



# VACCINE

## RESOURCE LINE

A QUARTERLY SUMMARY OF PEER-REVIEWED PUBLISHED LITERATURE

### Genital warts negatively affect well-being in men and women: PISCES study

*Sénécal et al. Loss of quality of life associated with genital warts: baseline analyses from a prospective study. Sex Transm Infect 2011;87:209-15.*

**G**enital warts (GWs) negatively affect well-being as reflected by poorer quality-of-life (QoL) scores compared with population norms, according to the Psychosocial Impact of Cervical Screening and Condylomas: an Epidemiological Study (PISCES), a Canadian prospective study.

Researcher Martin Sénécal, Montréal, Quebec, and multicentre colleagues examined the association between health-related QoL (HRQoL) detriments and the history and severity of GWs. Between September 2006 and February 2008, 42 physicians across Canada recruited 330 consenting patients with GWs either at first or follow-up visit for an initial or recurrent episode of GWs. Participants completed the EQ-5D, a generic measure widely used in cost-effectiveness analyses but which also includes a visual analogue scale—the EQ-VAS questionnaire. Subjects also responded to a modified version of the human papillomavirus (HPV) impact profile, a disease-specific measure designed for women who develop an HPV-related condition. Physicians also rated the severity of the GWs.

Some 270 of the recruits completed the study questionnaire. Approximately 47% of respondents were experiencing their first GW episode. The average lifetime number of episodes was 3.3 for those with recurrent GWs. “At recruitment, the mean time since self-reported onset of the first GW episode was 13.4 months for those experiencing a first episode and 50.9 months for recurrent cases,” the authors noted, “and participants reported an average 3.8 months between the onset of their first GW episode and first medical consultation.”

Results from the questionnaire showed that both males and females had significantly lower HRQoL scores ( $P<0.001$ ) than individuals in the general Alberta population of the same age and gender. HRQoL scores were mainly lower in the domains of pain and discomfort as well as anxiety and depression; to a lesser extent, scores assessing their ability to engage in usual activities were lower than population norms as well. Specifically, EQ-5D utility scores were on average 9.9% lower and EQ-VAS health status scores 6% lower for patients with GWs compared with age- and gender-specific Canadian population norms, investigators added.

“Our estimates of HRQoL lost to GWs using the EQ-5D is important for assessing the cost-effectiveness of HPV vaccination and therapeutic interventions against GWs,” the authors wrote, “...and our study suggests that the prevention or treatment of GWs has the potential to provide considerable benefits at the population level in terms of QoL gained.”

### Mumps outbreaks in Ontario, elsewhere: call for vigilance

*Deeks et al. An assessment of mumps vaccine effectiveness by dose during an outbreak in Canada. CMAJ 2011 May 16 [Epub ahead of print].*

**O**utbreaks of mumps occurring in Ontario and elsewhere should serve as a warning that public health officials cannot become complacent about vaccination programs, according to Canadian investigators.

Dr. Shelley Deeks, Ontario Agency for Health Protection and Promotion, Toronto, and multicentre colleagues assessed measles-mumps-rubella (MMR) vaccine effectiveness during a recent mumps outbreak in Ontario, where a total of 134 confirmed cases had occurred between September 1, 2009, and June 10, 2010. Information on receipt of the MMR vaccine was available for 114 of the cases, 63 (55.3%) of whom had received only 1 dose of the MMR vaccine and 32 (28.1%) of whom had received 2 doses. Only 19 (14.2%) had received no vaccination.

The mean age of the individuals affected was 25.9 years but 58.6% occurred in adolescents and adults between 15 and 24 years of age. Over 72% of the cases occurred in males. As investigators pointed out, vaccine effectiveness of 1 dose of the MMR vaccine against mumps ranged from 49.2% to 81.6% whereas the effectiveness of 2 doses ranged from 66.3% to 88%. “If we assume vaccine effectiveness of 85% for 2 doses of the vaccine, vaccine coverage of 88.2% and 98% would be

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needed to interrupt community transmission of mumps,” the authors confirmed.

As they also pointed out, most of the cases of mumps in this outbreak were in males, they occurred between the ages of 15 and 24 years and most subjects were not fully vaccinated. An active lifestyle of this age group therefore may have facilitated the transmission of disease while the preponderance of males in the cases likely reflects the settings in which males were exposed to the virus such as athletic events.

It has been 14 years since Ontario implemented a 2-dose policy for MMR vaccination; as such, “we are now at the point in the evolution of the program where we may begin to see the effect of waning immunity among recipients of 2 doses of the vaccine,” the authors observed.

During the same time interval, outbreaks of mumps also occurred in New York, New Jersey and Israel.

## Vaccine combinations in the elderly not more immunogenic than single vaccine doses

*Lazarus et al. A randomized study comparing combined pneumococcal conjugate and polysaccharide vaccination schedules in adults. Clin Infect Dis 2011;52(6):736-42.*

Schedules in which the 23-valent polysaccharide pneumococcal vaccine (23vP) and the 7-valent conjugate pneumococcal vaccine (PCV7) are combined do not enhance antibody concentrations over responses elicited by a single dose of either vaccine in older adults. These were among the findings of the first study to explore combinations of the 2 pneumococcal vaccines in the elderly.

Dr. Rajeka Lazarus, Oxford Vaccine Group, University of Oxford, UK, and multicentre colleagues assessed potential vaccination schedules using various combinations of the 2 vaccines in adults in an effort to improve immune responses to the vaccine serotypes. The study was designed as an open-label, randomized, parallel trial involving 348 adults between 50 and 70 years of age. “The primary objective of the study was the antibody response to 23vP after priming with 0, 1 or 2 doses of PCV7 for the 7 serotypes contained in PCV7,” the author stated. They also assessed the effect of administering the 23vP vaccine on subsequent antibody responses to a single dose of the PCV7 vaccine and to 2 sequential doses of PCV7.

Results showed that geometric mean concentrations (GMCs) of serotype-specific IgG 1 month after vaccination with a single dose of either the 23vP or the PCV7 vaccine were significantly higher for 4 of the 7 conjugate serotypes after PCV7 vaccination. Yet at 7 months’ follow-up, vaccination with a single dose of PCV7 prior to 23vP induced serotype-specific GMCs that did not differ significantly from those induced after a single dose of 23vP at 1 month, investigators reported.

At 13 months, vaccination with 2 consecutive doses of the PCV7 vaccine prior to administering the 23vP vaccine induced serotype-specific GMCs that were significantly higher for 3 of 7 serotypes compared with those induced by a single dose of the 23vP vaccine at 1 month. As investigators also noted, a dose of the PCV7 vaccine preceded by a single dose of the 23vP vaccine produced lower serotype-specific IgG levels for all serotypes except 19F at 7 months compared with serotype-specific IgG levels after an initial single dose of the PCV7 vaccine.

This was again the case at 13 months among subjects who received the 23vP vaccine followed by 2 doses of the PCV7 vaccine where serotype-specific IgG levels remained significantly lower than after a single initial dose of PCV7 for 4 out of the 7 vaccine serotypes. “In this study, combining PCV7 with the routinely used 23vP in older adults did not provide an immunological advantage using either a 1-dose or 2-dose priming schedule (PCV7-23vP; PCV7-PCV7-23vP),” the authors noted. They acknowledged that it is still not clear whether the enhanced immunogenicity achieved with the PCV7 vaccine against certain serotypes over that induced by the 23vP vaccine provides a potential advantage in the elderly.

The authors also pointed out that antibody concentrations induced by both vaccines wane rapidly in the first year after vaccination and that repeated doses of PCV7 vaccination may be necessary to sustain antibody concentrations against vaccine-specific serotypes.

## Fecal shedding of RV vaccine after first dose

*Yen et al. Detection of fecal shedding of rotavirus vaccine in infants following their first dose of pentavalent rotavirus vaccine. Vaccine 2011;29(24):4151-5.*

Fecal shedding of rotavirus (RV) vaccine after the first dose of the pentavalent RV vaccine occurs over a wider range of post-vaccinations days than previously studied. This finding has implications for the potential prevention of transmission of vaccine virus among immunocompromised household contacts of vaccinated infants, according to a US-based study.

Catherine Yen, Columbia University, New York, and colleagues from there and from the Centers for Disease Control and Prevention, Atlanta, Georgia, sought to detect fecal shedding of the pentavalent RV vaccine for 9 days following the first dose of vaccine in infants between 6 and 12 weeks of age. A total of 198 infants were enrolled in the study. Primary caretakers were given a stool collection kit and instructed to obtain swabs of the infant’s stool once daily for 9 days following receipt of the first dose of the pentavalent RV vaccine. “All stool samples were first tested for the presence of RV antigen [using an enzyme immunoassay (EIA)],” the authors noted.

Antigen-positive samples then underwent reverse transcription-polymerase chain reaction (RT-PCR) amplification and nucleotide sequencing of specific gene segments of RV strain WC3, the parent strain of the pentavalent RV vaccine. Some 103 stool collection kits were returned for analysis; slightly over half (57%) contained a complete set of 9 swabs. Of the 103 collection kits returned, 22 (21.4%) contained EIA-positive swabs on 1 or more post-vaccination days. “Of the 59 kits with a complete set of swabs, 12 (20.3%) had 1 or more positive swabs,” investigators reported.

Shedding occurred as early as the third day following receipt of the first dose of the RV vaccine and as late as the ninth day, with peak shedding occurring on post-vaccination days 6 through 8. The mean duration of shedding within the 9 days following receipt of the first dose of the RV vaccine was 2 days, investigators added. As they also noted, vaccine-type (WC3-like) RV alone was identified in all but 2 EIA-positive samples by RT-PCR.

In addition, 12 EIA-positive samples and 1 EIA-negative sample from 5 infants underwent RV cultivation; 75% of the positive samples and the 1 negative sample were culture-positive for vaccine-type RV.

“Our results demonstrate that the duration of vaccine virus shedding can extend beyond 6 days following vaccination, thus extending the time period for potential transmission of vaccine virus,” the authors observed. “[The fact that] we could efficiently cultivate vaccine virus from stool samples collected between days 6 and 9 post-vaccination suggests that sufficient infectious virus may be present for potential horizontal transmission of vaccine virus that may result in clinical disease.”

## No evidence concomitant use of the HZ/pneumococcal vaccines increases HZ risk

*Tseng et al. Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. Vaccine 2011;29(20):3628-32.*

**T**here is no evidence that patients receiving the herpes zoster (HZ) vaccine along with the pneumococcal vaccine are at greater risk of developing HZ because of a diminished immune response to the HZ vaccine, according to a large retrospective cohort study. These findings suggest that the product monograph should be revised to allow patients 60 years of age and older to receive both vaccines concomitantly and reduce barriers to recommended adult immunization schedules.

Dr. Hung Fu Tseng, Southern California Kaiser Permanente, Pasadena, and colleagues compared the incidence of HZ between Kaiser Permanente enrollees 60 years of age and older who received the HZ and the pneumococcal vaccine concomitantly and the incidence of HZ in those enrollees who did not receive the 2 vaccines concomitantly. For those who did not receive the 2 vaccines concomitantly, participants received the HZ vaccine during the same time interval as those who had received the 2 vaccines concomitantly but the non-concomitant group received a dose of the pneumococcal vaccine at some point within 365 to 30 days prior to receiving the HZ vaccine. In total, 7187 patients in the Kaiser Permanente cohort received the 2 vaccines concomitantly while 7179 others did not.

Over the study interval of January 1, 2007, to June 30, 2010, investigators documented 114 cases of HZ in total: 56 in the concomitant vaccination group and 58 in the non-concomitant group. At an average follow-up of 1.7 years, the incidence rate of HZ was 4.54/1000 person-years in those who had received the vaccines concomitantly vs. 4.51/1000 person-years for those who had not received the vaccines concomitantly.

In their fully adjusted analysis, the hazard ratio (HR) comparing the incidence rate of HZ in the concomitant vs. the non-concomitant cohort was 1.19, the authors added. The HR was lower in patients between the ages of 60 and 65 and highest in those between the ages of 70 and 75 but the differences between the 2 groups were not statistically significant.

“In this cohort study, we found no evidence of an increased risk of HZ in the population receiving a HZ vaccine and pneumococcal vaccine concomitantly on the same day,” the authors stated. “These results cast doubt about the necessity

of providing the 2 vaccines on separate dates.” The authors added that the safety profile of the HZ vaccine is not affected by the simultaneous administration of the pneumococcal vaccine either.

In an effort to avoid introducing barriers to these 2 important vaccines, the CDC continues to recommend that the HZ and the pneumococcal vaccine be given during the same visit if the patient is eligible for both vaccines.

## Accelerated hepatitis B schedule in high-risk pregnant women safe and effective

*Sheffield et al. Efficacy of an accelerated hepatitis B vaccination program during pregnancy. Obstet Gynecol 2011;117(5):1130-5. Cekmez et al. Response to hepatitis B vaccine differs by birthweight among neonates. Vaccine 2011;29(17):3096-7.*

**A**n accelerated hepatitis B vaccination schedule in high-risk pregnant women is safe and effective, providing comparable seroconversion rates to the standard hepatitis B vaccination schedule.

Dr. Jeanne Sheffield, The University of Texas Southwestern Medical Center, Dallas, and colleagues estimated the immunogenicity of an accelerated hepatitis B vaccination given at 0, 1 and 4 months in high-risk pregnant women who were hepatitis B surface antigen (HBsAg)-negative at presentation for prenatal care. Women were eligible for the study if they were less than 25 weeks' gestation and therefore could receive all 3 doses of the vaccine before delivery. Women also had a current diagnosis of a sexually transmitted disease, were current injection drug users or both, “high-risk” criteria for hepatitis B acquisition, as investigators pointed out. Two hundred women were enrolled, 84% of whom completed the 3-dose vaccine series.

As reflected by HBs antibody titres 10 MIU/mL or greater, seroconversion rates were 56% after 1 dose, 77% after 2 doses and 90% after the third dose. In comparison, seroconversion rates after administration of the standard 0-, 1- and 6-month hepatitis B vaccine schedule are 55%, 75% and >90%, based on results in a national cohort of healthy adults 40 years of age and under.

The vaccine was well tolerated and no serious adverse events were noted. Interestingly, body mass index (BMI) was inversely associated with seroconversion rates, although there was no single BMI cutoff above which seroconversion did not occur.

This latter observation was also reported by Cekmez et al. in neonates. He and colleagues observed response to the hepatitis B vaccine by birthweight. In a study comparing hepatitis B antibody titres of macrosomic infants vs. other infants, 96 infants were separated out by mean birthweights: group 1 at 2130 g, group 2 at 2920 g and group 3 at 4100 g. Median values of HBs antibody titres for groups 1, 2 and 3 were 1530 IU/mL, 1440 IU/mL and 1120 IU/mL, respectively.

“Our results show that macrosomic neonates achieve significantly lower titres of anti-HBs compared to [lower birthweight] infants after hepatitis B vaccine when the same needle was used for administration,” they concluded. “This supports the hypothesis that inadequate muscle penetration is responsible, at least in part, for lower immune responses to hepatitis B vaccine among macrosomic infants.”

## Herpes zoster incidence increasing across all age groups in the US

Leung et al. *Herpes zoster incidence among insured persons in the United States, 1993-2006: evaluation of impact of varicella vaccination*. Clin Infect Dis 2011;52(3):332-40.

The incidence of herpes zoster (HZ) is increasing across all age groups in the US but there is no evidence to suggest that the increase is in response to the varicella vaccine program now routinely offered to American children. Currently, varicella vaccination coverage among 19- to 35-month-old infants has increased from 68% in 2000 to 89% in 2006.

Dr. Jessica Leung, Centers for Disease Control and Prevention, Atlanta, Georgia, and multicentre colleagues used data from a large medical claims database from 1993, prior to the licensure of the varicella vaccine, to 2006, the year the HZ vaccine was licensed in the US. These data were used to track trends in HZ and better understand the impact of varicella exposure on the epidemiology of HZ. Investigators calculated the incidence of HZ using all enrollees in the MarketScan database who had received a diagnosis of HZ. This served as the numerator in the equation; the total MarketScan enrolment served as the denominator. HZ incidence was stratified by age and sex.

Between 1993 through 2006, there were 282,973 incidence cases of HZ in the study population. The mean age of those who developed HZ was 52.5 years in 1998 and 53.2 years in 2006. Specifically, the incidence of HZ increased from 1.7/1000 enrollees in 1993 to 4.4/1000 enrollees in 2006—a 98% increase in the overall incidence in 13 years, after standardizing by age and sex, as the authors pointed out. “Increases occurred among all age strata and both sexes, increasing more rapidly among females,” they reported. Importantly, age-specific HZ incidence did not differ between adults living in states with high varicella vaccine coverage and those living in low-coverage states.

As investigators pointed out, adults with dependents 12 years of age and under had a lower incidence of HZ when the varicella vaccine program was launched compared with adults without dependents. However, as the varicella program progressed, “the incidence in both groups became similar,” they stated, “and these ecologic analyses suggest that the varicella vaccination program has not influenced HZ incidence in the general population.”

Investigators also pointed out that their data show that increases in the incidence of HZ predated vaccine licensure and were most rapid during the early years of the vaccination program, before vaccine uptake reached high levels. □

### UPCOMING EVENTS

#### Sixth Annual Immunotherapeutics and Vaccine Summit

August 16-18, 2011 / Cambridge, MA

<http://www.healthtech.com/imt/clv>

#### European Scientific Working Group on Influenza (ESWI)

September 11-14, 2011 / St. George's Bay, Malta

[www.eswiconference.org/](http://www.eswiconference.org/)

#### XV International Congress of Virology

September 11-16, 2011 / Sapporo, Japan

[www.congre.co.jp/iums2011sapporo/data/general.html](http://www.congre.co.jp/iums2011sapporo/data/general.html)

#### AIDS Vaccine 2011

September 12-15, 2011 / Bangkok, Thailand

[www.hivaccineenterprise.org/conference/2011/about](http://www.hivaccineenterprise.org/conference/2011/about)

#### Vaccines for Enteric Diseases

September 14-16, 2011 / Cannes, France

[www.meetingsmanagement.com/ved\\_2011/index.htm](http://www.meetingsmanagement.com/ved_2011/index.htm)

#### 51st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)

September 17-20, 2011 / Chicago, IL

[www.icaac.org/](http://www.icaac.org/)

#### 27th International Papillomavirus Conference and Clinical Workshop

September 17-23, 2011 / Berlin, Germany

[www.hpv2011.org/index1.asp?siteid=1&pageid=1](http://www.hpv2011.org/index1.asp?siteid=1&pageid=1)

#### 14th Annual Meeting of the European Society for Clinical Virology

September 21-24, 2011 / Madeira, Portugal

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