COVID ANTIBODIES AND IMMUNITY

Name: Jenny Beck-Esmay, MD and Mizuho Morison, DO
Academic/Community Title: Assistant Residency Director, Mount Sinai Morningside-West
Email: jbeckesmay@gmail.com

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Summary: Dr. Mizuho Morrison & Dr.Jenny Beck Esmay both having had covid themselves, briefly discuss the clinical course and what presence of IgM vs. IgG signifies. They discuss what we currently know about antibody testing (national availability, reliability, sensitivity) as well as convalescent plasma transfusion (CPT) and criteria for donation vs. recipient.

Tags:
Immunology, Infectious disease ID

SHOW NOTES:

MIZ: Welcome to the free open access COVID website created by HIPPO education! Im Dr.Mizuho Morrison an an Emeregency physician and here with me today is Dr.Jenny Beck

Esmay a fellow EM physician joining us from NYC. It is May 11th 2020 and today we are going to dive into the topic of COVID ANTIBODIES and what does this mean in terms of immunity.

Let first talk about the difference between IgM and IgG and which one shows up first...
When infected by a virus like SARS-CoV-2, the cause of COVID-19, the body initially produces antibodies known as IgM (immunoglobulin-M), in an attempt to neutralize the virus. Later, as the body's adaptive immune system revs up, IgM levels go down and the body ramps up production of IgG, which more specifically targets the viral invader.

- Describe the current state of Antibody testing
    - National availability, reliability/sensitivity, etc
    - There are a multitude of different antibody tests for COVID-19 with variable performance. Tests vary in the viral antigen(s) they target, e.g., nucleoprotein (N protein) or spike protein (S protein). It is not yet clear which antibody responses, if any, are protective or sustained. (IDSA)
    - A "positive" test is exceptionally difficult to interpret because the performance of these tests is not well known. For some assays both sensitivity and specificity may be poor, or at the very least undefined. (IDSA)
    - Some FDA-authorized COVID-19 antibody tests are estimated to have 96-98% specificity, which would mean that a positive test result is more likely a false-positive result than a true positive result if the prevalence or pretest probability is 5% or less. (IDSA)
        - (Sinai test states - Our antibody test is very accurate, with a sensitivity of 94% and a specificity o f> 99%.)
    - The majority of samples >20 days post-symptom onset had detectable anti-SARS-CoV-2 antibodies, suggesting good to excellent sensitivity for all evaluated tests in hospitalized patients three or more weeks into their disease course. (covid testing project)
- As of mid May what do we believe to be true in terms of presence of IgG conferring immunity
    - While extrapolation from other coronavirus infections allows us to be optimistic that detection of an IgG response will likely confer at least some protection to most people, we have no direct evidence of this for SARS-CoV-2. (IDSA)
    - There is no data at the moment on whether some anti-SARS-CoV-2 IgG may confer immunity. It is important to differentiate antibody binding activity (what most of the current test is based on) from virus neutralizing activity.
    - What else is needed to confer this? Or prove presence of IgG = immunity
    - Understanding which antibodies (if any) are protective is required for vaccine development. There are many different SARS CoV-2 IgG antibodies that may be produced, and each may have a different role. This should also be a consideration in assessing the clinical utility of tests designed to target specific antibodies. (IDSA)

  - Determine limits of protective immunity (e.g., antibody amount, duration, and efficacy) and correlations with disease severity. (IDSA)
  - Address concerns about potentiation of cytokine release syndrome (CRS) by a vaccine or hyperimmune plasma administration: Patients with COVID-19 infection can develop CRS about day 7-10 of illness, which often leads to death. There is some concern that a vaccine against the "wrong" antigens or infusion of hyperimmune plasma from COVID-19 survivors could worsen the inflammatory immune response in patients with COVID-19 infection. This immune enhancement is seen for some flaviviruses such as dengue. (IDSA)
- Of course our biggest fear is repeat infection...what are the latest thoughts on this?
- Describe convalescent plasma transfusion (CPT) and criteria for donation vs. recipient
  - Passive immunization therapy has been successfully used to treat infectious diseases back to the 1890s.
  - Convalescent plasma containing neutralizing antibodies from recovered individuals can be administered in individuals with clinical disease to reduce symptoms and mortality.

Brief Literature Review - Hx of CPT

- A meta-analysis of studies performed during the 1918 ("Spanish") influenza pandemic found a possible decrease risk of death in patients with influenza pneumonia who received influenza-convalescent human blood products; however, studies were few and had many methodological limitations. (Luke)
- Past studies of convalescent serum therapy for pneumococcal pneumonia demonstrated that treatment was most effective if begun within 3 days of onset, and mortality could be reduced to 5% by administration of serum within the first 24 hours of the onset of symptoms, while administration of serum 4 to 5 days after symptoms began produced little clinical benefit. (Casadevall)
- A meta-analysis of 32 studies examining the use of convalescent plasma for 2003 SARS coronavirus infection or severe influenza revealed consistent evidence for a reduction in mortality, especially when convalescent plasma is administered early after symptom onset. Post hoc meta-analysis showed a statistically significant reduction in the pooled odds of mortality following treatment, compared with placebo or no therapy (odds ratio, 0.25; 95% CI, 0.14-0.45), with the caveat that studies were commonly of low or very low quality, lacked control groups, and/or had moderate or high risk of bias. (Jenkins)

- Treatment of severe H1N1 infection with hyperimmune immunoglobulin within 5 days of symptom onset was associated with a lower viral load and decreased mortality in a randomized controlled trial. (Hung)

So CPT has clearly been around a long time, but what do we know about CPT and COVID

Systematic Review of 5 Studies:

- 5 studies reporting CPT to COVID-19 patients. The main findings from available data are as follows: (1) Convalescent plasma may reduce mortality in critically ill patients (2) Increase in neutralizing antibody titers and disappearance of SARS-CoV-2 RNA was observed in almost all the patients after CPT therapy (3) Beneficial effect on clinical symptoms after administration of convalescent plasma. (Rajendran)

- Donor and Recipient Criteria likely vary by institution, but in general
  - **Donor criteria, go to American Red cross**

Donor Qualifications:

- **Evidence of COVID-19 infection**
- **Diagnostic test (Nasopharyngeal swab) at time of illness**

OR

- **Positive serological test for COVID-19 antibodies after recovery, if prior testing was not performed. The American Red Cross is now performing antibody testing on collections from donors who received a diagnosis of presumptive positive but never received a positive confirmatory test.**

List of approved testing can be found here.

AND

- **Resolution of COVID-19 symptoms (return to base-line health status).**
- **14 - 27 days with negative COVID-19 test results**

OR

- **28+ days: no further testing required**

AND

- **Defined COVID-19 neutralizing antibody titer (e.g. > 1:80)**

- **If neutralizing antibody titers cannot be obtained in advance, obtain a sample of the plasma and store for a later test date**
- **Donor must meet all routine allogeneic apheresis donor criteria per DHQ**
- **TRALI Mitigation: Males, females who are negative for anti-HLA antibodies (ARC performs this test)**
- **Aspirin restrictions apply if donor is undergoing a platelet/plasma-type collection (Determined at time of collection)**
- **Allowable collection every 28 days**

- **Recipient Criteria - EAP Per-Protocol Inclusion Criteria: (these are the criteria at Sinai)**
  - 18 years of age or older
  - Laboratory confirmed COVID-19 by SARS-CoV-2 RT-PCR
  - Hospitalized in an acute care facility for complications of COVID-19 disease
  - Severe or life-threatening COVID-19, or judged by the treating provider to be at high risk of progression to severe or life-threatening disease:
    - Severe disease is defined as:
      - dyspnea
      - respiratory frequency ≥ 30/min
      - blood oxygen saturation ≤ 93%
      - partial pressure of arterial oxygen to fraction of inspired oxygen (P/F) ratio < 300
      - lung infiltrates > 50% within 24 to 48 hours
      - life-threatening disease is defined as:
      - respiratory failure,
      - septic shock, and/or
      - multiple organ dysfunction or failure.

- Personal clinical insights into CPT
  - In talking with upstairs doctors from my institution, totally anecdotally, they are seeing tremendous response, drastic improvements in patients receiving the plasma transfusions.
  - JAMA article from March - case series of 5 critically ill patients with confirmed SARS-CoV-2 infection who were treated with 2 transfusions of ABO-compatible convalescent plasma.Viral load of the patients who received plasma transfusion improved 1 day after transfusion, and all 5 patients had undetectable viral loads after 12 days. Three of the five patients were discharged home. However, the

small cohort size and the absence of a control group limit the conclusions that can be drawn from this cohort. (Shen)

Miz OUTRO: thanks for listening to this FREE FOAM COVID podcast, ...we hope you will peruse through our other audio podcasts on this site, pertaining to everything covid, mini series in case you get called into the ED as well as video lectures and infographics that are useful. Go to https://covid.hippoed.com/ to check out those resources we've made JUST for you!

CME question:
COVID Antibody CME Question:
True or False: A positive antibody test (as of May 2020) indicates definitive immunity to SARS-CoV-2.
Answer: False

References:

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Additional references:

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- https://www.mountsinai.org/about/newsroom/2020/mount-sinais-blood-test-to-detect-antibodies-to-covid19-receives-emergency-use-authorization-from-us-food-and-drug-administration-pr