7:45 – 8:45 am
Preventive Medicine that Works: Adult Immunization
SPEAKER
Robert Hopkins, MD, FACP, FAAP

Immunization of Immunodeficient Adults: Avoiding Missed Opportunities to Optimize Care
Robert Hopkins, MD
Professor of Internal Medicine and Pediatrics
Director, Division of General Internal Medicine
University of Arkansas for Medical Sciences

Learning Objectives
- Discuss the current gap between national immunization goals and current immunization rates
- Use the current ACIP guidelines to vaccinate adult patients
- Implement strategies to improve immunization rates in clinician offices
- Review vaccination recommendations for immune compromised patients
  - Cancer
  - Autoimmune diseases/iatrogenic immune suppression
  - Immunodeficiency (Inherited, Acquired)
  - Transplant patients
  - Spleenectomy, Splenic Dysfunction

Influenza Vaccination Coverage among Adults: 2011-12 and 2012-13 Seasons

<table>
<thead>
<tr>
<th>Group</th>
<th>2011-12 (%)</th>
<th>2012-13 (%)</th>
<th>Difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons ≥ 18 yrs</td>
<td>38.8</td>
<td>41.5</td>
<td>+2.7*</td>
</tr>
<tr>
<td>Persons 18-49 yrs, all</td>
<td>28.6</td>
<td>31.1</td>
<td>+2.5*</td>
</tr>
<tr>
<td>Persons 18-49 yrs, high risk</td>
<td>36.8</td>
<td>39.8</td>
<td>+3.0*</td>
</tr>
<tr>
<td>Persons 50-64 yrs</td>
<td>42.7</td>
<td>45.1</td>
<td>+2.4*</td>
</tr>
<tr>
<td>Persons ≥ 65 yrs</td>
<td>64.9</td>
<td>66.2</td>
<td>+1.3*</td>
</tr>
</tbody>
</table>

* Statistically significant difference, P < 0.05.
Adult Vaccination Coverage, Selected Vaccines by Age and High-Risk Status, United States

Pneumococcal, HR 19-64yrs
Pneumococcal, ≥65 yrs
Herpes Zoster (Shingles), ≥60 yrs

Healthy People 2020 Targets: 90% PPV ≥65 yrs, 60% PPV HR 19-64 yrs, 30% Shingles.
Data Source: 2012 NHIS.

Herpes Zoster (Shingles), ≥60 yrs
Pneumococcal, ≥65 yrs
Pneumococcal, HR 19-64yrs

Healthy People 2020 Target: 50% HepB Healthcare Personnel (HCP).
Data Source: 2012 NHIS.

Non-Influenza Adult Vaccination Coverage: Vaccines with Increases from 2011 to 2012

HPV (≥1 dose), Women 19-26 yrs
Tdap, HCP 19-64 yrs
Herpes Zoster, ≥60 yrs
Tdap, 19-64 yrs

Healthy People 2020 Target: 90% PPV ≥65 yrs, 60% PPV HR 19-64 yrs, 30% Shingles.
Data Source: 2012 NHIS.

Why Review This Data?

• WE must be strong advocates for vaccination!
• WE need to work with our practice teams to improve vaccination
• ALL of us are needed to make improvements!!
  – Patients
  – Families
  – Primary Care
  – Specialists
  – Public health
  – Pharmacists
  – Team members

Influenza

Vaccine changes annually, Recommend yearly!!

• 1 dose for adults
  – (Children < 9 yrs, 1st year vaccinated = 2 doses)
• Vaccines: IIV = TIV, QIV, hdIIV, sqIIV, ‘egg-free’. LAIV = LQIV
• US ‘Season’: Vaccine avail. >> ‘disease passed’ (Aug/Sept-April)
• Predominant strain types (Dz and Vax) since 1977:
  – A H1N1, A H3N2, B
• 2013-14 Vaccine strains:
  – A/California/7/2009 (H1N1)-like virus
  – A/Victoria/361/2011 H3N2 virus
  – B/Massachusetts/2/2012–like virus
  – B/Brisbane/60/2008–like virus (QUAD Vaccines only)

IIV = Inactivated Influenza vaccine; QIV = Quadrivalent influenza vaccine; hdIIV = high-dose influenza vaccine; sqIIV = Subcutaneous influenza vaccine; LAIV = Live attenuated influenza vaccine (Quadrivalent).

Influenza Indications

• ALL 6 MONTHS AND OLDER = DON’T WANT FLU
• HEALTHCARE WORKERS
  – High risk for disease (symptomatic and asymptomatic)
  – High risk for transmission
  – If sick not available to provide healthcare...
• PATIENTS @ Greatest Risk severe illness/spread
  – Pregnant woman
  – Newborns and Children <2 years
  – Elderly
  – ‘Medical Comorbidities’
  – Household contacts of high-risk
  – Long-term care/institutionalized, Crowded living conditions
• VACCINATE ALL >6 months
  – IDSA: ‘it may not be beneficial to immunize patients NOT likely to respond’ e.g. current recipients of intensive CTX, patients receiving anti-B cell antibody within 6 months

**Tdap >> Tdap**

- All adults should have (had) a primary Tetanus Series
  - 3 doses of tetanus-containing vaccine over 6+ months
- Tdap Recommendation: All Adults
  - Single dose to replace one dose Td (booster or primary)
  - Including those 65 and older (Added in 2011)
  - May give <10 years following last Td
- Special emphasis: adults with infant contact:
  - HEALTHCARE, Parents, Child Care, etc.
- **2013: Tdap intrapartum** with each pregnancy
  - Regardless of interval prior Tdap (best @ 27-35 weeks)

**Estimated Number of Cases of Invasive Pneumococcal Disease (IPD)* in the US, 2008**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Estimated Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>4,157</td>
</tr>
<tr>
<td>5 to 24</td>
<td>3,417</td>
</tr>
<tr>
<td>25 to 64</td>
<td>14,777</td>
</tr>
<tr>
<td>65 &amp; over</td>
<td>15,418</td>
</tr>
</tbody>
</table>

*IPD: Bacteremia and meningitis.

**Invasive Pneumococcal Disease: Impact in Immune Compromised Patients**

<table>
<thead>
<tr>
<th>Population</th>
<th>Risk Factor</th>
<th>IPD Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults 18-64 years</td>
<td>Undifferentiated</td>
<td>3.8/100,000</td>
</tr>
<tr>
<td>Adults 18-64 years</td>
<td>Hematologic Malignancy</td>
<td>186/100,000</td>
</tr>
<tr>
<td>Adults 65+ years</td>
<td>Undifferentiated</td>
<td>36.4/100,000</td>
</tr>
</tbody>
</table>


**US Pneumococcal Vaccines:**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Body</th>
<th>Year</th>
<th>Population</th>
<th>Indication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPS14</td>
<td>FDA</td>
<td>1977</td>
<td>High risk</td>
<td>Prevent IPD</td>
<td>1st PNC vax</td>
</tr>
<tr>
<td>PPS23</td>
<td>FDA</td>
<td>1983</td>
<td>High risk adult, child</td>
<td>Prevent IPD</td>
<td>Initial then updated now</td>
</tr>
<tr>
<td>PPS23</td>
<td>ACIP</td>
<td>2000</td>
<td>Children 1-59 mo</td>
<td>Prevent PNC Infection</td>
<td>New Vaccine</td>
</tr>
<tr>
<td>PCV13</td>
<td>FDA</td>
<td>2010</td>
<td>Children 6 to 11 mo</td>
<td>Prevent PNC Infection</td>
<td>Changed and additional types</td>
</tr>
<tr>
<td>PCV13</td>
<td>ACIP</td>
<td>2010</td>
<td>Children 6 to 11 mo</td>
<td>Prevent PNC Infection</td>
<td>Changed and additional types</td>
</tr>
<tr>
<td>ACIP</td>
<td>2012</td>
<td>Adults 65+</td>
<td>Prevent IPD, Pneumonia</td>
<td>Immunogenicity Safety data</td>
<td></td>
</tr>
<tr>
<td>ACIP</td>
<td>2012</td>
<td>adults 65+</td>
<td>Prevent IPD</td>
<td>PCV1/13/PPS</td>
<td></td>
</tr>
<tr>
<td>ACIP</td>
<td>2012</td>
<td>adults 65+</td>
<td>Prevent IPD</td>
<td>PCV1/13/PPS</td>
<td></td>
</tr>
</tbody>
</table>

**PPS23 Vaccine Effectiveness**

- **7 Meta-Analyses of RCT (Most recent Cochrane 1/2013)**
  - Conclusions inconsitent: re: cause specific outcomes
  - Agreement: REDUCTION in IPD; NO reduction in ALL CAUSE mortality, pneumonia
- **3 Meta-Analyses of OBS studies**
  - Consistent results: vaccine is effective for prevention of IPD
- **Recent RCT Results**
  - Invasive PNC Dz: Odds ratio (consistent) 0.26 (CI 0.25-0.46)
  - Pneumonia: Odds ratio (signif. heterogeneity) 0.71 (CI 0.52-0.97)
  - Mortality: Odds ratio 0.87 (CI 0.69-1.10)
- **Summary**
  - Data = PPS prevents IPD, not compelling for Pneumonia, Mortality

**Pneumococcal Disease and Vaccination**

- >2000 Adults/yr 65+ die from Invasive Pneumococcal Disease
  - Bacteremia, Sepsis, meningitis
- PPS23 = ‘adult standard’ vaccine = purified capsular polysaccharide
  - 23 types = cause of 88% of bacteremic PNC disease
  - PPS23 has 60-70% efficacy vs. invasive disease (IPD)
  - Immunity lasts at least 5 yrs following 1 dose
  - Local reactions = only common AE
  - BOOSTER if imm before age 65; NOT ‘routinely’ if immunized @ 65+
- PCV13 = ‘pediatric standard’ vaccine = conjugated to protein
  - 13 types = ~50% IPD in immunocompromised adults
  - No published efficacy studies in adults (PCV7 data in HIV, reports)
- CAPITA is available in abstract form only
  - ACIP recommends – combined strategy with PPS23 – in adults
  - Details in subsequent slides

PCV13 Adult Vaccine Effectiveness

**CAPiTA**
- PC RCT PCV13 unimm. 65+ aged adults, Netherlands
  - PCV7 in Dutch infants since 6/2006 to PCV10 in March 2011
- 84,000+ participants PCV13 vs Placebo
  - Primary: 1st bacteremic CAP with vaccine-type PNC
  - Secondary: 1st non-bacteremic CAP, Other IPD
- Serologic and Urinary Ag used to identify PNC infection
- Met Primary and secondary endpoints, reduced PNC infection
- Presented, considered by ACIP pneumococcal group in summer 2014; abstract and secondary reports available.
- DID NOT address sequential PCV13/PPSV23 immunization
- FULL STUDY NOT YET PUBLISHED

Bonten, et al. COMMUNITY ACQUIRED PNEUMONIA IMMUNISATION TRIAL IN ADULTS (CAPiTA) (Abstract ISPPD-0541).

Pneumococcal Immunization

**PCV + PPSV23**
**HIGHEST Risk**
- Immune compromise (IC), Anatomic Risk
- Adults 65+ (NEW 9/2014)

**PPSV23 ONLY**
**INCREASED Risk**
- Smokers, Chronic Medical Conditions – Not Immunocompromised

NO PNEUMOCOCCAL VACCINE
**AVERAGE Risk**
- Young (<65)
- NO Chronic Medical Conditions

Pneumococcal Immunization I

**PPSV23 Alone for Increased Risk**
- All cigarette smokers ≥19 yo
  - Chronic conditions ≥19 yo: Diabetes
    - Lung disease: asthma, COPD
    - Cardiovascular disease
  - Kidney disease (except ESRD, nephrotic syndrome)
  - Immunocompromised: (except ESRD, nephrotic syndrome)
  - Cancer: solid tumors, hematologic malignancies, myeloma, etc.
  - HIV
  - INHERITED and OTHER immune deficiency (CVID, etc.)
  - End-stage kidney disease (ESRD), nephrotic syndrome
  - LTRERESE: Steroids (20 mg/d or greater), biologic immunomodulators, other
  - TRANSPLANTS: solid organ, bone marrow, stem cell

- Immunity lasts at least 5 yrs following 1 dose
- REVACCINATION ONCE after age 65 (PLUS 5 years after initial dose) for those vaccinated prior to age 65
- Adults 65 years and older are in this highest risk group

Pneumococcal Immunization II

**Sequential PCV13 + PPSV23 for Highest Risk**
- **Immunocompromised**
  - 1. Disease:
    - CA: solid tumors, hematologic malignancies, myeloma, etc.
    - HIV
    - INHERITED and OTHER immune deficiency (CVID, etc.)
    - End-stage kidney disease (ESRD), nephrotic syndrome
  - 2. Iatrogenic:
    - MEDS: Steroids (20 mg/d or greater), biologic immunomodulators, other
    - TRANSPLANTS: solid organ, bone marrow, stem cell
  - 3. Asplenia:
    - ANATOMIC: splenectomy (best if immunized prior to)
    - FUNCTIONAL: hemoglobinopathy, sickle cell, other
  - ADA: immunocompromised patients
  - HIV
  - CA: solid tumors, hematologic malignancies, myeloma, etc.
  - INHERITED and OTHER immune deficiency (CVID, etc.)
  - End-stage kidney disease (ESRD), nephrotic syndrome
  - MEDS: Steroids (20 mg/d or greater), biologic immunomodulators, other
  - TRANSPLANTS: solid organ, bone marrow, stem cell

- PCV13 recommended

Pneumococcal ‘Nuts and Bolts’

**INCREASED RISK**
- Pneumococcal polysaccharide (PPSV23) NOW
- Booster once at 65+ yrs/5+ years later (only if initial dose before 64)
- Pneumococcal polysaccharide (PPSV23) vaccine-naïve patients (best practice):
  - PCV13 followed by PPSV23 at least 8 weeks later
  - Booster PPSV23 in 5 yrs AND final PPSV23 at 5 yrs/65+ yrs
- Previously PPSV23-vaccinated patients:
  - PCV13 – at least 1 year after prior dose PPSV23 – followed by
  - Booster PPSV23 5 yrs after prior PPSV23 (and 6 yrs after PCV13)
  - AND final PPSV23 at 5 yrs/65+ yrs
- 65+
  - PCV13 (if Pneumococcal vaccine-naïve) followed 8-12 months later by PPSV23
  - PCV13 at least 1 year after prior (if any)/Pneumococcal vaccine
  - NO additional booster doses if sole indication is age ≥65 years

Flowsheet: Pneumococcal Vaccine

- **ADULTS 65+ YEARS old**
- **ADULTS WITH IMMUNODEFICIENCY**
- **ADULTS WITHOUT IMMUNODEFICIENCY**
- **NEW WHO recommendations**
- **Elderly>65 years**
- **No Prior Adult Pneumococcal Vaccine**
- **No Additional Immunization Needed**

- **No HIGHEST Risk Conditions**
- **HIGHEST Risk Conditions**
- **AVERAGE Risk Conditions**

- **No prior adult pneumococcal vaccine**
- **Recommended**

- **Cochlear Implant**
- **Splenectomy**
- **No other indications**
- **Modified ASPIRE Protocol**

- **1st dose**
- **2nd dose**
- **3rd dose**

*Pneumococcal vaccines should be completed at least 2 weeks prior to Cochlear Implant or Splenectomy, if possible. AMANDA, 1/2015.*
Flowsheet: Pneumococcal Vaccine

Flowsheet: Pneumococcal Vaccine

Centers for Disease Control and Prevention (CDC).
www.cdc.gov/vaccines/schedules/hcp/acip-recs/index.html.

‡65+: ACIP recommends PPSV23 6-12 months after PCV13: CM S payment approved for PCV13 + PPSV23 separated by 1 year.
†Persons receiving PCV13/PPSV23 for CSF leak and Cochlear implant should receive only 1 booster dose PPSV23 after age 65.
*Pneumococcal vaccination should be completed at least 2 weeks prior to Cochlear Implant or Splenectomy, if possible.

RHHMD

HiB Vaccine

• Haemophilus influenzae, type B
  – Highly contagious Gram-negative bacteria – common in children until vaccination
  – More common in adults since childhood vaccination routine
  • All children (3-4 doses) since ~1990

• Adult recommendations (NEW 2014)
  – Hematopoetic Stem Cell Transplant Recipient
  • 3 Dose series @ 6-12 months post transplant
  • Separate doses by minimum 4 weeks
  • Regardless of prior vaccination history
  – NOT Routinely recommended in HIV (Low risk)
  – Spleenectomy (Functional/Anatomic), Hemoglobinopathy
  • 1 dose if not previously vaccinated
  • At least 14 days prior to splenectomy


Meningococcal Indications: Adult

• College freshmen who will live in a dormitory
• Asplenia (anatomic or functional)
• Terminal complement deficiencies
• Travelers to ‘at-risk areas’: Sub-Saharan Africa, December-June
  – Required for entry into Saudi Arabia/Mecca during Hajj
• Microbiologists (possible occupational meningococcal contact)
• Prefer Conjugate for persons <56 and revaccination
  – Prefer Polysaccharide for those 56+ and needing only 1 dose
• HIV: NOT AN INDICATION (NEW 2014– Low absolute risk)

Meningococcal Vaccine

• 3 Current vaccines: Types A, C, Y, W-135
  – MPS4: Polysaccharide vaccine (subcut, 1 dose)
    • Available since 1978, fair efficacy, OK if conjugate not available
    • Preferred for primary vaccination >65 years
    • MCV4 (2 brands): Conjugate vaccines (intramuscular, 1 dose)
      • Approved 2005, 2010
      • Preferred for primary vaccination <65 years and boosters
      • Booster recommended @ 5 years if high risk persists
    • 1 Current vaccine: Type B
      • Approved fall 2014
      • Not incorporated into ACIP schedules (as of 2/2015)

ACIP Adult Hepatitis A, B Indications

Hepatitis A
– Chronic Liver Disease
  – Includes chronic HCV, HCC
  – MCM
  – Injection Drug Users
  – Travel to endemic area
  – Recipients of clotting factors
  – Lab workers

Diagnosis: HBV
– High dose vaccine: any ESRD pt
  – ICD-10: additional recommendations, immune compromised pt

Hepatitis B
– Diabetes mellitus (DID GVE, MD MAY give)
– Chronic Liver Disease Includes HCV
– MSM
– Injection Drug Users
– Travel to endemic area/smear
– Clothing factor recipients
– >1 sexual partner/6 mo, STD clinic
– HEALTHCARE WORKERS
– HIV
– Household and sexual contacts of HBV patients
– Make prison inmates, correction staff
– Developmental disability facility patients and staff
– Alaska and pacific island natives
– Any others that want to prevent HBV

http://www.cdc.gov/vaccines/schedules/hcp/prof/prof-hepb.html

Hepatitis A, B

• Vaccination currently recommended in all US children
• Vaccines
  – HAV (2 manufacturers)
  – HBV (2 manufacturers)
  – Combination HAV/HBV
  – HBV High-Dose (FDA, ACIP-> ESRD, IDSA has additional recommendations)
• Do NOT need to start over if series is delayed
• Multiple approved regimens: individually or in combination
  – HAV: 2 doses @ 6+ month interval
  – HBV: 3 doses @ 0, 1, 6 m
  – Dose and alternate regimens are different for Hemodialysis patients
  – Combination: 3 doses @ 0, 1 m, 6 m.
  – Accelerated Combo: 4 doses @ 0, 7 d, 21-30 d, booster @ 1 y


HPV

• Vaccines:
  – HPV4: Types 6,11,16,18 3 dose series @ 0, 2 m, 6 m
  – HPV2: Types 16,18 3 dose series @ 0, 1-2 m, 6 m
  – HPV5: Approved 12/10/2014
  – HPV4 or HPV2 in Women 11-12 (b-26):
    – Prevent Cervical CA (Pre-CA), Genital Warts, ‘other HPV disease’
  – Contraindications/Cautions:
    – Local reaction, syncope, bronchospasm reported
    – Not recommended in pregnancy- no proven AE (administer after delivery)
    – Immunosupression can reduce efficacy

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5602a1.htm.

MMR, Varicella

• 2 doses: immune competent children, selected adults
  – Healthcare workers, Int’l adoption, daycare workers, women (nonpregnant)
  – Most born before 1957 have immunity to M, M, R [1980 for V]
• Contraindications:
  – HIGHLY immune compromised
  – Acute/severe illness, allergy to vaccine component
  – Recent transfusion (ANY product which contains Ab)
  – Active untreated TB
  – Pregnancy
    – MMR: not pregnant x 3 months after vaccine- prevent NRS
    – Varicella: Avoiding all live vaccines (risk lower than MMR)

http://www.cdc.gov/mmwr/preview/mmwrhtml/00053391.htm.

Zoster

• Vaccinate HEALTHY 60+ adults
• ACIP: Not immune compromised
  – FDA approved from age 50 (Coverage? Cost/Benefit?)
  – Regardless of prior Zoster (opinion: wait 1 year)
  – No need to test and/or vaccinate for Varicella before administration
• Contraindications
  – Pregnancy
  – Anaphylactic Hypersensitivity to Neomycin, Gelatin
  – No need to defer for ‘at risk contacts’ – transmission risk low
  – No need to defer if recent transfusion, Ab containing products
• Adverse events
  – Occasional mild varicella-like rash at vaccine site
  – 1 DOSE. Frozen vaccine: Give within 60 minutes, 0.65 ml SQ,Deltoid
  – Duration of protection: At least 4 years. No booster.

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm.

Immunodeficiency (ID) Cartoon

<table>
<thead>
<tr>
<th>Immune Compromise</th>
<th>Humoral</th>
<th>Cellular</th>
<th>Complement</th>
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</thead>
<tbody>
<tr>
<td>Cancer (+: Cancer Treatment)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Stem Cell Transplant</td>
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<td>Splenectomy/Aplasia (Anatomic, Functional)</td>
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</tr>
<tr>
<td>Renal Failure/Nephrotic</td>
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<td>HIV</td>
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<tr>
<td>Immunosuppressive Treatment</td>
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<tr>
<td>Inherited Immunodeficiency</td>
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<tr>
<td>CSF Leak/Cochlear Imp</td>
<td>Anatomic Barrier Defect – Not ID…</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

= Impaired Immune Component

Highly Immunosuppressed

• Inherited combined immunodeficiency (SCID)
• Currently receiving cancer chemotherapy
• First 2 months after solid organ transplant
• HIV with CD4 <200 cells/mm³ (<15% in kids)
• Prednisone ≤20 mg/d (equivalent) x 14+ days
• Biologic Immunomodulators
  – Anti-B Cell Antibody, TNF-a Blocker, Others
• Variable interval after stem cell transplant (3+ mo)
  – More prolonged for allogeneic than autologous
  – More severe with GVHD, MUD

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm.
Low-Level Immunosuppression

- Asymptomatic HIV+ CD4 200-499 cells/mm^3
- Prednisone <20 mg/d (or equivalent) x 14+ days
  - Includes patients on alternate-day steroids
- Others:
  - Methotrexate <0.4 mg/kg/week
  - Azathioprine <3 mg/kg/d
  - 6-Mercaptopurine <1.5 mg/kg/d
  - Higher doses = Highly (Cancer Chemotherapy)

General Principles: Vaccination of Immune Compromised Adults

- Highly immunosuppressed: NO Live virus vaccines
  - Balance risk vs benefit in low-level immune suppression
- Evidence-based ‘rules’
  - MMR, VAR given to HIV patients with LOW-LEVEL immunosuppression
  - NO OPV in SCID (Proven high VAPP risk)
- Opinion/Theory-based recommendations
  - LAIV not recommended in Immunosuppression
    - Even if risk is low, we have other options!
  - VAR not recommended in Inflammatory Bowel Disease patients on 6-mercaptopurine
  - Theoretic risk of disseminated OKA (Vaccine)-strain varicella

- Vaccinate prior to immunosuppression if possible
- Live vaccines
  - Administer ≥4 weeks pre-immunosuppression
  - AVOID within 2 weeks of start of immune suppression
- Inactivated vaccines best given >2 weeks prior to immune suppression
- Evidence shows no causal relationship between onset or exacerbation of
  - MS, SLE, vasculitis, RA, Juvenile Idiopathic Arthritis
- With any of the following:
  - MMR
  - Tetanus (Includes Tdap, DTaP, DT, Tetanus Toxoid…)
  - Influenza
  - Hepatitis A
  - Hepatitis B
  - HPV
- Predominance of evidence
  - Vaccines are not important triggers of disease flares
  - AND should not be withheld

Vaccine Effectiveness and Safety in Immunocompromised 1

- Sickle Cell Disease
  - 93% reduction IPD with introduction of PCV 7
  - Direct benefit +/- herd immunity… 12
- ILV in HIV and in Heart Transplant
  - Reduction in disease 13
- VAR and reduction in severe varicella disease
  - Kidney and Liver transplants 16-18
  - Children with Leukemia and HIV 19-20

Rubin, et al. CID. 2014 58 (1Feb).
Vaccine Effectiveness and Safety in Immunocompromised 2

- A number of studies report ‘protective’ post-vaccine antibody levels vs pathogens
- BUT
  - Many VPD without established ‘protective Ab levels’
  - e.g. Pertussis
  - Some immunosuppressed conditions require higher ‘protective Ab levels’ than those established for patients without the condition
  - e.g. Splenectomy: Hib, Pneumococci
  - Imperfect correlation Ab levels with protection
  - Are Ab functional in immune suppressed?
  - Ab levels may not correlate with protection from diseases
  - e.g. Zoster

VDP = Vaccine-preventable diseases.

Rubin, et al. CID 2014;58 (1Feb).

Cancer and Immunization

Best to vaccinate prior to treatment: Live ≥4 weeks, Inactivated ≥2 weeks

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Prior to (During) Chemotherapy</th>
<th>≥3 mos CTX, ≥6 mo Anti-B-cell Ab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Vaccine</td>
<td>ACIP Schedule (NOT LAIV)</td>
<td></td>
</tr>
<tr>
<td>TetG, TetV Vaccine</td>
<td>ACIP Schedule (no GA specific recommendation)</td>
<td></td>
</tr>
<tr>
<td>Pre- pneumococcal vacs</td>
<td>PCV13 +PPSV23 then PPSV</td>
<td>ACIP Schedule (for Non-IC)</td>
</tr>
<tr>
<td>DTP Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>Varicella Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>Meningococcal vacs</td>
<td>PCV13 +PPSV23 then PPSV</td>
<td>ACIP Schedule (for Non-IC)</td>
</tr>
<tr>
<td>HPV Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>MMR Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
<tr>
<td>Hep A Vaccine</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>MMR Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
</tbody>
</table>

Immunization: Autoimmune Disease with Iatrogenic Immune Suppression

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>BEFORE Immunosuppression</th>
<th>LOW-LEVEL Immunosuppression</th>
<th>HIGH-LEVEL Immunosuppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Vaccine</td>
<td>ACIP Schedule</td>
<td>Annual using IIV (NO LAIV)</td>
<td></td>
</tr>
<tr>
<td>TetG, TetV Vaccine</td>
<td>ACIP Schedule (1st series, 1 adult TetG, q10 year Tet, qPreg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre- pneumococcal vacs</td>
<td>PCV13 +PPSV23 then PPSV</td>
<td>ACIP Schedule (for Non-IC)</td>
<td></td>
</tr>
<tr>
<td>DTP Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal vacs</td>
<td>PCV13 +PPSV23 then PPSV</td>
<td>ACIP Schedule (for Non-IC)</td>
<td></td>
</tr>
<tr>
<td>HPV Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>NOT RECOMMEND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hep A Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>NOT RECOMMEND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>NOT RECOMMEND</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hemoglobinopathy, Asplenia, CSF Leaks and Cochlear Implants

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Hemoglobinopathy, Asplenia</th>
<th>CSF Leaks and Cochlear Implants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Vaccine</td>
<td>Annual (IDSA: NOT LAIV)</td>
<td></td>
</tr>
<tr>
<td>TetG, TetV Vaccine</td>
<td>ACIP Schedule (1st series, 1 adult TetG, q10 year Tet, qPreg)</td>
<td></td>
</tr>
<tr>
<td>Pre- pneumococcal vacs</td>
<td>PCV13 +PPSV23 then PPSV</td>
<td>ACIP Schedule (for Non-IC)</td>
</tr>
<tr>
<td>DTP Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>Varicella Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>Meningococcal vacs</td>
<td>PCV13 +PPSV23 then PPSV</td>
<td>ACIP Schedule (for Non-IC)</td>
</tr>
<tr>
<td>Hep A Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>HPV Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>MMR Vaccine</td>
<td>ACIP Schedule (CACTX alone not indication)</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>NOT RECOMMEND</td>
<td></td>
</tr>
</tbody>
</table>

Solid Organ Transplants, ESRD, Nephrotic Syndrome

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Pre-Transplant</th>
<th>Start 2-4 Months Post-TXP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Vaccine</td>
<td>Annual (IDSA: NO LAIV)</td>
<td>Annual/Outbreak—Immediate</td>
</tr>
<tr>
<td>Tet, Tol Vaccines</td>
<td>ACIP Schedule (1st series, 1 adult Tol, 8-15 year Tol, q10yr)</td>
<td>Begin 4 months after Txp</td>
</tr>
<tr>
<td>Pneumococcal Vaccine</td>
<td>PCV13+PPV23 then PPV23 booster in 5 years and at 65+ years</td>
<td></td>
</tr>
<tr>
<td>HB Vaccine</td>
<td>ACIP Schedule (SOT Alone not indicated)</td>
<td></td>
</tr>
<tr>
<td>Meningococcal Vaccine</td>
<td>ACIP Schedule (SOT Alone not indicated)</td>
<td></td>
</tr>
<tr>
<td>Hep A Vaccine*</td>
<td>ACIP: Chr Liver or only. IDSA also in HAV nonimmune SOT Card</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>ACIP Schedule to age 26 (SOT Alone not indication)</td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td>ACIP: 2 doses +4 wks pre-TXP</td>
<td></td>
</tr>
<tr>
<td>VAR</td>
<td>ACIP: 2 doses +4 wks pre-TXP</td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>IDSA: Var immune HSV-1y, 4 wks pre-TXP</td>
<td></td>
</tr>
</tbody>
</table>

Pre-Stem Cell Transplants

- Stem cell transplant patients require more thorough 'immunologic ablation' than other transplants
- Stem cell recipient should be 'ACIP UTD' for all vaccines
  - Live virus vaccines (if indicated) ≥4 weeks prior to IS
  - NO MMR, VAR, ZOS within 4 weeks of stem cell harvest
  - Non-live virus vaccines ≥2 weeks before immune sup/TXP
  - DO NOT vaccinate donor to benefit recipient in allogeneic Txp
- ASSUME Immunologic 'restart' after Txp
  - 'Immunologically naive' immune system after stem cell engraftment
  - BUT immunization likely less effective than 'normals' with ongoing immunosuppression, esp. Chronic graft vs host disease

Post-Stem Cell Transplant

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendation</th>
<th>Interval AFTER Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Vaccine</td>
<td>IV Annualy (NO LAIV)</td>
<td>Begin 8 months after Txp</td>
</tr>
<tr>
<td>Tet, Tol Vaccines</td>
<td>3 dose series (1st)</td>
<td>Begin 8 months after Txp</td>
</tr>
<tr>
<td>Pneumococcal Conjugate*</td>
<td>3 dose series (4 if ChR-GVH)</td>
<td>Begin 3-6 months after Txp</td>
</tr>
<tr>
<td>Pneumococcal Pneumococcal Vaccine</td>
<td>3 dose series</td>
<td>Begin 3-6 months after Txp</td>
</tr>
<tr>
<td>Variola Polyvalent Vaccine*</td>
<td>1-dose (NOT Chronic GVH)</td>
<td>1 year after Transplant</td>
</tr>
<tr>
<td>Hep A Vaccine</td>
<td>ACIP Schedule</td>
<td>Begin 4 months after Txp</td>
</tr>
<tr>
<td>Meningococcal Vaccines</td>
<td>11-18 yr: 2 dose series</td>
<td>Begin 3-6 months after Txp</td>
</tr>
<tr>
<td>Hep A Vaccine</td>
<td>3-dose series, Bar (10-12yr)</td>
<td>Begin 3-6 months after Txp</td>
</tr>
<tr>
<td>HPV</td>
<td>ACIP Schedule (HPV 4)</td>
<td>Begin 4 months after Txp</td>
</tr>
<tr>
<td>MMR</td>
<td>IFP NA, HB b-C GVH, Neg = Ab</td>
<td>2 yrs after Txp, 8 mos afterIS</td>
</tr>
<tr>
<td>VAR</td>
<td>IFP IFD, HB b-C GVH, Neg = Ab</td>
<td>2 yrs after Txp, 8 mos afterIS</td>
</tr>
<tr>
<td>Zoster</td>
<td>IDSA: Var immune HSV-1y, 4 wks pre-TXP</td>
<td></td>
</tr>
</tbody>
</table>

Primary Immunologic Targets

- NO MMR, VAR, ZOS within 4 weeks of stem cell harvest
- 'Immunologically naive' immune system after stem cell engraftment
- BUT immunization likely less effective than 'normals' with ongoing immunosuppression, esp. Chronic graft vs host disease

Healthcare Workers

- Key in implementation of Adult Immunization
  - Education
    - Multiple studies: MD recommendation increases patient Vax uptake
  - Need preventive benefits 'for themselves'
    - Potential source for disease transmission
      - Patients
      - Other staff
      - Communities
      - Families
    - Potential for VPD to impair patient care
    - Adversely affect efficiency
    - Prevent Hcw from working with (their) patients

Household Contacts and Caregivers

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Vaccine</td>
<td>ACIP Schedule: IV, LAIV OK Except SCID, new/GV+SCT</td>
</tr>
<tr>
<td>Other Inactivated Vaccines</td>
<td>ACIP Schedule</td>
</tr>
<tr>
<td>MMR</td>
<td>ACIP Schedule</td>
</tr>
<tr>
<td>VAR</td>
<td>ACIP Schedule (IC avoid contact if skin lesions)</td>
</tr>
<tr>
<td>Zoster</td>
<td>ACIP Schedule (IC avoid contact if skin lesions)</td>
</tr>
<tr>
<td>RotaVirus</td>
<td>ACIP Childhood Schedule (IC Avoid diarrhea x 4 weeks)</td>
</tr>
<tr>
<td>OPV</td>
<td>SHOULD NOT BE ADMINISTERED</td>
</tr>
<tr>
<td>Travel</td>
<td>CDC Travel Schedule</td>
</tr>
<tr>
<td>Yellow Fever Vaccine</td>
<td>CDC Travel Schedule</td>
</tr>
</tbody>
</table>

Recommendations for Healthcare Workers

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>HCW Recommendation</th>
<th>Other Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Annual HCW vac. decr. risk to Pt +</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (PPS, PCV)</td>
<td>NO HCW Specific Rec.</td>
<td></td>
</tr>
<tr>
<td>MMR*</td>
<td>2 doses</td>
<td></td>
</tr>
<tr>
<td>VARicella</td>
<td>2 doses</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>NOT immune, born before '57, IS</td>
<td></td>
</tr>
<tr>
<td>Hep B</td>
<td>NOT immune, IS</td>
<td></td>
</tr>
<tr>
<td>HDV</td>
<td>NO HCW Specific Rec.</td>
<td></td>
</tr>
<tr>
<td>Td/Tdap</td>
<td>Rec, all women 9-28 yr</td>
<td></td>
</tr>
<tr>
<td>HAV</td>
<td>Only sel. lab workers</td>
<td></td>
</tr>
<tr>
<td>Meningococcal (MCV)</td>
<td>Only sel. lab workers</td>
<td></td>
</tr>
<tr>
<td>Zoster*</td>
<td>No HCW Specific Rec.</td>
<td></td>
</tr>
</tbody>
</table>

*Live Virus Vaccines

Adapted from data located at http://www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm.
Tools

- CDC Adult Immunization Scheduler
  - http://www.cdc.gov/vaccines/recs/Scheduler/AdultScheduler.htm
- CDC/ACIP Recommendations
  - http://www.cdc.gov/immunizations
  - http://www.cdc.gov/vaccines/pubs/ACIP-list.htm
- IAC Summary of Adult Immunization Rec’s
- IDSA Vaccination Rec’s for Immune compromise
  - CID 2014: 58 (1 FEBRUARY)