Update on Immunizations

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Greatest Medical Triumph of the 20th Century

<table>
<thead>
<tr>
<th>Disease</th>
<th>1998 Morbidity</th>
<th>% Decreased</th>
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</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>48164</td>
<td>100</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>175885</td>
<td>100</td>
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<tr>
<td>Pertussis</td>
<td>147271</td>
<td>95</td>
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<tr>
<td>Hemorrhagic</td>
<td>1974</td>
<td>61</td>
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<tr>
<td>Paralytic Polio</td>
<td>16316</td>
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<tr>
<td>Measles</td>
<td>503282</td>
<td>100</td>
</tr>
<tr>
<td>Mumps</td>
<td>152209</td>
<td>100</td>
</tr>
<tr>
<td>Rubella</td>
<td>47740</td>
<td>304</td>
</tr>
<tr>
<td>Hib</td>
<td>20000</td>
<td>61</td>
</tr>
<tr>
<td>Total</td>
<td>1112186</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

AAP, Red Book 2000

Types of Vaccines

<table>
<thead>
<tr>
<th>Live Attenuated</th>
<th>Killed Whole Organism</th>
<th>Purified Protein or Polysaccharide</th>
<th>Engineered</th>
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</thead>
<tbody>
<tr>
<td>Smallpox, 1798</td>
<td>Rabies, 1985</td>
<td>Typhoid, 1896</td>
<td></td>
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<tr>
<td></td>
<td>Cholera, 1896</td>
<td></td>
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<tr>
<td></td>
<td>Plague, 1897</td>
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<tr>
<td></td>
<td>BCG, 1927</td>
<td>Pertussis, 1926</td>
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<tr>
<td></td>
<td>Yellow fever, 1939</td>
<td>Influenza, 1936</td>
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<tr>
<td></td>
<td>Rickettsia, 1938</td>
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<tr>
<td>After World War II (Advance of cell culture)</td>
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<tr>
<td>Polio</td>
<td>Polio</td>
<td>Pneumococcus</td>
<td>Hepatitis B</td>
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<tr>
<td>Measles</td>
<td>Rabies</td>
<td>Meningococcus</td>
<td>Pertussis</td>
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<tr>
<td>Mumps</td>
<td>Japanese enceph</td>
<td>Hib</td>
<td></td>
</tr>
<tr>
<td>Rubella</td>
<td>Hepatitis A</td>
<td>Hepatitis B</td>
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<tr>
<td>Adenovirus</td>
<td>Tick-borne enceph</td>
<td>Typhoid (Vi)</td>
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<td>Ty21a</td>
<td></td>
<td></td>
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<tr>
<td>Pertussis</td>
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</tbody>
</table>

Plotkin and Orenstein, Vaccine, 1999

Disclosures

• None

MMWR 2011
Spacing the Administration of Killed and Live Antigens

- ≥ 2 Killed antigens
  - May be given at any interval between doses
- Killed and live antigens
  - May be given at any interval between doses
  - Exception: cholera and yellow fever
- ≥ 2 Live antigens
  - 4 weeks if not given simultaneously
  - Exception: OPV in relation to MMR or Ty21a

Mitigating Factors to Response

- Preformed antibodies
  - IV Ig, blood, plasma, and platelet products
  - MMR, TIG, VZIG, RIG, HBIG, RSV-Ig, anti-Rh(D)
- Impairs live viral replication
  - Varicella, measles >rubella, mumps >>yellow fever (YF), typhoid
- Recommendations
  - Ig and killed antigen: no time
  - Ig and live vaccines (depends on dose of Ig)
    - Live → Ig: none-OPV, YF, Ty21a; 3m-mumps, RA27/3; 5m-mumps, VZV
    - Consider follow-up serologic testing
- Antibiotic use
  - Live bacterial vaccines (e.g., Ty21a)

Contraindications

- Bleeding risks (e.g., IM injections)
  - Hemophilia, anti-coagulation
- Immunosuppressed
  - Medications, pregnancy, HIV, transplantation
- Infection, rejection, diminished responsiveness
- Live antigens: MMR, YF, OPV, VZV
  - Fetal risk: rubella, VZV (registry: 800-986-8999)
  - Household contacts: OPV, VZV
  - Prednisone (>20mg qd for ≥14 days, wait 1m post discontinuation)
- Hypersensitivity
  - Egg: influenza, YF, measles, mumps
  - Gelatin: MMR, YF, VZV
  - Abx: neomycin, streptomycin, or polymyxin B
  - Thimerosal: DTP, HBV, influenza, Japanese encephalitis
- Current moderate/severe illness

Specific Vaccines

- dT, Tdap
- MMR
- Influenza
- Pneumococcus, Menningococcus, HiB
- Varicella and Zoster
- HAV, HBV
- Rotavirus
- HPV
- Malaria

Case

30 yoM w/ no PMHx presents w/ diffuse muscle spasms
dT → Tdap

- **Dosing**
  - Boost every 10 years
  - 5 years if high risk behaviors anticipated

- **Who:** all adults
  - 45-65 cases tetanus annually in US w/ 60% in adults
  - Serologic studies show that >40% and 40-80% of 60+yo and 11% and 62% of 18-39yo w/o neutralizing antibody to tetanus and diphtheria respectively

- **PEP: Wound management**
  - History of <3 doses adsorbed tetanus toxoid
    - Clean, minor wounds: dT
    - Other wounds: TI (250 U IM) and dT
  - History of >3 doses
    - Clean, minor wounds: boost if >10 years since last dT
    - Other wounds: boost if >5 years

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**Pertussis**

- **N=2781, 1:1 randomization**
- **Acellular pertussis vaccine**
- **Median 22 months follow-up**
- **0.7 to 5.7% of illness due to pertussis**
- **Incidence of pertussis 370-450 per 100,000 pt-years**
- **Vaccine 92% effective**

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**Tdap**

- **2005 two formulations approved in US**
  - ADACEL (sanofi pasteur); licensed 7/10/05; single booster; 11-64 year olds. 0.5 mL IM
  - BOOSTRIX (GSK); single booster; 10-18 year olds

- **Reccs**
  - 19-64 yr olds -- use as next tetanus booster
  - Can be given as close as 2 years from last boost
  - Priority to boost following groups
    - Close contacts of infants/elderly and health care workers
  - Not licensed for decennial re-booster

- **Contraindications**
  - Allergy to prior tetanus vaccination;
  - Adults with history of unexplained encephalopathy w/ in 7 days of a vaccine with a pertussis component;
  - Ongoing/evolving neurologic condition

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**19yoM who arrived in Boston 2 days earlier from Italy. He is complaining of 2 days of fever, coryza and rash.**
MMR I

- **General**
  - Contains neomycin and gelatin, made from chick-embryo cell culture, live attenuated

- **Mumps (Jeryl Lynn strain)**
  - >95% w/ Ab after 1 dose
  - AEs: rarely orchitis, parotitis

- **Rubella (RA 27/3)**
  - >95% w/Ab after 1 dose
  - About 10% of young adults are not immune
  - AEs: Fever (5-15%), rash (5%), joint pain (up to 25% of young women 7-21d post vaccination)
  - Avoid in pregnancy

60yoM presents with SOB, fever, and cough productive of rusty-brown sputum

MMR II

- **Measles**
  - 95-98% w/ Ab after 1st dose, >99% post 2nd dose
  - 1963-7 inactivated vaccine – atypical measles
  - Recent IgG use interferes w/ immunogenicity
  - AEs: 5-15% w/ T>103 5-12d post vaccination, CNS <1/million doses, decreased plat seen 2-3 wks post vaccination, may decrease ppd reactivity for 4-6 weeks
  - Who
    - Everyone born after 1956, colleges typically require documentation of 2 dose
    - Recommended for HIV+ patients if not severely immunosuppressed

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  - >95% w/Ab after 1 dose
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Influenza

- **Inactivated, multivalent (2 type A and 1 B) adapted periodically to the strains expected to circulate in the winter (A/New Caledonia/311/01, A/Panama/2007/1, B/Hong Kong)**
  - 1 dose annually in autumn,
  - Efficacy: 56% resp illness, 50% pneumonia hosp, 68% death

- **Who**
  - Age≥50, CRF, DM, cardiac dz, pulm dz, HIV, immunosuppressed, nursing home residents
  - Health care workers, household contacts of at risk patients

- **AEs**: local reaction 10%
  - Caution in the setting of egg allergy

- **PEP**: consider chemoprophylaxis (rimant/aman, oseltamivir/zanamivir)
FluMist
- Cold adapted, live attenuated, intranasal, 2.5ml/nares
- Decrease febrile URI 24%, HCW visit 18-37%, Abx use 41-45%
- FDA approved (6/03) for healthy people, age 5-49
- AE: runny nose (45%), sore throat (28%), tiredness (26%), cough (14%), chills (9%)
- Contraindications: >50yo, pregnancy, egg allergy, h/o GBS, immunocompromised, recent resp illness (72h), or those w/cardiac, pulmonary, metabolic, or renal dz
- Possible transmission of vaccine strain thus avoid in those who are in contact w/ immunosuppressed patients
- Avoid antiviral therapy for 2 weeks
- Expensive

Pneumococcus
- Pneumovax
  - 23 valent polysaccharide vaccine
    - 88% of strains causing bacteremia/meningitis
  - 0.5mL IM (25ug of each polysaccharide)
  - About 70-81% effective, bacteremia
  - Consider boost in 5yrs
- Prevnar
  - 7 valent protein conjugated vaccine, rec for children
- Who?
  - Lung disease, CHF, age>65, immunosuppressed, DM, cirrhosis, corticosteroid use, transplantation, asplenic, nephrotic syndrome, renal failure, HIV, CSF leaks
  - About 1/3 of 50-64yo have an indication

Menningococcus and HiB
- Menningococcus
  - Serogroups A, C, Y, and W-135(50ug of each)
  - ?Boost in 5 years
  - Who: asplenic, hypocomplementemia, properdin deficiency, travelers, college students
  - Consider in setting of serogroup A/C outbreak
  - Types of vaccine
    - Polysaccharide
    - Conjugate (preferred in adults <55 years old)
- HiB
  - Part of the childhood vaccination schedule
  - Various conjugate formulations: HbOC, PRP-OMP, PRP-T, PRP-D
  - Who: consider in asplenic patients

Case
72 yoM w/ no PMHx developed right facial pain and rash over 1 week.

81 yoM w/ lymphoma developed cough and a disseminated rash.
Varicella Vaccine

- Oka strain, ~1350 pfu/dose
- Given SC, 0.5 mL
- Varivax (Merck) licensed 1995
  - Initially approved for
    - 1 dose in 1-12 year olds
    - 2 doses in >13 year olds
- Seroconversion
  - dose 78-82% after 1 dose
  - >99% after 2nd
- ProQuad (MMR-Varicella) licensed 2005
- Store frozen

Varicella Vaccine Recs

- 2 doses in children (12-15 m and 4-6 yrs of age)
- Catch-up for those who received 1 dose
- >13 years old w/o evidence for varicella immunity
- HIV infected individuals (CD4 >200)
- 2nd dose at 3 months
- Outbreak control
- PEP (within 3-5 days of exposure)
- Postpartum women
- School requirements

Vaccine for Zoster?

- Oxman et al NEJM 2005;352:2271-84
  - N= 38,546
  - Used Oka/Merck strain
    - Decreased incidence of zoster by 51.3%
    - Decreased postherpetic neuralgia by 66.5%

Varicella Vaccine

- Live attenuated, Oka strain, licensed 3/95
- 0.5 mL SQ/IM, 2 doses 4-8 weeks apart
- Seroconversion
  - 78-82% after 1 dose
  - >99% after 2nd dose
- Issues
  - Mild varicella syndrome in 1-4%, 5-26 days post vaccination
- Who
  - All children, occupation exposure, non-pregnant women of childbearing age, travelers
  - Immunocompromised patients and household contacts
  - 70-90% of individuals w/o h/o infection are seropositive

Burden of Varicella over Time

- MMWR: Vol 56 RR-4; June 22, 2007
- VZV: Varicella Vaccine
  - Live attenuated, Oka strain, licensed 3/95
  - 0.5 mL SQ/IM, 2 doses 4-8 weeks apart
  - Seroconversion
    - 78-82% after 1 dose
    - >99% after 2nd dose
  - Issues
    - Mild varicella syndrome in 1-4%, 5-26 days post vaccination
  - Who
    - All children, occupation exposure, non-pregnant women of childbearing age, travelers
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HZ Vaccine Recs

• **Who**
  – Persons ≥ 60 years old with a history of varicella

• **Contraindications**
  – Significant immunosuppression

HAV

• **Vaccines**
  – Havrix (1440 ELU) and Vaqta (50U):
    • 2 doses 1mL IM at 0 and 6-12m
    • Seroconversion at 15d 88-93% and 28d 95-99%

• **AEs:** local discomfort

• **Who**
  – Travelers, individuals under custodial care, persons with hepatitis B+C infection, chronic liver disease, high-risk behaviors (IVDU, MSM), or receive clotting factors

• **PEP**
  – ig w/in 14d of exposure (85% effective, 0.02 mL/kg)
  – Vaccination

HBV I

• **Recombinant vaccine to HBsAg**
  – Recombivax and Engerix-B
    • 10-20 ug/mL of antigen w/ aluminum hydroxide
    • 40 ug/mL formulation for dialysis and immunosuppressed patients

• **Series:** 3 doses at 0, 1, and 6 months
  – Do not vaccinate in buttock (diminished immunogenicity)

• **Obtain f/u serology in persons at risk thus PEP affected**
  (e.g., IVDU, MSM, STDs, health care workers)
  – If seronegative then revaccine up to 3 more times
  – Boost in hemodialysis pts when titer <10 mIU/mL

HBV II

• **Who**
  – Children, travel, hepatitis C infection, liver disease, household contacts of HBV infected persons, health care workers, high-risk behaviors (e.g., IVDU, MSM)

• **PEP**
  – Unimmunized or immunized nonresponder: HBIG (0.06 mL/kg) w/in 14d and vaccinate
  – Immunized and known responder: nothing
  – Immunized and unknown response: check titer if negative then Rx as nonresponder

• **First vaccine preventable cancer:** hepatoma

Rotavirus

• **Worldwide**
  – Most common cause of severe gastroenteritis in children
    – Accounts for ~1/3 hospitalizations for diarrhea
    – Responsible for >500,000 deaths/year in >5 year olds

• **Nearly every child in the US is infected by rotavirus by the age of 5 years**

Rotavirus Vaccines

• **Rotarix (GSK)**
  – Monovalent derived from human G1 strain
  – Replicates in GI tract, 50% children may shed briefly

• **Rotavirus**
  – Live, oral vaccine
  – 5 bovine (WC3) reassortant rotaviruses (G1, G2, G3, G4, G9)
  – ~2x10^6 infectious units of each component/dose
  – Stable in fridge for 24 months
  – No thimerosal

• **Rotateq (Merck); licensed 2006**
  – Live, oral vaccine
  – 5 bovine (WC3) reassortant rotaviruses (G1, G2, G3, G4, G9)
  – ~2x10^6 infectious units of each component/dose
  – Stable in fridge for 24 months
  – No thimerosal

MMWR: Vol 55 RR-12; Aug 2006
Rotavirus Vaccine Recs
- Rotateq
  - 3 dose regimen at 2, 4, and 6 months
  - 1st dose must be given between 6-12 wks of age
  - 3rd dose must be given before 32 wks of age
- Rotarix
  - 2 doses 4-8 weeks apart

HPV Associated Disease
- Estimated in US in 2007
  - 6.2 million new HPV infections
  - 11,000 new cases of cervical cancer
  - 3,700 cervical cancer deaths

HPV Vaccine(s)
- Gardasil (Merck)
  - Licensed 8/18/06
  - Quadravalent HPV L1 protein (major capsid protein) adjuvanted with alum
  - Serotypes 6, 11, 16, 18
  - Given 0.5 mL, IM at 0, 2, 6 months
- On the horizon – Cervarix (GSK)
  - Bivalent HPV L1 protein adjuvanted with AS04
  - Serotypes 16, 18
  - Given 0, 1, 6 months
Some HPV Vaccine Unknows

- Efficacy appears to be linked to vaccination prior to serotype exposure
  - Age of vaccination
- Duration of protection
- Role of vaccinating males
- Serotype replacement
- Impact on non-cervical HPV associated malignancies
- Impact on cervical cancer screening
Kaplan-Meier Curves Showing the Cumulative Incidence of at Least One Episode of Malaria Infection during the Study

References

2) Guide for Adult Immunization by the ACP
3) MMWR at www.cdc.gov/mmwr
   - Dec 2006;55(No.RR-15) Pg1-48 General Recommendations on Immunization (ACIP and AAFP)
4) Vaccines by Plotkin and Orenstein. WB Saunders 1999
5) Vaccines and Vaccinations, G Ada, NEJM 2001;345:1042-50

Q1) Which vaccine is not live attenuated?
   A) MMR
   B) Hepatitis B virus
   C) Zoster Vaccine
   D) Yellow Fever
   E) Oral Polio Virus
Q2) The Zoster vaccine is indicated for which patient group?

A) Those who have had zoster in the past
B) Those who are immunosuppressed
C) Anyone older than 50 years
D) Anyone older than 55 years
E) Anyone older than 60 years