Storage and Handling of the COVID-19 Vaccines

James Allen, MD
Medical Director, The Ohio State University Wexner Medical Center East Hospital
Professor of Internal Medicine
Division of Pulmonary and Critical Care Medicine
The Ohio State University Wexner Medical Center
Pfizer COVID-19 Vaccine

• Storage: -76° to -112° F
  – Temporary storage in dry ice
  – Cannot refreeze thawed vials
• Thawing:
  – In refrigerator: 35° to 46° F for 2-3 hours
    • Can store in refrigerator up to 5 days
    • Must use within 6 hours of dilution
  – Room temperature: 77° F for 30 minutes
    • Must use within 2 hours

Pfizer COVID-19 Vaccine

• Dilution:
  – Thaw vial
  – Invert vial *gently* 10 times
  – Add 1.8 ml 0.9% sodium chloride injection USP
    • NOT bacteriostatic sodium chloride injection
• Each vial contains 6 doses, 0.3 ml each
• Administer intramuscularly
1. No more than 2 hours at room temperature (up to 25°C / 77°F)

2. Gently x 10

3. 1.8 mL of 0.9% sodium chloride injection

4. Fill back plunger to 1.8 mL to remove air from vial
5. Gently x 10

6. Store at 35° to 77° F for up to 6 hours

7. Do not pool vaccine from multiple vials for any single injection
Pfizer COVID-19 Vaccine: What’s in the vial?

- Lipids
- Polyethylene glycol
- Cholesterol
- Potassium chloride
- Potassium phosphate
- Sodium chloride
- Sucrose
- 30 mcg mRNA to the spike glycoprotein
- Vial stopper does NOT contain natural rubber latex
- Vaccine is preservative-free

Moderna COVID-19 Vaccine

- Storage: -13° to 5° F
  - DO NOT store in dry ice or below -40° F
  - Can store refrigerated 36° to 46° F for 30 days
  - Cannot refreeze thawed vials
- Unpunctured vials 46° to 77° F for 12 hours
- Punctured vials 36° to 77° F for 6 hours
Modernas COVID-19 Vaccine

• Thaw in refrigerator 2 hours 30 minutes
  – After thawing, let stand 15 minutes at room temperature
• Alternatively thaw at room temperature 1 hour

Modernas COVID-19 Vaccine

• Swirl gently
  – DO NOT shake
• Each dose = 0.5 ml
• Vials contain 10 doses
• Administer intramuscularly
• FDA-approved for 18 years and older
Moderna COVID-19 Vaccine: What’s in the vial?

- Lipids
- Polyethylene glycol
- Cholesterol
- Tromethamine
- Acetic acid
- Sodium acetate
- Sucrose
- 100 mcg mRNA to the spike glycoprotein

- Vial stopper does **NOT** contain natural rubber latex
- Vaccine is preservative-free
Vaccine Administration Logistics

Ryan Haley, MBOE
Senior Director, Ambulatory Services
The Ohio State University Wexner Medical Center

Our First Doses Administered
Assembling the Teams

• Vaccine Prioritization: Dr. Nick Kman & Dr. Ryan Nash
  • Goal: Defining and Implementing the Prioritization of Vaccine
  • Met 3x week

• Vaccine Administration: Dr. Crystal Tubbs & Ryan Haley
  • Goals: Managing Supply Chain & Administration Process
  • Met 2x week but had multiple subgroups

• Vaccine Education: Beth Necamp
  • Goals: Developing education for internal and external groups
  • Established later in the process

Assembling the Workforce

• Vaccine Administration Roles
  • Manager
  • Scheduling (Call Center)
  • Pharmacist Station
  • Check-In / Registration Staff
  • Runner/Navigator
  • Vaccinator
  • Physician
  • Campus Police

• Indirect Support
  • IT
  • Marketing
  • Legal Services
  • Revenue Cycle
  • Volunteer / Staffing Management
The Vaccine Administration Process

• Before the Visit
  • Invitations / Notifications
  • Scheduling (Online vs Phone) w/screening questions
  • Reminders
• Day of the Visit
  • Arrival / Check-In
  • Review of Screening Questions
  • **Vaccine Administration**
    • Post-vax monitoring (15 min vs 30 min)
    • Full registration
    • Scheduling of 2\textsuperscript{nd} visit
• After the Visit
  • Billing for Service
  • Post-vax Nurse Line
  • Vsafe reporting

Safety

• Universal masking
• Physical distancing both in lines and at the vaccine stations
• Visual indicators to demonstrate whether vaccine station is clean or dirty
• One way traffic flow
• Vaccine screening questions
• Vaccine manufacturer double checks
Supply Chain / Schedule Management

• Managing the extreme variability of weekly supply (ranging from 975 in a week to 8850)
• Balancing allocated supply with specific number of appointment slots (how much risk do you take?)
• Multiple manufacturers
• 1st Dose vs 2nd Dose
• Visit Type by Manufacturer
• Goal to get all shipments out within 7 days or less of receipt
• ZERO DOSES WASTED from overdraws

Communication / education

• Town halls
• eLearning
• HealthBeat Hub FAQs
• Daily updates from chancellor
• Vaccine email address
OSUWMC’s Vaccine Hours Locations

• Initially used 3 different locations on campus
  • Biomedical Research Tower (capacity 900 patients per day)
  • East Hospital Conference Room (capacity 450 patients per day)
  • Ackerman Administrative Building (capacity 1100 patients per day)
• Days and Hours – somewhat dependent upon demand
  • M-F 7a-7p (12 hours, w/10.5 hours of vaccine uptime)
  • Saturdays 7a-3p (8 hours, w/7 hours of vaccine uptime)

Scaling Up: Shots at the Schott

• Schottenstein Center
  • 2 Concourses (~150-160 vaccine stations)
  • Max capacity in 12 hour shift ~ 3K
  • Goal of 2 table turns per hour
Schottenstein Center Pictures

Schottenstein Center Pictures
mRNA COVID-19 Vaccines

Nora Colburn, MD, MPH
Medical Director of Clinical Epidemiology, Ross Heart Hospital
Assistant Professor of Medicine, Department of Internal Medicine
Division of Infectious Diseases
The Ohio State University Wexner Medical Center
Traditional Vaccines

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Mechanism of Action</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live-attenuated</td>
<td>Weakened virus that infects cells and induces immune response.</td>
<td>Measles, Mumps, Rubella Variola (Smallpox)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Varicella (Chickenpox)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yellow Fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Influenza (intranasal)</td>
</tr>
<tr>
<td>Inactivated</td>
<td>Virus is inactivated. Not pathogenic to host, but can induce an immune response.</td>
<td>Hepatitis A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rabies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Influenza (IM)</td>
</tr>
<tr>
<td>Subunit (recombinant, polysaccharide, conjugate)</td>
<td>Antigenic material (sugar, protein, etc) that are components of the organism are used to induce an immune response</td>
<td><em>Haemophilus influenzae</em> type b</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HPV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pneumococcus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meningococcus</td>
</tr>
<tr>
<td>Toxoid</td>
<td>Toxin produced by the organism is inactivated and used to induce an immune response.</td>
<td>Diphtheria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tetanus</td>
</tr>
</tbody>
</table>

Nucleic Acid Vaccines

- Nucleic acid that encodes the desired antigenic protein is inserted into the cell.
- The cell uses its own machinery to transcribe and/or translate the nucleic acid into the protein.
  - DNA Plasmid
    - Examples: Zika, influenza
  - Viral Vector
    - Examples: Zika, HIV, Ebola, SARS-CoV-2
  - mRNA Vaccines

Source: https://cnx.org/contents/FPtK1zmh@8.25:fl13C80t@10/Preface
mRNA Vaccine Research

- 1990 - 1st successful use in animal model of mRNA was injected into mice and protein production was detected
- Very promising technology for vaccines against infectious agents, cancer therapies, and protein replacement therapies.

<table>
<thead>
<tr>
<th>Early Barriers</th>
<th>Advancements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid mRNA degradation</td>
<td>Development of cationic lipid/polymer molecules to usher the mRNA in the cell</td>
</tr>
<tr>
<td>Inefficient <em>in vivo</em> delivery into the cell</td>
<td></td>
</tr>
<tr>
<td>High innate immunogenicity</td>
<td>Immunogenicity can be down-regulated</td>
</tr>
</tbody>
</table>


Types of mRNA Vaccines

<table>
<thead>
<tr>
<th>1. Self-Amplifying</th>
<th>Delivery Method</th>
<th>Pathogens Studied</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complex to lipid nanoparticle and injected into host</td>
<td>RSV, influenza, CMV, HCV, HCV, rabies, HIV, Ebola, Zika <em>Toxoplasma gondii</em> Group A Strep, Group B Strep</td>
</tr>
<tr>
<td>2. Non-replicating</td>
<td><em>Ex vivo</em> loading of DC, then infusion into host</td>
<td>HIV, CMV</td>
</tr>
<tr>
<td></td>
<td>Complex to lipid nanoparticle and injected into host</td>
<td><em>Influenza</em>, rabies, HIV, <em>Zika</em></td>
</tr>
</tbody>
</table>

mRNA - promising alternative to traditional vaccine methodologies

- Safety
  - No potential risk of infection
  - Non-integrating platform
  - Degraded by normal cellular processes
  - High innate immunogenicity can be down-regulated

- Efficacy
  - mRNA can be modified to be more stable and highly translatable
  - Carrier/delivery molecules have been developed to efficiently deliver the mRNA into the cytoplasm before degradation can occur

- Production
  - Able to implement rapid, inexpensive, scalable manufacturing


SARS-CoV-2 Vaccine Candidates in Phase 3 Trials

<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Sponsor</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA</td>
<td>Pfizer</td>
</tr>
<tr>
<td></td>
<td>Moderna</td>
</tr>
<tr>
<td>Viral Vector</td>
<td>Astra Zeneca/Oxford</td>
</tr>
<tr>
<td></td>
<td>Janssen (J&amp;J)</td>
</tr>
<tr>
<td></td>
<td>CanSino</td>
</tr>
<tr>
<td>Recombinant Protein</td>
<td>Novavaxx</td>
</tr>
<tr>
<td>Inactivated</td>
<td>Sinovac</td>
</tr>
<tr>
<td></td>
<td>Wuhan Institute of Biological</td>
</tr>
<tr>
<td></td>
<td>Products</td>
</tr>
</tbody>
</table>

This media comes from the Centers for Disease Control and Prevention’s Public Health Image Library (PHIL), with identification number #23312.
https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines/
Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine

• Published in NEJM December 2020

• Multinational, placebo-controlled, observer-blinded efficacy trial
• 16 and older
• 1:1 randomization of placebo vs BNT162b2 vaccine candidate
  • Lipid nanoparticle-formulated, nucleoside-modified RNA vaccine that encodes the SARS-CoV-2 full-length spike protein


Primary Endpoints

• Efficacy
  • Confirmed COVID-19 at least 7 days after 2nd dose in subjects with no history of infection
  • Confirmed COVID-19 in all subjects regardless of past infection

• Safety
  • Solicited adverse events and use of antipyretics within 7 days of injection
  • Unsolicited adverse events through 1 month after 2nd dose and serious adverse events through 6 months after 2nd dose

Confirmed COVID-19 = at least 1 symptom + positive NAAT test

Interim Analysis 10/9/20

37,306 randomized

18,860 vaccine #1
18,556 vaccine #2

18,846 placebo #1
18,530 placebo #2

Male 50.6%
White 82.9%
Black 9.3%
Asian 4.3%
Hispanic 28.0%

Median Age
16-55 years 52.0 years (16-91)
>55 years 57.8%

BMI >30
≥1 Co-morbidity 35.1%
21%

Argentina 15.3%
Brazil 6.1%
South Africa 2.0%
US 76.7%


Pfizer-BioNTech COVID-19 Vaccine

## Primary and Secondary Endpoints

<table>
<thead>
<tr>
<th></th>
<th># cases BNT162b2</th>
<th># cases Placebo</th>
<th>Vaccine Efficacy, % (95% credible interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 at least 7 days after 2nd dose in subjects without evidence of past infection (n = 36,523)</td>
<td>8</td>
<td>162</td>
<td>95.0% (90.3-97.6)</td>
</tr>
<tr>
<td>COVID-19 at least 7 days after 2nd dose in subjects with and without evidence of past infection (n = 40,137)</td>
<td>9</td>
<td>169</td>
<td>94.6% (89.9-97.3)</td>
</tr>
<tr>
<td>Severe COVID-19 (n=10)</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>


## Vaccine Efficacy by Subgroup

<table>
<thead>
<tr>
<th></th>
<th># cases BNT162b2</th>
<th># cases Placebo</th>
<th>Vaccine Efficacy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-55 years</td>
<td>5</td>
<td>114</td>
<td>95.6%</td>
</tr>
<tr>
<td>&gt;55 years</td>
<td>3</td>
<td>48</td>
<td>93.7%</td>
</tr>
<tr>
<td>≥65 years</td>
<td>1</td>
<td>19</td>
<td>94.7%</td>
</tr>
<tr>
<td>≥75 years</td>
<td>0</td>
<td>5</td>
<td>100.0%</td>
</tr>
<tr>
<td>Male</td>
<td>3</td>
<td>81</td>
<td>96.4%</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>81</td>
<td>93.7%</td>
</tr>
<tr>
<td>White</td>
<td>7</td>
<td>146</td>
<td>95.2%</td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>7</td>
<td>100.0%</td>
</tr>
<tr>
<td>All others</td>
<td>1</td>
<td>9</td>
<td>89.3%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3</td>
<td>53</td>
<td>94.4%</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>5</td>
<td>109</td>
<td>95.4%</td>
</tr>
</tbody>
</table>

Between Dose #1-#2 = 52%

1st 7 days after Dose #2 = 91%
mRNA-1272 – Moderna Vaccine

- 27,817 participants
- 82% of subjects considered at occupational risk for exposure
  - 25.4% were HCW
- 22.3% with at least 1 risk factor for severe disease

<table>
<thead>
<tr>
<th></th>
<th># cases mRNA-1272</th>
<th># cases Placebo</th>
<th>Vaccine Efficacy, % (95% credible interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 at least 14 days after 2nd dose in subjects without evidence of past infection (n = 27,817)</td>
<td>5</td>
<td>90</td>
<td>94.5% (86.5-97.8)</td>
</tr>
<tr>
<td>18-64 years (n = 20,791) ≥ 65 years (n = 7026)</td>
<td>5 0</td>
<td>75 15</td>
<td>93.4% (83.7-97.3%) / 100%</td>
</tr>
<tr>
<td>Severe COVID-19 (n= 11)</td>
<td>0</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

After Dose #1 = 80.2%
Take home points:
• mRNA vaccines have been researched for years with significant recent advancements.
• 2 currently available vaccines with excellent and nearly identical efficacy and safety profiles.

Remaining questions:
• What is the efficacy for asymptomatic transmission?
• How long does immunity last?
• When will children be vaccinated?
COVID-19 Vaccine Safety

Jonathan P. Parsons, MD, MSc, FCCP
Professor of Internal Medicine
Executive Vice Chair for Clinical Operations
Department of Internal Medicine
Division of Pulmonary, Critical Care, and Sleep Medicine
The Ohio State University Wexner Medical Center

Adverse drug reactions in the news

2 Alaska Health Workers Got Emergency Treatment After Receiving Pfizer’s Vaccine
One of the workers, who did not have a history of allergies, remained in the hospital on Wednesday night. Some reactions to the vaccine were also reported last week in Britain.

Doctors encourage COVID vaccination despite reports of cosmetic facial filler swelling
About 2.7 million Americans get filler injections each year.

Four People Given the New COVID Vaccine in Clinical Trials Developed Bell’s Palsy—Should You Be Worried?
Here’s what to know about the condition, which causes temporary facial paralysis, and if a link has been established to the new vaccine.

VERIFY: Will the COVID-19 vaccine cause infertility in women?
A Facebook post claims a head researcher for vaccine manufacturer Pfizer has issued a warning that the company’s new COVID-19 vaccine would cause sterilization.
### Adverse drug reactions in clinical trials

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Moderna (n=15,185)</th>
<th>Pfizer (n=21,621)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1242 (8.2%)</td>
<td>4484 (20.7%)</td>
</tr>
<tr>
<td>Serious</td>
<td>6 (&lt;0.1%)</td>
<td>4 (&lt;0.1%)</td>
</tr>
<tr>
<td>Fatal</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Medically-attended</td>
<td>140 (0.9%)</td>
<td>Not assessed</td>
</tr>
<tr>
<td>Leading to study discontinuation after 1st dose</td>
<td>18 (0.1%)</td>
<td>Not assessed</td>
</tr>
<tr>
<td>Leading to study withdrawal after either dose</td>
<td>0</td>
<td>37 (0.2%)</td>
</tr>
<tr>
<td>Severe</td>
<td>71 (0.5%)</td>
<td>240 (1.1%)</td>
</tr>
</tbody>
</table>


### Adverse drug reactions in clinical trials

- Minor local (e.g., injection site pain) and systemic (e.g., fatigue, headache) side effects were common
  - Onset usually within first 24-48 hours
  - Mean duration 2-3 days

Serious reactions in trials: Moderna

- Occurred in 1.5% of Moderna vaccine recipients vs 1.1% placebo
  - Injection site rash, injection site urticaria
  - 1 anaphylactic reaction in each group
  - Facial swelling in 2 patients with history of dermatological fillers (onset 1 and 2 days after vaccination)
- 3 reports of Bell’s palsy in Moderna vaccine group
  - Onset: 22, 28, and 32 days after vaccination
  - Insufficient information to determine causal relationship with the vaccine


Serious reactions in trials: Pfizer

- 4 serious reactions related to Pfizer vaccine reported:
  - Shoulder injury related to vaccine administration
  - Right axillary lymphadenopathy
  - Paroxysmal ventricular arrhythmia
  - Right leg paresthesia

Anaphylactic reactions in practice

- 3 cases of anaphylaxis reported within first 24 hours after mass vaccination began in UK and US (Pfizer)
  - 2 females in UK with known food/drug allergies
  - 1 female in US with no known allergies
- Several more cases associated with Pfizer vaccine reported in US
  - Incidence ~1 in 100,000
  - Known stable incidence of anaphylaxis with other vaccines: ~1 in 1,000,000
- Too soon to identify similar potential signal with Moderna vaccine
  - Cases have been reported

Facial Fillers

- 3 patients with history of cosmetic filler injections reported facial swelling after receiving Moderna vaccine
  - Fillers injected 2 weeks, 6 months, and unknown period of time prior to COVID-19 vaccine
  - Onset 1-2 days after vaccination
  - All resolved

Safe Vaccine Administration: CDC Recommendations

- Vaccinated persons should be monitored
  - 30 minutes: history of immediate allergic reaction of any severity to a vaccine or injectable therapy OR anaphylaxis due to any cause
  - 15 minutes: all others

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html
Vaccination in Special Populations

<table>
<thead>
<tr>
<th>System</th>
<th>Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immuno-compromised</td>
<td>may administer if not otherwise contraindicated, but counsel about lack of data and potential for reduced immune response.</td>
</tr>
<tr>
<td>Autoimmune conditions</td>
<td>administer if not otherwise contraindicated.</td>
</tr>
<tr>
<td>History of Guillain-Barré</td>
<td>administer if not otherwise contraindicated.</td>
</tr>
<tr>
<td>History of Bell’s palsy</td>
<td>Cases observed in mRNA vaccine clinical trials, but no causality; frequency similar to that expected in general population. Administer if not otherwise contraindicated.</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>No safety concerns in animal models but lack of human data; may administer vaccine if patient wishes (risk/benefit discussion recommended).</td>
</tr>
<tr>
<td>Lactation</td>
<td>No data available; may administer vaccine if patient wishes.</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

Prevention: Triaging of mRNA Vaccine

Mandatory Reporting to Vaccine Adverse Event Reporting System (VAERS)

- Vaccine administration errors
- Serious (irrespective of attribution to vaccination)
  - Death
  - Life-threatening adverse drug event
  - Inpatient hospitalization or prolongation of existing hospitalization
  - Persistent or significant incapacity or substantial disruption of ability to conduct normal life functions
  - Congenital anomaly/birth defect
- Cases of COVID-19 that result in hospitalization or death

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html