

First Asia–Oceania Research Organisation on Genital Infections and Neoplasia (AOGIN) Meeting

The first AOGIN meeting was held in Kota Kinabalu, Malaysia, in July 2005. The conference covered regional issues relating to infection with the human papillomavirus (HPV)—epidemiology, virology and immunology, testing, screening and prevention strategies—as well as cervical cancer screening and its management.*

The meeting was generously supported by several pharmaceutical and diagnostic companies, and received helpful input from professional societies. Delegates from 23 nations attended the meeting and gave insights into HPV and cervical cancer epidemiology and management in their countries.

The Second Meeting will be held in Cebu, The Philippines, on 7–9 September 2006.

Introduction to AOGIN. Suzanne Garland

Cancer prevention and control are among the most important public health challenges facing the world today. Worldwide, carcinoma of the uterine cervix is the second most common cancer of women. Incident cases are estimated to be ~470 600 per annum, with almost 80% occurring in the developing world.

The AOGIN concept was based upon an expert multidisciplinary group developed overseas—the European Research Organisation on Genital Infection and Neoplasia (EUROGIN).

Cervical cancer and HPV—the essential epidemiology. Xavier Bosch

Globocan data suggest that around 470 000 cases of cervical cancer are diagnosed worldwide every year. While this is a far lower incidence than for breast cancer (1 050 000 diagnoses per year), cervical cancer remains the second most common cancer for women. Colon/rectal cancer, lung cancer and stomach cancer, which can affect both men and women, all have lower incidences at 446 000, 387 000 and 418 000, respectively.

HPV—virology and epidemiology. Ian Frazer

Papilloma viruses are double-stranded DNA viruses that replicate only in the skin cells of their host species. They do not grow in cell culture. There are many different immunologically distinct types of HPVs, which have been

linked to specific conditions—genital warts (HPV 6, 11), genital cancer (HPV 16, 18), epidermodysplasia verruciformis (EV; HPV 5, 8) and cutaneous warts (HPV 1, 2).

HPV DNA testing—assays and standards. Suzanne Garland

Laboratory procedures with known, consistent specificity and sensitivity for detecting and typing HPV are needed to conduct effective epidemiological surveys and vaccine evaluation. The standardisation of HPV assays is still evolving and requires external quality assessment.

HPV testing in clinical practice. Henry Kitchener

The most important clinical value of HPV testing in the lower genital tract is to distinguish women at very low risk of malignancy from those at some risk. In cervical screening, the principal roles that HPV testing may play are in primary screening, in following up the treatment of cervical abnormalities and in triage of mild abnormalities.

Baseline results of HPV DNA testing in European screening studies. Jack Cuzick, Christine Clavel, Ulli Petry, Peter Sasieni, Chris Meijer, Philippe Birembaut, Anne Szarewski, Achim Schneider, Shalini Kulasingam, Sam Ratnam, Thomas Ifner

The objectives for reviewing HPV screening trials were to determine the age-specific HPV prevalence in different European areas, to evaluate the sensitivity and specificity of HPV testing in women attending routine screening, and to compare the sensitivity and specificity of HPV testing with that of routine cytology.

Treatment of pre-invasive cervical lesions—is there any value in testing for HPV DNA post-treatment? Jeffrey Tan

A 2001 Cochrane report suggests there is no overwhelmingly superior surgical technique for eradicating cervical dysplasia (CIN). Regardless of treatment approach, the risk of persistent disease is greater when the lesion is large, or the patient is >30 years of age or has been treated previously and/or is a carrier of HPV types 16 or 18.

*A full version of the Proceedings is available from Infectious Diseases in Obstetrics and Gynaecology. (www.hindawi.com/GetJournal.aspx?journal=IDOG).

Singapore—cancer screening and epidemiology.
EH Tay

In Singapore, cancer causes more deaths than heart disease. Cervical cancer is the fourth most prevalent cancer in Singapore, and based on 1993–98 data, has an adult survival rate (ASR) of 14.3/100 000. Breast, lung, colorectal cancers and, in recent years, ovarian cancers, have a higher incidence. Breast, colorectal and ovarian cancer rates are increasing; lung and cervical cancer are decreasing, a trend believed to be linked to behavioural factors.

Organisational aspects of successful screening programs in developed countries—the English model.

Henry Kitchener

In planning a cancer screening program, each country will develop guidelines based on the best available estimates of costs, benefits and risks. Guidelines can be reviewed in light of emerging evidence as well as new diagnostic and treatment options. Evaluation of a program's coverage should consider the age of eligible participants, the frequency of testing, and community awareness of, and access to, the program. All will impact on cost and effectiveness.

Cervical cancer in the Philippines.
Genera A Manuel-Limson

In the Philippines, cervical cancer is the second most common cancer among women, behind breast cancer. The ASR is estimated to be 22.5/100 000. Incidence rises sharply in women >35 years of age. More than 7000 new cases and almost 4000 deaths are seen each year. There is a close link between neoplastic cervical changes and HPV persistence. Of 356 cases of SCC or ADC, 93.5% tested positive for HPV, compared with only 9.1% among a control group. HPV types 16 and 18 were most frequently associated with cervical cancer.

India—epidemiology and screening of cervical cancer.
Neerja Bhatla

Cervical cancer is the most common neoplasm in Indian women, with 126 000 new cases and 70 000 deaths each year. Incidence is higher than in Eastern Asia. Across India, age-adjusted rates (AARs) vary greatly from ~55/100 000 in Ambillikai to <18 in Mumbai and Trivandrum. Across India, cervical cancer is the commonest cancer reported from all cancer registries except those in Mumbai and Delhi, where breast cancer is the commonest.

China—HPV infection and cervical cancer screening studies. *You-lin Qiao*

Mortality data from the 1970s to the 1990s suggest that China suffers relatively high cervical cancer mortality, particularly in the rural mid-west. Wudu in Gansu province and Yangcheng in Shanxi had age-adjusted mortality rates of >40/100 000 in 1990–92. Better diagnosis and

treatment have reduced deaths from cervical cancer, but the improvement is not uniform and mortality rates are unchanged in some counties.

Hong Kong—cervical cancer screening.
Annie NY Cheung

Hong Kong has a population of 6.8 million. Life expectancy for women at birth was estimated to be 84.3 years in 2003. During the period 1988–92, Hong Kong's ASR for cervical cancer was ~17; this is lower than that of the Thai, Korean, Filipino and Singapore-Chinese populations, but higher than in Japan.

Screening Technologies to Advance Rapid Testing (START). *John Sellors*

This project aims to detect precancerous cervical lesions using newly developed rapid biochemical tests that are affordable, accurate, simple to use and appropriate for low-resource settings.

Costs of HPV DNA testing in cervical screening.
Jack Cuzick

HPV DNA testing has an estimated sensitivity of 96% and specificity of 92%, making it considerably more sensitive and only marginally less specific than cytology. There is sufficient evidence based on surrogate markers that the efficacy of HPV testing, using a validated system, as the primary screening modality can be expected to be at least as good as that of conventional cytology.

Emerging prevention strategies—promises of the quadrivalent HPV 6, 11, 16, 18 vaccine (GARDASIL). *Richard M Haupt*

A vaccine protecting against HPV types 6, 11, 16 and 18 is expected to substantially reduce the burden of HPV-related diseases. Merck's quadrivalent HPV L1 virus-like particle (VLP) vaccine, GARDASIL, has been well tolerated, immunogenic and effective against HPV infection in early studies. Phase III studies are underway to definitively evaluate the clinical and public health impact of GARDASIL in adolescent and adult men and women.

HPV 16/18 prophylactic cervical cancer vaccine—development update. *Hans Bock*

HPV types 16 and 18 are most frequently associated with cervical cancer, occurring in >70% cases globally. In some locations (the Philippines, Costa Rica, Bangkok), the odds ratio associating HPV and cervical cancer is >10 times that of cigarette smoking and lung cancer. The objective for vaccine development was to prevent persistent infection with HPV16/18, and thus avoid abnormal cytological and neoplastic changes in the cervix.

Immunotherapy for HPV—what is needed and why.
Ian Frazer

The only approach to preventing the consequences of persistent HPV infection currently widely available involves treatment following early detection of CIN. This requires regular screening using Pap smears, visual inspection, and/or HPV testing, followed by destructive therapy to kill cancerous cells. Prophylactic vaccines now in development use VLPs to prevent infection with specific HPV types.

Vaccination against cervical cancer—impact on screening. Jack Cuzick

Cytology is unfeasible for much of the developing world due to its cost, inadequate infrastructure and levels of expertise, and the very high level of inflammatory smears (false-positives). In an example from Recife, Brazil in 1991, ~63 000 women were screened using Pap smears. The incidence of inflammatory changes was 71%, compared with 6% of CIN or cancerous lesions. Only one in five women recorded 'normal' Pap smears.

Human Papillomavirus DNA testing—what are the psychosocial issues? Marian Pitts

A review of the role of HPV testing within a cervical screening program identified 'a lack of knowledge about the psychosocial issues involved in providing cervical screening in general and HPV testing in particular'. Public support for HPV testing and appropriate infrastructure and technology will need to be available before testing can become generalised; perhaps more important will be general knowledge and understanding.

Cervical cancer screening—women's perception, preferences and acceptance. Partha Basu

Cervical screening is a new concept in India. In order to assess the acceptability of cervical screening, perceptions and preferences among women, and reasons for non-compliance with screening, a review was undertaken wherein women were offered the opportunity to undergo a free screen.

Current problems for cervical cancer screening in Japan.
Ryo Konno

Mass screening for cervical cancer was introduced in Japan in the 1960s. In 1982, the government enacted the Health and Medical Service Law for the Aged, which supported annual screening for all women >30 years of age. Screening uses the Japanese Society of Obstetricians and Gynaecologist scheme to classify Pap test cytology with minor modification.

The Philippines—training needs for anti-cervical cancer medical education and community information.
Cecilia Ladines-Llave

The Philippines is an archipelago of 7167 islands, with a population of more than 87 million people. It is a young nation

by age—only 4% of the population are >65 years of age. Poverty is widespread, and communication and transport are difficult, particularly in rural areas. Pap smears cost P 400 (US\$ 7). The minimum daily wage is US\$ 3.57 and the average family income is US\$ 221 per month. Preventative health is a luxury.

Screening experiences—visual inspection with acetic acid (VIA). R Sankaranarayanan

Simple and less expensive methods of cervical screening based on visual examination of the uterine cervix are currently being investigated as alternatives in low-resource settings. VIA has been widely evaluated for accuracy in detecting CIN 2/3 lesions in research settings in low-resource countries.

Cervical cancer screening using a combination of Pap and DNA tests. Masaki Inoue

A nationwide cancer prevention program using annual Pap smears has dramatically reduced cervical cancer incidence and resultant mortality in Japan. However, the Pap test is not always accurate, and false-negative results can have serious implications. This has led to a re-evaluation of the cancer screening program in Japan.

Thailand—cervical cancer screening and epidemiology.
Somkeart Srisupundit

Data from 1996 showed that cervical cancer was the most common cancer in Thai women, with an ASR of 19.5, higher than that for breast cancer (ASR ~17.2). Within Thailand, incidence varies between regions, with Chiang Mai (ASR 25.6) and Lampang (23.6) having higher than national levels. The age prevalence is fairly consistent between regions, peaking at 45–55 years of age.

Korea—cervical cancer screening and epidemiology.
Hai Rim Shin

Since 1980, Korea has had a national tracking system for major cancers, which includes site-specific and regional tracking. The database for national cancer incidence is estimated to be 95% complete. Cervical cancer is the fourth most common cancer in Korean women.

Prevalence and impact of cervical HPV infections in Taiwan. Tang-Yuan Chu

In 1998–92, the AAR of cervical cancer in Taiwan (22.2/100 000) was higher compared with other Asian nations with Chinese populations, such as Singapore (16.3/100,000) and Hong Kong (15.3/100 000). In 1995, Taiwan instituted the National Cervical Screening Program for women aged >30 years.

Clinical algorithms for CIN1. Laurie Elit

Emerging evidence has changed the way low-grade cytological changes are viewed, but it has not clarified patient management. Members of the Ontario Cervical Screening Program reviewed the available evidence in order to optimise national guidelines.

Clinical algorithms for HSIL. Michael Quinn

Approaches to treatment for high-grade squamous intraepithelial lesions (HSIL) depend upon the type of histology (squamous, glandular, mixed), the size and accessibility of the lesion, the patient's stage of life and the surgical options available.

Genital warts—treatment modalities. Suzanne Garland

Genital warts (*Condylomata acuminata*) is one of the most common STIs worldwide, usually resulting from infection with HPV types 6 and 11. The highest rates of genital HPV infection are in sexually active women <25 years of age. Highest incidence for both genders is between 18 and 28 years of age. In developed countries, genital HPV infection has increased steadily since the 1950s. About 1% of all sexually active adults have had or currently have genital warts.

Cervical cancer—recommendations of IARC.

Albert Singer

The International Agency for Research on Cancer (IARC) 'Handbook of Cancer Prevention, Volume 10' was launched following a meeting in Lyon, France, in April 2004. The Working Group of the IARC concluded that screening for cervical cancer by Pap smear effectively prevents mortality from the disease. However, in order for a cytology screening program to reduce death optimally, it must be well organised and have quality control at every step throughout the process. If these prerequisites are met, an estimated 80% reduction in mortality can be achieved.

Practical colposcopy. Albert Singer

To improve colposcopy practice, it is necessary to consider the accuracy of colposcopy and biases that can arise. Studies of diagnostic and screening colposcopy provide insights

regarding the validity of visual signs, their reproducibility, quality control and how the process is taught.

The role of males in transmission of HPV infections and cervical cancer risk. Xavier Bosch

Over the years, both social and medical researchers have found statistical links between observed behaviours and the incidence of cervical cancer. As early as the 1850s, differences in incidence were noted between prostitutes and virgins/nuns.

Anogenital HPV infection and disease in HIV-positive women. Isabelle Heard

HIV infection is not uncommon in many Asian countries. At the end of 2003, Cambodia, Thailand, Myanmar, India, Nepal and Papua New Guinea had known prevalence levels >0.5%. As patients continue to survive longer following HIV infection, due to advances in treatment, health practitioners must consider the implications of anogenital HPV infection in HIV-positive women.

Single visit approach to cervical cancer prevention—lessons from Thailand.

Khunying Kobchitt Limpaphayom

The primary goal for Thailand is to reduce cervical cancer and mortality by detecting disease early, and treating it before it progresses to invasive cancer. Thailand has ~15 million women at risk for cervical cancer, only 5% of whom have been screened in the previous 5 years via the Pap smear campaign.

Global cervical cancer control. Edward Trimble

Four key areas will contribute to global cancer levels in coming decades: oncological infectious agents (i.e. hepatitis B, HPV, HIV, Epstein–Barr virus, schistosomes and *Helicobacter pylori*), carcinogens (most notably tobacco), lifestyle changes (particularly growing obesity and decreased exercise and physical fitness), and changing age structure in many societies in which smaller families and longer life-spans mean that cancer, generally a disease of old age, will grow in prevalence.