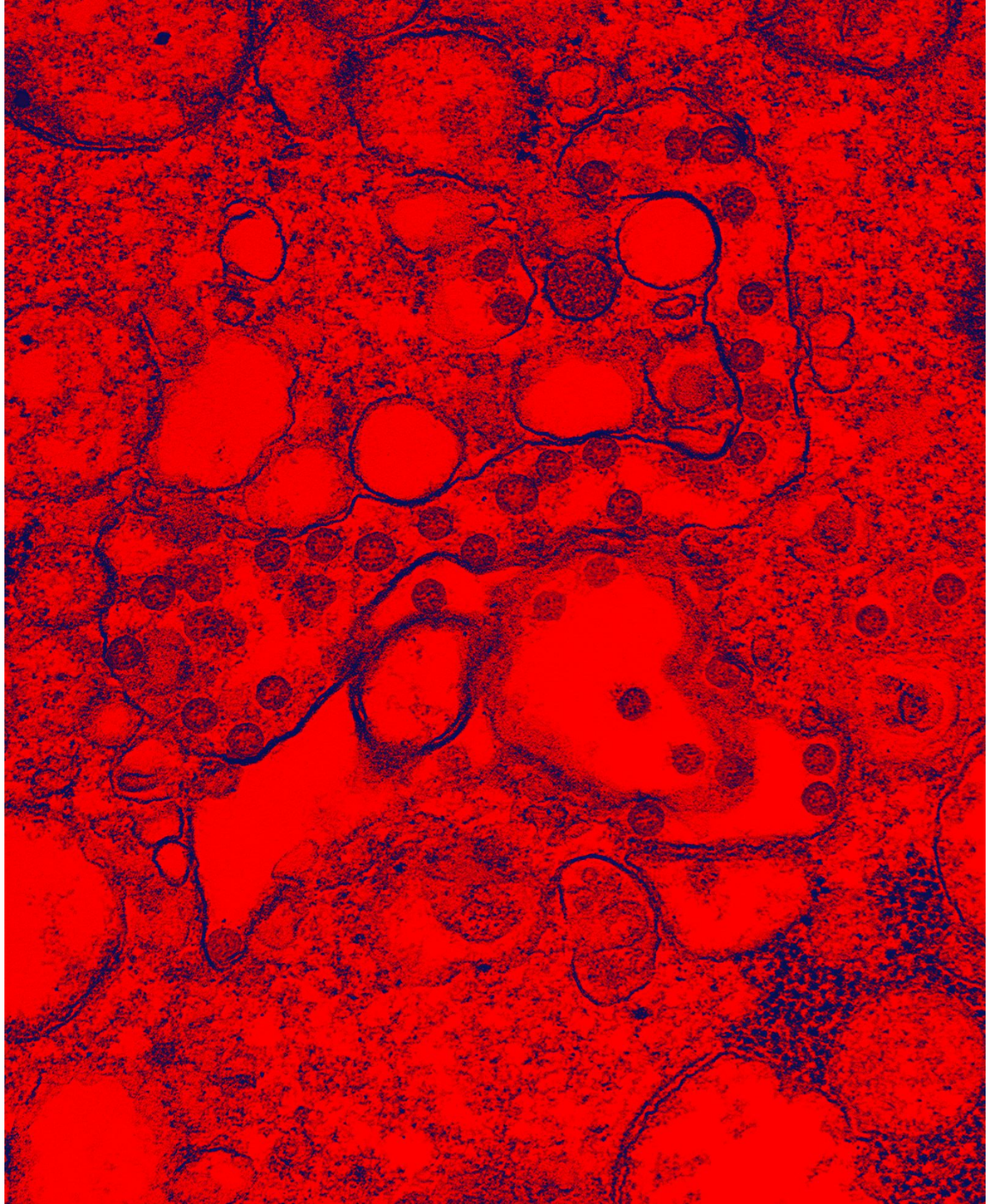

Varied Antibody Response to COVID-19: A Review

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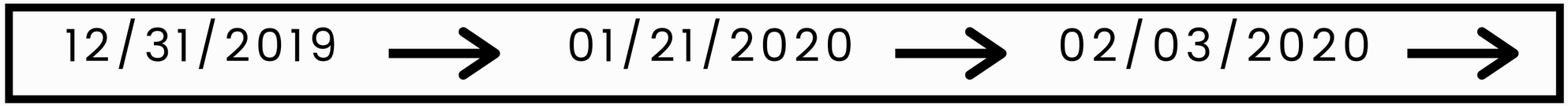
Our Agenda for Today

List of key concepts

- Background
- Grounds for Study
- Methods
- Results
- Conclusions
- Discussion and Future Study

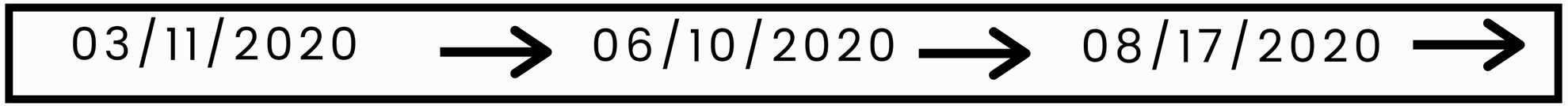
Timeline of COVID-19:



Case clusters first reported in China

First US case confirmed

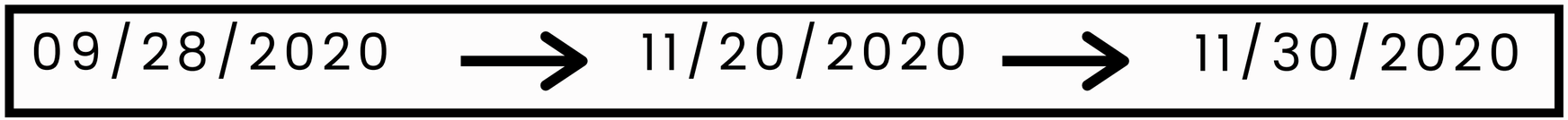
US declares Public Health Emergency



Pandemic declaration

2 million US cases

#3 leading COD in US



1 million deaths

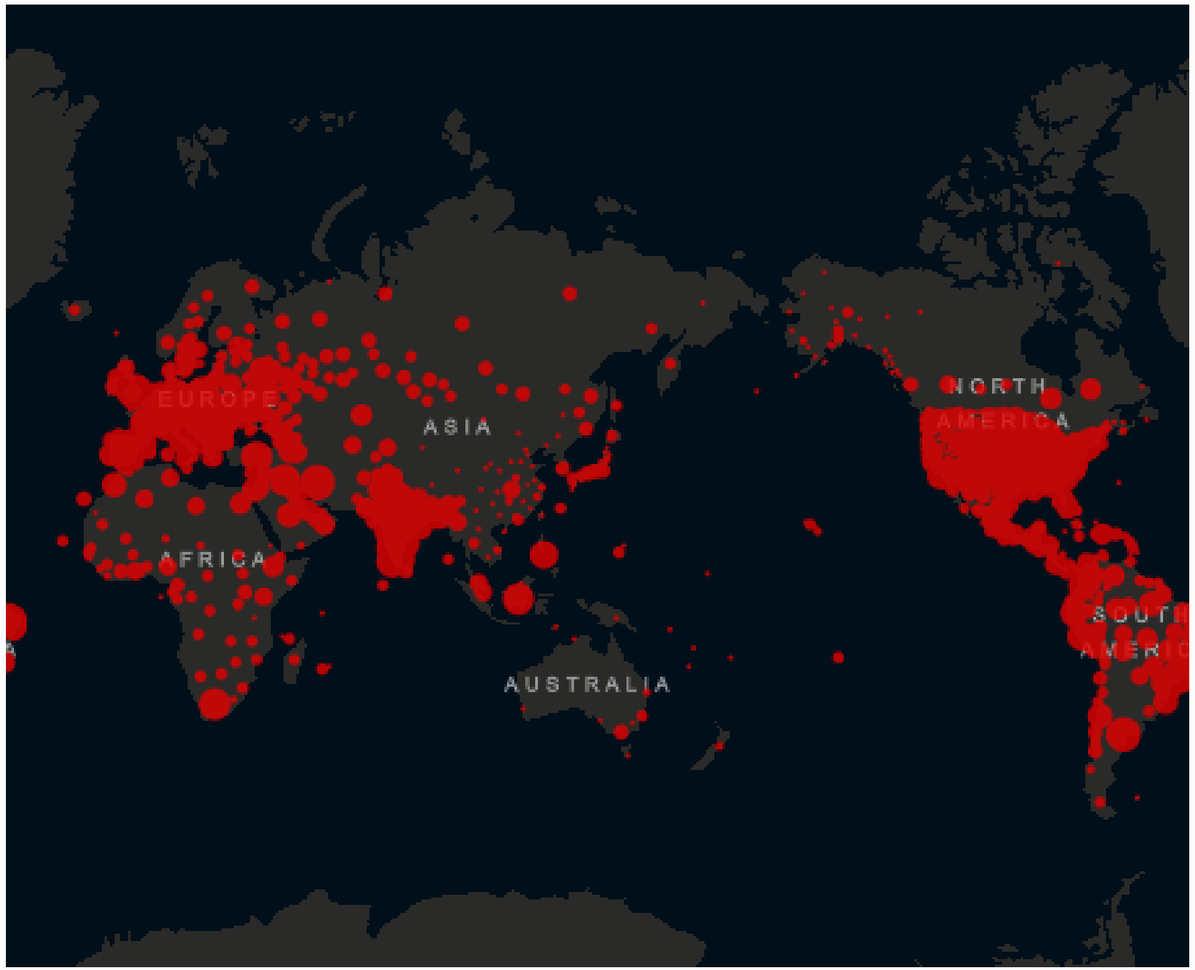
Pfizer submits for EUA

Moderna submits for EUA

(AJMC Staff, 2020)

Epidemiology of COVID-19:

As of December 8, 2020:

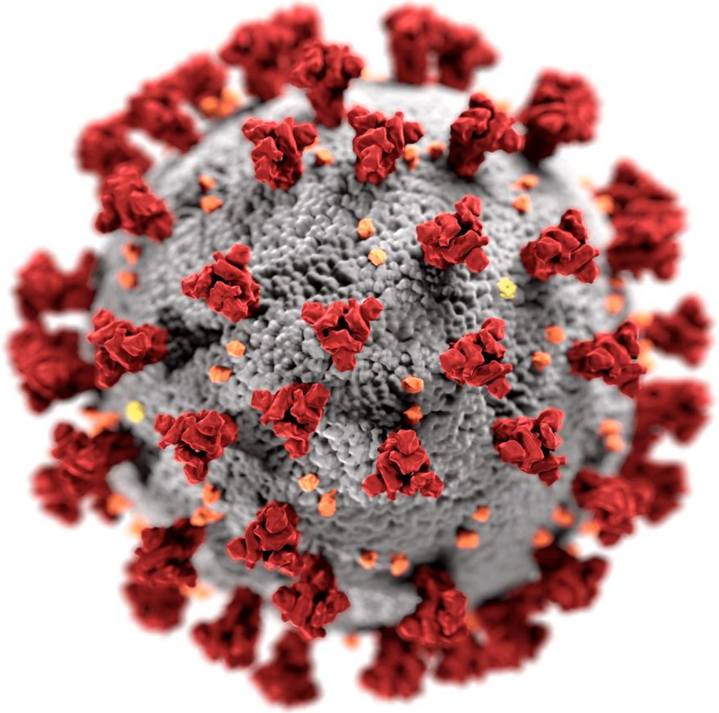


- 67,916,341 cases worldwide
  - 1. United States
  - 2. India
  - 3. Brazil
  - 4. Russia
  - 5. France
- 1,551,120 deaths worldwide
  - 1. United States
  - 2. Brazil
  - 3. India
  - 4. Mexico
  - 5. United Kingdom

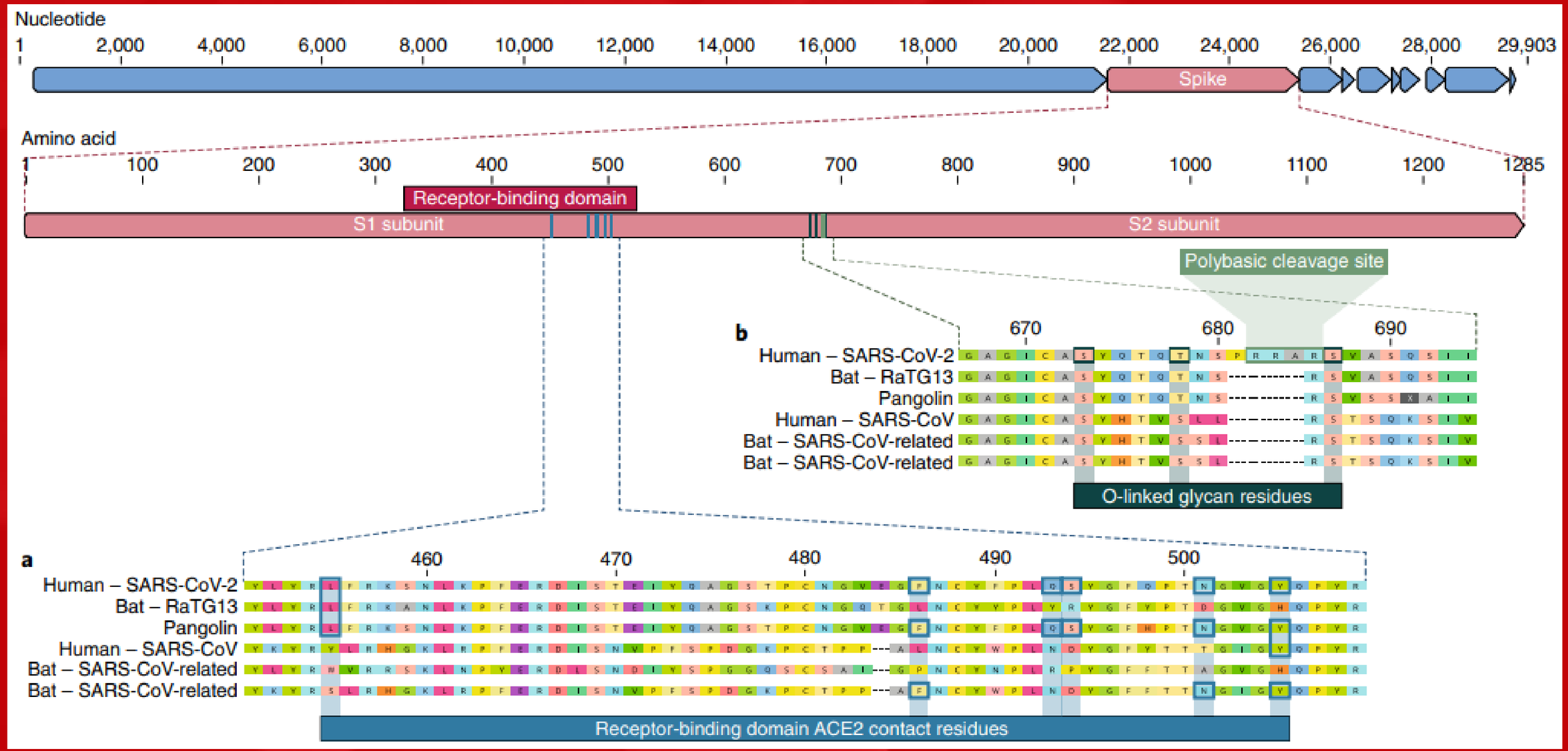
(Johns Hopkins University, 2020)

What Do We Know Now?

- Genetic similarities to past CoV
- Differential manifestations of illness
  - Unique shedding characteristics
  - Implications on immune response?
- Transmission
- Pathogenesis
  - S glycoprotein -> ACE2 receptor

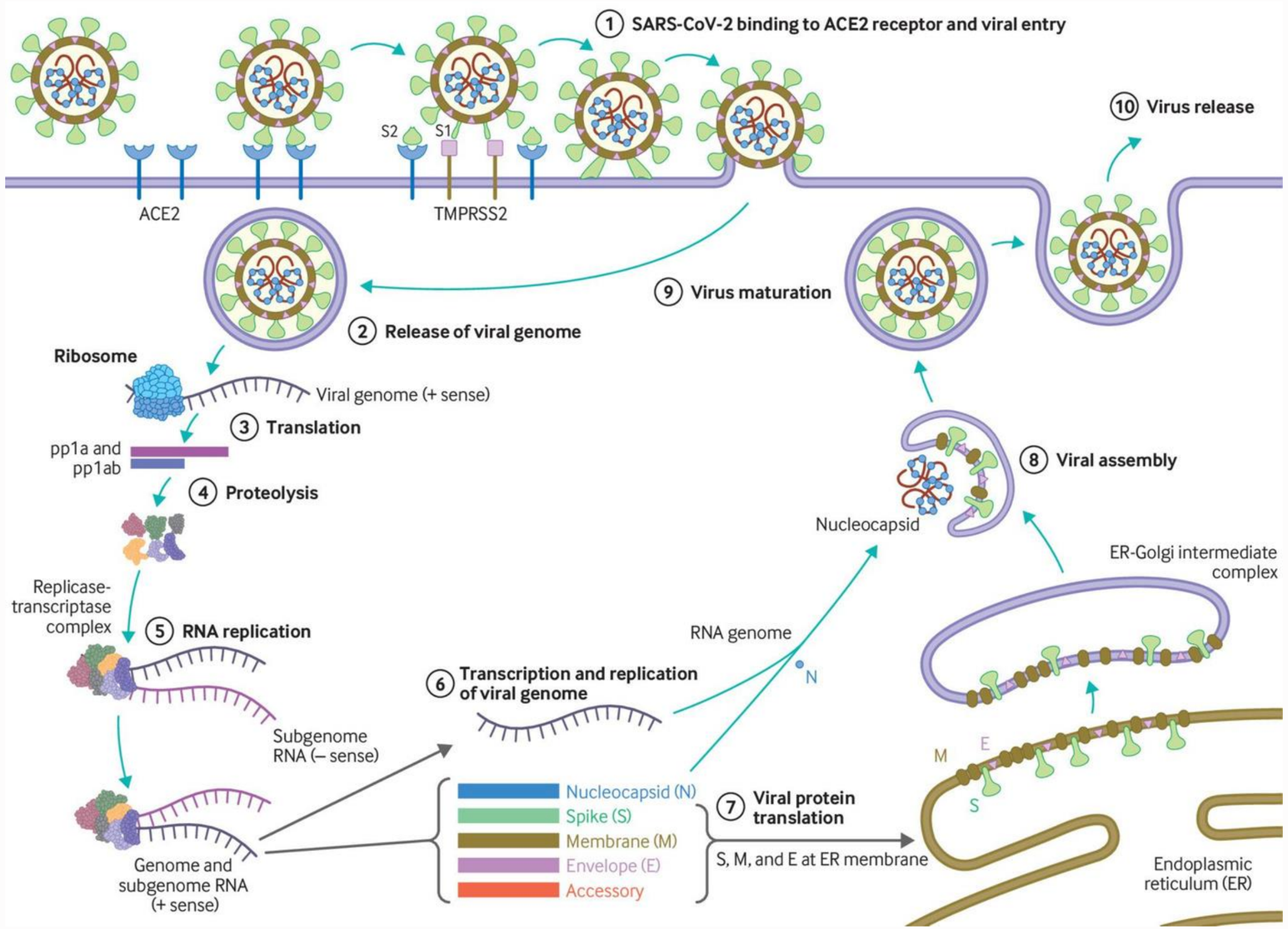


Genetic characteristics of SARS-CoV-2



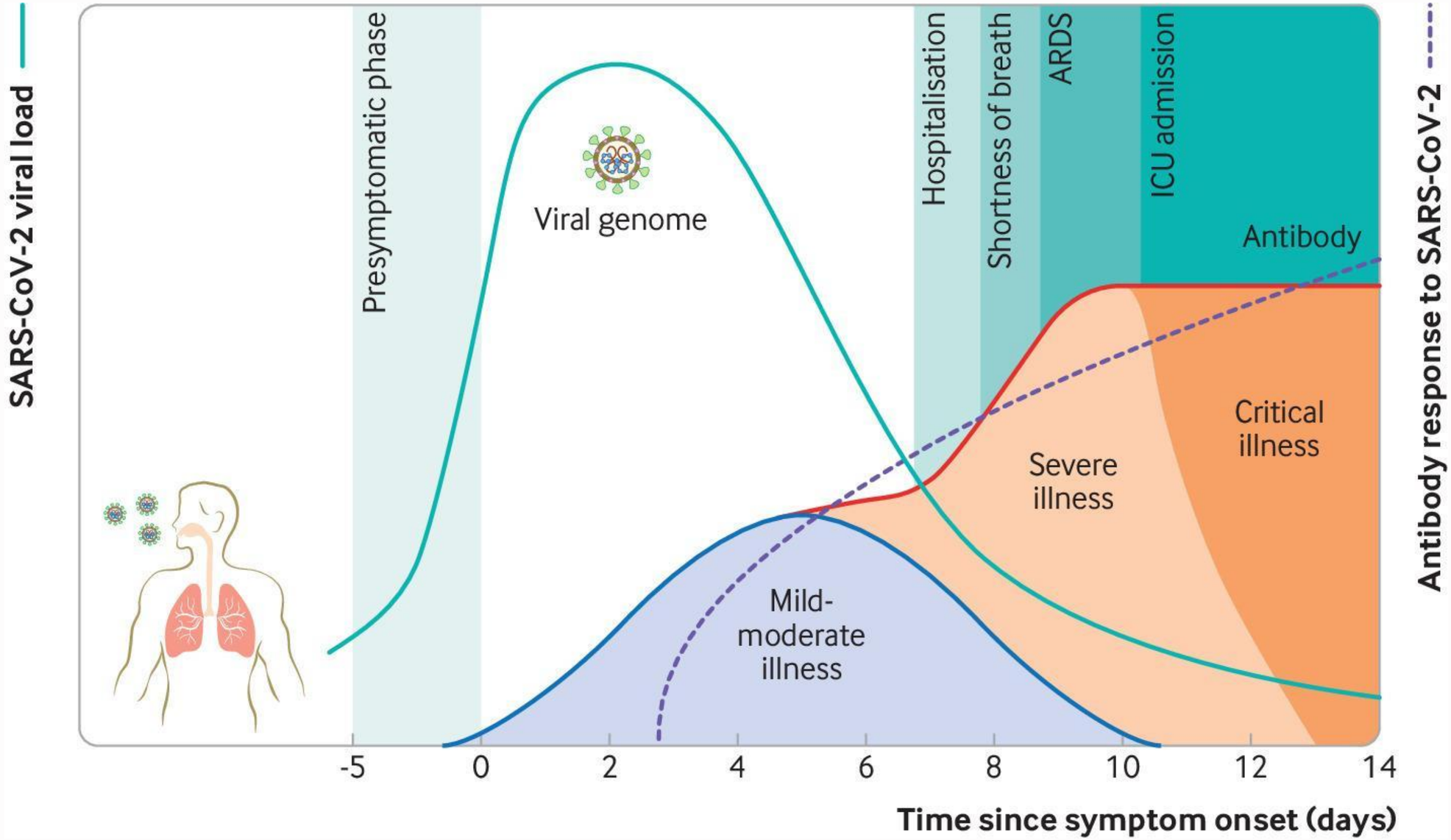
(Andersen et al., 2020)

Pathogenesis of SARS-CoV-2



(Cevik et al., 2020)

Pathogenesis of SARS-CoV-2



(Cevik et al., 2020)

Grounds for Review

- Little known on humoral response
- Observed variations
- Prognostic implications
- Immunity implications

METHODS

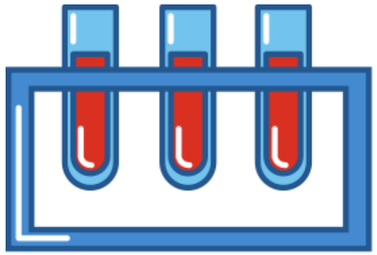
- Systematic search of PubMed
- Timeline: post-December 31, 2019
- Additional relevant references
- Pre-prints excluded

Findings

10 peer-reviewed studies were identified.

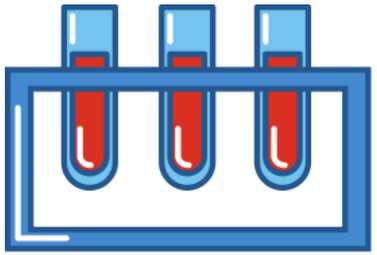
Author	Year	Title	N=
Yu et al.	May 2020	Distinct features of SARS-CoV-2-specific IgA response in COVID-19 patients	37
Zhao et al.	May 2020	Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019	173
Wang et al.	April 2020	Long-term coexistence of SARS-CoV-2 with antibody response in COVID-19 patients	26
Long et al.	June 2020	Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections	37
Lou et al.	May 2020	Serology characteristics of SARS-CoV-2 infection after exposure and post-symptom onset	80
Wang et al.	June 2020	Neutralizing Antibodies Responses to SARS-CoV-2 in COVID-19 Inpatients and	70
Ibarrondo et al.	September 2020	Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19	34
Long et al.	April 2020	Antibody responses to SARS-CoV-2 in patients with COVID-19	285
Suthar et al.	June 2020	Rapid Generation of Neutralizing Antibody Responses in COVID-19 Patients	44
Guo et al.	March 2020	Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19)	140

Topic 1: Seroconversion Time



Is it robust?

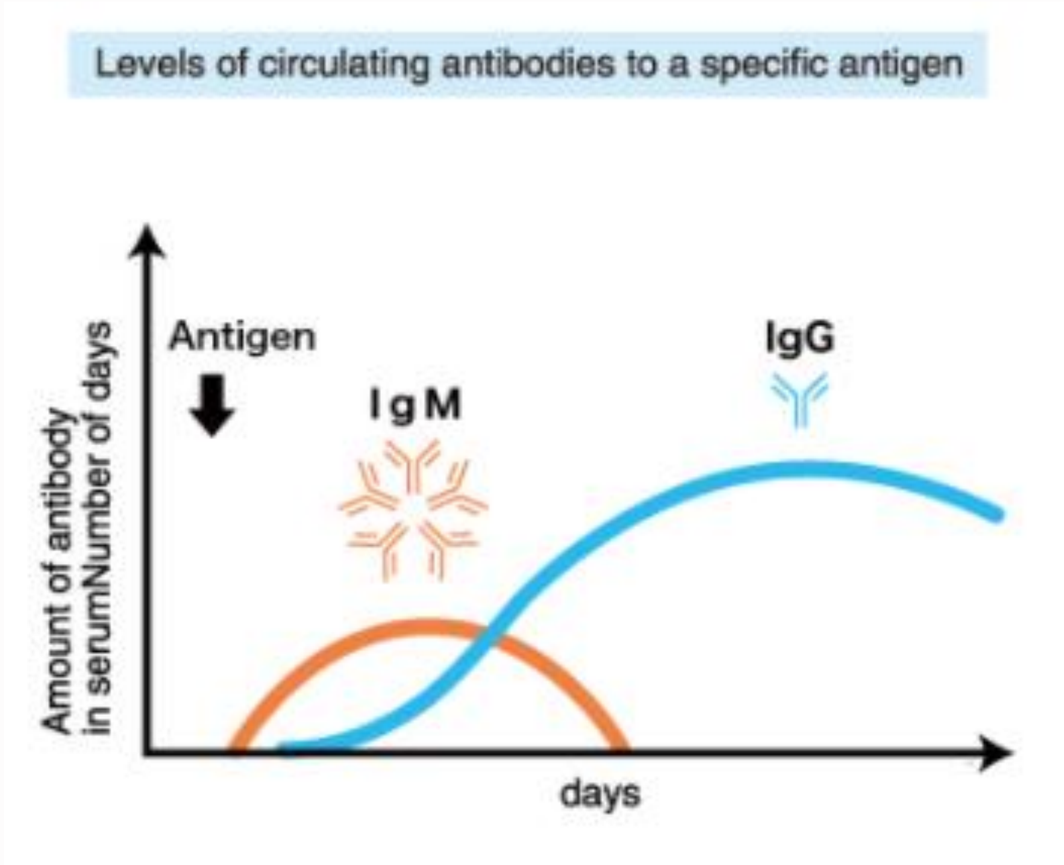
When does it happen?

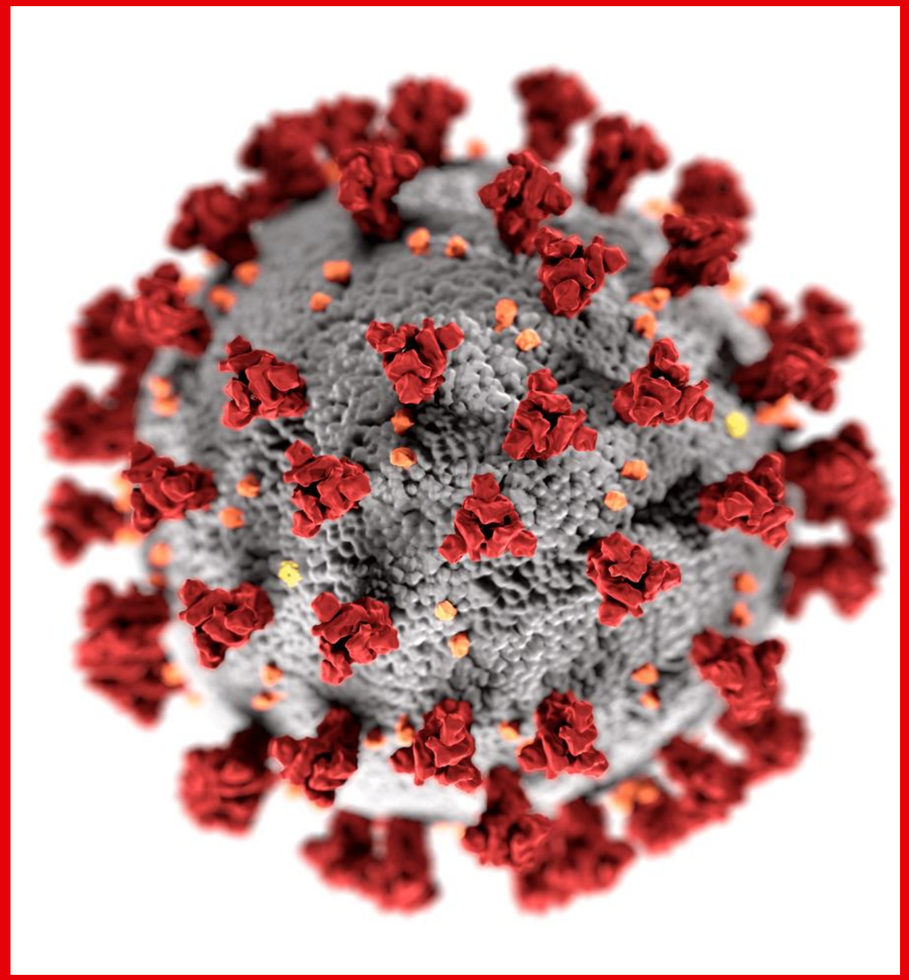


Differential by clinical manifestation?

Antibody Isotypes

- IgM: 1st response
- IgD: unknown
- IgG: most abundant, highest neutralization activities
- IgA: in mucosal tissues
- IgE: allergy response





- Early seroconversion of IgA
- Total antibody assays detected prior to specific estimates
- Peak 1-2 weeks post-onset
- 90% seroconversion seen within ~1 month
    - Greatest median time: IgG day 20

Interpret Cautiously...

- Antibody titers ≠ viral clearance
  - Detectable while convalescing OR
  - Achieve clearance prior to convalescent stage
- Implications re: innate immune response?

Topic 2: Clinical Presentation

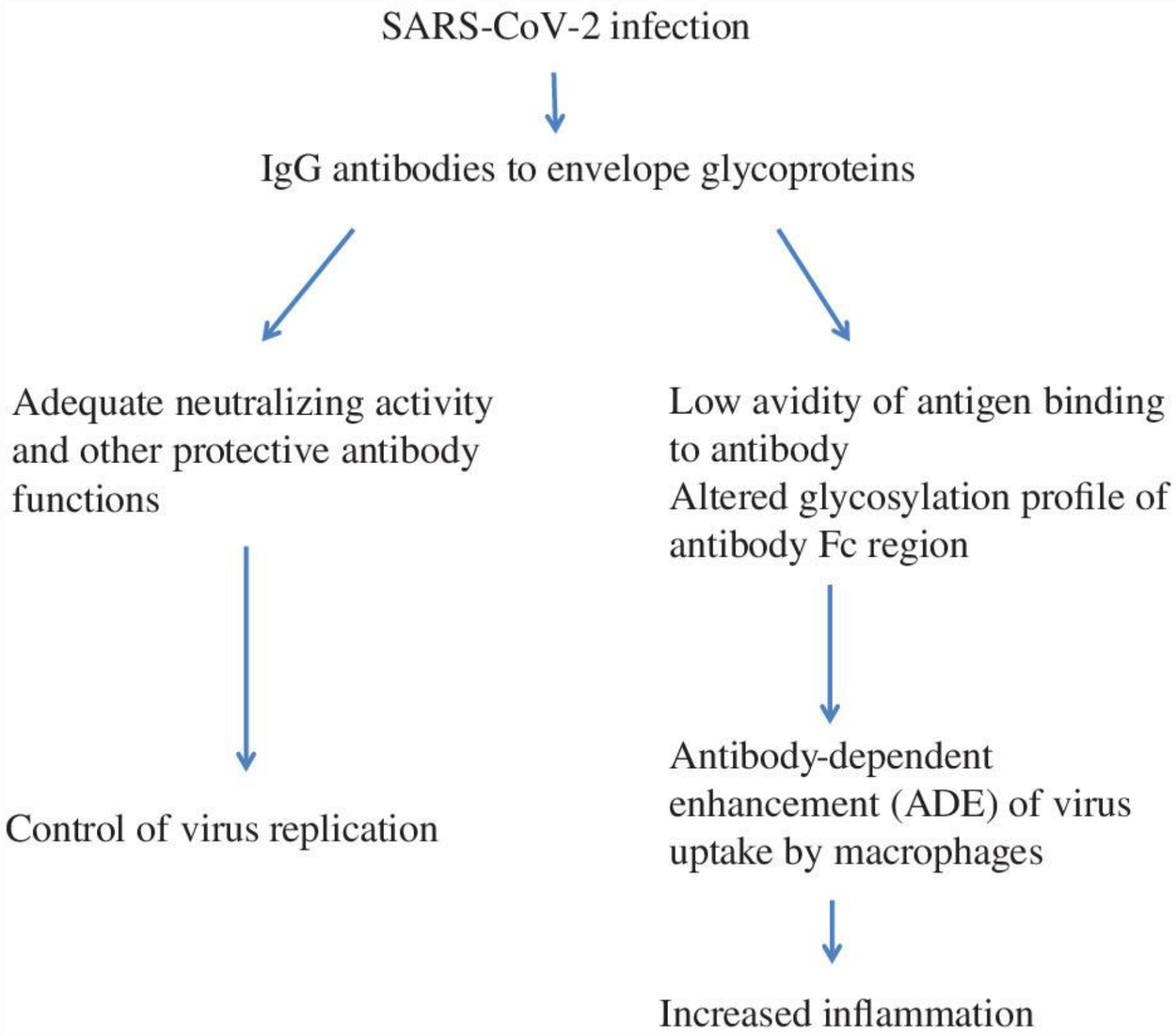
Can Ab response predict severity?

Which Ab may be responsible?

Mechanisms?

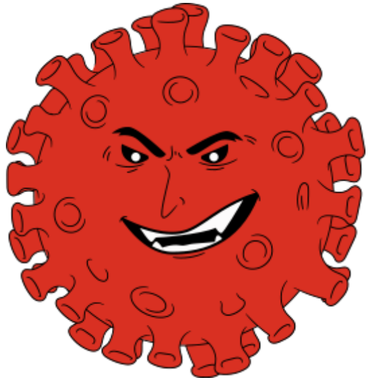
Dissecting the Differences

- Severe vs non-severe cases
  - Relative levels of total Ab, IgA, IgG ↑
  - 2 weeks post-onset
- Why?
  - Hypothesis: IgA and ADE



(French & Moodley, 2020)

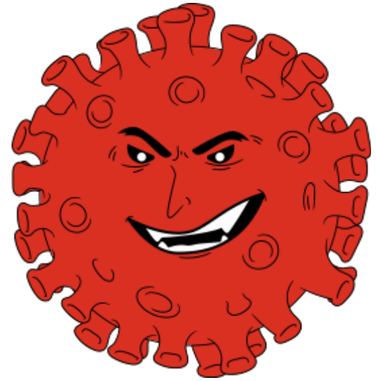
Topic 3: Lasting Immunity



Does IgM/IgG = neutralizing response?

Length of immunity?

Differentials by clinical presentation?



Evidence on Lasting Immunity

Neutralizing response

Correlation with IgG titers

→

Length of Immunity

~ 3 months

< SARS/MERS

→

By Clinical Severity

Faster Ab deterioration in asymptomatic

Topic 4: Diagnostic Relevance

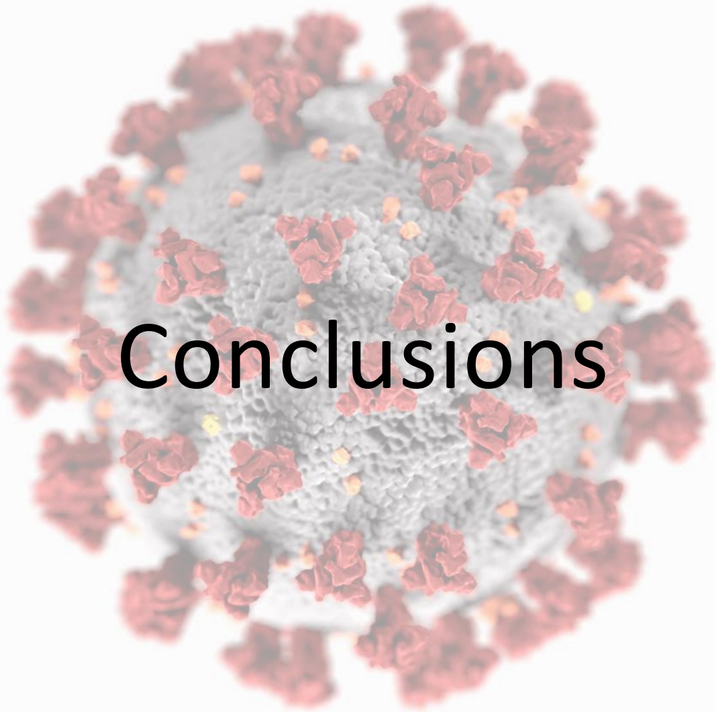
Shortfalls of RNA testing?

Capitalizing on timeline…

Implications on isolation protocol?

Issues + Proposed Modifications

- Viral load undetectable via NAT
- Time trade-off of qPCR to ELISA
- Ab results and de-isolation timeline
- RNA testing complemented by Ab assays



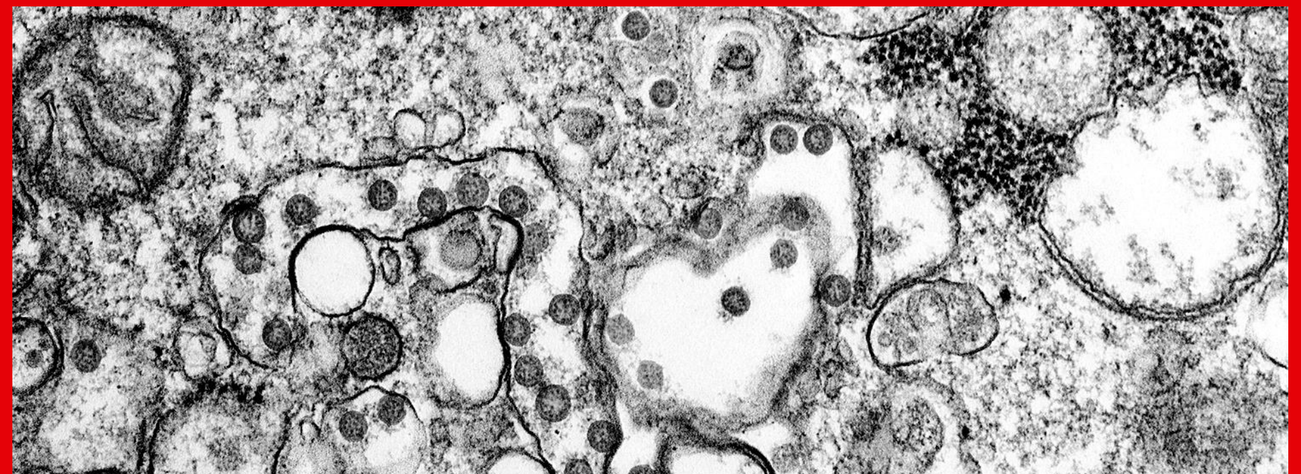
Conclusions

- **Immune response**
  Relatively typical
- **Pathogenesis**
  IgA + the inflammatory response role
- **Prognostic potential**
  Analysis of Ab titers as indicator of severity
- **Moving forward**
  Antibody assays as crucial supplementary element

Discussion + Future Study

- More work on neutralizing response needed
- More work on IgA mediation
- Expanded testing protocol = more data = better understanding
- Far from over
    - Mitigate excess damage

Questions?



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