EPI·WiN

WHO Information Network for Epidemics

World Health Organization

Coronavirus disease (COVID-19)

Laboratory/testing/diagnostics

23/04/2020

What do diagnostic tests for COVID-19 detect?

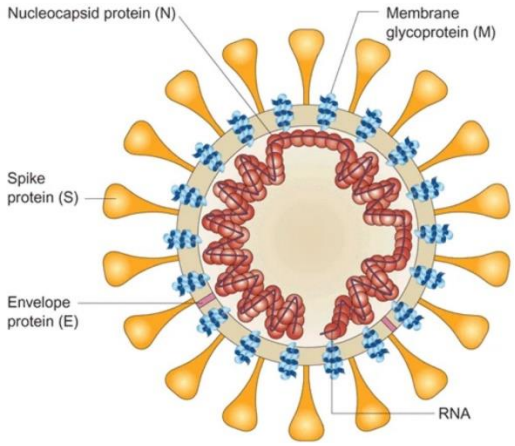
- Viral RNA detection by NAAT/RT-PCR
- COVID-19 viral antigen

Virus

- Antibodies against COVID-19 Antigen
  - Immunoglobulin M (IgM)
  - Immunoglobulin G (IgG)
  - Immunoglobulin A (IgA)

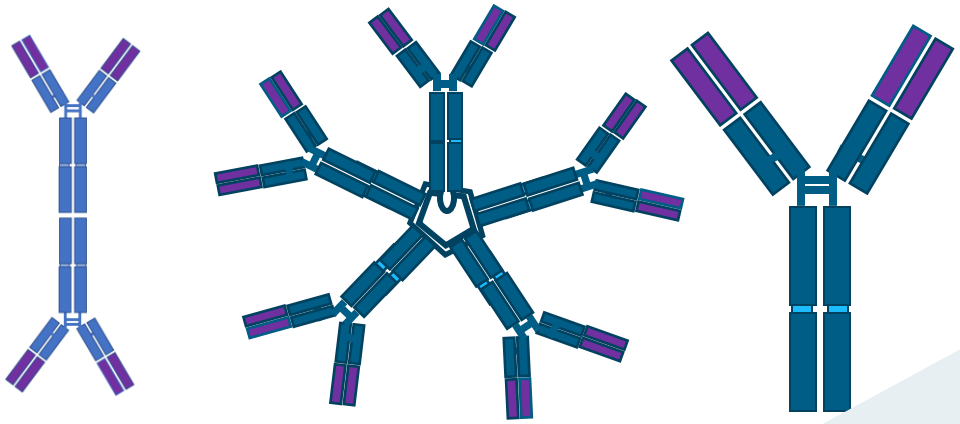
Immune response

Coronavirus



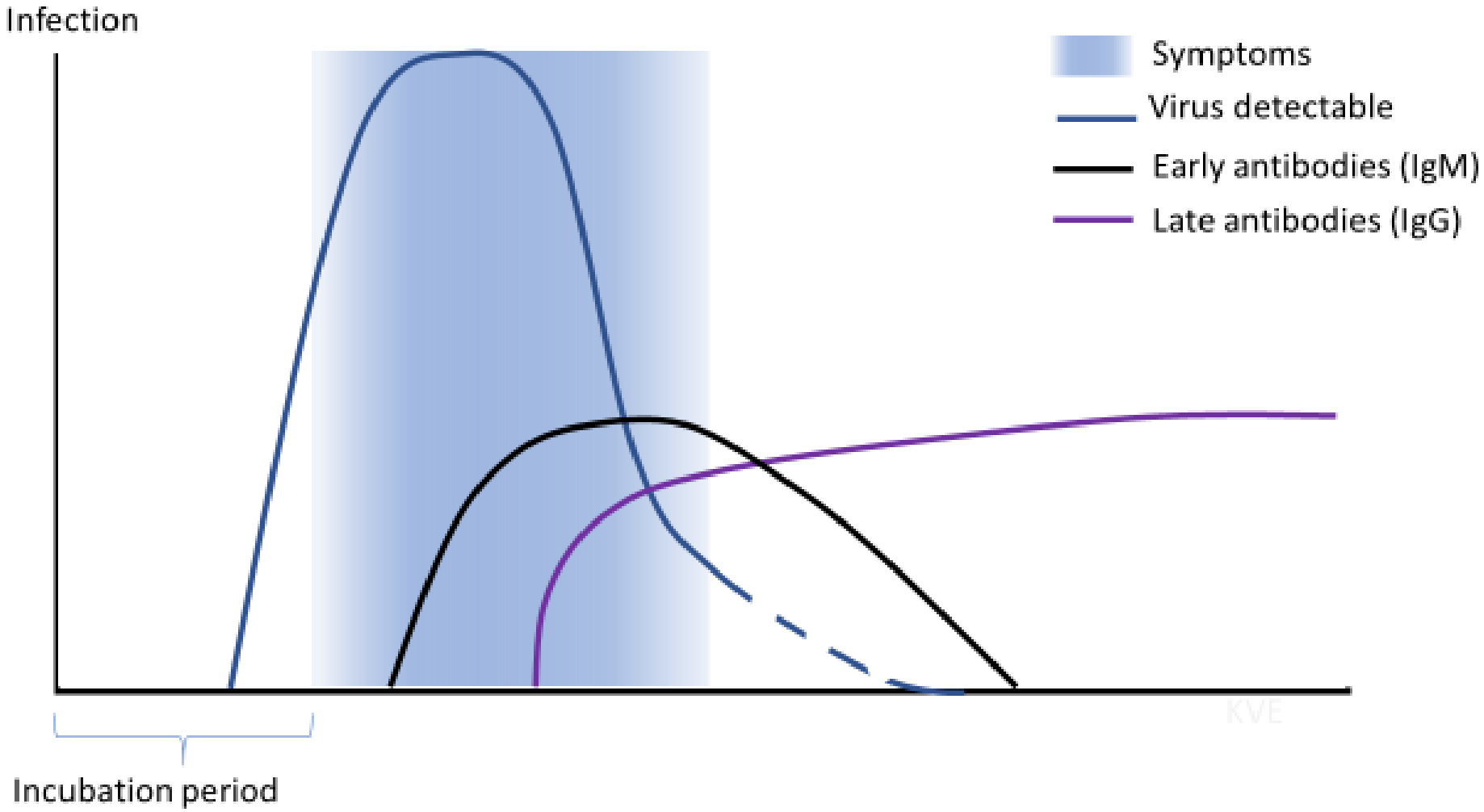
Monto, Cowling and Pereis. Coronaviruses. R.A. kaslow et al. (eds.), Viral infections in humans. https://link.springer.com/content/pdf/10.1007%2F978-1-4899-7448-8_10.pdf

Antibodies



IgA IgM

Molecular vs serology and their significance in terms of COVID-19



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Purpose of testing

- Detect acute infection → molecular test (maybe in the future antigen test*)
- Contact tracing → Molecular test (maybe in the future antigen test*)
- Serosurveillance → antibodies
- Immunity? → neutralizing antibodies? Insufficient understanding of strength and duration of protection, using inadequate testing can do more harm than good

Patient populations: mild vs severe disease, young versus old, healthy vs sick, ….

*Antigen test for other diseases (influenza and RSV) pooled sensitivity between 34-80%) this would be insufficient for clinical use.

Bruning AHL, Leeflang MMG, Vos JMBW, Spijker R, de Jong MD, Wolthers KC, et al. Rapid Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review and Meta-analysis. Clin Infect Dis [Internet]. 2017 Sep 15 [cited 2020 Apr 1];65(6):1026–32. Available from: http://academic.oup.com/cid/article/65/6/1026/3829590/Rapid-Tests-for-Influenza-Respiratory-Syncytial

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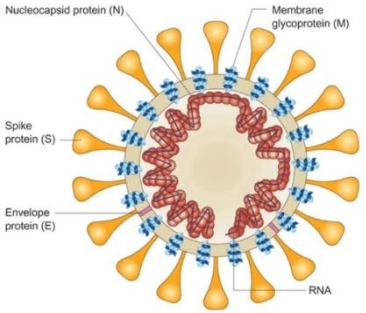

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Table 1: Considerations for laboratory testing for each transmission scenario*

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
Transmission scenario	No reported cases	One or more cases, imported or locally acquired	Most cases of local transmission linked to chains of transmission	Outbreaks with the inability to relate confirmed cases through chains of transmission for a large number of cases, or by increasing positive tests through sentinel samples (routine systematic testing of respiratory samples from established laboratories)
Public health aim	Stop transmission and prevent spread	Stop transmission and prevent spread	Stop transmission and prevent spread.	Slow transmission, reduce case numbers, end community outbreaks. Reduce health, social and economic impact of the outbreak. Minimize disruptions in health care for non-COVID-19 illness.
Testing strategy guidance documents	Test all individuals meeting the suspected case definition Test a subset of samples from SARI/ILI surveillance for COVID-19 Test patients with unexpected clinical presentation or an increase in hospital admissions in a specific demographic group that could be COVID-19	Test all individuals meeting the suspect case definition Considerations in the investigation of cases and clusters of COVID-19 Clinical management of severe acute respiratory infections when novel coronavirus is suspected. SARI/ILI surveillance for COVID-19 and reporting: see Interim operational considerations for COVID-19 surveillance using GISRS	Test all individuals meeting the suspected case definition Considerations in the investigation of cases and clusters of COVID-19. Clinical management of severe acute respiratory infections when novel coronavirus is suspected. SARI/ILI surveillance for COVID-19 and reporting: see Interim operational considerations for COVID-19 surveillance using GISRS.	If diagnostic capacity is insufficient, implement prioritized testing and measures that can reduce spread (e.g. isolation)., including: • people who are at risk of developing severe disease and vulnerable populations, who will require hospitalization and advanced care for COVID-19 (see Clinical management of severe acute respiratory infections when novel coronavirus is suspected). • symptomatic health workers (including emergency services and non-clinical staff) regardless of whether they are a contact of a confirmed case (to protect health workers and reduce the risk of nosocomial transmission) • the first symptomatic individuals in a closed setting (e.g. schools, long term living facilities, prisons, hospitals) to quickly identify outbreaks and ensure containment measures

Laboratory testing strategy recommendations for COVID-19

Interim guidance
22 March 2020

World Health Organization

Recommended testing method for identifying active infection is molecular testing, tailored molecular diagnostic solutions

Laboratory testing for coronavirus disease (COVID-19) in suspected human cases

Interim guidance
19 March 2020

World Health Organization

High-tech, high-throughput

Human resource-intensive, manual PCR

Automated PCR (sample in, answer out)

Purpose of testing

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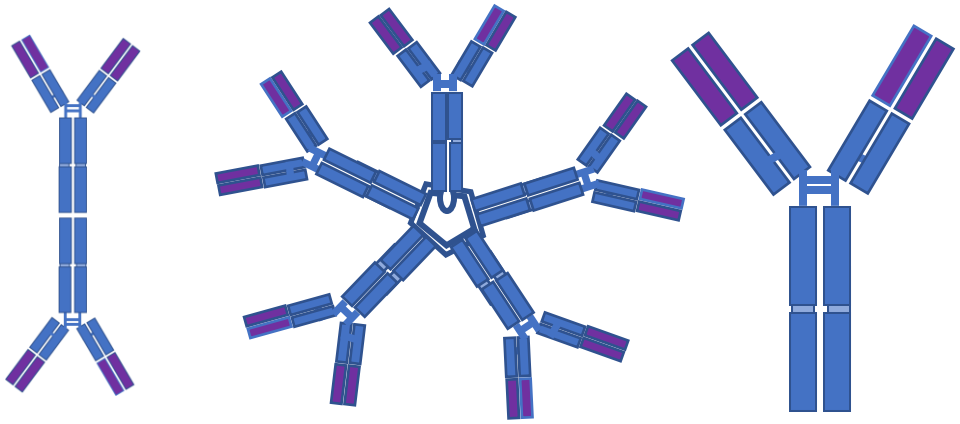

IgA IgM IgG

Immunity passports?

'Immunity passports' could speed up return to work after Covid-19

German researchers studying how lockdown restrictions could be lifted for some people

Serological tests

- Hundreds of immunoassays marketed for COVID-19 (ELISAs and mostly RDTs)
- First validation data available, often with limited sample set, not all with well characterized samples, different patient groups
- Patient group characteristics have influence on accuracy of a test:
  - -Sample timing after onset of symptoms
  - -Severity of disease
  - -Age of the tested patients (e.g. children, elderly)
  - -Suspected/proven infection with PCR

Table 3. Diagnostic indexes of SARS-CoV-2 IgG/IgM test kit in different subgroups according to the time from illness onset to sample collection (days).

	0 -7 days		8 - 15 days		>= 16 days	
	PCR +	PCR-	PCR+	PCR-	PCR+	PCR-
n	16	9	6	2	68	14
Both IgG/IgM Positive	2	1	5	1	25	3
IgG Positive	0	1	0	0	43	1
IgM Positive	1		1	0	0	1
Sensitivity	18.8%		100%		100%	
Specificity		77.8%		50%		64.3%
Accuracy	40%		87.5%		93.9%	

Figure 1. Result of Patient 1 was negative for both IgM and IgG antibodies. Result of Patient 2 was only IgM positive while results of patient 3 and 5 was only IgG positive. Result of patient 4 was positive for both IgM and IgG antibodies.

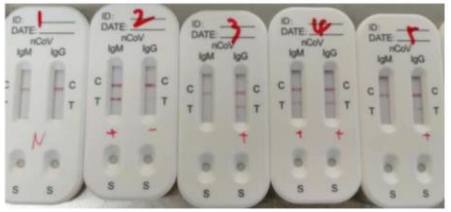

Figure 1. Representative picture for five patients blood testing results. Result of Patient 1 was negative for both IgM and IgG antibodies. Result of Patient 2 was only IgM positive while results of patient 3 and 5 was only IgG positive. Result of patient 4 was positive for both IgM and IgG antibodies.

Liu Ying et al, **Diagnostic Indexes of a Rapid IgG/IgM Combined Antibody Test for SARS-CoV-2.** medRxiv preprint doi: https://doi.org/10.1101/2020.03.26.20044883

Table 2. Accuracy in different subgroups.

	PCR Positive (n = 90)		PCR Negative (n = 89)		
	Mild/ common	Severe/ critical	Clinical confirmed	Suspected cases	Other disease
n	46	44	5	20	64
Both IgG/IgM Positive	11	21	1	4	0
IgG Positive	22	21	1	1	0
IgM Positive	1	1	0	1	0
Accuracy	73.9%	97.7%	60%	70%	100%

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WHE/HQ laboratory team

THE TIMES

CORONAVIRUS

Britain has millions of coronavirus antibody tests, but they don't work

World Health Organization

Advice on the use of point-of-care immunodiagnostic tests for COVID-19

Scientific brief

8 April 2020

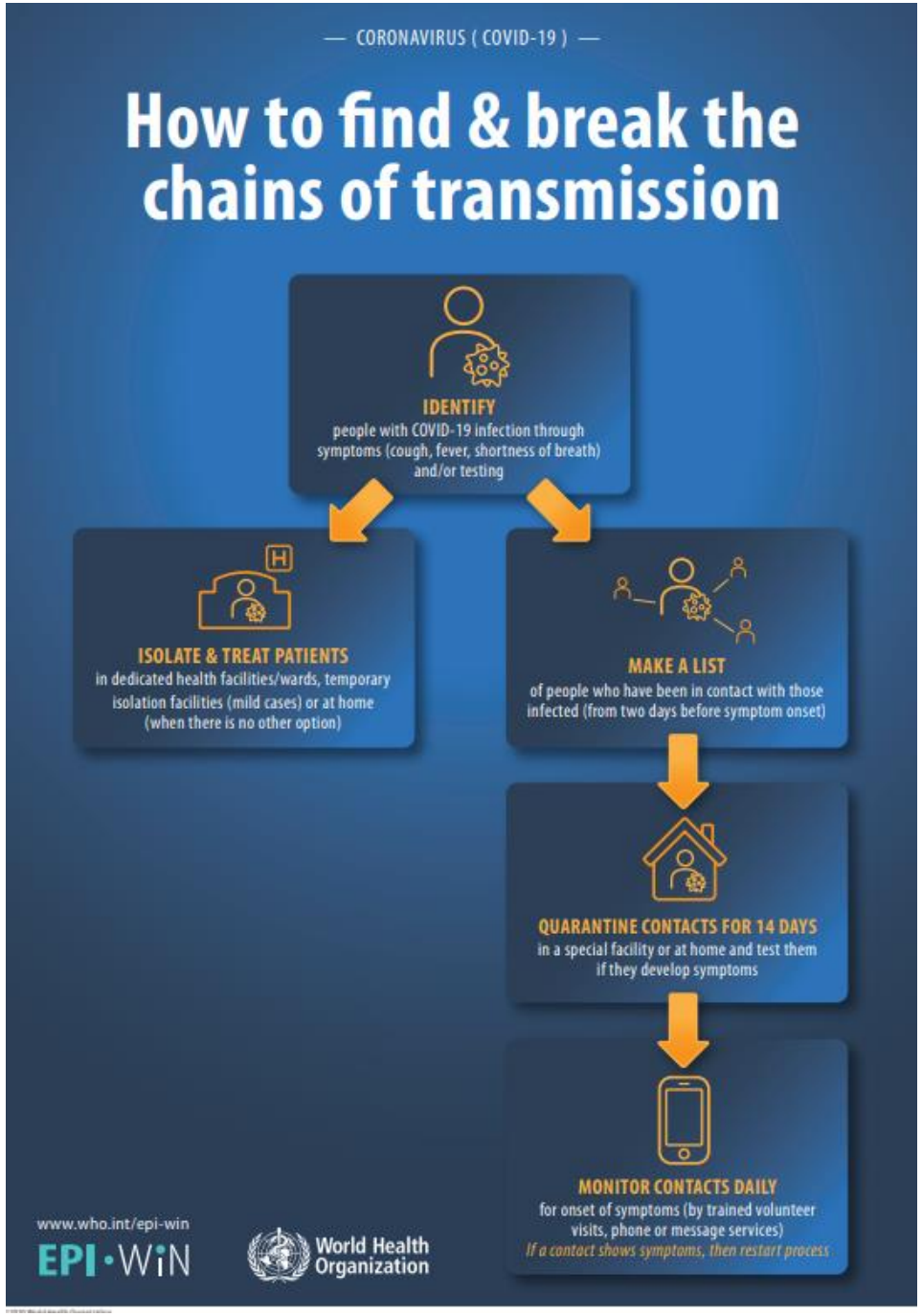
World Health Organization

In response to the growing COVID-19 pandemic and shortages of laboratory-based molecular testing capacity and reagents, multiple diagnostic test manufacturers have developed and begun selling rapid and easy-to-use devices to facilitate testing outside of laboratory settings. These simple test kits are based either on detection of proteins from the COVID-19 virus in respiratory samples (e.g. sputum, throat swab) or detection, in blood or serum, of human antibodies generated in response to infection.

WHO applauds the efforts of test developers to innovate and respond to the needs of the population.

However, before these tests can be recommended, they must be validated in the appropriate populations and settings. Inadequate tests may miss patients with active infection or falsely categorize patients as having the disease when they do not, further hampering disease control efforts. **At present, based on current evidence, WHO recommends the use of these new point-of-care immunodiagnostic tests only in research settings. They should not be used in any other setting, including for clinical decision-making, until evidence supporting use for specific indications is available.**

WHO continues to evaluate available immunodiagnostics tests for COVID-19 and will update this scientific brief when necessary.



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