

Immunization Update: National Perspective

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Disclosures

- **The speaker is a federal government employee with no financial interest or conflict with the manufacturer of any product named in this presentation**
- **The speaker will discuss the off-label use of rotavirus vaccines**
- **The speaker will not discuss vaccines not currently licensed by the FDA**

What's New in Immunization

- **Vaccine safety**
- **Measles outbreak**
- **New vaccines (Rotarix, Kinrix, Pentacel)**
- **Influenza vaccines**
- **Human papillomavirus vaccine**
- **Zoster vaccine**

Elements Needed To Assess Causation of Vaccine Adverse Events

| | <u>Disease</u> | <u>No disease</u> |
|-------------------|----------------|-------------------|
| <u>Vaccine</u> | a | b |
| <u>No vaccine</u> | c | d |

$$\frac{\text{Risk in "vaccine" group}}{\text{Risk in "no vaccine" group}} = \frac{a / a + b}{c / c + d}$$

If the rate in "vaccine" group is higher than the rate in the "no vaccine" group then vaccines may be the cause

Autism and Vaccines

- **Multiple population-based studies have examined the rate of autism among vaccinated and unvaccinated children**
- **Available evidence does not indicate that autism is more common among children who receive MMR or thimerosal-containing vaccines than among children who do not receive vaccines**

Studies of Autism and Vaccines*

Taylor, B, et al. Autism and measles, mumps, and rubella vaccine: no epidemiologic evidence for a causal association. *Lancet* 351:2026-2029, 1999.

Kaye JA, et al. Measles, mumps, and rubella vaccine and incidence of autism recorded by general practitioners: a time-trend analysis. *Brit Med J* 322:460-463, 2001.

Madsen KM, et al. A population-based study of measles, mumps, and rubella vaccination and autism. *N Engl J Med*. 2002;347:1477-1482.

Frambonne E, et al. Pervasive developmental disorders in Montreal, Quebec, Canada: prevalence and links with immunizations. *Pediatrics* 118:e139-50, 2006.

Thompson WW, et al. Early thimerosal exposure and neuro-psychological outcomes at 7 to 10 years. *N Engl J Med* 2007; 357(13):1281-92.

Schechter R, Grether JK. Continuing increases in autism reported to California's developmental services system: mercury in retrograde. *Arch Gen Psychiatry* 2008;65(1):19-24.

*partial listing of representative studies

Sources of Information about Autism

- **Centers for Disease Control and Prevention
Autism Information Center**
 - www.cdc.gov/ncbddd/autism/index.htm
- **American Academy of Pediatrics**
 - www.aap.org/healthtopics/autism.cfm
- **Vaccine Education Center at the Children's
Hospital of Philadelphia**
 - www.chop.edu/consumer/your_child/index.jsp
- ***Autism's False Prophets*, by Dr. Paul Offit
(Columbia University Press, 2008)**

Measles–United States, 2008*

- **137 cases reported from 17 states and DC**
- **88% imported (13%) or linked to imported case (76%)**
- **17 younger than 12 months of age (10 others 12 to 15 months)**
- **Only 11 (8%) cases had documentation of vaccination**
 - **48% unvaccinated because of religious or personal beliefs**
- **17% exposed in a healthcare setting**

MMWR 2008;57(No.33):893-6 and CDC unpublished data

*as of September 12, 2008

Impact of a HCP with Measles Pima County, Arizona

- **41 year old (born 1967) female patient care technician, unknown vaccination or immunity status**
- **Provided care to a 50 year old with undiagnosed measles in the ED**
 - **infected 2 additional persons (1 in hospital, one at home...**
 - **who infected 3 additional persons...**
 - **who infected 3 additional persons (8 total spread cases in 3 generations from a single infected HCP)**

CDC unpublished data

Measles 2008

- **Measles has been imported from Switzerland, Italy, Belgium, Italy, Israel, Germany, India, China, Pakistan, the Philippines, and Russia**
- **All international travelers should have evidence of measles immunity**
- **CDC recommends measles/MMR vaccination of 6-11 month old children traveling outside the United States**

Rotarix[®] Rotavirus Vaccine

- **Approved by FDA in April 2008**
- **Contains one strain of live attenuated human rotavirus (G1P[8])**
- **Two oral doses at 2 and 4 months of age (minimum interval 4 weeks)**
- **Minimum age 6 weeks**
- **Maximum age 24 weeks**

Provisional Rotavirus Vaccine Recommendations

| | Rotarix (RV1) | RotaTeq (RV5) | ACIP Recs |
|------------------------------|--------------------------|--------------------------|---------------------------|
| Doses | 2 | 3 | -- |
| Min age | 6 wks | 6 wks | 6 wks |
| Max age- 1st dose | 20 wks | 12 wks | 14 wks 6 days* |
| Max age- any dose | 24 wks | 32 wks | 8 mos 0 days* |

***off-label. See www.cdc.gov/vaccines/recs/provisional/**

Provisional Rotavirus Vaccine Recommendations

- Provider may not stock or may not know the brand of rotavirus vaccine received for previous dose or doses**
- If any dose in the series was RV5 (RotaTeq) or the product is unknown for any dose in the series, a total of three doses of rotavirus vaccine should be given**

KINRIX™ Vaccine

- **Approved by FDA in June 2008**
- **Contains DTaP (Infanrix) and IPV**
- **Approved ONLY for the 5th dose of DTaP and 4th dose of IPV in children 4 through 6 years of age***
- **Do NOT use for earlier doses in the DTaP or IPV series**
- **Single dose syringe contains latex**

***whose previous doses have been with Infanrix and/or Pediarix for the first 3 doses and Infanrix for the 4th dose**

KINRIX™ Vaccine

- **Use of KINRIX for any dose other than DTaP5 and IPV4 is off-label, and should be considered a medication error***
- **Medication errors should be reported to the Institute for Safe Medication Practices**
–www.ismp.org

***dose does not need to be repeated**

Pentacel[®] Vaccine

- **Approved by FDA in June 2008**
- **Contains DTaP, Hib, and IPV**
- **Approved for doses 1 through 4 among children 6 weeks through 4 years of age**
- **Do NOT use for in children 5 years or older**
- **Package contains lyophilized Hib (ActHib) that is reconstituted with a liquid DTaP (Daptacel)/IPV solution**

Pentacel[®] Vaccine

- **Do NOT use the Hib (ActHib) and liquid DTaP/IPV solution separately**
- **Hib must only be reconstituted with DTaP/IPV or specific ActHib diluent (NOT with MMR/varicella diluent or normal saline)**
- **Guidance for clinicians for the use of Pentacel**
 - www.cdc.gov/vaccines/pubs/pentacel-guidance.htm

Pentacel[®] Vaccine

- **Use of Pentacel for the first 4 doses of the DTaP series on schedule will also mean the 4th dose of IPV will be administered at 12-18 months of age**
- **At present, the 4th IPV at 12-18 months completes the series and another dose at 4-6 years is not needed***
- **This recommendation may change**

***unless the state requires a dose of polio vaccine on or after age 4 years**

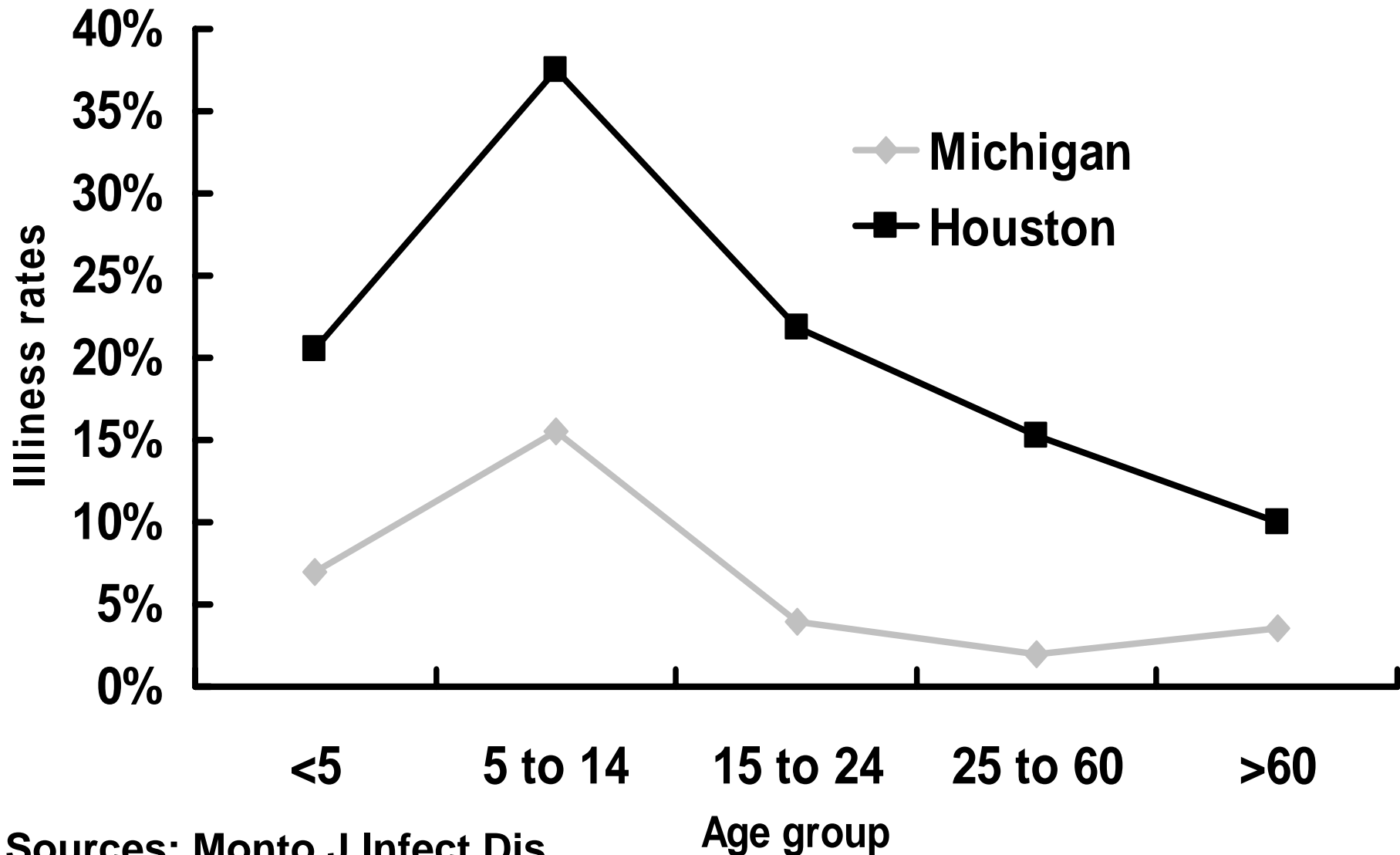
PedvaxHib[®] Shortage

- **Merck is experiencing a production problem with their Hib vaccine**
- **PedvaxHib is currently not available**
- **Improvement in the supply is expected during the 4th quarter of 2008**
- **Continue to defer the booster dose (including Pentacel) for healthy children**

The Evolution of Influenza Vaccination Recommendations

- Children 24-59 months were included for routine vaccination in 2007-2008**
- Healthy school-aged children are included for routine vaccination in 2008-2009**
- In 3-5 years annual influenza vaccination will be recommended for the entire U.S. population**

Average Influenza-Associated Illness Rates by Age Group*



Sources: Monto J Infect Dis
Glezen N Engl J Med

Burden of Influenza Among School-Aged Children

- **Few deaths and hospitalizations compared to younger children, elderly, or chronically ill**
- **5-7 outpatient visits per 100 children annually, frequently receive antibiotics**
- **10-30 illnesses per 100 children – frequently associated with school absenteeism**

Pediatric Influenza Deaths– 2007-2008

- **85 influenza-related deaths among children 0-17 years of age**
 - **Median age 6.4 years**
 - **23 (27%) younger than 24 months**
 - **44 (52%) 5 through 17 years of age**
- **Only 5 known to have been vaccinated according to 2007-2008 recommendations**

MMWR 2008;57(No. 25):692-7 and CDC unpublished data

Influenza Among School-Aged Children

- **Influenza outbreaks in schools are very disruptive and amplify the disease in the community**
- **Students with influenza expose household and other contacts to the infection**

ACIP Recommendations for Influenza Vaccine, 2008

- **All children aged 6 months through 18 years should receive annual influenza vaccination, beginning in 2008 if feasible, and beginning no later than during the 2009-2010 influenza season**

Inactivated Influenza Vaccines Available in 2008-2009

| Vaccine | Package | Dose | Age |
|--------------------------------|----------------------------------|---------------|----------|
| Fluzone (sanofi pasteur) | Multidose vial* | Age-dependent | ≥6 mos |
| | Single dose syringe* | 0.25 mL | 6-35 mos |
| | Single dose syringe and vial* | 0.5 mL | ≥36 mos |
| Fluvirin (Novartis) | Multidose vial | 0.5 mL | ≥4 yrs |
| | Single dose syringe | 0.5 mL | ≥4 yrs |
| Fluarix | Single dose syringe | 0.5 mL | ≥18 yrs |
| Flulaval (GSK) | Multidose vial | 0.5 mL | ≥18 yrs |
| Afluria (CSL) | Single dose syringe | 0.5 mL | ≥18 yrs |
| | Multidose vial | 0.5 mL | ≥18 yrs |

*inactivated vaccines approved for children younger than 4 years

Fluviron[®] Single-dose Syringes

- **Supplied with a fixed 5/8” needle**
 - **Needle length is acceptable for IM injection of persons weighing less than 130 pounds**
 - **A longer needle is preferred for persons weighing more than 130 pounds**
 - **Can use for heavier persons but proper injection technique is critical**

Inactivated Influenza Vaccine (TIV)

- All TIV packaged in multidose vials must contain a preservative**
- Thimerosal is used as a preservative for TIV**
- ACIP has not stated a preference for preservative-free vaccine for any group except persons with an anaphylactic allergy to thimerosal**

Trivalent Inactivated Influenza Vaccine (TIV) Schedule

| Age Group | Dose | # Doses |
|-------------------------|----------------|----------------|
| 6-35 mos | 0.25 mL | 1 or 2* |
| 3-8 yrs | 0.50 mL | 1 or 2* |
| 9 years or older | 0.50 mL | 1 |

TIV should only be administered by the intramuscular route.

***Doses should be separated by at least 4 weeks.**

MMWR 2008;57 (RR-7)

Influenza Vaccination of Children

- Children 6 months through 8 years of age who did not receive the recommended second dose of influenza vaccine LAST influenza season (2007-2008) should receive 2 doses during THIS influenza season**
- Children 6 months through 8 years of age who are being vaccinated two or more seasons after receiving an influenza vaccine for the first time should receive a single annual dose, regardless of the number of doses administered previously**

Influenza Vaccination of a 5 Year Old

Prior vaccination

- **1 dose in 2007 (first time)**
- **1 dose in 2006 (first time), 1 dose in 2007**
- **1 dose in 2006 (first time), none in 2007**

This year

2 doses

1 dose

1 dose

Live Attenuated Influenza Vaccine

- **Approved for healthy persons 2 years through 49 years of age who are not pregnant, such as**
 - **healthcare personnel**
 - **persons in close contact with high-risk groups**
 - **Healthy children**
 - **persons who want to reduce their risk of influenza**

LAIIV Schedule

| <u>Age Group</u> | <u>Number of Doses</u> |
|--|--------------------------------|
| 2 through 8 years -no previous influenza vaccine | 2 (separated by 4 weeks) |
| -previous influenza vaccine | 1 or 2 |
| 9 through 49 years | 1 |

Influenza Vaccine 2008-2009

- **Providers should begin vaccinating as soon as they receive vaccine, especially**
 - **children younger than 9 years being vaccinated for the first time (they need 2 doses)**
 - **healthcare personnel**
- **ACIP does not recommend a second dose during the same influenza season for any group except children younger than 9 years being vaccinated for the first time**

Human Papillomavirus Vaccine

- **Contains noninfectious HPV L1 major capsid protein of 4 HPV types (16 and 18 [oncogenic], 6 and 11 [genital warts])**
- **Produced using genetic engineering technology similar to hepatitis B vaccine**
- **Does not contain preservative or antibiotic**
- **Supplied in single-dose vials and syringes**

HPV Vaccination Schedule

- **Routine schedule is 0, 2, 6 months**
- **An accelerated schedule using minimum intervals is NOT recommended**
- **Intramuscular injection in the deltoid**
- **Minimum age is 9 years**
- **Maximum age is 26 years (may complete series after age 27 if begun before age 27)**

HPV Vaccine Intervals

- **There is no MAXIMUM interval between HPV vaccine doses**
- **If the interval between doses is longer than recommended you should just continue the series where it was interrupted**

Syncope Following Vaccination

- **An increase in the number of reports of syncope has been detected by the Vaccine Adverse Event Reporting System (VAERS)**
- **11-18 year old females have contributed most of the increase, many of whom received HPV vaccine**
- **Serious injuries have resulted**
- **Providers should strongly consider observing patients for 15 minutes after they are vaccinated**

HPV Vaccine Adverse Reactions

- **Mild local reaction most common** **84%**
 - Redness, soreness, itching at site
- **Fever** **10%***
- **No serious adverse reactions reported**

***similar to reports in placebo recipients (9%)**

HPV Vaccine VAERS Reports*

- **9,749 reports**
 - **94% classified as non-serious (local reactions, syncope, fatigue, etc)**
 - **6% classified as serious**
- **20 deaths reported**
 - **no common pattern to the deaths**
 - **the cause of death was explained by factors other than the vaccine**

***As of June 30, 2008**

www.cdc.gov/vaccinesafety/vaers/gardasil.htm

HPV Vaccine VAERS Reports

- **Guillain-Barré Syndrome (GBS)**
 - no evidence that HPV vaccine has increased the rate above that expected in the population
- **Thromboembolic disorders (blood clots)**
 - Most had known risk factors (e.g., oral contraceptive use)
 - Additional studies are being conducted

***As of June 30, 2008**

www.cdc.gov/vaccinesafety/vaers/gardasil.htm

Herpes Zoster Vaccine (Zostavax[®])

- **Administered to persons who had chickenpox to reduce the risk of subsequent development of zoster and postherpetic neuralgia**
- **Contains live varicella vaccine virus in much larger amount (14x) than standard varicella vaccine (Varivax[®])**
- **Requires freezer storage AT ALL TIMES**

ACIP Recommendations for Zoster Vaccine

- **Adults 60 years and older should receive a single dose of zoster vaccine**
- **Routine vaccination of persons younger than 60 years is NOT recommended**
- **Need for booster dose or doses not known at this time**
- **A history of herpes zoster should not influence the decision to vaccinate**

MMWR 2008;57(RR-5)

Zoster Vaccine

- **It is not necessary to inquire about chickenpox or test for varicella immunity before administering zoster vaccine**
- **Persons 60 years of age and older can be assumed to be immune regardless of their recollection of chickenpox**

Serologic Testing for Varicella Immunity

- **If a person 60 years or older is tested for varicella antibody and found to be negative**
 - **Administer 2 doses of regular varicella vaccine (not zoster vaccine)**
 - **Zoster vaccine is not indicated for persons whose immunity is based upon varicella vaccination**

CDC Vaccines and Immunization Contact Information

- **Telephone** **800.CDC.INFO**
(for patients and parents)
- **Email** **nipinfo@cdc.gov**
(for providers)
- **Website** **www.cdc.gov/vaccines/**
- **Vaccine Safety**
www.cdc.gov/od/science/iso/

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- **Vaccine Safety**
<http://www.cdc.gov/od/science/iso/>