VACCINATION SUCCESSES

Repercussions of Vaccines Introduced in 21st Century

David W. Scheifele MD

Director, Vaccine Evaluation Center, Vancouver
Chair, Canadian Association for Immunization Research and Evaluation (CAIRE)

OBJECTIVES

1. Provide a tangible reminder that the ultimate goal of immunization policy-making is safe, effective disease control

2. Recognize increasing challenges that newer vaccines pose for policy-makers and researchers

3. Two case studies: VZV, PnCV7

Cette présentation a été effectuée le 26 octobre 2006, au cours du Symposium "Mettre la science au service des programmes d'immunisation, le rôle des comités d'experts" dans le cadre des Journées annuelles de santé publique (JASP) 2006. L'ensemble des présentations est disponible sur le site Web des JASP, à l'adresse http://www.inspq.qc.ca/jasp.

TARGET: VARICELLA-ZOSTER INFECTIONS

Disease: Viremia with vesicular rash, minor complications 1/20, hospitalization 1/200

Complications: cellulitis, necrotizing fasciitis, encephalitis, cerebellitis, stroke, thrombocytopenia etc

Frequency: nearly universal, ~90% by age 16 years

Zoster (shingles): later painful reactivation in ~25%

PREVENTION TOOL: VZV VACCINE

- Live, attenuated vaccine, based on Oka strain
- Single dose, after 1 year (2 doses > 11 yrs)
- Good safety record, compatible with MMR
- Nearly 100% effective vs severe varicella, ~85% effective overall (mild disease with failures)

VZV VACCINE AVAILABILITY

- Freezer-stable version licensed 1995 (USA), late 1998 Canada
- Refrigerator-stable versions since 2000
- 2 products available (Varivax®, Varilrix®)
- NACI recommended universal programs in 1999, more strongly in 2002
- First programs delayed: PEI (2001), AB (2002)
- Other provincial programs started 2003-2004 (Quebec last to start, in early 2006)

WHY THE PROGRAM DELAYS?

- 1st vaccine not to offer net cost savings ($80/dose). Required re-thinking, measuring cost-effectiveness
- "Benign" disease, not well studied (non-reportable)
- 1st vaccine with persistent agent (risk of zoster)
- Duration of protection uncertain (only 10 yr follow-up)
- Formulation until 2000 impractical for programs
- Competing vaccines: PCV7, Tdap

VZV: "RECOMMENDED BUT NOT PROVIDED FREE" IS POOR POLICY

- Uptake limited as private purchase: 34% in Vancouver survey
- Ongoing morbidity after 2000: >300 hospitalizations/year at 12 IMPACT pediatric centers
- Ongoing deaths: 7 potentially preventable deaths at IMPACT centers, 2000-2006

EVIDENCE OF SUCCESS IN USA

- Licensed in 1995, widely used thereafter
- By 2001: deaths ↓ 92% in children 1-5 yrs
- By 2003: hospitalizations ↓ 88%
  ambulatory visits ↓ 59%
  costs ↓ 74% (by $63 million)

EVIDENCE OF SUCCESS IN CANADA?

VZV admissions at IMPACT pediatric centers

2002 . . . . . 389 (1 death)
2003 . . . . . 306 (0 deaths)
2004 . . . . . 340 (0 deaths)
2005 . . . . . 261 (1 death)
2006 (to Sept 30) . 109 (0 deaths)
(to year end, estimate 145cases)

PREVENTION TARGET: INVASIVE PNEUMOCOCCAL DISEASE, CHILDREN

Disease: bacteremia, sepsis, meningitis, joints etc
At risk: young children (< 5, mainly < 2 yr),
chronic conditions
Risk: cumulative risk ~1:450 to age 6 yrs
~110 per 100,000/yr for <24 month olds
Organisms: ~10 capsular types cause >95% cases
increasing rate of Pen^R (≥ 15%)

PREVENTION TOOL: 7-VALENT CONJUGATE VACCINE

- Conjugated capsular polysaccharide immunogenic in infants, elicits long-term, boostable memory
- 7 selected types match ~85% of cases 6-59 mos
- Requires 2-3 priming doses plus booster in 2nd year
- 7-in-1 vaccine very expensive (~$150 per dose)

7-VALENT CONJUGATE VACCINE

- Consistently immunogenic, well tolerated
- Pivotal P3 efficacy trial (Kaiser) convincing:
  - 94% ↓ in vaccine type infections
  - 89% ↓ in all invasive infections
  - some ↓ in pneumonia, otitis media
- Compatible with concurrently administered infant vaccines

PCV7: RAPID SUCCESS IN USA PROGRAMS

- Universal infant programs recommended in 2000
- By 2002, 77% ↓ in 7V invasive disease at children's hospital network (limited uptake)
- By 2003, 94% ↓ in 7V cases, 75% ↓ all types, < 5 yrs
- Strong indirect effect noted (62% ↓ 7V cases, > 5 yrs)
- Decreased rates of pneumonia, otitis media evident

PROGRAM IMPLEMENTATION IN CANADA

- PCV7 licensed in 2001, universal use recommended 2002
- AB and NVT implemented programs in Sept 2002
- BC program started Sept 2003
- Other provinces and territories followed in 2004-5
- Quebec chose innovative 2 plus 1 schedule to maximize cost-effectiveness

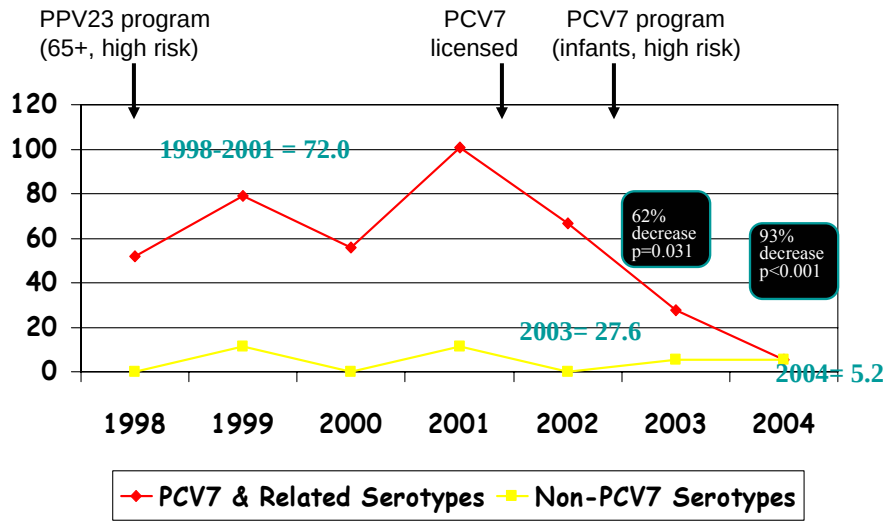
WHAT FACILITATED PCV7 PROGRAM DECISIONS?

- Severity of disease, age group affected, available disease burden data supported cost-effectiveness
- Short term data matched short term risk
- Likelihood of rapid effect, given US data
- Infusion of federal funding, with NIS

PCV7 SUCCESS: CALGARY

- By 2004, disease rate for children < 2 yrs
  - ↓ 82% for all types
  - ↓ 93% for 7V types
- With estimated 74% vaccination rate (4 doses) of < 2 year olds

ISP Incidence: Ages 6-23m



PCV7 SUCCESS: VANCOUVER

- By 2005, disease rate for children 6-23 months
  - ↓ 85% for all types
  - ↓ 93% for vaccine serotypes
  - not a single 7V type case in age-eligible children
  - uptake rate of vaccine pending

CONCLUDING COMMENTS

- Newer vaccines use sophisticated but expensive technology
- Newer vaccines target infrequent or less severe diseases than previous vaccines
- Newer vaccines are unlikely to be cost-saving
- Research on cost-minimization options is increasingly important for public programs
- Increasingly close scrutiny of unknowns, gaps
- Policy-making is an increasingly complex task!