


Capitalism is groovy, but at what cost?

Krishna Vedala, Phillip T Sobash , Shiyu Wang and Gilbert-Roy Kamoga

Department of Internal Medicine, White River Health System, Batesville, AR, USA

ABSTRACT

Due to the COVID-19 pandemic, the FDA was forced to bypass normal protocol and issue Emergency Use Authorization for diagnostic testing. As a result, we have seen an explosion in the number of available molecular diagnostic tests developed by various private enterprises. Our case reports of an 85-year-old female who was suffering from a multitude of comorbidities and underwent three different molecular diagnostic tests in a short timeframe. With little data on the precision and reliability of the multiple available tests, it has become extremely difficult to diagnose and guide management. Instead of focusing on commercial ventures, FDA in conjunction with the CDC should prioritize our resources to tackle COVID-19 as a public health crisis.

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The Covid-19 pandemic has exposed significant defects within the US Public Health System [1]. The lack of a cohesive testing strategy and preparation including insufficient training has complicated diagnosis and management of COVID-19. In order to meet the demands of the COVID-19 crisis, the FDA has been very active in rapidly making available various diagnostic tests, kits, assays and medical devices using Emergency Use Authorization (EUA) [2]. As a result, an even more concerning notion is the rise of a new entrepreneurial war between competing firms designing newer molecular diagnostic tests all in the name of capitalism. However, doing so has raised more questions especially regarding the utilization, accuracy, reliability, and financial burdens associated with the various diagnostic tests on the market now [2]. Here, we report a case that emphasizes how a fractured testing strategy based on the competition can lead to dire consequences.

Our patient is an 85-year-old female with a history of dementia, hypertension, hyperlipidemia and diabetes mellitus II who is also a nursing home resident. Due to an increase in positive COVID cases at the nursing home, she was tested for COVID19 twice in a span of eight days. She tested negative both times, but after her second test, she noticeably became more confused and exhibited bizarre behavior. One week after the second test, she suffered a witnessed seizure. She was then transferred to an Outside Hospital (OSH).

At OSH, she underwent significant workup for new-onset seizures and acute encephalopathy. A brain MRI revealed chronic microvascular changes and cerebral atrophy, but was negative for any acute

changes. Lumbar puncture showed elevated protein but was negative for meningitis. Transthoracic echocardiogram revealed a reduced ejection fraction with global hypokinesis but no thrombus or shunt. She was found to have a UTI and was treated with anti-epileptics and antibiotics. However, she also developed a 3.8 second pause on telemetry. Cardiology and Electrophysiology were worried about possible AV block in lieu of her symptoms and comorbidities and recommended permanent pacemaker placement. She was then transferred to our facility due to lack of neurology services at OSH, and with plan for pacemaker placement at our facility.

Further management at our facility revealed potential cholecystitis and bilateral aspirational pneumonia. With no cohesive diagnosis despite consultations with Cardiology and Neurology at our facility, decision was made to test the patient again for COVID two days after arrival. Using our in-house test, she tested positive. Unfortunately, her condition deteriorated quickly after the test results and expired 36 hours later, nearly a week after her admission at the OSH. Throughout her stay at our facility, patient was noted to be hemodynamically stable, saturating well with 2 L of oxygen, and non-oliguric urine output. A major concern was her persistent delirium or encephalopathy which made subjective assessment rather challenging. Her admission procalcitonin was <0.05, and only developed leukocytosis the last two days. She did spike a fever (t-max 102.1 F) soon after admission and on day of demise but was afebrile during the rest of admission. However, she was tachycardic and tachypneic for most of her hospitalization.

Our case shows many areas in this patient's care that warrant caution. A case can be made that the patient could have been exposed to the nursing home, the OSH or even our facility. Such a point would be difficult to prove for now which is also complicated by the lack of testing at the OSH. An ID specialist was consulted at OSH, but no mention of need for COVID testing was mentioned in documentation. Perhaps, the two negative tests from the nursing home discouraged further COVID testing at OSH. Another area of concern is the great variability in obtaining nasopharyngeal sample. A proper sample is often described as one that is inserted so deep into the nasal cavity that it elicits a tear-reflex [3]. At times, this can be a difficult procedure and is dependent upon the performer's experience and patient cooperativity. In addition, potential contamination of samples is always a possibility. Both tests from the nursing home were transported to different labs nearly 80 to 100 miles away, a task that enhances the risk of contamination [3].

Despite the issues listed above, the pressing concern is that each time she was tested with a different molecular test. As of 22 May 2020, the FDA has issued EUAs for 80 different molecular diagnostic tests for COVID-19 [4]. Each of these tests vary in terms of their target gene/region, the type, the test result time and the LoD (Limit of Detection). For her first test, the nursing home utilized the Thermofisher's Taqpath COVI19-combo kit from Gamma Laboratory. TaqPath is a multiplex real-time RT-PCR test that targets the ORFib, N, and the S genes [5]. Her second test from the nursing home was the CDC-developed CDC-2019 Novel Coronavirus Real-Time RT-PCR Diagnostic panel, which is a real-time RT-PCR test and targets the N gene [5]. It was also the first test issued an EUA by the FDA. Her third test that was done at our facility was CEPHEID'S Xpert Xpress SARS-CoV-2 test, which is another real-time RT-PCR test but it targets the N2 and E gene [5]. The Xpert results in roughly one hour, the CDC-2019 results in four hours and the Thermofisher results in three hours [5]. The LoD of each test also varies. The LoD is the smallest measured concentration of an analyte that can be reliably detected with acceptable certainty [6]. The Thermofisher's is 10 GCE/reaction, the Xpert is 250 copies/mL, and the CDC-2019 Novel is $10^{0.5}$ or $10^{1.0}$ RNA copies/microliter [7--9]. It is difficult to compare the three as each test has different targets and also differ in inherent design. In addition, the FDA and CDC have provided very minimal guidance on the selection of testing options.

With many available options under EUAs, there has been great indiscretion and irregularity in the type of test used. Even within our own facility, we have used the Roche Cobas SARS-CoV-2 and the

Abbot ID NOW COVID-19 in addition to the Xpert. Within a 100 mile-area (the nursing home, OSH, and our facility), there have been a minimum of five different tests used. The situation is also worsened by the fact that tests with EUA have not been thoroughly corroborated. According to Basu et al., the Abbot ID NOW when compared to Cepheid has been shown to have a sensitivity of 51.6% and a specificity of 98.6% [10]. Essentially, a positive test on Abbot has a high likelihood of being accurate (high positive predictive value), but a negative test on Abbot has a very poor likelihood of ruling someone out (low negative predictive value). On the other hand, the Xpert and the Roche test have been shown to have greater concordance with one another [11]. Unfortunately, very limited research has been conducted on analyzing available diagnostic tests, especially Thermofisher and CDC-2019 Novel. Therefore, it has been difficult to assess the validity and accuracy of these tests.

In conclusion, our case reinforces that the lack of uniform and reliable testing options complicates the diagnosis and management of COVID19. It would be beneficial if the FDA could develop a tool that provides an effective comparison of all molecular tests that have received EUAs. Of course, more research is always needed to test the efficacy of these various diagnostic tests and perhaps improving guidelines for FDA approval and EUA issuance. However, if we are to meet the urgent demands of this pandemic, there should be greater emphasis on seeing COVID-19 as a public health crisis rather than as a new battleground for competing capitalist ventures.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Phillip T Sobash  <http://orcid.org/0000-0001-9711-604X>

References

- [1] Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed.* 2020;91(1):157-160.
- [2] Mitchell SL, St. George K, Rhoads DD, et al. Understanding, verifying and implementing emergency use authorization molecular diagnostics for the detection of SARS-CoV-2 RNA. *J Clin Microbiol.* 2020;58(8). DOI:10.1128/JCM.00796-20
- [3] Tang Y-W, Schmitz JE, Persing DH, et al. The laboratory diagnosis of COVID-19 infection: current issues and challenges. *J Clin Microbiol.* 2020;58(6). DOI:10.1128/JCM.00512-20
- [4] US food and drug administration: emergency use authorizations. Test kit manufacturers and commercial laboratories table. 2020 May 22. Available from:

- <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd>
- [5] Linda J. Carter, Linda V. Garner, Jeffrey W. Smoot, Yingzhu Li, Qiongqiong Zhou, Catherine J. Saveson, Janet M. Sasso, Anne C. Gregg, Divya J. Soares, Tiffany R. Beskid, Susan R. Jervey, and Cynthia Liu. *ACS Central Science* 2020 6 (5), 591-605.
- [6] US food and drug administration: guidelines for the validation of chemical methods in food, feed, cosmetics, and veterinary products, 3rd edition. 2020 May 24. Available from: <https://www.fda.gov/media/81810/download>
- [7] US food and drug administration: taqPath™ COVID-19 combo kit instructions for use. 2020 May 24. Available from: <https://www.fda.gov/media/136112/download>
- [8] US food and drug administration: xpert xpress SARS-CoV-2 instructions for use. 2020 May 24. Available from: <https://www.fda.gov/media/136314/download>
- [9] US food and drug administration: CDC 2019-Novel Coronavirus (2019-nCoV) real-time RT-PCR diagnostic panel instructions for use. 2020 May 24. Available from: <https://www.fda.gov/media/134922/download>
- [10] Basu A, Zinger T, Inglima K, et al. Performance of Abbott ID Now COVID-19 Rapid Nucleic Acid Amplification Test Using Nasopharyngeal Swabs Transported in Viral Transport Media and Dry Nasal Swabs in a New York City Academic Institution. *Journal of Clinical Microbiology*. 2020 Jul;58(8). DOI: 10.1128/jcm.01136-20.
- [11] Moran A, Beavis KG, Matushek SM, et al. The detection of SARS-CoV-2 using the cepheid xpert xpress SARS-CoV-2 and Roche cobas SARS-CoV-2 assays. *J Clin Microbiol*. 2020;58(8). DOI:10.1128/JCM.00772-20