
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.

calculated using the so-called Corona Score)[7] should be regarded as an essential containment measure.

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## In Reply—Repeated Testing in SARS-CoV-2 Infection

***To The Editor:*** We appreciate the points raised by Lippi et al regarding our article describing repeated testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1] In summary, the authors emphasize that repeated testing may be helpful in improving the negative predictive value of testing and ensuring that cases of COVID-19 are identified. The authors include evidence supporting the conclusion that identification of the SARS-CoV-2 virus is directly related to the number of nasopharyngeal swabs that are collected and also emphasize the importance of case-finding in control of the pandemic. In general, we agree that repeated testing may be helpful in certain situations of ongoing high suspicion for active infection where alternative approaches are not feasible; however, we believe that testing should not be applied indiscriminately in a resource-constrained situation.

The results of several studies have suggested that the number of unique patient specimens tested for SARS-CoV-2 is directly related to the positive identification of the virus and that there may be a high false-negative rate of molecular testing.[2,3] The study by Zhang et al[2] reported 41 hospitalized patients with an initial negative polymerase chain reaction test who had at least 1 positive result on subsequent testing. However, the timing between tests was not reported in this article, which raises the possibility that some of the patients could have become infected after their first test. No laboratory test has 100% sensitivity, and we agree that the likelihood of detecting infected individuals will increase if they are tested more frequently. This characteristic of laboratory testing is not unique to SARS-CoV-2 but could be applied to molecular testing for many other infectious diseases. However, widespread indiscriminate repeated testing is not currently possible.

Unfortunately, supply chain challenges continue to limit the widespread availability of SARS-CoV-2 polymerase chain reaction testing in the United States. Tests should be used in an efficient manner and guided by principles of diagnostic stewardship.[4] We agree that there may be a role for repeated testing in patients with high clinical suspicion of coronavirus 19, and where a positive result would change clinical management. However, in situations with low pretest probability and limited resources, repeated testing of a sample collected from the same anatomical site demonstrated a low yield (2%) in our study. The clinical stage of illness can be used to determine whether an upper or lower respiratory specimen may provide more useful information, with detection of SARS-CoV-2 in lower respiratory sources becoming more likely as the disease progresses. The data on test characteristics in asymptomatic patients remain limited. Further studies are needed to identify the utility of repeated testing in this population.

Even in the absence of widespread test availability, there are a variety of strategies that have been proposed to mitigate the risk of false-negative testing, including strict infection control measures,

development of improved diagnostic tests, risk stratification of patients before testing, and the use of standardized protocols for the management of patients who test negative.[5] These strategies, combined with strategic use of repeated testing, will preserve limited resources and provide the best route toward ending the SARS-CoV-2 pandemic.

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## Severe Hyponatremic Encephalopathy in a Patient With COVID-19

***To The Editor:*** Coronavirus disease 2019 (COVID-19) has been declared a pandemic. The illness manifests mainly with fever and respiratory symptoms. We present the first reported case of life-threatening hyponatremia in a patient with COVID-19.

A 56-year-old woman was brought to the hospital for sudden-onset altered mental status. The patient had been at work on the day of admission. She had sore throat and, within hours, developed confusion and incoherent speech. Her only comorbidity was hypertension, for which she had been treated with hydrochlorothiazide for 3 years. She was taking no other medication or supplement. Vital signs were stable, with blood pressure of 110/70 mm Hg. On examination, she was obtunded and without focal neurologic deficits. Laboratory testing showed serum sodium 115 mEq/L, potassium 3.2 mEq/L A 55-year-old man with history of hyperlipidemia and previou, and magnesium 1.2 mmol/L. Serum osmolality was 247 mOsm/kg, whereas urine osmolality was 670 mOsm/kg. Computed tomography scan of the head and chest x-ray film showed no acute pathology. Urine toxicology results were negative. She was clinically euvolemic and diagnosed with acute-onset severe hyponatremia from an antidiuretic hormone (ADH)-dependent pathway. She was treated with 3% hypertonic saline and desmopressin. Being at the epicenter of the COVID-19 pandemic, SARS-CoV-2 testing was performed, and results came back positive. Computed tomography of the chest revealed ground-glass opacities bilaterally. Influenza testing, blood cultures, and urinalysis results were negative. Thyroid stimulating hormone level was normal, and serum cortisol was appropriately elevated. The patient's serum sodium and mental status normalized over the next 4 days, and she was advised to stop taking hydrochlorothiazide on discharge. She denied developing any respiratory symptoms on a telemedicine visit 10 days postdischarge.

Severe hyponatremia (<120 mEq/L) may present with manifestations of cerebral edema including obtundation, seizures, coma, respiratory arrest, and death. Thiazides are known to cause severe hyponatremia that can simulate a syndrome of inappropriate ADH-like picture associated with hypokalemia. The risk of thiazide-induced hyponatremia is present for as long as 10 years after initiation of therapy.[1] In patients on thiazides, severe hyponatremia could be precipitated by a lung infection, similar to our patient.[2] Pneumonia not only precipitates hyponatremia in patients on thiazides but can cause it independently by an ADH-dependent pathway. Although classically described in legionella pneumonia, hyponatremia occurs with a variety of bacterial, viral, and fungal lung pathogens.[3] Mechanisms and risk factors of thiazide- and pneumonia-induced hyponatremia and their interplay is shown in the Figure.[3,4]

As first-line antihypertensive agents, thiazides are widely prescribed. In 2012, in the United States alone, an