COVID-19 Clinical Update

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Questions

A staff member becomes infected with COVID-19 and then returns to work after the appropriate clearances/time. Will they need to continue wearing N95 masks for aerosols?

Since the virus has mutated will our current tests pick up the mutated virus antigens or antibodies?

Interested in learning more about plasma donation activities. What are most effective treatment studies so far?

Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19:
A Randomized Clinical Trial

Open-label, multicenter, randomized clinical trial performed in 7 medical centers in Wuhan, China, from February 14, 2020, to April 1, 2020: final follow-up April 28, 2020

103 participants with laboratory-confirmed COVID-19 that was severe (respiratory distress and/or hypoxemia) or life-threatening (shock, organ failure, or requiring mechanical ventilation)

Convalescent plasma in addition to standard treatment (n = 52) vs standard treatment alone (control, n = 51), stratified by disease severity

Terminated early: 103 of a planned 200 patients were enrolled

Results

103 patients: median age, 70 years; 58.3% male, 101 (98.1%) completed the trial

Clinical improvement occurred within 28 days in 51.9% (27/52) of the convalescent plasma group vs 43.1% (22/51) in the control group (difference, 8.8% [95% CI, −10.4% to 28.0%]; hazard ratio [HR], 1.40 [95% CI, 0.79-2.49]; *P* = .26).

- Among those with severe disease, the clinical improvement occurred in 91.3% (21/23) of the convalescent plasma group vs 68.2% (15/22) of the control group (HR, 2.15 [95% CI, 1.07-4.32]; *P* = .03)
- Among those with life-threatening disease the primary outcome occurred in 20.7% (6/29) of the convalescent plasma group vs 24.1% (7/29) of the control group (HR, 0.88 [95% CI, 0.30-2.63]; *P* = .83) (*P* for interaction = .17)

There was no significant difference in 28-day mortality (15.7% vs 24.0%; OR, 0.65 [95% CI, 0.29-1.46]; *P* = .30) or time from randomization to discharge (51.0% vs 36.0% discharged by day 28; HR, 1.61 [95% CI, 0.88-2.93]; *P* = .12)

Convalescent plasma treatment was associated with a negative conversion rate of viral PCR at 72 hours in 87.2% of the convalescent plasma group vs 37.5% of the control group (OR, 11.39 [95% CI, 3.91-33.18]; *P* < .001)

Conclusion: Among patients with severe or life-threatening COVID-19, convalescent plasma therapy added to standard treatment, compared with standard treatment alone, did not result in a statistically significant improvement in time to clinical improvement within 28 days

A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19

Does hydroxychloroquine prevent symptomatic infection after SARS-CoV-2 exposure?

Randomized, double-blind, placebo-controlled trial across the US and parts of Canada

Enrolled adults who had with confirmed Covid-19 at a distance of less than 6 ft for more than 10 minutes while wearing neither a face mask nor an eye shield (high-risk exposure) or while wearing a face mask but no eye shield (moderate-risk exposure)

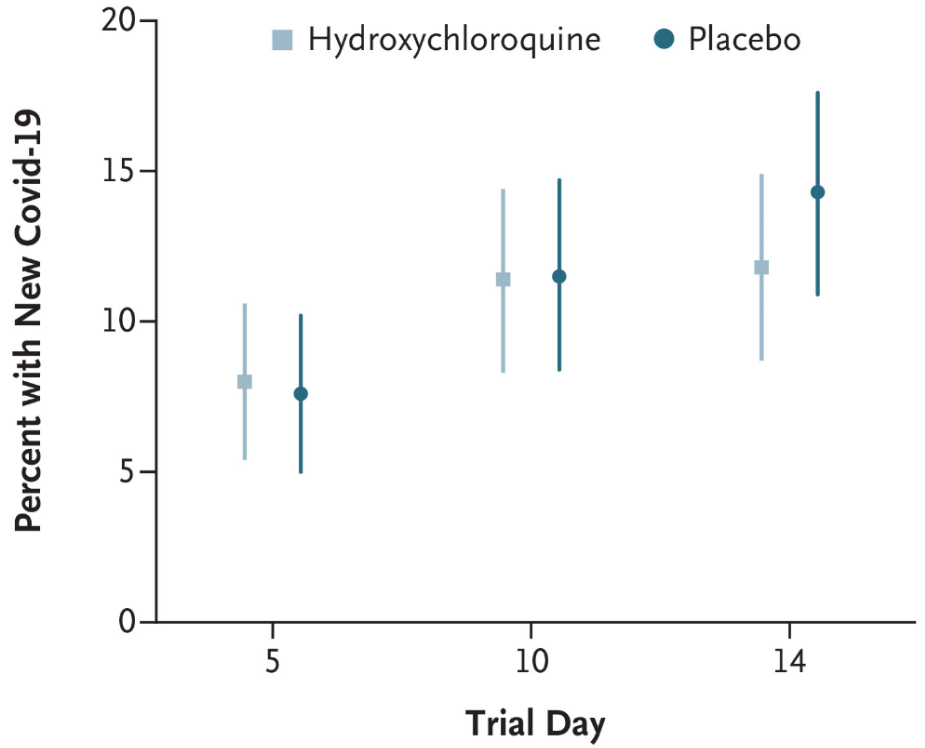
Within 4 days after exposure, randomly assigned participants either placebo or hydroxychloroquine (800 mg once, followed by 600 mg in 6 to 8 hours, then 600 mg daily for 4 additional days)

Primary outcome was the incidence of either laboratory-confirmed Covid-19 or illness compatible with Covid-19 within 14 days

Table 2. Outcomes of Hydroxychloroquine Therapy for Postexposure Prophylaxis against Covid-19.*

Outcome	Hydroxychloroquine (N=414)	Placebo (N=407)	P Value
	number (percent)		
Confirmed or probable Covid-19	49 (11.8)	58 (14.3)	0.35
Laboratory-confirmed diagnosis	11 (2.7)	9 (2.2)	0.82
Symptoms compatible with Covid-19	48 (11.6)	55 (13.5)	0.46
All new symptoms	57 (13.8)	59 (14.5)	0.84
Any hospitalization	1 (0.2)	1 (0.2)	0.99
Death	0	0	—

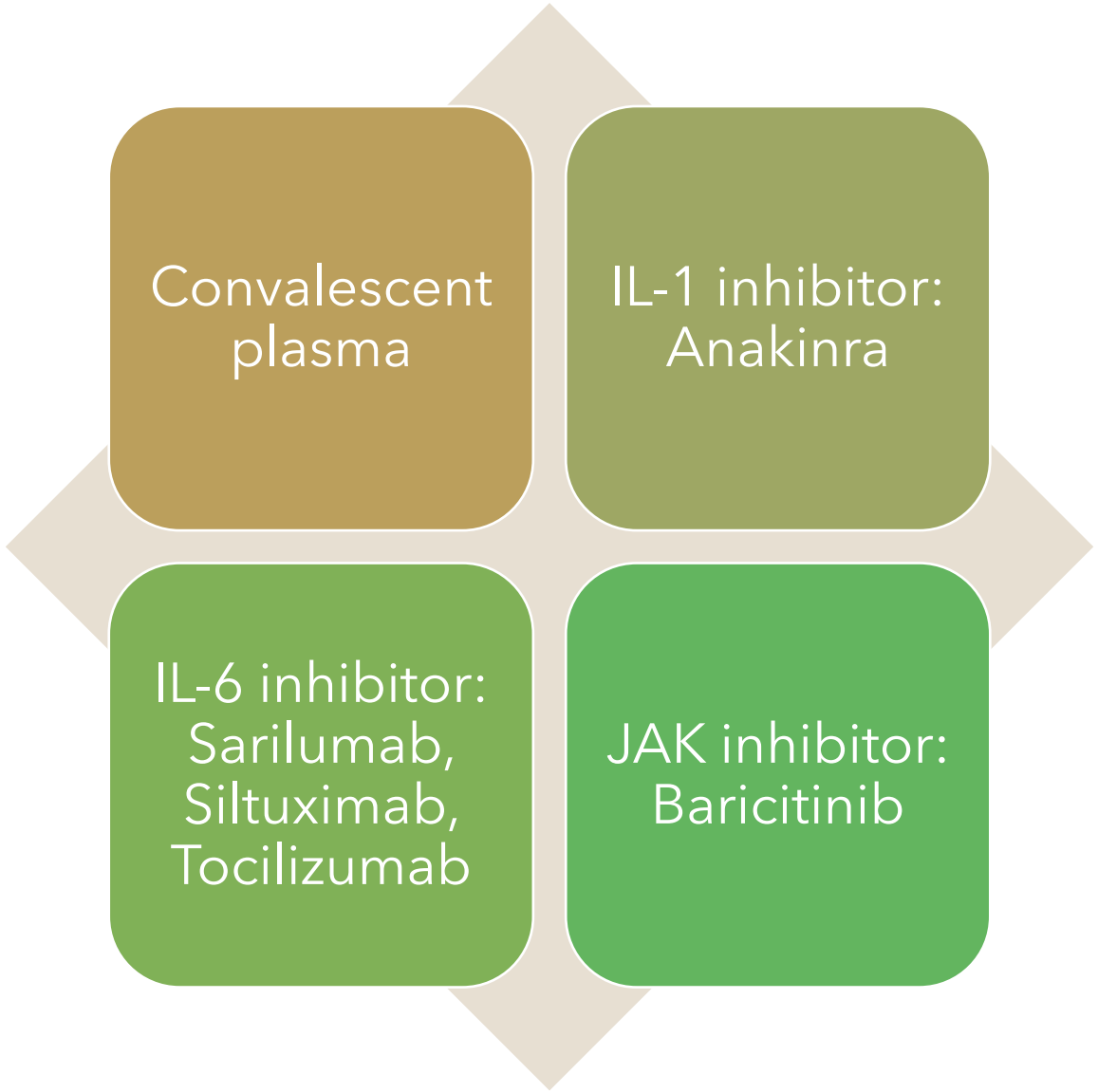
* Symptoms were adjudicated by four infectious disease physicians, who were unaware of the trial-group assignments, in accordance with U.S. Council of State and Territorial Epidemiologists case definition of probable Covid-19 after an epidemiologic link with a close contact.[15] (Descriptions of the symptom complex are provided in the Supplementary Appendix.) The median number of new symptoms reported in the hydroxychloroquine group was 4 (interquartile range, 2 to 6), as compared with 3 (interquartile range, 2 to 5) in the placebo group.



- 821 asymptomatic participants were enrolled
- 87.6% of the participants reported a high-risk exposure to a confirmed Covid-19 contact
- Incidence of new illness compatible with Covid-19 did not differ significantly:
  - Hydroxychloroquine (49 of 414 [11.8%])
  - Placebo (58 of 407 [14.3%])
  - Absolute difference was −2.4 percentage points (95% confidence interval, −7.0 to 2.2; P=0.35)
- Side effects were more common with hydroxychloroquine than with placebo (40.1% vs. 16.8%)
- No serious adverse reactions were reported

Results

Clinical Trials: Immune Based Therapy



References

- Boulware DR, Pullen MF, Bangdiwala AS, et al. A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19 [published online ahead of print, 2020 Jun 3]. *N Engl J Med*. 2020;10.1056/NEJMoa2016638. doi:10.1056/NEJMoa2016638
- Li L, Zhang W, Hu Y, et al. Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial. *JAMA*. Published online June 03, 2020. doi:10.1001/jama.2020.10044

RACIAL DISPARITIES IN COVID-19: FROM DIAGNOSIS TO DEATH

Black people disproportionately affected by COVID-19

Investigators at Ochsner Health System in Louisiana analyzed data from 3481 non-Hispanic black (NHB) and non-Hispanic white (NHW) patients diagnosed with COVID-19 between March 1 and April 11, 2020

- Mean age of patients - 54 years; 60% female
- Representing only 31% of the health system's population, NHB patients comprised 70.4% of COVID-19 patients

Price-Haywood EG et al. Hospitalization and mortality among black patients and white patients with Covid-19. *N Engl J Med* 2020 May 27; [e-pub]

RACIAL DISPARITIES IN COVID-19: FROM DIAGNOSIS TO DEATH

Among the COVID-19 subgroup

- NHB patients more likely than NHW patients to have preexisting conditions and to present with fever, cough, or dyspnea
- NHB patients nearly twice as likely to reside in a low-income area and three times as likely to have Medicaid insurance – factors associated with higher hospitalization

Of patients diagnosed with COVID-19,

- 40% required hospitalization; of these, 77% were NHB patients.
- 24% of patients hospitalized with the infection died 71% NHB

After risk-factor adjustments, in-hospital mortality independently associated with increasing age and with several clinical measures but not with black race

Price-Haywood EG et al. Hospitalization and mortality among black patients and white patients with Covid-19. *N Engl J Med* 2020 May 27; [e-pub]

Racial minorities disproportionately represented among pregnant women admitted to hospitals with confirmed COVID-19 in the UK

Demographics

- 430 women studied
- 56% black or other ethnic minorities
- 69% overweight or obese
- Most admitted during the third trimester or peripartum

Outcomes

- 10% required respiratory support and 1% died
- Of the women who delivered during the hospital stay, 25% did so preterm
- 5 babies overall died; 3 deaths unrelated to COVID-19, while the role of COVID-19 in 2 stillbirths not clear
- 5% of the babies tested positive for SARS-CoV-2, half within 12 hours of birth

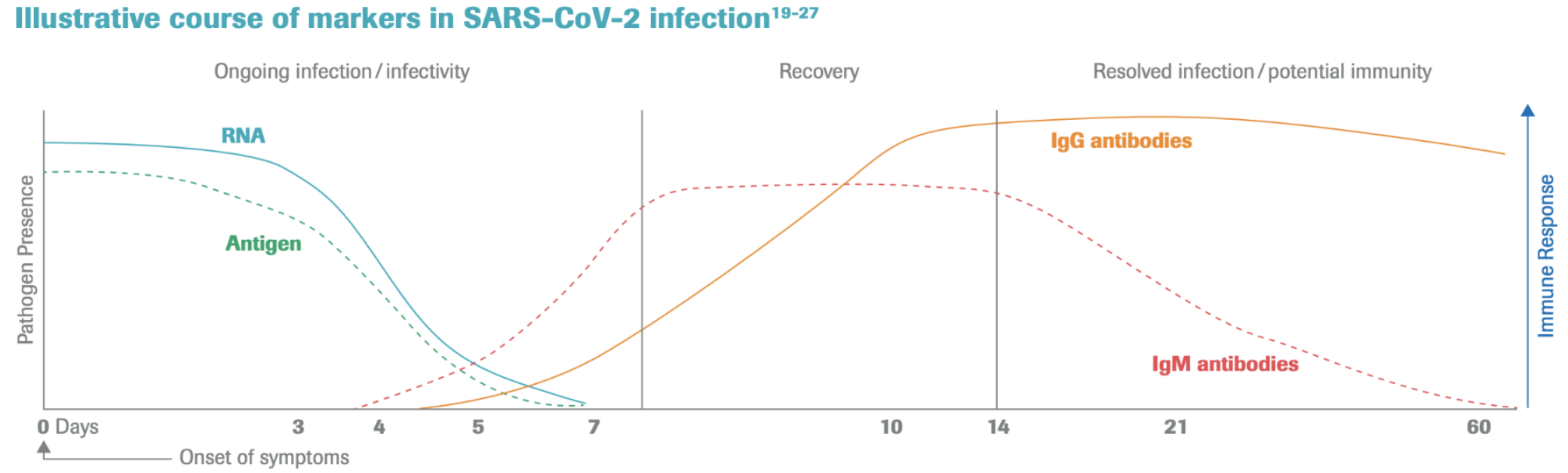
BMJ 2020

SARS-COV-2 INFECTIONS AND SEROLOGIC RESPONSES ON USS THEODORE ROOSEVELT

- CDC reports on the outbreak aboard the aircraft carrier the U.S.S. Theodore Roosevelt
- Risk for SARS-CoV-2 infection lower among service members who:
  - Reported a face covering (56% vs. 81% who didn't)
  - Avoided common areas (54% vs. 68%) and
  - Observed social distancing guidance (55% vs. 70%)
- Among those with an antibody response, 59% had neutralizing antibodies

Payne DC, Smith-Jeffcoat SE, Nowak G, et al. SARS-CoV-2 Infections and Serologic Responses from a Sample of U.S. Navy Service Members USS Theodore Roosevelt, April 2020. *MMWR Morb Mortal Wkly Rep*. ePub: 9 June 2020

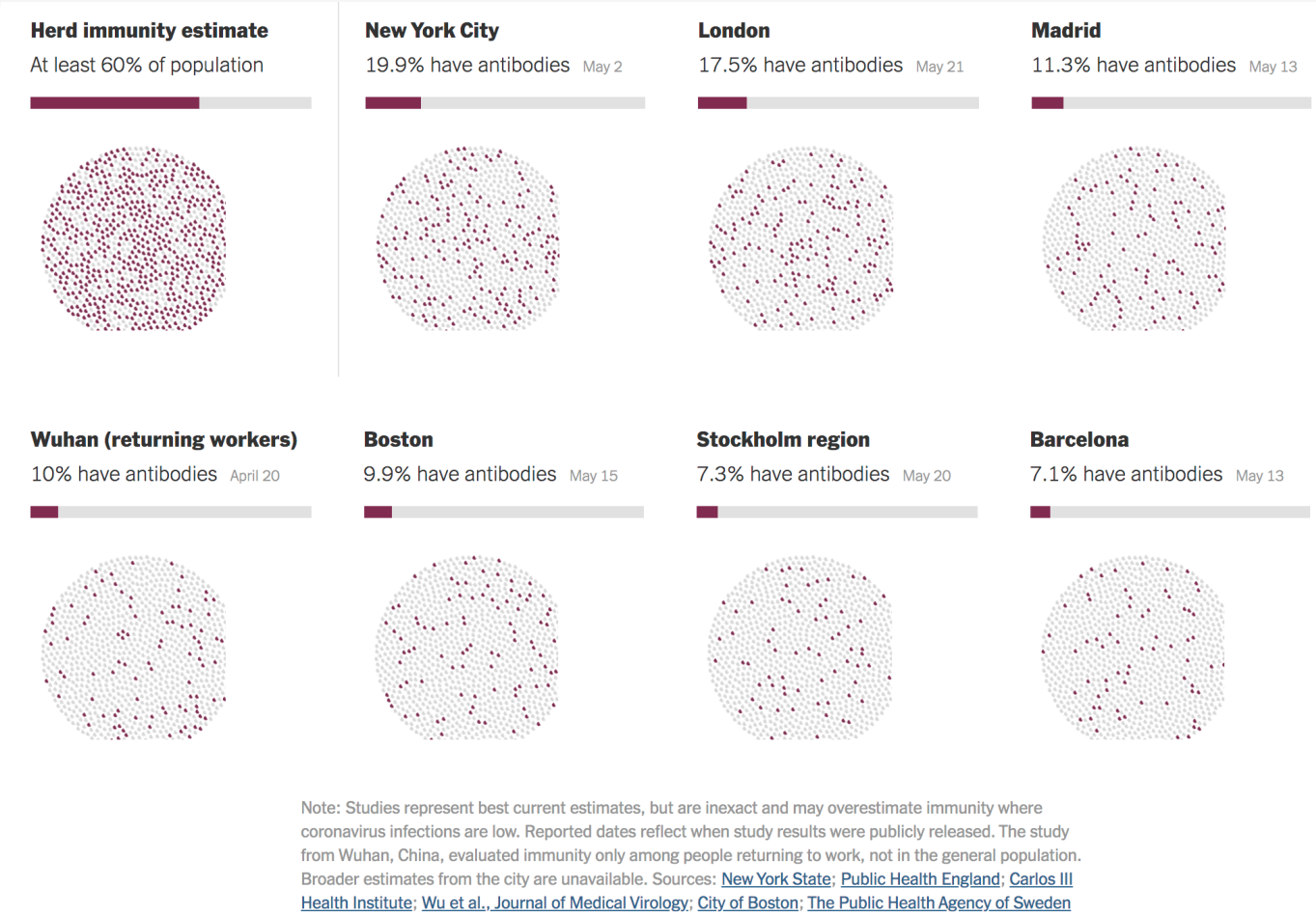
Dynamics of Infection Dictate Which Test to Use



Roche Elecsys Anti-SARS-CoV-2 package insert

Virology Education, COVID-19 Online Educational. Sanjat Kanjilal, MD, MPH, Daniel Kuritzkes, MD

Preliminary Estimates of SARS-COV-2 seroprevalence



New York Times

Public Health Uses of Serological Tests for COVID-19

Population-based serosurveys

- Important for understanding of epidemiology

No role in determining when to relax social distancing

- If current measures even modestly successful, the majority will be seronegative
- Seropositivity is not a guarantee of protection
- Duration of protective immunity (if it exists) is uncertain

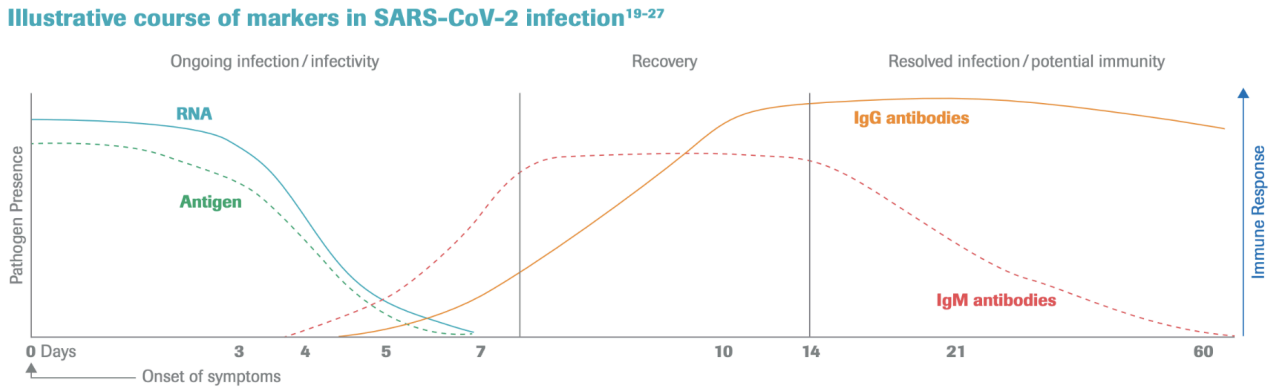
Clinical Applications of Serologic Tests for COVID-19

- Primary diagnosis
- Retrospective diagnosis
- Back to work?

Primary Diagnosis of COVID-19: Role of Serology

- Occasional patients may have a clinical syndrome strongly suggestive of COVID-19 but negative PCR for SARS-COV-2
- IgM and/or IgG may be useful in this setting if obtained > 7 days after symptom onset
- Reliability of the diagnosis entirely depends on performance characteristics of the serological test employed

Dynamics of infection dictate which test to use



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Back to Work?

- Results of serological testing should not be used as a criterion for determining who can come back to work
  - Majority likely to be seronegative
  - No guarantee of protection
  - Not a substitute for use of appropriate PPE

Retrospective diagnosis

- Early in the pandemic, persons with mild moderate symptoms not requiring urgent medical care may not have been tested
- Many such persons are interested in knowing if they had COVID-19
- SARS-Cov-2 IgG may be useful in this setting
- Some jurisdictions may require PCR testing to exclude active disease
- Many HCP want to know if they have been exposed and/or are immune
    - Most experience to date suggest a very small fraction will actually be positive
    - Rates of seropositivity will depend on availability and proper use of PPE