Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

pneumonia had not been the "friend of the aged." Nuland observed, "By and large dying is a messy business."

The stark contrast between the findings of the study by Heyland et al and the SUPPORT studies is troublesome. Is that difference due to cultural, attitudinal, and organizational differences for the delivery of critical care in Canada and America? The easy explanation that American patients want more treatment even at the risk of discomfort may or may not be true. After years of public and often acrimonious debate, á la Quinlan and Cruzan, physicians may feel unsettled with the following question. Are our medical practices regarding the dying more humane than they were 30 or 40 years ago?

Legally and ethically, a lot of ground has been covered. The death-with-dignity movement, living wills, durable power of attorney, and even assisted suicide (in Oregon) are society's attempts to deal with difficult bioethical issues. Yet why do most family members feel betrayed and burdened when their next of kin die in the ICU? The vigorous ethical debates do nothing for the anguish of surrogates caught in the maze of "full code" and "DNR" designations in the hospital. Practically, who decides the question of whether to institute mechanical ventilation or artificial feeding becomes more important than the essential goodness of the decisions.

Although the current study did not report too many out-of-control treatments, many families are fearful. Callahan[3] has referred to the illusion that we could master our medical choices: "Yet there is hardly below the surface, a remarkable and rising anxiety about dying—not necessarily death as such but the combination of an extended critical illness gradually transformed into an extended dying." His personal considerations border on accepting decline and death in an almost fatalistic manner, which is unusual in Western thought.

In an ever-shrinking world, we should not underestimate the effect of life-support technology and medical know-how in societies in which ethical and legal constraints are weak or nonexistent. One often hears of the "illegality" of discontinuing mechanical ventilation in dying patients! Yet, with few support systems, these interventions may be stopped abruptly after the financial ruin of the families. Unfortunately, the immorality of such practices is rarely questioned. Decision making in these highly paternalistic medical systems requires some scrutiny. I feel that we have an obligation to our colleagues in less affluent societies. A universal ethical code for the use of life-support technology in this young century is a laudable goal.

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Severe Acute Respiratory Syndrome

Severe acute respiratory syndrome (SARS) is an emerging infectious disease with a formidable morbidity and mortality. In March 2003, there was a serious outbreak of SARS in Hong Kong.[1] Within a month, the disease also spread to Singapore,[2] Vietnam, Taiwan, Germany, Canada,[3] and the United States. As of May 10, 2003, 7,296 cases have been reported in 30 countries, with a death toll of 526.[4]

Epidemiology

The early cases of SARS probably occurred in southern China. In November 2002, there were many cases of severe pneumonia of unknown etiology in Guangdong Province in southern China, with a high rate of transmission to healthcare workers.[5] A 64-year-old physician from southern China, who visited Hong Kong on February 21, 2003, and died 10 days later of severe pneumonia, is believed to have been the source of infection, causing subsequent outbreaks of SARS in Hong Kong,[1,6] Vietnam, Singapore,[2] and Canada.[3] The index patients of these cities had been exposed to the Guangdong physician while they were visiting China or had been staying on the same floor of the same hotel. While investigating the outbreak of SARS in Hanoi, Dr. Carlo Urbani unfortunately contracted the disease and died.

SARS appears to spread by close person-to-

person contact via droplet transmission or fomite.[7] The high level of infectivity of this viral illness is highlighted by the fact that 158 patients were hospitalized with SARS within 2 weeks as a result of exposure to one single patient on a general medical ward in Hong Kong. The use of a jet nebulizer for administering bronchodilators to the index case, who presented clinically with community-acquired pneumonia, could increase the droplet load around the patient and, together with the overcrowding condition on the hospital ward, had contributed to this major hospital outbreak.[1] A novel coronavirus (CoV) is now identified as the main pathogen responsible for SARS,[8–11] although the presence of a metapneumovirus also was inferred in studies from Canada[11] and Hong Kong.[1] Several laboratories have recently completed the sequencing of the genome of the CoV that has led to the global epidemic of SARS, and they have noted that the SARS-CoV is not closely related to any of the previously characterized CoVs.[12–14]

Clinical and Laboratory Features

The mean incubation period of SARS is estimated to be 6.4 days (95% confidence interval, 5.2 to 7.7), and the mean time from onset of clinical symptoms to hospital admission varied between 3 and 5 days.[15] The major clinical features on presentation include persistent fever, chills/rigor, myalgia, dry cough, headache, and dizziness. Less common symptoms include sputum production, sore throat, coryza, nausea and vomiting, and diarrhea.[1–3] Watery diarrhea has been reported in a subgroup of patients 1 week down the clinical course. This was reported in a cohort infected in a community outbreak that has been linked to a faulty sewage system, presumably due to involvement of the GI tract via the fecal-oral route.[16]

Lymphopenia (*ie*, the destruction of both CD4 and CD8 lymphocytes), features of low-grade disseminated intravascular coagulation (*ie*, thrombocytopenia, prolonged activated partial thromboplastin time, and elevated d-dimer levels), and elevated lactate dehydrogenase levels (reflecting lung injury) and creatinine kinase levels (reflecting myositis) are common laboratory features of SARS.[1–3,8,11]

The clinical course of SARS appears to follow a triphasic pattern. Phase 1 (viral replication) is associated with increasing viral load and is clinically characterized by fever, myalgia, and other systemic symptoms that generally improve after a few days. Phase 2 (immunopathologic damage) is characterized by the recurrence of fever, oxygen desaturation, and radiologic progression of pneumonia with falls in viral load. The majority of patients will respond to treatment with a combination of ribavirin and IV steroids, but 20% of patients may progress into the phase 3, which is characterized by ARDS necessitating ventilatory support.[16] Compared with adults and teenagers, SARS seems to run a less aggressive clinical course in younger children, with no children in one case series[17] requiring supplementary oxygen.

Pulmonary Features

The radiographic appearances of SARS share features in common with other causes of pneumonia. At fever onset, almost 80% of patients with SARS have abnormal chest radiographs, all of which show airspace consolidation. All patients will eventually develop airway opacities during the course of the disease. In our study, the opacities occupy a peripheral or mixed peripheral and axial location in 88% of patients.[18] The predominant involvement of the lung periphery and the lower zone, in addition to the absence of cavitation, hilar lymphadenopathy, or pleural effusion, are the more distinctive radiographic features of SARS.[1,18] Radiographic progression from unilateral focal airspace opacity to either multifocal or bilateral involvement during the second week of the disease course, followed by radiographic improvement with treatment, is commonly encountered.[1,18] In one case series,[16] 12% of patients developed spontaneous pneumomediastinum and 20% of patients developed evidence of ARDS over a period of 3 weeks. In general, the incidence of barotrauma in ICU admissions seems higher than expected despite treatment with low-volume and low-pressure mechanical ventilation. Chest radiographs and CT scans have not demonstrated excessive hyperinflation or bullous lung disease, and it is difficult to explain this observation.[19]

High-resolution CT scanning of the thorax is useful in detecting lung opacities in patients with unremarkable chest radiograph findings. Common findings include ground-glass opacification, sometimes with consolidation, and interlobular septal and intralobular interstitial thickening, with predominantly peripheral and lower lobe involvement. The characteristic peripheral alveolar opacities are very similar to those found in patients with bronchiolitis obliterans-organizing pneumonia.[1,19]

The postmortem examination of lung tissues in SARS patients has shown various levels of disease severity. Changes include gross consolidation of the lungs, the presence of interstitial mononuclear inflammatory infiltrates, desquamation of pneumocytes in alveolar spaces, pulmonary edema with hyaline membrane formation, and cellular fibromyxoid-orga-

nizing exudates in airspaces, indicating the organizing phase of alveolar damage. Viral inclusions were not detected.[1,10]

Diagnostic Criteria

The diagnosis of SARS is based on clinical, epidemiologic, and laboratory criteria that have been laid down by the Centers for Disease Control and Prevention.[20] The clinical criteria include the following: (1) asymptomatic or mild respiratory illness; (2) moderate respiratory illness (*ie*, temperature, $>100.4°F$ or $38°C$) and at least one respiratory feature (*ie*, cough, dyspnea, difficulty breathing, or hypoxia); (3) severe respiratory illness (features of the second criterion and radiographic evidence of pneumonia, the presence of respiratory distress syndrome, autopsy findings consistent with pneumonia, or the presence of respiratory distress syndrome without an identifiable cause). The epidemiologic criteria include travel (including transit in an airport) within 10 days of the onset of symptoms to an area with current, recently documented, or suspected community transmission of SARS, or close contact within 10 days of the onset of symptoms with a person known or suspected to have SARS infection. Laboratory criteria include the following: (1) the detection of an antibody to SARS-CoV in specimens obtained during acute illness or 21 days after illness onset; (2) the detection SARS-CoV RNA by reverse-transcriptase polymerase chain reaction (PCR) that was confirmed by a second PCR assay by using a second aliquot of the specimen and a different set of PCR primers; or (3) the isolation of SARS-CoV. A case of *probable SARS* is defined as having met the clinical criteria for severe respiratory illness of unknown etiology with onset since February 1, 2003, and epidemiologic criteria, irrespective of the laboratory result. A case of *suspect SARS* is defined as having met the clinical criteria for moderate respiratory illness of unknown etiology with onset since February 1, 2003, and epidemiologic criteria, irrespective of the laboratory result.[20]

Treatment

The treatment of SARS has been empirical during the recent outbreak. Anecdotal experience using a combination of ribavirin and steroids has been described by two studies in Hong Kong.[1,21] Oral ribavirin (1.2 g tid orally or 400 mg q8h IV) and corticosteroids (*ie*, prednisolone, 1 mg/kg/d) were prescribed as combination therapy.[1] During phase 2, when there was radiologic progression of pneumonia and/or hypoxemia, IV high-dose methylprednisolone, 0.5 g daily for up to 6 doses in most cases, is administered to prevent immunopathologic lung injury, with the rationale that progression of the pulmonary disease may be mediated by the host inflammatory response.[16] The majority of our cohort (90% of 138 patients) appeared to have a favorable response to the combination treatment with resolution of fever and lung opacities within 2 weeks, whereas about 23% and 14%, respectively, of the same cohort required ICU admission and invasive ventilatory support.[1] The use of ribavirin therapy in SARS patients is associated with significant toxicity, including hemolysis (76% of patients) and a decrease in hemoglobin of 2 g/dL (49% of patients), elevated transaminase levels (40% of patients), and bradycardia (14% of patients).[3] Any treatment regimen for SARS needs to be tested with a randomized placebo-controlled design. New antiviral agents and immunomodulating agents are also under investigation.

Noninvasive positive-pressure ventilation has been used for treatment with some success in a small number of SARS patients with respiratory failure.[21] However, therapy with noninvasive positive-pressure ventilation should be carried out only if there is adequate protection for the health-care workers (*eg*, an isolation room with adequate air exchange) because of the potential risk of viral transmission via mask leakage and flow compensation causing the dispersion of a contaminated aerosol.

Prognosis/Outcome

The calculation of case fatality rates in the situation of an emerging epidemic is difficult, but it has been estimated to be 13.2% (95% CI, 9.8 to 16.8%) for patients <60 years of age and 43.3% (95% CI, 35.2 to 52.4%) for those ≥ 60 years of age.[15] The prognostic factors associated with a poor outcome (*ie*, ICU admission or death) include age,[1,15,16] chronic hepatitis B treated with lamivudine,[16] high peak lactate dehydrogenase,[1] high neutrophil count on presentation,[1] or presence of diabetes mellitus or other comorbid conditions.[3]

In conclusion, with the recent onset of the SARS epidemic worldwide, research on the development diagnostic tests and an effective treatment is urgently needed. We hope that the availability of the genome sequence of the SARS-CoV[12–14] will facilitate efforts to develop new and rapid diagnostic tests, antiviral agents, and vaccines in the long run. SARS patients who have recovered from the acute illness should be monitored carefully for the possibility of continued viral shedding[16] and the potential development of pulmonary fibrosis or late postviral complications. The prevention of spread is most important for this highly infectious disease. Isolation facilities, strict precautions against droplet exposure (*ie*, hand hy-

giene, and the wearing of gowns, gloves, N95 masks, and eye protection) among health-care workers managing SARS patients,[22] the avoidance of the use of nebulizers on a general medical ward,[1] contact tracing, and quarantine isolation for close contacts are all important measures.

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