Pandemic Influenza Vaccines: Lessons Learned from the H1N1 Influenza Pandemic

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Global Influenza Vaccine Strategy

REDUCED DISEASE

VACCINATION POLICY DEVELOPMENT

DATA COMMUNICATED

DATA GENERATED

Population-based Surveillance

Enhanced Sentinel Surveillance

Basic Epidemiologic Surveillance

Laboratory Capacity

Capacity Surveillance Research

Special studies in selected countries, i.e., BoD & VE,
Presentation Themes: Pulling Detection Closer to Emergence & Vaccine Closer to Disease

- Challenges for early detection of novel viruses with pandemic potential
  - Validated diagnostic platforms for detection of novel influenza viruses and other emerging respiratory pathogens
  - Build partnerships to identify newly emerging influenza viruses in animals
  - Goal: earlier detection of emergence of pandemic influenza viruses suitable as vaccine candidates (H2, H4, H5, H6, H7, H9, H10, etc.)

- Challenges for vaccines - faster development & availability
  - Better growing vaccine viruses (focused R&D)
  - Library of pre-prepared HG vaccine candidates (clinical trials)
  - Stockpile potency testing reagents for library above
  - New platforms for streamlining the measurement of vaccine potency and sterility
  - Goal: earlier delivery of safe and effective pandemic vaccines

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Preventing for the Pandemic

- Developed New Diagnostic Tests
  - Part of national strategy for diagnostic preparedness
  - Two FDA approved devices

- Enhanced surveillance for human and animal-origin influenza
  - Increasing testing over last five years led to more swine flu detected (NEJM Shinde 2009)

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The Greatest Influenza Vaccine Challenge: Gearing up Production for a Pandemic

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Unique Features of Influenza Vaccines

- Current influenza vaccines target a rapidly changing seasonal viruses & unpredictable pandemic viruses
- Immunity acquired from vaccination is “strain-specific” (e.g., targeted to one antigenic variant per vaccine component)
- Broadening cross-protection has remained a challenge; oil in water adjuvants: our “best bet” for now
- The “holy grail” of a universal vaccine remains elusive; new targets identified, but unproven
- It remains a race against time to detect the emergence and spread of new influenza variants and to provide vaccine prior to disease
- Production of influenza vaccines is a high-risk, high-stress endeavor for manufacturers

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Estimated Timeline of H1N1pdm Vaccine Development and Delivery in the U.S.

- **April 15**: CDC isolates H1N1
- **April 27**: WHO H1N1 vaccine virus recommendation
- **April 25 and 28**: Vaccine virus reassortment started at CDC and NYMC
- **May 26 and 27**: CDC ships high growth reassortant viruses to mfrs (X-179A and RG-15)
- **June 20-30**: Working seed developed by vaccine manufacturers
- **August**: Monovalent concentrate
- **September 15 & 18 (N/sp)**: Pool monovalent concentrate
- **September 30**: FBER release Sept 15 & 18 (N/sp) filing September (at risk)
- **October 5**: Start Vaccination

(*) Manufacturers were transiently limited in their ability to develop seed viruses due to lack of facilities to grow virus in large volume at the required BSL3 biocontainment

($) Production of monovalent inactivated vaccine is a continuous process

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BRAND CAMP

THINK OUTSIDE THE BIN

GREAT BLUE SKY THINKING!
NOW, SORT YOUR IDEAS
AND GET BACK TO YOUR DESKS.

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Post Pandemic Blues

- After-action Reviews of the 2009 Pandemic Response
- President’s Council of Advisors on Science and Technology met resulting in “Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza” – August 2010
- Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Review
- Influenza Manufacturing Improvement – Coordinated by BARDA/HHS (NIH, FDA, CDC and many Academic and Industry Partners)
  - Optimization of Influenza Vaccine Donor and Candidate Viruses
  - Potency Assay Improvement
  - Rapid Sterility Testing - FDA

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Optimization of Influenza Vaccine Donor and Candidate Viruses

- Aim 1: Analyze Genetics of High Yield A/PR/8/34 Donor Viruses from Different Labs
- Aim 2: Produce and Evaluate High-yield Reassortant Viruses
- Aim 3: Combinatorial Optimization of Vaccine Candidates
- Aim 4: Establish Library of Validated High Growing Vaccine Candidates

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Developing a Risk Assessment Algorithm

- Identify the elements to consider in pandemic risk assessment
- Define each independent element
- Assign weight to each element and use variables for multi-factorial analysis
- Come up with a composite score
- For high scoring viruses develop “preparedness packages” (diagnostics and candidate vaccine libraries of high growth reassortants, clinical trial lots and vaccine trials, if high risk)
- For very high scoring viruses develop pre-pandemic vaccines
  - Candidate vaccine library useful for human and animal health
  - Vaccine stockpiles
Some Elements of a Risk Assessment Algorithm

- Secondary hosts infected by the novel virus (including poultry, swine and other mammals, especially humans)
- Transmissibility (using ferret models)
- Susceptibility of the population- seroprevalence
- Geographic spread of the virus in secondary hosts
- Severity of infection in humans and other mammals
- Virus characterization
  - Genetic features such as virulence markers
  - Genetic and antigenic variation
  - Receptor binding properties
  - Pathogenesis

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Improving Vaccine Antigen Standardization: Potency Testing

- Current methods for measuring the quantity of antigen in the vaccines are decades old and often cause significant delays in the availability of influenza vaccines.

- We need faster, more accurate methods for quantitating antigens contained in inactivated influenza vaccines.

- Need approaches that could be applied to all protein based influenza vaccines, including new vaccines:
  - HPLC
  - ELISA
  - Mass Spectroscopy-Isotope Dilution with
  - Antibody mediated pull down of intact HA

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Vaccine Lessons Learned from the H1N1 Pandemic

- In spite of many successes, once again too little vaccine, too late
- Uneven distribution of influenza vaccines globally
- Having influenza vaccines even 4-6 weeks earlier likely to make big difference in disease reduction and vaccine acceptance
  ✓ THE FUTURE
- Set goals: Move detection of novel influenza viruses closer to emergence & the availability of vaccines prior to disease occurrence:
  What do we need?
  ✓ Sustainable multi-use respiratory disease surveillance platforms for identification of novel virus emergence globally
  ✓ Library of truly HG reassortants tested and production-ready
  ✓ Streamline methods for measuring vax Ag content, suitable for all HA protein (HPLC, ELISA and MSID methods)
  ✓ Use of adjuvants to for Ag sparing & more robust immune response
  ✓ Improve vaccine capacity globally for vaccine equity (LAIV)
  ✓ Enhance partnerships domestically and globally

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Thanks for your attention.

Questions?

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