Fearless Defenders of the Immunocompromised Patient

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ADHS 2017 Immunization Conference
Phoenix, AZ

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Objectives

• Describe at least 2 components of the human immune system
• Name two vaccines that are contraindicated in immunocompromised patients
• Name one vaccine that should not be given to contacts of an immunocompromised patient
How Vaccines Are Made

• Toxoids
• Bacterial cultures
• Chicken eggs
• Cell-based
• Recombinant
  – Yeast
  – Insect vector
Live-attenuated Vaccines

- MMR
- Varicella/Zoster
- Nasal influenza (LAIV)
- Rotavirus
- Adenovirus
- Smallpox (vaccinia)
- Yellow fever
- Oral typhoid
- Oral Polio
- BCG

Inactivated/killed Vaccines

- Diphtheria-Tetanus-Pertussis
- Inactivated Polio
- *Haemophilus influenzae* type b
- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- Hepatitis A & B
- Human papillomavirus
- Most influenza
- Rabies
- Inactivated typhoid
- Japanese encephalitis
White blood cells

neutrophil  eosinophil  basophil  monocyte  lymphocyte
Principles of Vaccines and Immunity

• Live-attenuated vaccines are contraindicated in most cases of immunocompromised
• Inactivated vaccines
  – Safe in immunocompromised
  – Likely less effective when immunocompromised
  – Need more doses to maintain immunity
General Principles with Timing of Immunosuppressive Drugs and Live-Attenuated Vaccines

- Do not give live-attenuated vaccines in most cases on when patient has immunosuppression
- Wait ≥ 4 weeks after vaccine before starting immunosuppression
- Resolve immune suppression for adequate time before giving live-attenuated vaccines
General Principles with Timing of Immunosuppressive Drugs and Inactivated Vaccines

- Stop immune suppression ≥ 1 month before vaccinating
- Wait for 2-3 weeks after vaccinating to begin immunosuppression
- Pneumococcal and influenza vaccines are important even if immunosuppression
Low-level Immunosuppression

- Asymptomatic HIV with CD4 T-cells
  - 200-499 cells/μL for adults and ages ≥ 6 years old
  - 15-24% for infants and children

- Prednisone:
  - < 2 mg/kg/day for < 2 weeks
  - ≤ 20 mg/day for < 2 weeks

- Azathioprine: ≤ 3 mg/kg/day

- Methotrexate: ≤ 0.4 mg/kg/week

- 6-Mercaptopurine: ≤ 1.5 mg/kg/day

High-Level Immunosuppression

• Daily steroids ≥ 20 mg for ≥ 14 days
  – (Kids < 10 kg: ≥ 2mg/kg/day for ≥ 14 days)
• HIV: CD4 T-cells < 200 cells/µL (Kids < 15%)
• Cancer chemotherapy
• Immune modulators
• Within 2 months of solid organ transplant
• After Hematopoietic Stem Cell Transplant
  – Variable

Hematopoietic Stem Cell Transplant

• Inactive vaccines: ≥ 6 months after HSCT
  – DTaP/DT/Tdap/Td; polio; influenza
  – PCV13: Start 6-12 months after HCT: 3 doses
    • F/U with PPSV23 ≥ 8 weeks later
  – Hib: ≥ 6 months after HCT: 3 doses

• Live attenuated
  – MMR: ≥ 24 months
  – Varicella: ≥ 24 months on case-by-case

www.cdc.gov/vaccines/pubs/hemato-cell-transplts.htm
Measles Vaccine and Patients with Immune Suppression

- Risk of overwhelming infection
- MMR OK in HIV with CD4 $\geq 15\%$ or $\geq 200/\mu L$
- If measles exposure:
  - Pregnant or severely immune suppressed: IVIG 400 mg/kg within 6 days
- High dose prednisone: Wait for $\geq 1$ month before MMR
- Low dose prednisone: Wait 0-2 weeks before MMR

CDC. 2015 Pink Book
Varicella Vaccine and Patients with Immune Suppression

- Risk of severe infection
- Varicella vaccine OK in HIV with CD4 $\geq 15\%$ or $\geq 200$
- If varicella exposure:
  - VariZIG within 96 hours (up to 10 days) if immune suppressed; pregnant; premies & some newborns
- High dose prednisone: Wait for $> 1$ month before varicella vaccine

## Antibody-Containing Products & MMR and Varicella Vaccines

<table>
<thead>
<tr>
<th>Product/Indication</th>
<th>Dose (mg IgG/kg) and route*</th>
<th>Recommended interval before measles- or varicella-containing vaccine(^{1}) administration (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus IG</td>
<td>250 units (10 mg IgG/kg) IM</td>
<td>3</td>
</tr>
<tr>
<td>Hepatitis A IG</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Contact prophylaxis</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>International travel</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Hepatitis B IG</td>
<td>0.06 mL/kg (10 mg IgG/kg) IM</td>
<td>3</td>
</tr>
<tr>
<td>Rabies IG</td>
<td>20 IU/kg (22 mg IgG/kg) IM</td>
<td>4</td>
</tr>
<tr>
<td>Varicella IG</td>
<td>125 units/10 kg (60–200 mg IgG/kg) IM, maximum 625 units</td>
<td>5</td>
</tr>
<tr>
<td>Measles prophylaxis IG</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Standard (i.e., nonimmunocompromised) contact</td>
<td>0.25 mL/kg (40 mg IgG/kg) IM</td>
<td>5</td>
</tr>
<tr>
<td>Immunocompromised contact</td>
<td>0.50 mL/kg (80 mg IgG/kg) IM</td>
<td>6</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>RBCs, washed</td>
<td>10 mL/kg, negligible IgG/kg IV</td>
<td></td>
</tr>
<tr>
<td>RBCs, adenine-saline added</td>
<td>10 mL/kg (10 mg IgG/kg) IV</td>
<td>3</td>
</tr>
<tr>
<td>Packed RBCs (hematocrit 65%)(^{6})</td>
<td>10 mL/kg (60 mg IgG/kg) IV</td>
<td>6</td>
</tr>
<tr>
<td>Whole blood (hematocrit 35%–50%)(^{6})</td>
<td>10 mL/kg (80–100 mg IgG/kg) IV</td>
<td>6</td>
</tr>
<tr>
<td>Plasma/platelet products</td>
<td>10 mL/kg (160 mg IgG/kg) IV</td>
<td>7</td>
</tr>
<tr>
<td>Cytomegalovirus IGIV</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>IGIV</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Replacement therapy for immune deficiencies(^{5})</td>
<td>300–400 mg/kg IV(^{9})</td>
<td>8</td>
</tr>
<tr>
<td>Immune thrombocytopenic purpura treatment</td>
<td>400 mg/kg IV</td>
<td>8</td>
</tr>
<tr>
<td>Postexposure varicella prophylaxis**</td>
<td>400 mg/kg IV</td>
<td>8</td>
</tr>
<tr>
<td>Immune thrombocytopenic purpura treatment</td>
<td>1000 mg/kg IV</td>
<td>10</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>2 g/kg IV</td>
<td>11</td>
</tr>
<tr>
<td>Monoclonal antibody to respiratory syncytial virus F protein (Synagis (MedImmune))(^{11})</td>
<td>15 mg/kg IM</td>
<td>None</td>
</tr>
</tbody>
</table>

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Zoster Vaccine and Patients with Immune Suppression

- Vaccine decreases Zoster by 51%
- Prolonged pain by 66.5%
- Decreasing efficacy with increasing age
- Vaccine OK in HIV with CD4 $\geq 15\%$ or $\geq 200$
- OK in low-level immune suppression
Rotavirus Vaccine and Immune Suppression

- Do not give to infants with known or suspected immune deficiency
- Screen for family history of SCID
- OK to give to HIV-exposed infants
- OK to give if household has immune suppressed person
- Evaluate patients if persistent diarrhea after rotavirus vaccine
Human Papillomavirus Vaccine Age and Immune Competence

2 doses HPV Vaccine
• 1st dose 9-14 years old

3 doses HPV Vaccine
• 1st dose 15-26 years old
• Immune compromised

MMWR, December 16, 2016
Hepatitis B Virus Vaccine
Age and Immune Competence

Hepatitis B Virus Prevalence

Liver Cancer due to Hepatitis B

2012 CDC Yellow Book

CDC PHIL # 5606
Age-based and Immune Status Response to Influenza Vaccine

• Not < 6 months old
• If 1\textsuperscript{st} influenza vaccine in ages 6 months to 8 years old needs two doses
• Pandemic vaccine
• ≥ 65 year olds
• After hematopoietic cell transplantation
Asplenia or Splenic Dysfunction

CDC PHIL # 2840
Vaccines Needed for Asplenia and Splenic Dysfunction

**Prevnar®13 (PCV13)**

**Pneumovax®23 (PCV23)**

**Meningococcal Vaccines**

(MCV4 and Men B)

*Haemophilus influenzae type b (Hib)*
Pediatric PCV13 Schedule

- Standard: 2, 4, 6 months, 12-15 months
  
  **If no previous PCV13**

- 7-11 months: Two → booster 12-15 months

- 12-23 months: Two

- 24-59 months and healthy: One

- **24-71 months (at higher risk): Two**

www.immunize.org   Item # P2016


CDC. 2015 Pink Book
Unimmunized 24 Months-71 Months
Who Need 2 doses PCV13

• Chronic heart disease (esp. cyanotic & CHF), diabetes mellitus, chronic lung disease, asthma (with prolonged high dose oral steroids)
• Cochlear implant, cerebrospinal fluid leak
• Functional or anatomic asplenia
• Immune compromising conditions including chronic renal failure

➢ Children with risk factors: PPSV23 once 2 y.o

CDC. 2015 Pink Book.
Pneumococcal Vaccines in 6 yo-18 yo
Give 1 dose PPSV23*

• Chronic heart disease
  – Especially cyanotic congenital heart disease and cardiac failure
• Chronic lung disease
  – Asthma if prolonged high dose oral steroids
• Chronic liver disease
• Diabetes mellitus
• Alcoholism

*If not previously immunized with PPSV23

2017 CDC Schedule
Unimmunized 6 yo-18 yo Needs 1 dose PCV 13 and 1 dose PPSV23 if:

- Cochlear implant
- Cerebrospinal fluid leak

➢ PCV13 first when possible

2017 CDC Schedule
Unimmunized 6 yo – 18 yo
Need PCV13, PPSV23, and PPSV23 “Booster”

- Asplenia
- Sickle cell disease & hemaglobinopathies
- Immunodeficiency including HIV
- Chronic renal failure
- Nephrotic syndrome

- Leukemia, lymphoma
- Hodgkin disease
- Generalized malignancy
- Solid organ transplant
- Multiple myeloma
- Iatrogenic immune suppression
  - Medicines
  - Radiation

CDC 2017 Vaccine Schedule
Adult (19-64 yo) Risk Factors Needing Just PPSV23*

- Chronic heart disease (excluding hypertension)
- Chronic lung disease
  - Includes asthma, COPD, emphysema
- Chronic liver disease, cirrhosis
- Diabetes mellitus
- Alcoholism
- Cigarette smoking

*If PPSV23 was not previously given

MMWR, Oct. 12, 2012
Patient Risk Factors Needing Both PCV13* & PPSV23* but No PPSV23 Booster

- Cochlear implant
- Cerebrospinal fluid leak

*If PCV13 and PPSV23 were not previously given

CDC PHIL 13488

MMWR, October 12, 2012
Patient Risk Factors (2 yo – 64 yo) Needing PCV13, PPSV23, and PPSV23 “Booster”

• Asplenia
• Sickle cell disease & hemoglobinopathies
• Immunodeficiency
• HIV
• Chronic renal failure
• Nephrotic syndrome

• Leukemia, lymphoma
• Hodgkin disease
• Generalized malignancy
• Solid organ transplant
• Multiple myeloma
• Iatrogenic immune suppression
  – Medicines
  – Radiation

MMWR, October 12, 2012
CDC 2017 Vaccine Schedule
Pneumococcal Vaccination Tools

Recommendations for Pneumococcal Vaccine Use in Children and Teens

Table 1. Recommended Schedule for Administering Pneumococcal Conjugate Vaccine (PCV13)

<table>
<thead>
<tr>
<th>Child’s age now</th>
<th>Vaccination history of PCV13 and/or PCV7</th>
<th>Recommended PCV13 Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 through 6 months</td>
<td>0 doses</td>
<td>1 dose, 2, 4, 6 months, or 1 month and 6 months</td>
</tr>
<tr>
<td>7 through 11 months</td>
<td>0 doses</td>
<td>1 dose, at 2, 4, 6 months, or 1 month and 6 months</td>
</tr>
<tr>
<td>12 through 15 months</td>
<td>0 doses</td>
<td>1 dose, at 12 months</td>
</tr>
<tr>
<td>16 through 23 months</td>
<td>0 doses</td>
<td>1 dose, at 12 months</td>
</tr>
</tbody>
</table>

Table 2. Recommended Schedule for Administering Pneumococcal Polysaccharide Vaccine (PPSV23)

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Schedule for PPSV23</th>
<th>Revaccination with PPSV23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompetent children and teens with underlying medical condition</td>
<td>1 dose of PPSV23 at age 11-12 years</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Immunocompetent children and teens with immunocompromising condition</td>
<td>1 dose of PPSV23 at 11-12 years</td>
<td>Not indicated</td>
</tr>
</tbody>
</table>

Table 3. Underlying Medical Conditions that Are Indications for Pneumococcal Vaccination

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Condition</th>
</tr>
</thead>
</table>
| Immunocompetent children and teens with underlying medical condition | Chronic heart disease, chronic lung disease, diabetes mellitus, end-stage renal disease, immunocompromising condition, congenital immunodeficiency, congenital heart disease, chronic lung disease, diabetes mellitus, end-stage renal disease, immunocompromising condition, congenital immunodeficiency, congenital heart disease, chronic lung disease, diabetes mellitus, end-stage renal disease, immunocompromising condition, congenital immunodeficiency, congenital heart disease, chronic lung disease, diabetes mellitus, end-stage renal disease, immunocompromising condition, congenital immunodeficiency, congenital heart disease, chronic lung disease, diabetes mellitus, end-stage renal disease, immunocompromising condition, congenital immunodeficiency, congenital heart disease, chronic lung disease, diabetes mellitus, end-stage renal disease, immunocompromising condition, congenital immunodeficiency, congenital heart 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Pediatric vs Adult Intervals between PCV13 and PPSV23

• Pediatric 2-18 yo
  – PCV13 → PPSV23: Minimum of 8 weeks
  – PPSV23 → PCV13: Minimum of 8 weeks

• High Risk Adults 19-64 yo
  – PCV13 → PPSV23: Minimum of 8 weeks
  – PPSV23 → PCV13: Minimum of 1 year

• Adults ≥ 65 yo
  – PCV13 → PPSV23: Minimum of 1 year (Not high risk)
  – PPSV23 → PCV13: Minimum of 1 year

*Pediatrics, Dec 2014; MMWR Oct 12, 2012; MMWR Sept 4, 2015*
Meningococcal Vaccines and Immunocompromised Patients

- Quadrivalent (MCV4)
  - At least two doses for initial series
  - Indicated for HIV
- Mengincococcal B
  - Trumenba needs three doses
- Asplenics need both MCV4 and Men B
Meningococcal B

Meningococcal Vaccine Recommendations by Age and Risk Factor for Serogroup B Protection

Routine Recommendations for Meningococcal Serogroup B Vaccination

For teens and young adults ages 16 through 23 years who wish to be vaccinated. The preferred age is 16 through 18 years.

Give either 2 doses of Bexsero 4 weeks apart, or 2 doses of Trumena on a 0- and 6-month schedule.

Risk-based Recommendations for Persons with Underlying Medical Conditions or Other Risk Factors

For people ages 10 years or older with
- persistent complement component deficiencies
- anatomic or functional asplenia, including sickle cell disease,
- for people ages 10 years or older who are present during outbreaks caused by serogroup B,
- have prolonged increased risk for exposure (e.g., microbiologists routinely working with Neisseria meningitidis)

Give either 2 doses of Bexsero 4 weeks apart, or 3 doses of Trumena on a 0-, 2-, and 6-month schedule.

Note: The two brands of meningococcal B vaccine are not interchangeable. The series must be started and completed with the same brand of vaccine.

Footnotes:
1. Persistent complement component deficiencies include inherited or chronic deficiencies in C3, C5–C9, properdin, factor D, and factor H, or taking eculizumab (Soliris).
2. Seek advice of local public health authorities to determine if vaccination is recommended.

Meningococcal ACWY

Meningococcal Vaccine Recommendations by Age and Risk Factor for Serogroups A, C, W, Y Protection

Routine Recommendations for Quadivalent Meningococcal Conjugate Vaccine (MenACWY)

For teenagers 11 through 15 years
Give a total of 2 doses of MenACWY vaccine. (These 2 doses are recommended at 6–12 months.)

For ages 16 years
Give a total of 2 doses of MenACWY vaccine. (These 2 doses are recommended at 6–12 months.)

For the first year college students, ages 19 through 21 years, living in residence halls
If no history of prior vaccination with MenACWY, give 1 dose of MenACWY.

Risk-based Recommendations for Persons with Underlying Medical Conditions or Other Risk Factors

For people ages 10 years or older with
- persistent complement component deficiencies
- anatomic or functional asplenia, including sickle cell disease,
- for people ages 10 years or older who are present during outbreaks caused by serogroup ACWY,
- have prolonged increased risk for exposure (e.g., microbiologists routinely working with Neisseria meningitidis)

Give a total of 2 doses of MenACWY vaccine. (These 2 doses are recommended at 6–12 months.)

Note: The two brands of meningococcal ACWY vaccine are not interchangeable. The series must be started and completed with the same brand of vaccine.

Footnotes:
1. Persistent complement component deficiencies include inherited or chronic deficiencies in C3, C5–C9, properdin, factor D, and factor H, or taking eculizumab (Soliris).
2. Seek advice of local public health authorities to determine if vaccination is recommended.

www.immunize.org
**Haemophilus influenzae** type b

**Conjugate Vaccines**

- **Primary series**
  - 2 doses PRP-OMP
  - 3 doses PRP-Tetanus toxoid
- **All brands use same schedule ≥ 7 months old**
- **PRP-OMP preferred in Native American children for primary series**
- **Hib vaccine usually only ≤ 59 months**
People Who Need 1 Dose Hib Vaccine At Ages ≥ 5 Years Old

• “Unimmunized”
  – Not received primary series and booster, OR
  – Not received at least one dose of Hib vaccine at ≥ 15 months

• Asplenia
• Sickle cell disease, etc.
• HIV infection (< 19 yo)
• After HSCT (3 doses)

MMWR. February 28, 2014 (RR-1)
Post-exposure Rabies Vaccine

4 Doses

• Vaccine: 0, 3, 7, 14 days
• Rabies immune globulin
  – Day 0

Five doses

• Immune compromised
• Days 0, 3, 7, 14, 21-28
• Rabies immune globulin
  – Day 0

MMWR, March 19, 2010 (RR-2)
Yellow Fever Vaccine
Age and Immune Competence

• **Contraindicated**
  • < 6 months
  • Thymus disorder
  • Immunosuppression
  • HIV CDV < 200/µL

• **Precautions**
  • 6-8 months
  • > 60 years old
  • Pregnancy
  • Breast feeding
  • Asymptomatic HIV
    • CD4 200-499/ µL
    • CD4 15%-24% (< 6 y.o.)

CDC. 2016 Yellow Book
HIV/AIDS and Vaccines

- All recommended inactivated vaccines including influenza
- PCV13 and PPSV23
- Meningococcal (MCV4)
- MMR &/or Varicella once CD4 cells are:
  - $> 15\% \ (< 5 \text{ y.o.})$
  - $\geq 200/\mu\text{L} \ (\geq 5 \text{ y.o.})$
- Zoster vaccine OK if CD4 cells $\geq 200 /\mu\text{L}$

CDC. 2017 Immunization Schedule AAP 2015 Red Book
Chronic Granulomatous Disease

- White blood cells engulf bacteria
- Lysosomes in white blood cells lack hydrogen peroxide
- Unable to kill some bacteria and fungi
- Cannot have live bacterial vaccines; other vaccines OK
Immune Compromised Household Contacts and Vaccines

• Contraindicated
  – Smallpox (vaccinia)
  – Oral polio virus

• Precaution
  – + Varicella vaccine
  – + LAIV
  – + Oral typhoid vaccine
  – + Rotavirus vaccine
  – + Adenovirus
Pregnancy and Vaccines

**Influenza**

*Get the Shot, Not the Flu*

**Tdap**
Breastfeeding and Vaccines

- Contraindications
  - Smallpox (Vaccinia) Vaccine

- Precautions
  - Yellow fever vaccine

- Allowed
  - Other live-attenuated viral and bacterial vaccines

Questions?
CASE STUDY

• A 19-year-old man is on chemotherapy for Hodgkin’s lymphoma. What vaccines can he receive and what vaccines should he not receive?
CASE STUDY

• A 30-year-old woman is on chemotherapy for acute lymphocytic leukemia. She has several young children at home.

• What routine childhood immunizations should her children not receive?
CASE STUDY

• A 15-month-old boy with sickle cell anemia has just received his final Prevnar® 13.
• When does he need to get Pneumovax® 23?
• How many doses of Pneumovax® 23 does he need?
CASE STUDY

• A 62-year-old man with asthma received a course of prednisone, starting with a high dose (60 mg) and tapering off prednisone over twelve days. His last dose of prednisone was five days ago.

• Can this man receive a zoster vaccine today?
CASE STUDY

• A 24-year-old man has well-controlled HIV infection (CD4 cells > 500/µL, low viral load). He received all of his childhood vaccines, but he is seronegative for measles, varicella, and hepatitis B surface antibodies.

• Can he receive vaccines for any of these diseases?

• What other vaccines may he need?
THANK YOU

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