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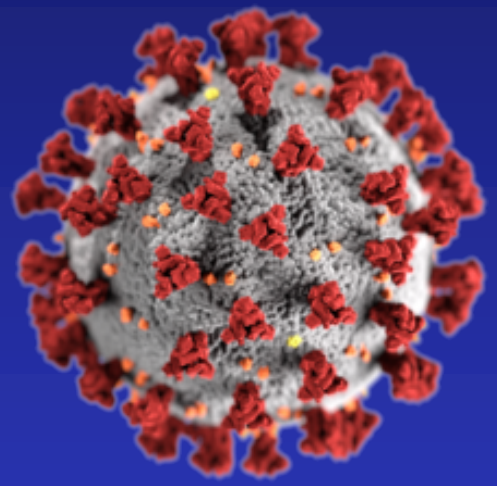
SARS-CoV-2

1. What is SARS-CoV-2 and how is it different from other coronaviruses ?

2. What is COVID-19 and what is unexpected in it?

3. How is our immune response dealing with this virus in adult and older populations (including duration of immunity)?

4. What is the basis of potential immune vulnerability in older adults? How will it relate to protection by vaccination?

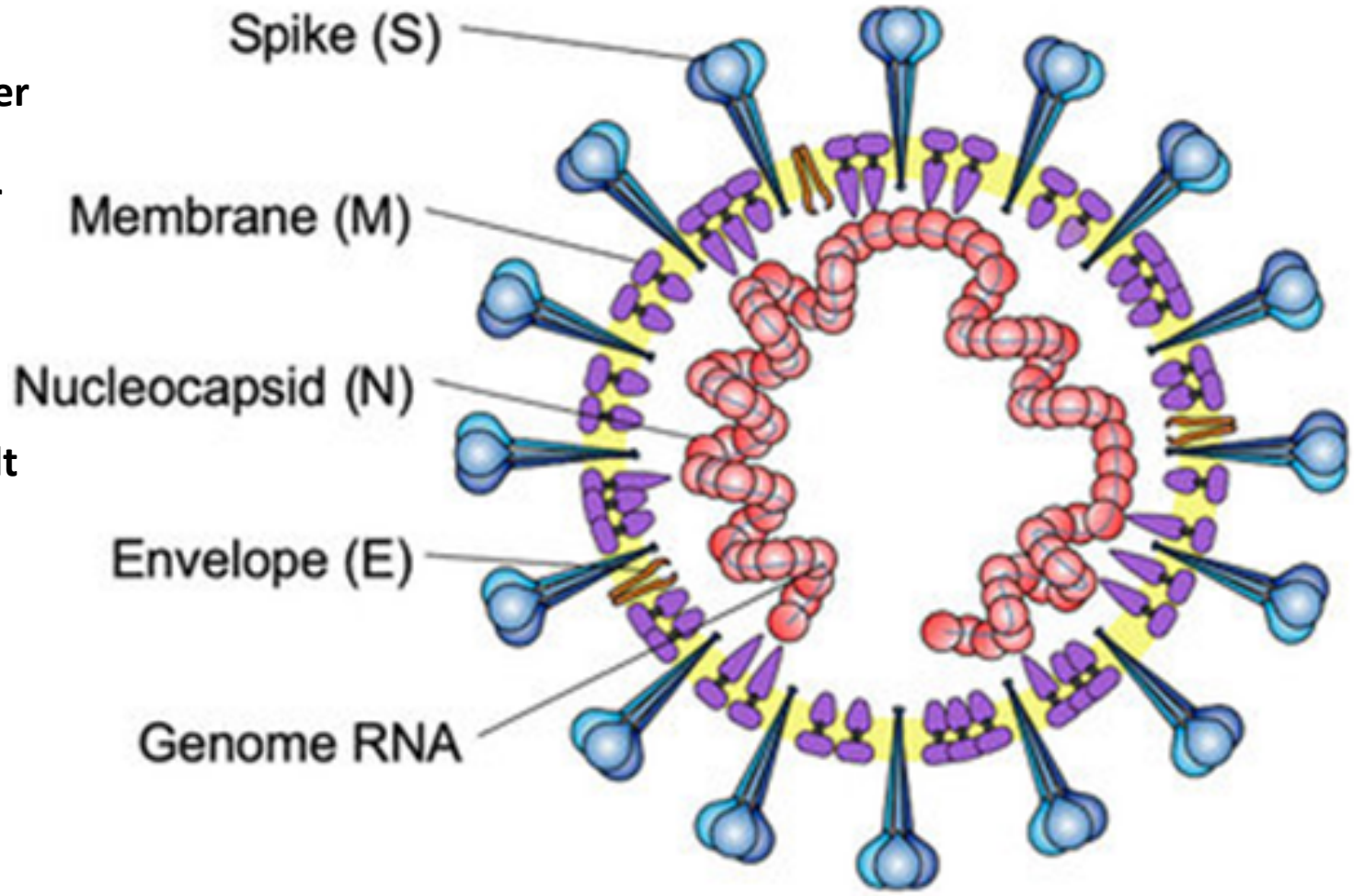


Alissa Eckert, Dan Higgins/CDC

Selecting antigenic targets for SARS-CoV-2 serological assays

What is new in this virus?

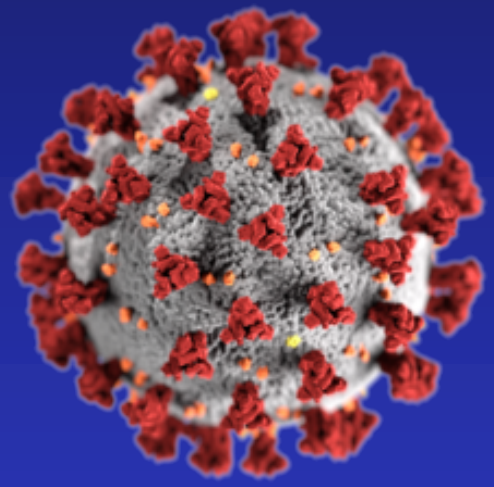
- **S RBD mutated, binds better to hACE2**
- **Persists and spreads better than SARS-1 or MERS**
- **Sheds from the infected person 2-3 days before symptoms**
- **Respiratory; always difficult to contain**
- **Asymptomatic spread (?)**



Xu et al., *Emerging Microbes and Infections*, 2019

SARS-CoV-2

- Severe acute respiratory syndrome coronavirus 2 (SARS-Cov2)
- Coronaviridae family
- Coronavirus disease 19 (COVID-19)
  - Fever
  - Cough
  - Fatigue
  - Shortness of breath; ARDS; cytokine storm



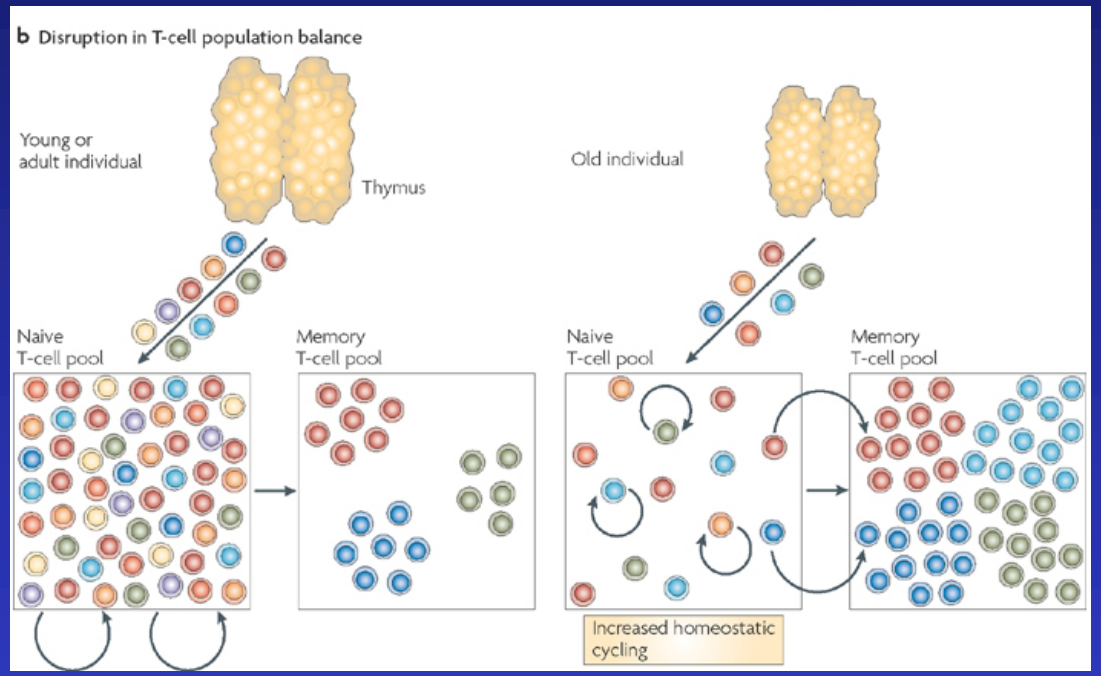
Alissa Eckert, Dan Higgins/CDC

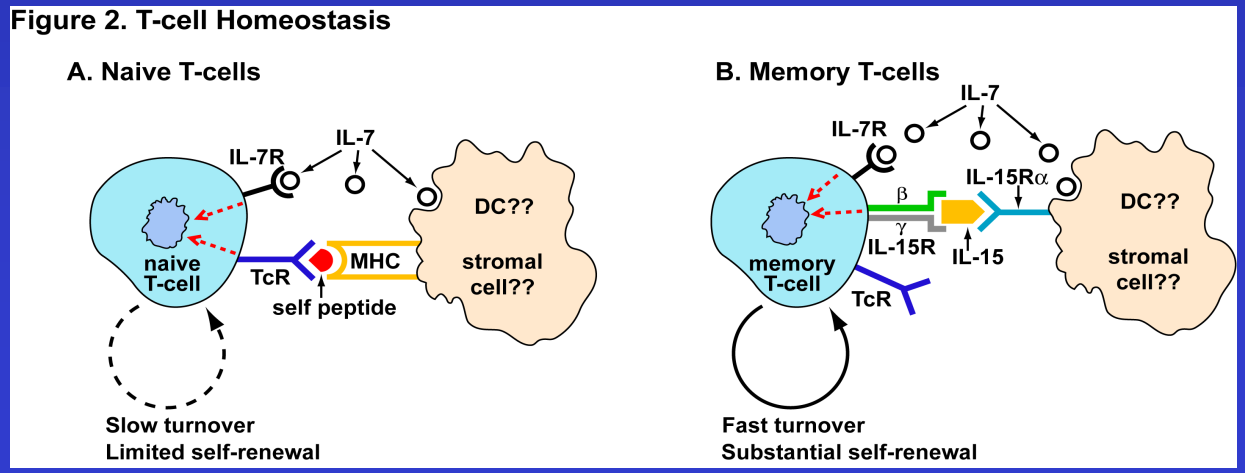
Pronounced vulnerability in older adults:

- **Ages 45-54 have 3x higher mortality than those 21-45;**
- **mortality goes up to 10-fold in those 55-64,**
- **Mortality culminates at 50-fold in those >65 years relative to adults 21-45 years old.**

Arizona Department of Health COVID Dashboard

T cell population maintenance with aging





New T cell production diminishes early (puberty). Peripheral maintenance takes over, but fails by the last third of life, with naïve T (Tn) cells reduced to 20-40% of youthful numbers in mice and men.....

NEW IMMUNE RESPONSES CRITICALLY DEPEND ON ACTIVATION OF NAÏVE T CELLS

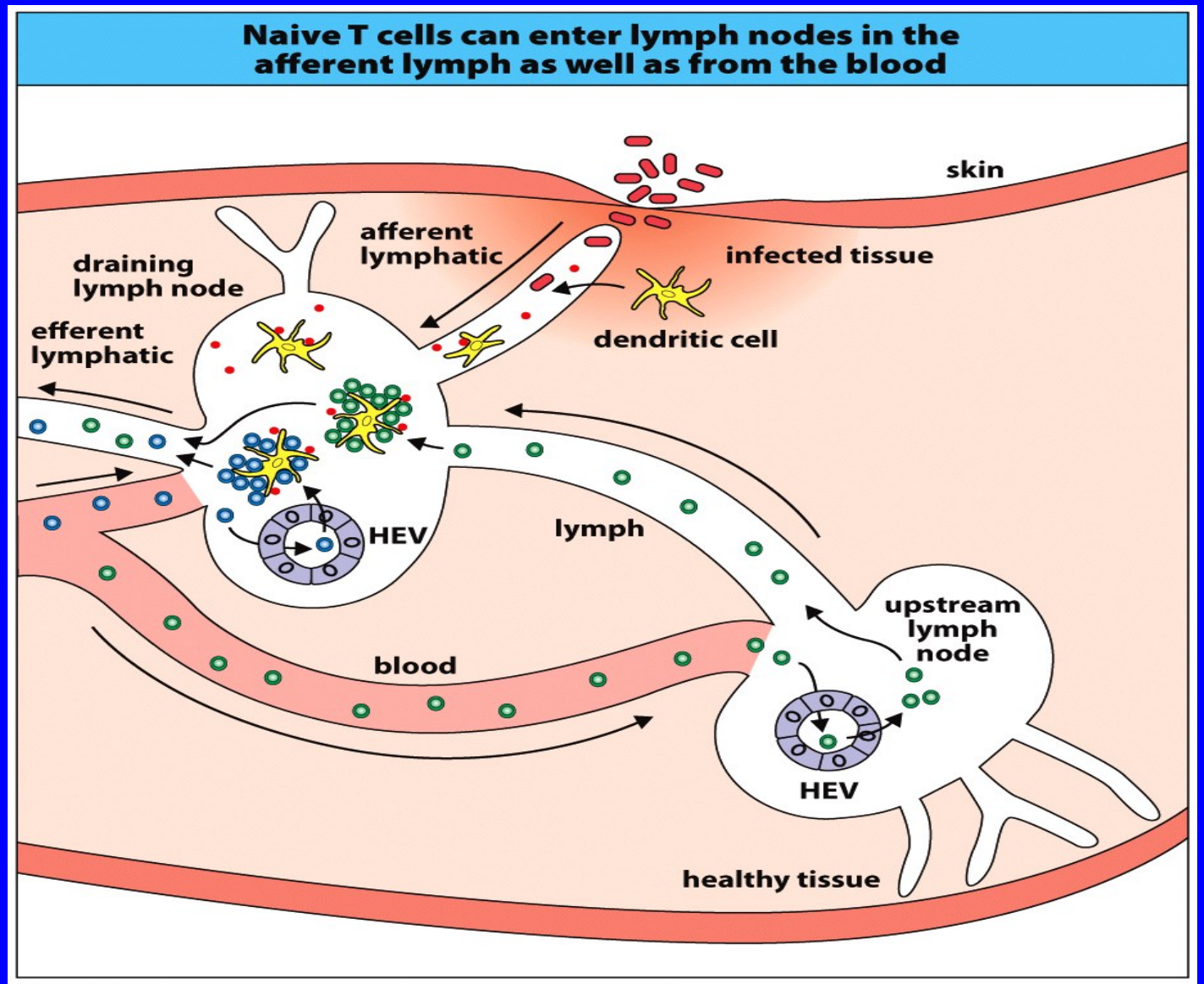
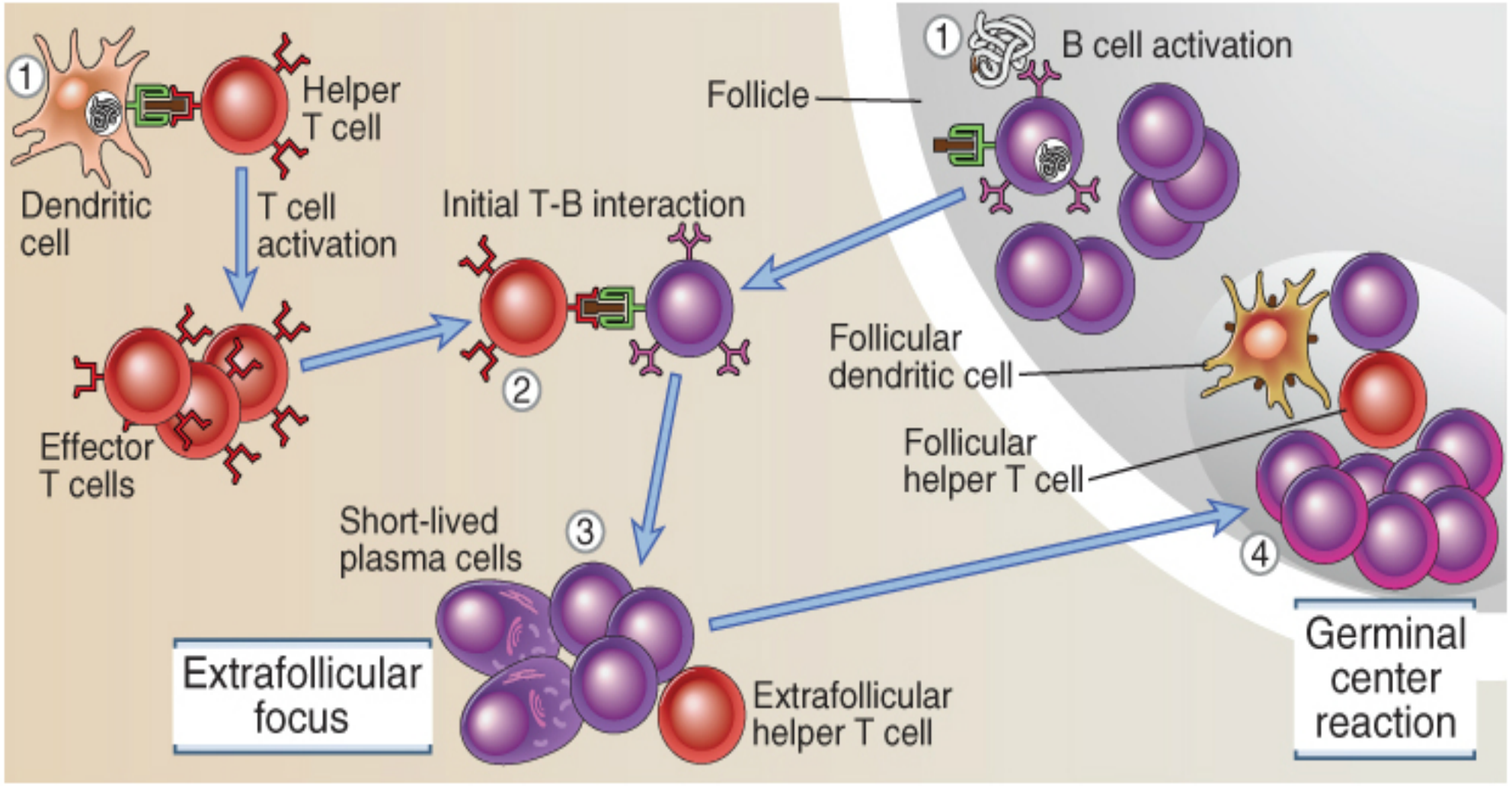


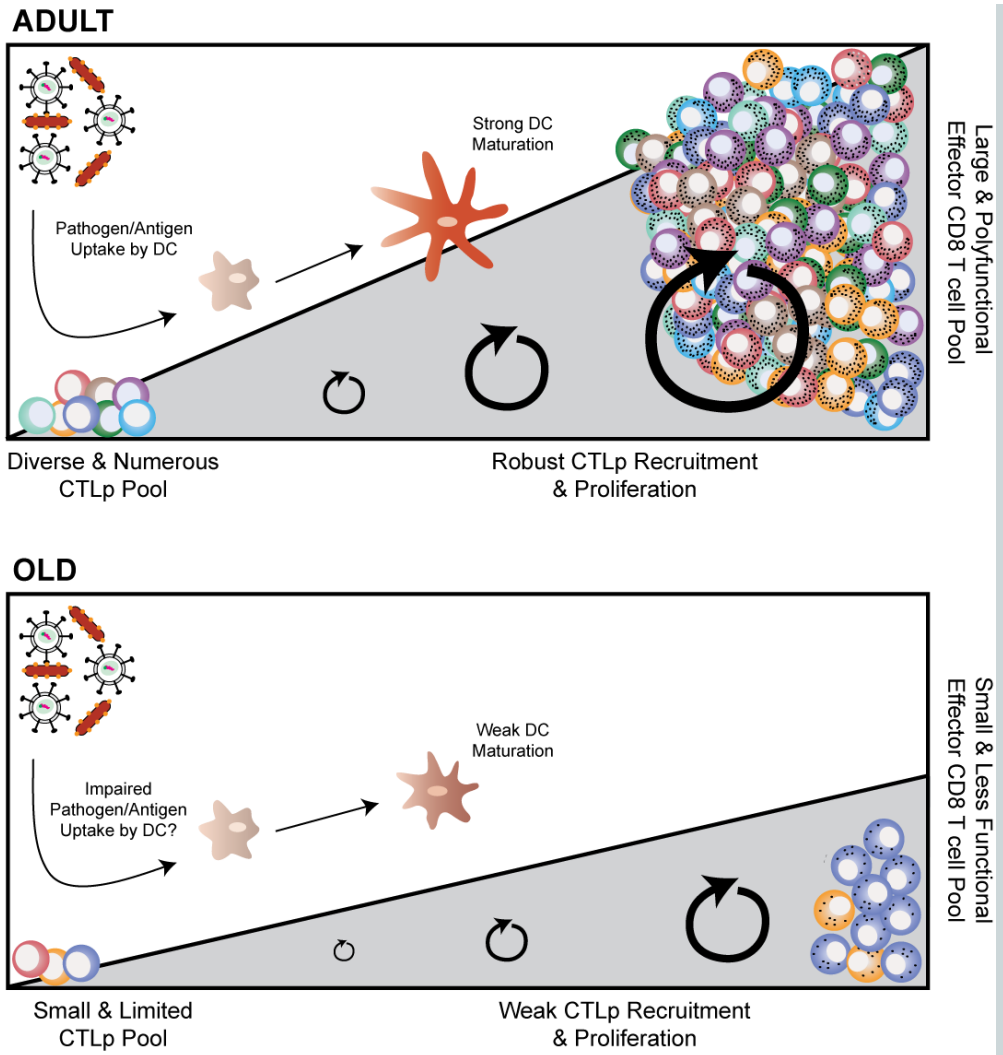
Figure 8.5 The Immune System, 3ed. (© Garland Science 2009)

- Upon infection, immature tissue DCs take up Ag from tissues, begin maturation and migrate into peripheral lymph nodes (LN).
- This is where they are scanned by thousands naïve T cells; the ones that can bind antigen on DC will get activated

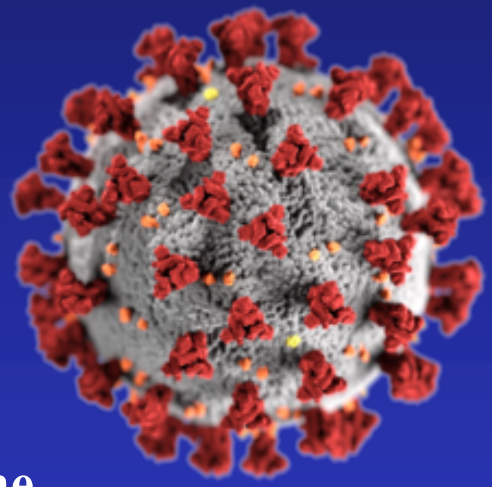
Mounting an immune response



CUMULATIVE PROBLEMS WITH AGING



SARS-CoV-2



Alissa Eckert, Dan Higgins/CDC

Late February/Early March 2020:

- **Can we detect immunity to this virus?**
- **What parts of the virus are targeted by the immune system (immunodominance, immune protection vs immune evasion)?**
- **What is the duration of immunity?**
- **Is there an immunological base to vulnerability to SARS-CoV2 (older adults primarily)?**

March 28, 2020—The Beginning of it All

HEALTH

UA researchers working on tests to detect COVID-19 antibodies in people without symptoms

Amanda Morris Arizona Republic

Published 6:00 a.m. MT Mar. 28, 2020 | **Updated 1:38 p.m. MT Apr. 1, 2020**

Because of limited resources and time, Nikolich said the UA's antibody testing will not be used to conduct widespread testing of the population to figure out who has and hasn't had the virus already. Instead, they will be coordinating with health care providers to select the best patients to test in order to have good data to analyze.

April 14, 2020—Wait, what?

Ducey says UofA will produce 250K tests for COVID-19 antibody

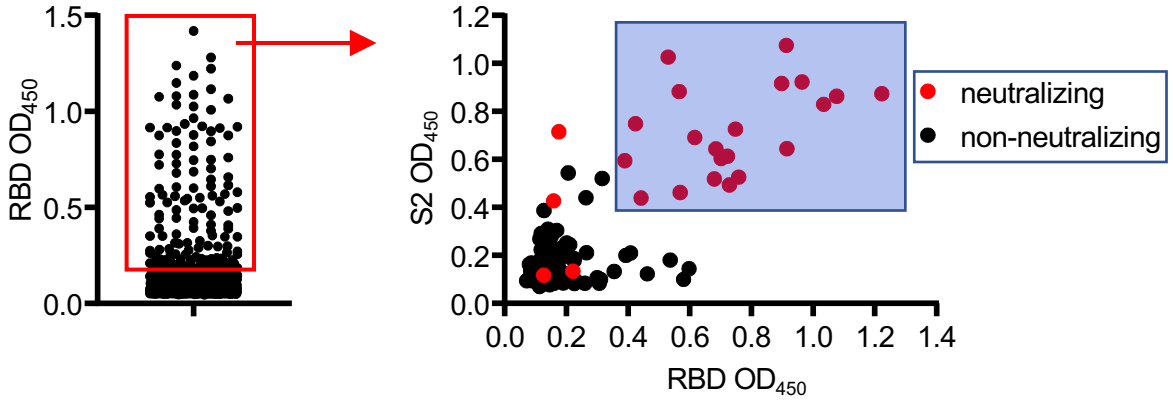
By **Jeremy Duda** - April 14, 2020

Last Updated: April 14, 2020 5:48 pm

Gov. Doug Ducey and Arizona Department of Health Services Director Dr. Cara Christ (right) give an update on the COVID-19 pandemic response during an April 14, 2020, press conference. Photo by Rob Schumacher/Arizona Republic | Pool photo

THE UNIVERSITY OF ARIZONA

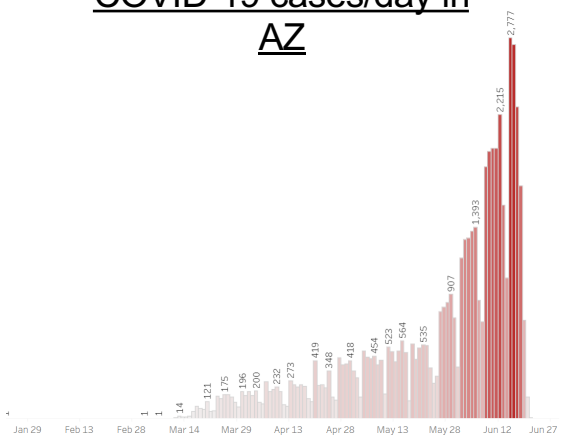
Highly accurate ELISA test for SARS CoV-2 exposure developed at University of Arizona



- Total Ig assay (A+G+M)
- False positives: <1/6000
- False negatives: ~5%
- FDA EUA filed 4/27/20; approved August, 2020
- PPV 100%, NPV 99%

- 20,102 healthcare workers, first responders, general public, and students tested by July 29, 2020
- Overall seroprevalence: 1.5%
- Student seroprevalence: 2.7%
- Seroprevalence May-mid-June ~1%; after mid-June >3%.

COVID-19 cases/day in AZ



HOME > POLITICS

Coronavirus herd immunity may be 'unachievable' after study suggests antibodies disappear after weeks in some people

Adam Payne Jul 7, 2020, 5:18 AM

Immunity to Covid-19 could be lost in months, UK study suggests

Exclusive: King's College London team found steep drops in patients' antibody levels three months after infection

Coronavirus – latest updates
See all our coronavirus coverage

Ian Sample *Science editor*

Sun 12 Jul 2020 12.31 EDT

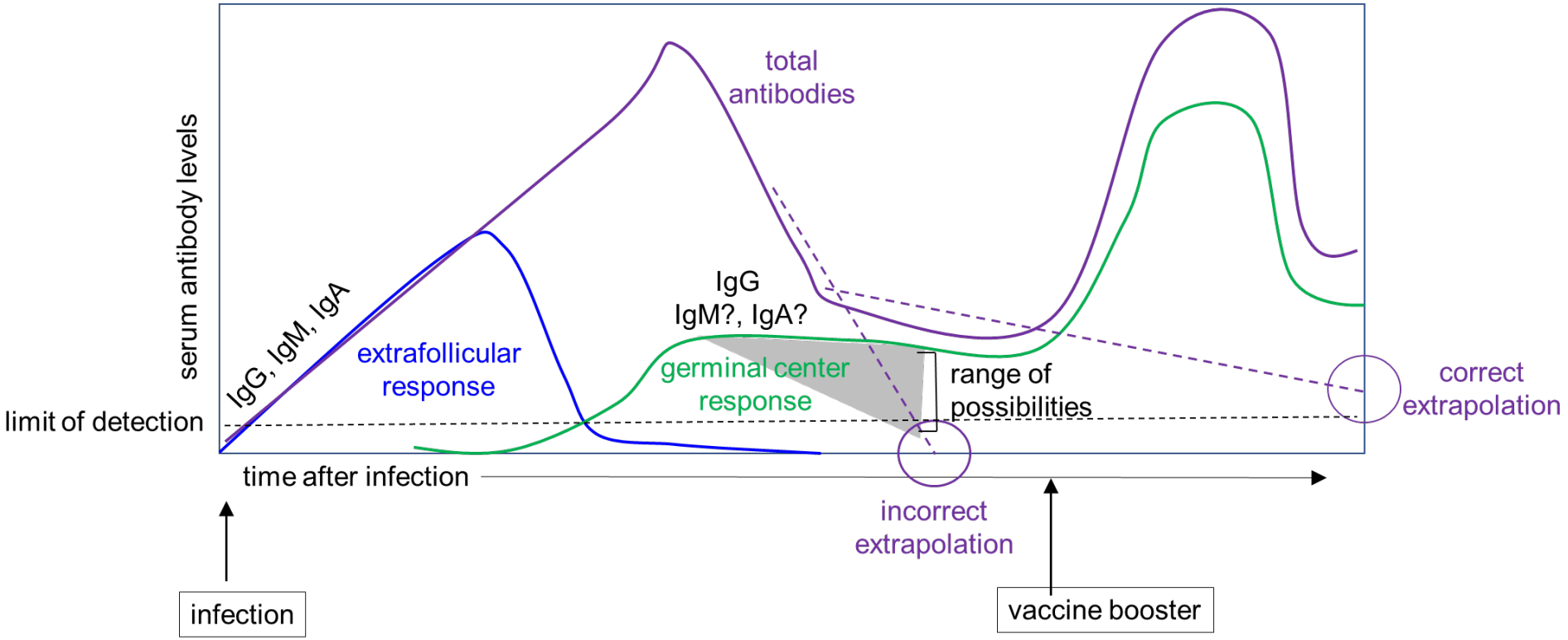
Duration of antibody production varies widely depending on the infection or vaccine

Table 2. Duration of Antigen-Specific Serum Antibody Production.*

Antigen	Protective Titer	Subjects Protected†	Antibody Half-Life‡			P Value
			Total Population	Men	Women	
	IU/ml	*no. (%)*	*year (95 percent confidence interval)§*			
Tetanus¶	0.01	42 (93)	11 (10–14)	12 (10–16)	10 (8–14)	0.23
Diphtheria¶	0.01	40 (89)	19 (14–33)	26 (17–51)	14 (8–42)	0.11
VZV	NA	NA	50 (30–153)	63 (28–∞)	41 (23–212)	0.51
Vaccinia	3.8	28 (62)	92 (46–∞)	99 (48–∞)	85 (31–∞)	0.91
Rubella	10.0	39 (87)	114 (48–∞)	85 (43–∞)	190 (35–∞)	0.60
EBV	NA	NA	11,552 (63–∞)	No decay (84–∞)	3648 (35–∞)	0.99
Mumps	NA	NA	542 (90–∞)	124 (53–∞)	No decay (89–∞)	0.16
Measles	0.2	41 (91)	3014 (104–∞)	369 (67–∞)	No decay (74–∞)	0.56

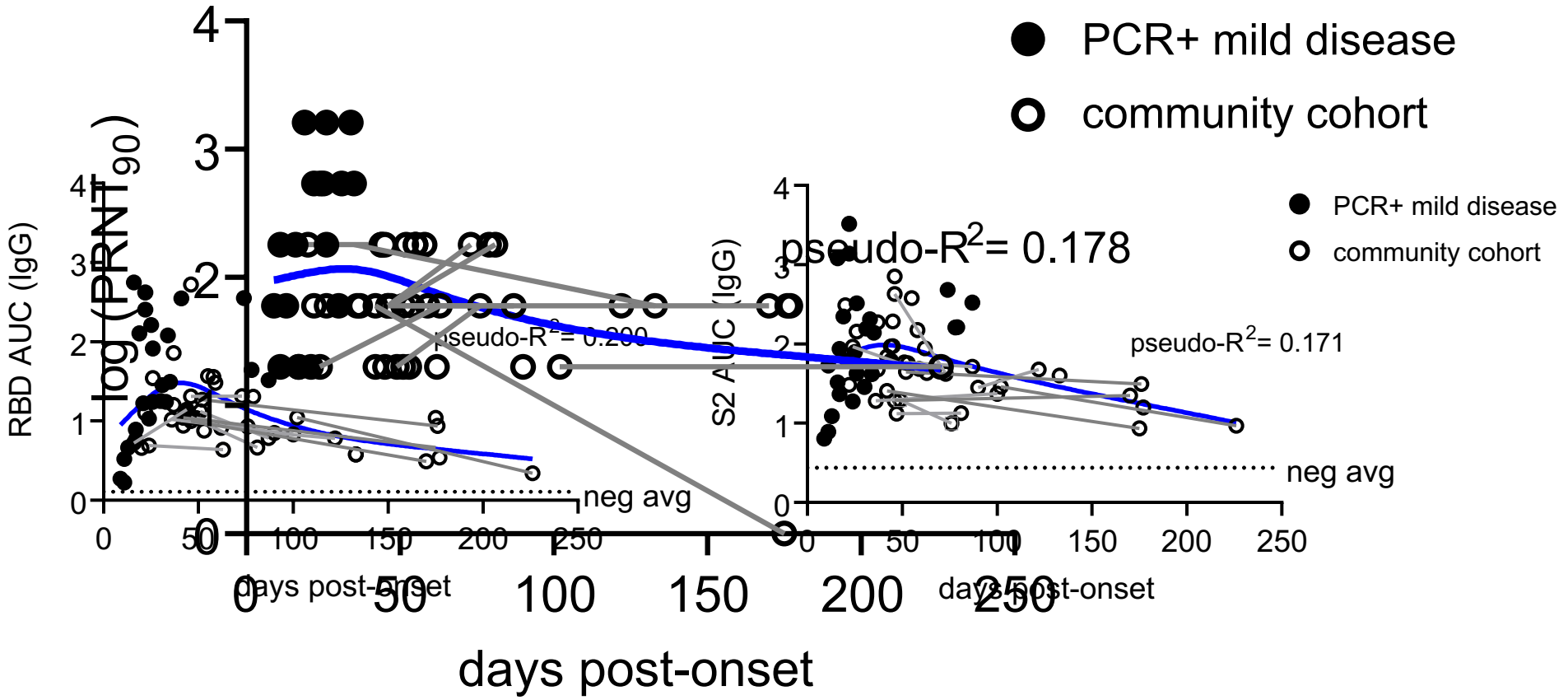
Ammana et al., NEJM, 2007

Antibody production decays in a non-linear pattern after acute infections



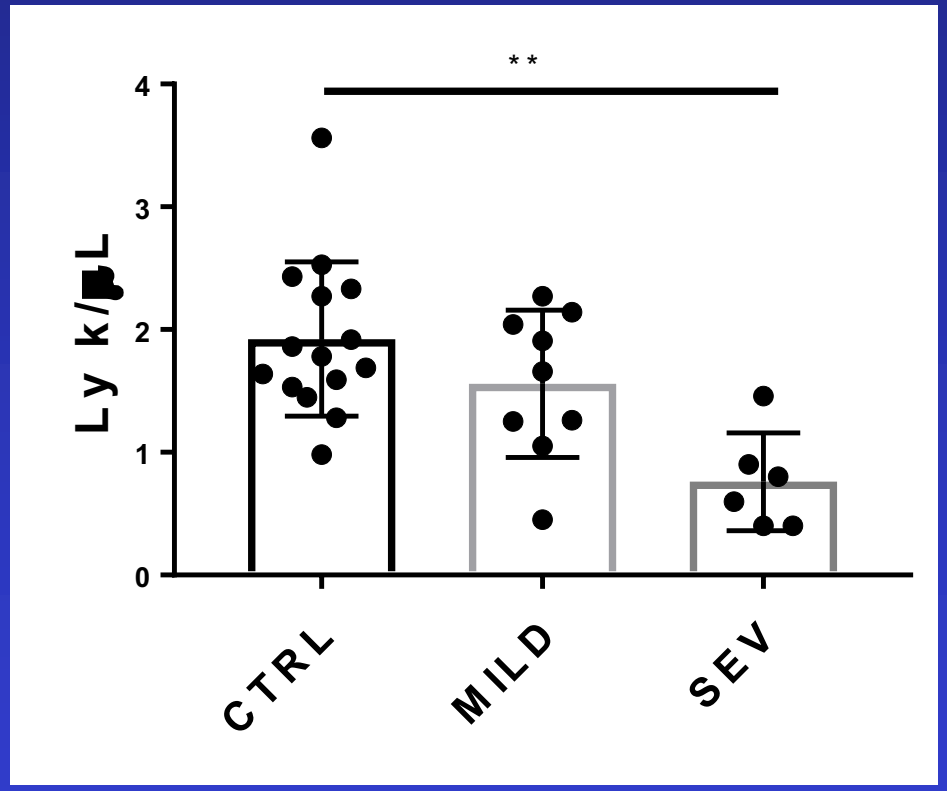
Baumgarth et al., JI, 2020

Stable α-Spike and neutralizing antibody titers over time following mild SARS-CoV-2 infections



Ripperger, Uhrlaub, Watanabe, Wong et al., Immunity, 2020

Confirmed lymphopenia in severeCOVID-19 cases



SQL and Hemavet combined data. Neutrophil counts mostly zero on our hemavet *

Preliminary conclusions

- Correlations between immunity and disease severity in the literature appear stronger than those with age, but studies well-controlled for age still rare
- Interpretation confounded by unknown viral loads (how much virus did you get initially and how well you are controlling it)
- Severe remodeling of immune cells in blood is found with severe diseases
- Signatures of innate and adaptive cell transcriptomes starting to provide initial clues
- Tons of things to do ……