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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Clinical presentations and outcome of severe acute respiratory syndrome in children

K L E Hon, C W Leung, W T F Cheng, P K S Chan, W C W Chu, Y W Kwan, A M Li, N C Fong, P C Ng, M C Chiu, C K Li, J S Tam, T F Fok

Hong Kong has been severely affected by severe acute respiratory syndrome (SARS). Contact in households and healthcare settings is thought to be important for transmission, putting children at particular risk. Most data so far, however, have been for adults. We prospectively followed up the first ten children with SARS managed during the early phase of the epidemic in Hong Kong. All the children had been in close contact with infected adults. Persistent fever, cough, progressive radiographic changes of chest and lymphopenia were noted in all patients. The children were treated with high-dose ribavirin, oral prednisolone, or intravenous methylprednisolone, with no short-term adverse effects. Four teenagers required oxygen therapy and two needed assisted ventilation. None of the younger children required oxygen supplementation. Compared with adults and teenagers, SARS seems to have a less aggressive clinical course in younger children.

Published online April 29, 2003. Lancet 2003; 361: 1701–03 http://image.thelancet.com/extras/03let4127web.pdf

Since late February, 2003, WHO has received reports of outbreaks of a severe form of atypical pneumonia in Vietnam, Hong Kong, and Singapore. Hong Kong is the most severely affected city. WHO has referred to this unusual form of severe pneumonia as severe acute respiratory syndrome (SARS).1 The surveillance case definition of SARS is: history of high fever (>38°C), one or more respiratory symptoms, including cough, shortness of breath, and difficulty breathing; and close contact within 10 days before onset of symptoms with a person who has been diagnosed with SARS, history of travel within 10 days before onset before symptoms to an area with SARS managed during the early phase of the epidemic in Hong Kong. All the children had been in close contact with infected adults. Persistent fever, cough, progressive radiographic changes of chest and lymphopenia were noted in all patients. The children were treated with high-dose ribavirin, oral prednisolone, or intravenous methylprednisolone, with no short-term adverse effects. Four teenagers required oxygen therapy and two needed assisted ventilation. None of the younger children required oxygen supplementation. Compared with adults and teenagers, SARS seems to have a less aggressive clinical course in younger children.

All children satisfied the WHO case definition for SARS and all had been in close contact with infected adults. The demographic, clinical, and laboratory data are shown in the table. Fever was a consistent symptom in all children, and lasted for a median duration of 6 days (range 3–11). There was no clinically significant drop in haemoglobin concentrations during treatment with ribavirin. In eight patients, corticosteroid was added to the regimen when fever did not subside. Pulse methylprednisolone was given to one young child (patient 2) and four teenagers (patients 6–9). Within 2 days of corticosteroid administration, all but one patient (patient 9) became afebrile. The same four teenagers developed respiratory distress and oxygen desaturation on day 5, 4, 6 and 7, respectively, after the onset of fever. These children were placed under strict isolation for 21 days and became asymptomatic before discharge.

Nine children had abnormal chest radiographs on presentation. The primary abnormality was air-space opacification. Of the five children aged 12 years or younger (patients 1–5), four presented with focal segmental consolidation. Patient 2 had ill-defined patchy air-space consolidation. All these patients had mild progressive consolidative change on serial chest radiographs but complete resolution was achieved within 14 days. The typical radiographic changes in one patient are shown in the figure. Three of the five teenagers (patients 7–9) presented with bilateral lower-lobe opacification at presentation, which progressed rapidly within days. Despite clinical improvement, these consolidative changes persisted into the 2nd week of the illness. Patient 10 showed no abnormality on chest radiography at presentation, but high-resolution CT confirmed focal consolidation in the right lower lobe. In CT of the thorax in patients 2 and 6, the characteristic features of peripheral and alveolar opacities simulated the radiological appearances of bronchiolitis obliterans organising pneumonia. Four teenagers required supplemental oxygen, one required bi-level positive airway pressure and intermittent positive-pressure ventilation. Respiratory distress developed 4–7 days after presentation.

Lymphopenia (0·3–3·0×10⁹/L) was reported in all patients, but the teenagers were generally more severely affected than the younger children. Lymphopenia mostly occurred between days 3 and 7, after the onset of fever. No bacteria, fungi, mycoplasma, chlamydia, or common respiratory viruses were detected by the laboratory investigations. Coronavirus was isolated by viral culture from the nasopharyngeal aspirates of patients 2 and 3. Reverse-transcriptase PCR targeting the novel coronavirus present in the nasopharyngeal aspirate samples was positive in four of six children tested (patients 1, 7, 9, and 10).
RESEARCH LETTERS

We noted two distinct patterns of clinical presentation among the children we studied. Teenage patients presented with symptoms of malaise, myalgia, chill, and rigor similar to those of adults, whereas the younger children presented mainly with cough and runny nose, and none had chills, rigor, or myalgia. The clinical course was much milder and shorter among younger patients, and radiological changes were milder and generally resolved more quickly than in the teenagers. All paediatric patients had clinically important lymphopenia, but it was more severe among the teenage children. However, since young children normally have higher lymphocyte counts than adults, the interpretation of results must take into account the patients’ ages. Furthermore, lymphopenia frequently resolves when the disease is improving. We adopted a treatment regimen of ribavirin and steroids similar to that used in adult SARS patients.

### Clinical features and treatment outcomes among SARS children

| Patient number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|----------------|---|---|---|---|---|---|---|---|---|----|
| Age (years)    | 1·5 | 3·2 | 5·1 | 6·2 | 7·5 | 13·2 | 13·3 | 15·6 | 15·6 | 16·4 |
| Sex (M/F)      | F | M | F | M | F | F | F | F |
| Clinical features | D | \| M |

### Laboratory findings

| Lowest lymphocyte count (<10^9/L) | Normal range 1·10–2·30 (day 3) | Lowest platelet count (<10^9/L) | Normal range 2·00–4·00 (day 3) | Highest serum LDH (U/L) | Normal range 2·00–4·00 (day 3) | Highest serum ALT (U/L) | Normal range 1·00–2·00 (day 3) |
|-----------------------------------|----------------------------------|---------------------------------|-------------------------------|-------------------------|-------------------------------|-------------------------|-------------------------------|
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |
| 3·0 (day 3)                       | 1·1 (day 3)                      | 1·1 (day 4)                     | 1·1 (day 3)                   | 1·2 (day 3)             | 0·8 (day 6)                   | 0·7 (day 4)             | 4·0 (day 6)                   |

### Radiological findings

| Initial chest radiograph | Right lower-zone focal | Right perihilar consolidation | Left middle-zone consolidation | Left upper-zone consolidation | Right upper-zone consolidation | Right lower-zone consolidation | Left and right lower-zone consolidation | Diffuse consolidation left and right lower zones |
|-------------------------|------------------------|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------------------|-----------------------------------------------|
| Progressive changes of chest radiograph | Increased right lower-zone consolidation (day 2) | Progress to involve right upper zone (day 8) | Increased left middle-zone consolidation (day 5) | Increased left upper-zone consolidation (day 4) | Increased right upper-zone consolidation (day 5) | Increased right lower-zone consolidation (day 5) | Left and right lower-zone consolidation | Diffuse consolidation left and right lower zones |

### Findings on CT of thorax

| None | None | None | None | None | None | None | None | None | Consolidation at right basal segments |

### Treatment and outcome

| Oral ribavirin | Prescribed | Prescribed | Prescribed | Prescribed | Prescribed | Not prescribed | Not prescribed | Not prescribed | Not prescribed |
|----------------|------------|------------|------------|------------|------------|----------------|----------------|----------------|----------------|
| IV ribavirin   | Not prescribed | Prescribed | Not prescribed | Not prescribed | Not prescribed | Prescribed | Not prescribed | Not prescribed | Not prescribed |
| Oral prednisolone/IV hydrocortisone | Prescribed | Prescribed | Prescribed | Prescribed | Prescribed | Prescribed | Prescribed | Prescribed | Prescribed |
| IV pulse methylprednisolone | Twice (day 10) | 6 | 7 | 3 | 6 | 6 | Three times (days 4–6) | 5 | Once (day 6) |
| Duration of fever (days) | 4 | 6 | 7 | 3 | 6 | 6 | Three times (days 4–6) | 5 | Once (day 6) |
| Ventilatory support | Not prescribed | Not prescribed | Not prescribed | Not prescribed | Not prescribed | Not prescribed | Not prescribed | Face mask (days 7–8; 12–15) | Bipap (days 8–12) |
| Maximum oxygen requirement | Air | Air | Air | Air | Air | 2 L/min | 3 L/min | 50% | 10%–13% |

LDH=Iactic dehydrogenase. ALT=alanine aminotransferase. IV=intravenous. BiPAP=bi-level positive airway pressure. IPPV=intermittent positive pressure ventilation.

*Mother of twin sisters (patients 8 and 9) is healthcare assistant. \(^\text{†}\)Normal range 110–230 U/L. \(^\text{‡}\)Normal range 1–40 U/L.
3 Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. http://content.nejm.org/cgi/reprint/NEJMoa030685v2.pdf (accessed April 24, 2003).

4 Cairo M, Branco F. Blood and blood-forming tissues. In: Rudolph AM, ed. Rudolph’s Pediatrics, 21st edn. New York: McGraw Hill, 2002: 1548.

5 Smith DW, Frankel LR, Mathers LH, Tang AT, Ariagno RL, Prober CG. A controlled trial of aerosolized ribavirin in infants receiving mechanical ventilation for severe respiratory syncytial virus infection. N Engl J Med 1991; 325: 24–29.

Departments of Paediatrics (K L E Hon FRCP, W T F Cheng MRCPCH, A M Li MRCP, P C Ng MO, C K Li MO, Prof T F Fok MO), Microbiology (PK S Chan MO, J S Tam PhD), and Diagnostic Radiology and Organ Imaging (W C W Chu MD), Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, Special Administrative Region, China; and Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong (C W Leung FRCPCH, Y W Kwak MRCP, N C Fong MRCP, M C Chiu FRCP)

Correspondence to: Prof T F Fok, Department of Paediatrics, Chinese University of Hong Kong, 6/F, Clinical Sciences Building, Prince of Wales Hospital, Shatin, Hong Kong, Special Administrative Region, China
(e-mail: taifaifok@cuhk.edu.hk)

Effect of gabapentin on nausea induced by chemotherapy in patients with breast cancer

Thomas Guttuso Jr, Joseph Roscoe, Jennifer Griggs

In an anecdotal report, complete resolution of chemotherapy-induced nausea was seen in a patient with breast cancer, after she was placed on the anticonvulsant gabapentin. On this basis, we did an open-label study in which oral gabapentin 300 mg thrice daily was given for every other chemotherapy treatment in nine patients with breast cancer. Six of the nine reported at least a three-point improvement in peak delayed nausea (on an eight-point nausea scale), and three patients had complete resolution of nausea when taking gabapentin. This preliminary evidence shows that gabapentin might have a role in treatment of chemotherapy-induced nausea.

Lancet 2003; 361: 1703–05

Delayed onset of nausea induced by chemotherapy remains a problem for about half of patients receiving moderately emetogenic chemotherapy, despite preventive treatment with a serotonin antagonist and dexamethasone.1 We describe an open-label study of therapy with the anticonvulsant gabapentin 300 mg thrice daily for acute (within 24 h) and delayed onset (days 2–5) nausea induced by chemotherapy.

The initial report came from a 59-year-old woman who began to have hot flushes soon after stopping oral oestrogen therapy because of newly diagnosed breast cancer. Chemotherapy consisting of doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² was given four times, the treatments separated by 3 weeks. Ondansetron 10 mg and dexamethasone 10 mg were given before each treatment. The patient reported severe nausea after the first two chemotherapy treatments. Prochlorperazine 10 mg taken thrice daily as required was ineffective. Midway between the second and third chemotherapy treatments, oral gabapentin 300 mg thrice daily was started for treatment of the patient’s hot flushes. Within 2 days, all such symptoms had resolved. Unexpectedly, she had no nausea after either the third or the fourth chemotherapy treatments. No other medication changes had been made.

We did an open-label study examining the effects of oral gabapentin 300 mg thrice daily on chemotherapy-induced nausea in breast-cancer patients who had not previously...