Fall 2009 Immunization Update: Novel Influenza A (H1N1)

September 16, 2009

Presented by:

Community Health Association of Mountain/ Plains States

colorado communityhealth network
quality care • quality investment

Colorado Children's Immunization Coalition

Influenza

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September 1, 2009

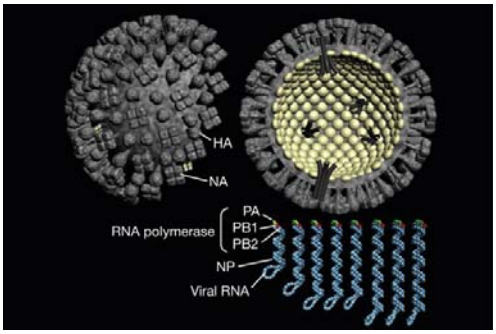
Influenza: Nomenclature

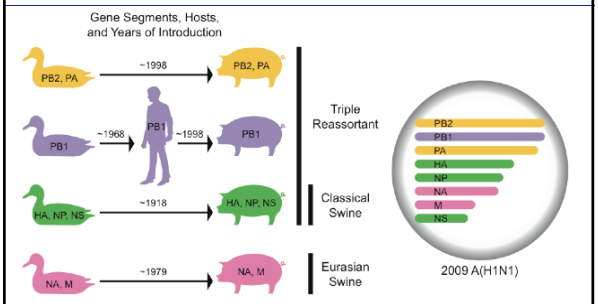
- Influenza A and B are human pathogens
- Subtypes of Influenza A classified by surface antigens H and N
  - H1N1, H2N3, H2N2
  - H5N1 (avian)
- Scheme used for naming strains
  - A/Sydney/5/93(H1N1)
  - Type/Origin/strain sequence/year/H/N

Influenza: Biology

- Segmented viral RNA – 8 segments
- Infection with one or more two different strains (pig, avian, human) leads to new viruses with RNA segments from different sources.
- Hemagglutinin (cell entry) and Neuraminidase (cell escape) are surface antigens.
  - Antibody against these antigens confer immunity.
  - Immunity is short not long lived
  - Mutation in the H and N antigens occurs frequently (antigenic shift and drift)

What is the origin of the new pandemic strain?





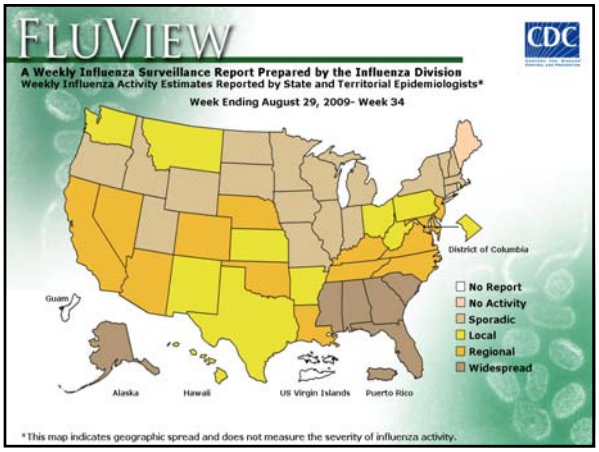
Garten RJ et al. Science 2009;325: 197

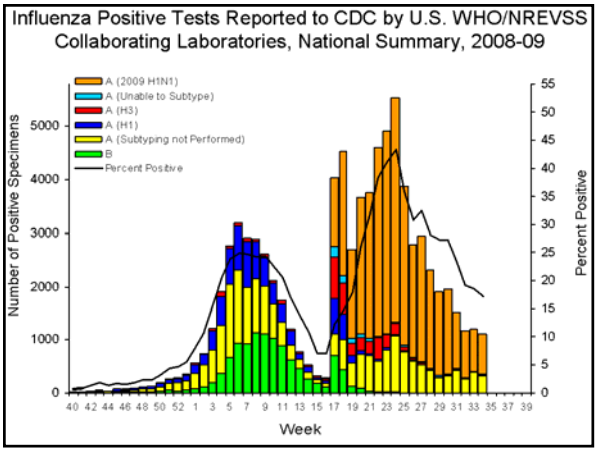
H1N1 Epidemiology/Incidence

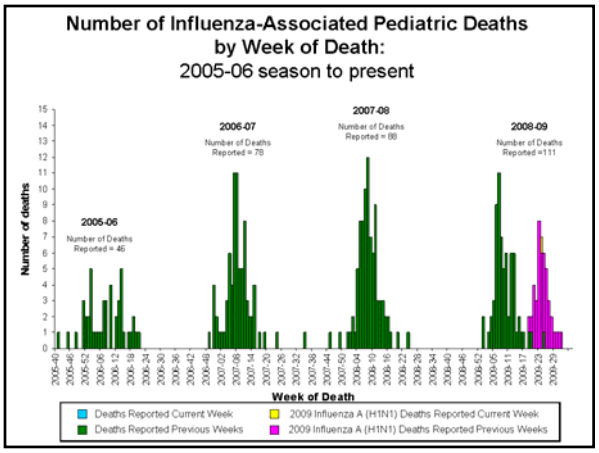
- 8,843 H1N1 influenza hospitalizations in 2009
  - 556 total deaths
- 110 pediatric deaths since Sept. 28, 2008
- 42 pediatric deaths from H1N1 2009
- WHO reports 209,438 lab-confirmed H1N1 cases
  - 2,185 deaths
- Probably undercounts cases 20-50 fold with apparent overestimate of mortality rate
  - CDC August 28, 2009

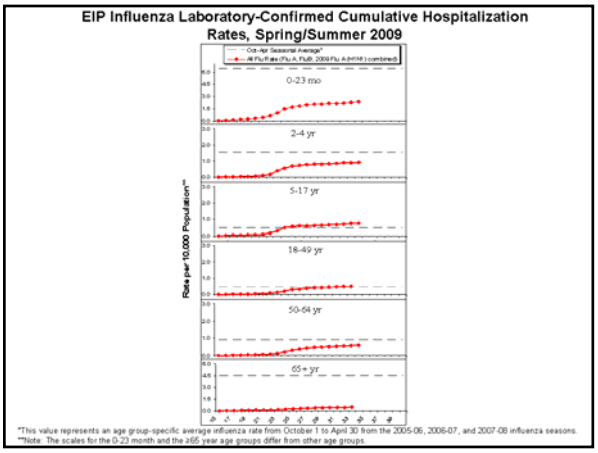
H1N1 Epidemiology/Outcomes

- Total hospitalizations similar to seasonal flu
- Mortality rate similar to seasonal
- Both seasonal and novel expected to circulate
  - Currently all viruses in US are novel H1N1
  - Some circulation of the seasonal flu in Southern Hemisphere
- No significant mutational change in Southern Hemisphere virus









Transmission of Influenza

- Person to person
- Large droplets fall out within 3 feet
- Fomites persist until drying 8-48 hrs
  - Self-inoculation of conjunctivae and nasal mucosa is efficient
- Incubation Period 18 hrs - 5 days (usually 2-3 days)

Clinical Signs and Symptoms Presentation

- **Clinical Symptoms**
  - **Fever** **371/394 (94%)**
  - **Cough** **365/397 (92%)**
  - **Sore Throat** **242/367 (66%)**
  - **Diarrhea** **82/323 (25%)**
  - **Vomiting** **74/293 (25%)**

NEJM 360:2605, 2009

Diagnostic Testing for Influenza

- Rapid Antigen Detection Tests on nasopharyngeal secretions are highly specific, but lack sensitivity (30-70%).
- PCR testing is more sensitive (95%) but costly ($100). PCR is a rapid lab test but often 1-5 days if sent to reference lab.

Diagnostic Testing: Conclusions

- No testing of healthy outpatients
- Very selective testing of chronically ill or immune compromised patients. Test only if it will change management
- Seriously ill patients (ICU on ventilator)
- Hospitalized patients if it will change management

Antiviral Susceptibility

	Amantadines	Oseltamivir	Zanamivir
Seasonal A H1N1 -	***Susceptible***	***Resistant***	***Susceptible***
Novel A H1N1 -	***Resistant***	***Susceptible***	***Susceptible***
Seasonal A H3N2 -	***Resistant***	***Susceptible***	***Susceptible***
Seasonal B -	***Resistant***	***Susceptible***	***Susceptible***

Anti-Viral Medication: Who to Treat

- Seriously ill, hospitalized patients
- Patients with serious underlying disorders
- Pregnant women
- Children younger than 2 years
- Treat within 48 hours
- Expense: Treatment of adults for 5 days ~ $100

Efficacy of Antiviral Treatment in Children

- **Oseltamivir given within 48 hours shortens illness 36 hours, fever 22 hours**
  - **Peds ID J 20:127, 2001**
- **Zanamivir given within 36 hours shortens illness 1.25 days**
  - **Peds ID J 19:410, 2000**
- **Retrospective analysis of Oseltamivir treatment of children with various chronic medical conditions 1-17 years reduced hospital admissions, otitis media and respiratory conditions other than pneumonia.**
  - **Pediatrics 124:170, 2009**
- **10 day course of prophylaxis was associated with a 8% decrease in in confirmed symptomatic influenza. NNT =13**
  - **BMJ 339:b3172, 2009**

Anti-Viral Medication: Prophylaxis

- Household contacts, infants < 6 months
- Pregnant women
- Patients with serious underlying disorders

BUT…

- How many courses of prophylaxis will we give? How many will be exposed multiple times?

H1N1 Vaccination: An Evolving Picture

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September 16, 2009

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Disclosures

No relevant financial relationships with any commercial interests are present

Novel influenza A (H1N1) vaccine is not currently licensed by the Food and Drug Administration (FDA);
therefore this talk *will reference* the use of medications not currently licensed by the FDA

H1N1 vaccination is a constantly changing topic; all organizations and healthcare providers should seek updated information for as long as H1N1 infections persist in the community

H1N1 Immunity and Seasonal Influenza Vaccine

- **Limited data from serologic studies indicates seasonal influenza vaccines will not provide protection against novel H1N1 infection**
- **In persons vaccinated with seasonal vaccine, percent with adequate antibody against H1N1:**
  - **18-64 years old: 6-9%**
  - **>60 years old: 33%**
  - **Children: 0%**

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

Influenza A (H1N1) 2009 Monovalent Vaccine

- **H1N1 vaccination likely to be best way to prevent H1N1 infection and its consequences**
- **H1N1 vaccines being produced using methods similar to those used to make seasonal vaccine**
- **Licensure based on same standards used for seasonal vaccines**

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

H1N1 Vaccine

- Both inactivated (injectable) and live, attenuated (intranasal) H1N1 vaccines will be available
- No adjuvants will be used (no adjuvants in seasonal vaccine either)
- If vaccines with adjuvants are available later in season, will be under different scenario (public health threat; special documentation)

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

H1N1 Vaccine Dosing

- Number of doses required for immunity not known at this time
- Possibly 2 doses will be required
- Whether 1 vs. 2 doses needed may vary by age
- Interval between 1st and 2nd dose not known (range could be >21 days, >28 days, or longer)
- Vaccine should not be "held in reserve" for those needing 2nd doses

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

Seasonal and H1N1 Influenza Vaccine: Simultaneous Administration

- Inactivated (injectable): simultaneous admin. of seasonal and H1N1 vaccines permissible if different anatomic sites used
- Live attenuated (intranasal): simultaneous admin. of seasonal and H1N1 vaccines not recommended
- Give seasonal as soon as available

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

Anticipated H1N1 Vaccine Supplies

- 45-55 million doses by mid-October
- 20 million doses weekly after that
- Up to total of 190 million doses nationwide
- Volume distributed on a proportional basis by state
- However, these estimates based on many assumptions (production, trials, licensure)

Vaccine Distribution

- A "blended" model of public and private
- Distribution centralized through vaccine distributors
- Similar to process used to ship vaccines through routine childhood immunization program
- Private providers need to sign up
- Minimum order (~100 doses?)

Recommendations for H1N1 Vaccine Use

- ACIP recommends 5 targeted groups for initial H1N1 vaccination, based on risk of complications, or risk of contact and spread
- Targeted groups:
  - Pregnant women
  - Persons caring for infants <6 months of age
  - Healthcare personnel
  - Persons 6 months-24 years of age
  - Persons 25-64 years of age with chronic medical conditions (same definition as used for seasonal)

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

If H1N1 Vaccine Supplies Initially Limited

- Not anticipated, but may occur if demand exceeds supply
- Targeted while local supplies limited:
  - Pregnant women
  - Persons caring for infants <6 months of age
  - Healthcare personnel with direct patient contact
  - Persons 6 months-4 years of age
  - Persons 5-18 years of age with chronic medical conditions

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

Expanding Vaccination Efforts

- Decisions should be made at local level
- Once vaccination programs and providers meeting demand for 5 targeted groups
- Expand vaccination to all persons 25-64 years of age
- Local areas can consider vaccinating all persons ≥65 years, after reassessing supply and demand

Ref: ACIP, *MMWR*, 2009:58:RR10:1-7

Financing and Billing

- All H1N1 vaccine will be paid for by the federal government
- Patients/insurers should not be charged for vaccine itself
- Admin. fee can be billed; should be reimbursed at the rate set by Medicare for seasonal influenza vaccine administration
- H1N1-specific vaccination codes have been established (both the vaccine codes, and the administration codes)

Monitoring the Safety of Influenza A (H1N1) 2009 Monovalent Vaccine

Novel H1N1 Influenza Teleconference
September 16, 2009

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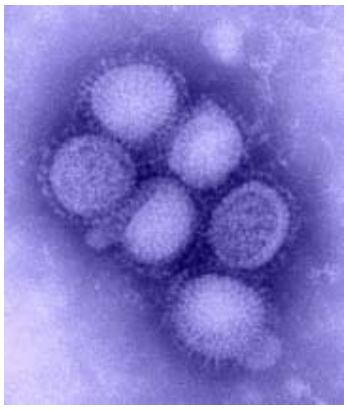

Background

- When seasonal influenza vaccines are administered according to licensed indication and usage information they are safe.
- It is anticipated that the safety profile of licensed influenza A (H1N1) 2009 monovalent vaccine (2009 H1N1 vaccine) will be similar to seasonal influenza vaccines.
  - Serious adverse events after vaccination are uncommon.
- Vaccine safety monitoring is an important component of the pandemic (H1N1) 2009 influenza response

Components of H1N1 Vaccine Safety Monitoring

- **VAERS**
- **Vaccine Safety Datalink (VSD)**
- **Vaccine Analytic Unit**
  - Collaboration with DoD/CDC/FDA
  - Utilizes Defense Medical Surveillance System
  - U.S. military personnel (~1.5 million active duty personnel)
- **Real Time Immunization Monitoring System**
  - Automated web-based active surveillance for certain sub-populations of vaccinees (CDC & Johns Hopkins)
- **Other**

Using the Vaccine Adverse Event Reporting System (VAERS) during the Pandemic (H1N1) 2009 Influenza Response

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Immunization Safety Office, CDC

VAERS Background

- **US post licensure vaccine safety surveillance**
  - **Collects voluntary reports of adverse events following immunization**
  - **Co-managed by CDC and the Food and Drug Administration (FDA)**
- **Healthcare providers are encouraged to report clinically significant adverse events after vaccination**
  - **Anyone can submit a report to VAERS**
- **Receives ~23,000 reports per year (2005-2008 average)**
- **Data publicly available**

VAERS Strengths

- **Can detect very rare adverse events**
- **Generates hypotheses**
  - **Helps identify new and/or rare adverse events following immunization**
  - **Helps determine if further investigations are needed**
- **Monitors trends of already known adverse events**
- **Monitors vaccine lot safety**

VAERS Limitations

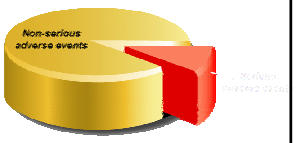
- **Risk of underreporting**
- **Stimulated reporting due to media attention and other factors**
- **Possibly incomplete or inaccurate data on report form**
- **Lack of availability of denominator data**
  - **No information on number of persons vaccinated**
  - **No information on background rates of adverse events in the population**
- **VAERS generally cannot determine if an adverse event was coincidental or caused by a vaccine**

VAERS "Non-Serious" Reports

92% of VAERS reports are "non-serious"

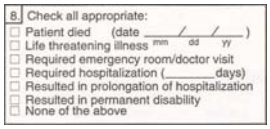
Most frequent adverse events (bases on 91,000 VAERS reports received 2005 – 2008):

- **Local reactions**
- **Fever**
- **Rashes or itching**
- **Headache**
- **Dizziness**



VAERS definition of "Serious" Reports*

- **Death**
- **Life-threatening illness**
- **Hospitalization**
- **Prolonged existing hospitalization**
- **Persistent or significant disability**
- **Certain other medically important conditions**



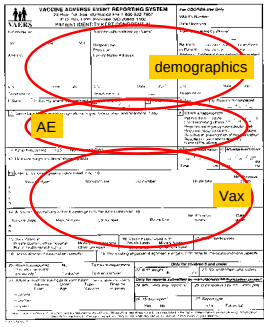
*Code of Federal Regulations Title 21 (21CFR 314.80)

What to Report to VAERS

- **Report any clinically significant adverse event following immunization (www.vaers.hhs.gov)**
  - Adverse event of concern to the healthcare provider or vaccinee/caregiver or other VAERS reporter
- **The National Childhood Vaccine Injury Act of 1986 mandates that healthcare providers report specific adverse events that occur after immunization for some vaccines.**
  - Events listed in the vaccine package insert
  - http://vaers.hhs.gov/pdf/ReportableEventsTable.pdf
  - No events are listed in the table for seasonal influenza vaccines
  - The National Childhood Vaccine Injury Act does not apply to 2009 H1N1 vaccines

What to Report to VAERS (cont.)

- **Submit reports of adverse events, even when not sure whether the vaccine caused the adverse event**
- **Include as much information as possible in the report (vaccination location, date, vaccine type, lot number and dose number)**
  - Reports with incomplete information accepted
- **Report as soon as possible but no time limit on reporting**



How to submit a VAERS report:

1) Online via a secure website at
https://vaers.hhs.gov

2) Download a reporting form:
www.vaers.hhs.gov/pdf/vaers_form.pdf
Fax a completed form: 877-721-0366
Mail a completed VAERS form to VAERS, P.O. Box 1100, Rockville, MD, 20849

To request a reporting form or for VAERS assistance: call 800-822-7967 or email: info@vaers.org

VAERS Follow-up

- **Follow-up conducted for reports of serious adverse events or for vaccines or adverse events designated for enhanced surveillance**
  - **Medical records**
  - **Autopsy reports**
- **Letter sent to reporters to check recovery status for all reports with "no" or "unknown" recovery listed on initial VAERS form (60 days and 1 year)**

Other Safety Monitoring Plans: Enhanced 2009 HINI Vaccine Safety Surveillance System (timely identification and rapid evaluation)

- Collaboration with the CDC and the FDA to increase the capacity to monitor vaccine safety in real-time
- Link exposure data (vaccine registry data) to outcome data available in large health care plans in selected states

Other Safety Monitoring Plans:

- Clinical Immunization Safety Assessment (CISA) Network
  - Collaboration between CDC and 6 academic centers with vaccine safety experts
  - Provide vaccine safety clinical expertise in the evaluation of serious adverse events following 2009 H1N1 vaccination (e.g., assist with review of complex serious cases reported to VAERS)
- Field investigations as needed
  - In collaboration with state/local health departments if CDC assistance is requested

Vaccine Safety Monitoring in Pregnant Women after 2009 H1N1

- Rapid Assessment
  - VAERS
  - VSD (selected outcomes)
  - Real-time Immunization Monitoring System
- Prospective study
  - Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) will be used to monitor seasonal and 2009 H1N1 vaccine safety in pregnant women and their infants
  - Office of the Biomedical Advance Research and Development Authority

Guillain-Barré Syndrome (GBS)

- Immune-mediated acute demyelinating polyneuropathy affecting the peripheral nervous system
- Estimated annual incidence rate: 1 case per 100,000 population
- In 1976, a type of influenza vaccine was causally associated with GBS (Institute of Medicine)
  - 1 additional case per 100,000 persons vaccinated
- Subsequent studies of influenza vaccines have found small or no increased risk of GBS
  - if there is a risk of GBS from seasonal influenza vaccines, it would be no more than ~1 additional case per million people vaccinated

GBS Active Case-Finding

- Emerging Infections Program
  - Active GBS case finding (other adverse events as necessary)
  - Ascertainment of vaccination status
  - Identify risk factors for GBS (e.g., antecedant infection)
  - >50 million US population
  - 10 states
- American Academy of Neurology (AAN)
  - Increase VAERS awareness to enhance GBS reporting
  - Active case finding is an option
- Provisional Brighton Collaboration GBS case definition being used*

*http://www.brightoncollaboration.org/internet/en/index/definition___guidelines.html

Summary Systems and Strategies for Monitoring 2009 H1N1 Vaccine Safety

Objective	System/ Strategy
Timely identification of adverse event	- Vaccine Adverse Event Reporting System (VAERS) - Vaccine Safety Datalink (VSD) - Vaccine Analytic Unit (VAU) - Real time immunization monitoring system (RTIMS) and Enhanced Safety Surveillance System
Rapid evaluation of serious adverse events	- VSD, VAU, and RTIMS, Enhanced safety surv. - Clinical Immunization Safety Assessment Network - Special studies and field investigations in collaboration with states as indicated
Evaluation of GBS	- Case finding through the Emerging Infections Program and American Academy of Neurology - VSD
Communication	- Communications materials; partnerships and collaborations

Summary
2009 H1N1 Vaccine Safety Monitoring

- Established vaccine safety infrastructure will be utilized, enhancements planned
- New collaborations being developed
- CDC to provide support to states and territories during 2009 H1N1 vaccination program
- Vaccine risk communication is an important component of the vaccine safety monitoring effort.

Vaccine Safety Risk Communication During the Pandemic (H1N1) 2009 Influenza Response

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The Landscape

- Concept of being a well educated parent
- Encouraged to be critical consumers of healthcare
- More information than ever available 24/7
- More virtual peer-to-peer interactions
- General distrust of government, pharmaceutical companies, and others
- Healthcare system that might not allow time for communication and relationship-building

Perception of Risk

Less Risk Perceived
- **Voluntary**
- **Personal control**
- **Familiar**
- **Natural origin**
- **Reversible**
- **Endemic**
- **Generated by trusted institution**

More Risk Perceived
- **Involuntary**
- **Controlled by others**
- **Exotic**
- **Manmade**
- **Permanent**
- **Epidemic**
- **Generated by a mistrusted institution**

Perceived Safety Concerns: 2009 H1N1 Vaccine

- **Vaccine hesitancy driven by safety and disease threat**
- **Ingredients (e.g., thimerosal)**
- **Safety testing concerns**
- **Special populations (e.g., pregnant women, children)**
- **What is the government doing**
- **Where to find accurate information**

CDC's Communication Response: Guiding Principles (1)

- Acknowledge uncertainties and the unpredictable nature of influenza, including 2009 H1N1
  - recognize the amount of uncertainty is more than everyone would like
  - trust the public to tolerate incomplete and potentially upsetting information
  - do anticipatory guidance even in the face of uncertainty

CDC's Communication Response: Guiding Principles (2)

- Share challenges and dilemmas
- Address fears and concerns (vs. attempting to minimize them)
- Maintain transparency and communicate early and frequently
- Utilize multiple channels and partners to increase reach and visibility of recommendations and messages

Available Communication Resources

PandemicFlu.gov

http://flu.gov/news/rcommunication.html

- **Crisis & Emergency Risk Communication (CERC) Training – CDC**
- **Pandemic Influenza Pre-Event Message Maps – CDC**
- **Effective Media Communication during Public Health Emergencies - WHO**
- **WHO Outbreak Communications Guidelines**
- **Communicating in a Crisis: Risk Communication Guidelines for Public Officials - SAMSA**

Crisis and Emergency Risk Communications Training

Crisis and Emergency Risk Communication Training

- **Module available Online**
- **In-person trainings**
- **Web site: http://emergency.cdc.gov/cerc/**
- **Email: cercinfo@cdc.gov**

Lessons Learned from Vaccine Refusing Parents & Their Doctors

- **Don't patronize or act defensively**
- **Show empathy – acknowledge that parents' fears are real – do not dismiss them**
- **Parents want doctors to present both sides – it is important for providers to be honest and describe the risks of vaccination – no medication is 100% safe**
- **If comfortable, discuss your own children – it's powerful when concerned parents know you vaccinated your own children**
- **Don't just use data, use anecdotes, especially around your own experiences caring for children with vaccine-preventable diseases**

Lessons Learned from Vaccine Refusing Parents & Their Doctors (cont'd)

- **$ - some parents think doctors are paid for each vaccine administered. It is important to communicate that vaccines are not a profitable business and the motivation behind vaccination is to protect children even if it means losing money.**
- **Community Benefit (Herd Immunity): immunizing helps to protect the community, particularly children too young to be vaccinated.**

H1N1 Vaccine Delivery & Coordination

Nancy Gilbert
Emergency Preparedness Manager
Colorado Community Health Network

Region VIII H1N1 Vaccine State Contact Information

- Colorado
  http://www.cdphe.state.co.us/epr/h1n1.html
  Colorado Immunization Program
  303-692-2650
- Montana
  Not yet identified
- North Dakota
  Molly Sanders
  800-472-2180 or 701-328-3386
  msander@nd.gov

Region VIII H1N1 Vaccine State Contact Information

- South Dakota
  Not yet identified
- Utah
  Linda Abel
  801-538-9450
  label@utah.gov
- Wyoming
  www.immunizewyoming.com
  Immunization Section
  307-777-7952

Federal Plans for H1N1 Vaccine Distribution

- **McKesson will distribute the H1N1 vaccine**
- **Providers interested in distributing the vaccine need to register with their state**
- **Providers will also receive:**
  - **Needles**
  - **Syringes**
  - **Alcohol Wipes**

H1N1 Vaccine State and Local Plans

- **Plans are still be being developed**
- **At this time vaccine will be sent to providers**
- **Some states/counties are still considering setting up points of distribution (PODs)**
- **Maintain connections with local health departments for new developments**

Administration & Documentation

- **Storage and Handling**
- **Administration of the Vaccine**
- **Documentation**

Additional H1N1 Information Resources

- **For posters, flyers and other immunization information: http://www.childrensimmunization.org/index.php?s=86&item=157**
- **Good resource for up to date guidance for providers on testing, medications, and vaccines: http://www.cdc.gov/**
- **Web site dedicated to flu information for the US. A source for archived flu briefings: http://www.flu.gov/**

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