Core Document

Appendix 1

Clinical, Epidemiologic, and Virologic Features of SARS-CoV

Emergence of SARS-CoV

SARS first came to global attention on February 11, 2003, when Chinese officials informed WHO of the occurrence of 305 cases of atypical pneumonia and 5 deaths in Guangdong Province since November 2002 (WHO 2003). On February 21, a Chinese physician with SARS traveled from Guangdong to Hong Kong and spent the night in a hotel there. During the next two days, he developed increasingly severe respiratory symptoms and was hospitalized in a Hong Kong hospital, where he died from his illness. His one-night stay in a Hong Kong hotel led to infection by yet unexplained mechanisms in several other guests, who subsequently traveled to and seeded SARS outbreaks in Vietnam, Singapore, Hong Kong, and Canada (CDC 2003a; Hsu 2003; WHO 2003). In these areas, local spread was initiated and maintained in hospitals, where healthcare personnel, patients, and visitors – unaware of the emergence of a new disease – acquired SARS-CoV from persons with unrecognized infection (Booth 2003; CDC 2003b; CDC 2003c; Lee 2003; Varia 2003). During March-May, the spread of the virus from Guangdong to other parts of China established additional foci of infection, such as Beijing and Taiwan (CDC 2003d).

Once SARS was recognized in these locations and widespread community transmission was noted in several outbreak sites, the spread of SARS-CoV was controlled by aggressive community infection control measures including active case finding, contact tracing and monitoring, travel restrictions, and quarantine and other containment strategies. These measures were implemented in many geopolitical jurisdictions and involved intense, sustained collaboration among institutions and persons beyond the traditional public health infrastructure. Areas with high transmission rates experienced severe economic consequences and social disruption rivaling that seen in other global epidemics (e.g., plague) of centuries past.

On March 14, 2003, CDC launched an emergency public health response and established national surveillance for SARS to identify case-patients in the United States and discover if domestic transmission was occurring. Through July 2003, a total of 159 suspect and 33 probable cases had been reported in the United States. Of the 33 probable cases, only 8 had laboratory evidence of SARS-CoV infection (CDC 2003e; CDC 2003f; CDC 2003g; CDC 2003h). All of the eight cases with documented SARS-CoV infection occurred in persons who had traveled to SARS-affected areas. One of these case-patients might have acquired infection either abroad or from her spouse, who was one of the other seven SARS-CoV-positive cases. Except for this one person with possible transmission from a household contact, no evidence of SARS-CoV infection was detected by serologic testing of household contacts of SARS cases or of healthcare workers who cared for SARS patients.

During the global epidemic, transmission of SARS-CoV in hospitals was a major factor in the amplification of outbreaks and the initiation of spread into the community (Booth 2003; CDC 2003b; CDC 2003c; CDC 2003d; Lee 2003). In areas characterized by extensive outbreaks, early SARS-CoV transmission occurred predominantly among healthcare workers, patients, and visitors; these groups accounted for 18% to 58% of all SARS cases in the five countries with the largest outbreaks. The concentration of illness in previously healthy hospital staff placed an enormous strain on hospital facilities and staff. The apparent ease of nosocomial transmission – added to the far-reaching public health ramifications of SARS-CoV transmission in single hospitals – posed great challenges for healthcare institutions in maintaining high levels of vigilance and infection control.

Clinical, Epidemiologic, and Virologic Features of SARS-CoV
(continued from previous page)

Clinical Features

The median incubation period for SARS appears to be approximately 4 to 6 days; most patients become ill within 2 to 10 days after exposure (Booth 2003; CDC 2003b; Donnelly 2003; Varia 2003). The clinical presentation of SARS-CoV infection has some but not enough distinctive features to enable diagnosis by clinical signs and symptoms alone (Hsu 2003). Respiratory symptoms typically do not begin until 2 to 7 days after onset of systemic symptoms such as fever, headache, myalgias. Respiratory complaints usually include a non-productive cough and dyspnea but not upper respiratory symptoms such as rhinnorhea and sore throat (Booth 2003; Donnelly 2003; Drosten 2003a; Lee 2003; Peiris 2003a; Poutanen 2003; Rainer 2003; Tsang 2003). Almost all patients with laboratory evidence of SARS-CoV infection evaluated thus far developed radiographic evidence of pneumonia (Poutanen 2003; Rainer 2003), and most (70% -90%) developed lymphopenia (Booth 2003; Lee 2003; Peiris 2003a; Poutanen 2003; Tsang 2003; Wong 2003). The overall case-fatality rate of approximately 10% can increase to >50% in persons older than age 60 (Peiris 2003a).

Transmission

Epidemiologic features of SARS provide keys to its diagnosis and control. The pattern of spread suggests that SARS-CoV is transmitted primarily through droplets and close personal contact (Seto 2003; Varia 2003). Studies documenting stability of the virus for days in the environment suggest the possibility of fomite transmission. There is also suggestive evidence that, in a few instances, SARS-CoV may have been transmitted by small-particle aerosols. Epidemiologic data suggest that infected persons do not transmit SARS-CoV before the onset of symptoms and that most transmission occurs late in the course of illness when patients are likely to be hospitalized (Peiris 2003a). The lack of transmission before symptom onset and during early illness explains the infrequency of community transmission and the preponderance of hospital-associated transmission. Although evidence indicates that most patients do not transmit SARS-CoV efficiently (Lipsitch 2003), documentation of “super-spreaders” and “super-spreading events” shows that, in certain situations, viral transmission can be highly efficient (CDC 2003b).

Control Strategies

The rapidity with which SARS spread globally and the severity of the disease require a rapid and integrated global response to SARS. SARS anywhere in the world can potentially affect all other global regions. In response to the 2003 SARS epidemic, WHO orchestrated a rapid and intense effort to control transmission, which ultimately was effective in stopping all global spread by early July 2003. The classic public health control measures of isolation, contact tracing and monitoring, infection control, and quarantine were an important part of the global control of SARS and will be the key to controlling SARS if it returns.

The Virus and Its Re-emergence

SARS is caused by the newly identified SARS-associated coronavirus (SARS-CoV) (Drosten 2003b; Ksiazek 2003). As SARS-CoV is distantly related to all previously described coronaviruses, it is likely that the virus or its parent virus has been circulating in some location for a long period. Antibodies to SARS-CoV were not found in human serum samples banked before the SARS outbreak, suggesting that the virus is new to the human population. Evidence suggests that it is a previously unknown coronavirus, probably from an animal host, that crossed the species barrier and somehow acquired the ability to infected humans. No one knows if SARS-CoV will reappear, but the most likely potential sources for its reintroduction are: 1) the original animal or a new animal reservoir; 2) undetected transmission in humans; 3) persistent infection in humans; or 4) the laboratory (as occurred recently in Singapore). Since most other respiratory viruses are seasonal, with outbreaks in fall, winter, or spring that spontaneously resolve, it is possible that SARS may also be seasonal and spread more efficiently during the respiratory virus season.

Clinical, Epidemiologic, and Virologic Features of SARS-CoV
(continued from previous page)

Recurrence of or concern about SARS during respiratory virus season will likely challenge the healthcare and public health communities with large numbers of SARS-like illnesses.

Laboratory Diagnostics

Laboratory diagnostics are essential for detecting and documenting a resurgence of SARS, responding to and managing outbreaks of SARS, and addressing concerns about SARS in patients with other respiratory illnesses. Two assays are most often used to diagnose SARS CoV infection: PCR assays for viral RNA and serologic testing for virus-specific antibodies (Drosten 2003b; Ksiazek 2003; Peiris 2003b). Both assays can be very specific and sensitive in detecting RNA and antibodies, respectively. However, because of the low titer of virus in clinical specimens from most patients and the time it takes persons to mount an antibody response to infection, neither assay can reliably detect SARS-CoV infection early in illness (Ksiazek 2003; Peiris 2003). Interpretation of these assays needs to account for the possibility of false-negative results, which are frequent occurrences early in infection, and false-positive results, which are especially important concerns for PCR assays.

Prophylaxis and Treatment

No vaccines have yet been developed for SARS and no anti-viral treatment has been shown to be effective. CDC, the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and academicians are developing protocols to assess antiviral drugs that show activity in vitro against SARS-CoV. It is not yet clear whether persons who recover from SARS-CoV infection develop long-lasting protective immunity or whether they are susceptible to re-infection and disease, as is the case with other human coronaviruses.

References

Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose D, et al. Clinical features and short-term outcomes of 144 patients with SARS in the Greater Toronto area. JAMA 2003;289:2801-9.

CDC. Outbreak of severe acute respiratory syndrome – worldwide, 2003. MMWR 2003a;52:241-8.

CDC. Severe respiratory syndrome – Singapore, 2003b. MMWR 2003b;52:405-11.

CDC. Update: severe acute respiratory syndrome – Toronto, Canada, 2003. MMWR 2003c;52:547-50.

CDC. Severe acute respiratory syndrome –Taiwan, 2003. MMWR 2003d;52:461-6.

CDC. Severe acute respiratory syndrome (SARS) and coronavirus testing – United States, 2003. MMWR 2003e;52:297-302.

CDC. Update: severe acute respiratory syndrome – United States, 2003. MMWR 2003f;52:357-60.

CDC. Update: severe acute respiratory syndrome – United States, May 28, 2003. MMWR 2003g;52:500-1.

CDC. Update: severe acute respiratory syndrome – United States, June 11, 2003. MMWR 2003h;52:550.

Donnelly CA, Ghani AC, Leung GM, Hedley AJ, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Lancet 2003;361:1761-6.

Drosten C, Gunther S, Preiser W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 2003a;348:1967-76.

Clinical, Epidemiologic, and Virologic Features of SARS-CoV

(continued from previous page)

Drosten C, Preiser W, Gunther S, Schmitz H, Doerr HW. Severe acute respiratory syndrome: identification of the etiological agent. Trends Molec Med 2003b;9:325-7.

Hsu LY, Lee CC, Green JA, et al. Severe acute respiratory syndrome in Singapore: clinical features of index patient and initial contacts. Emerg Infect Dis 2003;9:713-7.

Ksiazek TG, Erdman D, Goldsmith C, Zaki SR, et al. A novel coronavirus associated with severe acute respiratory syndrome. N Engl J Med 2003;348:1953-66.

Lee N, Hui D, Wu A, Chan P, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348:1986-94.

Lipsitch M, Cohen T, Cooper B, Robins JM, et al. Transmission dynamics and control of severe acute respiratory syndrome. Science 2003;300:1966-70.

Peiris JSM, Chu CM, Cheng VCC, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet 2003a;361:1767-72.

Peiris JSM, Lai ST, Poon LLM, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet 2003b;361:1319-25.

Poutanen SM, Low DE, Henry B, Finkelstein S, Rose D, et al. Identification of severe acute respiratory syndrome in Canada. N Engl J Med 2003;348:1995-2005.

Rainer TH, Cameron PA, Smit D, Ong KL, et al. Evaluation of WHO criteria for identifying patients with severe acute respiratory syndrome out of hospital: prospective observational study. Br Med J 2003;326:1354-8.

Seto WH, Tsang D, Yung RWH, Ching TY, et al. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). Lancet 2003;361:1519-20.

Tsang KW, Ho PL, Ooi GC, Yee WK, et al. A cluster of cases of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003;348:1977-85.

Varia M, Wilson S, Sarwal S, McGeer A, et al. Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. Can Med Assoc J 2003;169:285-92.

WHO. WHO issues a global alert about cases of atypical pneumonia [Press release, 12 March 2003]. Geneva: 2003. http://www.who.int/csr/sars/archive/2003_03_12/en/

Wong RS, Wu A, To KF, Lee N, et al. Haematological manifestations in patients with severe acute respiratory syndrome: retrospective analysis. Br Med J 2003;326:1358-62.

For more information, visit www.cdc.gov/ncidod/sars or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)