If at first you do not succeed…. Repeat SARS-COV2 PCR testing

Stephanie Shea, MD[1]; Gopi Patel, MD[2]; Sarah Schaefer, MD[2]; Michael Nowak, MD[1]; Emilia Sordillo, MD, PhD[1]; Alberto Paniz-Mondolfi, MD, PhD[1]; Melissa R. Gitman, MD[1]

[1]Department of Pathology, Molecular, and Cell Based Medicine, Icahn School of Medicine at Mount Sinai, New York, NY;

[2]Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, New York, NY

ABSTRACT

Background: Nucleic Acid Amplification Tests (NAATs) of nasopharyngeal specimens (NPS) have become standard for diagnosis of SARS-COV2. IDSA guidelines suggest repeat testing after 24-48 h when initially negative and clinical suspicion persists. We characterized patients from whom initial NPS were NAAT-negative, but repeats were NAAT-positive, in order to identify which patients might benefit from repeat NAAT for SARS-CoV-2, and the appropriate interval.

Methods: We conducted an IRB-approved retrospective review of laboratory and electronic medical record data for all patients evaluated for SARS-CoV-2 infection at the Mount Sinai Health System, whose initial NAATs were done between March 16 – March 30, 2020, and who were retested within one month. NAATs were performed on NPS in viral transport medium using the Roche Diagnostics cobas® 6800 SARS-CoV-2 Test. Baseline patient characteristics, clinical and radiographic findings were identified.

Results: Of 235 patients eligible for inclusion, 172 (70.5%) were initially NAAT-negative, and 118 (68.6%) remained NAAT-negative over 1 month follow up. 54 (31.4%) converted to NAAT-positive over the next 1-month. Of patients who became NAAT-positive, 31 (57.4%) were inpatients who converted results within a single admission; the average interval was 6d 7h between the NAAT-negative and NAAT-positive results, and the minimum interval was 10.5 h. Symptoms examined for correlation for conversion to NAAT-positive were: fever, cough, shortness of breath, and combined nausea/vomiting/diarrhea. Duration of symptoms reported at triage did not appear to affect time to conversion to NAAT-positive. No individual symptom was more likely to be associated with conversion to NAAT- positive. However, time to conversion to NAAT-positive was shorter for patients with multiple symptoms. In general, chest radiography (CXR) findings correlated with NAAT results; interval to NAAT-positive was shorter for patients with worsening CXR findings.

Conclusion: Our data supports repeat testing in patients with multiple clinical symptoms suggestive of SARS CoV-2 infection and negative initial NP test results. Further studies are needed to determine the true clinical sensitivity and specificity of SARS-CoV-2 NAAT assays.

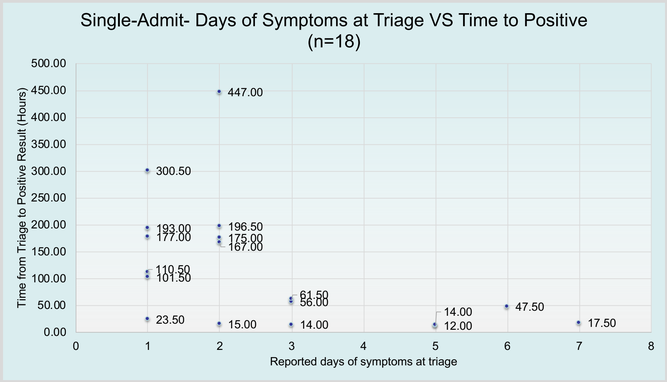
Patient Inclusion

All patients with repeat NP testing in March n=272 → With accurate MRN for chart review n=244 → Excluding patients with "flip-flopping" results n=235 → Initial Negative Result n=172 (70.5% of 235) → Always Negative n=118 (68.6%) Convert to Positive n=54 (31.4%)

Negative to Positive Results n=54

- Single-Admit- n=31 (57.4%) inpatients with conversion during same admission → *Result change interval:* Minimum - 10.5 h; Average - 6 d 7 h; Maximum - ~32 d
- Multi-Admit – n=15 (27.8%) inpatients with conversion over multiple admissions → *Result change interval:* Minimum - 69 h; Average - 12 d 2 h; Maximum - ~25 d
- Outpatient – n=8 (14.8%) outpatient testing only (limited history) → *Result change interval:* Minimum - 20 h; Average - 4 d 20.5 h; Maximum - ~28 d

Common Symptoms and Time to Positive Result?



Which Symptom?	Single Admit (n)	Triage to Positive (hours)	Multi Admit (n)	A1 Triage to Positive (hours)
Unknown	2	37.5	2	416.5
N/V/D*	7	45	4	332
SOB	12	131.5	5	242
Fever	13	155	6	276
Cough	17	230	7	330
None	5	300	1	388

*Nausea/vomiting/diarrhea was always associated in association with other symptoms

Number of Symptoms	Single Admit (n)	Triage to Positive (hours)
0	5	330
1	10	337
2	6	120
3	4	102
4	4	65.5
Unknown	2	36
	31	

Chest X-Rays and Time to Positive Result?

Chest X-Ray Comparison	Single Admit (n)	Triage to Positive (hours)	Multi Admit (n)	A1 Triage to Positive (hours)	Combined Admit (n)	Triage to Positive (hours)	Outpatient
No CXR	4	61	0	x	4	61	1
Clear x2	1	110.5	1	233.5	2	172	2
Worsening	7	181	5	345	12	249.5	2
Findings x2	17	267	9	286.5	26	273.5	3
Improving	2	307	0	x	2	307	0
	31		15		46		8

CONCLUSIONS

- The majority of patients with a Negative NAAT test for SARS-CoV-2 will remain Negative.
- There is value to repeat testing if first test is Negative and there is clinical suspicion.
  - New positive result seen for some samples collected less than 24 hours later.
- Common SARS-CoV-2 symptoms were considered (Fever, Cough, Shortness of Breath, Nausea/Vomiting/Diarrhea):
  - Duration of symptoms at triage did not predict time to Positive result.
  - No clear correlation between type of symptoms and time to Positive result.
  - Increasing number of these symptoms reported at triage associated with shorter time interval to Positive result.
- Most patients had abnormal chest x-ray findings before Negative and Positive results.
  - Interval to Positive result was generally shorter for patients with worsening CXR findings compared to similar or improving findings.
- This study did not identify a clear predictor of which patients will convert from a Negative to a Positive result or what testing interval is ideal to capture conversion.
  - Choice to repeat testing should reflect overall clinical suspicion.

DISCLOSURE

The authors declare no conflicts of Interest.