolving situation and intends to make any revisions or additions as needed to preserve the safety and availability of the blood supply, based on the best available information. For example, FDA's guidance may be modified based on further scientific research on whether the causal agent of SARS may be present in blood of the types of persons subject to this interim deferral.

Those interested in commenting on the guidance may submit their comment to Dockets Management Branch (HFA-305) Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. As always, FDA strongly encourages eligible donors to give blood regularly. Blood transfusion is often life-saving, and the blood supply is limited. For patients who need blood transfusions, the benefits outweigh the risks.



SARS: Availability and use of laboratory testing

From www.who.org

17 April 2003

Researchers in several countries are working towards developing fast and accurate laboratory tests for the SARS. However, until those tests have been adequately field tested and shown to be reliable, SARS diagnosis remains dependant on the clinical findings of an atypical pneumonia not attributed to another cause and a history of exposure to a suspect or probable case of SARS or their respiratory secretions and other bodily fluids. This requirement is reflected in the current WHO case definitions for suspect or probable SARS . However several countries (Canada, France, Germany, Hong Kong SAR, Japan, the Netherlands, Singapore, United Kingdom and the United States of America) are testing samples for suspected and probable SARS cases in research settings.



Interpretation of test results

Positive test results indicate that SARS patients are, or recently were, infected with the SARSvirus. Specificity of the different tests still needs to be established.

Negative test results: A negative SARS virus test does not mean that the patient does not have SARS. The reasons for negative test results in a patient with SARS include the following: - The patient is not infected with the SARS -virus; the illness is caused by another infectious agent (virus, bacterium, fungus) or non-infective cause. - Test results are incorrect ("false-negative"). Current tests need to be further developed to improve sensitivity. - Specimens were not collected at a time when the virus or its genetic material was present (pertains to PCR and cell culture). The virus and its genetic material may be present for a brief period only, depending on the type of specimen tested. - Specimens were collected early in the course of the illness and before antibodies had been produced (pertains to ELISA and immunofluorescence assays).

Sampling for research To enhance the future understanding of the SARS disease process, WHO recommends that clinicians collect and store sequential samples from patients with SARS for testing when diagnostic tests become readily available. This is particularly important for the first case(s) recognised in countries that have not previously reported SARS.

Guidelines on sample handling of suspected or probable SARS patients, can be found at the website from Centres for Disease Control and Prevention (CDC) , United States of America.

Status of laboratory tests currently under development

1 Antibody tests

- ELISA (Enzyme Linked Immunosorbant Assay) detects antibodies in the serum of SARS patients reliably as from day 21 after the onset of clinical symptoms and signs.
- Immunofluorescence Assays detect antibodies in serum of SARS patients after about day 10 of illness onset. This is a reliable test requiring the use of fixed SARS-virus, an immunofluorescence microscope and an experienced microscopist. Positive antibody tests indicate that the patient was infected with the SARS -virus.

2 Molecular tests (PCR)

PCR can detect genetic material of the SARS -virus in various specimens (blood, stool, respiratory secretions or body tissue). Primers, which are the key pieces for a PCR test, have been made publicly available by WHO network laboratories on the WHO web site . The primers have since been used by numerous countries around the world. A ready-to-use PCR test kit containing primers and positive and negative control has been developed. Testing of the kit by network members is expected to quickly yield the data needed to assess the test's performance, in comparison with primers developed by other WHO network laboratories. Existing PCR tests are very specific but lack sensitivity. That means that negative tests can't rule out the presence of the SARS virus in patients. Various WHO network laboratories are working on their PCR protocols and primers to improve their reliability.

3 Cell culture

Virus in specimens (such as respiratory secretions, blood or stool) from SARS patients can also be detected by infecting cell cultures and growing the virus. Once isolated, the virus must be identified as the SARS virus with further tests. Cell culture is a very demanding test, but the only means to show the existence of a live virus.