

clinical condition improved; he had no fever and could walk without dyspnea. The infiltrate in the left lung diminished in density, and the dose of methylprednisolone was reduced to 40 mg twice daily on April 19.

On April 29, the patient was again dyspneic, and radiographs showed a left basilar infiltrate. Bone marrow aspiration revealed suppression of all three cell lineages. On May 4, the patient was transferred to a university teaching hospital. Methylprednisolone (240 mg twice daily) was given, but the next day the oxygen saturation fell to 60 percent, and endotracheal intubation was performed to allow mechanical ventilation. The patient showed signs that were consistent with the presence of tentorial herniation; his pupils were fixed and dilated. Computed tomographic examination of the cranium showed diffuse cerebral edema with localized hemorrhage. Enzyme-linked immunosorbent assay and indirect immunofluorescence established the presence of specific antibodies against a SARS-associated virus in the serum. The fungal culture of sputum obtained on April 14 was negative; the bacterial cultures of sputum obtained on May 2 and May 4 were negative as well. Despite massive supportive care, the patient died on May 7.

Autopsy showed SARS-associated pathologic changes,^{1,2} including consolidation, hemorrhage, and edema of the lungs; proliferation and desquamation of alveolar epithelial cells; exudation of monocytes, lymphocytes, and plasma cells in alveoli; and formation of hyaline membranes. In addition, there were multiple lung abscesses containing aspergillus (Fig. 1). There was also cerebral edema,

diffuse cerebral hemorrhage, aspergillus meningitis, and multiple brain abscesses containing aspergillus. Multiple abscesses containing aspergillus were also found in the heart, liver, kidney, spleen, stomach, pancreas, and adrenal glands.

In this patient, it is likely that SARS infection induced mild immunosuppression³ and that immune function was further suppressed by high-dose corticosteroid treatment. At this time, it has not been established whether corticosteroid treatment has an effect on SARS-associated mortality,⁴ although it may decrease clinical morbidity.⁵ We speculate that use of corticosteroids over the course of many weeks led to the serious secondary aspergillus infection that contributed to the death of this patient. We urge caution and restraint in the use of corticosteroids in the treatment of SARS.

Huijun Wang, M.D.

Yanqing Ding, M.D.

Xin Li, M.D.

Lei Yang, M.D.

Wenli Zhang, M.D.

Wei Kang, M.D.

First Military Medical University
Guangzhou 510515, People's Republic of China
hjwang@fimmu.com

1. Ding Y, Wang H, Shen H, et al. The clinical pathology of severe acute respiratory syndrome (SARS): a report from China. *J Pathol* (in press).
2. Nicholls JM, Poon LM, Lee KC, et al. Lung pathology of fatal severe acute respiratory syndrome. *Lancet* 2003;361:1773-8.
3. Panesar NS. Lymphopenia in SARS. *Lancet* 2003;361:1985.
4. Oba Y. The use of corticosteroids in SARS. *N Engl J Med* 2003;348:2034-5.
5. Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;348:1986-94.

Profile of Specific Antibodies to the SARS-Associated Coronavirus

TO THE EDITOR: A novel coronavirus called the severe acute respiratory syndrome (SARS)-associated coronavirus (CoV) has been identified as the causal agent of SARS.¹⁻³ To understand the humoral immunity to this virus, we studied the profile of IgM and IgG antibody responses to SARS-CoV. IgM and IgG antibodies were analyzed by an indirect enzyme-linked immunosorbent assay in 20 patients with SARS from week 1 of their illness to week 12 and in 103 healthy contacts.

All 20 patients tested negative for IgM and IgG at week 1 after the onset of symptoms. Of these pa-

tients, 16 tested positive for IgM and 17 tested positive for IgG at week 2 (Fig. 1). All 20 patients were IgG-positive after week 3 and continued to have high levels of IgG up to three months after the onset of symptoms. The IgG titers were low at the beginning of week 2 (mean, 1:40, with the cutoff for a positive result being 1:10), increased to an average of 1:256 at week 3, and peaked at 1:640 at week 12. The IgM titers peaked during the acute or early convalescent phase and then declined with IgM disappearing by the end of week 12. All 103 healthy contacts tested negative for IgM and IgG.

Our results suggest that 100 percent of patients had antibody responses to SARS-CoV during the convalescent phase. The SARS-specific IgG antibody persisted for a long time, but the SARS-specific IgM remained measurable for a much shorter period, suggesting that IgG antibody to SARS-CoV may represent the primary humoral immune response protecting patients against SARS. The profile of antibodies against SARS-CoV was consistent with common findings with regard to acute viral infectious diseases such as hepatitis A.⁴ The profile of anti-SARS antibodies may be helpful in the diagnosis and in epidemiologic surveys. The presence of high titers of IgG antibody to SARS-CoV in the patients at the convalescent stage also suggests that a live attenuated or inactivated vaccine for active immunization and a concentrated human SARS-specific IgG antibody for passive immunization could be developed for the treatment of SARS.

Gang Li, M.D., Ph.D.

Xuejuan Chen

Anlong Xu, Ph.D.

Sun Yat Sen University
Guangzhou 510275, China
ligangzh@pub.guangzhou.gd.cn

1. 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.
2. Drosten C, Günther S, Preiser W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med* 2003;348:1967-76.

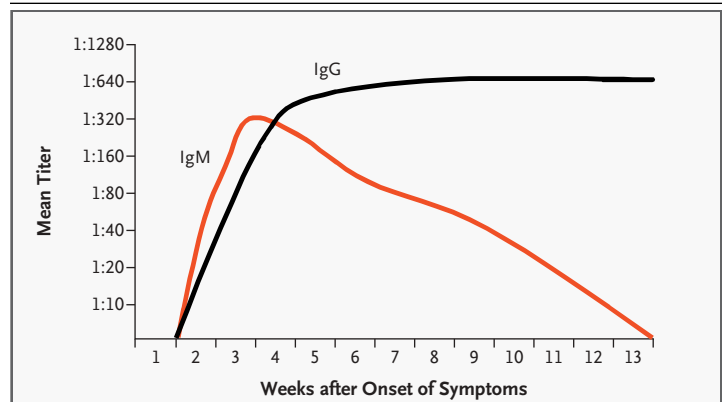


Figure 1. Changing Titers of IgM and IgG Antibodies to the SARS-Associated Coronavirus from the Onset of Illness through the Convalescent Phase.

IgM and IgG were measured at weeks 1, 2, 3, 4, 8, and 12; the mean IgG titer was 1:40 at week 2, 1:256 at week 3, 1:368 at week 4, 1:640 at week 8, and 1:640 at week 12. The mean IgM titer was 1:120 at week 2, 1:320 at week 3, 1:160 at week 4, and 1:40 at week 8. The cutoff value for a positive result was 1:10, and patients with negative results were considered to have a titer of 0 for the calculation of the mean titer.

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

4. Kawai H, Feinstone SM. Acute viral hepatitis. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. 5th ed. Vol. 1. Philadelphia: Churchill Livingstone, 2000:1279-97.

Correspondence Copyright © 2003 Massachusetts Medical Society.

INSTRUCTIONS FOR LETTERS TO THE EDITOR

Letters to the Editor are considered for publication, subject to editing and abridgment, provided they do not contain material that has been submitted or published elsewhere. Please note the following: •Letters in reference to a *Journal* article must not exceed 175 words (excluding references), must be received within three weeks after publication of the article, and must be submitted over the Internet at <https://secure.nejm.org/letters>. Letters not related to a *Journal* article must not exceed 400 words and may be submitted over the Internet or sent, typewritten and triple-spaced, by mail. •A letter can have no more than five references and one figure or table. •A letter can be signed by no more than three authors. •Financial associations or other possible conflicts of interest must be disclosed. (Such disclosures will be published with the letters. For authors of *Journal* articles who are responding to letters, this information appears in the original articles.) •Include your full mailing address, telephone number, fax number, and e-mail address with your letter.

Our address: **Letters to the Editor • New England Journal of Medicine • 10 Shattuck St. • Boston, MA 02115**

Our Web address: <https://secure.nejm.org/letters>

Our fax numbers: **617-739-9864** and **617-734-4457**

We cannot acknowledge receipt of your letter, but we will notify you when we have made a decision about publication. Letters that do not adhere to these instructions will not be considered. Rejected letters and figures will not be returned. We are unable to provide prepublication proofs. Submission of a letter constitutes permission for the Massachusetts Medical Society, its licensees, and its assignees to use it in the *Journal's* various print and electronic publications and in collections, revisions, and any other form or medium.