

DEVELOPMENT OF A TREATMENT PROTOCOL FOR SARS

Investigators developed a standard treatment protocol for patients with severe acute respiratory syndrome (SARS). Between March 9 and March 29, 2003, 31 patients meeting the then-current World Health Organization criteria for probable SARS were admitted to a Hong Kong hospital. Sixteen of these patients were traced to an index patient admitted on March 2 and who died March 16. On March 12, the initial protocol was launched, consisting of combination treatment with a broad-spectrum antiviral (ribavirin) and an immunomodulating agent (methylprednisolone). Patients received antibacterial agents before recognized pathogens were excluded. Methylprednisolone dosing and weaning schedules were adjusted based on the experience in treating the first 11 cases and index case. The index patient's death suggested that delayed administration of combination treatment was ineffective. The final protocol was implemented on March 18. Patients were followed for a mean of 18.9 days. Thirty of 31 patients needed combination therapy at 1.7 days after admission and 5 days after symptom onset. Rapid, sustained response (1–2 days) to combination therapy occurred in 17 patients. Two patients required increased methylprednisolone dosing and 11 received pulsed methylprednisolone for severe disease. Sixteen patients required oxygen and 4 required short periods (2–5 days) of noninvasive mechanical ventilation at 8 to 10 cm H₂O expiratory pressure. One patient who was seropositive for the novel coronavirus and viral RNA in nasopharyngeal aspirates recovered on levofloxacin alone. No patients required intubation or mechanical ventilation, and none died after using the standard treatment protocol. The death of the index case was attributed to late diagnosis and treatment that did not conform to the subsequent protocol.

So LK, Lau AC, Yam LY, et al. Development of a standard treatment protocol for severe acute respiratory syndrome. *Lancet* 2003;361:1615–7.

NOVEL CORONAVIRUS ASSOCIATED WITH SARS

Researchers tested clinical specimens from patients in 7 countries using virus-isolation techniques, electron-microscopic and histologic studies, and molecular and serologic assays to determine an etiologic agent of the SARS outbreak. All specimens were from patients meeting the SARS case definition. Cytopathologic features were observed in Vero E6 cells inoculated with throat-swab specimens. Immunohistochemical and immunofluorescence staining revealed reactivity with group I coronavirus polyclonal antibodies. Electron microscopy demonstrated characteristic coronavirus particles in the endoplasmic reticulum and vesicles. Reverse-transcription polymerase chain reaction (RT-PCR) identified the isolate as a unique coronavirus that is

distantly related to previously sequenced coronaviruses. Nineteen patients with SARS were identified as infected by the new coronavirus by virus isolation, RT-PCR, or serologic tests; all patients were directly or indirectly linked to the SARS outbreak in Hong Kong or Guangdong Province, China. In 12 patients identified with the novel coronavirus infection by RT-PCR, the sequences from a limited region of the polymerase gene were identical, which is consistent with point-source outbreak. Evidence indicates that a novel coronavirus associated with the outbreak has an etiologic role in SARS.

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

EFFECT OF PREVIOUS ANTIBIOTIC USE ON PENICILLIN-NONSUSCEPTIBLE *S. PNEUMONIAE* INFECTION

The authors evaluated the impact of treatment duration of all major classes of antibiotics on the risk of acquiring penicillin-nonsusceptible *Streptococcus pneumoniae* (PNSP) infection. A retrospective cohort of 303 pediatric and adult patients was identified at 4 tertiary centers in New Orleans, LA. Penicillin-susceptible *S. pneumoniae* and PNSP, respectively, accounted for 205 (68%) and 98 (32%) bacteremic episodes. Using penicillin or its derivatives, any β -lactam, sulfonamides, or macrolides within the previous month or the previous 6 months before zero time (the date of the patient's first positive blood culture) was significantly associated with PNSP infection ($P < .05$), as was cephalosporin use within 6 months before zero time. Fluoroquinolone use within the previous month or the previous 6 months before zero time was not associated with PNSP infection ($P = .34$ and $P = .18$, respectively). PNSP infections were associated with taking 1 or ≥ 2 courses of β -lactam or macrolides or taking ≥ 2 courses of sulfonamides ($P < .001$). Patients who received short-term therapy with β -lactams also had a significantly greater chance for developing PNSP bacteremia ($P = .014$). Regression analysis revealed that using β -lactams ($P < .001$) or macrolides ($P < .004$) in 6 months prior to zero time were independent risk factors for PNSP bacteremia. Risk for acquiring PNSP depends on the antibiotic class as well as treatment duration. More cautious use of β -lactams and macrolides may lower the incidence of PNSP infection.

Ruhe JJ, Hasbun R. *Streptococcus pneumoniae* bacteremia: duration of previous antibiotic use and association with penicillin resistance. *Clin Infect Dis* 2003;36:1132–8.

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