COVID-19 Immunity
&
Clinical Manifestations

CORONAVIRUS (COVID-19) UPDATE NO. 24
1 May 2020

Current global situation

- More than 3 million confirmed cases globally
- More than 200 000 deaths

Top ten countries with the highest number of new cases (last 24 hours)

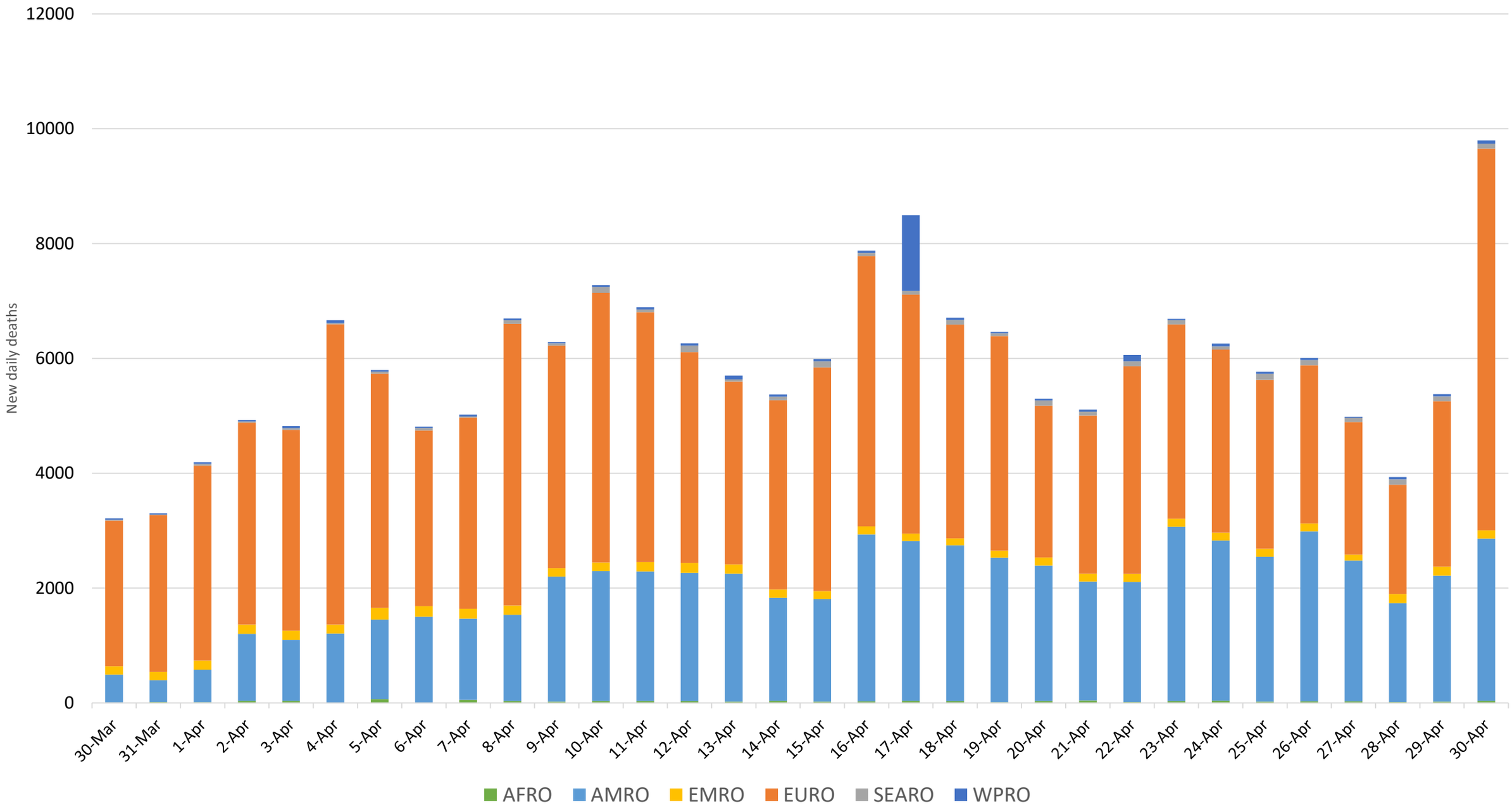
. USA – 20 517
. Russian Federation – 7 099
. Brazil – 5 017
. UK – 4 076
. Turkey – 2 936
. Peru - 2 491
. Spain – 2 144
. Italy – 2 086
. India - 1 718
. France – 1 602

For the latest data, please access:

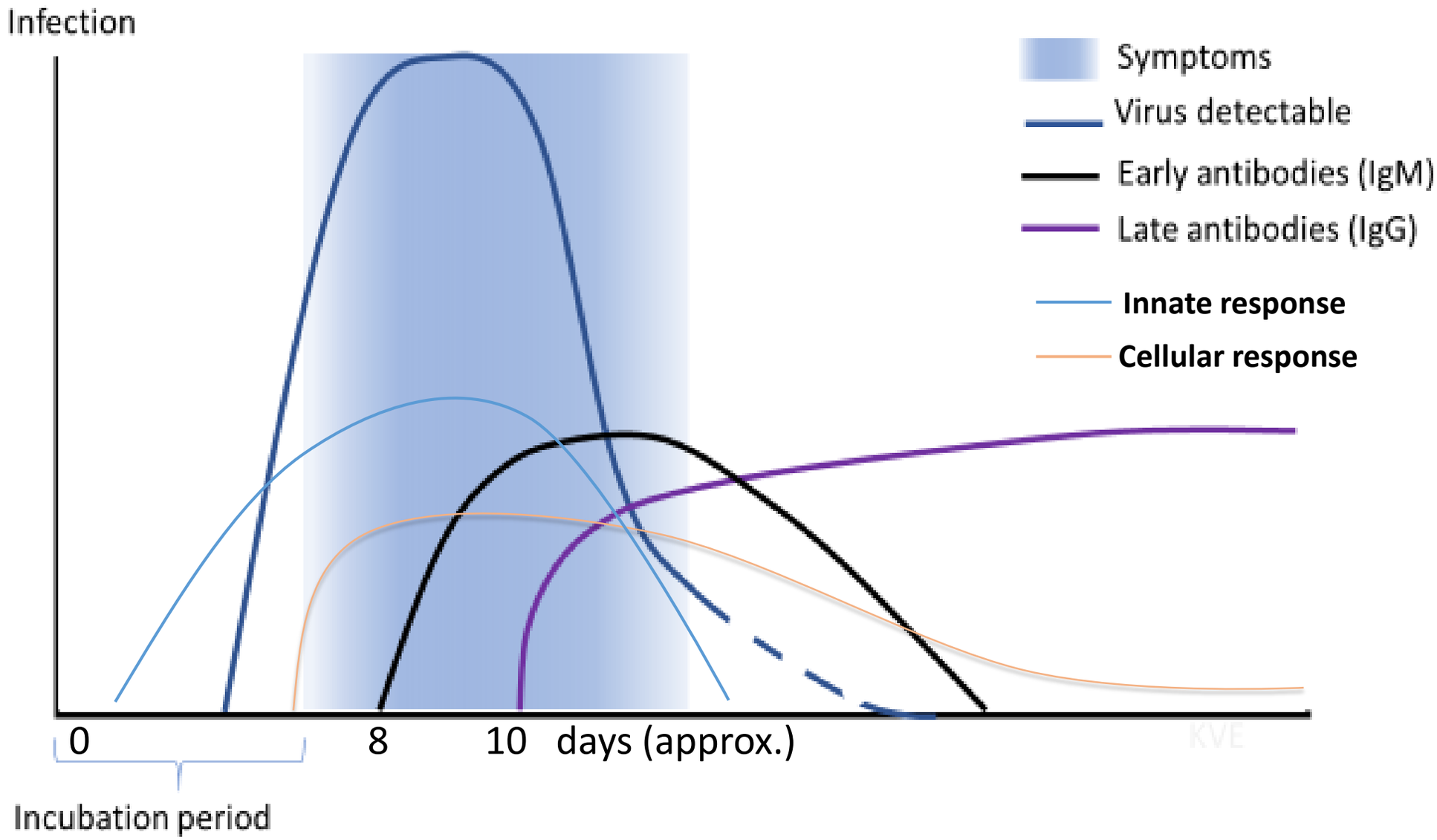
WHO situation dashboard
WHO situation reports
UNWFP world travel restrictions

Data as of 01.05.2020

Number of new deaths of COVID-19 per day, by WHO region



The immune response to viral infections



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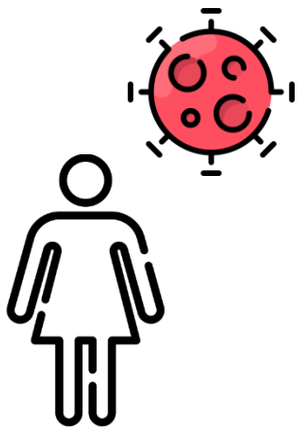


Step 1

Innate immune response:

- general response to ANY infection
- Innate immune response cells secrete **interferons and other chemicals (cytokines)**
- Interferons interfere with virus replication

THE INFECTION CAN BE STOPPED AT THIS STAGE

- **STEP 2** is triggered

Step 2

Adaptive immune response:

- specific response to the infection
- starts after 6-8 days
- involves two types of white blood cells (T-cells and B-cells)

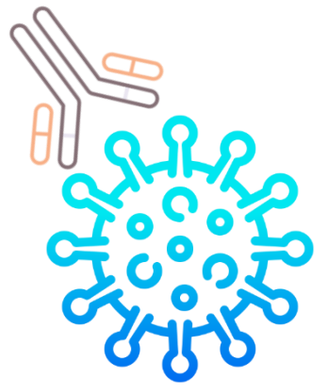
- ❑ **Interferons and cytokines cause fever, muscle ache, etc - the early symptoms of infection**
- ❑ **A 'weak' innate response (elderly people or those with underlying health problems) may result in a delayed stimulation of the adaptive response.**

Adaptive immune response:

T-cells (cellular response)

T-cells recognize cells infected with a specific virus (eg SARS-CoV-2) and rapidly replicate. Two different types of T-cells are responsible for 2 functions:

1. **CD8 cells kill** the SARS-CoV-2 infected cells thereby killing the virus
2. **CD4 cells stimulate** the B-cells



B-cells (antibody response)

B-cells produce antibodies (Abs) specific to the virus:

1. **IgM** antibodies are produced first and then disappear after a few weeks
2. **IgG** antibodies are produced a couple of days later and can remain for months-years

The effectiveness of the antibody response depends on:

Quality of Abs: do the Abs stop the virus from entering cells and multiplying (neutralizing Abs)

Quantity: how much Ab is produced

Duration: how long the Abs persists in the body

Antigen stability: if viruses mutate over time, the viral proteins (antigens) to which the antibodies bind may become unrecognizable

- **After infection, T and B-cells decline but some "memory" cells remain enabling a more rapid response if the virus is encountered a second time**

What we know, so far, about the immune response to Sars-CoV-2

- Most patients who recover from COVID-19 have antibodies to the virus detectable in their blood.
- Most COVID-19 patients develop antibodies about 10-15 days after symptoms start. This is around the time when many patients start to recover.
- The levels of the important NEUTRALIZING antibodies appear to be higher in patients who had more severe disease.
- Patients who had mild or asymptomatic COVID-19 have low levels of NEUTRALIZING antibodies (or even undetectable levels) with current tests[1].
- In these patients it is possible the innate immune response and the T-cell response cleared the virus (this is similar to what happens with MERS[2]).
- Most antibody tests cannot differentiate between neutralizing vs non-neutralizing antibodies.
- Rapid antibody detection tests do not measure the quantity (levels) of antibodies.
- More complicated tests such as ELISA tests can inform on level of antibodies, but not necessarily on different kind of antibodies (neutralizing vs non-neutralizing) .

1.Wu F, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. medRxiv 2020: 2020.03.30.20047365.
2. Zhao J et al.Recovery from the Middle East respiratory syndrome is associated with antibody and T cell responses. Science Immunology 2017:2, 1-10.

Can antibodies against SARS-CoV-2 protect us from being infected again?

No-one knows yet!

What we do know, at present:

- Generally, a person who recovered from a viral infection is protected against new infection or against severe disease. However, this requires antibodies to be of adequate quality (neutralizing antibodies) and quantity (high levels)
- Changes in the virus sequence can make prior immunity less effective (eg influenza).
- Protection from re-infection with the common cold (endemic coronaviruses) is short-term (sometimes less than a year)[1,2]
- For other coronaviruses, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) - antibodies have been detected a few years later.

For the emerging coronaviruses we do not YET have enough data to confirm that antibodies protect, what antibody levels are required, or how long this will last.

1. Callow, K. A. Effect of specific humoral immunity and some non-specific factors on resistance of volunteers to respiratory coronavirus infection. J. Hyg. 1985: 95, 173–189.
2. Galanti M and Shaman J 2020. Direct observation of repeated infections with endemic coronaviruses. http://www.columbia.edu/~jls106/galanti_shaman_ms_supp.pdf

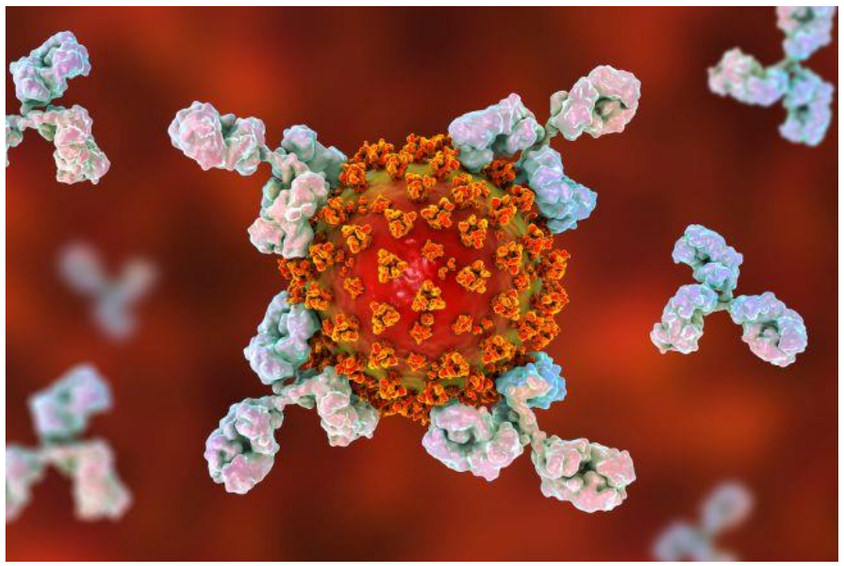
What does a positive antibody test tells us?

It tells us:

- The person was infected in the past with SARS-CoV-2 *
- If IgM and IgG positive: recent infection (within past few weeks)
- If IgM negative and IgG positive: more distant infection (several weeks at least).

It does NOT tell us:

- If the person has recovered (does not preclude persistent infection).
- If the antibodies are neutralizing (unless a specific assay is used).
- What the antibody levels are (unless a specific assay is used (ELISA)).



A coronavirus being attacked by antibodies.
Shutterstock

What does a negative antibody test tells us?

Not too much……

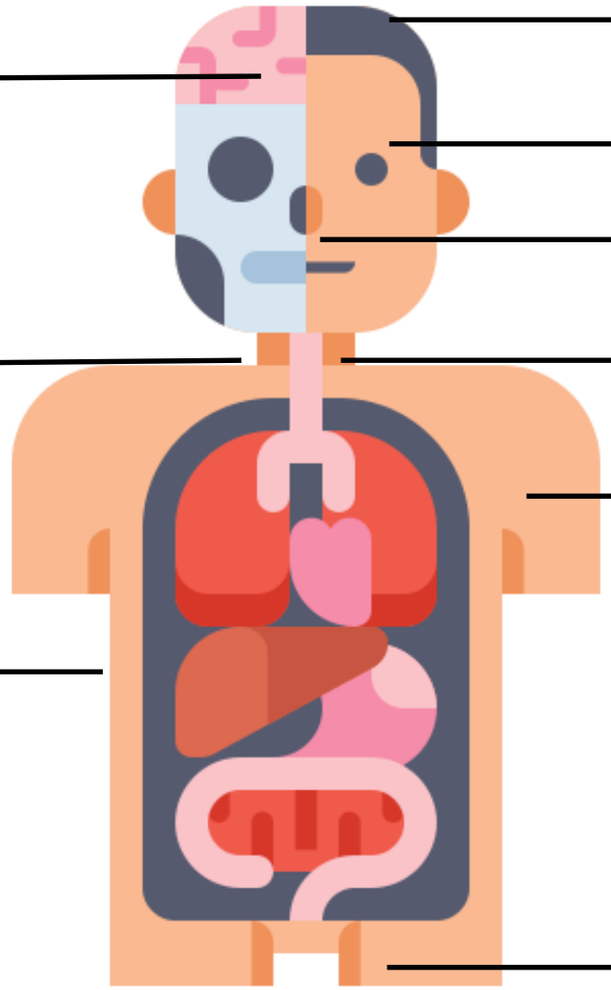
It could mean:
That the person has not been infected,
Or
That the person was very recently infected (less than 8-10 days),
Or
That the person was infected but cleared the virus without mounting an antibody response (ie innate and T cell response cleared the virus)
Or
That the person was infected and mounted an antibody response but the antibody levels are below the level of detection of the test.

It does not tell us if the person is susceptible to infection.

Clinical manifestations linked to COVID-19

MOST COMMON

- fever
- dry cough
- tiredness



LESS COMMON

- headache
- red or irritated eyes
- loss of taste of smell
- sore throat
- aches and pains
- diarrhea

Approximately 1 in 5 people become very ill and develop serious symptoms such as shortness of breath, chest pain or loss of speech or movement.

Emerging clinical manifestations linked to COVID-19

As we learn more about COVID-19, we also learn about less common manifestations linked to COVID-19 for example:

Thromboembolic events

- The available data on thrombotic risk in severely ill COVID-19 patients is limited and based on case series from China[1], The Netherlands[2] and France[3]. These studies may indicate an increased thrombotic risk, including pulmonary embolism and stroke in hospitalized COVID-19 patients.

Skin manifestations

- Data on skin lesions as a symptom of COVID-19 are limited. In one study, of 88 patients testing positive for COVID-19, 18 patients (20%) developed skin rashes like rash and hives[4]. There are also anecdotical accounts of purple toe lesions (purpura fulminans) in suspected COVID-19 patients.
- WHO is collecting information on rashes, and the American Academy of Dermatology has established an international registry to report cases.

1 https://doi.org/10.1111/jth.14830
2 https://doi.org/10.1016/j.thromres.2020.04.013
3 https://www.esicm.org/wp-content/uploads/2020/04/863_author_proof.pdf
4 https://onlinelibrary.wiley.com/doi/epdf/10.1111/jdv.16387

COVID-19 compared to other diseases and conditions

Relative frequency of symptoms in different infectious or allergic conditions.

SYMPTOMS	COVID-19	FLU	COMMON COLD	MALARIA	DENGUE	ALLERGIES
Fever	Common	Common	Rare	Common	Common	Rare
Dry Cough	Common	Less common	Less common	Rare	Rare	Less common
Tiredness	Common	Common	Less common	Common	Common	Less common
Shortness of breath	Less common	Less Common	Rare	Rare	Less common	Less common
Aches and pains	Less common	Common	Rare	Less common	Common	Rare
Headache	Less common	Common	Rare	Common	Common	Less common
Sore throat	Less common	Less common	Common	Rare	Rare	Rare
Diarrhea	Less common	Less common	Rare	Common	Rare	Rare
Stuffy nose	Rare	Less common	Common	Rare	Rare	Common
Runny nose	Rare	Common	Common	Rare	Less common	Common
Sneezing	Rare	Rare	Common	Rare	Rare	Common

New Guidance

WHO issued *a scientific brief on the 'immunity passport' concept in the context of COVID-19* as WHO continues to review evidence on antibody responses to SARS-CoV-2.

Addressing Human Rights as Key to the COVID-19 Response: key health and human rights considerations with regards to COVID-19 pandemic, including addressing stigma and discrimination, prevention of violence against women, support for vulnerable populations; quarantine and restrictive measures and shortages of supplies and equipment.

COVID-19 and Food Safety: Guidance for competent authorities responsible for national food safety control systems: temporary measures that can be introduced to contain widespread food safety risks and reduce serious disruption to national food safety programmes

Water, sanitation, hygiene and waste management for the COVID-19 virus

Information resources

WHO WhatsApp messaging service

Receive the latest news and information on COVID-19. To subscribe:

text 'hi' to +41 79 893 1892

EPI-WIN website

Access to timely, accurate, and easy-to-understand advice and information from trusted sources

www.who.int/epi-win

Previous webinars

Immunity passports in the context of COVID-19 (01.05.20)

Recording:

https://who.zoom.us/rec/share/vvx6Car97m1IYM_JuW_9RIpxDtnJT6a80Xcb-aEKyUnzJdTHpEzt2C2PyKmGzIH2

COVID-19 and schools (30.04.20)

Recording:

https://who.zoom.us/rec/share/tZIrDev22W9JZZHk9GDcQbEQXd3qX6a8hCJP_aUOxEd4RKIAiZOrtDiqCkJy7Oim