Meeting of the Advisory Committee on Immunization Practices (ACIP)

Feb 24-25, 2021

Stan Grogg, DO, Liaison for American Osteopathic Association (AOA), unedited, draft minutes.

Rabies Vaccine
ACIP approved the following recommendations:
-ACIP recommend a 2-dose (0,7 days) intramuscular rabies vaccine series in immunocompetent person in persons 18 years of age for whom rabies vaccine pre-exposure prophylaxis (PrEP) is indicated.
-ACIP recommends an intramuscular booster dose of rabies vaccine, as an alternative to a titer check, for immunocompetent persons 18 years and older who have sustained and elevated risk for only recognized rabies exposures (i.e., those in risk category #3 of rabies PrEP recommendations table). The booster dose should be administered no sooner that day 21 but no later than 3 years after the 2-dose PrEP series.

Dengue Vaccine
Results of dengue test independent evaluation by Dr. Freddy Medina (CDC). The Dengue vaccine is only good if patients have had Dengue disease. Thus, an appropriate test is needed. Three anti-DENV IgG tests performed with high specificity (97%-98%) and moderate sensitivity (68%-82%) with low Zika cross-reactivity (6%-8%). No decision was made at this time.

Tick-borne Encephalitis (TBE) vaccine

TBE epidemiology: endemic to Europe and Asia. Can be transmitted by unpasteurized dairy products, slaughter of animals, transfusion or transplantation, breastfeeding and laboratory exposure.
Clinical features: Biphasic illness with fever then neurologic illness in Europe and monophasic neurologic illness in Far Eastern and Siberian subtypes. Neurologic illness include meningitis, encephalitis and meningoencephalomyelitis. Case fatality rates: 1-20% with 10-80% neurologic sequelae. Children are usually milder disease than adults.
TBE among military personnel and dependents from 2006-2020: 9 cases with 5 confirmed and 4 probable.
Possible future vote: Should TBE vaccine be recommended for use in persons aged ≥1 year traveling to or residing in TBE risk areas and in laboratory staff working with TBE virus? No vote at this time.

Ebola Vaccines

Several surveys asking groups if Ebola was serious and who would get the vaccine if available.

Conclusion: 54% of the study population expressed interest in receiving the vaccine if eligible and offered the vaccine today**.** When people were given the choice to get vaccinated at different time points (when there was an EVD case in the U.S. or their state), interest in vaccine increased to **81%**

1st Vaccination Policy Issue for Consideration

Should pre-exposure vaccination with the rVSVΔG-ZEBOV-GP vaccine ***be recommended*** for individuals ≥ 18 years of age working as HCP in state-designated Ebola Treatment Centers?

– or –

Should pre-exposure vaccination with the rVSVΔG-ZEBOV-GP vaccine ***be recommended with shared clinical decision making*** for individuals ≥ 18 years of age working as HCP in state-designated Ebola Treatment Centers?

2nd Vaccination Policy Issue for Consideration

Should pre-exposure vaccination with the rVSVΔG-ZEBOV-GP vaccine **be recommended** for individuals ≥ 18 years of age working as staff in facilities within the Laboratory Response Network that handle replication competent Ebola virus (species *Zaire ebolavirus*)?

– or –

Should pre-exposure vaccination with the rVSVΔG-ZEBOV-GP vaccine ***be recommended with shared clinical decision making*** for individuals ≥ 18 years of age working as staff in facilities within the Laboratory Response Network that handle replication competent Ebola virus (species *Zaire ebolavirus*)?

Hepatitis Vaccine

Discussion but no vote was, “Should all unvaccinated adults receive hep B vaccination or should just unvaccinated adults age 59 and under receive Hep B Vaccination.”
Vaccines provide >90% protection among healthy adults who complete the 3-dose series. Rare side effects.

Tomorrow the following vaccines will be discussed:

1. Pneumococcal Vaccines
2. Zoster Vaccines
3. Influenza Vaccines
4. Cholera Vaccine
5. Orthopoxviruses Vaccines

Day 2 of Feb. 25 of ACIP meeting with minutes by Stan Grogg, DO; AOA's liaison member.

6. **Agency Updates**

7. **Pneumococcal Vaccines**
    a. Introduction by Dr. Kathy Poehling (ACIP, WG Chair)
    b. Current epidemiology of pneumococcal disease and pneumococcal vaccine coverage in US Adults by Mr. Ryan Gierke (CDC)
    c. PCV20 Phase study results in adults by Dr. Wendy Watson (Pfizer)
    d. PCV15 Phase 2/3 study results in adults, including adults with underlying conditions by Dr. Ulrike Buchwald (Merck)
    e. Considerations for PCV15 and PCV20 use in adults by Dr. Miwako Kobayashi (CDC)

8. **Zoster Vaccines**
    a. Introductions by Dr. Grace Lee (ACIP)
    b. Risk of Guillain-Barre syndrome (GBS) following recombinant zoster vaccine by Dr. Richard Forshee (FDA)
    c. RZV risk-benefit analysis by Dr. Lisa Prosseer (Univ of Michigan)
    d. Work group interpretation by Dr. Tara Anderson (CDC)
    e. Introduction of the Evidence to Recommendations framework for use of RZV in immunocompromised adults by Dr. Anderson (CDC)

9. **Influenza Vaccines**
    a. Introductions by Dr. Keipp Talbot (ACIP, WG Chair)
    b. Influenza surveillance update by Dr. Lisa Grohskopf (CDC)
    c. Work group considerations by Dr. Grohskopf

10. **Cholera Vaccine**
    a. Introduction by Dr. Pablo Sanchez (ACIP)
    b. Introduction to cholera and cholera vaccines by Dr. Jennifer Collins (CDC)
    c. Vaxchora safety and immunogenicity data by Dr. James McCarty (Emergent BioSolutions)
    d. Work group plans by Dr. Jennifer Collins (CDC)

11. **Orthopoxviruses Vaccines**
    a. Introduction by Dr. Beth Bell (ACIP, WG Chair)
    b. Workgroup considerations by Dr. Brett Petersen (CDC)
    c. Updated policy questions and progress on systematic review by Dr. Agam Rao (CDC)
    d. Summary and next steps by Dr Brett Petersen (CDC)

Day 2 of Feb. 25 of ACIP meeting with minutes by Stan Grogg, DO; AOA's liaison member.

CDC comment:

Problem with children catching up with immunizations

Record number of influenza vaccines given this year and low influenza season

1. **Pneumococcal Vaccines**: anticipated Pfizer PCV and Merck PCV 15 Oct. 2021 ACIP meeting.

Incident if Invasive pneumococcal in children 5 years of age or younger has decreased significantly from 2007-2018 with introduction of PCV13 for children in 2010.

Incident amount adults 19-64 years of age 65 years and older has decreased, too, from 2007-2018 due to PCV13 in children.

Common disease among adults 19-64 years of age 19-64 is 003 (35%), 004 (26%) 19A (11%) and 19F (11%) and 50-64 years if age us 003 (53%), 19A (11%), 004 (10%) and 19F (9%)

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	2	8	9N	10A	11A	12F	15B	17F	20	22F	33F
PCV13																								
PPSV23																								
PCV15																								
PCV20																								

Summary of PCV20

- PCV20 contains PCV13 components + 7 additional serotypes to broaden disease coverage for IPD and pneumonia in adults
- FDA granted Breakthrough Designation for PCV20 recognizing the benefit of conjugate technology in long term protection and importance for prevention of pneumonia
- PCV20 is well tolerated and has a safety profile similar to PCV13 regardless of prior pneumococcal vaccination, and across subgroups of age, sex, and race
- PCV20 is immunogenic across all ages, including in those with chronic medical conditions and regardless of prior pneumococcal vaccination
- PCV20 offers a potentially simplified and impactful approach to the prevention of pneumococcal disease in adults, particularly pneumonia
- PCV20 is currently under review by the FDA for the prevention of IPD and pneumonia in adult 18 years of age and older with target action date of June 8, 2021

Adult PCV20 and PCV 15 will be provided first followed in 2 years for pediatric formulation.

2. **Zoster Vaccines**: 41.3 million doses distributed in U.S from launch – end of 2020. Guillain Barre Syndrome (GBS) is rare. Based on available date, there was consensus among the work group that no change to the current zoster vaccination is warranted at this time. Continued safety monitoring of RZV in VAERS and VSD is warranted.
3. **Influenza Vaccines:** 2020-2021 has been a very low incidence of influenza and the highest number of influenza vaccines given in the US. Only 1 child death for the season. Due to low incidence of influenza, the effectiveness of this year's vaccine is unknown.
4. **Cholera Vaccine:** in June 2016 Vaxchora was recommended by Vaxchora for adult travelers 18-64 years old. FDA for Vaxchora for children and adolescents 2-17 years old Dec 2020. ACIP

reviewing information to possibly recommend for 2 years and older. Choler is endemic in more than 50 countries. Between 2012-2018 64 US patients were identified. Severe form of disease is deadly if not treated with fluids immediately. Vaxchora is a single-dose vaccine with demonstrated safety and efficacy.

5. **Orthopoxviruses Vaccines:** expect ACIP to have vote for vaccine Oct. 2021. Species known to infect humans: Variola (smallpox), Vaccinia (smallpox vaccine, Monkeypox, cowpox and newly discovered aperies (e.g., Akhmeta virus, Alaskapox virus). Monkeypox is increasing in incidence in central and eastern Africa. Two FDA approved vaccines presently: ACAM2000 (indicated for active immunization against smallpox disease for person determined to be at high risk for smallpox infection and Jynneos and indicated for prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection.

Considerations for Revaccination of Laboratory and Healthcare Personnel with JYNNEOS

- **Greater importance for protection of persons working with more virulent orthopoxviruses (e.g., variola and monkeypox)**
  - Individual level - severe systemic disease
  - Societal level - contagious pathogens with epidemic potential
- **Difficult to precisely define the duration of protection for vaccines**
- **JYNNEOS duration of protection is not known**
  - Neutralizing antibodies generally do not persist beyond 6 months following primary vaccination with JYNNEOS
  - A single booster dose of JYNNEOS given 2 years following primary vaccination with JYNNEOS produces a robust increase in neutralizing antibodies
  - Data suggests that a robust anamnestic immune response is present 2 years following primary vaccination

Considerations for Orthopoxvirus Response and Healthcare Teams

- **Working group recognizes the benefit of having cadres of vaccinated public health and healthcare personnel available to respond and care for orthopoxvirus infected individuals**
  - The recent increase in monkeypox cases in Africa and importation into other countries (UK, Israel, and Singapore) suggests the risk of monkeypox exportation is increasing
- **Desire to avoid being overly prescriptive in defining who and how many such persons be vaccinated as assessments of the threat level of these pathogens changes over time**
- **Empower appropriate local, state, and federal public health and antiterrorism authorities to make decisions**

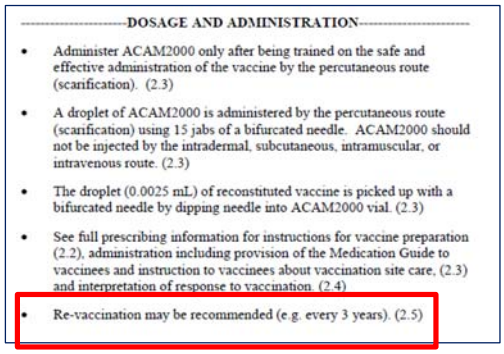
Updated policy questions and progress on systematic review by Dr. Agam Rao (CDC)

Proposed policy question #1

Should persons who are at occupational risk for Orthopoxviruses be offered JYNNEOS® as a vaccination option

Booster doses

- ACAM2000 licensed for smallpox
  - Revaccination recommendations for every 3 years in that population
- JYNNEOS licensed for smallpox and for monkeypox
  - No re-vaccination recommendations

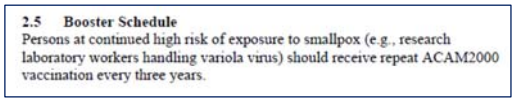


----------DOSAGE AND ADMINISTRATION----------

- Administer ACAM2000 only after being trained on the safe and effective administration of the vaccine by the percutaneous route (scarification). (2.3)
- A droplet of ACAM2000 is administered by the percutaneous route (scarification) using 15 jabs of a bifurcated needle. ACAM2000 should not be injected by the intradermal, subcutaneous, intramuscular, or intravenous route. (2.3)
- The droplet (0.0025 mL) of reconstituted vaccine is picked up with a bifurcated needle by dipping needle into ACAM2000 vial. (2.3)
- See full prescribing information for instructions for vaccine preparation (2.2), administration including provision of the Medication Guide to vaccinees and instruction to vaccinees about vaccination site care, (2.3) and interpretation of response to vaccination. (2.4)
- Re-vaccination may be recommended (e.g. every 3 years). (2.5)

Figures: Screenshots from ACAM2000 package inserts (accessed 2/20/2021)

- ACIP recommendations for ACAM2000 boosters
  - Made through extrapolation of data for Dryvax



2.5 Booster Schedule
Persons at continued high risk of exposure to smallpox (e.g., research laboratory workers handling variola virus) should receive repeat ACAM2000 vaccination every three years.

Proposed policy question #2

Should persons who are at continued risk for occupational exposure to more virulent orthopoxviruses such as smallpox or monkeypox receive a booster dose of JYNNEOS® two years after the primary JYNNEOS series?

– CDC laboratorians who work with smallpox or monkeypox – Research laboratorians who work with monkeypox – Laboratory Response Network (LRN) laboratorians at state health departments who are designated to test for smallpox

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Proposed policy question #4

Should persons who are at continued risk for occupational exposure to orthopoxviruses, *and who received an ACAM2000 primary vaccination,* receive a booster dose of JYNNEOS® as an option to a booster dose of ACAM2000?

Policy question #4

Policy question: Should persons who are at continued risk for occupational exposure to orthopoxviruses, *and who received an ACAM2000 primary vaccination,* receive a booster dose of JYNNEOS® as an option to a booster dose of ACAM2000?

Anticipated Timeline

Meeting of the advisory committee on immunization practices
Feb. 28,2021 (Day 1 of 2)
Highlights, unedited by Stan Grogg, DO liaison for American Osteopathic Association

Welcome and Introduction by Dr. Jose Romero, Chair and Dr. Amanda Cohn (CDC) Executive Secretary. *Before the start of the ACIP meeting, Rochelle P. Walensky, MD, MPH, Director of the Centers for Disease Control and Prevention thanked the ACIP members for their services.*

On Feb 27, 2021, the FDA issued Emergency use authorization (EUA) for. Use of the Janssen COVID-19 vaccine for individuals 18 years of age and older.

Overview of Janssen's single dose COVID 19 Vaccine, Ad26.COV2.S.

Uses Coronavirus spike protein and given I.M via a non- replicating adenoviral vector. After a single dose, vaccine offer substantial protection against COVID-19 as follows:

> **85% vaccine efficacy (VE) against severe disease after 7 days after vaccination and 100% protection hospitalizations and death**.

Most common adverse events included tenderness, redness and swelling around injection site. Some transient systemic events lasting 1-2 days included fatigue, headache, myalgia, nausea and fever.

After reviewing all of the safety and efficacy data, the ACIP voted to recommend the Janssen COVID19 vaccine for 18 years and older.

Next emergency meeting of ACIP tomorrow, March 1, 2021

Monday, March 1, 2021 Emergency meeting of ACIP
Highlights of the March 1, 2021 emergency meeting

Implementation considerations for COVID19 vaccines

ACIP states no preference for any of the 3 authorized vaccines.

Janssen COVID-19 Vaccines: 1 dose, transport and storage at 2-8 C, no diluent/reconstitution necessary.

Clinical Considerations for use of COVID19 vaccines (73 million COVID-19 vaccine doses have been administering in the US through Feb. 27)

a. **Delay the second dose?**

Pros	Cons
Could provide 1 dose protection to a larger number of people over the next several months. If 1 dose protection is high and persists, this could prevent more infections and deaths[1].	Lower neutralization antibodies could be protective against 'wild-type' COVID-19, but not novel variants[2-4]. 1-dose vaccination could leave individuals susceptible to variants, providing selective pressure to increase community transmission of variants[5].
Boosting still likely to be effective, even at longer interval	Estimates of effect for a single dose are imprecise and duration of protection after the 1st dose is unknown.
	Would contradict FDA's Emergency Use Authorization (2-dose series, 3 or 4 weeks apart)

Currently, there are insufficient data to recommended intervals. Important uncertainty around protection from the variants following 1 dose of mRNA COVID-19 vaccines However, if it is not feasible to adhere to the recommended interval, the second dose of Pfizer-BioNTech and Moderna COVID-19 vaccines **may be scheduled for administration up to 6 weeks (42 days) after the first dose.**

Single dose of mRNA vaccine for individuals with confirmed prior SARS-coV-2 infection?

Pros	Cons
Could 'free up' 2nd doses for seropositive persons to be provided to seronegative persons	Current studies included individuals with confirmed antibodies to SARS-CoV-2. Performing large-scale antibody screening prior to vaccination is not feasible
Seropositive persons would not receive 2 doses of reactogenic vaccine	Correlate of protection currently unknown; difficult to extrapolate antibody studies to vaccine effectiveness
	Limited data (small studies) currently
	Would contradict FDA Emergency Use Authorization (2-dose series, 3 or 4 weeks apart)

There are insufficient data to support changes to guidance or recommendations .

Immunocompromised persons: individuals should be counseled about unknow vaccine safety and efficacy profiles in immunocompromised persons (HIV)
Persons with underlying medical conditions: no contraindications to vaccination.

Persons who previously received passive antibody therapy: Vaccination should be deferred for at least 90 day
Persons with known current COVID Infection: Vaccination should be deferred until recovery from the acute illness, no minimal interval between infection and vaccination.
Coadministration of COVID-19 vaccines with other vaccines: COVID-19 vaccine should be administered with minimum interval of 14 days before or after administration of other vaccines. A shorter period interval may be used in situations where the benefits of vaccination are deemed to outweigh the potential of unknown risks. (I.e., tetanus for wound management)
Safety: Local and systemic reactions continue to be most commonly reported following vaccination (VAERS).
Anaphylaxis :reporting rate 2.5 – 4.7 cases per million doses. Several agencies both public and private are reviewing safety data and no significant issues have been detected with any of the FDA approved vaccines.
Pregnancy: COVID during pregnancy has an increased risk of severe illness. Currently, there is limited data on safety of COVID-19 vaccines during pregnancy. Vaccines are inactivated but data is limited and is being studied by vaccine pharmaceuticals. Pregnant people may choose to receive COVID-19 vaccine when eligible. No unexpected pregnancy or infant outcomes have been observed to CAOVID-19 vaccination has been observed as of Feb. 28, 2021.

Contraindications and precautions for COVID-19 vaccines

CONTRAINDICATION TO VACCINATION	PRECAUTION TO VACCINATION	MAY PROCEED WITH VACCINATION
History of the following: • Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to component of the vaccine† • Immediate allergic reaction* of any severity after a previous dose or known (diagnosed) allergy to a component of the vaccine† Actions: • Do not vaccinate. • Consider referral to allergist-immunologist. • Consider other vaccine alternative.†	Among persons without a contraindication, a history of: • Any immediate allergic reaction* to other vaccines or injectable therapies‡ Note: persons with a contraindication to mRNA COVID-19 vaccines have a precaution to Janssen COVID-19 vaccine, and vice versa# Actions: • Risk assessment • Consider referral to allergist-immunologist • 30-minute observation period if vaccinated	Among persons without a contraindication or precaution, a history of: • Allergy to oral medications (including the oral equivalent of an injectable medication) • History of food, pet, insect, venom, environmental, latex, etc., allergies • Family history of allergies Actions: • 30-minute observation period: persons with history of anaphylaxis (due to any cause) • 15-minute observation period: all other persons

Most commonly adverse events reported to VAERS:

Pfizer-BioNTech

Adverse event†	N (%)
Headache	2,322 (20.0)
Fatigue	1,801 (15.5)
Dizziness	1,659 (14.3)
Pyrexia	1,551 (13.4)
Chills	1,508 (13.0)
Nausea	1,482 (12.8)
Pain	1,464 (12.6)
SARS-CoV-2 Test Positive	1,002 (8.6)
Injection Site Pain	997 (8.6)
Pain in Extremity	923 (8.0)

Moderna

Adverse event†	N (%)
Headache	1,353 (23.4)
Pyrexia	1,093 (18.9)
Chills	1,056 (18.3)
Pain	945 (16.3)
Fatigue	888 (15.4)
Nausea	884 (15.3)
Dizziness	792 (13.7)
Injection Site Pain	671 (11.6)
Pain in Extremity	576 (10.0)
Dyspnoea	487 (8.4)

SARS-CoV-2 variants: Feb. 28, 2021 prevalence estimated at 1-2%. Because viruses constantly mutate, new variants are expected. Seem to be greater infectivity, likely increased transmissibility (20%), NOT more clinically severe, current vaccines highly effective.

Variant	Reported cases	No. of states
B.1.1.7	2,400	46
B.1.351	53	16
P.1	10	5

as of Feb. 28, 2021.

Next ACIP scheduled meeting for 2020 are June 24-25 (virtual) and October 28-29, which may be virtual ore live.

Any questions, do not hesitate to contact me at Stanley.Grggg@okstate.edu. Stan