SARS CoV-2 immunity from a clinical perspective

Corine Geurts van Kessel, MD PhD
Clinical virologist, Erasmus MC Rotterdam
c.geurtsvankessel@erasmusmc.nl
The use of SARS CoV-2 serology in clinical practice
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1. How good is SARS CoV-2 serology?

2. Use of IgG binding as correlate of protection in HC?
The use of SARS CoV-2 serology in clinical practice

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2. Use of IgG binding as correlate of protection?
Validation of SARS CoV-2 serology...this was just the start

Okba et al. EID 2020
Validation of SARS CoV-2 serology: virus neutralization
Determining functionality of antibodies by virus neutralization

<table>
<thead>
<tr>
<th>titer</th>
<th>n</th>
<th>POS</th>
<th>NEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1:20</td>
<td>31</td>
<td>27 (87%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>1:20</td>
<td>10</td>
<td>4 (40%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>1:40</td>
<td>7</td>
<td>2 (29%)</td>
<td>5 (71%)</td>
</tr>
<tr>
<td>1:80</td>
<td>2</td>
<td>0 (0%)</td>
<td>2 (100%)</td>
</tr>
<tr>
<td>1:160</td>
<td>4</td>
<td>0 (0%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>1:320</td>
<td>11</td>
<td>0 (0%)</td>
<td>11 (100%)</td>
</tr>
<tr>
<td>1:640</td>
<td>9</td>
<td>0 (0%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>1:1280</td>
<td>14</td>
<td>0 (0%)</td>
<td>14 (100%)</td>
</tr>
<tr>
<td>1:2560</td>
<td>16</td>
<td></td>
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</tr>
</tbody>
</table>

Probability <5% when PRNT is at least 1:80

Van Kampen et al, Nat Comm 2021
Timing
Severity of disease
Used antigen

Validation of SARS CoV-2 serology: assay comparison
Validation of SARS CoV-2 serology: assay comparison

DiaSorin Trimeric SARS CoV-2 IgG anti Spike

DiaSorin Trimeric CoV2 IgG : 7.8125-250 BAU/ml
Validation of SARS CoV-2 serology: current situation

Wild type virus

Liaison Trimeric S
Validation of SARS CoV-2 serology: current situation

- Wild type virus
- Delta
- Omicron

**Liaison Trimeric S**

**S-specific IgG (BAU/ml)**

- PRNT50 (titer)
- $10^1$, $10^2$, $10^3$, $10^4$, $10^5$

**Liaison Trimeric S**

**S-specific IgG (BAU/ml)**

- PRNT50 - DELTA (titer)
- $10$, $40$, $160$, $640$, $2560$, $10240$, $40960$

**Liaison Trimeric S**

**S-specific IgG (BAU/ml)**

- PRNT50 - OMICRON (titer)
- $10$, $40$, $160$, $640$, $2560$, $10240$, $40960$
Single shot mRNA BNT162b is sufficient for vigorous immune responses in COVID-19 recovered individuals.

Polyclonal sera have 2-3 fold reduced functionality against VOC B.1.351.

- **CD4+ T cells** retain reactivity to VOC B.1.1.7 and B.1.351.

Determining functionality of antibodies by virus neutralization:

- Type of SARS CoV-2 variant
- Type of cells
- Incubation
- Live virus or pseudotyped
The use of SARS CoV-2 serology in clinical practice

1. How good is SARS CoV-2 serology?

2. Use of IgG binding as correlate of protection?
- **Correlates of protection:**
  Measurable signs that a person is immune, in the sense of being protected against becoming infected and/or developing disease

- **Antibodies**
  - SARS-CoV-2-specific antibodies bind to the virus, and can prevent infection of cells

- **T-cells**
  - SARS-CoV-2-specific T-cells recognize infected cells, leading to viral clearance
- **Correlates of protection:**
  Measurable signs that a person is immune, in the sense of being protected against becoming infected and/or developing disease

- **Antibodies**
  - SARS-CoV-2-specific antibodies bind to the virus, and can prevent infection of cells

- **T-cells**
  - SARS-CoV-2-specific T-cells recognize infected cells, leading to viral clearance
Interpretation of serological results

• Kinetics of antibody levels in time, stratified by vaccine platform

• Functionality of antibodies (binding versus neutralizing antibodies)

• Comparison of methods and standardization

• Patient characteristics: immune suppression/COVID treatment
Kinetics of binding antibody responses in healthy individuals

AZ  Janssen  Moderna  Pfizer

GeurtsvanKessel et al. Science Imm. 2022
Determining functionality of antibodies by virus neutralization

**A**

- **ChAdOx-1 S (28d)**
  - GMT: 411, 365, 329, 20
  - PRNT50 (titer): 40960

- **Ad26.COV2.S (56d)**
  - GMT: 163, 140, 137, 15
  - PRNT50 (titer): 20480

- **mRNA-1273 (28d)**
  - GMT: 1997, 1808, 827, 58
  - PRNT50 (titer): 40960

- **BNT162b2 (28d)**
  - GMT: 802, 766, 301, 26
  - PRNT50 (titer): 40960

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**B**

- **Convalescent (6m)**
  - GMT: 336, 400, 419, 42
  - PRNT50 (titer): 40960

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**C**

- **WT delta beta omicron**
  - GMT: 27x, 11x, 34x

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Geurtsvankessel et al. Science Imm. 2022
Booster response in healthy individuals

GeurtsvanKessel et al. Science Imm. 2022
Binding antibodies upon heterologous boosting of Janssen vaccinees

3 months after 1x Janssen

Sablerolles et al NEJM 2022
Binding antibodies upon heterologous boosting of Janssen vaccinees

3 months after 1x Janssen

28 days after boost

Sablerolles et al NEJM 2022
5 months upon booster vaccination

Sablerolles et al NEJM 2022
Breakthrough infections

Positivity Rate in vaccinated/unvaccinated people

Unvaccinated

Vaccinated
Immune responses in risk populations

- Department of Viroscience directly involved in multiple vaccination studies:
  - Healthy individuals
    - **HCW**: follow-up of healthcare workers vaccinated with different vaccines
    - **HCW boost**: follow-up of healthcare workers boosted with Pfizer
    - **SWITCH**: improving immune responses in Janssen vaccinated individuals
  - Immunocompromised patients
    - **RECOVAC**: immune responses after vaccination in kidney disease patients
    - **COVALENT**: immune responses after vaccination in lung transplant recipients
    - **VACOPID**: immune responses after vaccination in patients with primary immunodeficiencies
    - **VOICE**: immune responses after vaccination in cancer patients
    - **COVIH**: immune responses after vaccination in HIV patients
Serological cut off based on virus neutralization

Modernata vaccinated at 28 days post 2nd vaccination

- Optimal responder
- (sub) Optimal responder
- Low responder
- Non-responder

**Cut-off for seropositivity**

<table>
<thead>
<tr>
<th>S1 in BAU/ml (WHO/NIBSC units)</th>
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<tbody>
<tr>
<td>0.1</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>1000</td>
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</tbody>
</table>

**Study X**
Comparative serology 28 days after Moderna vaccination

XLA: failure of B-lymphocyte precursors to mature into B-lymphocytes and ultimately plasma cells

Unpublished data
Comparative T cell immunology 28 days after Moderna (IGRA)

XLA: failure of B-lymphocyte precursors to mature into B-lymphocytes and ultimately plasma cells.
Vaccination-induced S-specific T-cells equally recognized VOC including Omicron
The use of serology in clinical practice

1. Use of IgG binding as correlate of protection in HC?

2. Use of IgG binding as correlate of protection in immune compromised patients

Requirements:

1. Standardised quantitative assay (calibrated with NIBSC)
2. Fixed timing → 28 days post vaccination?
3. Analysis based on type of vaccine
4. Definition of risk groups?
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