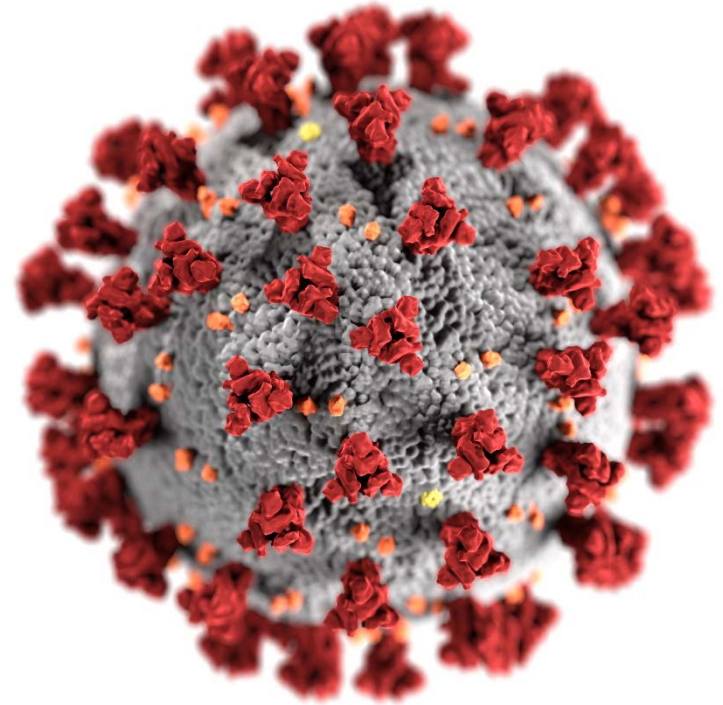


Adaptive immunity and SARS-CoV-2

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ACIP

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cdc.gov/coronavirus

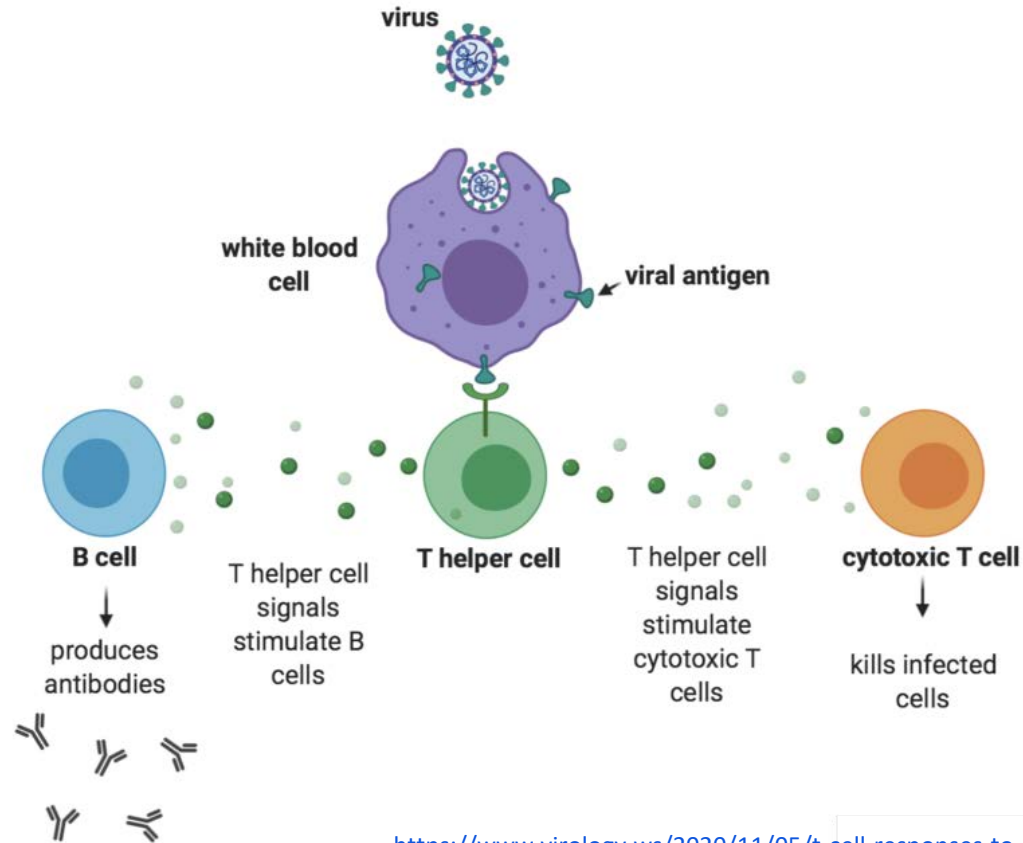
Outline

- Adaptive cellular and humoral immunity
- Correlates and contributors to immunity
- Immune durability
- Age-related immunosenescence
- Variant circulation might affect immunity
- Conclusions

Adaptive cellular and humoral immunity

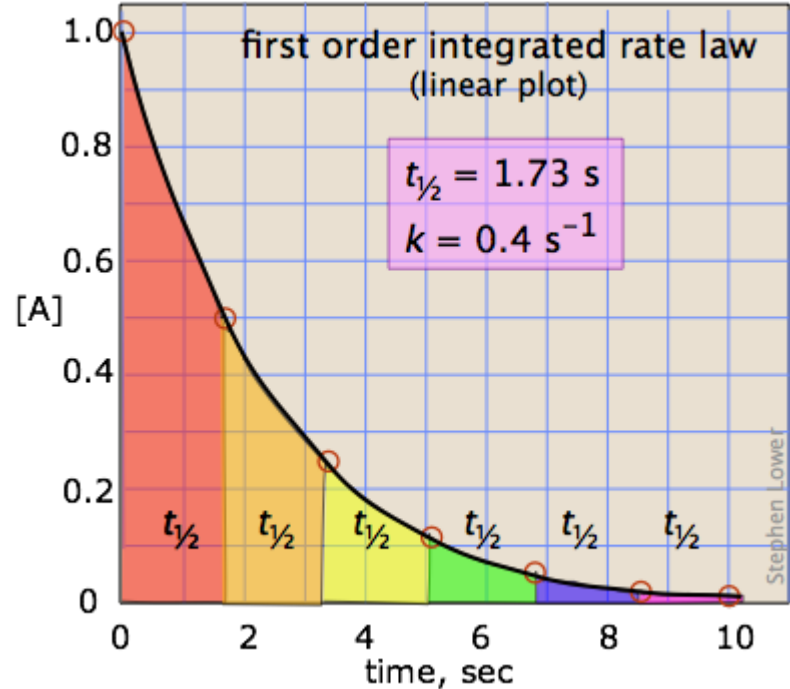


Adaptive immunity includes cellular and humoral responses

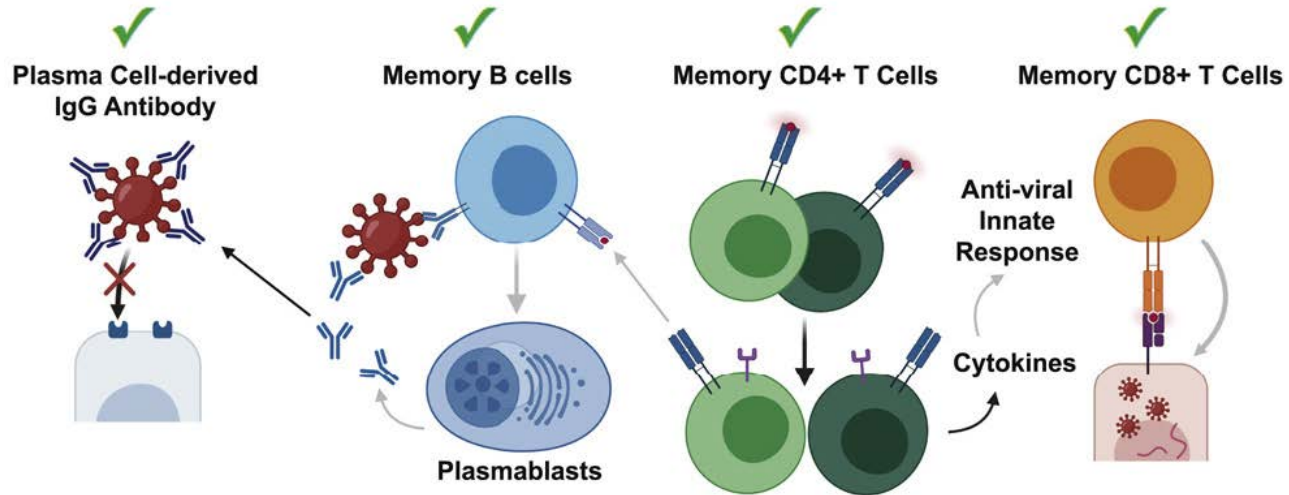


Antibodies decay with a known half-life

Immunoglobulin	Approximate half-life (days)
IgM	5-6
IgA	5-6
IgG1	21
IgG2	21
IgG3	7
IgG4	21



Memory T and B cells are generated, which can initiate anamnestic responses after re-exposure



Immunity – correlates and contributors

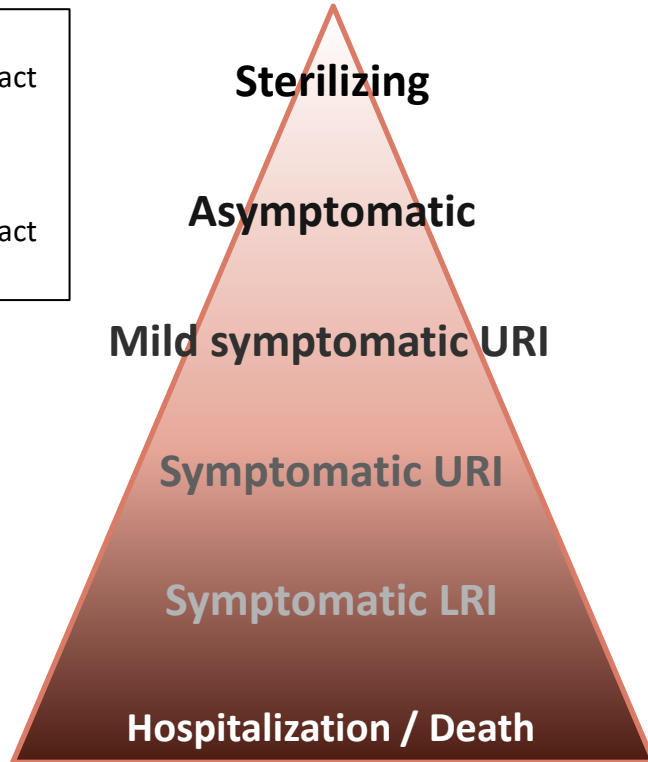


Immunity is a gradient

Levels of immunity

URI – upper respiratory tract infection

LRI – lower respiratory tract infection



Contributors

Antibody levels

Antibody isotypes

**Antibody functionality
(neutralizing / epitopes / affinity)**

Antibody location

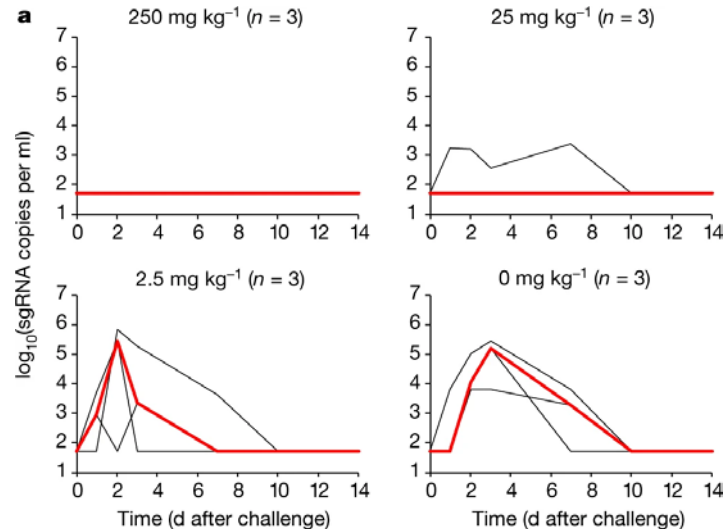
Number and specificity T cells

T cell ratios



Transfer of IgG with high neutralization titer is sufficient to protect against SARS-CoV-2 challenge of rhesus macaques

Lower respiratory tract



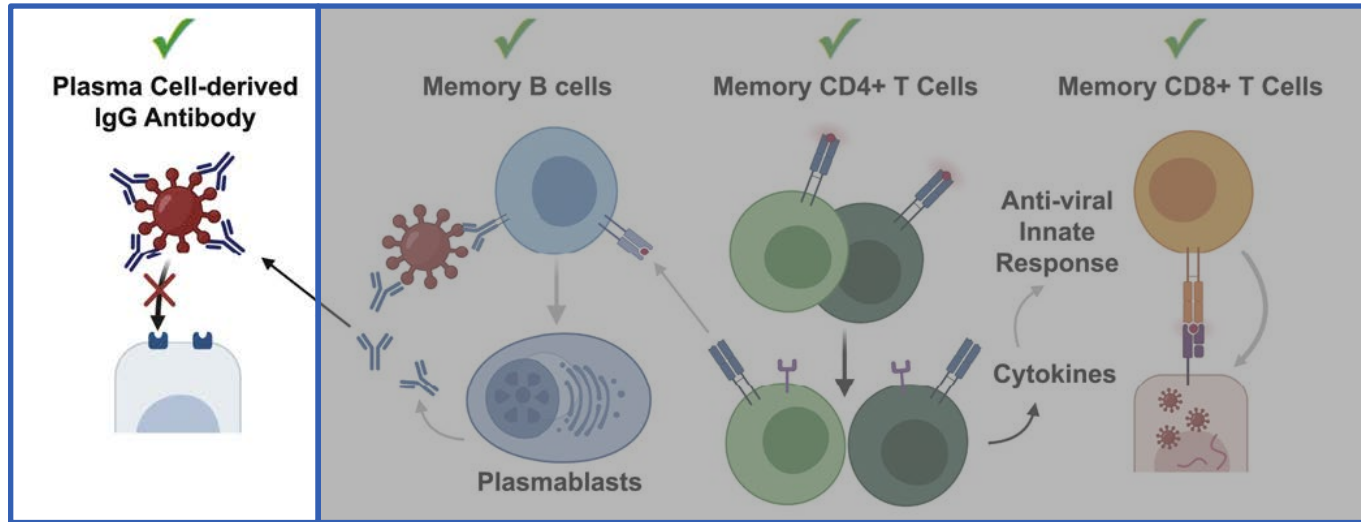
Anti-spike antibodies are correlates of risk

- [Khourey et al.](#) normalized neutralizing antibody titers after vaccination with different vaccine products to mean convalescent titers. Used these normalized values to compare vaccine efficacy (VE) estimates. Used the normalized values to estimate the level of neutralizing antibodies required for 50% protection against infection.
- [Goldblatt et al.](#) assayed binding and neutralization in participants who had received BNT162b, mRNA1272, AZD1222, or Ad26Cov2.S and used a population-based method to estimate a protective threshold (60 BAU/ml anti-spike IgG).
- [Feng et al.](#) calculated the levels binding and neutralizing antibodies required for 50, 60, 70, 80, and 90% VE from symptomatic infection after vaccination with AZD1222.

Correlates analysis of mRNA-1273 indicates 68% of VE mediated through serum neutralizing antibodies

- Day 29 and Day 57 correlates analysis examining inhibitory concentrations 50% (IC50) with neutralization assays
- VE was estimated to be 45 – 60% for vaccine recipients without detectable binding or neutralizing antibodies
- Increased to >98% VE in recipients with highest neutralization titers
- Analysis estimated 68% of VE against symptomatic infection was mediated through Day 29 neutralization titers

Correlates studies focus on humoral arm of adaptive immunity, but that is not the only contributor

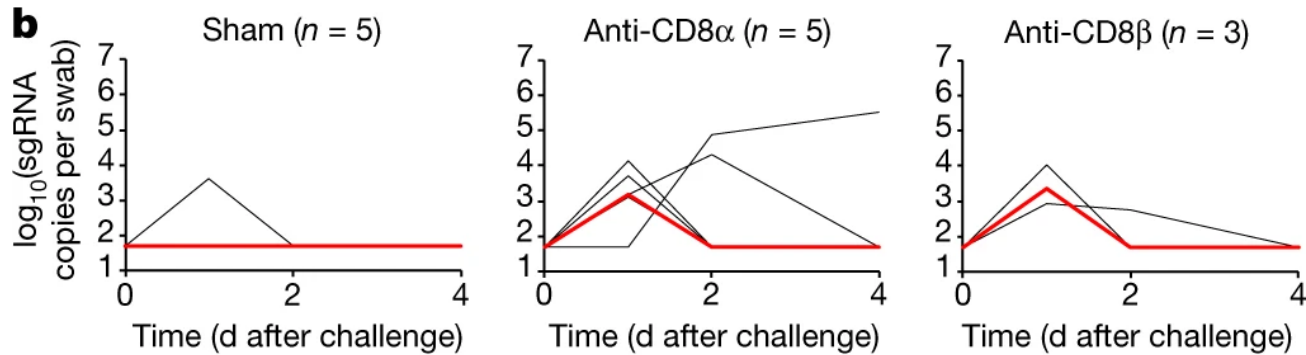


≈ 68%

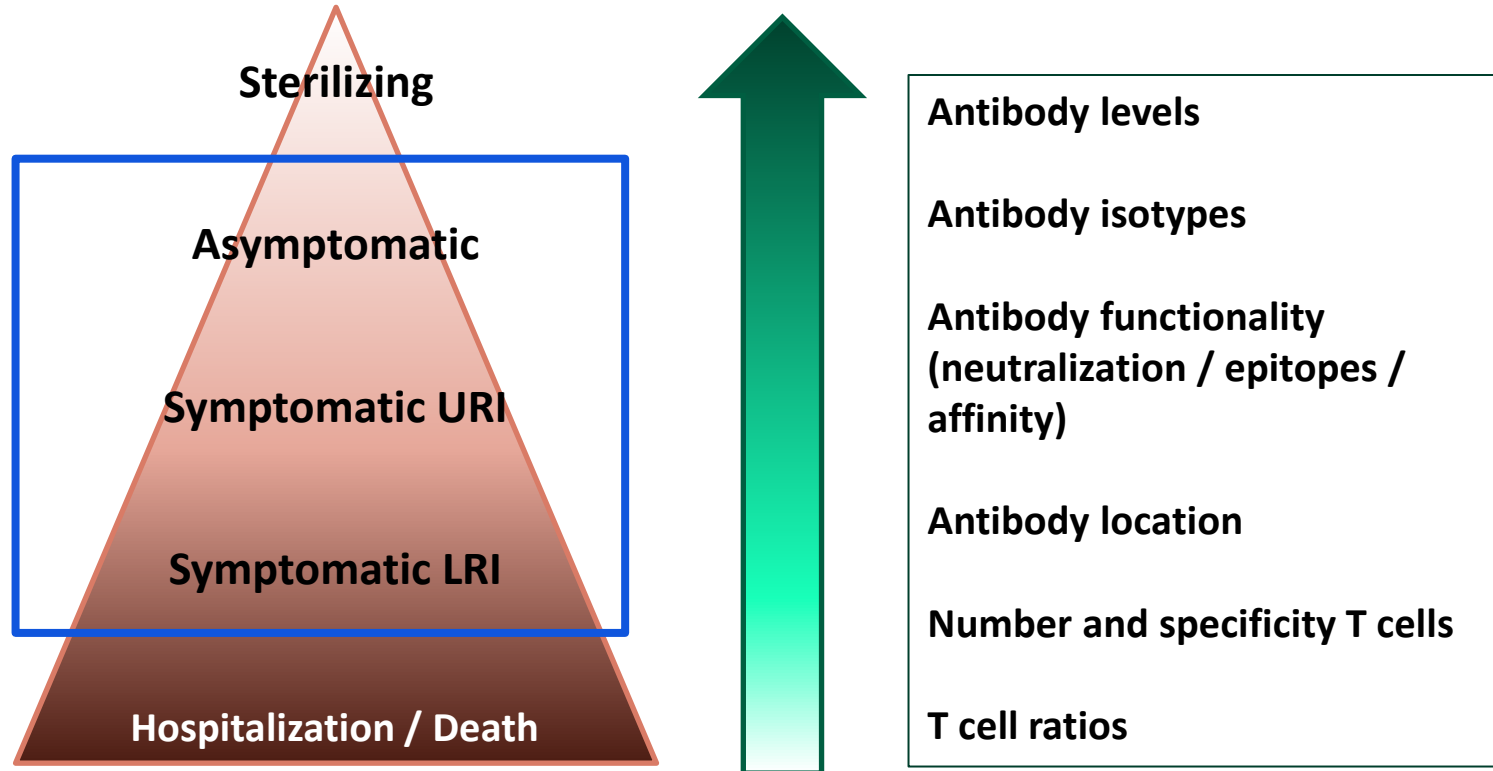
≈ 32%

In previously infected macaques with low levels of antibodies, CD8+ T cells contribute to protection

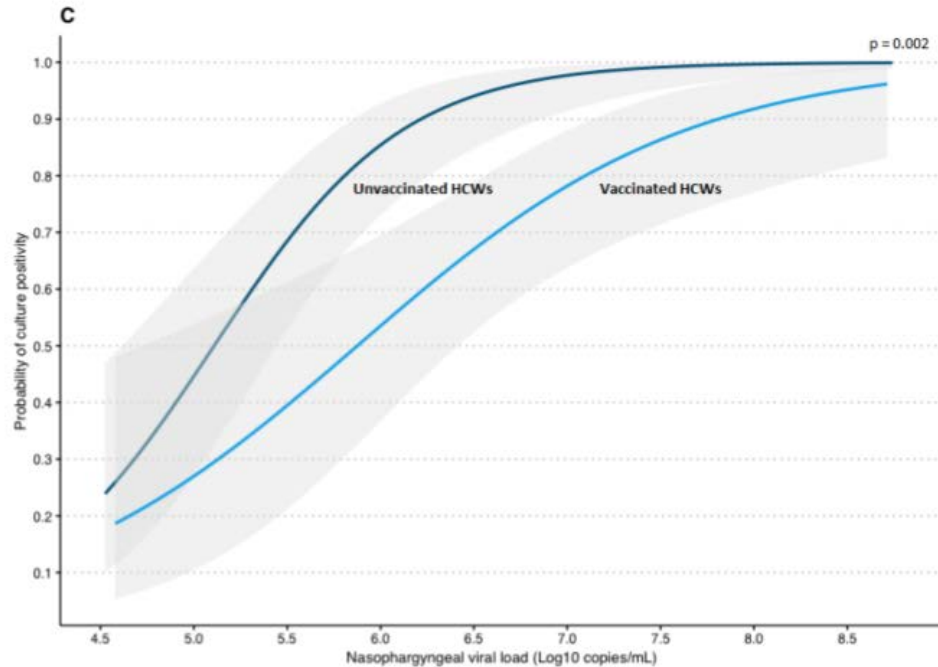
Upper respiratory tract



What happens during infections in vaccinated people?



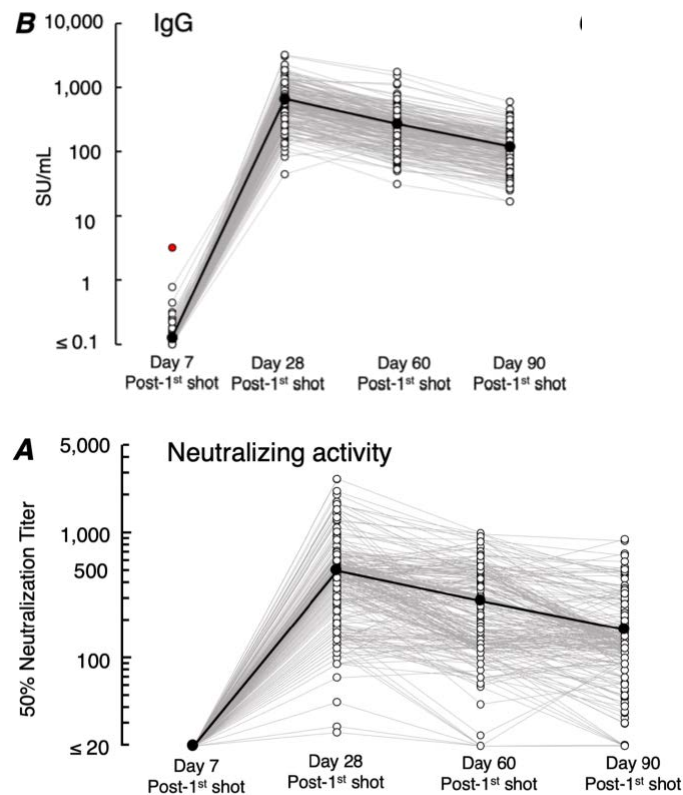
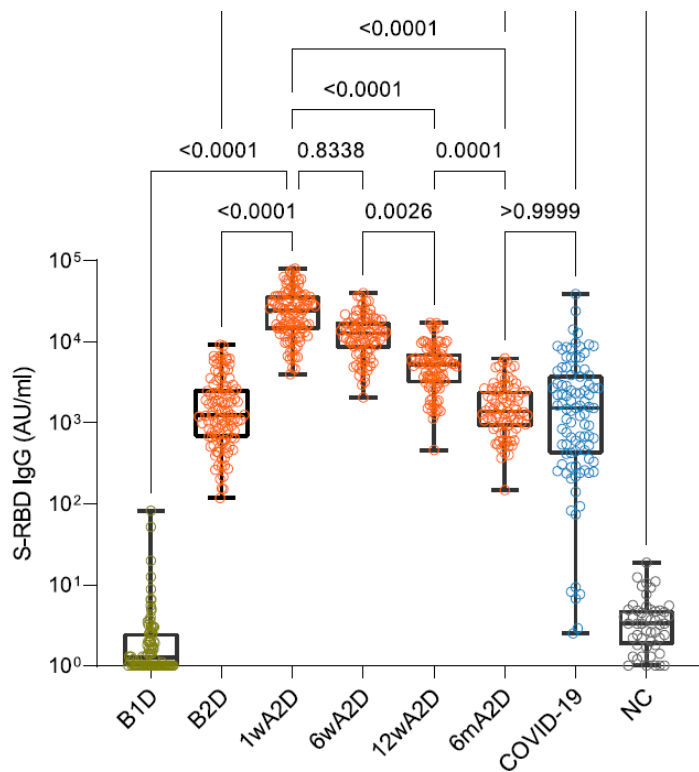
Culturable virus recovered from unvaccinated and vaccinated infected health care workers



Immune durability

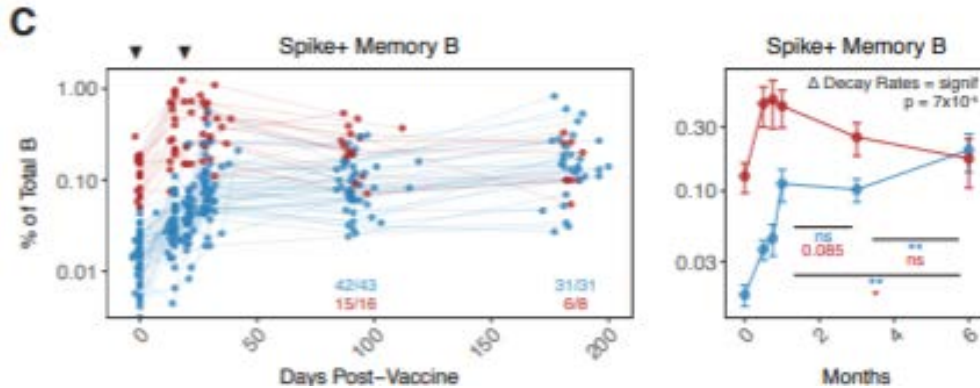


Anti-spike antibodies decay after BNT162b2 vaccination

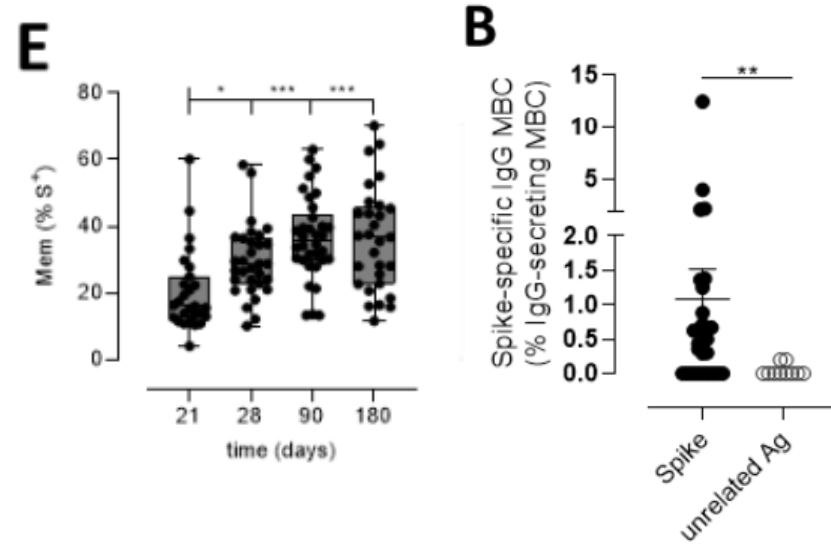


mRNA vaccine recipients maintain spike-specific memory B cells at 6 months

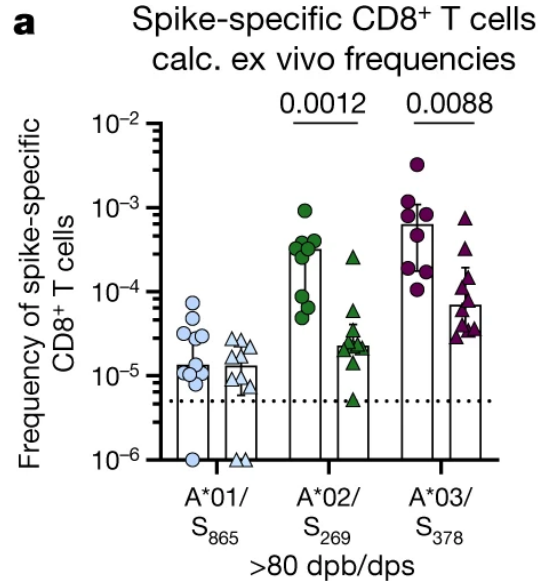
Moderna



Pfizer-BioNTech



BNT162b2 mRNA vaccine recipients generate spike-specific early memory CD8⁺ T cells



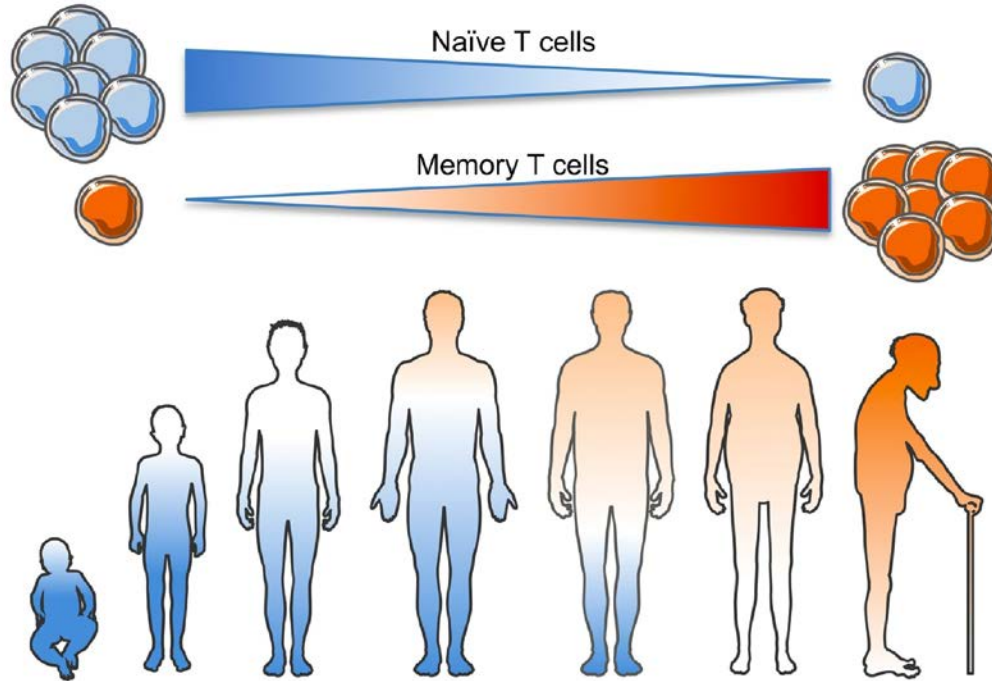
Durability

- Serum antibodies decrease over time
- Memory B cells are maintained out to 6 months post-vaccination
- Early memory CD8+ T cells are detected >80 days after vaccination with BNT162b2

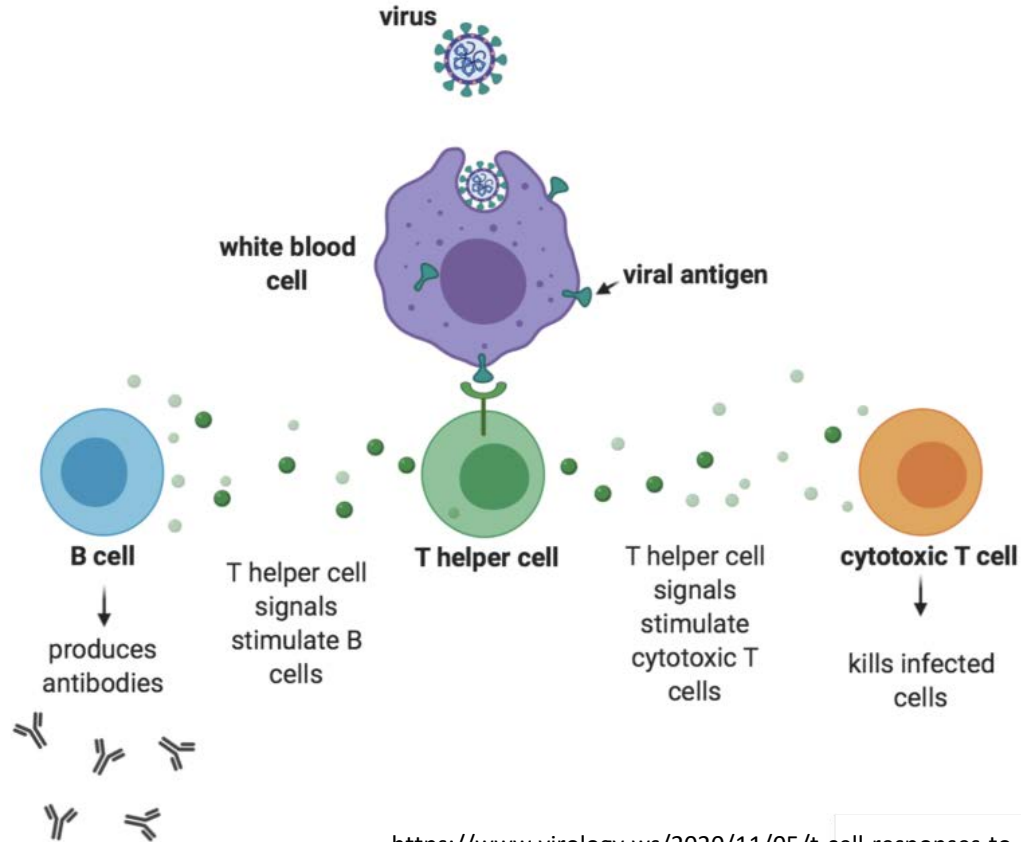
Immunosenescence



Pool of naïve T cells diminished with age

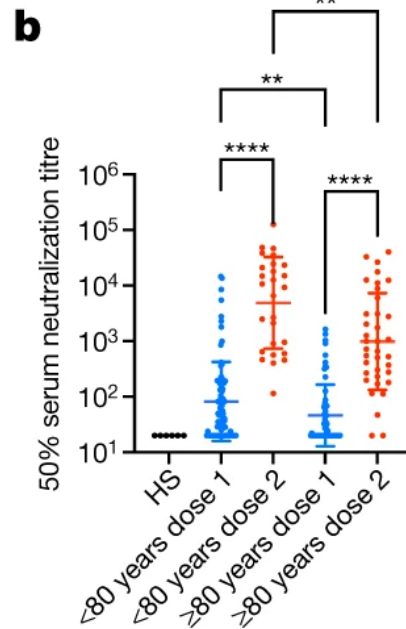
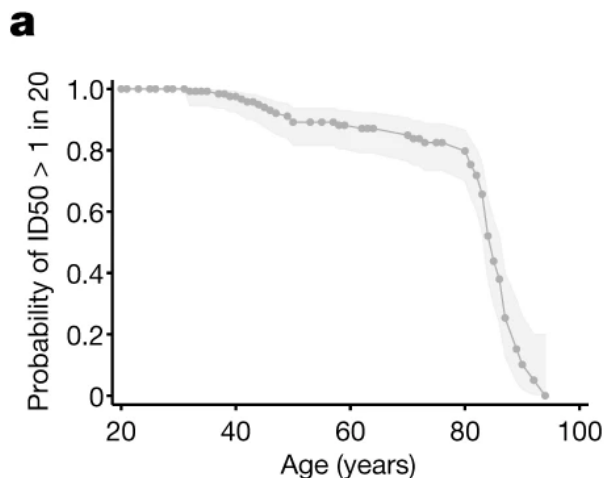


Adaptive immunity includes cellular and humoral responses



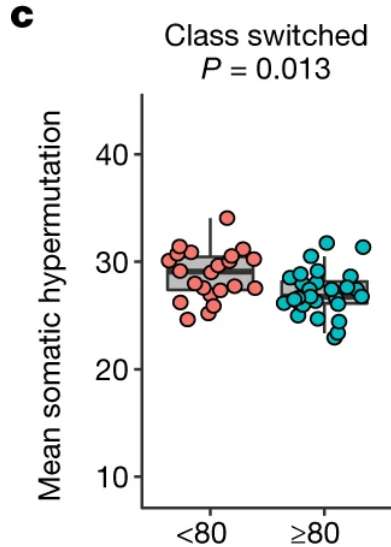
Adults ≥ 80 years have reduced neutralization titers compared to younger adults after BNT162b2 vaccination

Probability of +
neutralization after 1 dose

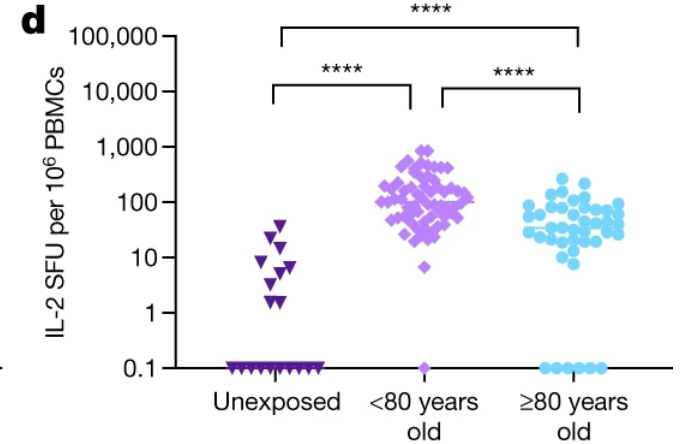
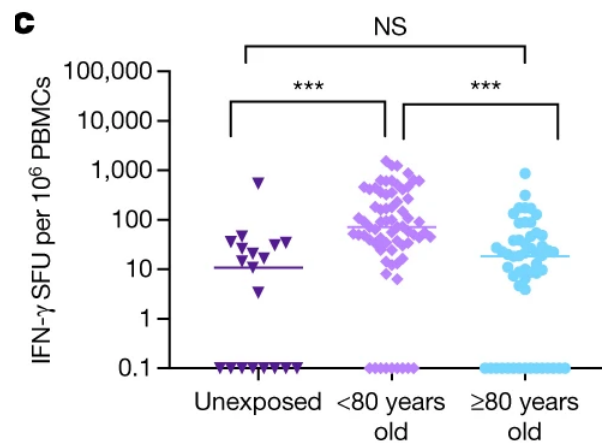


Adults ≥ 80 years had less mature antibodies and fewer functional T cells after BNT162b2 vaccination

B cells



T cells

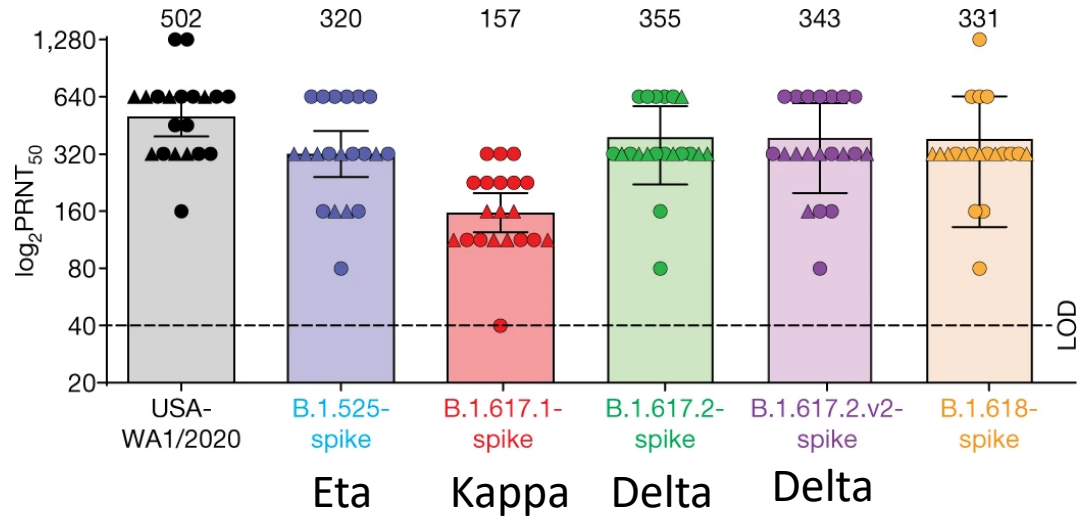


Variants

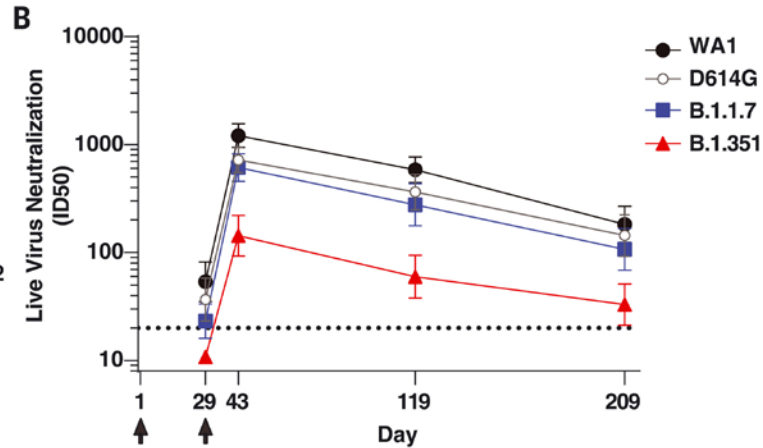
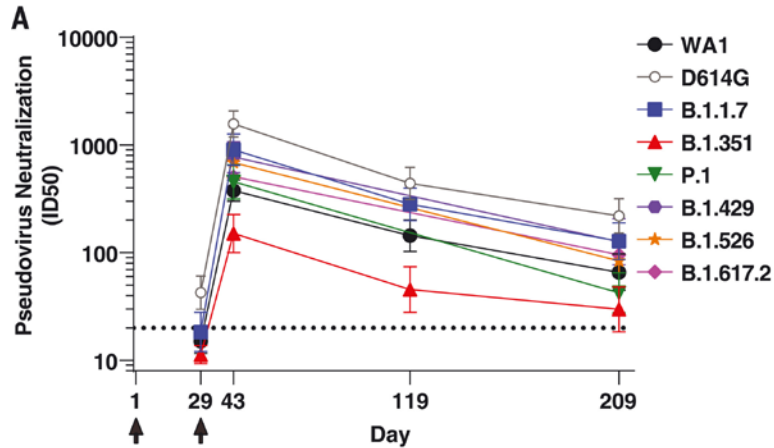


Decay of neutralizing antibodies could be confounded by circulation of variants of concern

- Some variants have amino acid changes near the spike receptor binding domain that could result in reduction in neutralization titers.
- Neutralization loss ranges from nil (alpha) to about 7-fold (beta). Delta is approximately 1.5-2-fold reduction.



Antibody decay plus reduction in neutralization titers yield lower titers at six months after mRNA-1273 boost



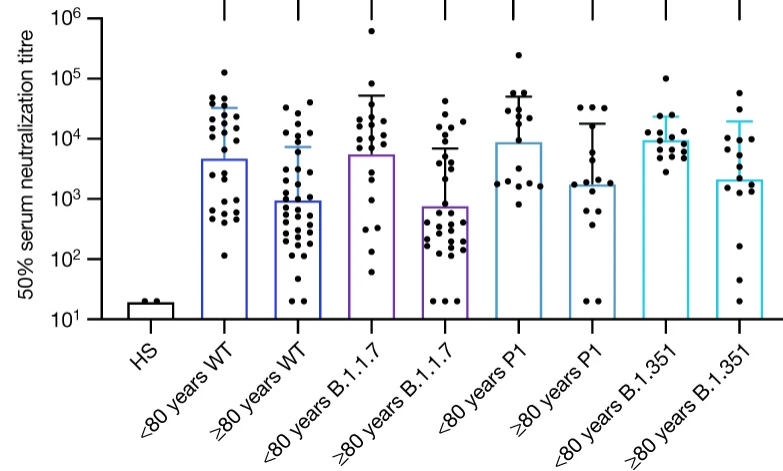
WHO label	Lineage #
Alpha	B.1.1.7
Beta	B.1.351
Gamma	P.1
Delta	B.1.617.2
	AY.1
	AY.2
Eta	B.1.525
Iota	B.1.526
Kappa	B.1.617.1
Mu	B.1.621



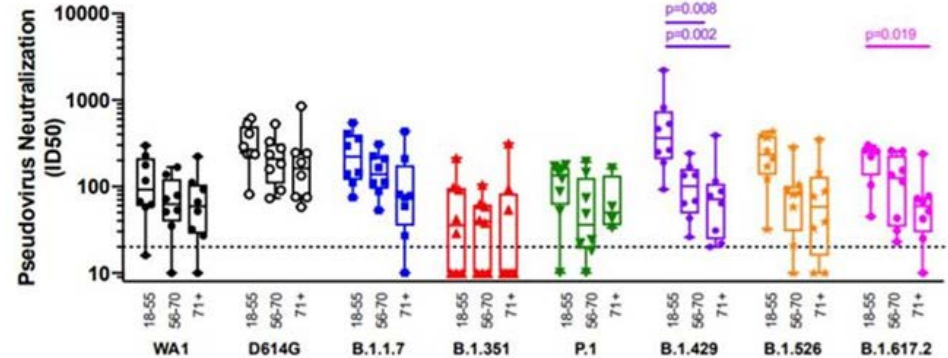
Reduced titers in older adults can also be further confounded by variant circulation

Peak BNT162b2

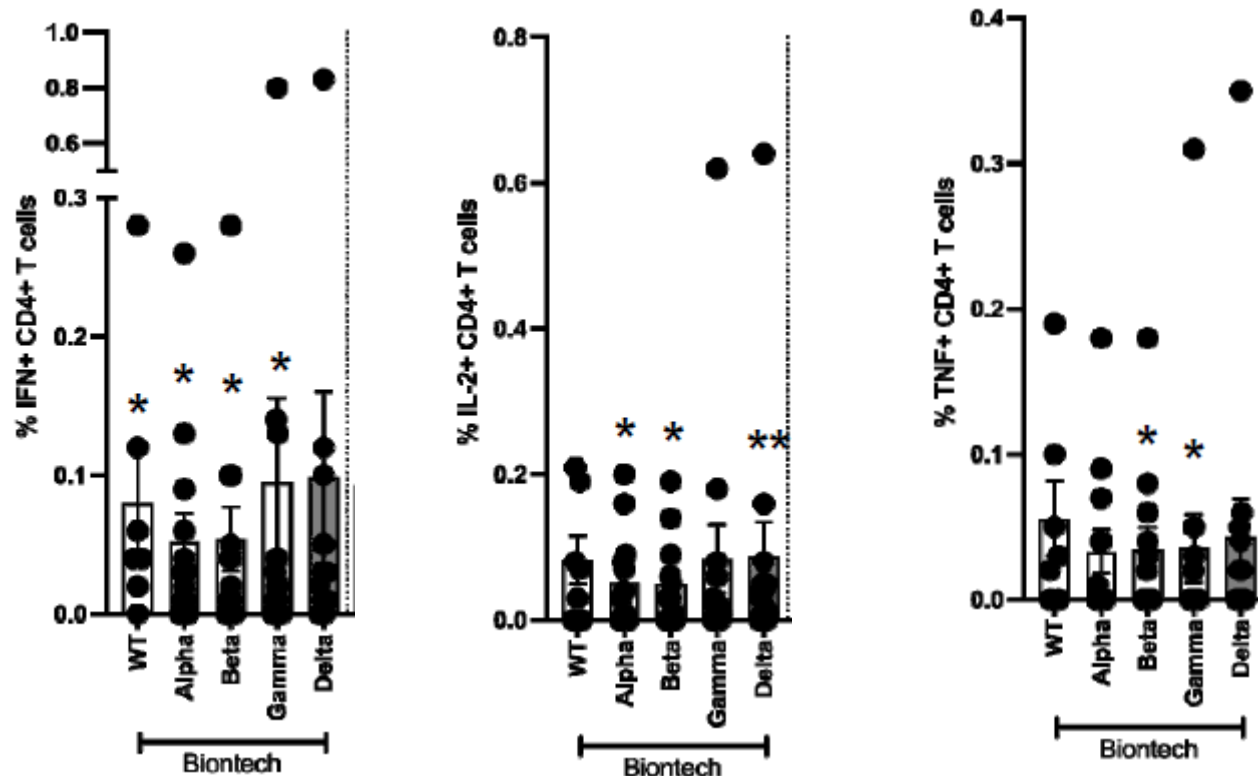
Two doses



Six months mRNA-1273



T cell activity maintained against variant spikes after BNT162b2 vaccination



Summary



Conclusions 1 of 3

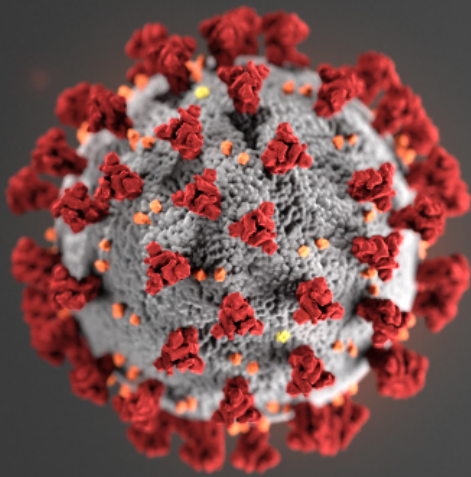
- There are degrees of protection from different outcomes based on a person's level of immunity.
- Multiple components of the immune system are required to prevent infection and illness; these components are complex and dynamic.
- When a vaccinated person becomes infected, they may shed culturable virus, and therefore may be infectious.

Conclusions 2 of 3

- Antibodies decrease over time in all age groups; cellular memory is maintained after waning.
- Neutralizing antibodies likely confer a majority of, but not all, immunity.
- Cellular responses likely contribute to protection against severe disease through anamnestic response even after antibodies wane.

Conclusions 3 of 3

- Older adults
 - Start with lower neutralization titers than younger adults.
 - Because they start at lower titers, they may be faster to fall below the lower limit of detection.
 - May have less robust cellular memory generation because of immunosenescence and therefore may be more dependent on humoral immunity.
 - Reduced neutralization of variant viruses may confound antibody waning in all age groups.



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

