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Foresight Dialogues
Web Series 2020

Immunology of Covid-19
Dr Gareth Kantor
Sept 1, 2020

UNCERTAINTY

Immunology / immunity

Issues & implications

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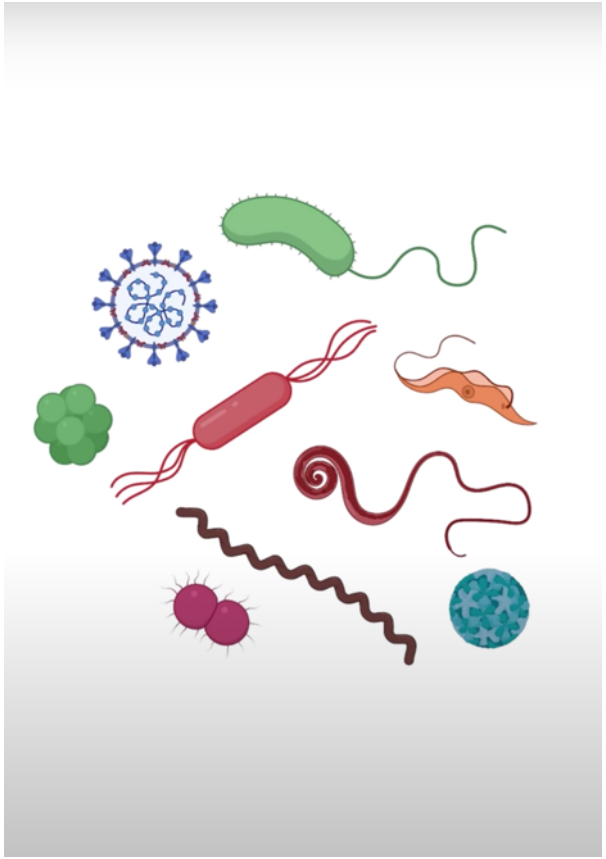
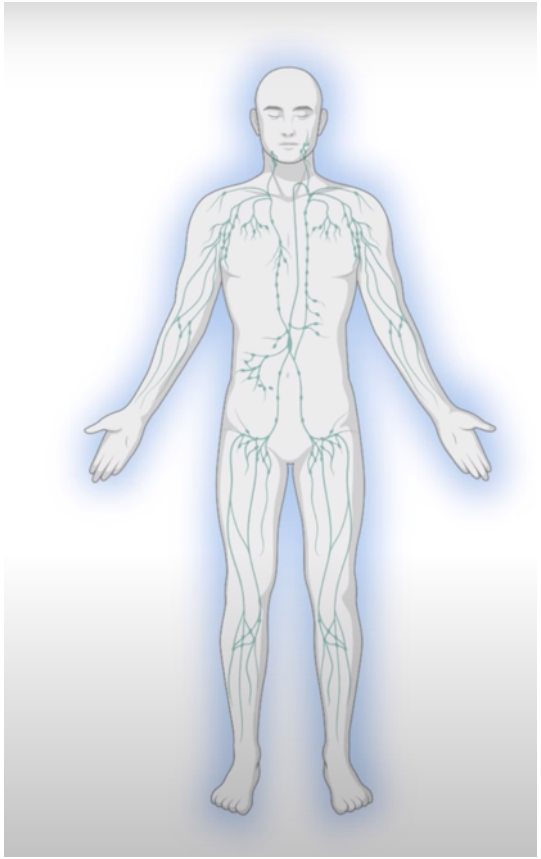
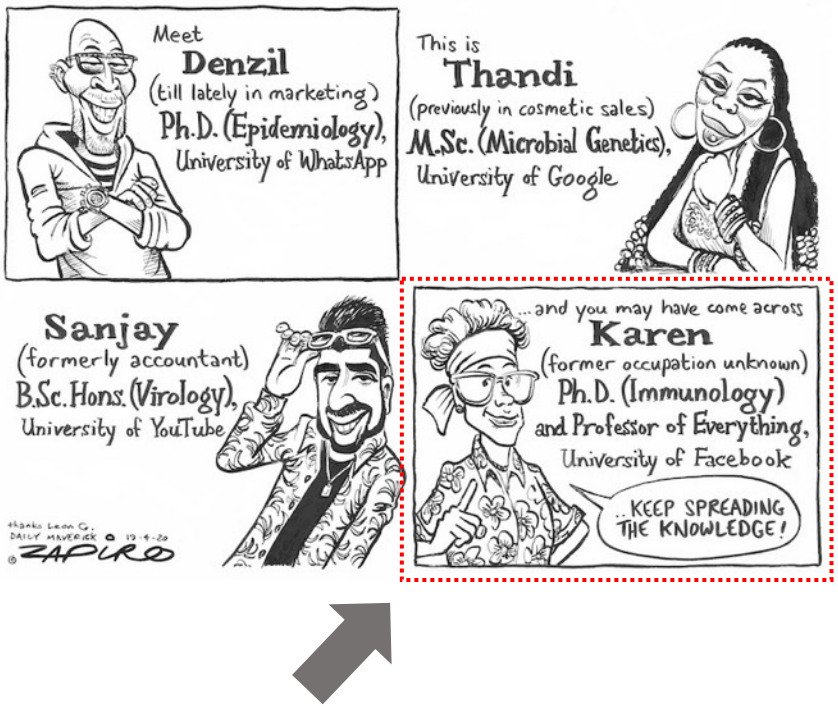


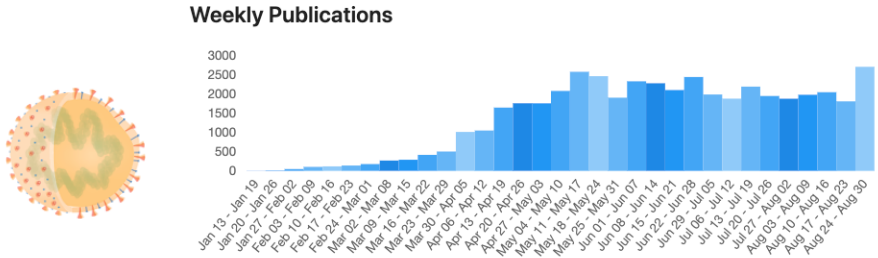


Immunology 101 for non-immunologists (Iwasaki: Yale)



NIH NLM

LIT COVID



46,586 publications

August 30

https://www.ncbi.nlm.nih.gov/research/coronavirus/

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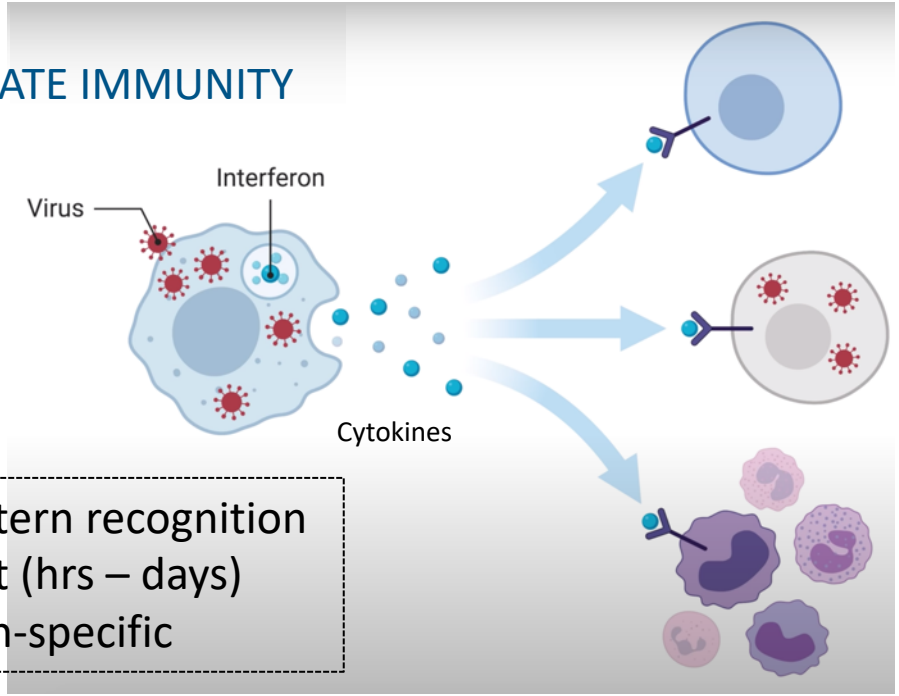
1. INNATE IMMUNITY



Pattern recognition
Fast (hrs – days)
Non-specific

Image: Iwasaki (Yale)

Signal neighbouring cells to put up barriers

Signal infected cells die

Recruit white blood cells to stimulate long lasting immunity

(+ INFLAMMATION)

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2. ADAPTIVE IMMUNITY

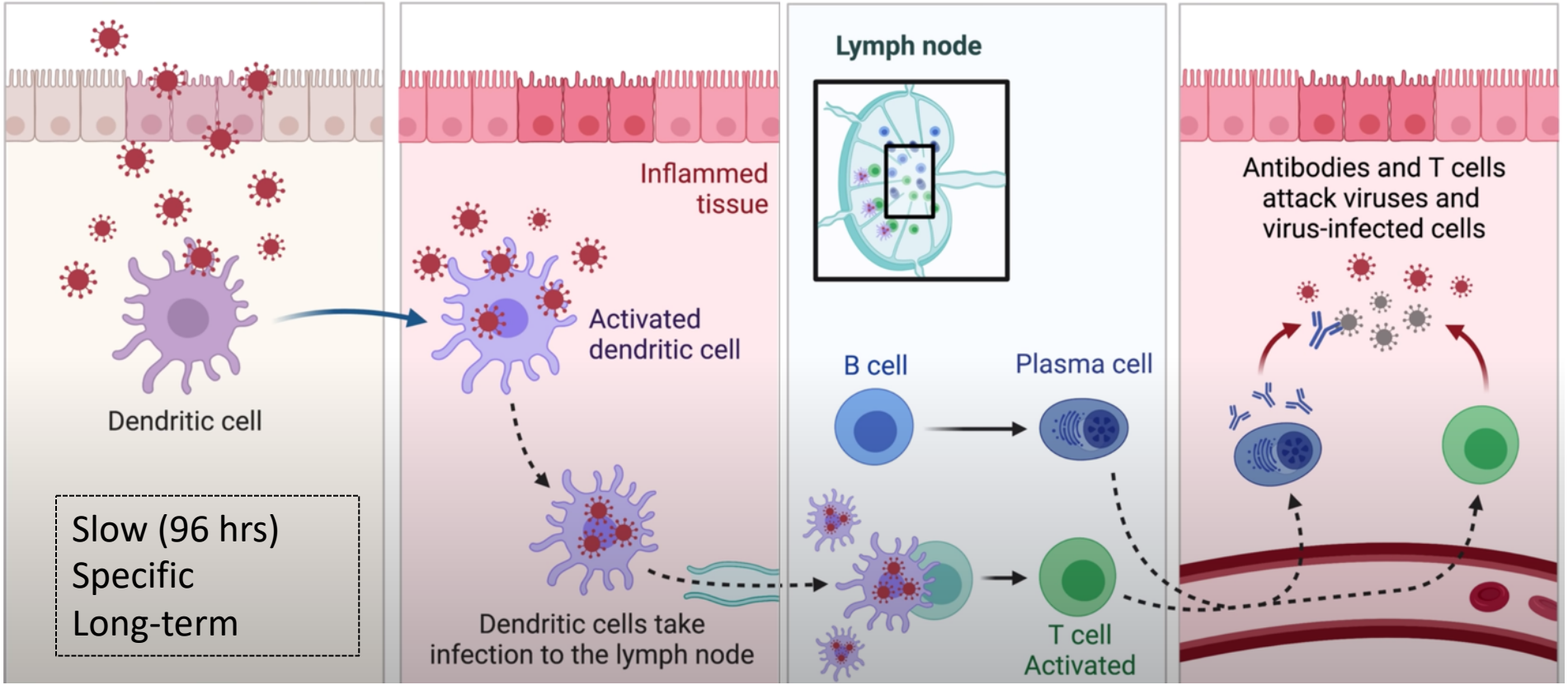
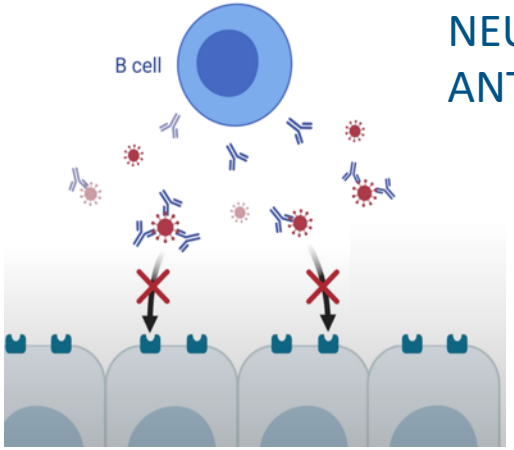
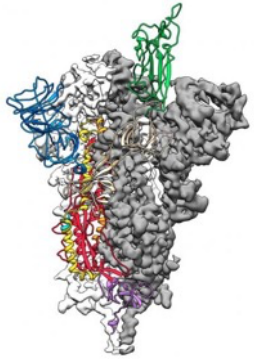


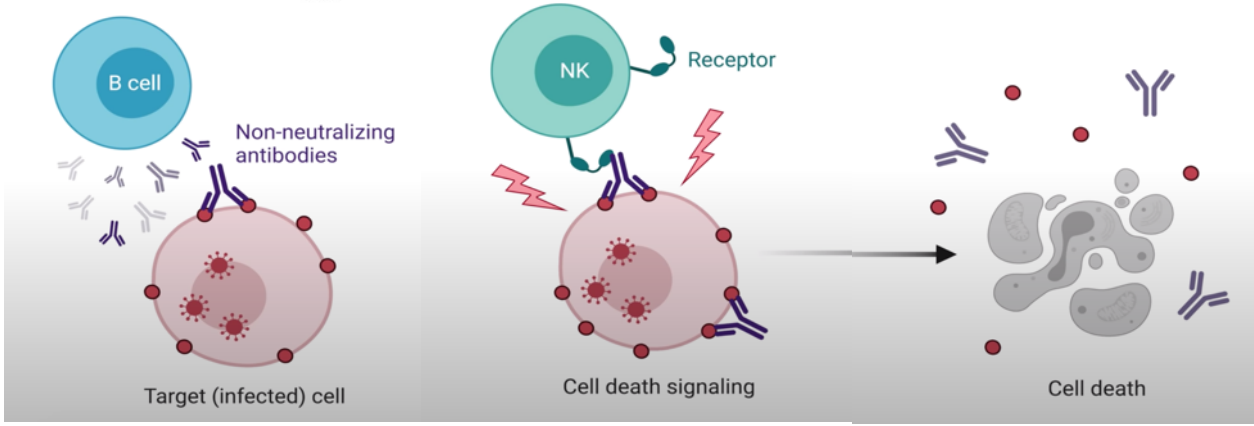
Image: Iwasaki (Yale)

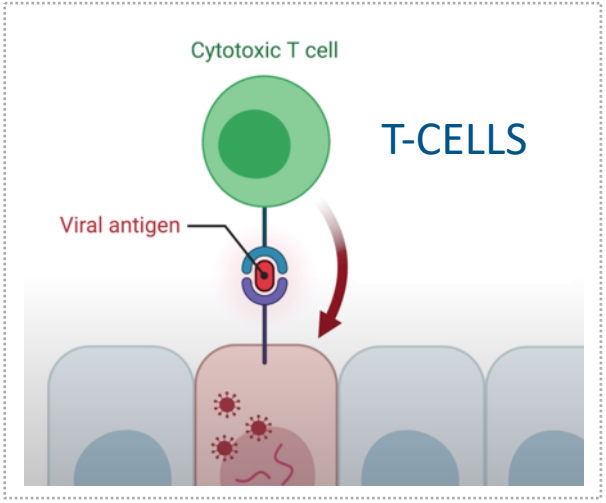


NEUTRALIZING ANTIBODIES



NON-NEUTRALIZING ANTIBODIES





T-CELLS

Images: Iwasaki (Yale)

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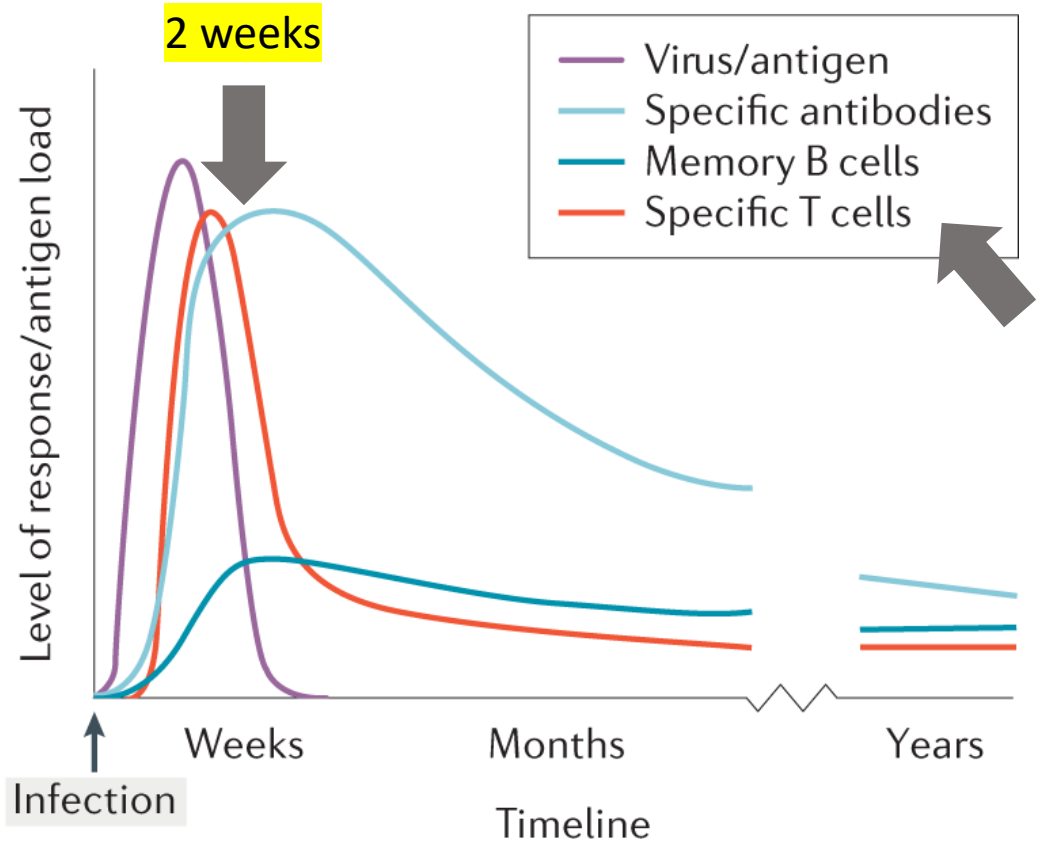
TIME COURSE

Almost all produce antibodies

Amount correlates with severity

↓ over time



Nat Rev Immunol (2020). https://doi.org/10.1038/s41577-020-00436-4

IMMUNITY

response

protection

sterilizing immunity
functional immunity

waning immunity
lost immunity

a matter of degrees, not absolutes

https://www.statnews.com/2020/08/25/four-scenarios-on-how-we-might-develop-immunity-to-covid-19/

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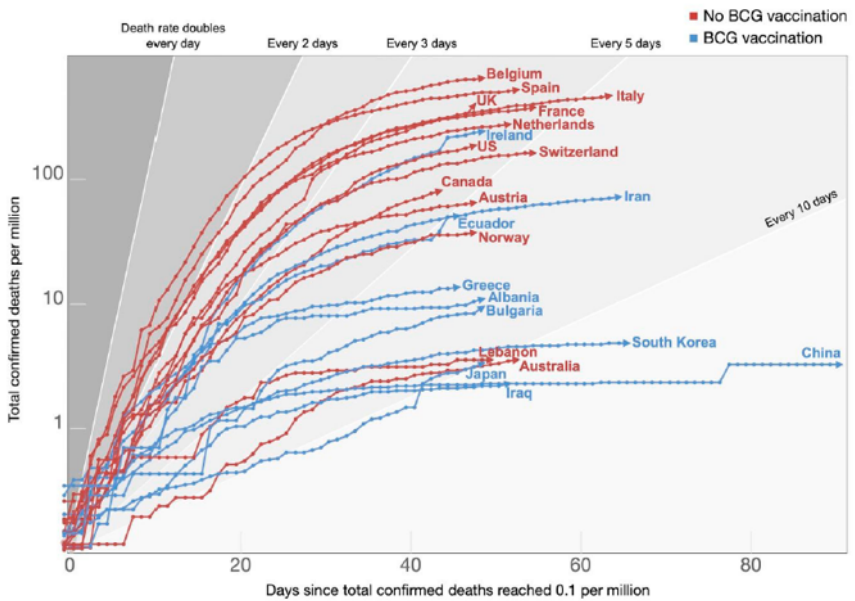
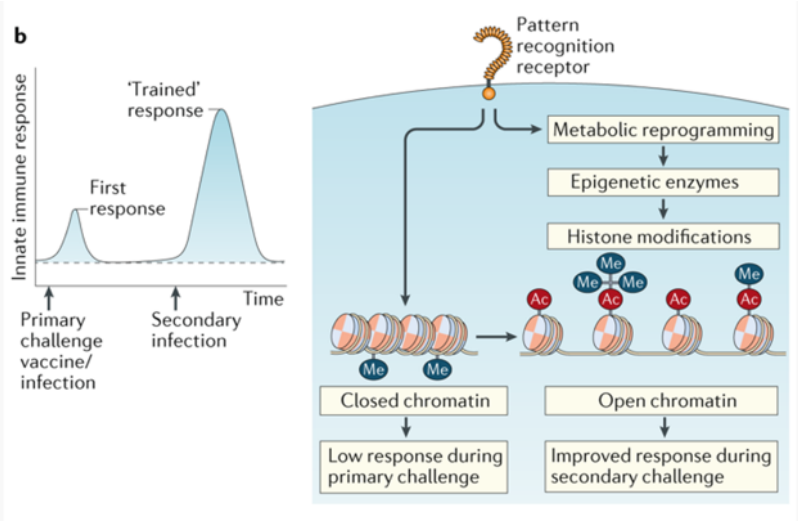
BCG VACCINATION





Epigenetic and metabolic programming of innate cells

trained immunity

↑ cytokines
↑ activation
↑ functional response

https://www.medrxiv.org/content/10.1101/2020.04.10.20060905v2

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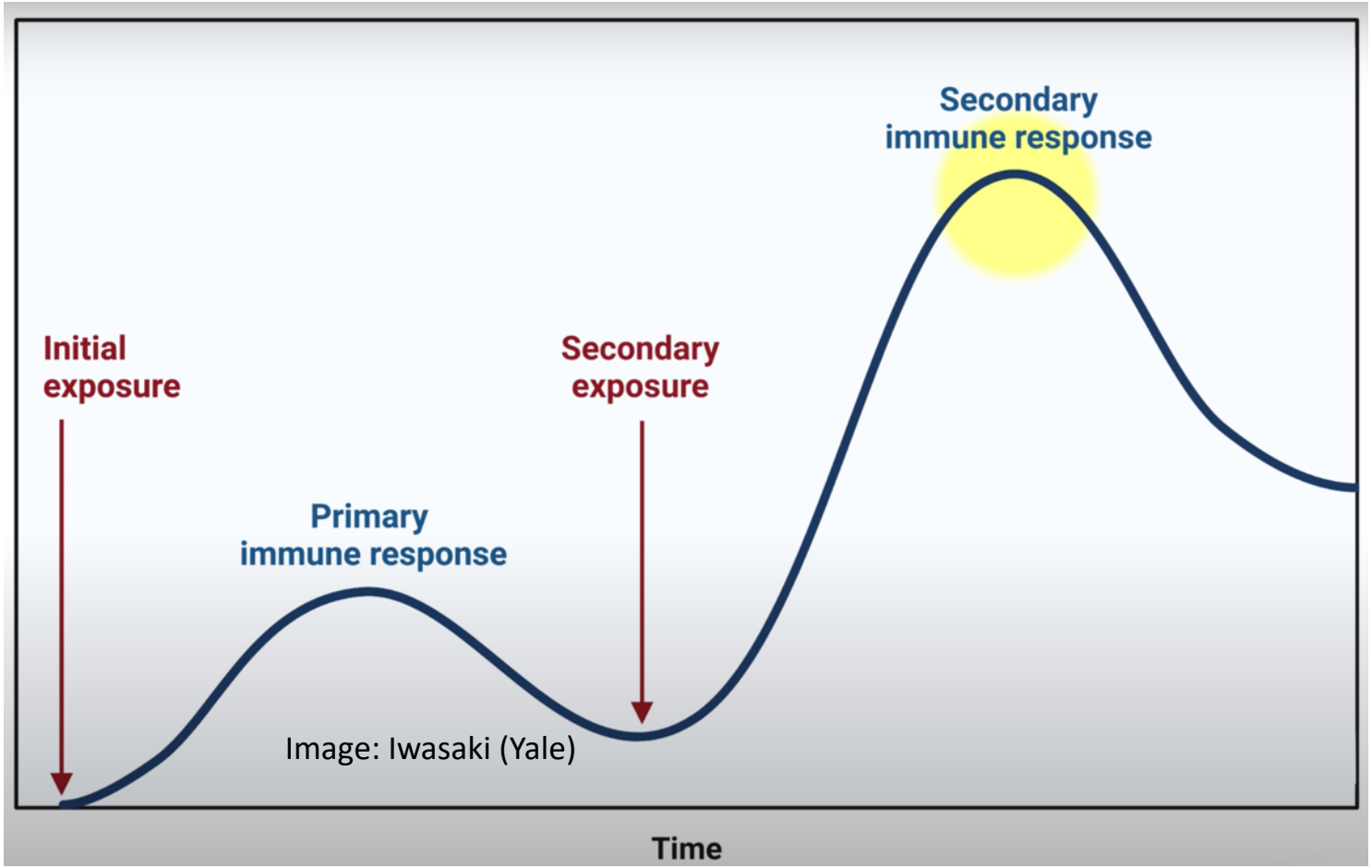

Image: Iwasaki (Yale)

3. MEMORY

B cells
T cells

etc

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CYTOKINE STORM

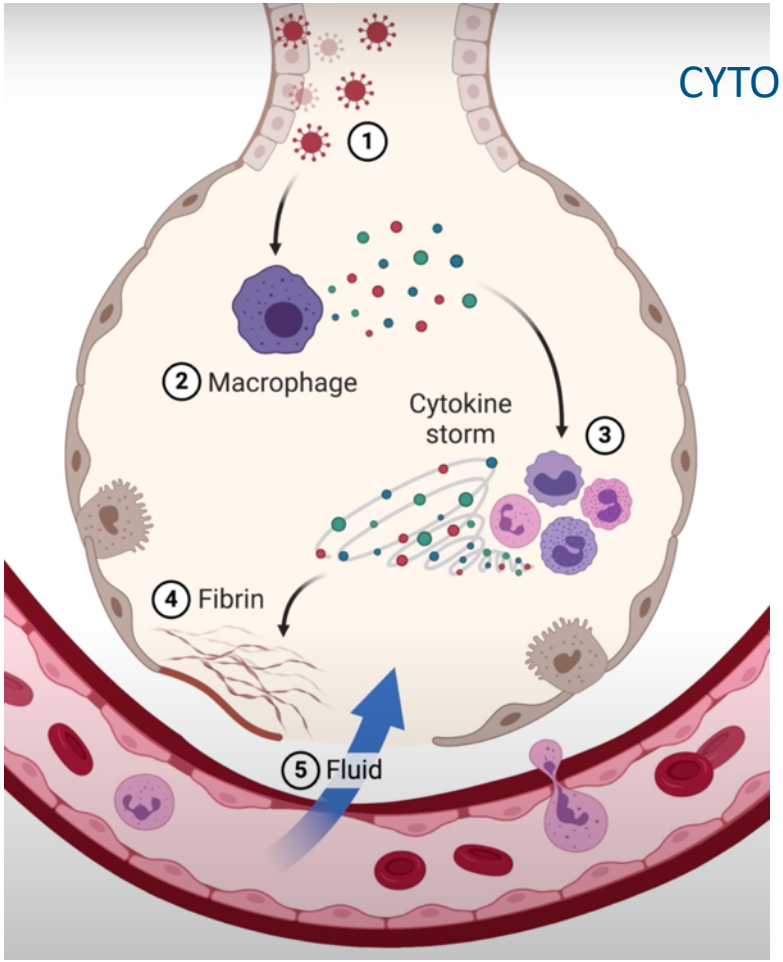

Image: Iwasaki (Yale)

a. **Delayed innate response; less interferon; “exhausted” T-cells**
b. **Both innate and adaptive systems compromised**
c. **More virus; migration to other tissue**
d. **Prolonged immune system activation**

Treatment implications

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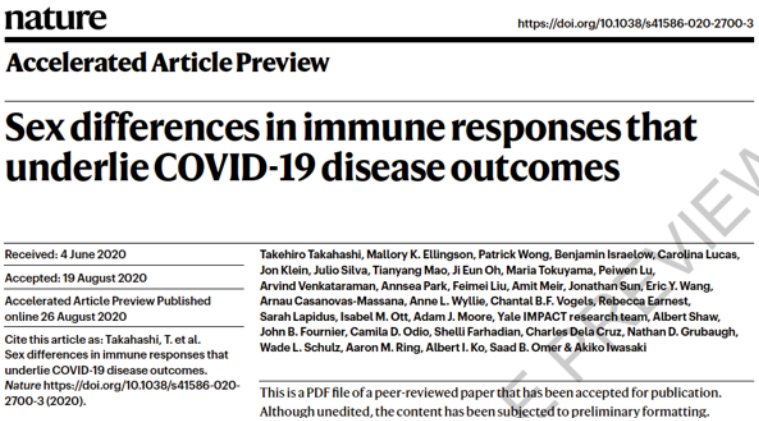
REINFECTION

- Months later (140 days)
- Not sick
- Different strains

- New infection vs persistence
- Immunity is not absolute “sterilizing”

GENDER
AGE



nature

https://doi.org/10.1038/s41586-020-2700-3

Accelerated Article Preview

Sex differences in immune responses that underlie COVID-19 disease outcomes

Received: 4 June 2020

Accepted: 19 August 2020

Accelerated Article Preview Published online 26 August 2020

Cite this article as: Takahashi, T. et al. Sex differences in immune responses that underlie COVID-19 disease outcomes. *Nature* https://doi.org/10.1038/s41586-020-2700-3 (2020).

Takehiro Takahashi, Mallory K. Ellingson, Patrick Wong, Benjamin Israelow, Carolina Lucas, Jon Klein, Julio Silva, Tianyang Mao, Ji Eun Oh, Maria Tokuyama, Peiwen Lu, Arvind Venkataraman, Annsea Park, Feimei Liu, Amit Meir, Jonathan Sun, Eric Y. Wang, Arnau Casanovas-Massana, Anne L. Wyllie, Chantal B.F. Vogels, Rebecca Earnest, Sarah Lapidus, Isabel M. Ott, Adam J. Moore, Yale IMPACT research team, Albert Shaw, John B. Fournier, Camila D. Odio, Shelli Farhadian, Charles Dela Cruz, Nathan D. Grubaugh, Wade L. Schulz, Aaron M. Ring, Albert I. Ko, Saad B. Omer & Akiko Iwasaki

Implications for
vaccine dosing

"Female patients mounted significantly more robust T cell activation than male patients during SARS-CoV-2 infection, which was sustained in old age"

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THE CHECKUP

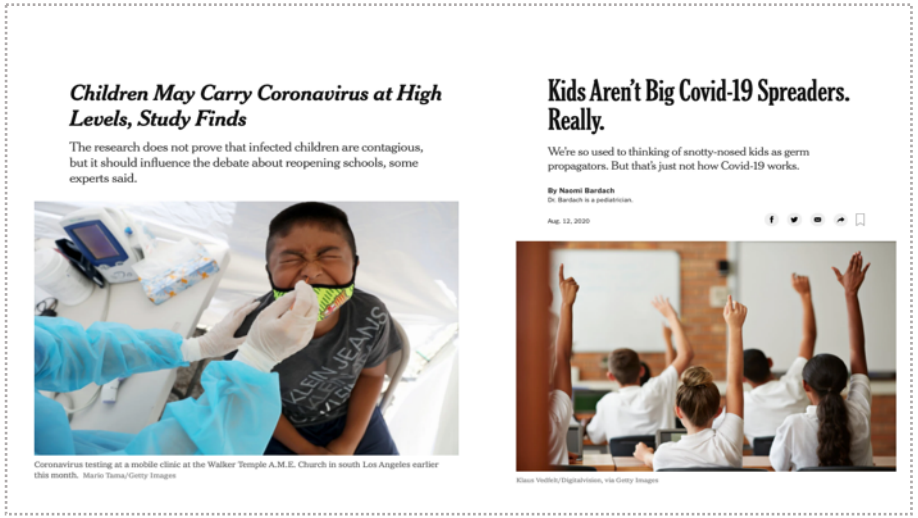
Caring for Children With Multisystem Inflammatory Syndrome

Now, nearly two months after the first cases were reported, doctors can reassure parents that the syndrome remains rare, while continuing to urge vigilance.

Getty Images

By Perri Klass, M.D.

June 29, 2020



Children May Carry Coronavirus at High Levels, Study Finds

The research does not prove that infected children are contagious, but it should influence the debate about reopening schools, some experts said.

Coronavirus testing at a mobile clinic at the Walker Temple A.M.E. Church in south Los Angeles earlier this month. Mario Tama/Getty Images

Kids Aren't Big Covid-19 Spreaders. Really.

We're so used to thinking of snotty-nosed kids as germ propagators. But that's just not how Covid-19 works.

By Naomi Bardach

Dr. Bardach is a pediatrician.

Aug. 12, 2020

Klaus Vedfelt/Digitalvision, via Getty Images

KIDS

- Less susceptible
- Less sick
- MIS-C

- More vigorous immune response
- May carry/transmit - but less

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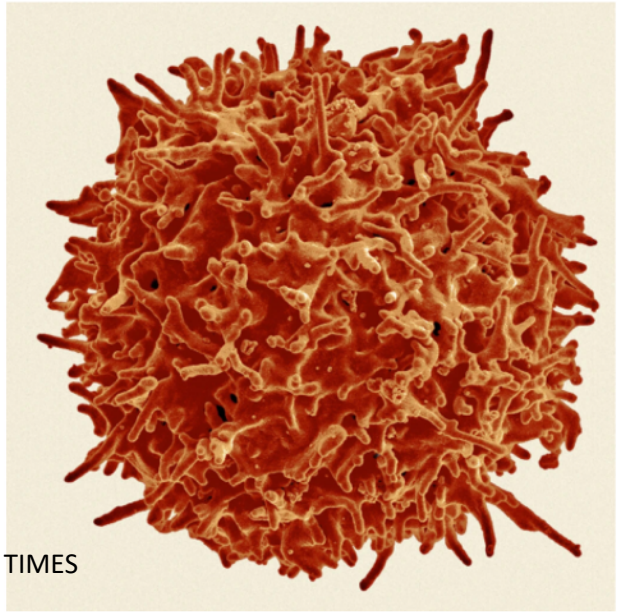
The Coronavirus Is New, but Your Immune System Might Still Recognize It

Some people carry immune cells called T cells that can capitalize on the virus's resemblance to other members of its family tree.



A colorized scanning electron micrograph of a human T cell. Encounters with other coronaviruses may prime the immune system to fight the virus that causes Covid-19. Science Source

IMAGE: NY TIMES

PRE-EXISTING IMMUNITY

20 – 50 % of people who were never exposed to SARS-CoV-2 have significant numbers of T-cells that can recognize it.

Common human coronaviruses (229E, NL63, OC43, HKU1) cause mild/moderate upper-respiratory tract illnesses like the common cold.

Functional relevance?

+/-

Nat Rev Immunol (2020). https://doi.org/10.1038/s41577-020-0389-z.

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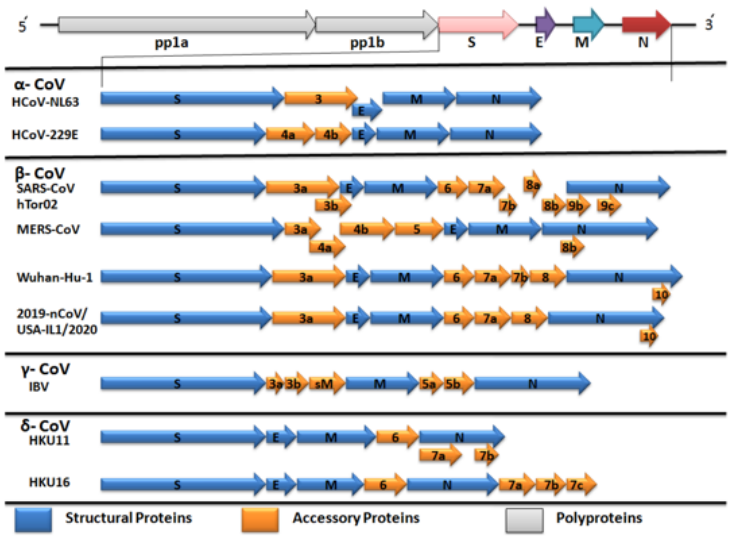


https://www.mdpi.com/2076-0817/9/3/240/htm

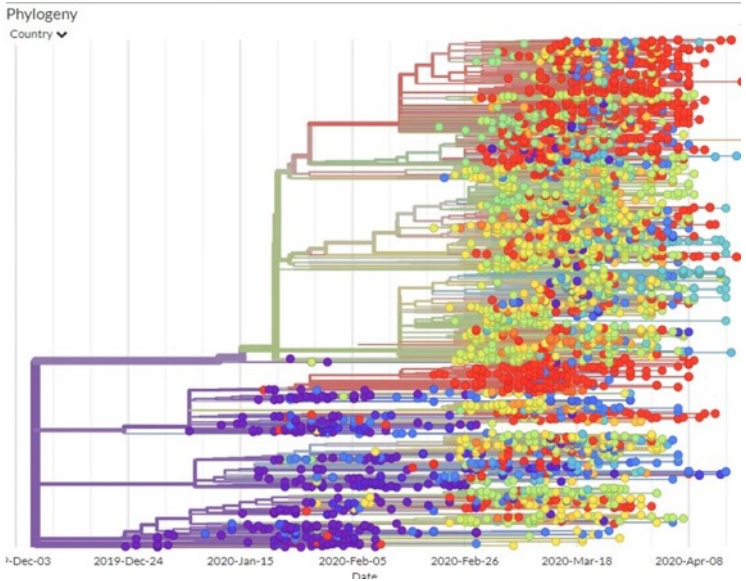


Image: conversation.com

GENETICS

Gene variants associated with respiratory failure

1. Region of genome that determines ABO blood type.
2. Near genes that encodes a protein that interacts with the ACE receptor the virus uses to enter human cells
3. Near genes that encode immune response

ANTIBODY TESTING

Aug 26 launch by private labs
+ Single point of care test

SAHPRA
South African Health Products Regulatory Authority

MAVERICK CITIZEN OP-ED

The False Hope of Antibody Testing

By Greg Kew & Jonny Myers • 15 July 2020

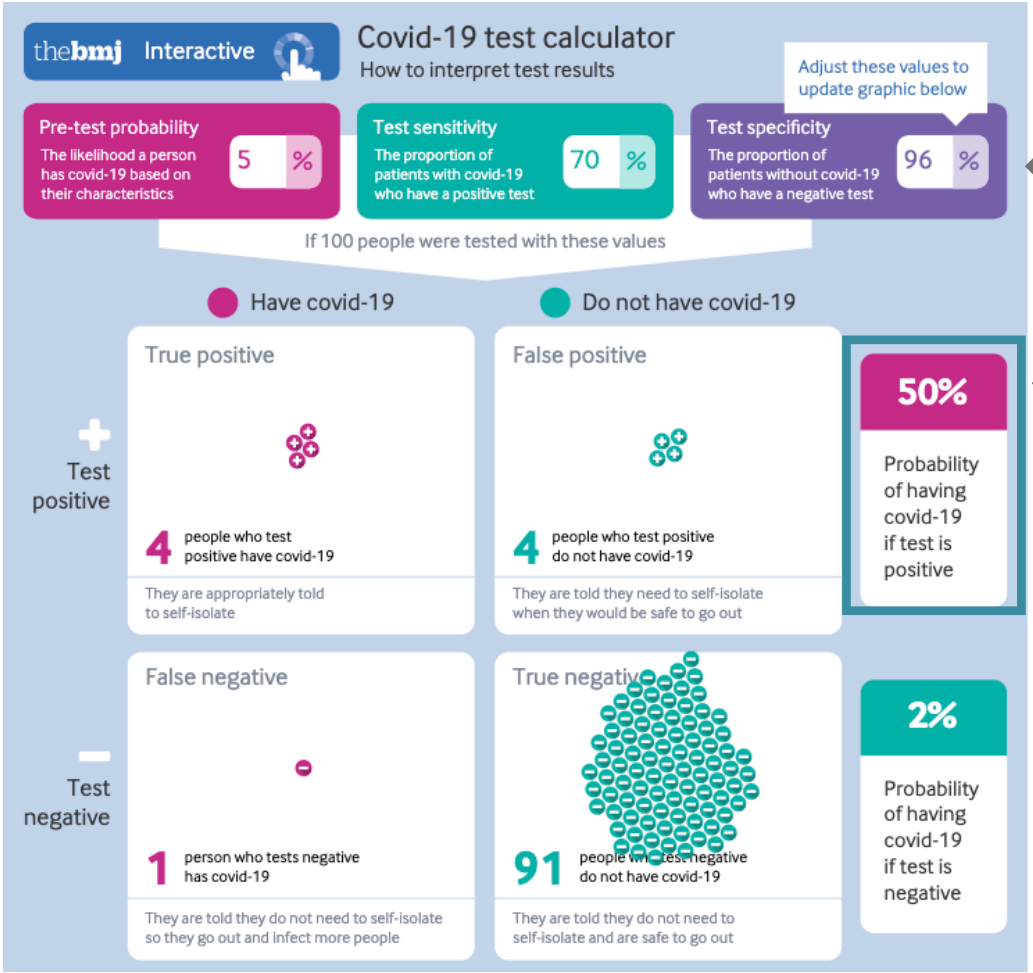
- Professional use only
- Epidemiologic study (PREVALENCE)
- Not diagnostic
- Not predictive of immunity

"Diagnose COVID-19 retrospectively in patients who have recovered from a COVID-19 compatible illness".

Diagnose COVID-19 in patients in who are "admitted with suspected SARS-CoV2 infection but who test negative [RT-PCR]".

Children with multi-inflammatory syndrome

PREVALENCE



https://www.bmj.com/content/369/bmj.m1808/infographic

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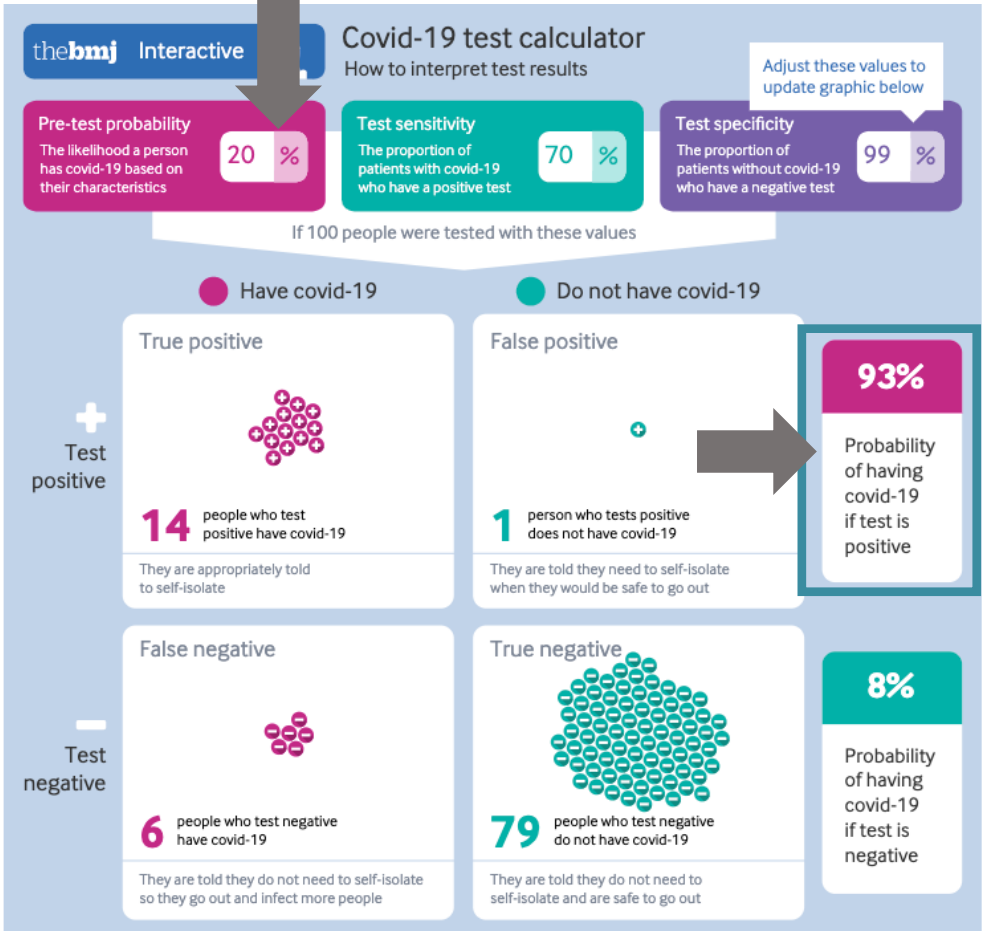
PREVALENCE (pre-test probability)



https://www.bmj.com/content/369/bmj.m1808/infographic

The crucial thing is not the test itself but what you do in response.

Quarantine (stop transmission)
Diagnose and treat
Admit to a COVID ward
"Immunity passport" X

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HERD IMMUNITY

+ distancing

+ VACCINE

LONG COVID

- 10-20%
- Residual damage
- Ongoing inflammation?

Research Letter

July 9, 2020

Persistent Symptoms in Patients After Acute COVID-19

Angelo Carfì, MD[1]; Roberto Bernabei, MD[1]; Francesco Landi, MD, PhD[1]; et al

» Author Affiliations | Article Information

JAMA. 2020;324(6):603-605. doi:10.1001/jama.2020.12603

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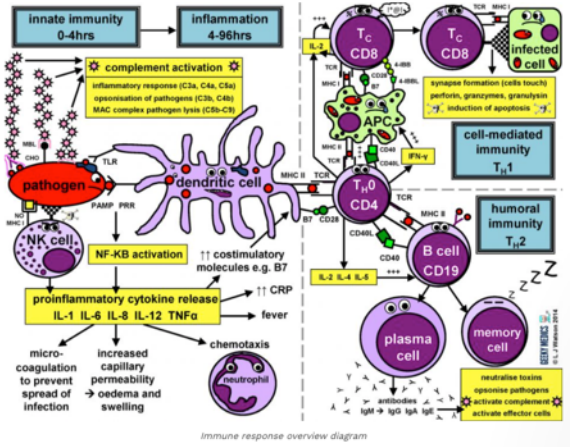
SUMMARY



Immune response overview diagram

Complicated, amazing system
Three phases – innate, adaptive, memory
Balance and timing; in severe COVID-19 is lost
Immunity is degrees not absolutes

Uncertainty for medicine and policy
Answers emerging

https://geekymedics.com/immune-response/

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