New Mexico Medical Advisory Team (MAT) Assessment

MAT Workgroup Name: Testing **Date:** April 20, 2020

Questions or requests:
What approach should New Mexico take to serologic coronavirus antibody testing?
What are the appropriate uses of the testing?
Should NM seek to purchase serologic testing kits in bulk?

Recommendations:

- At the present time, serologic testing has a defined role in the following settings only: subset of acutely ill patients; focused epidemiologic surveillance during the ongoing outbreak and post-outbreak in vulnerable populations; general epidemiologic surveillance; as an important tool in studying long-term outcomes in individuals with symptomatic and asymptomatic COVID-19 disease.
- Serologic testing should be diversified to multiple platforms and at the same time focused on high-throughput hospital and reference lab-based testing as determined by criteria listed below, from reliable manufacturers (DiaSorin, Abbott, Roche) who have or are expected to have FDA Emergency Use Authorizations (EUA) for their tests.
- NM reference labs should independently evaluate test characteristics to ensure high sensitivity (positive in people with disease) and specificity (negative test in people without disease)
- Lateral flow point-of-care rapid testing kits available now and heavily marketed via email have NOT been sufficiently tested and should NOT be considered for purchase unless and until rigorous independent evaluation of their performance characteristics is available through FDA and CDC.
- The State of NM can assist state labs to procure testing kits at this time (given predictable multiple supply chain interruptions due to overwhelming demand for reagents). The Scientific Laboratory Division of the Department of Health (DOH) is in negotiation with Abbott to purchase serologic test reagents when they become available and receive an EUA from FDA.
- DOH should provide specific guidance as to the proper use of antibody tests to the provider community and the general public (to be attached)

Assessment:

Expected APPROPRIATE uses of Antibody Testing	**Non-Value-Added Uses of Antibody Testing**
Focused epidemiologic surveillance during the ongoing outbreak and post-outbreak in vulnerable/special populations/locations (estimated need = 5000 tests)	To determine who can return to work – limited by the fact that we do not yet know whether the presence of antibody following disease is an indication of cure or protection from subsequent infection
General epidemiologic surveillance (estimated need = 5000 tests)	To satisfy curiosity about "Did I have COVID?"
Limited use: subset of acutely ill patients, as a complement to nucleic acid amplification testing to increase the sensitivity of lab diagnosis [they could be used in a complementary manner – both obtained at the same time since both will take a while to come back] (estimated need = 500 tests)	To determine who does and does not need a vaccine – limited by the fact that the presence or absence of an antibody response may not enter into population-level vaccination policy
To study long-term outcomes of individuals with both symptomatic and asymptomatic COVID-19 disease (estimated need = 500 tests)	-

- The MAT recommends these criteria for selecting a reliable antibody test:
  - High sensitivity and specificity, as well as high positive and negative predictive value (these depend on prevalence)
  - Ability to be run in a high-throughput environment (ELISA methodology testing NOT recommended)
  - Highest possible probability that positive AND negative tests results will be automatically reported to DOH (which is not the case for point-of-care testing)
  - There is an established and reliable supply chain for necessary test reagents
  - Highly reliable manufacturer with a wide distribution of machines in New Mexico. First tier = DiaSorin, Abbott, Roche; second tier = Beckman Coulter, Siemens, Bio-Rad
- Antibody testing can be IgM (positive within 5-7 days of initial symptoms) and/or IgG (positive within 10-21 days of initial symptoms). IgG antibody testing is preferred over IgM antibody testing in this context because it is likely to have a lesser false positive rate but with comparable sensitivity for detection of acute infection. In a small sample, one NM reference lab found 8/9 (89%) positive IgG tests at >=10 days post positive-PCR test with 4/4 (100%) positive at >=14 days, and 100% negative tests in 19 individuals with positive respiratory virus screening for a non-coronavirus infection. NM labs can quickly validate newer tests coming onto the market.
- Blood specimens should be tested in both reference labs AND hospital labs throughout the state.
- New Mexico's use of antibody testing should be diversified to at least three manufacturers to avoid the effects of supply chain interruptions as demand increases.

Manufacturer	Testing Equipment Model Name/#	Antibody Testing Methodology	Reagents Needed	Throughput (tests/day)*	Reference Labs with Equipment	Number of NM Hospitals with Equipment	Estimated Cost per Test
DiaSorin	Liason XL	Automated serology platform	DiaSorin kits, $12 each	800	TriCore	1	$47
Abbott	i1000	Automated serology platform	Abbott kits, $6.50 each	900	SLD	0	$6.50 (no other costs included)
Roche	Cobas e411	Automated serology platform	Roche kits	600	TriCore	2	$TBD
Beckman Coulter	DxI800	Automated serology platform	Beckman kits	3,000	TriCore	1	$TBD
Siemens	Centaur XP	Automated serology platform	Siemens kits	TBD by Siemens when test complete	TriCore	3	$TBD

Throughput per day will depend on reagent availability and allocations. As of 4/19/20 only DiaSorin and Abbott are shipping (or are about to ship) reagents. Others are expected in early May (Roche), late May (Siemens), and mid-summer (Beckman).

It is important to have guidance for both providers and the public regarding the appropriate use of antibody testing. Guidance to providers has been created and is available on MAT website. Public guidance is near completion, and will be posted on MAT website.

Red flags and concerns:

- At the present time, state officials and others receive multiple daily e-mails marketing point-of-care testing with lateral-flow COVID-19 serologic antibody testing. Almost all of these tests have not received an EUA from FDA, and when they are, the approval is due to very relaxed criteria and zero to minimal actual scientific evaluation of individual tests.
- It is not known whether antibodies to coronavirus (COVID-19) predict immunity to the disease. Some viral illnesses (e.g., mumps) can occur when antibodies are present.
- The duration of immunity for COVID-19 after infection is not known. Other viral respiratory illnesses and their related vaccine (e.g., influenza) may confer immunity for only one year, which is why annual influenza immunization is recommended or required.

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Resources/Reference:

From FDA on 4/19/2020:
Letter to Health Care Providers
https://www.fda.gov/medical-devices/letters-health-care-providers/important-information-use-serological-antibody-tests-covid-19-letter-health-care-providers
FAQs on Diagnostic Testing for SARS-CoV-2
https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2
FDA Fact Sheet - Serological Testing for Antibodies to SARS-CoV-2 Infection
https://www.fda.gov/media/137111/download
Serological Test Validation and Education Efforts
https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-test-validation-and-education-efforts

Additional References:
Antibody Test, Seen as Key to Reopening Country, Does Not Yet Deliver
https://urldefense.com/v3/__https://www.nytimes.com/2020/04/19/us/coronavirus-antibody-tests.html?referringSource=articleShare__;!!NYT1fPLx!uS9H3kOwAeBZrQNzie9-F4tKLIAN_bcdBsWxtUHzMgECn_1CJN8xLUdIbgzdw-V4bkU3TQ$

Wölfel, S, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. https://doi.org/10.1038/s41586-020-2196-x

Also See Attached

nature medicine

BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0869-5

Check for updates

Temporal dynamics in viral shedding and transmissibility of COVID-19

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We report temporal patterns of viral shedding in 94 patients with laboratory-confirmed COVID-19 and modeled COVID-19 infectiousness profiles from a separate sample of 77 infector–infectee transmission pairs. We observed the highest viral load in throat swabs at the time of symptom onset, and inferred that infectiousness peaked on or before symptom onset. We estimated that 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases' presymptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home. Disease control measures should be adjusted to account for probable substantial presymptomatic transmission.

SARS-CoV-2, the causative agent of COVID-19, spreads efficiently, with a basic reproductive number of 2.2 to 2.5 determined in Wuhan[1,2]. The effectiveness of control measures depends on several key epidemiological parameters (Fig. 1a), including the serial interval (duration between symptom onsets of successive cases in a transmission chain) and the incubation period (time between infection and onset of symptoms). Variation between individuals and transmission chains is summarized by the incubation period distribution and the serial interval distribution, respectively. If the observed mean serial interval is shorter than the observed mean incubation period, this indicates that a significant portion of transmission may have occurred before infected persons have developed symptoms. Significant presymptomatic transmission would probably reduce the effectiveness of control measures that are initiated by symptom onset, such as isolation, contact tracing and enhanced hygiene or use of face masks for symptomatic persons.

SARS (severe acute respiratory syndrome) was notable, because infectiousness increased around 7–10 days after symptom onset[3,4]. Onward transmission can be substantially reduced by containment measures such as isolation and quarantine (Fig. 1a)[5]. In contrast, influenza is characterized by increased infectiousness shortly around or even before symptom onset[6].

In this study, we compared clinical data on virus shedding with separate epidemiologic data on incubation periods and serial intervals between cases in transmission chains, to draw inferences on infectiousness profiles.

Among 94 patients with laboratory-confirmed COVID-19 admitted to Guangzhou Eighth People's Hospital, 47/94 (50%) were male, the median age was 47 years and 61/93 (66%) were moderately ill (with fever and/or respiratory symptoms and radiographic evidence of pneumonia), but none were classified as 'severe' or 'critical' on hospital admission (Supplementary Table 1).

A total of 414 throat swabs were collected from these 94 patients, from symptom onset up to 32 days after onset. We detected high viral loads soon after symptom onset, which then gradually decreased towards the detection limit at about day 21. There was no obvious difference in viral loads across sex, age groups and disease severity (Fig. 2).

Separately, based on 77 transmission pairs obtained from publicly available sources within and outside mainland China (Fig. 1b and Supplementary Table 2), the serial interval was estimated to have a mean of 5.8 days (95% confidence interval (CI), 4.8–6.8 days) and a median of 5.2 days (95% CI, 4.1–6.4 days) based on a fitted gamma distribution, with 7.6% negative serial intervals (Fig. 1c). Assuming an incubation period distribution of mean 5.2 days from a separate study of early COVID-19 cases[1], we inferred that infectiousness started from 2.3 days (95% CI, 0.8–3.0 days) before symptom onset and peaked at 0.7 days (95% CI, −0.2–2.0 days) before symptom onset (Fig. 1c). The estimated proportion of presymptomatic transmission (area under the curve) was 44% (95% CI, 25–69%). Infectiousness was estimated to decline quickly within 7 days. Viral load data were not used in the estimation but showed a similar monotonic decreasing pattern.

In sensitivity analysis, using the same estimating procedure but holding constant the start of infectiousness from 1 to 7 days before symptom onset, infectiousness was shown to peak at 0–2 days before symptom onset, and the proportion of presymptomatic transmission ranged from 46% to 55% (Extended Data Fig. 1).

Finally, simulation showed that the proportion of short serial intervals (for example, <2 days) would be larger if infectiousness were assumed to start before symptom onset (Extended Data Fig. 2). Given the 7.6% negative serial intervals estimated from the infector–infectee paired data, start of infectiousness at least 2 days before onset and peak infectiousness at 2 days before to 1 day after onset would be most consistent with this observed proportion (Extended Data Fig. 3).

Here, we used detailed information on the timing of symptom onsets in transmission pairs to infer the infectiousness profile of COVID-19. We showed substantial transmission potential before symptom onset. Of note, most cases were isolated after symptom onset, preventing some post-symptomatic transmission.

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