Non-IgE Mediated Vaccine Reactions 2012 Updates

Learning Objectives
Participants will be able to . . .

- Discuss non-IgE mediated adverse reactions to vaccines and their management
- Describe the 2011 Institute of Medicine findings on causality of adverse event-vaccine pairs reviewed including a new approach to categorizing evidence and classifying level of evidence for or against a causal association.
- Understand the importance of live virus vaccines and their risk to some but not all immunodeficient patients.

Vaccines & 21st Century
Evolving Standards & Knowledge

- Prescription drugs
  - Diversity of responses seen post-marketing
  - Vaccines as "orphan prescription drugs"
  - Apply standards for prescribing any drug to vaccines
- Safe and effective: population to individual
  - FDA & Public Health/CDC perspectives
  - Operational medicine perspective
  - Provider perspective
  - Patient/Individual vaccinee perspective
- Need: improved life cycle safety surveillance
  - Understanding gender, racial/ethnic/genetic differences
  - Evidence-based practice improvements

Knowledge Gaps & Unmet Needs
Beyond Epidemiology and FDA Guided Studies

"Undermining the public trust . . . "
1st: "Inadequate ongoing, credible education of the public and health professions concerning the known and unknown benefits and risks of vaccines."
2nd: grossly insufficient investment in research on the safety of immunization.

Adverse Event Following Immunization
AEFI – International "VAERS"

All AEFI Reports (not yet assessed for link to vaccine)

Adverse Reaction versus Adverse Event

Side Effect
Versus
"Serious or Impacting"
Adverse Reaction Impact Criteria?
Level of Pain?
Quality of Life?
Duration?
Recurrence?

From the desk of RJM Engler, MD: 2013
Non-IgE Mediated Vaccine Reactions 2012 Updates

Many Items to Consider for Complex Reactions

Cause or Coincidence?

The Xs & Y of Immune Response to Viral Vaccines


YFV Vaccination Induces TLR-Interferon Signaling F>M

Genes expressed in women (pink), men (blue), or both (white) 2–10 days after YFV17D vaccination


Muscle aches 416 Male – 185 Female 2.0% - 3.0%
Fatigue 1.2% - 2%
Headache 1.4% - 0.5%
Joint ache 1.4% - 1.4%
Loss of appetite 0.2% - 0.5%
Nausea and vomiting 0.6% - 1.4%
Fever 1.1% - 4.5%
Chills 0.3% - 0.8%
Diarrhea 0.3% - 0.8%
Shortness of breath 0.3% - 0.2%
Itching over entire body 0.5% - 0.6%

TAMC Anthrax Vaccine Study 601 HCW’s: Severity “4”

Gender Difference in Immune Responses and Side Effect Severity

Gender
More important determinant of immune response than dose or age groups

Reduced dose influenza vaccine ↓ impacting side effects for women ↓ Local reactions ↓ Impacting systemic side effects

Clinical Relevance
Individuals with Complaints of More Severe, Impacting FLU-like Symptoms after Influenza Vaccine: Should dose be lowered?

Geometric Mean Titers: 18-49 Years

Geometric Mean Titers: 50-64 Years
An Expanding Platform of Challenges in Immunization

- Updates and Highlights
  - Tdap/Td: New vaccine information sheet 24Jan12
  - Tdap: Fever over 102°F (about 1 in 100 adolescents and 1 in 250 adults), Headache (1 in 300), nausea, vomiting, diarrhea, stomach ache (up to 3 in 100 adolescents and 1 in 100 adults)
  - Dose after 20 weeks pregnancy, elderly in contact with infants
  - NEW: with each pregnancy even if less than 3 years apart!
  - Risk of repeated Tdap every few years with new guidelines
- Influenza vaccine ingredients:
  - Flumist: egg, MSG, gentamicin, gelatin, thimerosal (multi-dose), latex (single)
  - Fluzone: egg, formaldehyde, gelatin, thimerosal (multi-dose), latex (single)
- Afluria: egg, neomycin, polymyxin B, thimerosal (multi-dose vials)
- Influenza vaccines
  - Oculorespiratory syndrome: not anaphylaxis

Oculo-respiratory Syndrome

2000 Canadian Case Definition of ORS
- At least one of the following symptoms: bilateral conjunctivitis, respiratory problem (chest tightness, difficulty breathing, wheezing), and oropharyngeal edema, or any combination of these conditions within 24 hours of receiving the vaccine.

Evolved case definition to 2 symptoms for discrimination between patients

- Attack Rate of 3.4% (95% CI 2.4-4.4%)
- Evolved case definition to 2 symptoms for specificity
- Age-group distribution (years) of ORS cases for 2000-2001 to 2003-2004 influenza seasons (n=3264)

Canadian Influenza Vaccines Oculo-Respiratory Syndrome

Randomized crossover DBPC trial (vaccine-placebo 7 days apart): Recurrence Rates?
- 2 FLU Vaccines used
- Risk difference in ORS symptoms 24 hours after receiving vaccine vs placebo
- Recurrence 34% (21-47%) vs placebo 15% (9-28%)

Deoxycholate
- Virus-splitting acid
- Used in vaccines linked to febrile seizures in Australia and Canadian ORS
- Manufacturing changes linked with reductions in ORS

Etiology Identified?
Vaccine Production with Deoxycholate -- Linked to Febrile Seizures & ORS;
AEFI Prevented Through Vaccine Modifications!

Symptoms in Primary & Revaccinated Smallpox Vaccine Recipients

(A) Percentage With Indicated Symptom And
(B) Mean Number of Clinic Visits

At Which Symptom Was Reported

Cytokine Response to Smallpox Vaccine • JID 2010:201 (15 April) • 1183-1191

New Onset Systemic Symptoms Following Smallpox (SPX) Immunization

Many Unmet Needs
- Personalized Medicine
- Issues within the Immunization Clinical Mission
- Targeting Safety, Efficacy & Acceptability
- Evidence Based Practice Improvements & Enhance Adverse Events Reporting

Kinetics of Serum Cytokines after Primary or Repeat Vaccination with the Smallpox Vaccine

J Infect Dis. 2010; 201:1183-1191

IFN-γ, TNFα, P-10, MIG, IL-6, etc.

Host

Cytokine Patterns Associated with Adverse Events after Smallpox Immunization

Pattern of 4 cytokines (108 cytokines and chemokines measured pre/post 1st SPX)
- Discriminated between patients with and without Adverse Events (fever, adenopathy, rash):
  - ICAM-1, CD54
  - G-CSF
  - Eotaxin
  - TIMP-2

TIMP-2: Natural inhibitors of the matrix metalloproteinases - a group of peptidases involved in degradation of the extracellular matrix and with ability to directly suppress the proliferation of endothelial cells and of quiescent tissues in response to angiogenic factors.
**Myocarditis After Smallpox Vaccine**

<table>
<thead>
<tr>
<th>Data Source</th>
<th>N</th>
<th># Cases</th>
<th>Percent %</th>
<th>Cases: 1 in</th>
</tr>
</thead>
<tbody>
<tr>
<td>New York - 1947</td>
<td>-6,000,000</td>
<td>1</td>
<td>0.00002%</td>
<td>~50,000</td>
</tr>
<tr>
<td>Finland 1877-1879</td>
<td>60,000</td>
<td>10</td>
<td>0.02%</td>
<td>~5,000</td>
</tr>
<tr>
<td>CDC-Dryvax® 2004 (Epi)</td>
<td>40,449</td>
<td>21</td>
<td>0.05%</td>
<td>~2,000</td>
</tr>
<tr>
<td>DoD-Dryvax 2004 @ (Epi)</td>
<td>~1,200,000</td>
<td>140</td>
<td>0.01%</td>
<td>~10,000</td>
</tr>
</tbody>
</table>

Prospective Studies¹

Helle (Finland) 1974 | 234 | 8 | 3.4% | ~30 |
Ahborg (Sweden) 1963 | 286 | 3 | 1.0% | ~100 |
Acambis FDA Data²³⁴ | All Studies | 15 punctures |
Acambis-Dryvax®All¹ | 868 | 3 | 0.35% | ~289 |
Acambis-ACAM²⁰⁰⁹¹² | 2983 | 7 | 0.23% | ~426 |


**Associated with Eosinophilic Hypersensitivity Myocarditis**

**Antibiotic** | **Anti-inflammatory** | **Others To Consider**
--- | --- | ---
Amprolium B | Indomethacin | Vaccinia, vaccines?
Ampicillin | Oxphenbutazone | Other drugs?
Chloramphenicol | Phenylbutazone | Parvovirus B19
Penicillin | Dicetan | Other viruses?
Streptomycin | Chlorothalidone | Acetaminophen | Metfudopa
Cephalosporin | Hydrochlorothiazide | Phenindione | Sulfonamide
Sulfasalazine | Spironolactone | Sulfasalazine | Other
Sulfisoxazole | Antimyelopine | Anticonvulsant | Methyldopa
Anticonvulsant | Methyldopa | Pheneridine | Sulfonamide
Anticonvulsant | Methyldopa | Phenytoin | Sulfonamide
Carbamazepine | Oxyphenbutazone | Carbamazepine | Sulfonamide
Antibiotic | Oxyphenbutazone | Carbamazepine | Sulfonamide
Para-amino-salicylic acid | Amphenyline | Antibiotic | Sulfonamide

**Inactivated Trivalent Influenza Vaccine and Pneumococcal Vaccine (PCV13)**

- **Febrile Seizures**
  - Occur in 2-5% of all children: generally benign outcome
  - INCREASED RATE in children, especially 12-23 months, compared with those who received vaccines separately
  - ACTUAL RISK: 1 additional seizure in every 2225 children vaccinated
  - WHAT IS RISK of delaying one vaccine at well-baby visits?

- **Why Vaccinate with FLU Vaccine?** MMRW Sep 16, 2011
  - 2010-11: 115 children in US died from influenza
  - 50% of deaths occurred in children < 5 years of age
  - 17/74 (23%) had been vaccinated with TIV

- **Why Vaccinate with Pneumococcal Vaccine?**
  - Pneumococcal disease: 1 million deaths annually worldwide (<5 yrs)
  - 13% of all infections in children, major cause of pneumonia
  - Rates of disease reduced in all ages with vaccine: 20% ↓ pneumonia

**Autoimmune Responses Influenza Vaccine** (Lupus. 2012;21(2):175-83.)

- **Autoimmune Inflammatory Rheumatic Disease (AIRD)**
  - Prospective cohort study with 6 months follow-up: 218 patients AIRD
  - 50 vaccinated with seasonal FLU, 6 with H1N1, 104 with both
  - 58 non-vaccinated controls
  - Healthy controls: 41 subjects (9 seasonal FLU, 3 H1N1, 18 both)

- **Outcome Measures: Autoantibodies**
  - ANA, ENA, aCL IgG/IgM, anti-beta2-glycoprotein
  - Antinuclear antibody (ANA), anti-extractable nuclear antigen (anti-ENA), antinuclearpil (aCL) IgG/IgM antibodies, anti-beta 2-glycoprotein I (anti-B2GPI)
  - Baseline, 1 (AIRD only) and 6 month post vaccine

- **Results**
  - Transient changes in autoantibody production in AIRD & controls
  - Small subset: tendency toward anti-ENA development (ANA+ pts)
  - H1N1 – aCL induction in some

**Non-IgE Mediated Vaccine Reactions 2012 Updates**

**Neurologic Immune Inflammatory Reactions**

**Recurrent Guillain-Barré Syndrome Following Vaccination**

- GBS: acute polyradiculopathy, probably autoimmune
  - Reported as a rare but serious vaccine adverse event
  - ACIP recommends no influenza vaccine to individuals with a prior history of GBS within 6 weeks of a prior FLU vaccine if not at higher risk of severe complications from influenza illness

- **Northern California Kaiser Study** Clin Infect Dis 2012;54(8):800-4
  - 1995-2006: hospital discharge diagnoses, neurology reviewed GBS
  - 550 cases of GBS over 33 million person-years, 6 with recurrence
  - 898 vaccines given to 279 of these individuals with 405 TIV vaccine doses given to 107 individuals with prior Dx of GBS
  - 15 had GBS with 6 weeks following FLU vaccine – 2 revaccinated without recurrence
  - Limitations of study: selection bias so at greatest risk for recurrence were not revaccinated

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[From the desk of RJM Engler, MD: 2013](http://cid.oxfordjournals.org/content/54/6/800)
Non-IgE Mediated Vaccine Reactions 2012 Updates

### Adverse Events Following 12 & 18 Months Vaccinations

- Population-based, self-controlled case series
  - 271,495 12-month vaccinations
  - 184,312 18-month vaccinations
- Relative incidence of ER visits or hospital admissions
  - Consecutive one day intervals following vaccination
  - Compared to control period 20-28 days later
  - Post-hoc analysis: reasons for ER visits, average acuity score for 12-month vaccines. NOTE: No increase in hospitalizations seen
- Results
  - 4-12 days post 12 months vaccines, RR incidence: 1.33 (1.29-1.38)
  - 10-12 days post 18-month vaccines: RRI 1.25 (1.17-1.33)
  - 1 excess event for every 730 children vaccinated
- Future Studies: Risk Factors and/or Prevention?

### Defining Vaccine Injury: Evidence of Causality

- 2008 Table of Reportable Events Following Vaccination
  - Based on independent review of existing evidence
  - [http://vaers.hhs.gov/resources/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf](http://vaers.hhs.gov/resources/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf)
- 2011 Institute of Medicine (IOM) Report
  - 12000 peer-reviewed articles considered, 158 vaccine AE pairs
  - Goal: Updated scientific basis for review and adjudication of claims of vaccine injury by the VICP
- Lesson learned: “some issues simply cannot be resolved with currently available epidemiologic data, excellent as some of the collections and studies are.”
- Outcomes: 134 “insufficient evidence to accept or refute a causal relationship”, 24 consensus for or against causal association

### 2011 Institute of Medicine

#### Adverse Effects of Vaccines: Evidence & Causality

  - New Categories of Causation: Agreed on:
    - Reviewed 8 of 12 covered vaccines: varicella zoster, influenza (not H1N1), hepatitis B, HPV, MMR, Hepatitis A, meningococcal, tetanus-containing vaccines (AP)
- Evidence convincingly supports a causal relationship
  - Example: paralytic polio and oral polio vaccine
- Evidence favors acceptance of a causal relationship
  - Evidence is strong and generally suggestive, although not firm enough to be described as convincing or established.
- Evidence is inadequate to accept or reject a causal relationship
  - The evidence is not reasonably convincing either in support of or against causality; evidence that is sparse, conflicting, of weak quality, or merely suggestive—whether toward or away from causality—falls into this category. Where there is no evidence meeting the standards described above, the committee also uses this causal conclusion.
- Evidence favors rejection of a causal relationship
  - The evidence is strong and generally convincing, and suggests there is no causal relationship.

### IOM Report Summary – 1

#### Evidence Supports Causal Relationship

Evidence Convincingly Supports a Causal Relationship

- Varicella Vaccine:
  - Disseminated varicella infection rash after vaccination
  - Disseminated varicella infection with subsequent infection resulting in pneumonia, meningoitis, or hepatitis in individuals with demonstrated immunodeficiencies
  - Vaccine strain viral reactivation (appearance of chickenpox rash months to years after vaccination)
  - Vaccine strain viral reactivation with subsequent infection resulting in meningitis or encephalitis (inflammation of the brain)
  - MMR Vaccine
  - Linked to disease called measles inclusion body encephalitis
    - In very rare cases, can affect people whose immune systems are compromised and usually occurs within a year of acute infection or vaccination

#### Evidence Favors Acceptance of a Causal Relationship

(Evidence favors acceptance of 4 vaccine AEFI: strong and generally suggestive but not firm enough to be convincing)

- HPV vaccine and anaphylaxis
- MMR vaccine and Transient Arthralgia (temporary joint pain) in female adults
- MMR vaccine and transient arthralgia in children
- Certain trivalent influenza vaccines used in Canada in some recent years and mild/temporary ocuiorespiratory syndrome
  - Conjunctivitis, facial swelling, upper respiratory symptoms including cough and wheezing

### IOM Report Summary – 2

#### Evidence Supports Causal Relationship

Evidence Convincingly Supports a Causal Relationship

- MMR Vaccine
  - Linked to disease called measles inclusion body encephalitis
    - In very rare cases, can affect people whose immune systems are compromised and usually occurs within a year of acute infection or vaccination
    - Linked to febrile seizures
    - Generally benign and hold no long term consequences
    - NOTE: enhanced risk when MMRV used versus MMR & V
- 6 Vaccines Linked to Anaphylaxis
  - MMR, varicella zoster, influenza, hepatitis B, meningococcal, tetanus-containing vaccines
- Injection of Vaccine, Independent of Antigen Involved
  - Syncope (risk of fall complications described)
  - Deltoide bursitis (frozen shoulder); shoulder pain, loss of motion

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From the desk of RJM Engler, MD: 2013
Non-IgE Mediated Vaccine Reactions 2012 Updates

IOM Report Summary – 1
Evidence Favors Rejection of a Causal Relationship

- MMR vaccine and
  - Autism
  - Type 1 diabetes
- DTaP vaccine and
  - Type 1 diabetes
- Inactivated influenza vaccine
  - Bell’s palsy (weakness of facial nerve)
- Inactivated influenza vaccine
  - Exacerbation of asthma or reactive airway disease episodes in children and adults

IOM Report Summary – 2
Evidence Favors Rejection of a Causal Relationship

- MMR vaccine and
  - Autism
  - Type 1 diabetes
- DTaP vaccine and
  - Type 1 diabetes
- Inactivated influenza vaccine
  - Bell’s palsy (weakness of facial nerve)
- Inactivated influenza vaccine
  - Exacerbation of asthma or reactive airway disease episodes in children and adults

Human Statue of Liberty 1918
18,000 men preparing for war at Camp Dodge, Iowa

Base to Shoulder: 340 feet
Right Arm: 340 feet
Widest part of arm holding torch: 12 1/2 feet
Right thumb: 35 feet
Thickest part of body: 29 feet
Left hand length: 30 feet
Face: 60 feet - Nose: 21 feet
Longest spike of head piece: 70 feet
Torch and flame combined: 980 feet

Number of men in:
Flame of torch: 12,000
Torch: 2,800
Right arm: 1,200
Body, head & balance of figure only: 2,000

TEAMWORK & COMMUNICATION
Questions?

Vaccine Healthcare Centers Network
Supporting Quality Immunization Healthcare
Building Trust Through Improved Understanding of Biodiversity in Vaccine Responses

www.VHCinfo.org/www.vaccines.mil
Clinical Consultations 24/7: 1-866-210-6469

Countermeasure Injury Compensation Program (CICP)

- Health Resources and Services Administration
  - HRSA houses CICP: created by PERP Act
    - PERP: Public Readiness & Emergency Preparedness Act
  - PERP Act (http://www.hrsa.gov/countermeasurescomp/)
    - Provides compensation to individuals for serious physical injuries or deaths from pandemic, epidemic, or security countermeasures
    - Identified in declarations issued by Secretary of HHS
    - Pursuant to section 319F-3(b) of the Public Health Service Act
    - Provides broad liability protections to cover
      - Manufacture and testing
      - Development and distribution
      - Use of designated covered countermeasures

- Vaccine Injury Compensation Program (VICP): distinct

CICP Coverage
Populations and Countermeasures

- Coverage: Secretarial declaration specifies . . .
  - Categories of threats or conditions for which countermeasures are recommended.
  - The time period of liability protections are in effect
  - The population of individuals protected
  - The geographic areas for which the protections are in effect.
- Countermeasures currently covered include vaccines, antibiotics or devices used to protect against the following:
  - Influenza (pandemic, not seasonal)
    - Seasonal influenza vaccines covered by VICP
  - Anthrax
  - Botulism
  - Smallpox
  - Acute Radiation

Filing deadline: Within 1 year of vaccination
If a possibility, FILE as placeholder!
Contact or refer patients to the Vaccine Healthcare Centers Network

Immunization Tool Kit (7th Edition)

The VHCN offers four ways for military healthcare professionals to view and receive the comprehensive immunization information included in the Tool Kit:

1. Order a Printed Tool Kit
   - The Tool Kit is a pocket-sized immunization reference book
   - Printed, bound for flexibility in what you carry, laminated (can spill coffee on it); ideal for use in the field.

2. Download the Tool Kit (pdf format)
   - The Tool Kit is a pocket-sized immunization reference book

3. View Tool Kit as a book online
4. Access Immunization Tool Kit Online
   - Access for links to online information & resources
Viewing the Tool Kit on an iPhone

1. On the iPhone, go to the Apple Store and search for PDF Reader Lite.
2. Install the PDF Reader application on your iPhone.
3. Go to www.vhcinfo.org using Safari on your iPhone and click on Tool Kit on the main menu.
4. Click on "Download Tool Kit (pdf). Item # 2
5. When the main page of the Tool Kit appears, touch the screen on the iPhone once. In the top corner you will see "Open in Adobe Reader", tap this and the Tool Kit will now be viewable in Adobe Reader.
6. Any time you open the Adobe Reader application on your iPhone, you will be able to access the Tool Kit.

Users will not need Wi-Fi or internet connection to view the Tool Kit once it is saved to Adobe Reader. Use the tools available with the Adobe Reader application to search or bookmark pages in the Tool Kit for quick and easy access.

COMING SOON: Apps for iPod, android, etc.


Outcomes of Immunizations in Infancy & Childhood

JAMA. 2007;298(18):2155-2163

Vaccination with 7 of the 12 routinely recommended childhood vaccines prevents an estimated 33 000 deaths and 14 million cases of disease in every birth cohort, saves $10 billion in direct costs in each birth cohort, and saves society an additional $33 billion in costs that include disability and lost productivity.

International Focus
Immunization Safety Importance

• Brighton Collaboration
  – Adverse Events Following Immunization (AEFI) Case Definitions
• World Health Organization (WHO)
  – Immunization Safety Priority Project
  – Vaccine safety and quality
• WHO Causality Assessment Clinical Guidelines
  – http://www.who.int/vaccines-documents/DocsPDF05/815.pdf

Alternate Vaccination Schedule
Preferences Among Parents of Young Children

• Results of Survey (748 parents responded, 61%)
  – 13% of parents reported alternative vaccine schedules
  – 53% refused certain vaccines and/or delayed some vaccines until the child was older (55%)
  – 17% reported refusing all vaccines: factors associated
    – Not having a regular health care provider
    – Nonblack race
  – Large proportion of alternative schedule vaccinators followed initial recommendations
    – 28% thought delaying vaccine was safer & 22% disagreed with experts

Adverse Reaction Rates to Smallpox Vaccine (per Million)

Estimates reviewed: Military Medicine 2000; 165:4:287
• Encephalitis: 0.2-8 with 0 in healthy revaccinates
  – Lower rates related to age/re-vaccinates
• Vaccinia necrosum: 1-4 per million
• Eczea vaccinatum: 2-15 with highest in Israel
• Generalized vaccinia: 2-30 (highest in Puerto Rico experience 1967-68)
• E multiforme: 3-24 (Puerto Rico ↑)
• Inadvertent inoculation: 2-13
• Secondary infection: 6 (in IDF experience)
  – US Total 46 per million
2009-2010 Influenza Vaccine Safety Network

- Vaccine Adverse Event Reporting System (VAERS)
- Real Time Immunization Monitoring Systems (RTIMS)
- Vaccine Safety Datalink (VSD),
- Department of Defense (DoD) Defense Medical Surveillance System (DMSS)
- Post-Licensure Rapid Immunization Safety Monitoring (PRISM),
- Indian Health Service (IHS),
- Department of Veteran Affairs (VA),
- Centers for Medicaid and Medicare Services (CMS), and
- CDC’s EIP.

MMWR Report 2010 Jun
H1N1 Vaccine Safety Surveillance: Limitations

1. Misclassification of some cases, particularly in young
   - Impact: Underestimation of GBS cases
2. Inaccurate reporting of date of vaccination
   - Impact: Overestimation or underestimation of cases in risk window
3. Rate ratio relies on vaccination coverage estimates
   - BFRSS and NHFS data, not actual dose delivery – 2-3% diff
   - Impact: Underestimation of the rate ratio
4. Incomplete case ascertainment or reporting bias
   - Active case finding surveillance
5. None of vaccine monitoring systems currently in use, including EIP, can fully account for other confounding risk factors for GBS
   - Cannot prove causal relationship between vaccination & GBS

Immunization 2012
New Framework for Evidence Based Guidelines

- Advisory Committee on Immunization Practices (ACIP)
  - Expert advice/guidance to Director CDC and Secretary, HHS
  - Basis of Evidence Based Recommendations:
    - Grading of Recommendations, Assessment, Development, Evaluation (GRADE)
      - Balance of benefits and harms; Type of evidence
      - Values and preferences of people affected
      - Health economic analyses
    - Category A: for all persons in an age- or risk-factor-based group
    - Category B: “for individual clinical decision making and do not apply to all members of an age- or risk-factor-based group, but in the context of a clinician-patient interaction, where vaccination may be found appropriate for a person”
- New: Balance Considering Not Just Quality of Evidence

Vaccine Recommendations
GRADE Evidence Approach

- Evidence Tables To Summarize
  - The benefits and harms
  - The strengths and limitations of the body of evidence.
  - ACIP unanimous vote to adopt GRADE approach: Oct 2010
    - Quality of evidence for benefits & harms only 1 factor in developing recommendations: balance with values, health economics
- New Evidence Framework Goals
  - Enhance the ACIP’s decision-making process by making it
    - More transparent, consistent and systematic.
  - Response to challenges and criticisms
    - A move towards personalized/subpopulation-focused medicine?
  - Online Review of GRADE
    - http://www.cdc.gov/vaccines/recs/acip/GRADE/about.htm

New Framework for Development of ACIP Guidelines for Vaccines

Advisory Committee on Immunization Practices
From Online Presentation At
Email: fahmed@cdc.gov

From the desk of RJM Engler, MD: 2013