

## SARS-CoV-2 RNA more readily detected in induced sputum than in throat swabs of convalescent COVID-19 patients

In China, the most common method for diagnosing coronavirus disease 2019 (COVID-19) is the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in throat swabs. This technique has a rate of false-negative results that might enable convalescent COVID-19 patients to meet the criteria<sup>1</sup> for discharge from hospital and release from quarantine, resulting in the spread of disease.

In patients with COVID-19, whether SARS-CoV-2 RNA tests of sputum samples are more sensitive than viral RNA tests of throat swabs is uncertain. Furthermore, most of these patients do not have sputum, especially during the convalescent period.<sup>2</sup> We resolved this problem in two patients by inducing sputum production. To our knowledge, this is the first report of such a technique in patients with COVID-19.

Our first case was a 54-year-old man with a history of diabetes who was admitted to our hospital (Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong, China) for treatment and quarantine on Feb 1, 2020, because of self-reported fever for the previous 3 days. On admission, his white blood cell count was  $6.62 \times 10^9$  per L, lymphocyte count was  $2.02 \times 10^9$  per L, C-reactive protein level was 26.6 mg/L (normal range 0–8.0 mg/L), and fasting blood glucose level was 12.5 mmol/L. Lung CT showed multiple ground-glass opacities in both lungs and lesions that were primarily distributed along the pleura (appendix pp 1–2). On Feb 3, a China Food and Drug Administration-approved viral RNA detection kit confirmed mild COVID-19 in this

patient. Symptoms resolved after treatment with oxygen, lopinavir-ritonavir, moxifloxacin, and hypoglycaemic drugs. 3 days later, the patient's fever decreased and C-reactive protein levels normalised. After four follow-up lung CT scans, the patient's lungs showed substantial lesion resorption (appendix pp 1–2). Beginning Feb 13, three consecutive throat swabs (>24 h intervals) and one anal swab tested negative for viral RNA. On Feb 21, induced sputum (ie, 10 mL of 3% hypertonic saline was inhaled through a mask with oxygen at a flow rate of 6 L/min for 20 min or until the sputum was produced) was positive for viral RNA.

Our second case was a 42-year-old woman who was admitted to our hospital on Jan 27, 2020, because of self-reported fever for the previous 4 days. On admission, her white blood cell count was  $4.01 \times 10^9$ /L, lymphocyte count was  $0.71 \times 10^9$ /L, and C-reactive protein level was 2.58 mg/L. Lung CT showed scattered inflammation in both lungs and lesions that were primarily distributed along the pleura (appendix pp 1–2). On Jan 28, viral RNA was detected in a throat swab, confirming a mild case of COVID-19. Her fever subsided the day after treatment with oxygen, lopinavir-ritonavir, and moxifloxacin, and her symptoms gradually resolved. After four follow-up lung CT scans, her lungs showed lesion resorption and improvement (appendix pp 1–2). Beginning Feb 10, three consecutive throat swabs (>24 h intervals) and one anal swab tested negative for viral RNA. On Feb 21, we induced 3 mL of sputum, as described before for our first case, and viral RNA was detected.

Sputum induction is a safe and simple non-invasive method for detecting various lung diseases.<sup>3</sup> Moreover, the risk of medical staff exposure to COVID-19 is lower with sputum induction than with nasal or throat swabs and bronchoalveolar lavage methods. Here we showed sputum induction might be more

helpful than throat swabs for the detection of SARS-CoV-2 RNA in convalescent patients; to confirm our findings, more patients should be tested using this method to further test its viability for clinical application. Our study also showed that patients with COVID-19 might be contagious despite being clinically cured and having multiple negative throat swabs. To reduce the risk of disease spread, viral RNA tests of induced sputum—not throat swabs—should be assessed as a criterion for releasing COVID-19 patients.

We declare no competing interests. Written informed consent was obtained from the patients. We thank Prof Liehua Deng and Prof Dongming Li who were involved in the diagnosis and treatment of COVID-19. We also thank the patients.

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See Online for appendix