COVID-19 Education Module 2
COVID-19 outpatient evaluation and management of acute illness in adults

• Our understanding of management is rapidly evolving with limited data informing outpatient management strategies

• Approaches are based upon clinical experience and rapidly evolving evidence

• Doctors should take into account the individual patient's clinical and social circumstances as well as available resources

• COVID-19 patients without severe disease can generally remain at home for management depending on symptoms
COVID-19 outpatient evaluation and management of acute illness in adults

<table>
<thead>
<tr>
<th>ED Referral (≥1 high risk condition)</th>
<th>Outpatient Clinic Evaluation</th>
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<tbody>
<tr>
<td>• Severe shortness of breath (at rest, interfering with the ability to speak in complete sentences)</td>
<td>• Mild shortness of breath in a patient with an oxygen level on room air between 91 to 94 percent</td>
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<tr>
<td>• Oxygen saturation on room air of ≤90 percent, regardless of severity of shortness of breath</td>
<td>• Mild shortness of breath in a patient with any risk factors for severe disease</td>
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<tr>
<td>• Confusion, change in behavior, difficulty in waking up or other signs and symptoms (eg, falls, low blood pressure, dehydration or chest pain)</td>
<td>• Moderate shortness of breath in any patient</td>
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<td>• Symptoms concerning enough to warrant in-person evaluation but not severe enough to require emergency department referral</td>
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COVID-19 outpatient evaluation and management of acute illness in adults

• Reinforce the importance of infection control and self-isolation

• Symptomatic, non-hospitalized COVID-19 patients with mild to moderate illness and specific risk factors for severe disease, may be candidates for early therapy (monoclonal antibody therapy)
  • Monoclonal antibody therapy should be given as early as possible after diagnosis and within seven days of symptom onset
  • Monoclonal antibodies have been seen to reduce the severity of the disease.
COVID-19 outpatient evaluation and management of acute illness in adults

• Corticosteroids (like Prednisone) are not routinely used in mild cases

• Antibiotics are typically not necessary in mild cases

• Anticoagulation or antiplatelet therapy (blood clot treatment) are also not routinely indicated for outpatient COVID-19 therapy

• The role of anti-viral medications should be considered and is generally reserved for the inpatient setting
How are Vaccines Developed?

• Vaccines may contain an active component (the antigen) which generates an immune response, or may contain the blueprint for making the active component (i.e. mRNA Vaccines)
  • The antigen may be a small part of the disease-causing organism, like a protein or sugar, or it may be the whole organism in a weakened or inactive form.
Vaccine Development

- Vaccine development progresses through preclinical evaluation and three distinct clinical stages:

  - **Phase I trials** — The vaccine is given to a small number of volunteers to assess its safety, confirm that it will create an immune response, and determine the right dosage.

  - **Phase II trials** — The vaccine is then given to several hundred volunteers to further assess its safety and ability to generate an immune response. There are usually multiple trials in this phase to evaluate various age groups and different formulations of the vaccine.

  - **Phase III trials** — The vaccine is next given to thousands of volunteers — and compared to a similar group of people who did not get the vaccine but received a placebo (non-active substances) — to determine if the vaccine is effective against the disease it is designed to protect against and to study its safety in a much larger group of people.
Vaccine Development

• Traditionally, these steps do not overlap (each taking years), however, COVID-19 development has been accelerated **without skipping any step!**
  • Phase I and II and phase II and III studies have frequently been combined with a seamless transition from one phase into the next

• Safety criteria remains stringent
  • Data Safety and Monitoring Committees (DSMCs) assess adverse events that are reported in each phase of clinical study and approve advancement

• In the United States, the Food and Drug Administration must also approve progression to each next step in human trials
There are many different types of vaccines

- Vaccines are being developed using traditional and newer platforms including:
  - Inactivated vaccines
  - Live attenuated vaccines
  - Recombinant protein vaccines
  - Vector vaccines
  - DNA vaccines
  - RNA vaccines
mRNA vaccines have been in development for years

• RNA vaccines were the first vaccines for SARS-CoV-2 to be produced and represent a new vaccine approach

• Vaccine development for SARS-CoV-1 and Middle East respiratory syndrome coronavirus (MERS-CoV) paved the way for rapid development of COVID-19 vaccines roughly 12 years ago
  • Testing was done for SARS-CoV-1 vaccines
  • Two vaccines were evaluated in human trials

• The antigenic target for both SARS-CoV-1 and MERS vaccines was the large surface spike protein
  • The same protein is also present in SARS-CoV-2
How does the mRNA coronavirus vaccine work?

The RNA vaccine contains messenger RNA, which contains an instruction to make a SARS-CoV-2 spike protein.

For messenger RNA (mRNA) to enter the muscle cell at the injection site, it is packaged inside a very small fatty particle.

Spike protein
Antibody

Messenger RNA instructs cells to produce a coronavirus spike protein.

The body's defence system recognises the spike protein as foreign and begins to protect itself against it.

Source: Finnish Institute for Health and Welfare 2020

https://thl.fi/documents/533989/5805321/THL-korona-RNA-rokote_02_EN_21122020.png/e1d5088a-c56c-cfbc-7fb3-ca85471d545b?t=1610716016942
Vaccines in the United States

- COVID-19 vaccines in the US granted Emergency Use Authorization (EUA):
  - Pfizer-BioNTech COVID-19 vaccine - BNT162b2 (mRNA)
    - Indicated for individuals aged 12 years or older
  - Moderna COVID-19 vaccine - mRNA-1273 (mRNA)
    - Indicated for individuals aged 18 years or older
  - Janssen COVID-19 vaccine (Johnson & Johnson) - Ad26.COV2.S (adenoviral vector)
    - Indicated for individuals aged 18 years or older

- The choice between vaccines is based on availability
  - They have not been compared directly
Most Vaccine Trials only have Thousands of Participants
Even though under “Emergency Use”, the studies on the current COVID-19 vaccine have far exceeded any prior vaccine studies

- **4.46 BILLION vaccines** have been given, as of August 8, 2021
  - 2,340,887,061 **people** have received at least one dose
  - 1,206,027,798 **people** have been fully vaccinated

- In the United States (as of August 8, 2021):
  - 194,886,738 **people** have received at least one dose
  - 166,477,481 **people** have been fully vaccinated

- In the United States, Vaccine Adverse Event Reporting System (VAERS) is used to monitor for adverse events

- **Adverse events with the COVID-19 vaccine have been rare.**
Rare adverse events

• Janssen vaccine has rarely been associated with thrombosis with thrombocytopenia and possibly Guillain-Barre syndrome (as indicated in the following slides)

• The mRNA vaccines (Pfizer and Moderna) have rarely been associated with myocarditis
  • The risks of these events are extremely small, and the benefits of the vaccine outweigh them (as indicated in the following slides)

• Individuals who have a contraindication to a vaccine in one class (i.e. an mRNA vaccine) should not receive other vaccines in that class but can receive a vaccine in the other class with precautions
Vaccine Safety: Thrombosis with Thrombocytopenia are rare

- Reported with Janssen COVID-19 vaccine (Johnson & Johnson)

- After administration of **8.7 million doses** in the United States, 28 cases of thrombosis with thrombocytopenia syndrome have been reported
  - This is **3.2 cases per 1 million people**
  - **12.4 cases per million** for females 30 to 39 years old
  - **9.4 cases per million** for females 40 to 49 years old
  - The risk in other age groups and males ranged from **1.3 to 4.7 cases per million**
  - Symptom onset was usually one to two weeks after vaccination (range 3 to 15 days)
Risk of Central Venous Sinus Thrombosis is Extremely Low

<table>
<thead>
<tr>
<th>Population</th>
<th>Cases</th>
<th>Population Size</th>
<th>Probability</th>
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<tbody>
<tr>
<td>US population vaccinated with J&amp;J</td>
<td>6</td>
<td>6.8M</td>
<td>0.000088%</td>
</tr>
<tr>
<td>General population</td>
<td>5</td>
<td>1M</td>
<td>0.0005%</td>
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Combined information from Johns Hopkins, CDC, Cleveland Clinic, WebMD
There is a much higher risk of blood clots in commonly used medications than with the COVID-19 vaccine.

There is also a much higher risk of blood clots with severe COVID-19 than with the COVID-19 immunization.

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<tr>
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<th>Risk of any type of blood clot</th>
<th>PCT.</th>
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<tbody>
<tr>
<td>Women not on birth control</td>
<td>Up to 5 out of every 10K</td>
<td>0.01% to 0.05%</td>
</tr>
<tr>
<td>Women on birth-control pills</td>
<td>Up to 1 out of every 100</td>
<td>0.3% to 1%</td>
</tr>
<tr>
<td>ICU patients with severe COVID-19</td>
<td>31 out of every 100</td>
<td>31%</td>
</tr>
</tbody>
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Combined information from Johns Hopkins, CDC, Cleveland Clinic, WebMD
The Risk of Myocarditis and Pericarditis is very low

- Reported following receipt of the mRNA vaccines: Pfizer and Moderna
  - 267 reported cases of myocarditis/pericarditis following one dose of an mRNA vaccine (this is 267 cases with over 191 million doses given as of 8/2/21) (Incidence 0.0000014)
    - Average age of 30 years old
  - 827 following two doses (this is 827 cases with over 164 million doses given in the US in people who have had 2 doses) (Incidence 0.00000504)
    - Average age of 24 years old
  - The estimated rate of myocarditis/pericarditis among males 12 to 29 years of age was 41 cases per million (Incidence 0.0000041) following a second dose of an mRNA vaccine

- Onset was generally within the first week after vaccine receipt

- Most reported cases were mild

- The benefits of mRNA vaccination greatly exceed the small increased risk for those who develop myocarditis or pericarditis following a first dose of an mRNA vaccine
Guillain-Barre Syndrome (GBS)

- A potential association with adenovirus vector vaccine Janssen/Johnson & Johnson
- There had been 100 preliminary reports of GBS among Janssen recipients with over 12.5 million doses given (Incidence 0.000008)
  - Average age was 54 years
  - Time to onset was 14 days following vaccination
  - Only 10 had severe disease (only one fatality)
- This has not been observed with mRNA vaccines
- US FDA, CDC and European regulators affirm that the benefits of these vaccines outweigh their risks

AAMC and AACOM Recommendations

• **AAMC COVID 19 vaccine recommendations for medical schools and teaching hospitals** is strongly advising for medical students and health care providers to receive the vaccine in order to protect both patients and health care personnel.

• **AACOM strongly encourages COVID 19 vaccination** for individuals in order to protect themselves and their communities.
Nearly 60 Health Care Associations have signed on to a recommendation for all healthcare workers to be vaccinated

- Recommendation is made for the safety of patients

- Recommendation is made for the safety of health care workers

- Includes the American Medical Association, American Nursing Association and nearly 60 other reputable organizations


- [https://www.acponline.org/acp_policy/statements/joint_statement_covid_vaccine_mandate_2021.pdf](https://www.acponline.org/acp_policy/statements/joint_statement_covid_vaccine_mandate_2021.pdf)
COVID-19 Vaccine Safety in Pregnancy

• COVID-19 vaccinations are recommended for pregnant women
  • Especially those with increased risk for severe infection, but also for pregnancy in general

• Scientific literature does not claim any link to COVID-19 vaccine and infertility. The American College of Obstetricians and Gynecologists (ACOG) recommend pregnant patients receive the COVID-19 vaccine
Information regarding concerns pertaining to stem cell use in vaccine research

• The concern is similar to that of Rubella vaccines and the use of information gathered from stem cell lines obtained in the 1960’s

• This link provided below mentions both stem cell use related to the Rubella vaccine as well as stem cell references related to the COVID-19 vaccine

• https://www.usccb.org/moral-considerations-covid-vaccines
Useful Vaccine Information Resources

• Understanding of COVID-19 is evolving and interim guidance has been issued by the World Health Organization and CDC

• COVID-19 Advisory Committee on Immunization Practices: Vaccine Recommendations

• Centers for Disease Control and Prevention: COVID-19 Vaccination Page

• U.S. COVID-19 Vaccine Product Information

• Center for Disease Control and Prevention: Ensuring COVID-19 Vaccine Safety in the US