Severe Acute Respiratory Syndrome
SARS Coronavirus 1
and
SARS Coronavirus CoV-2  COVID-19
Mutations and Vaccines

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CORONAVIRUSES – worldwide, many animals
SARS: Number of Current Probable Cases as of 9 June 2003, 18:00 GMT+2

438 cases, 44 deaths

United States of America: 33
Canada: 69
Thailand: 1
China: 802
China, Taiwan: 342
China, Hong Kong SAR: 100
Russia Federation: 1
Germany: 1
France: 1
Singapore: 6

Number of current probable cases
- 1 - 60
- 61 - 200
- 201 - 500
- 501 - 1000
- More than 1000

Data Source: World Health Organization
Map Production: Public Health Mapping Team
Communicable Diseases (CDS)
© World Health Organization, June 2003

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SARS Pandemic
2003

32 countries
>8,000 cases
774 deaths

5-27% mortality
For patients >60,
50% mortality

MERS CoV 2012
SARS-CoV2 2019
HEALTH ALERT NOTICE
SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

HEALTH CANADA MESSAGE FOR INTERNATIONAL TRAVELLERS
ARRIVING IN OR RETURNING TO CANADA

Self-assessment questionnaire:
(1 questionnaire per family)

Please circle YES or NO to the following questions:

1. Do you have a fever?  YES  NO

2. Do you have one or more of the following symptoms:
cough, shortness of breath OR difficulty breathing?  YES  NO

3. Have you been in contact with a SARS-affected person in the last 10 days?  YES  NO

This Health Alert Notice will be given back to you by the Custom's Agent. Please save it for 10 days.

Version 4
Date: August 8, 2003
**TABLE 2** Clinical profile at admission to hospital for SARS (adapted from Reference 54)*

<table>
<thead>
<tr>
<th>Clinical profile</th>
<th>Frequency in Toronto n = 144</th>
<th>Frequency in Hong Kong n = 138</th>
<th>Frequency in Hong Kong n = 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45/34–57 (median/IQR)</td>
<td>39.3/16.8 (mean/SD)</td>
<td>39.8/12.2 (mean/SD)</td>
</tr>
<tr>
<td>Fever</td>
<td>99.3%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Nonproductive cough</td>
<td>69.4%</td>
<td>57.3%</td>
<td>22%</td>
</tr>
<tr>
<td>Myalgias</td>
<td>49.3%</td>
<td>60.9%</td>
<td>68%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>41.7%</td>
<td>NR</td>
<td>4%</td>
</tr>
<tr>
<td>Headache</td>
<td>35.4%</td>
<td>55.8%</td>
<td>15%</td>
</tr>
<tr>
<td>Malaise</td>
<td>31.2%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Chills and rigors</td>
<td>27.8%</td>
<td>73.2%</td>
<td>65% and 56%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>23.6%</td>
<td>19.6%</td>
<td>1%</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>19.4%</td>
<td>19.6%</td>
<td>NR</td>
</tr>
<tr>
<td>Sore throat</td>
<td>12.5%</td>
<td>NR</td>
<td>11%</td>
</tr>
<tr>
<td>Arthalgia</td>
<td>10.4%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Chest pain</td>
<td>10.4%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Productive cough</td>
<td>4.9%</td>
<td>29.0%</td>
<td>NR</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4.2%</td>
<td>42.8%</td>
<td>4%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3.5%</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Rhinorrhea or coryza</td>
<td>2.1%</td>
<td>22.5%</td>
<td>NR</td>
</tr>
</tbody>
</table>

Loss of smell, pneumonia, clotting, heart attacks, strokes
SARS Coronavirus
SARS Genome and Proteins

The Genome Sequence of the SARS-Associated Coronavirus, SCIENCE

400+ mutations
Published
Jan 11, 2020
SARS CoV-2 in US

US 87 k/mil
Canada 22 k/mil
Europe 28-46 k/mil

https://www.worldometers.info/coronavirus/country/us/
Daily New Deaths in the United States

Daily Deaths
Deaths per Day
Data as of 0:00 GMT+8

Total 515,000

https://www.worldometers.info/coronavirus/country/us/
Asymptomatic transmission

The diagram illustrates the transmission of SARS-CoV-2 before and after symptom onset. Detection of the virus is unlikely before symptom onset. After symptom onset, PCR tests are likely positive for a short period, followed by a negative PCR test in subsequent weeks. Antibody detection occurs over time, with IgM antibodies appearing before IgG antibodies. The diagram also shows the increasing probability of detection over time.
COVID Diagnostics

• Detect genome RNA – RT-PCR
• Detect proteins/antigens
  – Not very sensitive

• Detect antibodies ~ 10 days
A negative test doesn’t mean you’re not infected. It means there’s not enough virus right now.

Quarantine is recommended for 10 (14) days because you could become positive any one of those days.
COVID Prevention

- Wear a mask
- Keep distance
- Wash your hands, sanitizer
- Avoid people/crowds
- Outdoors safer than indoors
- Even after vaccination…

To be really careful:
Assume everyone is infected and everything is contaminated with virus
Exposure, whereas universal masking results in the least exposure.

Particle size (μm)

100 10 1 0.1

Infected, asymptomatic

Healthy

Maximum exposure

Minimum exposure

GRAPHIC: V. ALTOUNIAN/SCIENCE
## Transmission of SARS-CoV-2 Infections in Households — Tennessee and Wisconsin, April–September October 30, 2020. CDC

Carlos G. Grijalva, MD\(^1,\)*; Melissa A. Rolfes, PhD\(^2,\)*; Yuwei Zhu, MD\(^1\); Huong Q. McLean, PhD\(^3\); Kayla E. Hanson, MPH\(^3\); Edward A. Belongia, MD\(^3\); Natasha B. Halasa, MD\(^1\); Ahra Kim, MPH\(^1\); Carrie Reed, DSc\(^2\); Alicia M. Fry, MD\(^2\); H. Keipp Talbot, MD\(^1\)

<table>
<thead>
<tr>
<th>Index patient age group, yrs</th>
<th>%Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12</td>
<td>53 (31–74)</td>
</tr>
<tr>
<td>12–17</td>
<td>38 (23–56)</td>
</tr>
<tr>
<td>18–49</td>
<td>55 (46–64)</td>
</tr>
<tr>
<td>≥50</td>
<td>62 (44–77)</td>
</tr>
</tbody>
</table>
COVID Treatment

- Remdesivir
- IFN beta inhalant
- Antibody treatments (i.v.)
- Steroids – dexamethasone if serious inflammation –
  - Immunosuppressive? Virus shedding?

NOT hydroxychloroquine – no data to support
Viruses do 2 things:
- Replicate
- Spread

sickness?

Evolution - mutating over time

Spring 2020

# Genomic Architecture and Variant SARS-CoV-2

## Mutations

<table>
<thead>
<tr>
<th>gene</th>
<th>nucleotide</th>
<th>amino acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORF1ab</td>
<td>C3267T</td>
<td>T1001I</td>
</tr>
<tr>
<td></td>
<td>C5388A</td>
<td>A1708D</td>
</tr>
<tr>
<td></td>
<td>T6954C</td>
<td>I2230T</td>
</tr>
<tr>
<td></td>
<td>11288-11296 deletion</td>
<td>SGF 3675-3677 deletion</td>
</tr>
<tr>
<td>spike</td>
<td>21765-21770 deletion</td>
<td>HV 69-70 deletion</td>
</tr>
<tr>
<td></td>
<td>21991-21993 deletion</td>
<td>Y144 deletion</td>
</tr>
<tr>
<td>A23063T</td>
<td>N501Y</td>
<td></td>
</tr>
<tr>
<td>C23271A</td>
<td>A570D</td>
<td></td>
</tr>
<tr>
<td>C23604A</td>
<td>P681H</td>
<td></td>
</tr>
<tr>
<td>C23709T</td>
<td>T716I</td>
<td></td>
</tr>
<tr>
<td>T24506G</td>
<td>S982A</td>
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<tr>
<td>G24914C</td>
<td>D1118H</td>
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<tr>
<td>Orf8</td>
<td>C27972T</td>
<td>Q27Stop</td>
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<tr>
<td>G28048T</td>
<td>R52I</td>
<td></td>
</tr>
<tr>
<td>A28111G</td>
<td>Y73C</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>28280 GAT-&gt;CTA</td>
<td>D3L</td>
</tr>
<tr>
<td></td>
<td>C28977T</td>
<td>S235F</td>
</tr>
</tbody>
</table>

## UK Variant 2020

- Naqvi TAT, et al. BBA – Molecular Basis of Disease 1866.2020; 165878

![Diagram of a virus with annotations](image-url)
Larger clades were named based on marker variants:
S ... ORF8-L84S
G ... S-D614G
V ... NS3-G251V

Full genome tree of all outbreak sequences
2020-04-01

Notable changes:
2,794 full genomes (+360)
(excluding low coverage, out of 3,136 entries)

- S clade 672 (+107): 80
  USA/WA, 24 Canada, 2
  USA/VA, 1 Japan

- G clade 1221 (+157): 48
  Belgium, 35 England, 29
  USA/WA, 20 Canada, 8
  Switzerland, 5 USA/UT, 5
  Australia/QLD, 5 Ireland, 2
  Spain

- V clade 294 (+59): 53
  England, 2 Ireland, 1 Belgium, 1 Canada,
  1 Hong Kong, 1 USA/WA

- Other clades 607 (+37): 15
  Hangzhou, 11 England, 4
  Belgium, 4 Canada, 2
  Australia/QLD, 1 USA/WA

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.
Indicates that antibodies to this protein have been detected in SARS patients.
COVID Vaccines

- Most target spike protein
- Phase III Trials ~30,000 people
- Safety and efficacy
- Wait to see if vaccinated people are protected compared to placebo vaccine
Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.
ALL VACCINES AVAILABLE IN THE US MUST PROVE SAFETY AND EFFICACY TO FDA BEFORE RELEASE

CDC (ACIP) RELEASES GUIDELINES

Advisory Committee on Immunization Practices
Vaccine types

• Killed virus - flu shot (examples)
• Viral protein – Shingrix, HPV vaccine
• Recombinant virus- Ebola vaccine, HIV DNA - RNA - protein
• DNA vaccine: DNA - RNA - protein
• RNA vaccine: RNA – protein NEW
• Live attenuated safe – measles, mumps, rubella, polio… (not safe for CoV)
Vaccine Platform Refresher

DNA-based vaccines work by inserting synthetic DNA of viral gene(s) into small DNA molecules (called plasmids). Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognized by the immune system, and prepare it to respond to disease exposure.

Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating), which delivers the viral protein to the vaccine recipient, triggering an immune response.

RNA vaccines introduce an mRNA sequence coded for a disease-specific antigen. Once this antigen is reproduced within the body, it is recognized and triggers an immune response.

Subunit vaccines introduce a fragment of the virus into the body. This fragment is enough to be recognized by the immune response and stimulate immunity.

Inactivated vaccines consist of the whole virus, which has been killed with heat or chemicals so it can't cause illness.

Live attenuated vaccines are made up of whole viruses that have weakened in a lab. They tend to elicit a stronger immune response than inactivated vaccines.
Influenza vs Coronavirus

• Flu vaccine – every year
  – 8 genome pieces

• Coronavirus – maybe repeats
  – 1 piece genome
COVID Vaccine Safety

- RNA disappears, unstable
- Long term safety?
- 6 months and now 50 million vaccinations
- Allergic reactions, about 1 in 100,000 people, usually allergy history to vaccine
Indicates that antibodies to this protein have been detected in SARS patients
COVID Vaccines

• RNA vaccines - Pfizer, Moderna
  – 2 shots - 95% symptoms

• Recombinant viral vaccine -
  – Johnson & Johnson 1 shot - 85% serious effective against S. African variant
Get your shot!