

HKU study on HPV testing

Speakers:

Professor Hextan NGAN, Yuen-sheung

Tsao Yin-Kai Professor in Obstetrics and Gynaecology
Clinical Professor and Head
Department of Obstetrics and Gynaecology,
The University of Hong Kong Li Ka Shing Faculty of Medicine

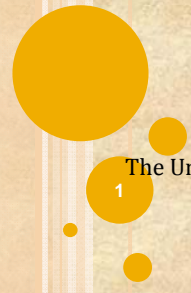
Professor Annie CHEUNG Nga-yin

Clinical Professor
Department of Pathology
The University of Hong Kong Li Ka Shing Faculty of Medicine

Guest speaker:

Professor Harald zur Hausen

Recipient of Nobel Prize in Physiology or Medicine in 2008



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PART I

HKU'S STUDY ON WOMEN'S PERCEPTION AND
ACCEPTANCE OF HPV/HPV TESTING

Prof Hextan NGAN Yuen-sheung

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CERVICAL CANCER: A GLOBAL HEALTH PROBLEM

In 2008, worldwide...

- The 3rd most common female cancer
- 530,000 new cervical cancer cases
- 275,000 related deaths

(IARC, GLOBOCAN 2008)

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CERVICAL CANCER: COMMON IN HONG KONG

- The 7th most common female cancer
- 453 new cases, 128 deaths in 2009

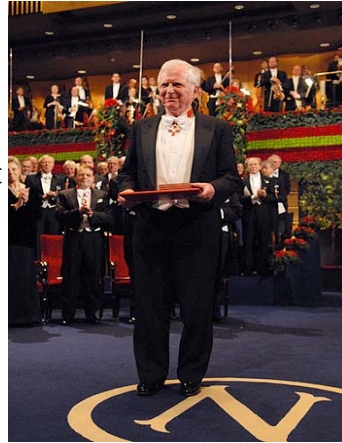
(HK Cancer Registry, 2009)

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NOBEL PRIZE: DISCOVERY OF HPV CAUSING CERVICAL CANCER

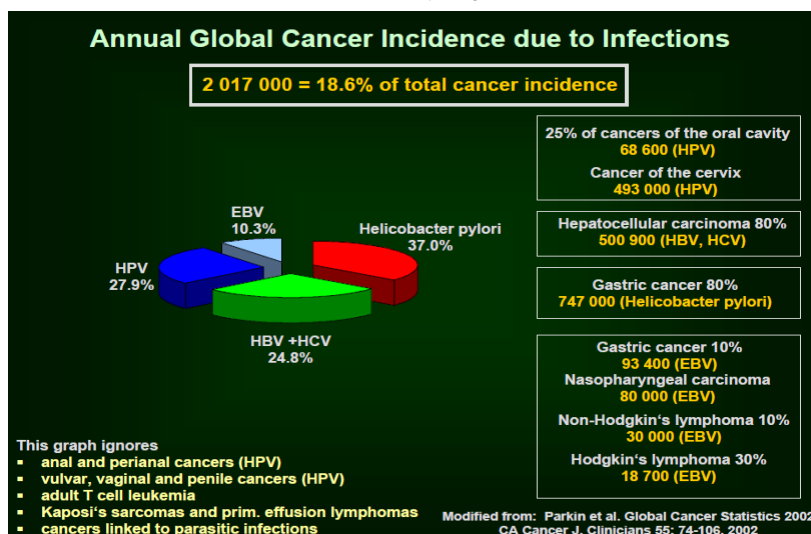
- In 2008, Professor Harald zur Hausen was awarded the Nobel Prize in Physiology or Medicine for his discovery of the causative agent of cervical cancer –

Human Papilloma Viruses (HPV)



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Around 19% of the cancers in the world originated from several kinds of infectious diseases. *Helicobacter pylori* causes 80% of stomach cancer, Hepatitis B & C leads to 80% of liver cancer. And cervical cancer, the 3rd most common cancer in female, almost 100% caused by High-risk HPV.

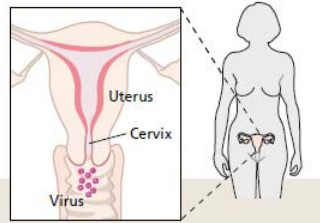


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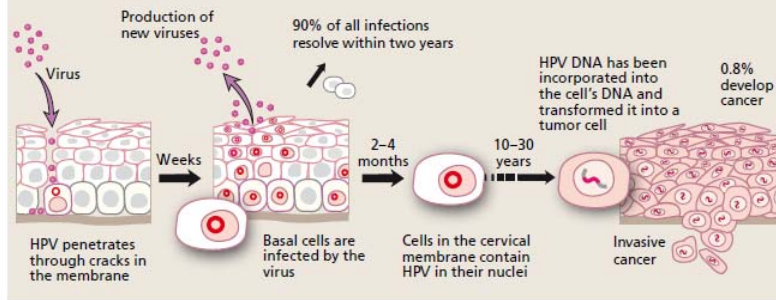
Adapted from Prof. Harald zur Hausen's Nobel Lecture on 7 Dec 2008 in Stockholm entitled "The Search for Infectious Causes of Human Cancers: Where and Why"

HPV infection

The virus infects cells deep within the cervical membrane. If a certain part of the viral DNA is incorporated into the cell's genetic material, a tumor will form.

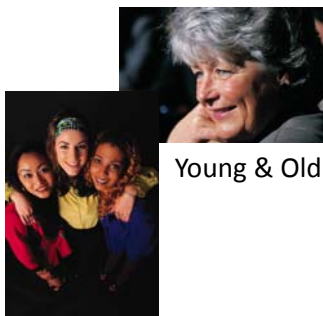


From infection to malignant tumor



Adapted from: http://www.nobelprize.org/nobel_prizes/medicine/laureates/2008/popular-medicineprize2008.pdf

WHO MAY BE INFECTED WITH HIGH-RISK HPV?



Young & Old



Male & Female



More than 1 partner

1 partner only



- Any individuals who are sexually experienced may be infected
- Those who have been sexually inactive may also be tested positive for high-risk HPV



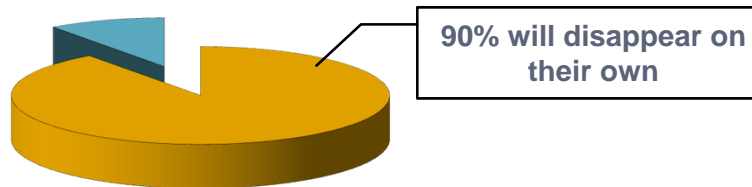
HPV infection is very common. It has been estimated that the lifetime chance of HPV exposure for any sexually experienced individuals could be as high as 50-80%.



*Stanley M. Pathology and epidemiology of HPV infection in females. GynecolOncol (2010) 117:S5-S10

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- People who are infected with HPV are unaware of it for there are no symptoms, and most infections disappear on their own.



*Stanley M. Pathology and epidemiology of HPV infection in females. GynecolOncol (2010) 117:S5-S10

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- Overseas studies estimated that about 1 in 10 women might be persistently infected with high-risk HPV
- What is the impact on health if the infection persists?

*Stanley M. Pathology and epidemiology of HPV infection in females. GynecolOncol (2010) 117:S5-S10

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Persistent high-risk HPV infection → Precancerous changes → Cervical cancer

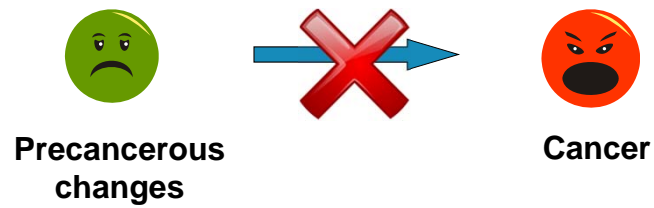


through 10 to 20 years



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Regular cervical screening allows early detection and management of abnormalities, and thus can prevent cancer!



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CERVICAL CANCER SCREENING

- Traditionally, cervical screening is done by the cytology method, also called a Pap smear test
- The principle behind is rather simple. A cell sample is taken from the surface layer of the cervix. The sample is examined under the microscope for any “abnormal-looking” cells
- Women with an abnormal cytology result may required further in-depth investigation, namely colposcopy, to delineate the nature and severity of the problem and to determine necessary follow-up

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WHO NEEDS CERVICAL SCREENING?

- Women who are 25 years of age or above, and who are sexually experienced should begin to attend screening
- Women will initially be screened once every year for the first 2 years. If both results are normal, then they can be screened once every 3 years thereafter

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REGULAR SCREENING IS THE KEY

- Screening needs to be done regularly throughout lifetime until reaching 65 years of age
- Women should be screened at least once every 3 years so that any abnormalities in the cervix may be detected early before they turn cancerous

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PREVENTIVE MEASURES

Primary prevention: HPV vaccination

- The current HPV vaccines prevent cervical cancer by offering protection against two most common cancer-causing HPV types – HPV 16 & 18
- Adolescents girls and women who have not had sex before are most suitable for HPV vaccination.
- Older women may also be vaccinated but the protective effect may vary
- Both vaccines require 3 injections to be given in 6 months
- Research has shown that the protective effect lasts for at least 7 years after vaccination

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PREVENTIVE MEASURES

Secondary prevention: Regular cervical screening

- Cytology testing
- HPV testing
 - (1) used in conjunction with cytology testing for women aged 30 years or above
 - (2) as a second line test in case of an ASC-US (atypical squamous cells of undetermined significance)

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HKU RESEARCH ON WOMEN'S PERCEPTION OF HPV

- In 2009, the Department of Obstetrics & Gynaecology, The University of Hong Kong Li Ka Shing Faculty of Medicine conducted a randomized controlled trial
- to study local Chinese women's perceptions towards HPV and HPV testing, and whether they would accept this new measure
- Nearly 300 Chinese women who attended the Family Planning Association of Hong Kong (FPA) Wanchai Clinic joined the study.

Kwan TT, Tam KF, Lee PW, Lo SS, Chan KK, Ngan HY (2010) De-stigmatising human papillomavirus in the context of cervical cancer: a randomized controlled trial. *Psycho-Oncology*. 19:1329-1339.

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METHODS

- Women were asked to read an educational message about HPV and HPV testing
- Method of assessment: Self-administered questionnaires given before and after message reading
- Outcomes assessed: Beliefs towards individuals with high risk HPV infection, knowledge, intention to be HPV-tested

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RESULTS

- Total number of participants (N = 292)
- Participants' characteristics:
 - Mean age = 38 years
 - 74% married
 - 64% secondary educated
 - 95% have attended cervical screening before

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RESULTS

Mean knowledge score before reading (max. 6) 1.53
Mean knowledge score after reading (max. 6) 4.25

	YES (No.)	NO (No.)
Ever heard of HPV (before reading message)	59% (172)	41% (120)
Willing to be tested for HPV (before reading)	93% (237)	7% (17)
Willing to be tested for HPV (after reading)	97% (260)	3% (9)

N=292

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MISCONCEPTIONS LED TO BIAS TOWARDS INDIVIDUALS WITH HPV INFECTION

Misconceptions	Agreed (No.)
Infected individuals are sexually easy	22% (63)
Women are infected because they have more than 1 sexual partner	22% (63)
Women are infected because their partners have been unfaithful	17% (48)
One should keep a social distance from those who are infected	12% (33)
An individual with only 1 lifetime sexual partner will not be infected	10% (30)

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MISCONCEPTIONS MAY HARM WOMEN

- HPV-infected individuals may be stigmatized by others
- Individuals may incur undue psychosocial burden on themselves following a positive HPV test result
- Women may avoid cervical screening altogether for fear of stigmatization

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PUBLIC EDUCATION

- The benefits of HPV testing and women's positive acceptance would likely lead to its increased use in Hong Kong
- **Mass HPV education** needs to go hand-in-hand with widespread testing in Hong Kong
- The design of public HPV messages should:
 - Focus on cervical cancer prevention
 - Appropriate for the Chinese culture
 - Specifically target and correct misconceptions
 - Comprehensible to the general public

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HPV RESEARCH CONTINUES*

- A study on the use of HPV testing as a first-line cervical screening tool is currently recruiting
- Participants will receive a free HPV test when they have their Pap smear test done at designated FPA clinics
- Who may join:
 - Ethnic Chinese women aged 30-60 (HKID card holder)
 - Not pregnant
 - Did not need follow up or treatment due to an abnormal Pap smear result in the past 1 year
 - Do not have cancer or congenital anomalies of the genitourinary tract
- Details of the study and eligibility are available at the following FPA clinics : 1) Wanchai, 2) Ma Tau Chung, 3) Tseun Wan, 4) Wong Tai Sin and 5) Tai Wai
- Please browse through the Department of Obstetrics and Gynaecology's website : <http://www.obsgyn.hku.hk/>
- For enquiries, please call: 2255 4265

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*Supported by the Wong Check She Charitable Foundation

PART II
HPV DNA TEST

Prof Annie Cheung Nga-yin

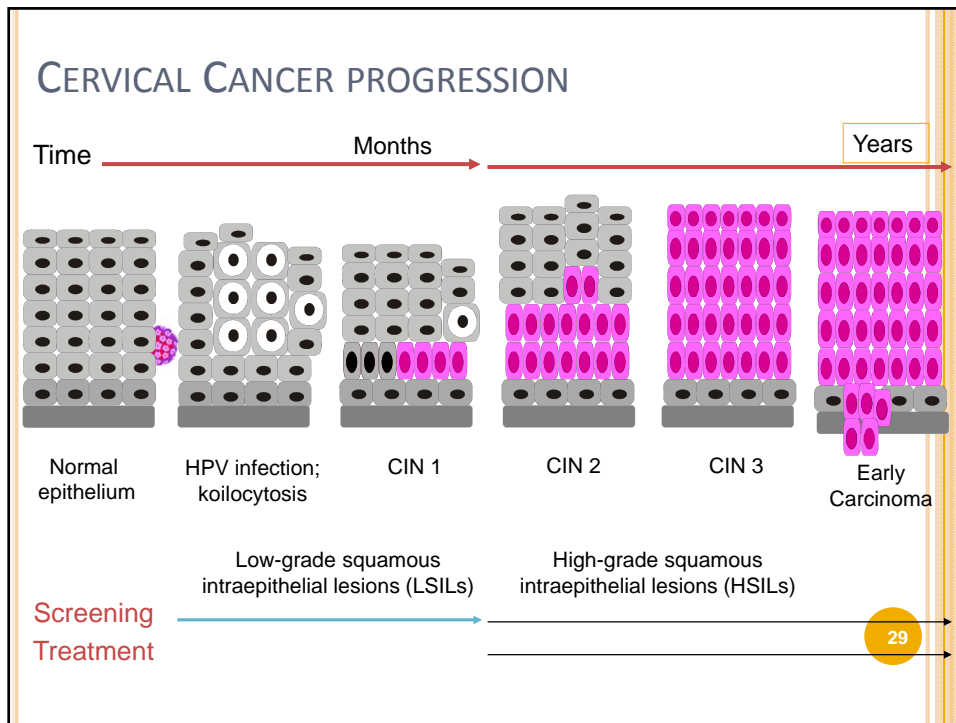
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HPV DNA TESTING

- Many different types of HPV DNA test
 - High risk HPV pooled DNA detection
 - High risk HPV pooled DNA detection + HPV 16/18 genotyping
 - HPV genotyping
- Each type of HPV DNA test will have its own advantage and limitation
- None of the HPV DNA test could test all types of HPV infection (200 + types HPV)
- ***Quality control in diagnostic settings is most important

Wong GW et al. J Clin Virology 2011
Wong GW et al. J Clin Microbiology 2012

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CLINICAL APPLICATION OF HPV DNA TEST

- **Triage of ASC-US**
- **Primary screening / Co-testing with smear**
- **Test of Cure - Determine risk for persistent / recurrent disease**

➔

Detection of HSIL/CIN3

Note:
 HSIL = High-grade squamous intraepithelial lesions (HSILs)
 CIN3= Cervical intraepithelial neoplasia, is the potentially premalignant transformation and abnormal growth (dysplasia) of squamous cells of the surface epithelium of the cervix

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ASC-US is the most common cervical cytological abnormality

ASC-US = atypical squamous cells of undetermined significance

HKU conducted a study in 2003
About 400,000 cervical cell samples from clinics of Family Planning Association (FPA) were analysed

- ✓ ASC-US was found in 3-4% of the smears
- ✓ ASC-US account for 60-80% of all abnormal cytology

Cheung et al. Cancer Cytopathology 2003

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Another HKU study in 2004



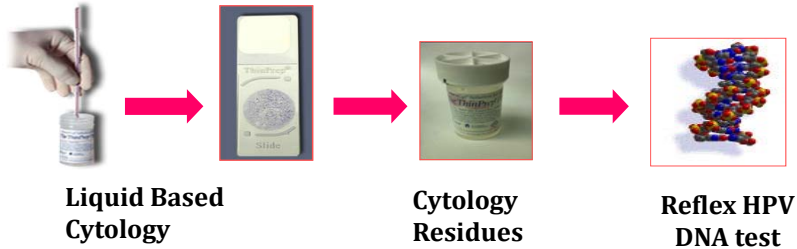
Results:

- Women with ASC-US has higher risk of subsequent confirmation of LSIL or HSIL compared with general women population
- Follow up results show that women with ASC-US have 10 times higher relative risk in having HSIL when compared with general women population

Cheung et al. Cancer Cytopathology 2004

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HPV DNA Test - Triage of ASC-US



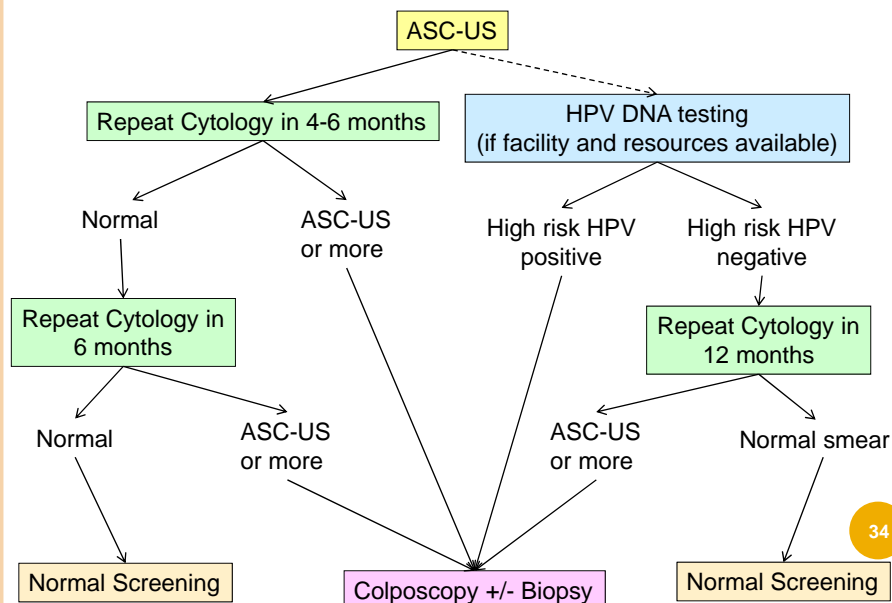
- Reflex HPV DNA test on **10,000 women** diagnosed with ASC-US in FPA clinics from 2007 to 2012 by Department of Pathology, HKU
- Supported by SK Yee Medical Foundation
- Result:

• 56% of the 10,000 women with ASC-US were positive for HR-HPV

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Ngan et al. HKCOG 2009

HPV DNA Test - Triage of ASC-US



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FOLLOW UP STUDY BY HKU

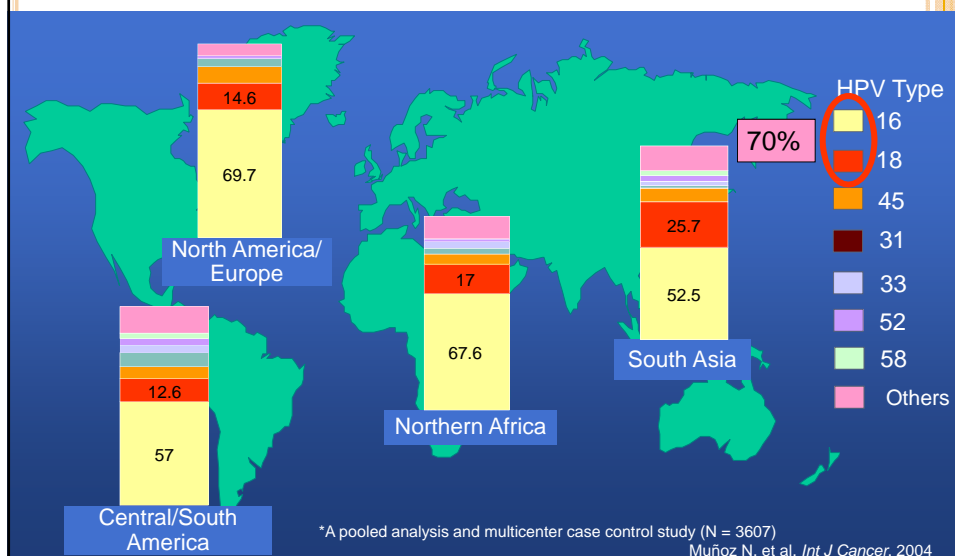
- A follow up study successfully analyzed 2,447 cases with ASC-US (from the 10, 000 cases from 2007-2012)

	≥HSIL detected	≥HSIL not detected	Total:
Pooled HPV Negative -	12	858	870
Pooled HPV Positive +	199	1,378	1,577
Total:	211	2,336	2,447

- Women with ASC-US and High risk-HPV +ve are more likely to have HSIL or above detected at follow up (p = 0.001)
- The risk is about 20 times higher than women with ASC-US but High risk HPV -ve
- Advantages:
 - ✓ ↓ anxiety of patients
 - ✓ earlier diagnosis of HSIL+ cases

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HPV 16 AND 18 CAUSE 70% OF CERVICAL CANCER



HPV 16/18 GENOTYPING WAS ALSO PERFORMED IN CASES POSITIVE FOR POOLED HPV DNA

- The sensitivity and negative predictive value of the HPV DNA test approach 100%.
- The specific identification of HPV 16 or 18 genotypes further ↑ the specificity and positive predictive value of identifying cases which harbour HSIL/CIN2+, the risky precancerous lesion.

Follow up findings	Test	Sensitivity	Specificity	PPV	NPV
HSIL/CIN2+	Pooled HPV DNA (A)	100%	15.25%	9.57%	100%
	Pooled HPV DNA (B)	100%	20.83%	14.93%	100%
HSIL/CIN2+	HPV16/18 (A)	35.00%	76.23%	11.67%	92.90%
	HPV16/18 (B)	30.00%	86.11%	23.08%	89.86%

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RESEARCH PROSPECT

- In the long run, scientist will investigate whether the use of HPV testing as a first-line screening tool will improve cervical screening accuracy
- **Stage 1**
- HPV test as a second line test in case of an ASC-US
- **Stage 2**
- Use HPV test in conjunction with cytology testing for women (co-test)
- **Stage 3**
- HPV testing as a first-line screening tool
- At current stage, regular Pap smear is still advisable
- Continue research for evidence to support whether co-test or even first line screening is more effective

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2012 CONFERENCE OF ASIA OCEANIA RESEARCH ORGANISATION ON GENITAL INFECTIONS AND NEOPLASIA

Date July 13-15, 2012 (Fri-Sun)
Venue Cheung Kung Hai Conference Centre, G/F, William MW
Mong Block, 21 Sassoon Road, Pokfulam, HK
Keynote speaker Professor Harald zur Hausen
Recipient of Nobel Prize in Physiology or Medicine in 2008



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Patient Sharing

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Q & A

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