HPV 2014
CONFERENCE REVIEW

Making Education Easy

August 20–25, 2014, Seattle, USA

In this review:

- *HPV vaccine dosing schedules*
- *9HPV vaccine*
- *Primary HPV screening*
- *The 'invisible' man*
- *Head and neck*
- *Update on current vaccines*

Abbreviations used in this issue

CIN = cervical intraepithelial neoplasia
GI = gastrointestinal
GP = general practitioner
HPV = human papillomavirus
MSM = men who have sex with men
OPC = oropharyngeal cancer

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Welcome to this review of the 29th Annual International Papillomavirus Conference and Public Health and Clinical Workshops, held over 6 days. The meeting brought together >1200 of the world's leading researchers, funders and policymakers involved in HPV to exchange and debate information and set directions for the field. This review summarises some of the presentations/abstracts from the conference. Selection and commentary has been provided by Min Lo who attended the conference in Seattle, USA.

We hope you enjoy this Conference Review. Please feel free to send us your feedback and comments.

Kind regards
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Summary of Conference Review

Two-dose schedule

- Data from randomised trials have demonstrated noninferiority of two doses of 2HPV and 4HPV compared with three doses in girls aged 9–13 years.
- The WHO SAGE (Strategic Advisory Group of experts) in April 2014 recommended a two-dose schedule for adolescent girls aged <15years. A three-dose schedule is still recommended for those aged >15 years or who are HIV-positive.
- There are many countries that have now implemented a two-dose schedule – Canada, Netherlands, Italy, Austria, UK, France, Switzerland, South Africa, Brazil, Columbia and Mexico.

9HPV (9 valent vaccine)

- The 9HPV vaccine has completed clinical trials and is currently under review by the US FDA and other countries. It is expected to become available in 2015 as a three-dose vaccine.
- It is expected to provide 90% protection against cervical disease (the 2HPV and 4HPV provide 70% protection).
- In the future the 2HPV and 4HPV vaccines will be phased out.

Cervical screening

- HPV testing is steadily taking over as the primary screening tool instead of cervical smears.

Male vaccination

- Implemented by three countries only (Austria, Canada and Australia). Austria is the only country to have implemented a gender-neutral two-dose programme. Reports from these countries suggest very good acceptance and relatively problem-free rollout.

Anal and oral HPV related cancers

- These predominantly affect males more than females, and the rates continue to increase. Data from the US show that oropharyngeal cancers related to HPV in men is now at a rate comparable to that of cervical cancer. The HPV vaccine has high efficacy against anal disease, but it is not known yet what the outcomes are for oropharyngeal disease. There is no method of screening for HPV disease in males, and primary prevention through vaccination is the only way.

Update from Australia

- Australia is now in its eighth year since HPV vaccination was initiated in 2007. Monitoring of outcomes (data from 2014) shows national vaccination coverage of 70% (NZ 56%). Studies in Australia monitoring HPV prevalence, CIN disease and rates of external genital warts are showing a dramatic decline in rates.

Natural history

- A 'negative' HPV test does not necessarily mean there is no infection. Undetectable virus may reflect latency. Positive HPV tests may reflect either new acquisition of infection, 'blipping' or shedding of virus or persistent high activity.

HPV VACCINE DOSING SCHEDULES

Two-dose schedules – why might two doses work?

Presenter: Stanley M

Summary/comment:

- Any vaccination must induce robust immune memory to provide at least 20–30 years of protection
- The best age to give the HPV vaccine is 9–11 years. This age group has an immunogenicity response that is two-fold higher than 18- to 26-year olds. After the age of 11 years, antibody response to vaccination is 'downhill all the way'.
- Clinical trials on two-dose schedules are based on girls aged 9–14 years using a 0,6 schedule. The data show an immunogenicity response that is as good as the usual three-dose schedule with a good safety profile.
- As is the case with the current three-dose vaccines, we don't know what the duration of protection will be.
- NZ currently delivers a three-dose schedule at 0,1/2,6 months. Skipping the third dose after receiving the first two doses at 0 and 1–2 months is not considered adequate as the minimum interval should be 6 months.
- Following the WHO recommendation in April 2014, GAVI the Vaccine Alliance has changed its alliance scheme to only support a two-dose schedule. There are now 20 African countries and one Asian country that now must switch to a two-dose schedule.
- Monitoring of immunogenicity and clinical endpoints will be required to make sure the reduced level of dosing actually works – best to let other countries who are already set up with good research teams do this and report back.
- Quebec City have been doing 0,6,60 since 2007 and monitored for immunogenicity. Results show 100% seroconversion with good antibody titres after the second 6-month dose, which persists at the third follow-up (after the third dose). The increase in immunogenicity after the third dose is not much higher than after the second.
- There are no current data on two-dose schedules for males, although in theory there is no reason why they should be different.
- Austria is the only country at present to be delivering a gender-neutral (boys and girls) programme in a two-dose schedule.

Preconference Workshop and Interactive session

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Romanowski B et al. Immune response to the HPV-16/18 AS04-adjuvanted vaccine administered as a 2-dose or 3-dose schedule up to 4 years after vaccination: results from a randomized study. Hum Vaccin Immunother 2014:10(5);1155–65

World Health Organisation. Meeting of the Strategic Advisory Group of Experts on immunization, April 2014 – conclusions and recommendations. Weekly Epidemiological Record 2014;89(21):221–36

Other dosing schedules of HPV vaccine

Summary/comment

- In theory, a 0,12-month schedule would also work (although this was not part of trial data). A once-a-year programme may seem logistically easier, but there has been concern that this reduces the opportunity for nurses to 'mop up the stragglers'. Many schools also have problems with truancy, and individuals will need to see their GP if the second dose is missed.
- The UK is moving to a two-dose schedule at 0,12 months. Public health nurses will now be only going to schools once a year, when they used to go in three times a year.
- Can the schedule be extended from the current three-dose schedule of 0,2,6 to 0,6,12 or 0,12,24 months? Yes, this can be done. Data for the 0,12,24-month schedule are not yet published. This may be useful for some school-based programmes.

Satellite Session

HPV16 antibody avidity following one and two doses of HPV16/18 vaccine: results from the Costa Rica HPV16/18 Vaccine Trial (CVT)

Authors: Safaeian M et al.

Summary: This research investigated HPV16 antibody avidity at 48 months among HPV 16/18 vaccine recipients who received one of the four following schedules: i) one-dose (n=78); ii) two-doses separated by 1 month (2[0/1]; n=140); iii) two-doses separated by 6 months (2[0/6]; n=52); and (iv) three scheduled doses (n=100). The geometric mean HPV16 avidity values at 48 months in the respective groups were 2.17, 2.35, 2.30 and 2.61 (p=0.003 for trend). The respective ratios of HPV16 geometric means for the three-dose schedule versus the 2(0/1), 2(0/6) and one-dose schedules were 0.90 (95% CI 0.82, 0.98), 0.88 (0.78, 0.99) and 0.83 (0.74, 0.93).

Comment: Would one dose work? Results from a trial in Costa Rica have found that in girls who received only one dose of vaccine there was a good antibody response; the titres were lower than for a two- or three-dose schedule, but follow-up showed no decline at 4 years.

Public Health Science Oral Abstract 02.04; Vaccines 1

9-VALANT HPV (9HPV) VACCINE

Current and next generation HPV vaccines

Presenter: Markowitz L

Summary/comment

- 9HPV vaccine has now completed clinical trials and is currently under review by the US FDA and other licensing authorities around the world. It is expected to become available in 2015.
- The vaccine doesn't have a name yet and the cost is unknown.
- The vaccine includes an additional five HPV types – 31/33/45/52/58.
- Globally, these five HPV types together contribute to 30% of CIN2+ and 20% of invasive cervical cancer, so there is potential benefit to prevent a total 90% of pre-invasive cervical disease.
  - These five types also contribute to about 11% of other invasive cancers (penile, anal, oral, vulva, vaginal).
- The trial data in women aged 16–26 years show 97% efficacy for HPV 31/33/45/52/58-associated disease outcomes, good immunogenicity and safety profile.
- Trial data on boys aged 9–15 years show good immunogenicity and safety.
- 9HPV vaccine will be more useful for females than males because the '5 other types' mainly contribute to cervical disease and not so much to anal/OPC or penile cancers. However, this doesn't mean that in the future there will be one vaccine for girls and a different one for boys; the quadrivalent vaccine will probably be phased out.
- Countries will start moving to the 9HPV vaccine when it becomes available.
- The 9HPV vaccine will be licensed as a three-dose schedule. Studies on 9HPV vaccine in a two-dose schedule are currently underway.
- The availability of the current vaccines in a two-dose schedule and the new 9HPV vaccine in a three-dose schedule is causing confusion for many countries.

Plenary session

9HPV VACCINE *(CONTINUED)*

Efficacy and immunogenicity of a novel 9-valent HPV L1 virus-like particle vaccine in 16–26 year old women

Authors: Joura E et al.

Summary/comment: This is the key paper on 9HPV vaccine trial data. The Protocol 001 trial enrolled 14,204 women aged 16–26 years to receive 9HPV vaccine or quadrivalent HPV injections on day 1, month 2 and month 6. Noninferiority was seen between the two vaccines for anti-HPV 6/11/16/18 responses, but there were 30 cases of HPV 31/33/45/52/58-related high-grade cervical/vulvar/vaginal disease among quadrivalent HPV vaccine recipients compared with just one case (96.7% efficacy) among 9HPV vaccine recipients. The respective efficacy rates against HPV 31/33/45/52/58-related any-grade cervical/vulvar/vaginal disease and 6-month persistent infection in the per-protocol efficacy population were 97.1% and 96.0%.

Public Health Science Oral Abstract 02.01; Vaccines 1

Efficacy of a novel 9-valent HPV L1 vaccine against disease irrespective of HPV type

Authors: Giuliano A et al.

Summary: This analysis of Protocol 001 study data (see previous summary) evaluated the potential for the 9HPV vaccine to decrease the overall risk of cervical, vulvar and vaginal disease. In a historical placebo group (regardless of HPV), 9HPV vaccine was found to reduce the risk of any-grade cervical disease by 47.1%, high-grade cervical disease (CIN ≥2) by 62.8%, condyloma by 94.6%, Pap test abnormalities (ASCUS HR HPV positive or worse) by 44.3% and high-grade lesions (atypical squamous cells of high grade or worse) by 63.8%.

Comment: Does the 9HPV vaccine have efficacy against **any** HPV type, even those types that are not in the vaccine? The answer was yes.

Public Health Science Poster Discussion Abstract 04.05; Vaccination/Screening/Epidemiology

An open-label, randomized study of a nine-valent human papillomavirus vaccine given concomitantly with REPEVAX in healthy adolescents aged 11–15 years

Authors: Kosalaraksa P et al.

Summary: Children aged 11–15 years stratified 1:1 by gender were randomised 1:1 to receive IM 9HPV vaccine 0.5mL on day 1, month 2 and month 6 plus IM diphtheria/tetanus/acellular pertussis/inactivated poliomyelitis vaccine (REPEVAX®) 0.5mL in the opposite deltoid either on day 1 (n=526) or at month 1 (n=528). Noninferiority was demonstrated between the two groups for anti-HPV geometric mean titre and seropositivity rate across all 9HPV antigens, and the seroconversion rates for the 9HPV vaccine types were ≥99.8% in both groups. Noninferiority for immune response was established for diphtheria, tetanus and all polio and pertussis antigens between the groups. No vaccine-related serious adverse events were reported.

Public Health Science Poster Abstract 06.30; Vaccination

Immunogenicity and tolerability of a novel 9-valent HPV vaccine given concomitantly with MENACTRA and ADACEL in 11 to 15 year old boys & girls

Authors: Schilling A et al.

Summary: In a similar study, children aged 11–15 years were randomised to receive 9HPV vaccine on day 1, month 2 and month 6, along with *Neisseria meningitidis* serotypes A, C, Y and W-135 vaccine (Menactra®) and diphtheria/tetanus/acellular pertussis vaccine (Adacel®) in the opposite limb on day 1 (n=621) or month 1 (n=620). Noninferiority was demonstrated between the groups for: i) geometric mean titres for all nine HPV types in the 9HPV vaccine 4 weeks after the third dose; ii) the proportions of recipients with a ≥4-fold increase in titres for four *N. meningitidis* serotypes 4 weeks after Menactra® injection; and iii) the proportions of recipients with antibody titres to diphtheria and tetanus ≥0.1 IU/mL and geometric mean titres for pertussis antigens 4 weeks after Adacel® injection. No vaccine-related serious adverse events were reported, and the safety profiles were generally comparable between the two groups.

Public Health Science Poster Discussion Abstract 04.04; Vaccination/Screening/Epidemiology

Comment: Can the HPV vaccine be co-administered with other teenage vaccines (at the same visit)? In NZ, this would be tetanus/diphtheria/pertussis (Boostrix®) given at age 11 years. The answer is yes, this is safe, and would provide an alternative and easy platform to deliver HPV vaccine.

Immunogenicity and safety of a 9-valent HPV vaccine in prior quadrivalent HPV vaccine recipients

Authors: Luxembourg A et al.

Summary: Females aged 12–26 years were randomised in a 2:1 ratio to receive 9HPV vaccine (n=618) or placebo (n=306). Compared with placebo recipients, 9HPV vaccine recipients had a higher injection-site adverse event rate 1–5 days postvaccination (91.1% vs. 43.9%), but similar vaccine-related systemic adverse event rates 1–15 days postvaccination (30.6% vs. 25.9%) and adverse-event related discontinuation rate (0.5% vs. 0%). There was one vaccine-related serious adverse event in each group. Four weeks after the third dose, >98% of 9HPV vaccine recipients were seropositive for HPV 31/33/45/52/58, with marked increases in geometric mean titres to these HPV types. Recipients of 9HPV vaccine who had not previously received quadrivalent HPV vaccine had lower anti-HPV 31/33/45/52/58 geometric mean titres.

Comment: Can I (or my child) have the 9HPV vaccine if I have previously completed GARDASIL®? The answer is yes you can. This appears to have predictably good immune response with the usual mild side effect profile. Can I switch to 9HPV vaccine if I am halfway through the GARDASIL®? The answer is 'don't know'.

Public Health Science Poster Abstract 06.37; Vaccination

PRIMARY HPV SCREENING

Natural history of HPV in women – implications for screening practices

Presenter: Cox T

Summary/comment

- Age to begin screening
  - In mid-20s (2012 guidelines from ACS, ACOG, USPSTF) – need to prevent harm and balance gains.
  - It is important not to screen the under 20s, as the harms caused by colposcopy and biopsy outweigh any benefit.
- Screening interval
  - Ranges from seven screens per lifetime in the Netherlands to ~20 in the US.
  - Three-year interval with cytology is a good balance between detecting disease and causing harm by overscreening.
  - If using cotesting (cytology plus HPV), the screening interval can be longer.
- When to stop screening
  - Despite a slight increase in HPV and CIN, in early 60s – a woman who has been well screened by age 65 years has very little risk of developing invasive cancer and there is little to be gained with ongoing screening.
- New options
  - Screening with HPV alone (primary HPV testing).

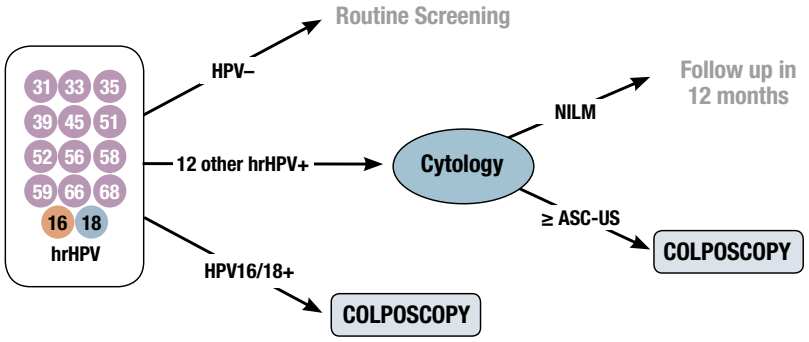
Preconference workshop

PRIMARY HPV SCREENING *(CONTINUED)*

A new era in cervical cancer prevention: implementing HPV primary screening into practice

Summary/comment

- Primary screening with HPV is more sensitive than cytology and is equivalent to cotesting (cytology followed by HrHPV testing)
- There are now substantial data that support HPV primary screening for cervical cancer, including the ATHENA trial, which enrolled more than 47,000 women. The US FDA reviewed these data and in April 2014 approved the Cobas HPV test for use as the first-line primary screening test in women aged 25 years and older. Guidelines on the use of HPV screening as a primary screening tool are currently being developed by the SGO and ASCCP.
- A negative HPV result will go on to routine screening (interval to be determined at either 3 or 5 years)
- A positive HrHPV test will be triaged by HPV 16/18 genotyping. Those who are positive for HPV 16/18 will go on to colposcopy. Those who are positive for the other 12 HPV types will be further triaged by either by cytology or dual staining with p16/Ki-67. Women who have negative cytology or staining will have follow-up in 12 months
- HPV primary screening is already being implemented in the following countries.
  - The Netherlands – starting 2016.
  - Australia (pending final approval) – HPV primary screening with 16/18 genotyping starting at age 25 years up to age 70–74 years with a 5-year interval.
  - US – approved by the FDA beginning at age 25 years; awaiting recommendations by guidelines groups.
  - Italy – already in use.



Lunch symposium

THE 'INVISIBLE' MAN

Natural history of HPV in men – genital anus and oral mucosa

Presenter: Giuliano A

Summary/comment

- The prevalence of HPV remains high in men regardless of age (unlike women where prevalence is high in younger age and decreases with age).
- Men develop poorer antibody response to natural infection compared with women.
- There is no routine screening available for men and no option for prevention, except for vaccination.
- Anal HPV can be detected in heterosexual men (10% prevalence) compared with 50% of MSM.
- The prevalence of oral HPV is lower than anal (~4%), but is more likely to be persistent.
- HPV at different sites has markedly different natural history in terms of rates, clearance and persistence regardless of gender.

Preconference workshop

Male vaccination

Summary/comment

- Only three countries have implemented national immunisation for boys – Australia, Canada (only in two provinces) and Austria.
- Austria has implemented a gender-neutral programme in a two-dose schedule.
- Males are affected by a range of HPV-related diseases, with a rising incidence of anal and oropharyngeal disease.
- The quadrivalent vaccine has been shown to be very effective in males.
- MSM are not affected by vaccination of female population.
- Herd immunity is often quoted as a reason not to require vaccination for boys, but the reality is that this is not realistic in most countries.
- Modelling from Australia shows that vaccination of boys provides more effective population coverage.
- Australia started vaccination for boys in 2013, and reports show that this has gone well – as at August 2014, 760,000 doses had been given.
- At present, there are no data available for two-dose schedules in males, although there is no reason why this would also not be useful.

Preconference workshop

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Palefsky JM et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. N Engl J Med 2011;365(17):1576–85

Smith MA et al. The predicted impact of HPV vaccination on male infections and male HPV-related cancers in Australia. Vaccine 2011;29(48):9112–22

Anal cancer in HIV-infected men

Presenter: Palefsky J

Summary/comment

- Anal cancer is generally uncommon and comprises 2.5% of all digestive tract system cancers. Amongst the general HIV-negative heterosexual population, anal cancer is more common in women than men.
- From an aetiological standpoint, anal cancer has more in common than GI tract tumours, as risk is associated with HPV infection, lifetime number of sexual partners, genital warts, cigarette smoking, receptive anal intercourse and HIV infection.
- The rate of anal cancer in HIV-negative men and women is 1.5/100,000 (compared with cervical cancer ~2–5/100,000). The rates of anal cancer are much higher in MSM, HIV-positive heterosexual men and women at about 30–40/100,000, which is as high as the rate of cervical cancer was before cervical cytology screening began.
- The incidence of anal cancer in HIV-positive MSM is especially high – 130/100,000.
- The prevalence of HPV in the anal canal in HIV-positive MSM is almost 90%, and rates of high grade AIN2+ lesions are about 50%.
- Almost all anal cancers are caused by HPV, mostly HPV-16.

Preconference workshop

THE 'INVISIBLE' MAN *(CONTINUED)*

HPV and HIV

Presenters: Palefsky J & Kojic M

Summary/comment

- We are doing a better job at controlling HIV infection, and people are living longer in the post-ART era. However, there is no corresponding decrease in HPV-related complications.
- It is now recognised that an 'undetectable' HIV viral load does not mean a person has 'no virus'. HIV proteins are present in the epithelium and cause inflammation and disruption in immune barrier function. At this tissue level, there is an increase in the risk of HPV infection and also direct effects between HIV and HPV viruses. This means existing high-grade changes related to HPV will continue to progress with time, regardless of how high or good the CD4 count is.

Preconference workshop

HEAD AND NECK

Oral HPV natural history and its progression to oropharyngeal cancer

Presenter: Kreimer A

Summary/comment

- Globally, the incidence of HPV-related OPC is increasing. In contrast, non-HPV-related OPC (e.g. from smoking) is decreasing.
- In the US, the incidence of OPC in males is now more common than for cervical cancer.
- In the US, 60–70% of OPCs are due to HPV, but this figure could be as high as 90% in some settings.
- HPV prevalence in the oropharynx is three times more common in males than females.
- HPV-related cancers occur primarily in the tonsils and base of the tongue.
- Oral HPV incidence is most common in age 40–50 years.
- In contrast to genital HPV, there is no peak in HPV in the oropharynx after sexual debut, and the incidence is stable across all age categories.
- The majority of OPCs are due to HPV-16, and there is high seropositivity to HPV-16 E6 in individuals with OPC.

Plenary

UPDATE ON THE CURRENT VACCINES

Current and next generation HPV vaccines

Presenter: Markowitz L

Summary/comment

- HPV vaccination induces very good immune memory response. The current bivalent and quadrivalent vaccines are at 8–10 years of follow-up, safety profiles remain excellent and there is no evidence of waning protection.
- To date (2014) there are 54 countries that are providing HPV vaccination.
- Population impact data are now starting to come through from countries able to provide surveillance data. They show that there are decreasing rates of HPV prevalence from four countries, external genital warts from six countries and cervical lesions from two countries.

Preconference workshop

Effects of the HPV vaccination programme in Australia: evidence to date

Presenter: Brotherton J

Summary/comment

- In 2007, Australia was the first country to start a fully funded vaccination programme in girls aged 12–26 years.
- The programme is currently in its eighth year.
- National coverage is ~70% across the country (80% in Northern Territory).
- Coverage is also good in lower socioeconomic populations and remote areas.
- Lowest coverage is in indigenous girls aged 12–17 years.
- Evaluation endpoints include data on DNA prevalence, CIN disease and external genital warts.
- There are two studies reporting on DNA prevalence.
  - One showed a dramatic drop in cervical HPV prevalence in vaccinated populations, including nonvaccine types.
  - Another showed a fall in HPV-16 prevalence in the prevaccinated population.
- There has been dramatic decline in high-grade cervical disease in the 20- to 24-year age group. This used to be the age group with the highest rates of cervical disease, but has now dropped below the 25- to 29-year olds.
- The incidence of external genital warts in females aged <21 years has dropped to almost zero (Melbourne Sexual Health).

Plenary

REFERENCES

Garland S et al. (see following summary)

Tabrizi SN et al. Assessment of herd immunity and cross-protection after a human papillomavirus vaccination programme in Australia: a repeat cross-sectional study. Lancet Infect Dis; published online Aug 6, 2014

Assessing the impact of HPV vaccination on HPV genotype status in CIN3 cases in Australian women

Authors: Garland S et al.

Summary: The VACCINE (Vaccine Against Cervical Cancer Impact and Effectiveness) study is assessing the effectiveness of the vaccine programme in Victoria, Australia, for reducing CIN3 lesions positive for vaccine-specific HPV types.Vaccine-eligible women who have undergone sequential CIN3/AIS cervical biopsies submitted for histopathology are being tested for HPV DNA detection and genotypes using whole-tissue section processing. This abstract reported an interim analysis showing that the HPV-16 prevalence in 202 CIN3/AIS lesions (of 500 targeted) did not differ significantly from the prevalence seen in 205 prevaccine age-matched CIN3 samples (59% vs. 63% [p=0.47]), but the prevalence among women aged 18–25 years was almost statistically significantly lower (69% vs. 55% [p=0.06]).

Comment: A study was done on HPV DNA prevalence, showing that HPV-16 in a group of young prevaccinated girls was only 1.6%, compared with 18% in the prevaccination era.

Public Health Science Poster Abstract 06.20; Vaccination

UPDATE ON THE CURRENT VACCINES *(CONTINUED)*

Natural history of HPV

Summary/comment

- Natural infection does not always result in seroconversion or in an immune response that is protective.
- Seroconversion occurs more commonly in females (70–80%) than in males (30–40%).
- Antibody response after natural infection is slow, weak and not generally protective.
- There continue to be many questions and no clear answers. There are conflicting thoughts as to whether HPV is an infection that truly 'clears', and does a 'negative' HPV test simply reflect undetectable latent virus?
- Is finding HPV DNA a definition of 'infection'?
- It is likely that most individuals have undetectable HPV infection that is controlled by the immune system. Loss of immune control results in detectable virus and a person can be shedding intermittently (or blipping) or be persistently positive.
- Risk of high-grade disease is likely to be related to detectable virus that is not only persistent but also high in copy number.
- Just being positive over two points in time may not represent a true increase in the risk of disease.

Preconference Workshop

Reliable categorization of CIN to address diagnostic problems of CIN 1 and 2 by combining molecular biomarkers P16 and PANHR-HPV E4

Authors: van Baars R et al.

Summary: This research conducted on 500 lesional and normal epithelial areas from 116 cervical specimens investigated whether combining biomarkers of productive HPV infection and transformation (E4, MCM and p16INK4a) is more reliable for CIN categorisation than histology. The interobserver agreement among the three pathologists who performed histological diagnoses ranged from moderate to substantial, whereas interobserver agreement for biomarker scoring was good to excellent. Distinct immunostaining patterns were related to CIN grades. There was complete agreement that histologically negative regions were E4 negative; 82% were p16-negative and had only basal MCM staining. The agreed CIN1 cases were usually E4-positive with limited p16 staining below the MCM-positive layers, indicating productive hrHPV infection. Some of the CIN1 cases resembled CIN2 and were E4- and p16-positive. CIN2 cases were divided into intermediate lesions (expressing E4 and p16) and transforming lesions (expressing p16 but not E4). CIN3 cases had consistently high MCM and p16 levels with little or no superficial E4 staining, indicating transforming lesions. Biomarker assessments identified missed lesions in several cases.

Comment: CIN2 is not homogenous and there two major categories of transformation, with and without evidence of viral production. What this paper suggests is that the current paradigm of 'clearance' may not be true and HPV latency may be more common than we think.

Clinical Science Oral Abstract 06.04; Cervix 2

Pre-vaccination type-specific HPV prevalence in confirmed cervical high grade lesions in the Māori and non-Māori populations in New Zealand

Authors: Kang Y-J et al.

Summary: These researches identified women aged 20–69 years with an index high-grade cytology report (ASC-H, HSIL+, AGC or AIS) during 2009–2012 from NZ's National Cervical Screening Programme register. Among the 730 women who consented and had a valid HPV test result, 418 had histologically confirmed CIN2/3 lesions, including 149 Māori and 269 non-Māori women. The respective prevalences of oncogenic HPV, HPV-16 and HPV-18 in both Māori and non-Māori women with confirmed CIN2/3 were 96%, 54% and 11%. Age-specific patterns of infection for HPV-16/18 differed between Māori and non-Māori women (p=0.02 for interaction), with a lower prevalence in younger versus older Māori women (57% in 20–29 years vs. 75% in 40–69 years), but a higher prevalence in younger versus older non-Māori women (70% in 20–29 years vs. 49% in 40–69 years).

Comment: These are prevalence data from NZ. HPV-16 and HPV-18 contribute 62% of high-grade lesions (54% for HPV-16 and 11% for HPV-18), with no difference between Māori and non-Māori women.

Public Health Science Poster Abstract 05.05; Social/Behavioural

Independent commentary provided by Dr Min Karen Lo

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Min graduated from Auckland University in 1993 and completed specialist qualifications as a Fellow of the Royal Australasian College of Physicians (FAChSHM) in 2004.

She is a colposcopist (investigation and treatment of abnormal cervical smears and cervical cancer) at Counties Manukau Super Clinic.

She is also a forensic physician and is a medical examiner for the NZ Police in the area of sexual assault. She has a Masters in Forensic Medicine from Monash University in Melbourne.

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