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Severe acute respiratory syndrome and dentistry

A retrospective view

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Microbial threats continue to emerge, reemerge and persist. Some organisms are newly recognized pathogens that have existed for centuries (for example, *Helicobacter pylori*, which causes gastric ulcers). Others are old organisms that have learned new tricks (for example, multidrug-resistant tubercle bacilli). A third category consists of totally new organisms.[1]

The dental community must be constantly aware of impending infectious threats that may challenge the current infection control regimen.

This last group of alarming new infectious agents that are virulent and deadly have emerged in rapid succession during the last few years. Some of these, such as the Ebola virus infection,[2] are still smoldering in some remote corners of the world,[3] while others, such as the H5N1 (and H7N7) influenza A bird flu virus and the West Nile virus infections, are emerging in different parts of the world.[4]

Severe acute respiratory syndrome, or SARS, is the latest addition to this deadly assortment of new diseases. In the face of these infectious threats, in particular the pandemic of HIV infection, the dental community has reacted swiftly by adopting standard precautions. Dentists follow a uniform infection control protocol to treat all patients, irrespective of their medical histories.[5]

However, in the face of a new infection that is considered highly contagious, it is prudent to review infection control procedures. The objective of this article, therefore, is to describe the epidemiology, clinical features,

ABSTRACT

Background. Severe acute respiratory syndrome, or SARS, which has created panic in Asia and in some parts of North America, is the first epidemic of the new century. Although it has been well-contained, sporadic cases continue to emerge.

Objectives. The authors trace the emergence of the SARS outbreak from southern China and its spread worldwide, discuss the viral etiology of the infection and its clinical features, and review the infection control guidelines issued during the outbreak by the health authorities in Hong Kong, the Centers for Disease Control and Prevention, the World Health Organization and the American Dental Association. They also review the prospects for a new outbreak and preventive measures.

Overview. The disease, which is caused by a novel coronavirus termed the "SARS coronavirus," or SARS-CoV, essentially spreads through droplet infection and affects people of any age. It has a mortality rate ranging from 10 to 15 percent. A major hallmark of this disease has been the rate at which it has affected health care workers through nosocomial transmission; in some countries, up to one-fourth to one-third of those infected were in this category. However, no dental health care worker has been affected by SARS in a nosocomial or dental setting.

Conclusions and Clinical Implications. Researchers believe that a combination of factors, including the universal infection control measures that the dental community has implemented and/or the low degree of viral shedding in the prodromal phase of SARS, may have obviated the spread of the disease in dental settings. The dental community should reflect on this outbreak to reinforce the currently applied infection control measures.

etiology and prevention of SARS, as well as to evaluate the current infection control protocols used in dentistry in view of the facts related to the spread of this infection.[6] We also explore the prospects for recrudescence of the disease, its treatment modalities and the promise of a SARS vaccine.

BRIEF HISTORY OF SARS

We do not know with certainty how, where and when the disease now known as SARS manifested in humans, although theories abound. In February 2003, the World Health Organization, or WHO, coined the term "severe acute respiratory syndrome" for the flulike condition that developed into pneumonia.[7] Nonetheless, researchers and clinicians generally believe that the first few cases may have originated in China. These sporadic cases were described sometime in the fall of 2002 in the Guangdong province in southern China.

Symptomatically, the illness appears to have two phases: an early, prodromal febrile phase and a secondary lower-respiratory phase.

For decades, the Guangdong province had a large concentration of people, pigs and fowl living in close proximity because of mixed farming traditions that date back for centuries.[1] This region also has the dubious distinction of being the deadly source of the Asian flu, caused by the H2N2 virus, which killed about 1 million people worldwide in 1957 and 1958.[8] In 1997, the avian flu (caused by the H5N1 virus), which killed six people, also originated in the Guangdong province.[9]

The recent outbreak. The SARS outbreak has been identified in more than 30 countries in five continents, affecting more than 8,000 people, predominantly in Asia (especially China), with mini-outbreaks in North America and a few cases in Europe. The disease has led to more than 700 deaths worldwide. Clusters of cases are particularly common among close associates of patients and the health care workers who treated them and their household contacts. Because of the alarming global spread of the disease, WHO issued a global alert in March 2003 and instituted worldwide surveillance.[6]

Patient characteristics. Most patients identified up to now were previously healthy adults aged 25 through 70 years.[10] A few cases of SARS have been reported among children (≤ 15 years of age), in whom the clinical course now is thought to be less aggressive.[11] We provide a summary of the major clinical characteristics of patients with SARS, although the information should be considered preliminary because of the broad and nonspecific case definition.

Clinical features. The incubation period for SARS is widely considered to be two to seven days, but occasionally may last up to 10 days. Symptomatically, the illness appears to have two phases: an early, prodromal febrile phase and a secondary lower-respiratory phase. In pathological terms, however, it is a triphasic disease with a primary viral replicative phase, a secondary immune hyperactive phase and a pulmonary destructive phase.[12] The disease generally begins with a prodrome of typically high fever (> 38 C) that may be accompanied by chills and rigors. Headache, malaise and myalgia also are common. At the onset of the illness, some patients have mild respiratory symptoms. In a few cases, the febrile prodrome may be accompanied by diarrhea, although rash and neurologic or gastrointestinal findings are absent.

After three to seven days, the secondary lower-respiratory phase begins with a dry, nonproductive cough or dyspnea that may be accompanied by, or progress to, hypoxemia. In up to one-fifth of the cases, the respiratory illness is severe enough to require intubation and mechanical ventilation.

The fatality rate among patients with illness that meets the current WHO definition for probable and suspected cases of SARS ranges from 3 to 10 percent, depending on the age group and possibly other, yet unconfirmed, factors.[10] Furthermore, the mortality rate is higher among those with underlying illnesses and among the very elderly.

Typically, chest radiographs appear normal during the febrile prodrome and, in some patients, throughout the course of the illness. However, in the majority of patients, the respiratory phase is characterized by early focal infiltrates that progress to more generalized, patchy, interstitial infiltrates, sometimes leading to consolidation in the very late stages.[13]

In general, in the early phase of the disease, patients may have either a normal or decreased white blood cell count, with a reduction in the absolute lymphocyte count. At the peak of the

lower respiratory phase, up to one-half of patients exhibit leukopenia and thrombocytopenia or platelet counts at the low end of the normal range (50,000 to 150,000 per microliter). Renal function appears to remain normal in the vast majority of patients.

The box shows the second interim case definition for SARS, provided by the Centers for Disease Control and Prevention, or CDC.[14] It is based on clinical, epidemiologic and laboratory criteria.[14] However, in areas such as Hong Kong, where there has been significant disease activity, the CDC criteria have been amended to include patients who do not respond to appropriate antibiotic therapy for atypical pneumonia caused by conventional agents (such as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*) and/or are in direct contact with another patient with SARS.

Treatment and prevention. A number of treatment regimens have been explored for SARS. These include a variety of antibiotics to presumptively treat known bacterial agents of atypical pneumonia, as well as antiviral agents such as oseltamivir and ribavirin. Steroids also have been administered in combination with these antimicrobial agents. However, the most beneficial regimen remains to be determined.[15]

Researchers have confirmed that a new strain of virus belonging to the family *Coronaviridae* is the prime agent of severe acute respiratory syndrome.

Until reliable diagnostic tests, an effective vaccine and antiviral drugs are available, control of the epidemic depends on early identification of suspected and probable cases, quarantine of patients (and their close contacts) and effective infection control measures, particularly after patients are admitted to a health care facility.

Etiology. Researchers have confirmed that a new strain of virus belonging to the family *Coronaviridae* is the prime agent of this disease.[16-19] Although other viruses belonging to paramyxoviruses such as metapneumovirus have been implicated, these appear to play only a secondary role, if any, in the disease process.

DETECTION OF CORONAVIRUS AS THE PUTATIVE AGENT OF SARS

The coronaviruses—so named for the crown of spikes they carry on their surface[20]—attracted the interest of researchers when they noted that the virus rapidly infected cells in culture, a phenomenon not common among other human coronaviruses.[16] Medical workers in Hong Kong, Toronto and Germany noted this effect when they inoculated lung tissue of patients into cultured monkey kidney cells.[16-18] This phenomenon leads to a classic cytopathic effect in which the confluent cell layers in laboratory cell cultures are broken down, causing patchy denudation and detachment of cells.[16-18]

Immunofluorescence testing of the infected cells indicated that they were indeed infected with a new form of the coronavirus, which has been termed "SARS coronavirus," or SARS-CoV. Furthermore, antibodies to the SARS-CoV were found almost exclusively in patients with SARS during their convalescence, but not in human serum samples from healthy patients or in samples banked before the outbreak,[16] suggesting that the infection is new to humans.

Until now, human coronaviruses have caused the relatively innocuous common cold.[20] However, coronaviruses that infect other mammals and birds are more virulent. These include avian infectious bronchitis (a major problem in the poultry industry), transmissible gastroenteritis of pigs and feline infectious peritonitis.[21] Although there was initial speculation that close contact between poultry and humans in the Chinese province of Guangdong (where SARS is thought to have originated) may have resulted in the virus' crossing the species barrier from poultry to humans, evidence now indicates that the Himalayan palm civet cats that are consumed as a delicacy and sold widely in animal markets in China are the source of the infection.[22] However, the SARS-CoV is not a recombinant of known coronaviruses. Analyses of the genetic signatures of the viral strains from different geographic regions indicate that immunological pressure might modulate the evolution of the virus in human population cohorts.[23,24]

Other candidate organisms such as paramyxovirus and chlamydia have been implicated in the disease process, but the consensus is that they play a very small role, if any, in the pathogenesis of SARS.[23]

General properties of *Coronaviridae*. *Coronaviridae* are a family of RNA viruses that have been associated etiologically with respiratory ill-

BOX

UPDATED INTERIM U.S. CASE DEFINITION FOR SEVERE ACUTE RESPIRATORY SYNDROME, OR SARS.*

CLINICAL CRITERIA

Early Illness

- Presence of two or more of the following features: fever (might be subjective), chills, rigors, myalgia, headache, diarrhea, sore throat or rhinorrhea

Mild-to-Moderate Respiratory Illness

- Temperature of > 100.4 F (> 38 C); and
- One or more clinical findings of respiratory illness (for example, cough, shortness of breath, difficulty breathing)

Severe Respiratory Illness

Meets clinical criteria of mild-to-moderate respiratory illness and one or more of the following findings:

- Radiographic evidence of pneumonia;
- Respiratory distress syndrome;
- Autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause

EPIDEMIOLOGIC CRITERIA

Possible Exposure to SARS-Associated Coronavirus, or SARS-CoV

One or more of the following exposures in the 10 days before the onset of symptoms:

- Travel to a foreign or domestic location with documented or suspected recent transmission of SARS-CoV;
- Close contact† with a person with mild-to-moderate or severe respiratory illness and history of travel in the 10 days before onset of symptoms to a foreign or domestic location with documented or suspected recent transmission of SARS-CoV

Likely Exposure to SARS-CoV

One or more of the following exposures in the 10 days before onset of symptoms:

- Close contact with a person with confirmed SARS-CoV disease;
- Close contact with a person with mild-to-moderate or severe respiratory illness for whom a chain of transmission can be linked to a confirmed case of SARS-CoV disease in the 10 days before onset of symptoms

LABORATORY CRITERIA

Tests to detect SARS-CoV are being refined and their performance characteristics assessed; therefore, criteria for laboratory diagnosis of SARS-CoV are changing. The following are general criteria for laboratory confirmation of SARS-CoV:

- Detection of serum antibody to SARS-CoV by a test validated by the Centers for Disease Control and Prevention, or CDC (for example, enzyme immunoassay); or
- Isolation in cell culture of SARS-CoV from a clinical specimen; or
- Detection of SARS-CoV RNA by a reverse transcriptase polymerase chain reaction test validated by CDC and with subsequent confirmation in a reference laboratory (for example, CDC)

CASE CLASSIFICATION

- Probable case: meets the clinical criteria for severe respiratory illness of unknown etiology and epidemiologic criteria for exposure; laboratory criteria confirmed or undetermined
- Suspect case: meets the clinical criteria for moderate respiratory illness of unknown etiology and epidemiologic criteria for exposure; laboratory criteria confirmed or undetermined

EXCLUSION CRITERIA

A case may be excluded as a suspect or probable SARS case if:

- An alternative diagnosis can fully explain the illness;
- The case has a convalescent-phase serum sample (that is, obtained > 28 days after symptom onset), which is negative for antibodies to SARS-CoV;
- The case was reported on the basis of contact with an index case that was subsequently excluded as a case of SARS, provided other possible epidemiologic exposure criteria are not present

* Adapted from the Centers for Disease Control and Prevention.[14]

† Close contact is defined as having cared for or lived with a person who has SARS, or having a high likelihood of being in direct contact with respiratory secretions and/or body fluids of a person with SARS (during encounters with the patient or through contact with materials contaminated by the patient), either during the period in which the individual was clinically ill or within 10 days of resolution of symptoms. Examples of close contact include kissing or embracing, sharing eating or drinking utensils, close conversation (less than 3 feet apart), physical examination, and any other direct physical contact between people. Close contact does not include activities such as walking by an individual or sitting across a waiting room or office for a brief time.

ness in humans and with other diseases in domestic animals. Interestingly, they also are associated to some extent with human diarrheal diseases.[21] Structurally, they are 80 to 160 nanometers in diameter, positive-stranded and about 30 kilobases in length.[21] Their genome is the largest of all RNA viruses, and high-frequency recombination between related coronaviruses leads to the generation of much genetic diversity.

The virus has three major proteins. The nucleocapsid protein is enclosed within the viral envelope with the RNA in a helical nucleocapsid. The other two proteins are the membrane glycoproteins and the spike glycoprotein.[21] The spike glycoprotein is responsible for the characteristic fringe of crownlike projections. Antibodies that elicit spike glycoprotein are thought to confer protection against infection. Because the human strains are relatively difficult to culture compared with animal strains, the extent of strain variation in human coronaviruses is unclear.[25]

There are three serologically and genetically distinct groups of coronaviruses associated with animal and human disease. In general, they are species-specific, although there are a number of examples of viruses crossing species barriers and establishing themselves in new hosts.[21, 25] Once the host is infected, the virus may produce localized disease that often is restricted to the respiratory epithelium or the gastrointestinal tract, or they may produce disseminated infection causing systemic disease.[21]

Coronavirus was confirmed as the etiologic agent in SARS via serologic techniques demonstrating a rise in antibody titer, its growth in tissue culture, a determination of reverse transcriptase–polymerase chain reaction, or RT-PCR, specific for this virus using molecular genetic techniques, and animal studies.[23]

Animal studies have helped to satisfy Koch's postulates, which are necessary to prove disease causation.[19] These postulates stipulate that to be the causal agent, a pathogen must meet four conditions: it must be found in all cases of the disease, it must be isolated from the host and grown in pure culture, it must reproduce the original disease when introduced into a susceptible host, and it must be found in the experimental host so infected. However, further studies that include control groups are required to determine the role of other agents, if any, in causality or as cofactors for severe disease.

Virus infectivity and survival. The rapid spread of SARS worldwide within a few months points to the contagious nature of the disease. The infectivity during the incubation period is still unclear, and it appears that the risk of transmission during the prodrome is low. In contrast, in coronaviruses that cause the common cold, the viral shedding period usually precedes the onset of clinical symptoms by one to two days, although the peak viral excretion occurs during the symptomatic phase.[21,23,26] The infectivity of SARS during convalescence appears to be low and remains to be determined.

Some data on the survival and infectivity of the SARS coronavirus[27] indicate that, unlike other coronaviruses, it is a rather robust organism that is stable in feces (and urine) at room temperature for at least one to two days. It is more stable (up to four days) in stool from patients with diarrhea (which has a higher pH than does normal stool). However, the virus loses infectivity five minutes after being exposed to commonly used disinfectants and fixatives, including 10 percent formaldehyde, 10 percent hypochlorite, 75 percent ethanol and 2 percent phenol. Heat at 56 C kills the SARS coronavirus at around 10,000 units per 15 minutes (considered to be a quick reduction).[27]

Spread of the disease. The available epidemiologic data suggest strongly that the main routes of virus spread are droplets, direct contact and fomite (indirect contact) transmission, although airborne transmission has not been ruled out completely.[28] Researchers believe that the cause of the large outbreaks among health care workers was the transmission of droplets through aerosol-generating medical procedures, such as the use of nebulizers.[28,29]

No firm data exist regarding the infectivity of contaminated saliva (as opposed to sputum from the respiratory tract) through the droplet route. In some patients, the infection manifests itself as a mild form of diarrhea, and coronavirus particles have been recovered from fecal matter. Hence, it is possible that fecal contamination could lead to the spread of the disease, although more data are needed to confirm this route of transmission. It is interesting that some animal coronaviruses are spread through the fecal-oral route.[21]

Laboratory diagnosis. The mainstay of the SARS diagnosis is its characteristic clinical features mentioned above. However, a number of laboratory tests—including serologic tests, cell culture and molecular diagnostics—can be used to

confirm the clinically suspicious or probable cases.[16,23] These tests include the following.

Enzyme-linked immunosorbent assay, or ELISA, test. From about 20 days after the onset of clinical signs, ELISA tests can be used to detect immunoglobulin, or Ig, M and IgA antibodies in the serum samples of patients with SARS. Early antibodies are detected in some patients within two weeks.

Immunofluorescence assay. SARS virus–infected Vero cells can be used to detect IgM antibodies in serum samples of patients after about day 10 of the onset of the disease. This test is reliable, yet demanding, because the live virus must be grown in cell culture; in addition, subsequent immunofluorescence needs to be demonstrated.

Cell culture. Laboratory workers can detect virus in specimens (for example, respiratory secretions, blood) from patients with SARS by infecting cultured Vero-E6 or fetal rhesus kidney 4, or Frhk-4, cells.

Molecular tests. Laboratory workers can use PCR assays that detect genetic material of coronavirus in patient specimens (such as respiratory secretions, blood or stool samples). Primers that are required for this test now are available widely through various Web sites (for example, the CDC, The University of Hong Kong and the Governmental Viral Unit of Hong Kong).

Interpretation of test results. Clinicians must exercise caution when interpreting laboratory test results, because the key to diagnosis is clinical evaluation and possible exposure to an infected person. A positive laboratory test result indicates that the patient is, or has been, infected with the SARS-CoV, while a negative test result does not necessarily rule out SARS.[16,23]

Seroconversion of paired serum samples with convalescent serum samples obtained more than 21 days after onset of symptoms is a reliable, sensitive and specific diagnostic method. However, the current diagnostic option of choice for early and rapid diagnosis is RT-PCR detection of virus in respiratory or fecal specimens. This test has low sensitivity, and a negative test result does not exclude the diagnosis.

Many laboratories are addressing the problem of sensitivity and specificity of the SARS diagnostic tests, and it will take some time before a highly sensitive, specific, quick and simple diagnostic test is available. It is possible that, as is the case with HIV infection, saliva could be used as a diagnostic fluid in this context.

To date, there have been no documented cases of severe respiratory syndrome transmitted in a dental setting.

IMPLICATIONS FOR DENTISTRY

Many people have been alarmed by the spread of SARS in clinical facilities, where a disproportionately large number of health care workers (sometimes up to one-third) have been infected. However, it is reassuring that, to date, there have been no documented cases of SARS transmitted in a dental setting. This may be the result of a combination of factors.

First, transmission has not been documented during the incubation period before the appearance of febrile symptoms. It is unlikely that patients with SARS would visit a dentist for elective treatment while they are in the acute phase of the disease, because of the high fever and other, rather debilitating, attendant symptoms. Seto and colleagues[29] conducted a case-control study in which they showed that proper use of standard precautions is adequate to prevent the nosocomial spread of SARS in the absence of aerosol-producing procedures.

However, as health care providers, dental personnel should be wary of the disease and should know how it is spread, how to identify patients with SARS and what modifications need to be made to the practice to prevent transmission of the disease. Although SARS is well-controlled now, it may emerge insidiously, as has been the case with many other coronavirus infections.

We review below the infection control measures that dentists and dental staff members now follow, in light of new epidemiologic data about SARS, particularly its spread through aerosols and droplets. Our recommendations are based on the recent ADA guidelines,[30] the CDC's recent report of recommended infection control practices for dentistry[31] and our own experience in Hong Kong related to the last outbreak.

Identification of patients with SARS. As health care providers, dentists should be able to identify a suspected case of SARS. The CDC's current interim diagnostic criteria for SARS are shown in the box.[14] They are subject to change as more is learned about the disease, and should be reviewed periodically by visiting the ADA or CDC Web sites.

As stated above, we doubt that patients with SARS who are in the acute febrile phase of the disease will visit a dentist. In the unlikely event that this does occur, the dentist should not treat the patient in the dental office, but should refer him or her to a health care facility as soon as possible for diagnosis and care. Dentists also have a duty to report the case to state or local health departments.[32]

Patient evaluation. As always, dentists should take a thorough medical history from each patient and update it at each recall appointment.[5] The questionnaire used for this purpose may have to be modified to incorporate targeted screening questions regarding SARS. Although these questions may appear superfluous during the current abeyance of the outbreak, they are important as a guide if there is another outbreak of SARS or an outbreak of a similar new disease. These questions may include the following:

- Do you have fever?
- Have you experienced a recent onset of a respiratory problem, such as a cough or difficulty breathing?
- Have you, within the last 10 days (that is, the incubation period for SARS), traveled internationally or visited an area where documented or suspected community transmission of SARS is occurring?
- Have you come into contact with a patient with SARS in the past 10 days?

In the event that the patient recently has returned from a geographic region with documented or suspected community transmission of SARS, the clinician can defer elective treatment until the incubation period is over. Dentists can provide emergency treatment, provided they use routine barrier precautions and avoid spatter or aerosol-generating procedures. This emergency treatment should be limited to the control of pain and infection. Dentists should not treat patients in the dental office who are suspected of having SARS.

If a patient replies "yes" to the first two screening questions, the dentist should wear a surgical mask, discuss his or her potential concerns with the patient, call an area medical facility (such as a hospital) and inform the staff that he or she is referring a patient suspected of having SARS so that arrangements can be made for transportation and care of the patient. Patients with SARS need ground emergency medical services.[32]

These screening questions should be asked routinely of all patients, because questioning only a select group of patients, for whatever reason, may undermine the early detection of infection and might be construed as a discriminatory practice. Clinicians should delay treating convalescing patients for at least one month after they are released from the hospital. Convalescing patients are instructed to remain at home for seven days after discharge from the hospital, and during this period they are requested to stay indoors and keep contact with others to a minimum.[33]

Preprocedural rinsing. A preprocedural antimicrobial mouthrinse (with 0.12 to 0.2 percent chlorhexidine gluconate) is believed to reduce the number of microbes that are released into the operatory environment. This has been shown in a number of studies in which a long-lasting mouthrinse (for example, chlorhexidine gluconate with povidone iodine and essential oils) has reduced the disseminated microbial load during procedures such as ultrasonic scaling.[34,35] However, no concrete data show that a preprocedural mouthrinse reduces infection among dental health care workers or patients. A preprocedural rinse would be most useful in situations in which a rubber dam cannot be used, such as when a prophylaxis cup or an ultrasonic scaler is used, and in the absence of assisted, high-volume suction.

Hand hygiene. Microflora on the skin can be divided into two categories: the transient flora colonizing the superficial layers of the skin and mainly acquired through environmental routes, and the residential flora thriving on the deeper layers of the skin and hair follicles.[36] The exogenous, superficial flora are harmful and pathogenic, but are removed easily with clinical hand-washing procedures. By contrast, the endogenous residential flora are almost impossible to remove completely, but are less likely to be associated with infections.[36]

The single most important method of preventing transmission of any infectious agent, including the SARS coronavirus, is hand washing and appropriate hand care. Studies have found that even in critical care units, hand-washing compliance is relatively low, sometimes approaching 40 percent.[37] By contrast, a dramatic reduction in the prevalence of health care–associated infections has been shown when regimented hand hygiene measures were introduced.[38] Thus, appropriate hand hygiene is the

mainstay of a good dental infection control program.

Furthermore, recent data indicate that the SARS virus, compared with other coronaviruses, is a relatively robust organism and may survive on nonporous surfaces for up to 48 hours.[39] This reinforces the need for good hand hygiene, as well as the importance of thorough surface disinfection.

Hand hygiene for routine dentistry. For routine dentistry, which entails examinations and nonsurgical procedures, plain soap and water are adequate. Recently, the CDC recommended that if the health care worker's hands are not visibly soiled, an alcohol-based hand rub could be used for routine decontamination, because this is as effective as hand washing and also saves time.[40] Also, clinicians should decontaminate their hands both before and after removing gloves, because humidity and moisture cause bacteria to multiply rapidly under the glove surface.

Hand rubs that are based on alcohol alone should not be used owing to their rapid evaporation and lack of residual effect. Consequently, hand rubs must be laced with agents such as chlorhexidine, octenidine or triclosan to achieve the needed effect.[41] After using an alcohol-based hand rub, the clinician must dry his or her hands thoroughly before putting on gloves, because any residual alcohol may increase the risk of glove perforation.[42]

Recent experience has shown that vast numbers of health care workers acquired the infection in hospital settings, either as a result of inadequate barrier protection methods or the improper use of these methods.

Personal protective equipment. Personal protective equipment, or PPE, is designed to protect the skin and mucous membranes of the eyes, nose and mouth from exposure to potentially infectious material. Recent experience with the SARS coronavirus has shown that vast numbers of health care workers acquired the infection in hospital settings, either as a result of inadequate barrier protection methods or the improper use of these methods.[29] This barrier protection equipment consists of protective eyewear, masks, gloves, face shields and protective overwear. We should note that general work clothes such as uniforms do not protect against a hazard and should not be considered PPE. We describe below the relevant aspects of PPE that pertain to protection against airborne hazards.

Masks. Face masks were first worn by surgeons to minimize postsurgical infection in patients due to microbes that were exhaled or shed by the surgical team.[43] However, the realization that face masks protect the health care worker as well as the patient has led to the routine use of this protective measure in many clinical settings including dentistry.

Transmission of airborne infection depends on factors such as the virulence of the organism, as well as the number of organisms, transmitted.[44] In the case of coronavirus-induced pneumonia leading to SARS, airborne droplet transmission of infection is considered to be the main route of spread.[45]

Various types of masks and face shields are available. Surgical masks usually provide adequate protection in dental care settings, where highly transmissible infectious diseases are not typically encountered.

Particulate respirators. However, surgical masks are not designed to provide adequate protection against exposure to airborne infectious agents such as tubercle bacilli or droplet nuclei smaller than 5 micrometers. For such purposes, particulate respirators (for example, N-95 masks) must be used. During the SARS outbreak in Hong Kong, the vast majority of dental practitioners in that country used N95 masks for routine dentistry. However, these masks are uncomfortable to wear for extended periods because of the difficulty in breathing through a thick impervious fabric, and are not recommended for routine dental office settings.

Rubber dam isolation. Rubber dams help minimize the production of saliva- and blood-contaminated aerosol or spatter. Samaranayake and colleagues[46] reported an up-to-70-percent reduction in airborne particles around a 3-foot diameter of the operational field when a rubber dam was used. A split-dam technique may be used in situations in which gingival areas are involved, such as Class V restorations and crown-and-bridge preparations.

Aerosol-generating procedures should be avoided as much as possible if rubber dam isolation is not feasible. Some of these procedures include ultrasonic scaling, root-surface débride-

ment, and high- or low-speed drilling with water spray.

UNRESOLVED QUESTIONS AND FUTURE RESEARCH DIRECTIONS

There is no doubt that coronavirus research has gained an unprecedented and urgent momentum owing to the lethality of SARS and its nearly worldwide spread within a few months. Consequently, laboratories throughout the world are working in unison to provide answers to many unresolved questions, as well as to develop a new preventive vaccine. In dentistry, in particular, a number of questions remain to be resolved, including the following:

- Does the virus survive in human saliva, and, if so, for how long?
- Is the virus shed in saliva during the early incubation period or during the convalescent phase of the disease?
- Do human salivary constituents such as lysozyme, lactoferrin and the salivary leukocyte protease inhibitor have anticoronavirus activity?
- Could the virus spread in a dental clinic environment because of aerosols, and, if so, are additional barrier protection measures required to prevent such spread?
- What are the more efficacious disinfectants that kill or inhibit the viral activity?
- How long does the virus survive on surfaces, and what factors, such as humidity, affect its survival?

CONCLUDING PERSPECTIVES

Response of the clinical community. Although the global threat of SARS has peaked for the most part, it is helpful to review the response of the community to this novel disease. It is fortunate that SARS was not sufficiently infective to cause a repeat of the 1918 influenza pandemic that killed millions. Even so, we might be able to attribute the relatively low death rate in large part to the worldwide surveillance networks and patient isolation efforts that were introduced rapidly in most countries. In retrospect, an overreaction seems to have been a better option than allowing the disease to run out of control, as was the case with the AIDS pandemic.

Culmination of the outbreak. The WHO lifted all its travel advisories[47] as of June 15, 2003, and since then, only three new cases of SARS have been reported. Two of these—one in Singapore and the other in Taiwan—were accidental, laboratory-acquired infections in research technicians working with the organism, while the third patient—from Guangdong province in southern China—is thought to have acquired the infection through contact with contaminated rodents.

Because the initial symptoms of SARS mimic those of many variants of atypical pneumonia, a high degree of suspicion by the medical establishment, intense surveillance and immediate quarantine of all close contacts of patients should ward off another, large-scale winter outbreak. If SARS does return, its epidemiology may be different from that of the current strain. For instance, the genome of the new SARS-CoV may differ, and the virus may be more or less infective than the original strain that emerged in 2003. Furthermore, we do not know how long the acquired immunity to SARS persists. Also, will those exposed to the virus be carriers of the disease in the face of a new infection? How many will be silent healthy carriers of the virus? Will an emergent strain or strains behave similarly to the older counterpart? We do not have the answers to these questions.

Mutation of the SARS-CoV. The reason for the pandemic spread of HIV is its ability to mutate rapidly from one generation to another so it can escape the immune surveillance mechanisms of the host, as well as the prescribed antiviral medications. The SARS virus, on the other hand, seems to be remarkably invariant; the genome sequence of isolates from patients in Singapore, Toronto, China and Hong Kong has not revealed any changes of major consequence.[23] This does not mean that the SARS virus is incapable of mutation; rather, because the virus has encountered little resistance from new human hosts, there is less selective pressure for new mutants to emerge and persist.

Drugs and vaccines for SARS. Many researchers are working on potential drugs and vaccines to treat patients with SARS. However, their approach has been scattered for the most part, as they screen the multitude of available drugs and compounds for their ability to destroy the SARS-CoV. Thus far, a few have had success. One group reported that the compound glycyrrhizin, which is derived from licorice roots, can rid cultured monkey kidney cells of the SARS virus.[48] Other researchers, using in silico research, have proposed that the newly described proteinase of the SARS virus (which converts

viral proteins into the active form required for viral replication)[49] could be inhibited by drugs.

Animal models are essential for experimentation and drug discovery; thus far, the only validated model has been cynomolgus macaque (*Macaca fascicularis*).[20] A smaller and less expensive animal model for SARS research has yet to be defined.

Although vaccines exist for animal coronavirus infections, it may take a few years before a vaccine for SARS is developed. It is comforting to note that the existing technology and know-how for animal coronavirus vaccines could be translated directly toward the manufacture of a SARS vaccine. Furthermore, implicit evidence shows that the vaccine approach to preventing SARS is feasible, because patients' conditions appear to improve when they are given hyperimmune serum from recovered patients with SARS.

SARS vaccines could be based on a killed SARS virus or on an attenuated virus that is sufficiently potent to replicate itself in humans and initiate a successful antibody response, but not potent enough to cause disease. Another option would be to re-engineer a harmless candidate virus to contain genetic sequences of the SARS virus. This approach has been used to produce a prototypic vaccine against a coronavirus that causes bronchitis in chickens.[50] Should there be a renewed threat of SARS, a vaccine would be a most-welcomed weapon by health care workers.

CONCLUSION

SARS is the first readily transmissible infectious disease that the global community has confronted in the new millennium. This, surely, will not be the last contagion that we will encounter. The fact that no dental health care worker or dental patient has thus far contracted SARS in a dental setting is a testament to good infection control measures that have been implemented in the vast majority of dental offices. However, the dental community cannot let down its guard, and must be constantly aware of impending infectious threats in various guises, as well as recrudescence of disease, that may challenge the current infection control regimen. ■

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