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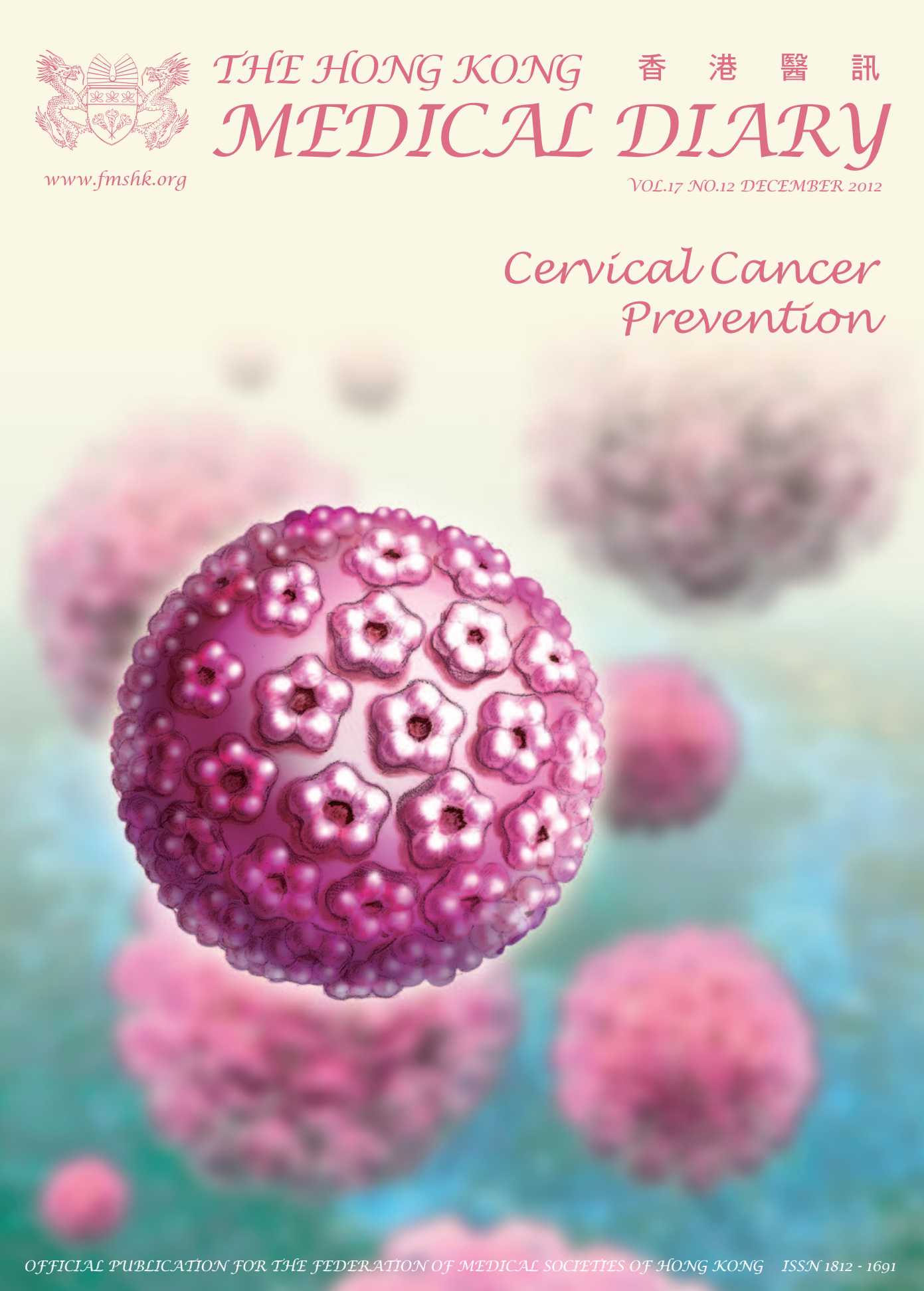
THE HONG KONG MEDICAL DIARY

香 港 醫 訊

VOL.17 NO.12 DECEMBER 2012

Cervical Cancer Prevention



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References:

1. Bachmann G, et al. Contraception 2004; 70(3): 191-8
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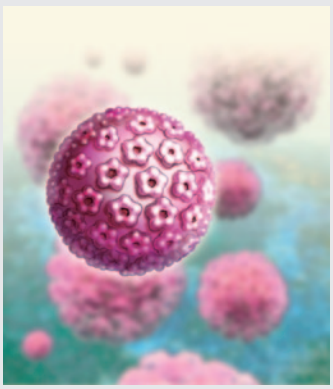

The cover photo shows the image of the HPV virus. Most of the cervical cancers and pre-malignant diseases are related to the infection of this high risk HPV, for example, HPV types 16 and 18. By understanding its basic epidemiology and microbiology, we can mount strategies to control and prevent cervical cancers, namely, primary prevention by HPV vaccination, secondary prevention by cervical cytology (+/- HPV DNA test) and lastly early referral of diseased patients for treatment (colposcopy, LEEP and/or cancer treatment).

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Editorial

Dr. Siu-keung LAM

President, Hong Kong Society for Colposcopy and Cervical Pathology (www.hksccp.org.hk)
Specialist in Obstetrics and Gynaecology

Editor

Dr. Siu-keung LAM

The Hong Kong Society for Colposcopy and Cervical Pathology was inaugurated in 2000 under the leadership of the founding President, Professor Hextan NGAN. I was the third President after Professor Annie CHEUNG. The aim of the Society is to enhance the knowledge and skill in cervical cancer prevention, organise regular educational activities for our members, doctors, nurses and laboratory staff. In conjunction with the Hong Kong College of Obstetricians and Gynaecologists, accreditation exercises are organised for specialist colposcopists and refresher courses on colposcopy are held regularly. The Society also accredits nurses as smear takers after completion of the relevant theoretical and practical training.

The field of colposcopy and cervical cancer screening has undergone many changes in the past 12 years. First and foremost was the availability of HPV vaccines as primary prevention. Although the uptake of HPV vaccines is relatively slow probably because of the cost, more and more parents are willing to bring their young kids for vaccination. Only with a high coverage rate then can we be able to decrease the cervical cancer incidence further. In her paper, Dr. Assumpta WONG discussed the rationale and efficacy of the 2 HPV vaccines used in Hong Kong. Without a proper understanding of the relationship between HPV and cervical cancer, it will be difficult to link the HPV infection, co-carcinogens and the gradual deterioration of cervical premalignant changes to malignant changes. Prof. Annie CHEUNG in her paper gave a very detailed explanation on the epidemiology and pathophysiology of the cervical malignant transformation and the current method for detection be it by cytology or by molecular tests.

The secondary prevention by regular Pap smears (cytology) is the cornerstone of the conventional cervical cancer screening programme. The addition of HPV DNA test either as a reflex test or co-test (cytology and HPV DNA at the same time) was further proven to improve the sensitivity and specificity of cervical cancer detection. I described some of the recent advances in the screening methodology abroad particularly in USA and the Netherlands. The screening strategy will obviously be different in different localities e.g. Hong Kong, China Mainland or Africa, depending on the HPV incidence, HPV epidemiology, disease burden, patient availability and most important of all the medical infrastructure.

The last defence will be the early referral of patients with abnormal smears and/ or abnormal looking cervixes for colposcopy and/ or cervical cancer treatment. Dr. Mandy CHU and Dr. Karen CHAN described the updates in the management of abnormal smears in Hong Kong and Dr. SF YIM of The Chinese University of Hong Kong highlighted some of the recent advances in the management of cervical cancer.

The ultimate objective of the Society is to decrease the incidence of premalignant and malignant diseases of the cervix thus improving the quality of life of women at large.

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Reference:
1.Cetin I, Koletzko B. Long-chain omega-3 fatty acid supply in pregnancy and lactation. Curr Opin Clin Nutr Metab Care. 2008;11(3):297-302. 2.Murcia M, Rebagliato M, Iñiguez C, et al. Effect of iodine supplementation during pregnancy on infant neurodevelopment at 1 year of age. Am J Epidermiol. 2011;173(7):804-814. 3.Lozoff B, Georgieff MK. Iron deficiency and brain development. Semin Pediatr Neurol. 2006;13(3):158-165. 4. Greer FR, Krebs NF; American Academy of Pediatrics Committee on Nutrition. Optimizing Bone Health and Calcium intakes of Infants, Children, and Adolescents. Pediatrics. 2006;117(2):578-585. 5.Mulligan ML, Felton SK, Riek AE, et al. Implications of vitamin D deficiency in pregnancy and lactation. AM J Obstet Gynecol. 2010;202(5):429.e1-9. 6.Lowdon J. Getting bone health right from the start! Pregnancy, lactation and weaning. J Fam Health Care. 2008;18(4)137-141. 7.USDA. USDA National Nutrient Database for Standard Reference. NDB No. 01211. Release 22 (2009). 8.Obican SG, Finnell RH, Mills JL, et al. Folic acid in early pregnancy: a public health success story. FASEB J. 2010;24(11):4167-4174.

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Updates on Cervical Cancer Screening and Management of Abnormal Cervical Smears

Dr. Siu-keung LAM

President, Hong Kong Society for Colposcopy and Cervical Pathology
Specialist in Obstetrics and Gynaecology

Dr. Siu-keung LAM

This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 December 2012.

Introduction

In 2008, cervical cancer was the tenth most common cancer among women in Hong Kong. According to the Hong Kong Cancer Registry, there were 358 new cases of cervical cancer, accounting for 3.1% of all new cancer cases in females. The crude incidence rate was 9.7 per 100 ,000 female population. The age-standardised incidence rate was 6.9 per 100, 000 standard population. The median age at diagnosis was 53 years old. In 2009, cervical cancer was the ninth most common female cancer death. There were 128 deaths in females due to this cancer, accounting for 2.5% of all cancer deaths in females. In 2009, the crude death rate was 3.5 per 100 ,000 female population and the age-standardised mortality rate was 2.2 per 100 ,000 standard population. The incidence was gradually decreasing over the years probably because of the increasing cervical smear screening coverage.

Screening strategy

Before the establishment of the government's cervical smear screening programme opportunistic screening had already been carried out. Patients attending private doctors, family planning clinics, gynaecology clinics, antenatal clinics and emergency gynaecology admissions were offered cervical smears but not in an organised manner. Patients will not be called back on a regular basis except for those having abnormal smears. Colposcopy examinations were not widely available in the government hospitals as in the present situation.

In March 2004 the Department of Health, in collaboration with other health care professionals, started to organise the **Cervical Smear Screening Programme (CSSP)** to facilitate and encourage women to have regular cervical smears with the ultimate aim of decreasing the incidence of cervical cancer in Hong Kong.

The programme objectives include:

1. To raise public awareness on the need for cervical cancer screening;
2. To improve the overall coverage of the target population;
3. To promote more equitable and efficient screening across the target population.
4. To build a quality assurance mechanism for better quality screening services in smear-taking, cytological examinations, referrals and follow-up management of abnormal smears; and
5. To provide better support to the private sector and relevant stakeholders

The screening protocol proposed by the Department of Health and Hong Kong College of Obstetricians and Gynaecologists was simple: cervical smear screening from the age of 25 with the first two smears one year apart, then three yearly thereafter. The screening can be stopped at the age of 65 if the latest three smears were all negative. Women over 65 should have at least one smear if never done before. Women with no sexual experience or women having had hysterectomy can be excluded from the programme. A flowchart is enclosed for your reference.[1]

Figure 1: The screening flowchart recommended by Department of Health

Please note this protocol refers to healthy women and the frequency of cervical smear screening can be increased in patients with abnormal smears, after

treatment and clinically suspicious cases.

Other than the publicity and promotion on cervical smear screening, the Department of Health also collects useful data on the number of clients having regular cervical smears in Hong Kong. Up till now there are 436,461 clients recorded in the **Cervical Screening Information System** (but please note that the reporting is voluntary and the total number of clients having cervical smears in Hong Kong is more than this number).

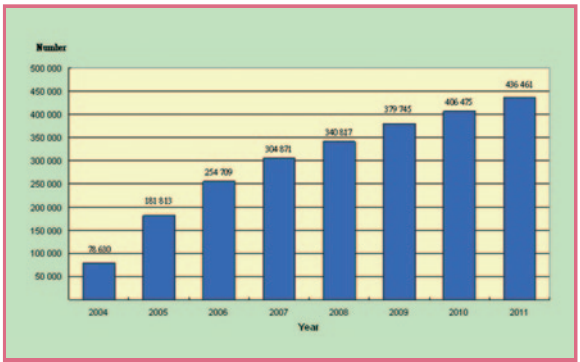

Figure 2: Cumulative total number of women registered with the Cervical Smear Screening Programme (total: 436461, source from Department of Health)

The age range of the clients in the Cervical Screening Information System is shown in the chart below with the majority of women in the reproductive age group. Although the screening should start at the age of 25, a small proportion of clients have cervical smears under the age of 25 because of other risk factors e.g. multiple partners, smokers etc.

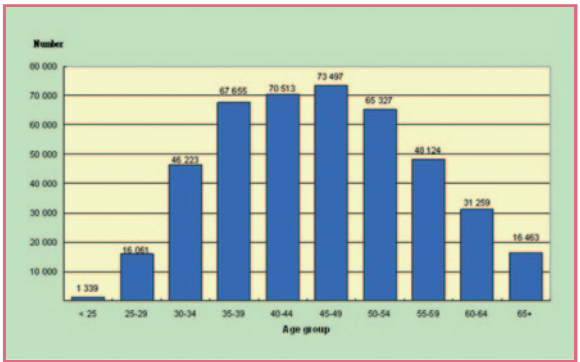

Figure 3: Number of women registered with the Cervical Smear Screening Programme by Age group (total = 436 461, source from Department of Health)

Since the establishment of the government's cervical smear screening programme in 2004, the average coverage rate (i.e. women with cervical smear screening in their previous three years) was also analysed. It seems the average rate has reached a plateau of 60% and health care workers may need to work hard to reach the remaining at risk population. Only by increasing the population screening, we can aim to decrease the incidence of malignant and premalignant cervical lesions. The target objective is to reach 80% of the at risk population.

Figure 4: Percentage of respondents with last cervical smear taken within three years with the latest figure plateau at 60%

The method for cervical cancer screening

Conventional Pap smear taking is by taking cervical cells by the wooden Ayre spatula and spreading on a glass slide and fixed by alcohol or other fixatives. The liquid base cytology (LBC) has almost completely replaced the conventional glass slide in Hong Kong as the latter's unsatisfactory rate is lower and the quality of smear is better and easier to be read by the pathologist. As some of the laboratory procedure can be automated, the turnaround time can be shortened. The remaining aliquot can be used for HPV DNA testing if needed without calling back the patient for another sample (reflex testing)

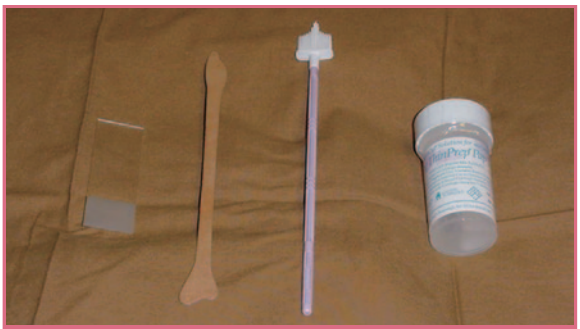

Figure 5: the traditional glass slide and wooden spatula on the left hand side and the plastic brush and liquid base cytology bottle on the right hand side (preferred method for collection)

HPV DNA tests were used in the triage of low grade smears (i.e. refer for immediate colposcopy or observation), test of cure after LEEP (loop electrosurgical excision procedure) and co-testing in the past but its role is now further widened with more reliable HPV DNA tests. The current HPV genotyping test is able to differentiate each type of the high risk HPV DNA e.g. HPV 16 or HPV 18 as compared with the previous basket test (Digene test which indicated presence of high risk HPV but will not specify which type).

As there are many new HPV DNA test kits available, clinicians should be careful in the selection of the test kits and the interpretation of the results.

Management of abnormal cervical smears in Hong Kong

Patients with abnormal cervical smears will be managed according the recommended protocol of the Hong Kong College of Obstetricians and Gynaecologists. Basically for low grade lesions, observation is the norm especially for young patients. For high grade abnormality CIN II or III, excision treatment (LEEP) under LA or GA is recommended. Some clinicians may elect a see and treat policy in selected cases. Cryotherapy and LASER treatment (ablative treatment) are not much used nowadays.

Changes in the screening methodology

The screening strategy will be different in different countries according to the local disease prevalence, HPV epidemiology and medical infra-structure.

There are recent updates on the screening strategy that may be worthwhile for Hong Kong to consider:

Co-testing rather than pap smear alone

In the **POBASCAM** trial [2] 45,000 women aged 29 to 56 years attending routine cervical screening in the Netherlands between 1999 and 2002, were equally randomised to receive either HPV DNA testing and cytology or cytology alone. The researchers wanted to see if HPV testing would result in fewer high grade lesions and cancers in the second round of screening 5 years later because of earlier detection and treatment of lesions after the first round. They then assessed the most appropriate age for starting HPV testing. In the second round, HPV testing and cytology were done on all women.

In the first screening, HPV testing identified significantly more cancer precursors (CIN 2 or worse) than cytology alone (267/19999 vs 215 /20106, p=0.015) Five years later, significantly fewer women had CIN grade 3 or worse (88/19579 vs 122/19731, p= 0.023) and cervical cancers (4/19579 vs 14/19731, p=0.031) in the HPV group, compared with cytology alone.

HPV DNA testing definitely has a role in the cervical cancer screening because of its higher sensitivity but how it can be incorporated in the screening strategy in Hong Kong has yet to be decided. Nevertheless the American Cancer Society, American Society for Colposcopy and Cervical Pathology and American Society for Clinical Pathology all have already recommended changes to the screening strategy for women aged 30 to 65 as follows: [3]

(1) HPV and cytology co-testing every five years (preferred method for routine screening)

Group (A): if HPV positive, and cytology ASCUS and >= LGSIL, consider colposcopy

Group (B): if HPV positive, cytology negative
Option (1) 12 month follow ups with co-testing
Option (2) Test for HPV 16 or HPV 16/18 genotype
If HPV 16 or HPV 16/18 positive, refer for colposcopy
If HPV 16 or HPV 16/18 negative, 12 month follow ups with co-testing

Group (C): Co-test negative or HPV negative ASCUS, rescreen with co-testing in 5 years

Definition: Co-test: cytology and HPV DNA test at the same time (same specimen)
ASCUS = Atypical squamous cells of unknown significance
LGSIL = Low grade intraepithelial neoplasia

(2) Cytology alone every three years (acceptable)

Patients with normal smears but positive HPV DNA 16 or 16/18 might be put on cytology surveillance in the past but some recent studies showed that this group of patients having the HPV 16 and or 18 (i.e. the two most oncogenic viruses) may harbour a significant risk of CIN and cancer. The 12 month risk for CIN 3+ following an HPV-positive cytology-negative co-test ranged from 0.8%[4] to 4.1%[5]. The estimated 12-month risk of cancer was 0.08%[4]. The consensus group therefore recommends immediate colposcopy for patients with positive HPV 16 or positive HPV 16/18 even if the smear is negative. If immediate colposcopy is not feasible, than repeat co-testing in 12 months' time.

HPV DNA as primary screening

HPV DNA as primary screening is not widely used in the world except the Netherlands where they will change to primary HPV DNA screening starting from age 30 and cytology as back up (reflex cytology, if cytology abnormal, refer for colposcopy). The number of colposcopy will be unacceptably high if all HPV positive women are referred for colposcopy. The result of the new screening strategy of the Netherlands will be useful for other countries in adopting a new screening paradigm (from the gold standard cytology which was used for 50 years to the HPV DNA test). There are even suggestions to send the patients a kit to take vaginal swab for HPV DNA at home to increase the uptake rate (patient self collection).

Conclusion

Without a national HPV vaccination programme, it will be unlikely for Hong Kong to cover a significant proportion of males and females and the reduction on the cervical cancer incidence will take a long time to be achieved. We should therefore rely on a reliable cervical screening strategy most likely a combination of cytology and HPV DNA test (exact model which is suitable for our locality to be worked out). Prompt referrals to colposcopy and/or cancer treatment will further reduce the incidence of cervical cancers on a long run.

References

1. Department of Health website: http://www.cervicalscreening.gov.hk/english/about/abt_screening.html (accessed 20th October 2012)
2. Rijkaart DC, Berkhof J, Rozendaal L et al. Human papillomavirus testing for the detection of high grade cervical intraepithelial neoplasia and cancer: final results of the POBASCAM randomised controlled trial. Lancet Oncol 2012; 13(1): 78-88.
3. Debbie Saslow et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention of Early Detection of Cervical Cancer. CA Cancer J Clin 2012; 62 (3): 147-172.
4. Katki HA, Kinney WK, Fetterman B et al. Cervical cancer risk for women undergoing concurrent testing for HPV and cervical cytology: a population based study in routine clinical practice. Lancet Oncol 2011; 12: 663-672.
5. Wright TC Jr, Stoler MH, Sharma A, Zhang G, Behrens C, Wright TL; ATHENA (Addressing THE Need for Advanced HPV Diagnostics) Study group. Evaluation of HPV 16 and HPV 18 genotyping for the triage of women with high risk HPV cytology negative results. Am J Clin Pathol. 2011; 136: 578-586.

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Updates on Cervical Cancer Screening and Management of Abnormal Cervical Smears" by Dr. Siu-keung LAM and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 December 2012. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. The number of death due to cervical cancer in Hong Kong was around 300 each year
2. The current coverage rate for cervical smear screening in HK was 80%
3. Almost all the cervical cancer is related to HPV infection
4. Women with hysterectomy should have regular smear after the operation still
5. The liquid base cytology LBC is the preferred method for cells collection
6. HPV DNA tests can be done in the same specimen (bottle) for cervical smear
7. The most common treatment for cervical intraepithelial neoplasia is cryotherapy
8. The POBASCAM trial showed HPV DNA tests and cytology was better than cytology alone
9. Co-testing referred to the combination of cytology and HPVDNA test together
10. In Netherlands, HPV DNA tests will be used as primary screening with cytology as adjunct

ANSWER SHEET FOR DECEMBER 2012

Please return the completed answer sheet to the Federation Secretariat on or before 31 December 2012 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Updates on Cervical Cancer Screening and Management of Abnormal Cervical Smears

Dr. Siu-keung LAM

President, Hong Kong Society for Colposcopy and Cervical Pathology
Specialist in Obstetrics and Gynaecology

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

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Answers to November 2012 Issue

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HPV Vaccine Updates

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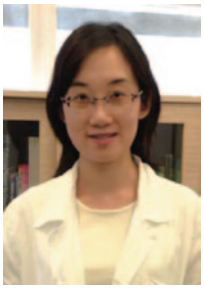

Dr. Assumpta SM WONG Dr. William WH LI

Introduction

Cancer of the cervix is the second most common cancer in women worldwide, with about 500 000 new cases and 250 000 deaths each year[1]. Almost 80% of cases occur in low-income countries. In Hong Kong, there were 453 new cases of cervical cancer and 128 cases of mortality resulted from the disease in the year 2009[2]. Virtually all cervical cancer cases (99%) are linked to genital infections with the human papillomavirus (HPV).

HPV are DNA viruses that infect skin or mucosal cells. There are more than 100 known HPV genotypes, at least 15 of which (HPV-16,-18,-31,-33,-35,-39,-45,-51,-52,-56,-58,-59,-68,-73 and -82) can cause cancer of the cervix and are associated with other anogenital cancers; they are called "high-risk" genotypes. The two most common of these (genotypes 16 and 18) cause approximately 70% of all cervical cancers. HPV (especially genotypes 6 and 11) also cause genital warts, a common benign condition of the external genitalia that causes significant morbidity.

HPV vaccines

Two prophylactic HPV vaccines were launched and licensed since 2006 with the aim of preventing high risk HPV infections and cervical precancerous lesions by inducing high level of serum neutralising antibodies. They are prepared from virus-like particles (VLPs) that do not contain any live biological product or DNA, and so are non-infectious. A quadrivalent vaccine (Gardasil®, which protects against high risk HPV types 16 and 18, and low risk HPV types 6 and 11) and a bivalent vaccine (Cervarix®, which mainly protects against high risk HPV types 16 and 18) are currently available in the market.

Efficacy

Both vaccines showed high efficacy (>90%) against HPV-16/18 related high grade cervical intraepithelial neoplasia (CIN) and adenocarcinoma in situ (AIS), which served as the surrogate endpoint of analysis.

The overall efficacy of the bivalent vaccine against CIN3+ (CIN3 and AIS) was 100% (for HPV16/18 associated lesion) and 93.2% (irrespective of HPV type in the lesion, including lesion with no HPV DNA detected), for women aged 15-25 years who have no evidence of HPV infection at baseline. In women who has unknown HPV DNA status and cervical cytology at baseline (including those who are sexually active and have received at least one vaccine dose) the efficacy of preventing CIN 3+ lesion was 45.7% for HPV16/18 associated lesions and 45.6% irrespective of HPV type[3].

One study of the quadrivalent vaccine demonstrated an efficacy of 99% protection against HPV16/18 related CIN2/3, AIS or cervical cancer in women who were HPV DNA 16/18 negative at baseline and had received all three doses of vaccine[4]. The efficacy against vaccine-related VIN 2-3 or VAIN2-3 was 95.4% and vaccine related genital warts was 96.4%[5].

Cross protection

Non-vaccine HPV types account for ~30% of cervical cancers; cross protection against these types would potentially enhance primary cervical cancer prevention.

Vaccine efficacy of the bivalent vaccine against CIN2+ associated with the composite of 12 non-vaccine HPV types (31,33,35,39,45,51,52,56,58,59,66 and 68), with or without HPV-16/18 co-infection, was 46.8% in those who received all 3 doses of vaccine and 56.2% in those who received at least one vaccine dose and were HPV naïve at baseline. The corresponding figure of efficacy after excluding HPV 16/18 co-infection was 24.1% and 17.1% respectively.[6]

For the quadrivalent vaccine, the study showed that there was a 32.5% reduction in CIN2+ lesions associated with 10 non-vaccine HPV types (HPV 31,33,35,39,45,51,52,56,58,59), other than HPV type 16 and 18, in women who were negative for the HPV tested at baseline[7].

Immunogenicity and duration of protection

Antibodies against vaccine-related HPV were persistently high and remained at or several fold above those following natural infections after 5-9.4 years[8-10]. Mathematical modelling studies predicts that both vaccines would have a high and sustained antibody level for at least 20 years.[11,12]

A recent study comparing the 2 vaccines for immunogenicity in women who were seronegative and DNA-negative at baseline (for the HPV type analysed),

seropositivity rates of neutralising antibodies were across all age strata, 100% (HPV-16/18 vaccine) and 97.5-100% (HPV-6/11/16/18 vaccine) for HPV-16, and 99.0-100% (HPV-16/18 vaccine) and 72.3-84.4% (HPV-6/11/16/18 vaccine) for HPV-18. The neutralising antibody level at 24 months was 2.4-5.8-fold higher for HPV-16 and 7.7-9.4-fold higher for HPV-18 with the bivalent vaccine versus the quadrivalent vaccine[13]. However, there are no data correlating antibody titres or memory B-cell response with clinical efficacy.

Target population

The quadrivalent vaccine (Gardasil®) is a vaccine indicated in girls and women from the age of 9 years through 45 years. It is indicated in boys and men from the age of 9 through 26 years for the prevention of genital warts. The efficacy of prevention against vaccine related (HPV6/11/16/18) anogenital warts and penile/ perineal/ perianal intraepithelial neoplasia was 89.4% and 100% respectively for those who have received all three vaccinations and were HPV naïve at baseline[14].

The bivalent vaccine (Cervarix®) is a vaccine for use from the age of 9 years onwards.

Safety

Currently available data showed that both vaccines are safe. Injection site reactions, headache, syncope, nausea, vomiting, diarrhoea, abdominal pain, itchiness, rash, urticaria, myalgia, arthritis, fatigue and fever are the most frequently reported adverse effects for both vaccines. They are usually transient and do not affect compliance with the three-dose vaccination schedules[15]. A study of vaccine safety carried out in Hong Kong showed that the vaccine (bivalent vaccine) was well tolerated and compliance was high (99%). Pain was the most common local symptom while fatigue and myalgia were the most frequent general symptoms. There was no serious adverse event that was related to the vaccination[16].

Psychosocial issues

The acceptance of the vaccine plays a key role in cervical cancer prevention. HPV knowledge and awareness of cervical cancer were significant predictors of readiness to accept HPV vaccines[17]. A cross-sectional questionnaire survey has shown that women in Hong Kong are most concerned about the efficacy of the vaccine, duration of protection and long term side effects. The degree of concern is proportional to educational level[18].

Public health implication

Both the quadrivalent vaccine and the bivalent vaccine were implemented in many countries e.g. UK[19], Australia, New Zealand, Canada etc. as part of their regional or national immunisation programmes against cervical cancer since their licensing from the year 2006. An ecological study in Australia showed that the incidence of high grade cervical abnormalities (CIN2/3 or AIS) in girls aged 18 or younger was decreased from 0.8% to 0.42% (47.5% decrease) within 3 years of launching the Quadrivalent HPV vaccination programme. However, further studies are needed to confirm whether this ecological observation is attributable to vaccination[20].

Human papillomavirus (HPV) types 6 and 11 cause up to 90% of cases of genital warts[21,22] . The incidence of genital warts in Hong Kong was estimated to be 203.7 per 100,000 person-years (292.2 and 124.9 per 100,000 person-years for males and females respectively)[23]. Analysis of national sentinel surveillance data in Australia showed a 59% decline in the number of diagnoses of genital warts in young female residents (age 12-26 years) after introduction of the quadrivalent HPV vaccination programme. There was also a 39% decline in the proportion of heterosexual men (aged 12-26) diagnosed with genital warts during the vaccine period[24], suggesting HPV vaccine may provide protective effects in heterosexual men through herd immunity.

Conclusion

Both vaccines demonstrate a high efficacy against HPV-16/18 related high grade cervical intraepithelial neoplasia and adenocarcinoma in situ (AIS). Currently, HPV vaccination is not included in the Hong Kong Childhood Immunisation Programme. Local study data may help in policy implementation for control and prevention of cervical cancers and genital warts in Hong Kong. On the other hand, it should be noted that vaccination only protects against selected HPV types and pre-cancerous cervical lesions are usually asymptomatic, the role of regular cervical cancer screening cannot be replaced by vaccination.

References

1. World Health Organization. Website: http://www.who.int/reproductivehealth/topics/cancers/en/index.html or http://globocan.iarc.fr/factsheets/populations/factsheet.asp
2. Hong Kong Cancer Registry. Cervical Cancer in Hong Kong. Website: http://www3.ha.org.hk/cancereg/e_cx.pdf
3. Lehtinen M. Paavonen J. Wheeler CM. Jaisamrarn U. et al. HPV PATRICIA Study Group. Overall efficacy of HPV-16/18 AS04-adjuvanted vaccine against grade 3 or greater cervical intraepithelial neoplasia: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncology 2012; 13(1):89-99.
4. Villa, L;Perez, G;Kjaer, S;Lehtinen, et al Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomized clinical trials. The Lancet; 2007; 369, 9576
5. Munoz N. Kjaer SK. Sigurdsson K. et al. Impact of human papillomavirus (HPV)-6/11/16/18 vaccine on all HPV-associated genital diseases in young women. Journal of the National Cancer Institute2010; 102(5):325-39.
6. Wheeler CM. Castellsague X. Garland SM. Szarewski A. et al. HPV PATRICIA Study Group. Cross-protective efficacy of HPV-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by non-vaccine oncogenic HPV types: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncology 2012; 13(1):100-10.
7. Brown DR. Kjaer SK. Sigurdsson K. et al. The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in generally HPV-naive women aged 16-26 years. Journal of Infectious Diseases 2009; 199(7):926-35.
8. De Carvalho N. Teixeira J. Roteli-Martins CM. et al Sustained efficacy and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine up to 7.3 years in young adult women. Vaccine 2010; 28(38):6247-55.

9. Naud P et al. HPV-16/18 Vaccine: Sustained immunogenicity and efficacy up to 9.4 years. Abstract presented in 27th IPV congress, Berlin, Germany, Sept 2011
10. Villa LL. Costa RL. Petta CA. et al. High sustained efficacy of a prophylactic quadrivalent human papillomavirus types 6/11/16/18 L1 virus-like particle vaccine through 5 years of follow-up. British Journal of Cancer 2006; 95(11):1459-66.
11. Fraser C. Tomassini JE. Xi L. et al. Modeling the long-term antibody response of a human papillomavirus (HPV) virus-like particle (VLP) type 16 prophylactic vaccine. Vaccine 2007; 25(21):4324-33.
12. David MP. Van Herck K. Hardt K. et al. Long-term persistence of anti-HPV-16 and -18 antibodies induced by vaccination with the AS04-adjuvanted cervical cancer vaccine: modeling of sustained antibody responses. Gynecologic Oncology 2009; 115(3 Suppl):S1-6.
13. Einstein MH. Baron M. Levin MJ. et al. Comparative immunogenicity and safety of human papillomavirus (HPV)-16/18 vaccine and HPV-6/11/16/18 vaccine: follow-up from months 12-24 in a Phase III randomized study of healthy women aged 18-45 years. HPV-010 Study Group. Human Vaccines 2011; 7(12):1343-58.
14. Giuliano AR. Palefsky JM. Goldstone S. et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males New England Journal of Medicine 2011; 364(5):401-11.
15. Einstein MH. Baron M. Levin MJ. et al. Comparison of the immunogenicity and safety of Cervarix and Gardasil human papillomavirus (HPV) cervical cancer vaccines in healthy women aged 18-45 years. HPV-010 Study Group. Human Vaccines 2009; 5(10):705-19.
16. Ngan HY. Cheung AN. Tam KF et al. Human papillomavirus-16/18 AS04-adjuvanted cervical cancer vaccine: immunogenicity and safety in healthy Chinese women from Hong Kong. The Hong Kong Medical Journal 2010; 16(3):171-9.
17. Iliyasu Z. Abubakar IS. Aliyu MH. Galadanci HS et al. Cervical cancer risk perception and predictors of human papilloma virus vaccine acceptance among female university students in northern Nigeria. Journal of Obstetrics & Gynaecology 2010; 30(8):857-62.
18. Chan KK. Kwan TT. Yao TJ. Tam KF. Cheung AN. Ngan HY. Human papillomavirus vaccine: What are women most concerned about? Journal of Obstetrics & Gynaecology Research 2012; 38(1):23-30.
19. UK will use Gardasil in its HPV vaccination programme from next September. Kmietowicz Z. BMJ 2011; 343:d7694.
20. Brotherton JM. Fridman M. May CL. et al. Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study. Lancet 2011; 377(9783):2085-92.
21. Lacey CJN, Lowndes CM, Shah KV. Burden and management of non-cancerous HPV-related conditions: HPV-6/11 disease. Vaccine 2006; 24 (suppl 3): 35-41.
22. Aubin F, Pretet J-L, Jacquard A-C, et al. Human papillomavirus genotype distribution in external acuminata condylomata: a large French national study (EDiTH IV). Clin Infect Dis 2008; 47: 610-15.
23. Lin C. Lau JT. Ho KM. et al.Incidence of genital warts among the Hong Kong general adult population. BMC Infectious Diseases 2010; 10:272.
24. Donovan B. Franklin N. Guy R.et al. Quadrivalent human papillomavirus vaccination and trends in genital warts in Australia: analysis of national sentinel surveillance data. The Lancet Infectious Diseases 2011; 11(1):39-44.

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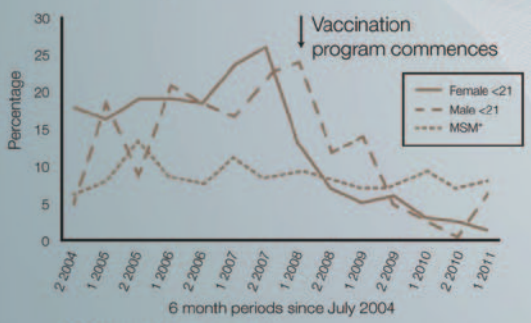
Significant impact on high grade cervical disease and genital warts

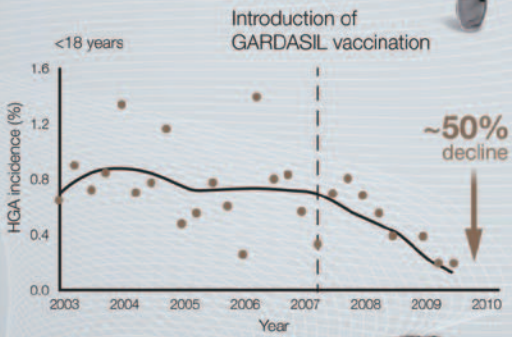
The near disappearance of genital warts in young women 4 years after commencing GARDASIL vaccination programme in Australia[2]

Female <21: ↓90% Male <21: ↓87%



*MSM=Men who have sex with men
Adapted from Read et al.[2]

First report of a decrease of CIN 2/3 or AIS after commencing GARDASIL vaccination program in Australia[3]



HGA = high-grade cervical abnormalities (cervical intraepithelial neoplasia of grade 2 or worse or adenocarcinoma in situ)
Adapted from Brotherton et al.[3]

UK switches to GARDASIL for national HPV vaccination in Sept 2012 following a competitive tendering exercise[4]

Before prescribing, please consult the full prescribing information.

GARDASIL is contraindicated in individuals with hypersensitivity to any vaccine ingredients or after a previous dose of GARDASIL. It is not recommended for pregnant women and pregnancy should be avoided during the vaccination period. This vaccine will not protect against diseases that are not caused by HPV and is not intended to be used for treatment of active genital warts; cervical, vulvar, or vaginal cancers; CIN, VIN, or VaIN. Routine cervical screening should be continued. Vaccinees should be carefully observed for approximately 15 minutes after administration of GARDASIL. Common adverse reaction in clinical trials were: headache, dizziness, nausea, pain in extremity, pyrexia, injection site reactions: erythema, pain & swelling; pruritus & hematoma which were mild to moderate. Post-marketing reports: dizziness, headache, syncope, nausea & vomiting, arthralgia, asthenia, lymphadenopathy, urticaria

References:
1. HKPC **2.** p.1, Column 1, 'Conclusion', Read TR, The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme. Sex Transm Infect 2011;87:544-547. Doi:10.1136/sextrans-2011-050234 **3.** p.4, Figure2, graph 1, Julia ML Brotherton, Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study. The Lancet 2011;377:2085-92 **4.** HPV vaccine to change in September 2012, UKDOH. Available at http://mediacentre.dh.gov.uk/2011/11/24/hpv-vaccine-to-change-in-september-2012. Accessed on January 2012.

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Management of Abnormal Smears

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Introduction

Cervical cancer is the seventh most common female cancer in Hong Kong. According to the Hong Kong Cancer Registry, there were 453 new cases of cervical cancer, and caused 128 deaths in the year of 2009[1].

Cervical cancer is one of the few cancers that can be prevented by regular screening The natural history of cervical cancer is well understood. In most cases, there is a premalignant condition, cervical intraepithelial neoplasia (CIN), which can persist for many years before becoming invasive. The cervical smear, a simple and non-invasive screening test, can readily identify this pre-malignant condition, which can be easily treated before it becomes malignant. Therefore, the correct management of abnormal cervical smears is crucial in the prevention of cervical cancers, while avoiding unnecessary treatment with its potential physical and psychological morbidities.

Current Cervical screening programme in Hong Kong

The target population for cervical smear screening includes all women who have never had sexual experience. Screening should start from the age of 25 or the time of their first sexual exposure (whichever is later). Nevertheless, women with high-risk profiles may consider starting below the age of 25. The Department of Health in Hong Kong recommends annual smears for two consecutive years, and if both are normal, the woman should have cervical smears every three years. Screening may be discontinued after the age of 65 if they have normal smears for three consecutive smears.

It should be noted that a cervical biopsy, rather than a cervical smear, should be taken if an obvious growth is noted on examination.

Patients with abnormal cervical smears

Most laboratories in Hong Kong use The Bethesda System[2]. The cervical cytology abnormalities can be broadly divided into squamous cell or glandular cell abnormalities. The management of abnormal cervical smears depends on the likelihood of the patients having a high-grade lesion, which may progress to invasive carcinoma.

Squamous cell abnormalities

The categories of squamous cell abnormalities are listed in Table 1.

Table 1: Categories of abnormal squamous cytology and its significance[3, 11]

Atypical squamous cells of undetermined significance (ASCUS)	CIN 2-3: 7-12%
Atypical squamous cells, cannot exclude HSIL (ASC-H)	CIN 2-3: 26-68%
Low-grade squamous intra-epithelial lesion (LSIL)	CIN 2-3 or above: 12-17%
High-grade squamous intra-epithelial lesion (HSIL)	CIN 2-3 or above: 53-97% Invasive cancer: 2%
Squamous cell carcinoma	Invasive cancer: 55.7%

For women with a single smear showing ASCUS, the incidence of high grade CIN (i.e. CIN 2/3) is around 11%[3], with a very low incidence of invasive cancer of 0.1-0.2%.

Two management options are available:[4]

1) Reflex HPV Testing# for high-risk oncogenic HPV types. Refer to colposcopy if HPV test is positive.
2) Repeat cytology in 6 months. Refer to colposcopy if the repeated smear is abnormal.

Reflex HPV testing is preferred as it eliminates the need for the woman to return to the clinic for a repeat smear, and it can reassure many women that they do not have a significant lesion. Reflex HPV testing is also a more cost-effective strategy in detecting high grade CIN when compared with a repeated cytology.[5]

For women with smears showing squamous cell abnormalities other than ASCUS, there is a significant proportion of them having high grade CIN or invasive cancers (Table 1), therefore, all of them should be referred to colposcopy and biopsy[4].

Glandular cells abnormalities

The two most common sources for glandular cells on cervical smears are the endocervix and the endometrium. Less commonly, atypical glandular cells can also be found in women with neoplasms of the fallopian tubes or the ovaries.

The 2001 Bethesda System classifies glandular cell abnormalities into 4 different categories, and pathologists will try to indicate whether the origin of the glandular cells is endocervical, or endometrial:

- Atypical glandular cells, NOS

- Atypical glandular cells, favour neoplastic
- Adenocarcinoma-in-situ
- Adenocarcinoma

AGC is associated with CIN and squamous cell carcinoma, adenocarcinoma-in-situ and adenocarcinoma of the cervix, endometrial hyperplasia and endometrial carcinoma. The incidence of significant pathology was significantly higher in women with smears showing AGC-favour neoplasia (68-74%), than those with AGC-NOS (19-33%) [6,7]. Therefore, all patients with AGC should be referred for endocervical sampling, colposcopy and biopsy. Endometrial sampling should also be performed for women older than 35 years old or if they are at risk of endometrial neoplasia (e.g. abnormal vaginal bleeding or conditions with chronic anovulation)[5]. One exception to this is for women with AGC-endometrial cells, endometrial sampling should be performed first, and to refer for colposcopy if the endometrial sampling is negative[4,5]. Because of the high incidence of significant pathology in women with AIS or AGC-favour neoplasia, a diagnostic cold knife cone should be performed if all the workup is negative.

Colposcopy

A colposcope is a low-power binocular microscope that allows magnification of the lower female genital tract (Fig. 1). The aim of colposcopy is to identify the worst area for biopsy and to assess the extent of the lesion. The transformation zone is the area of the cervix where the columnar epithelium is replaced by metaplastic squamous epithelium, and almost all squamous lesions occur in this area. For a colposcopic examination to be satisfactory, the whole transformation zone has to be examined. It is also important to examine the vagina at the time of colposcopy.

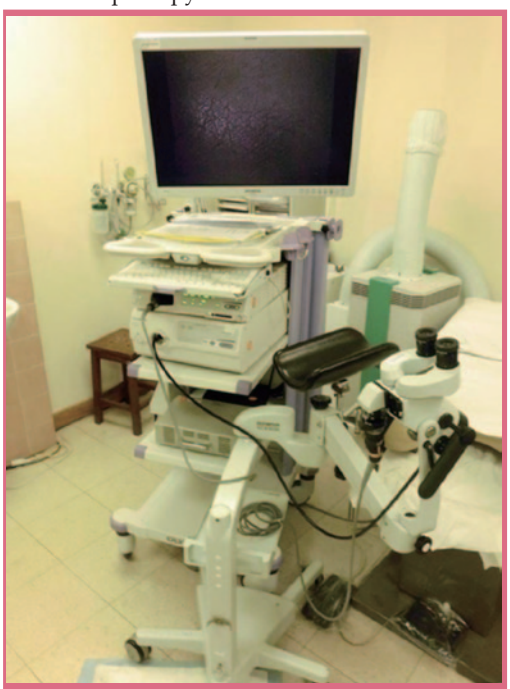

Figure 1: Colposcope

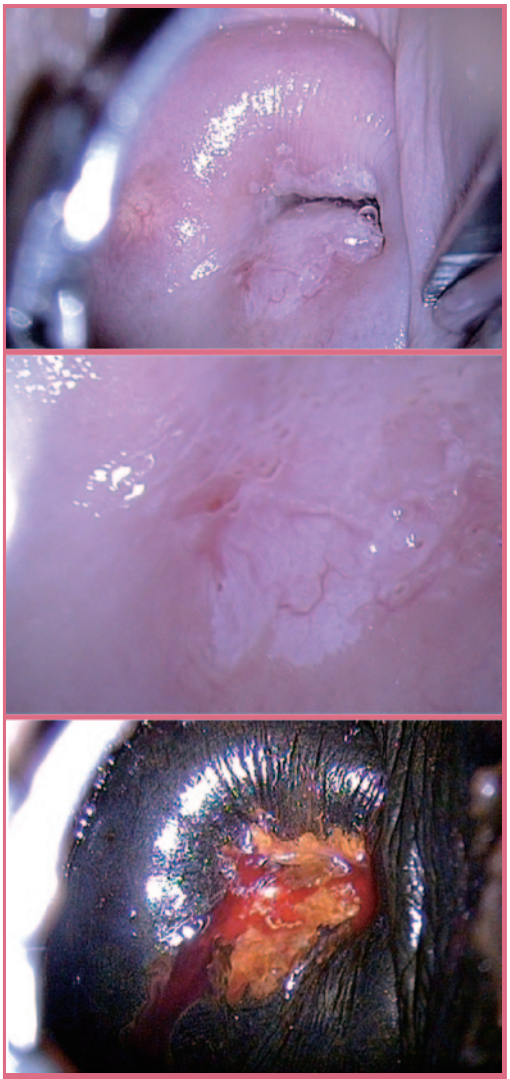

Figure 2: High grade lesion (at 7 o'clock position) appears as an aceto-white and iodine-negative lesion (upper – aceto-white lesion; middle – aceto-white lesion with abnormal vessels (on higher power); lower – iodine-negative are corresponding to the aceto-white lesion)

The cervix is first examined under the colposcope for any abnormal vessel pattern, which is best visualized with the use of a green filter. Afterwards, 5% acetic acid, followed by Lugol's iodine, are applied to the cervix. Typically, CIN appears as an aceto-white lesion, which is iodine negative. Higher grade lesions may be associated with abnormal vascular patterns. (Fig. 2) For glandular lesions, there are no reliable, widely accepted colposcopic features. Moreover, most AIS occur in the endocervical canal, which makes colposcopic examination even more difficult.

Special population

Pregnant women

The incidence of abnormal cervical cytology in pregnant women is around 5% and is similar to the non-pregnant population. Studies have shown that a large proportion of cervical dysplasia regressed during pregnancy

(53-64%)[8] and the progression rate from high-grade lesions to invasive cancer is extremely low (0-0.4%)[9]. Colposcopy is more difficult in pregnant women because of the changes in the cervix associated with pregnancy, and hence it should be performed by an experienced colposcopist. The main aim of colposcopy during pregnancy is to exclude invasive disease.

For pregnant women with ASCUS / LSIL on smears, it is reasonable to defer colposcopy until 6 weeks after delivery because of the low risk of malignancy and high rate of spontaneous regression[4,5].

For pregnant women with smears showing HSIL / AGC, they should be referred for colposcopy as non-pregnant women to exclude invasive diseases. Repeat Colposcopy at the early third trimester may be considered[4,5].

Although cervical biopsy has been shown to be safe during pregnancy in the evaluation of abnormal smears, there are concerns about the risks of excessive bleeding because of the hypervascular cervix. Therefore, cervical biopsy is recommended only if a malignant lesion is suspected during colposcopy[4].

Adolescents (20 years or less)

Adolescents have a very low risk of cervical cancer. In Hong Kong, there were only 4 cases of cervical cancer diagnosed in girls younger than 20 years old for the period of 1999-2009[1].

The prevalence of HPV infection is high in adolescent women. Up to 80% of sexually active young women will be HPV DNA positive at some point after initiating sexual activities[10]. However, most of the HPV infections clear spontaneously after 2 years. Therefore, immediate referral for colposcopy is discouraged in adolescents unless the cervical smear shows HSIL[4,5], because of the potential harm from over-investigation and over-treatment. Instead, they should have a follow-up smear every 12 months[4].

Adolescents who have a HSIL smear or persistent abnormal cervical cytology for 2 years should be referred for colposcopy[4].

Conclusion

Cervical cancer is a largely preventable disease. The correct management of abnormal cervical smears is an important element in the prevention of this potentially lethal condition. Clinicians should be familiar with the indications for referral for further investigations (e.g. colposcopy) for an abnormal smear, so that high-grade pre-invasive conditions can be identified and managed accordingly before they progress to truly invasive disease, while avoiding over-investigation and over-treatment in the women causing unnecessary psychological and physical morbidities.

Reflex HPV Testing - Testing either the original liquid-based cytology residual specimen or a separate sample co-collected at the time of the initial screening visit for HPV testing.

References

1. Hong Kong Cancer Registry, Hospital Authority
2. faceto
3. Solomon D et al. The 2001 Bethesda system – Terminology for reporting results of cervical cytology. JAMA 2002; 287: 2114-19
4. Solomon D et al. Comparison of three management strategies for patients with atypical squamous cells of undetermined significance: Baseline results from a randomised trial. J Natl Cancer Inst 2001; 93(4): 293-99
5. Guidelines on the Management of Abnormal cervical cytology. Hong Kong College of Obstetricians and Gynaecologists. 2008
6. Wright TC et al. 2006 Consensus Guidelines for the Management of Women With Abnormal Cervical Screening Tests. J Low Genit Tract Dis. 2007; 11(4): 201-22
7. Tam KF et al. A retrospective review on atypical glandular cells of undetermined significance (AGUS) using the Bethesda 2001 classification. Gynecol Oncol 2003; 91: 603-7
8. Lai CR et al. Clinical significance of atypical glandular cells by the 2001 Bethesda System in cytohistologic correlation. Acta Cytol 2008; 52(5): 563-7.
9. Fader AN et al. Cervical dysplasia in pregnancy: a multi-institutional evaluation. AJOG 2010; 203(2): 113.e1-e6
10. Yang K. Abnormal Pap smear and cervical cancer in pregnancy. Clin Obstet Gynecol 2012; 55(3): 838-48
11. Burchell AN et al. Chapter 6: epidemiology and transmission dynamics of genital HPV infection. Vaccine 2006; 24(suppl 3): S52-S61
12. SJ Johnson et al. How predictive is a cervical smear suggesting invasive squamous cell carcinoma? Cytopathology. 200; 12(3): 144-50

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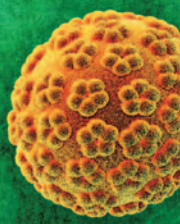

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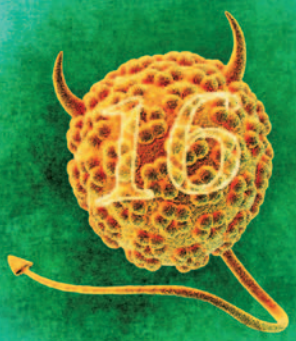

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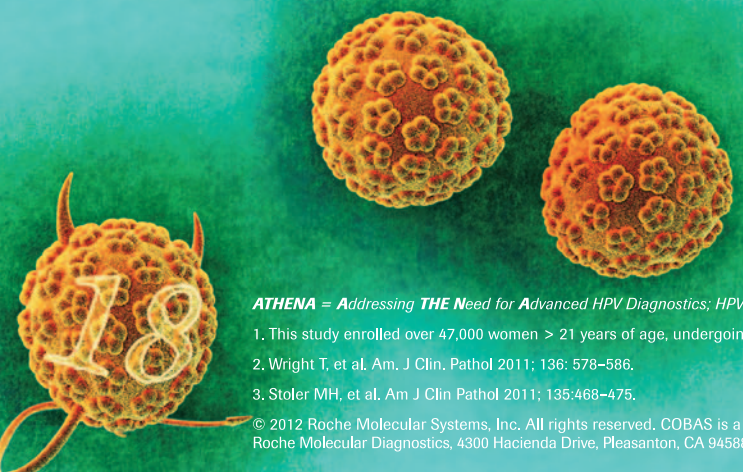
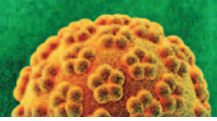


***ATHENA** = **A**ddressing **THE N**eed for **A**dvanced HPV Diagnostics; HPV = Human Papillomavirus;*

1. This study enrolled over 47,000 women > 21 years of age, undergoing routine cervical cancer screening
2. Wright T, et al. Am. J Clin. Pathol 2011; 136: 578–586.
3. Stoler MH, et al. Am J Clin Pathol 2011; 135:468–475.



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Update on the Management of Cervical Cancer in Hong Kong

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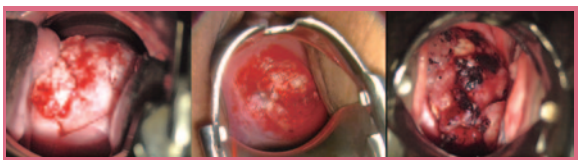
Introduction



Advances in medicine have made cancer survivors going back to community sooner and longer than what we had expected in the old days. Women are now delaying their child bearing and fertility conserving treatment for gynaecological cancers are being increasingly requested.

Cervical cancer is the second most common cancer in women aged between 15 and 44 worldwide[1] and in Hong Kong, it is the fourth most common cancer in women aged between 20 and 44[2]. Therefore, it is a nightmare to women, not only because of its high mortality rates, around 30% of all cases[2], but also because of the loss of fertility after treatment. Recently, if the disease can be diagnosed at an early stage, fertility conserving treatment can result with similar survival rates[3-5] and an acceptable reproductive outcome[6-9].

Problems in Hong Kong, data extracted from the Cancer Registry in Hong Kong, Hospital Authority[2]

Cervix Cancer in Hong Kong

Table 1. Incidence and Mortality of Cervix Cancer in 2009

	New Case	Death
Number of cases registered	453	128
Rank	7	9
Proportion of all cancer	3.7%	2.6%
Median age (years)	53	65.6
Crude rate*	12.3	3.5
Age-standardized rate (World)**	9.4	2.2
Lifetime risk before age 75	1 in 127	1 in 498
Mortality : Incidence ratio (2005-09)	0.29	

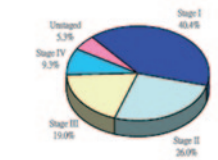


Fig 1. Stage Distribution of Cervix Cancer in 2009

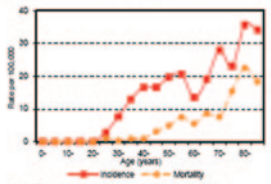


Fig 2. Age-specific Rate for Cervix Cancer in 2009

*Rates are standardized to the age distribution of the WHO 2000 World Standard Population.

Fig 3. Incidence and Mortality Trends for Cervix Cancer, 1995-2009

With the help of colleagues who actively advise or perform cervical smear screening for our local population, we are seeing a steady decline in the incidence of the disease.

Table 2. 2009 FIGO staging for Cervical Cancer[10]

Table 2
Carcinoma of the cervix uteri

Stage I	The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)
IA	Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≤ 5 mm and largest extension ≥7 mm
IA1	Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm
IA2	Measured stromal invasion of >3.0 mm and not > 5.0 mm with an extension of not >7.0 mm
IB	Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA *
IB1	Clinically visible lesion ≤4.0 cm in greatest dimension
IB2	Clinically visible lesion >4.0 cm in greatest dimension
Stage II	Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina
IIA	Without parametrial invasion
IIA1	Clinically visible lesion ≤4.0 cm in greatest dimension
IIA2	Clinically visible lesion >4 cm in greatest dimension
IIB	With obvious parametrial invasion
Stage III	The tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney **
IIIA	Tumor involves lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney
Stage IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV
IVA	Spread of the growth to adjacent organs
IVB	Spread to distant organs

*All macroscopically visible lesions—even with superficial invasion—are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.00 mm and a horizontal extension of not >7.00 mm. Depth of invasion should not be > 5.00 mm taken from the base of the epithelium of the original tissue—superficial or glandular. The depth of invasion should always be reported in mm, even in those cases with "early (minimal) stromal invasion" (~1 mm).
The involvement of vascular/lymphatic spaces should not change the stage allotment.
**On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. All cases with hydronephrosis or non-functioning kidney are included, unless they are known to be due to another cause.

This is a clinical staging as most of the cases are to be treated by primary radiotherapy or chemo-irradiation. Stage 0 has been deleted from the staging as these cases should not be treated as cervical cancer.

Treatment

Treatment of cervical cancer depends on the stage of the disease, risk factors of the disease and the fertility wish of the patient.

Primary surgery can be performed for surgically fit cases up to stage IIa1, non- bulky disease (tumour size < or = 4cm). For stage IA1 disease, they can be treated by conisation of the cervix or simple hysterectomy as the chance of metastasis or lymph nodes involvement is almost negligible. For stage IA2, IB1 and IIa1 disease, they will be offered a radical hysterectomy and pelvic lymphadenectomy. If she wishes to preserve her fertility and the tumour is smaller than 2cm without lymph node involvement, a radical trachelectomy and pelvic lymphadenectomy can be considered.

However, if the patient is not surgically fit, primary radiotherapy can be offered with similar survival rates.

Primary Chemo-irradiation should be offered for stage IIB or bulky disease (tumour size > 4cm) in women who are medically fit for chemotherapy. The dosage of chemotherapy is lower than normal treatment and it is used as a radio-sensitising agent to improve the survival outcomes when compared to primary radiotherapy alone[11-15].

Fertility conserving treatment

Professor Daniel Dargent, a pioneer of radical trachelectomy in treatment of early stage cervical cancers, had published his early works in 1994[3]. Since then, there are more than 1000 reported cases of radical trachelectomy with similar survival rates when compared to radical hysterectomy for the same stage. The pregnancy rate is around 30% with half of those results in take home babies[16].

The laparoscopic route has replaced most of the abdominal route treatment in view of the better morbidity profile but similar surgical and survival outcomes[17-19]. A robotic route has now been used to adjuvant the laparoscopic route with comparable outcomes to abdominal and laparoscopic routes[20-21]. It was found that the robotic route results in a significantly lower morbidity profile than the laparoscopic route including lower conversion rates (conversion to laparotomy during operation), lower blood transfusion rates, less vaginal cuff dehiscence rates and shorter hospital stay[22-24]. Therefore, it is a better option for treatment of such oncological patients.

Robotic assisted laparoscopic radical hysterectomy has shown to have comparable outcomes to abdominal or laparoscopic radical hysterectomy[25-26]. The learning curve for a robotic assisted laparoscopic hysterectomy is found to be significantly shorter than conventional laparoscopic hysterectomy with shorter operative times and lower morbidity such as blood loss and hospital stay[27-28].

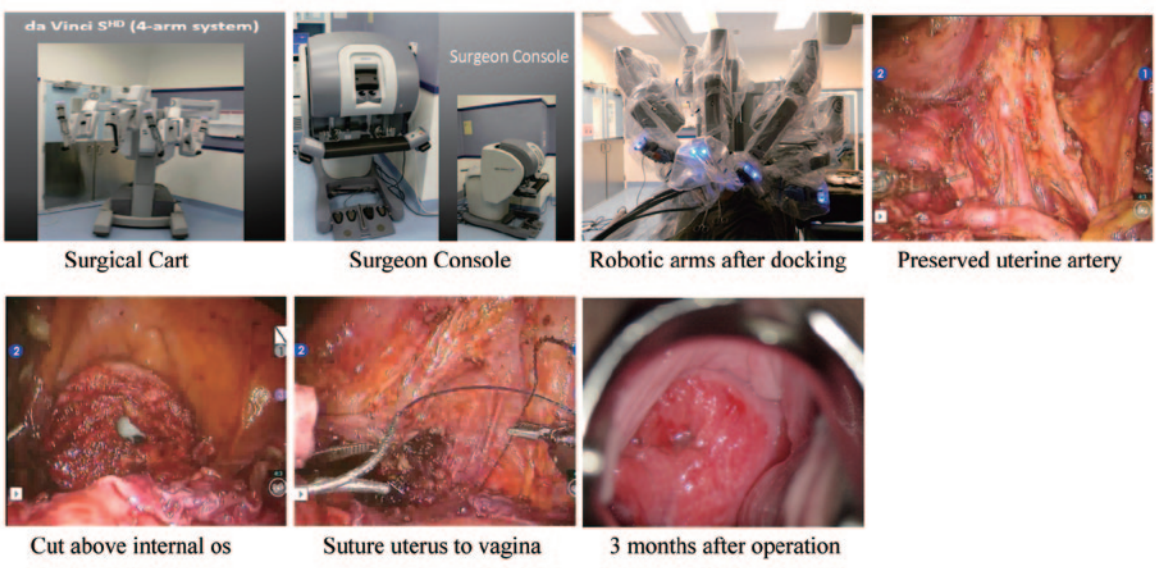
The technical aspect of a radical trachelectomy is much more complicated than a radical hysterectomy and the functional outcome is much more important than a radical hysterectomy, therefore the benefit of a robotic route can be estimated to be more in a radical trachelectomy than a radical hysterectomy[16]. Using the robotic system, the surgeons have better ergonomics, dexterity and angles of movement to perform selective resection and fine and complex suturing procedures in a narrow pelvis. The Hospital Authority will subsidise the use of the da Vinci Surgical System to assist in this procedure.

Treatment for recurrence

Last but not least, after primary treatment, one third still recurs. Only one third of those will be centrally located local pelvic recurrence that is suitable for a total exenteration with a 6-10% operative related mortality and 20-40% 5 years survival[29-32].

References

1. WHO. 2010 [cited: Available from: http://apps.who.int/hpvcentre/statistics
2. HK Cancer Registry. Oct 2011 [cited: Available from http://www.ha.org.hk/cancereg
3. Dargent D, Brun JL, Remy I. Pregnancies following radical trachelectomy for invasive cervical cancer. Gynecol Oncol 1994;52:105
4. Dargent D, Martin X, Sacchetoni A, Mathevet P. Lpaoaroscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. Cancer 2000;88:1877-1882
5. Mathevet P, Laszlo de Kaszon E, Dargent D. Fertility preservation in early cervical cancer. Gynecol Obstet Fertil 2003;31:706-712
6. Shepherd JH, Crawford RA, Oram DH. Radical trachelectomy in early stage carcinoma of the cervix: Outcome as judged by recurrence and fertility rates. Br J Obst Gynecol 2001;108:882-885
7. Shepherd JH, Spencer C, Herod J. Ind TEJ. Radical vaginal trachelectomy as a fertility-sparing procedure in women with early-stage cervical cancer-cumulative pregnancy rate in a series of 123 women. Br J Obst Gynecol 2006;113:719-724



da Vinci surgical system and operative views

8. Plante M, Renaud MC, Francois H, Roy M. Vaginal radical trachelectomy: An oncologically safe fertility-preserving surgery. An update series of 72 cases and review of the literature. Gynecol Oncol 2004;94:614-623
9. Hertel H, Kohler K, Grund D, Hillemanns P, Possover M, Michels W, Schneider for the German Association of Gynecologic Oncologists. Radical vaginal trachelectomy combined with laparoscopic pelvic lymphadenectomy: Prospective multicenter study of 100 patients with early cervical cancer. Gynecol Oncol 2006;103:506-511
10. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging of carcinoma of the cervix. International Journal of Gynecology and Obstetrics 2009;105:103-104
11. Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 1999;340:1154-61
12. Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based ra diotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med 1999;340:1144-53
13. Morris M, Eifel PJ, Lu J, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med 1999;340:1137-43
14. Thomas G, Dembo A, Ackerman I, et al. A randomized trial of standard versus partially hyperfractionated radiation with or without concurrent 5-fluorouracil in locally advanced cervical cancer. Gynecol Oncol 1998;69: 137-45
15. Meta-Analysis Group. Medical Research Council Clinical Trials Unit, London, UK. Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: A systematic review and meta-analysis of individual patient data from 18 randomized trials. Chemoradiotherapy for cervical cancer meta-analysis collaboration. J Clin Oncol. 2008;265802-5812
16. Yim GW, Kim SW, Nam EJ. Role of robot-assisted surgery in cervical cancer. Int J Gynecol Cancer 2011;21:173-81
17. Fram KM. Laparoscopically assisted vaginal hysterectomy versus abdominal hysterectomy in stage I endometrial cancer. Int J Gynecol Cancer 2002;12:57-61
18. Zullo F, Palomba S, Russo T, et al. A prospective randomized comparison between laparoscopic and laparotomic approaches in women with early stage endometrial cancer: a focus on the quality of life. Am J Obstet Gynecol 2005;193:1344-52.
19. Malzoni M, Tinelli R, Cosentino F, et al. Total laparoscopic hysterectomy versus abdominal hysterectomy with lymphadenectomy for early stage endometrial cancer: a prospective randomized study. Gynecol Oncol 2009;112:126-33
20. Bogges JF, Gehrig PA, Cantrell L, et al. A comparative study of 3 surgical methods for hysterectomy with staging for endometrial cancer: robotic assistance, laparoscopy, laparotomy. Am J Obstet Gynecol 2008;199:360.e1-9
21. DeNardis SA, Holloway RW, Bigsby Ge 4th, et al. Robotically assisted laparoscopic hysterectomy versus total abdominal hysterectomy and lymphadenectomy for endometrial cancer. Gynecol Oncol 2008;111:412-7
22. Seamon LG, Fowler JM, Richardson DL, et al. A detailed analysis of the learning curve: Robotic hysterectomy and pelvic-aortic lymphadenectomy for endometrial cancer. Gynecol Oncol 2009;114:162-7
23. Boggess JF, Gehrig PA, Cantrell L, et al. A comparative study of 3 surgical methods for hysterectomy with staging for endometrial cancer: robotic assistance, laparoscopy, laparotomy. Am J Obstet Gynecol. 2008;199:360.e1-9
24. Cardebas-Goicoechea J, Adms S, Bhat SB, et al. Surgical outcomes of robotic assisted surgical staging for endometrial cancer are equivalent to traditional laparoscopic stagina at minimally invasive surgical center. Gynecol Oncol. 2010;117:224-8
25. Magrina JF, Kho RM, Weaver AL, et al. Robotic radical hysterectomy: comparison with laparoscopy and laparotomy. Gynecol Oncol 2008;109:89-91
26. Maggioni A, Minig L, Zanagnolo V, et al. Robotic approach for cervical cancer: Comparison with laparotomy. A case control study. Gynecol Oncol 2009;115:60-4
27. Seamon LG, Fowler JM, Richardson DL, et al. A detailed analysis of the learning curve: Robotic hysterectomy and pelvic-aortic lymphadenectomy for endometrial cancer. Gynecol Oncol 2009;114:162-7
28. Lim P, Kang E, Park DH. A comparative detail analysis of the learning curve and surgical outcome for robotic hysterectomy with lympahdenectomy versus laparoscopic hysterectomy with lymphadenectomy in treatment of endometrial cancer: A case-matched controlled study of the first one hundred twenty two patients. Gynecol Oncol 2011;120:413-8
29. Soper JT, Berchuck A, Creasman WT, Clarke-Pearson DL. Pelvic exenteration: factors associated with major surgical morbidity. Gynecol Oncol 1989;35:93-98
30. Lawhead RA Jr, Clark DG, Smith DH, Pierce VK, Lewis JL Jr. Pelvic exenteration for recurrent or persistent gynecologic malignancies: a 10-year review of the Memorial Sloan-Kettering Cancer Center experience (1972-1981) Gynecol Oncol 1989;33:279-282
31. Shingleton HM, Soong SJ, Gelder MS, Hatch KD, Baker VV, Austin JM Jr. Clinical and histopathologic factors predicting recurrence and survival after pelvic exenteration for cancer of the cervix. Obstet Gynecol 1989;73:1027-1034
32. Stanhope CR, Webb MJ, Podratz KC. Pelvic exenteration for recurrent cervical cancer. Clin Obstet Gynecol 1990;33:897-909

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(Effective from October 2009)

Venue or Meeting Facilities	Member Society (Hourly Rate HK$)			Non-Member Society (Hourly Rate HK$)		
	Peak Hour	Non-Peak Hour	All day Sats, Suns & Public Holidays	Peak Hour	Non-Peak Hour	All day Sats, Suns & Public Holidays
Multifunction Room I *(Max 15 persons)*	150.00	105.00	225.00	250.00	175.00	375.00
Council Chamber *(Max 20 persons)*	240.00	168.00	360.00	400.00	280.00	600.00
Lecture Hall *(Max 100 persons)*	300.00	210.00	450.00	500.00	350.00	750.00
Non-Peak Hour: 9:30am - 5:30pm Peak Hour: 5:30pm - 10:30pm						
LCD Projector	500.00 per session					
Microphone System	50.00 per hour, minimum 2 hours					

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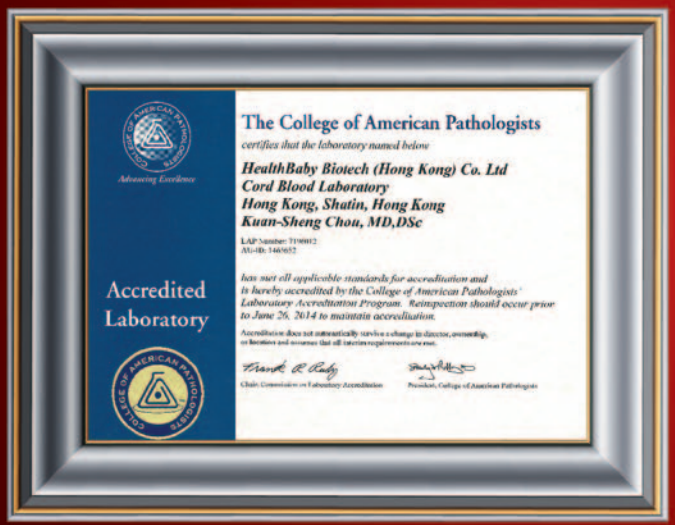

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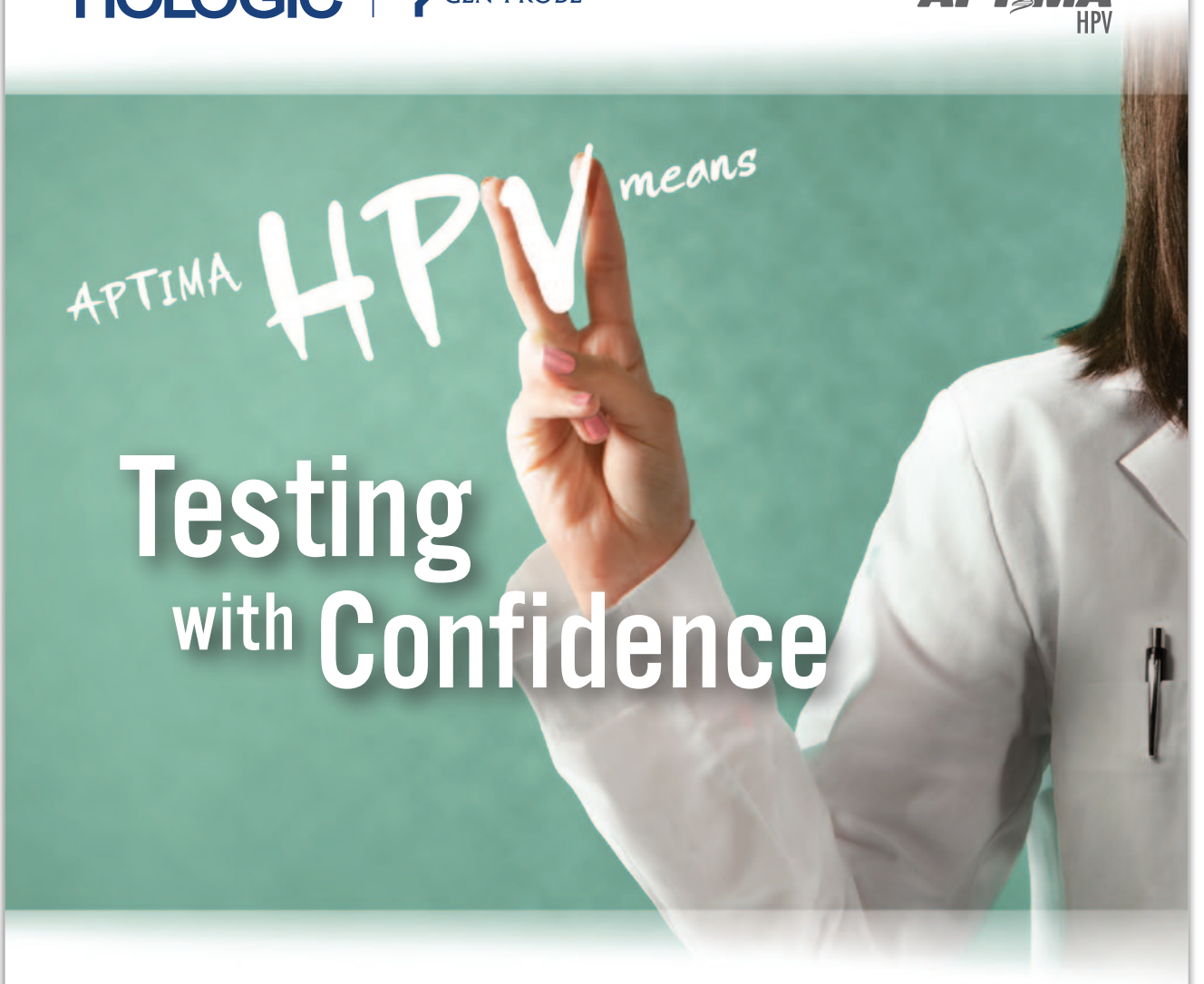

Testing with Confidence

"The **majority** of HPV detection tests...cannot **delineate between** transient and potentially **transforming** infection. To **improve** the **specificity** of an HPV test would clearly be of **clinical value.**"

–Cuschieri and Wentzensen Cancer Epidemiol Biomarkers Prev 2008

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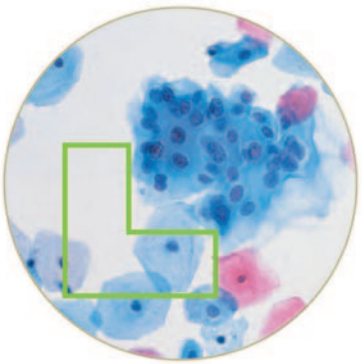

ThinPrep® plus imaging with dual review...

- **Increased productivity and disease detection, reduction in false negative fraction with the** ThinPrep Imaging System (TIS) with dual review vs. manually screened ThinPrep slides (TP) vs. conventional slides (CS)

Roberts et al - 2007 (Diag CytoPath)	
TIS vs TP	↑ 27% increased productivity
TP vs CS	↑ 54% increased productivity
TIS vs CS	↑ 44% increase in sensitivity
TIS vs CS	↓ 64% reduction in false negative fraction

"We have shown that the ThinPrep Imaging System assisted screening of ThinPrep slides shows significantly improved disease detection of high grade disease over the conventional pap smear."

Jennifer M. Roberts, et al. The Three Armed trial of the ThinPrep Imaging System, Diagnostic Cytopathology Vol.35. No.2. 2007.

- **Biopsy comfirmed data show improved disease detection[1]** with the ThinPrep Imaging System with Dual Review over manually screened ThinPrep slides

Author	Year	Disease detection[2]
Dziura[2]	2006	↑ 31% LSIL ↑ 20% HSIL

27, 525 manually screened ThinPrep slides compared to 27, 725 slides processed on the ThinPrep Imaging System with dual review

Author	Year	Disease detection[3]
Lozano[3]	2006	↑ 46% LSIL ↑ 38% HSIL

87, 267 manually screened ThinPrep slides compared to 37, 717 slides processed on the ThinPrep Imaging System with dual review

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Updates on Pathology Tests in Prevention of Cervical Cancers

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Background

Laboratory testing is a crucial element in the prevention of cervical cancers, by identification of cervical cancer cells or their pre-invasive lesions in cervical cytology and detection of the human papillomavirus (HPV), the necessary causative factor. Early identification of women at risk enables efficient treatment and enhances survival.

Cervical cancer screening is probably the most durable and effective cancer screening programme in medical history. The cervical cytology test, or the "Pap" test, refers to the collection of cells from the cervix (Figure 1), and transfer to a glass slide for detection of cancer and precursor cells. This principle has remained unchanged since its launch eight decades ago. In nearly all countries with good screening indexes, a remarkable reduction in the incidence of cervical cancers is achieved. Cervical cytology screening accounts for up to 80% reduction in mortality due to cervical cancer (Sasieni et al., 2009). The sensitivity and specificity of conventional cervical cytology for detecting CIN 2 to 3 is estimated to be 44-80% and 91-96%, respectively (Rodriguez et al., 2010).

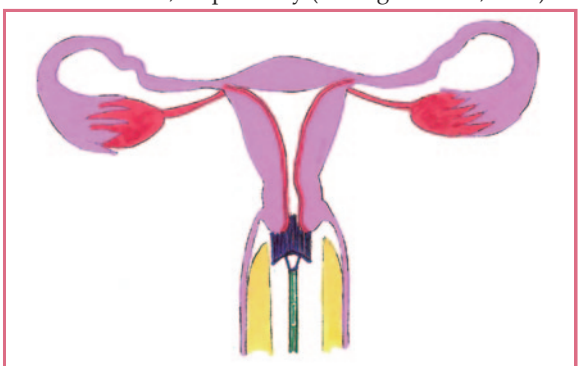

Figure 1. The uterine cervix is relatively accessible to periodic collections of cells for cancer screening.

Among cervical cancers, the incidence of squamous cell carcinomas is particularly reduced by screening although the effect on adenocarcinomas and adenosquamous carcinomas is less obvious (Smith et al., 2000). This may be due to the deeper location of the latter two cancers in the endocervix and their detection is less effective. Cervical smears can occasionally detect cancers of the uterine corpus, ovaries or even extra-genital organs (Tam et al., 2003; Wang et al., 2002). However, cervical cytology should not be considered as a screening tool for these malignancies.

Enhancement of cervical cancer screening

Infrastructure of cervical cytology screening: Cervical cytology is a good screening test but a single negative smear cannot exclude cancer (Castle et al., 2009). Both health care providers and patients need to understand the fact that successful cervical cancer screening relies on repeated cervical cytology testing and this should be done at suitable intervals. To ensure the success of cervical cytology screening, it is necessary to have a well-organised screening programme of good coverage, an adequate number of qualified cyto-technicians and pathologists, and matching resources for management with emphasis on quality assurance.

Evolution of cervical cytology reporting system: A cervical cytology reporting system has evolved since its introduction due to the identification of the link between HPV and cervical cancers as well as the merging of dysplasia and carcinoma-in-situ into a spectrum CIN (Figure 2) (Nucci and Crum, 2007) The most widely practised cervical cytology reporting system is The Bethesda System (TBS). It was initially introduced by the National Cancer Institute (NCI) of USA in 1989 (Solomon et al., 2002; Workshop, 1989) in which a binary classification of SIL in cytological reporting was adopted. Low-grade SIL (LSIL) includes abnormal cells from HPV infection and CIN I (Figure 3) whilst high-grade SIL (HSIL) refers to abnormal cells from CIN 2 and CIN 3 (Figure 4) (Table 1). A more significant modification was further made in 2001 incorporating the increasing use of new processing methods, ancillary techniques and automated screening devices (Solomon et al., 2002). The unified terminology enables accurate communication between cyto-pathologists and gynaecologists, and between cervical cytology laboratories. Quality of samples and education notes on clinical follow-ups should also be included, with reference to consensus management guidelines prepared by local authorities. In Hong Kong, corresponding management guidelines were produced by the Hong Kong College of Obstetricians and Gynaecologists in 2002 and 2008 (Ngan et al., 2008).

Development of new laboratory techniques: To improve the sensitivity and specificity of cervical cancer screening, there is a blooming of techniques (Figure 5) (1) to improve the quality of the sample by liquid-based cytology; (2) to increase the efficiency of screening for abnormal cells by automated screening platform; (3) to detect risk factors particularly human papilloma virus (HPV) and (4) to provide predictive molecular markers.

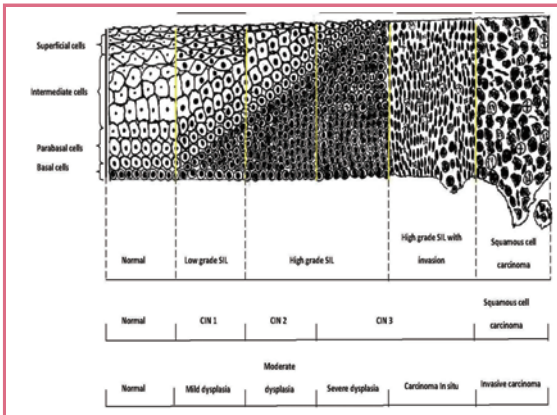

Figure 2. The spectrum of cervical intraepithelial neoplasia and squamous cell cancer.

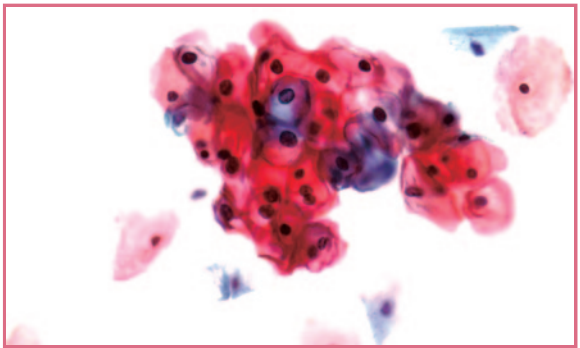

Figure 3. Koilocytes with perinuclear halo and atypical nuclei are considered a diagnostic feature of HPV infection in cervical smear or biopsy.

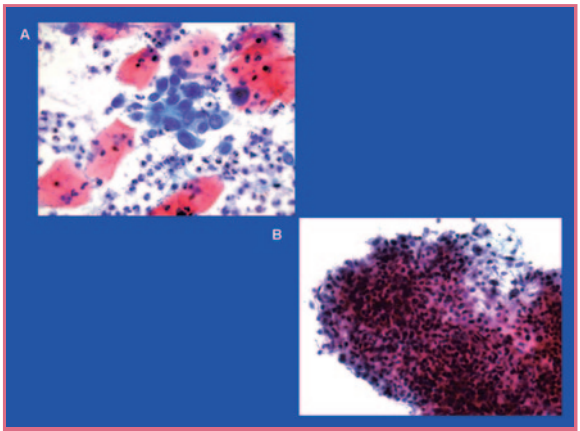

Figure 4. High-grade SIL (HSIL) and squamous cell carcinoma cells found in a screening cervical smear.

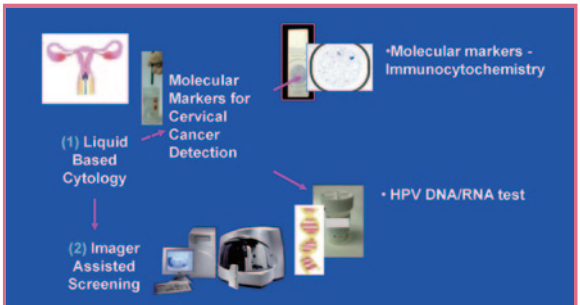

Figure 5. New technologies including liquid- based cytology, computer assisted screening and molecular markers are increasingly applied to cervical cancer detections.

Table 1. A concise version of The 2001 Bethesda System (Solomon et al., 2002)

Squamous adequacy
- Satisfactory for evaluation
- Unsatisfactory for evaluation
  - Specimen rejected/not processed (specify reason)
  - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

General Categorisation
- Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormality
- Other

Interpretation/Result
- Negative for Intraepithelial Lesion or Malignancy
  - Organisms
  - Other non-neoplastic findings, e.g. inflammation, radiation, intrauterine contraceptive device
  - Glandular cells status post-hysterectomy
  - Atrophy

Epithelial Cell Abnormalities
- Squamous cell
  - Atypical squamous cells (ASC) of undetermined significance (ASC-US) cannot exclude HSIL (ASC-H)
  - Low-grade squamous intraepithelial lesion (LSIL), including HPV cytopathic effect and CIN 1
  - High-grade squamous intraepithelial lesion (HSIL), including CIN 2 and 3
  - Squamous cell carcinoma
- Glandular cell
  - Atypical glandular cells (AGC) (*specify endocervical, endometrial, or not otherwise specified*)
  - Atypical glandular cells, favor neoplastic (*specify endocervical or not otherwise specified*)
  - Endocervical adenocarcinoma in situ (AIS)
  - Adenocarcinoma
- Other

Endometrial cells in a woman 40 years of age
Automated review and ancillary testing
Educational notes and suggestions

New laboratory techniques

Liquid-based cytology

Sampling or preparation errors have been shown to significantly affect the accuracy of cytology reporting (Gay et al., 1985; Linder and Zahniser, 1998). Conventional smears are traditionally taken with a wooden spatula, and the collected cellular material being smeared directly onto glass slides. The remaining collected cells were discarded together with the spatula but it has been reported that only 6.5% to 62.5% of the epithelial cells collected on the sampling spatula are deposited on the glass slide. Such sampling errors are responsible for a significant portion of false negative cervical cytology tests (Hutchinson et al., 1994).

The development of liquid-based cytology system represents an important milestone in the practice of gynaecology and laboratory medicine. Liquid-based cytology was initially developed in the 1990s as a preparation exclusively for use with automated screening devices. Ever since its introduction, however, it has performed so well in clinical trials against the conventional Pap smear, and it is now marketed independently to automated screening.

Liquid-based cytology involves direct rinsing of cells from the collecting device in the fixation/ transport medium from which thin layer smears are produced. This approach increases the number of cells subsequently deposited on the glass slides (Figure 6), eliminates air-drying artifacts and removes obscuring factors due to abundant blood and inflammatory cells in the sample or thick cell smears in conventional smears (Figure 7). Therefore, reduction of the unsatisfactory rate is usually achieved, particularly in populations with high rates of unsatisfactory smears, for example due to high incidence of genital infections.

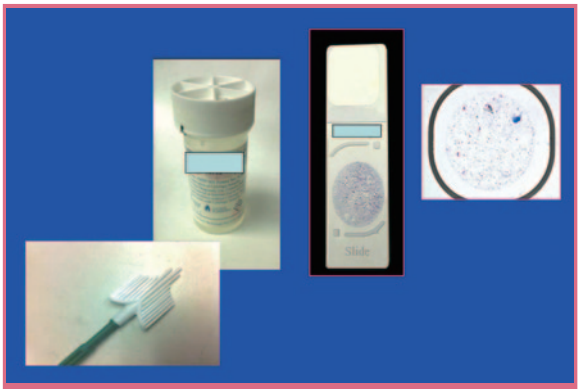

Figure 6. Cervical epithelial cells are being collected by a broom device and then rinsed in a vial of fixative transport medium. Thin layer smears with a clear background are produced for microscopic evaluation.

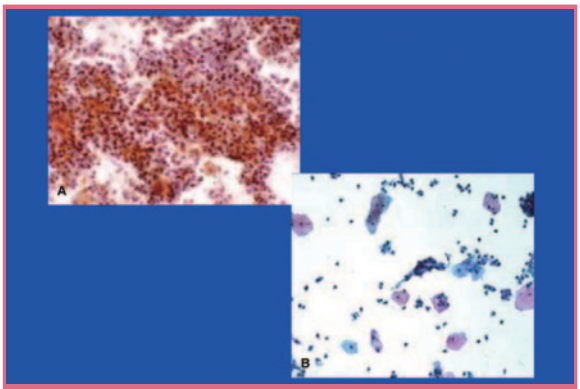

Figure 7. A conventional smear (A) with abundant polymorphs and a liquid- based cytology smear (B) with a clean background.

Globally, the two most widely used liquid-based cytology devices include the ThinPrep and the BD SurePrep which were approved by the United States Food and Drugs Administration (FDA) for cervical cancer screening in 1996 and 1999, respectively (Cibas, 2009). In Hong Kong, liquid-based cytology is now extensively used and contributes to around 70% of cervical cytology evaluation (Tay et al., 2008). There are several other liquid-based preparations currently available in the market but the majority is yet to be approved by FDA for cervical cancer screening.

In 1996, ThinPrep (Hologic, Marlborough, MA, previously Cytyc Corporation) was the first liquid-based system approved by the Food and Drug Administration (FDA) for cervical cancer screening. Instead of spreading directly onto a glass slide as in the conventional Pap smear, the cellular samples, usually collected with a cervix brush, are fixed in a methanol-based preservative (PreservCyt) and subsequently processed in a manufacturer-specified instrument (ThinPrep 2000 or ThinPrep 3000). Newer models are capable of batch processing. Using a filtering mechanism, the cells are vacuumed from the container against a filter, and then transferred onto a glass slide, followed by staining. The cells are spread over a circular area 20 mm in diameter in an almost monolayer sheet.

Becton Dickinson Diagnostic currently owns the BD SurePath Pap test system, which is a merged company between the former AutoCyte Prep and CytoRich in the late 1990s. The specimen collection method is identical to ThinPrep but the cellular samples are fixed in an ethanol-based fixative (CytoRich) supplied by the manufacturer. The specimens are then processed by the manufacturer-supplied system, the BD PrepStain slide processor, which is a fully automated system capable of batch processing. The samples are centrifuged in a density reagent and then converted into an enriched cell pellet before deposition of the cellular material onto a glass slide over a circular area 13 mm in diameter.

The MonoPrep Pap test is the most recent liquid-based system approved by FDA for cervical cancer screening. The collection method is similar to other liquid-based systems, but special collection instruments, the endocervical cytobrush and plastic cytospatula, are used. The transport medium is a buffered alcohol-based solution. The specimens are processed in a manufacturer-supplied, fully automated MonoPrep Processor capable of batch processing. The slide preparation is very similar to the ThinPrep system that involves the use of a filtering mechanism.

Although there is an overall improvement of quality with liquid-based preparations, they each have their inherent problematic issues, such as those related to specimens that are rich in mucus or blood. Each system has its own way of reducing this artifact.

Liquid-based cytology was found to be significantly more effective for the detection of LSIL and more severe lesions in several populations when compared with conventional smears, including our earlier study(Cheung et al., 2003; Gutman, 2000; Laverty et al., 1995; Lee et al., 1997; McGoogan and Reith, 1996; Wilbur et al., 1994). Liquid-based cytology has also been reported to increase the sensitivity of detecting adenocarcinomas of the cervix (Schorge et al., 2002) and micro-organisms (Cheung et al., 2003).

The almost monolayer property of the liquid-based system preparations ensures their successful use with automated screening devices, such as the ThinPrep Imaging System and the BD FocalPoint Slide Profiler for ThinPrep and SurePath, respectively. Apart from their superior quality to the conventional Pap smear at a microscopic level, the liquid-based system has the added advantage of being able to produce additional preparations for use in educational or quality assurance programmes. The residual cellular samples may also be used for additional laboratory tests.

The residual exfoliated cells in liquid-based cytology also facilitates application of ancillary techniques for cervical

cancer screening (Figure 5) (Cheung, 2007; Cheung et al., 2003; Cheung et al., 2004b; Cheung et al., 2010; Keyhani-Rofagha and Vesey-Shecket, 2002), such as detection of HPV, chlamydia, and gonorrhoea. Such approach is accepted for providing reflex HPV tests for women whose Pap tests are found to harbour atypical squamous cells of undetermined significance (ASC-US) (Ngan et al., 2008; Solomon et al., 2001; Wright et al., 2007)

Automated screening of cervical cytology

Cervical cytology evaluation is probably the only big volume medical test that has not been automated. There is high motivation to develop computer assisted evaluation of cervical smears (Baldwin et al., 2003; Wilbur, 2003). (1) The most important motivation is an attempt to reduce human errors. In a screening population, abnormal smears constitute a small portion (≈6%) of smears evaluated. Moreover, cyto-technicians need to evaluate more than 30,000 cells in one smear (Lozano, 2007) without knowing which smears harbour abnormal cells nor the nature of the abnormal cells. This combination of screening and interpretation procedures can be compared to the challenge of searching needles in haystacks (Figure 8). (2) Then there is the drive to reduce the manpower required for screening. The imager assisted screening is particularly helpful in handling the labour intensive and tiring screening process so that effort can be focused on interpreting the abnormal cells selected by the imager.

Figure 8. Needle in a haystack.

As noted earlier, the currently popular liquid-based cytology preparations were initially developed as a by-product of automated screening devices. It is understandable that automated screening only works well on smears with clear background and little cell overlap.

The PAPNET system is the first generation of commercialised automated smear screening system. The system scans the slides and identifies 128 most suspicious fields for the cyto-technicians or pathologists to check on a television monitor.

The AutoPap /FocalPoint™ slide profiler, after scanning the smears on glass slides, ranks them according to potential abnormalities. It allows a certain portion (25%) of smears to be archived without review (Brown and Garber, 1999). It has been approved by FDA to be used as a primary cervical cytology screening tool.

Using the ThinPrep Imaging System, the cells stained by DNA sensitive dyes are automatically screened. In every smear, 22 Fields of View (FOV) considered most worrying are identified and their x-y axis recorded. These 22 FOV are then recalled using the Review Scope and evaluated by cyto-technicians (Figure 9). If no abnormal cells are found in these 22 FOV, the smear can be reported as negative after the quality control procedures have been followed. Otherwise, the whole smear will need to be manually checked for abnormal cells.

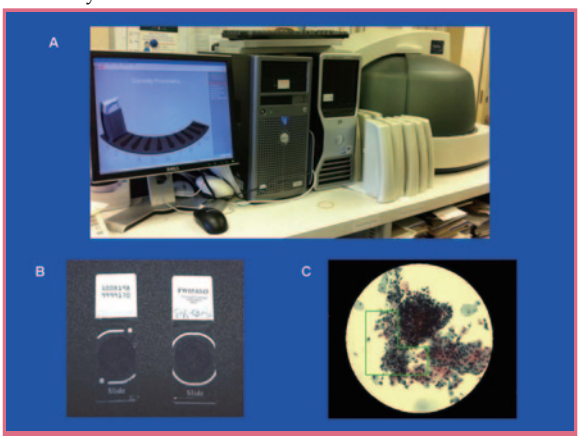

Figure 9. Computer assisted screening. (A) The ThinPrepR Imaging System is composed of the Image Processor, computer and automated Review Scopes. (B) Liquid- based cytology slides bear fiducial marks for location of the field of view. (C) An aggregate of HSIL cells identified by the imager in an electronically marked field of view.

Irrespective of the type of imager being used, cases with abnormal cells found and cases with significant clinical concern have to be referred to cyto-pathologists for evaluation and reporting. All negative cases should undergone quality control rescreening before reports are issued.

Detection of HSIL/LSIL

In most studies, a significant increase in detection of HSIL or above lesions can be found after the use of imager assisted screening (Biscotti et al., 2005; Chivukula et al., 2007; Davey et al., 2007; Dziura et al., 2006; Lozano, 2007; Miller et al., 2007). In fact, a very low detection rate of high risk HPV DNA (1.9% to 3.9%) was found in women whose liquid-based cytology smears were reported to be negative by imager assisted screening (Bansal et al., 2009; Cibas et al., 2007; Zhao et al., 2007). These findings support the high negative predictive value of image assisted screening for HPV related cytological changes.

HPV tests

There has been a remarkable advancement in the molecular detection and genotyping of HPV in recent years (Cheung, 2007; Cuschieri et al., 2005). HPV DNA testing with HC2 can be performed in the liquid-based cervical cytology cellular residues or direct samples (Sherman et al., 1997). HPV tests have been increasingly used for triage of borderline smears of ASC-US, primary screening and as a test of cure. However, clinicians and health care professionals need to understand the advantages and limitations of different HPV tests for the benefit of our women (Table 2).

Table 2. Summary of HPV molecular testing

HPV test	Manufacturer	HPV Detection	HPV Genotyping	Identify Multiple Infections in 1 test
Hybrid Capture 2	Qiagen	13 HR HPV	NA	NA
Amplicor	Roche	13 HR HPV	NA	NA
Cervista	Hologic	14 HR HPV	HPV16/18	NA
Cobas HPV	Roche	14 HR HPV	HPV16/18	NA
Realtime HR HPV	Abbott	14 HR HPV	HPV16/18	NA
Aptima HPV	GenProbe	14 HR HPV	NA	NA
Linear Array	Roche	Multiple HPV	Yes	Yes
HPV Chips	Various	Multiple HPV	Yes	Yes
PCR-Sequencing	-	Yes	Yes	NA

NA Not available

Different types of HPV tests

Historically, HPV infection was first identified by morphological identification of koilocytes (Figure 3) in either cytology or tissue biopsy samples. Electron microscopy, immunohistochemistry and various molecular biology methods were subsequently employed (Cheung, 2007) (Figure 10).

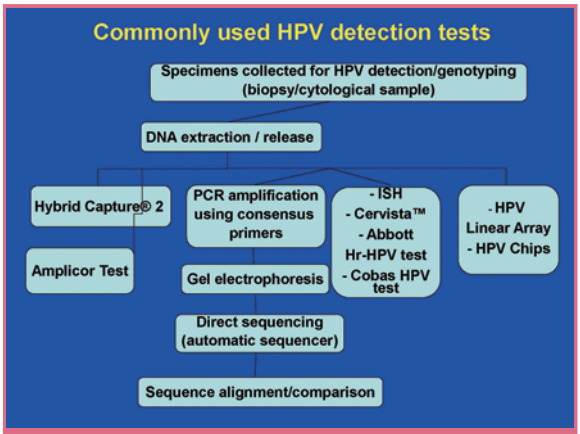

Figure 10. Commonly used HPV detection tests.

For HPV ***In situ*** **hybridisation** (ISH), complementary DNA or RNA labelled probes are applied directly onto tissue sections or cytology smears (Bewtra et al., 2005; Kong et al., 2007). The Ventana Inform HPV assay, for example, is a commercially available chromogenic ISH test that has been reported to enhance the sensitivity of HSIL (Davis-Devine et al., 2005; Guo et al., 2008).

PCR and/or Sequencing: DNA can be extracted from a direct cervical swab sample, liquid-based cytology residue, archival cervical smears, formalin-fixed paraffin-embedded or frozen tissue samples (Tabrizi et al., 2010). Amplification of the DNA template by PCR with general or consensus primers, such as GP5/6 and modified GP5+/6+, MY09/11 or modified PGMY09/11, and SPF primer set, targeting the L1 region of HPV, are commonly applied for the detection of HPV (Liu et al., 2008; Ngan et al., 2002). PCR products of different sizes due to different HPV types are amplified. Comparison of the HPV DNA sequence in the sample with sequences of known HPV genotypes enables identification of the HPV genotype (Figure 11) (Liu et al., 2008; Ngan et al., 1999a; Ngan et al., 1999b; Ngan et al., 1999c). However, PCR and/or Sanger sequencing are labour intensive and may not be suitable for high throughput processing. Moreover, it cannot detect multiple HPV infections in a sample. Nevertheless, PCR and/or sequencing is considered a good quality control tool.

Figure 11. DNA sequencing from a cervical cytology sample matched that of HPV 16.

The Hybrid Capture assays (HC2) is currently still the most widely adopted HPV test. It is the first HPV test that was approved by FDA and can identify 13 high-risk HPV types (Figure 12) or 5 low risk HPV types. This chemiluminescent-based signal amplified assay has been reported to perform at a level of sensitivity comparable to that of polymerase chain reaction (PCR) (Peyton et al., 1998) with less problems of contamination.

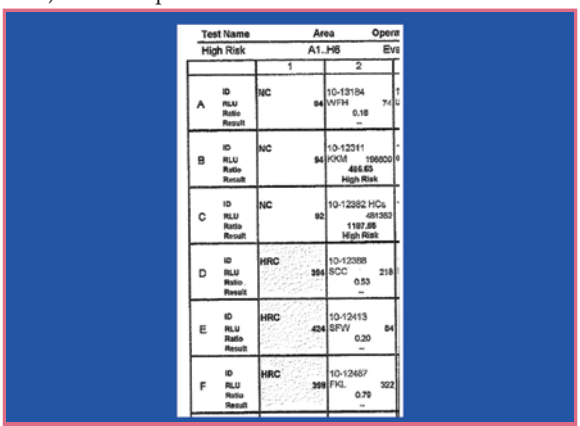

Figure 12 Hybrid capture 2 print out showing status of samples with 13 HR HPV with positive and negative controls.

To enhance the specificity for cervical cancer detection, inclusion of HPV16 and 18 genotyping is incorporated in various techniques (Cuzick et al., 2010; Stoler et al., 2011; Wong et al., 2011). This is because HPV16 and HPV18 have been identified in about 50% and 20% of cervical cancers and high grade CIN/SIL, respectively (Chan et al., 2009a; Chan et al., 2009b; de Sanjose et al., 2007; IARC, 2007; Liu et al., 2008; zur Hausen, 1994).

The Cervista™ HPV HR Test is another signal amplified technology that was approved by FDA (Day et al., 2009). Besides detecting 14 HPV high risk types, it can also detect the presence or absence of HPV 16/18. It is claimed to achieve high sensitivity and negative predictive value (NPV) in detecting CIN3+ or above as well as absence of cross-reactivity with common low risk HPV types (Kinney et al., 2010).

Similarly, the Abbott RealTime High Risk HPV is a qualitative in vitro PCR assay ?that 14 high risk HPV

genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68)? and can partially genotype HPV 16 and 18 from other 12 high risk genotypes (Wong et al., 2011).

The Roche cobas® 4800 HPV Test is an automated, PCR-based, qualitative multiplex assay which has been recently approved by FDA. It provides genotyping information for HPV 16 and 18 besides detecting the presence of 12 other HR-HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) at clinically relevant infection levels (Figure 13) (Stoler et al., 2011).

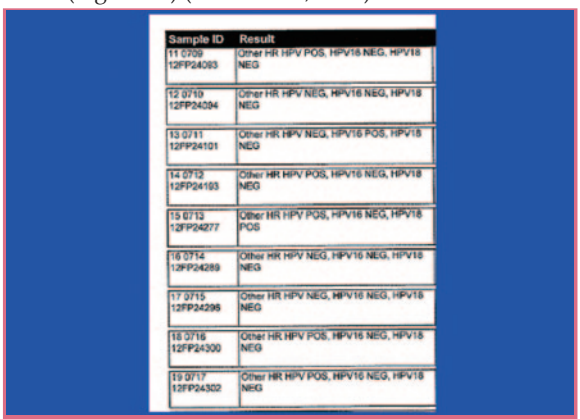

Figure 13. Cobas 4800 HPV test print out showing HPV status of samples with 13 HR HPV +/- 16/18.

HPV genotyping: The Roche linear array incorporates PGMY09/11 PCR with a line blot assay and detects 37 HPV genotypes (Figure 14) (Stevens et al., 2007; Stevens et al., 2006). It is widely used as a validation assay for various HPV genotyping kits (Wong et al., 2012). It can identify multiple HPV infections and is often used in epidemiological studies.

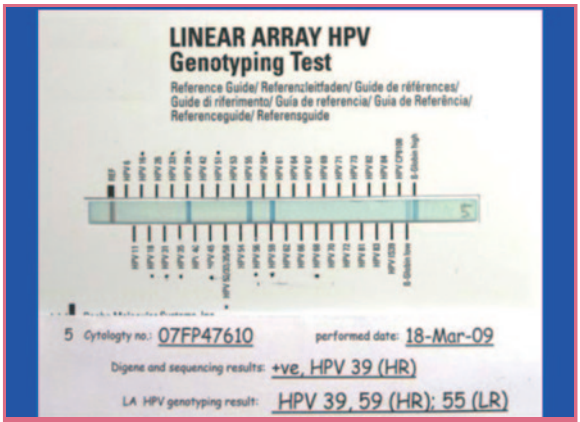

Figure 14. Roche linear array strips showing presence of multiple infections of HPV 39, 59 and 45. The former two are high risk HPV.

HPV DNA chips constructed from consensus PCR products of L1 and E6/E7 gene sequences of HPV are reported to be reliable for the detection and genotyping of HPV as a high-throughput screening test. Locally developed HPV DNA arrays such as SNIPER® HPV Genotyping Biochip Assay (Yip et al., 2010); GenoArray human papillomavirus (HPV) genotyping assay (Liu et al., 2010) and GenoFlow human papillomavirus (HPV) test (Wong et al., 2012) (Figure 15) are reported to demonstrate sensitivity and specificity similar to that of the Roche Linear Array HPV genotyping assay .

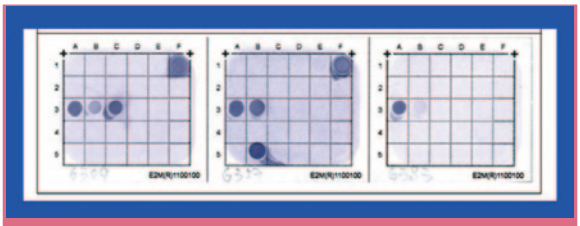

Figure 15. Three Genoflow HPV chips showing presence of HPV 16, HPV 58 and absence of HPV (from left to right).

While the above tests evaluate the existence of HPV DNA, detection of HPV RNA is also important. Active HPV infection can be detected by RNA transcription of specific HPV genes using RT-PCR or real time PCR. Commercially available E6/E7 mRNA assays such as the Pretect® HPV Proofer (NorChip) for 5 HR HPV types and APTIMA (Gen-Probe) for 14 HR HPV types have been found to be more specific for the detection of CIN3 when compared with DNA genotyping (Ratnam et al., 2010; Ratnam et al., 2011). RNA transcript detection at a single time point has also been reported to identify persistent infections without the need for repeated testing (Cuschieri and Wentzensen, 2008).

Impact of psychosocial factors

Health care professionals should be aware of the potential psychosocial impact of abnormal cervical cytology or HPV test results (Gath et al., 1995; Kwan et al., 2011; Kwan et al., 2012; Pirotta et al., 2009). Besides the fear for cancer, women found to be positive for HPV or diagnosed to have HPV related diseases may experience guilt and anger due to the stigmata of HPV infection as a sexually transmitted infection. Local studies in Hong Kong have shown that our women community has limited knowledge on cervical cancer or HPV and its related diseases (Kwan et al., 2009; Kwan et al., 2008; Lee et al., 2007). On the other hand, most women trust their doctors or health service providers for HPV related information (Pitts et al., 2007). Therefore, we should be active in learning about HPV and educate the public on the issue.

Molecular markers for cervical cancer detection

The most common abnormal cytological finding encountered in a screening programme is ASC-US. ASC-US is diagnosed in about 3-4% of screening smears (Cheung et al., 2003) and is associated with a significantly higher chance of harbouring cervical cancer and HSIL (Cheung et al., 2004b). HPV DNA testing is an option in the triage of women with ASC-US. If the ASC-US samples are positive for HPV, the women can be referred for colposcopy directly while women who are HPV negative can be reassured (Ngan et al., 2008). This practice allows early referrals for colposcopy and earlier diagnosis of HSIL or even cancer and relieve the anxiety of those women while they wait for their repeat cytology tests (Maissi et al., 2004). High risk HPV DNA testing has also been suggested to be a test for primary screening and as a test of cure in communities with enough resources. However, high risk HPV can be found in 8% of our local population and 50% of ASC-US cases (Heider et al., 2011; Liu et al., 2008). To improve specificity of identifying women who harbour cancer precursors, additional markers are being explored to distinguish cancer or dysplastic cells from reactive cells

and to predict whether a CIN will progress or regress. ProExC and p16INK4a were widely studied.

ProEx C (BD Tripath) is a cocktail immunocytochemical test that evaluates the expression of topoisomerase II-A and minichromosome maintenance protein 2 (MCM2) which are associated with host DNA integrity and cell cycle regulation (Kelly et al., 2006). It can be used in cytology and surgical pathology specimens.

p16INK4a is a cyclin-dependent kinase inhibitor. Upon HPV infection, Rb is inactivated by E7 causing paradoxically raised levels of p16INK4a (Klaes et al., 2001; Wentzensen et al., 2005). Overexpression of p16INK4a was demonstrated in both CIN and cervical cancer and has become a surrogate marker of HPV infection. Immunocytochemistry for Ki-67, another marker for cell cycle progression, can be applied to liquid-based cervical cytology to enhance the detection of carcinoma cells and precursors (Cheung et al., 2004b) (Cheung et al., 2004a). p16INK4a and Ki67 co-expression (CINtec® PLUS) are being explored for identifying dysplastic cells (Loghavi et al., 2012; Wentzensen et al., 2007).

Quality control in cervical cancer screening tests

Quality control is important for all tests including cytology, HPV tests and biomarker analysis. A modern cytology laboratory of high standard should have means to monitor its quality to ensure issued reports are accurate, reliable and informative and delivered in a timely manner.

For cervical cytology evaluation, these include prospective rescreening of negative cases before issue of reports (random 10% negative or 100% rapid rescreen of all negative cases), retrospective review of all negative cytology in the past 5 years for a new case diagnosed with high-grade lesion or carcinoma, and cytologic-histologic correlation exercises. There should be a policy on how these different quality control exercises are carried out and stated in the standard operating procedure manual. False-negative cases should be documented, reviewed and recorded and followed by a revised report. The results of these quality control exercises can be used as performance indicators for cyto-technologists/ pathologists and for the laboratory.

Similarly, a molecular pathology laboratory reporting HPV tests must also have a written quality control programme for detection of errors. One need to bear in mind that false negative and positive results can occur in molecular pathology tests including HPV tests. For instance, false negative HPV test results can occur due to insufficient cellularity in the samples, L1 gene deletion, PCR competition and inhibition of the assays. All steps of the HPV tests from specimen collection (pre-analytical) to inclusion of proper controls (analytical) and proper issuing of patients' reports (post-analytical) should be monitored. Both the molecular pathology laboratory and the referring physician should understand the limitations of the methodology being employed.

Laboratories with high standards are usually accredited by either one or the other local or overseas laboratory accreditation bodies. These include Tthe College of American Pathologists (CAP), National Association of Testing Authorities, Australia (NATA) and Hong Kong Laboratory Accreditation Scheme (HOKLAS).

Future Perspective in the post HPV Vaccine era

Future cervical cancer screening is likely to be affected by the discovery and launching of the HPV vaccine (Schiffman, 2007). With the decreasing prevalence of HPV16 and HPV18 infections in the population, it is possible that serious cytology abnormalities, particularly HSIL and carcinoma, caused by these two vaccine covered genotypes will disappear. The remaining cytological abnormalities are likely to be of low grade or equivocal after vaccine is implemented. Moreover, obvious and reliable colposcopic abnormalities that are often caused by HPV16 will also be disappearing. Even for cocktail HPV tests such as HC2, the PPV will decrease, since the clinically significant cases due to HPV16/18 and related types will most likely be prevented by the vaccine.

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References

Baldwin, P., Laskey, R., and Coleman, N. (2003). Translational approaches to improving cervical screening. Nat Rev Cancer 3, 217-226.

Bansal, M., Austin, R. M., and Zhao, C. (2009). High-risk HPV DNA detected in less than 2% of over 25,000 cytology negative imaged liquid-based Pap test samples from women 30 and older. Gynecol Oncol 115, 257-261.

Bewtra, C., Xie, Q., Soundararajan, S., Gatalica, Z., and Hatcher, L. (2005). Genital human papillomavirus testing by in situ hybridization in liquid atypical cytologic materials and follow-up biopsies. Acta Cytol 49, 127-131.

Biscotti, C. V., Dawson, A. E., Dziura, B., Galup, L., Darragh, T., Rahemtulla, A., and Wills-Frank, L. (2005). Assisted primary screening using the automated ThinPrep Imaging System. Am J Clin Pathol 123, 281-287.

Brown, A. D., and Garber, A. M. (1999). Cost-effectiveness of 3 methods to enhance the sensitivity of Papanicolaou testing. JAMA 281, 347-353.

Castle, P. E., Rodriguez, A. C., Burk, R. D., Herrero, R., Hildesheim, A., Solomon, D., Sherman, M. E., Jeronimo, J., Alfaro, M., Morales, J., et al. (2009). Neither one-time negative screening tests nor negative colposcopy provides absolute reassurance against cervical cancer. Int J Cancer 125, 1649-1656.

Chan, K. Y., Liu, W., Long, J. R., Yip, S. P., Chan, S. Y., Shu, X. O., Chua, D. T., Cheung, A. N., Ching, J. C., Cai, H., et al. (2009a). Functional polymorphisms in the BRCA1 promoter influence transcription and are associated with decreased risk for breast cancer in Chinese women. J Med Genet 46, 32-39.

Chan, P. K., Ho, W. C., Yu, M. Y., Pong, W. M., Chan, A. C., Chan, A. K., Cheung, T. H., Wong, M. C., To, K. F., and Ng, H. K. (2009b). Distribution of human papillomavirus types in cervical cancers in Hong Kong: current situation and changes over the last decades. Int J Cancer 125, 1671-1677.

Cheung, A. N. (2007). Molecular targets in gynaecological cancers. Pathology 39, 26-45.

Cheung, A. N., Chiu, P. M., Tsun, K. L., Khoo, U. S., Leung, B. S., and Ngan, H. Y. (2004a). Chromosome in situ hybridisation, Ki-67, and telomerase immunocytochemistry in liquid based cervical cytology. J Clin Pathol 57, 721-727.

Cheung, A. N., Szeto, E. F., Leung, B. S., Khoo, U. S., and Ng, A. W. (2003). Liquid-based cytology and conventional cervical smears: a comparison study in an Asian screening population. Cancer 99, 331-335.

Cheung, A. N., Szeto, E. F., Ng, K. M., Fong, K. W., Yeung, A. C., Tsun, O. K., Khoo, U. S., Chan, K. Y., and Ng, A. W. (2004b). Atypical squamous cells of undetermined significance on cervical smears: follow-up study of an Asian screening population. Cancer 102, 74-80.

Cheung, A. N., Tsun, K. L., Ng, K. M., Szeto, E., Siu, M. K., Wong, E. S., and Ngan, H. Y. (2010). P634A4 and TAp73 immunocytochemistry in liquid-based cervical cytology--potential biomarkers for diagnosis and progress prediction of cervical neoplasia. Mod Pathol 23, 559-566.

Chivukula, M., Saad, R. S., Elishaev, E., White, S., Mauser, N., and Dabbs, D. J. (2007). Introduction of the Thin Prep Imaging System (TIS): experience in a high volume academic practice. CytoJournal 4, 6.

Cibas, E. S. (2009). Cervical and vaginal cytology

3rd edition edn: Saunders Elsevier).

Cibas, E. S., Hong, X., Crum, C. P., and Feldman, S. (2007). Age-specific detection of high risk HPV DNA in cytologically normal, computer-imaged ThinPrep Pap samples. Gynecol Oncol 104, 702-706.

Cuschieri, K., and Wentzensen, N. (2008). Human papillomavirus mRNA and p16 detection as biomarkers for the improved diagnosis of cervical neoplasia. Cancer Epidemiol Biomarkers Prev 17, 2536-2545.

Cuschieri, K. S., Cubie, H. A., Whitley, M. W., Gilkison, G., Arends, M. J., Graham, C., and McGoogan, E. (2005). Persistent high risk HPV infection associated with development of cervical neoplasia in a prospective population study. J Clin Pathol 58, 946-950.

Cuzick, J., Ambroisine, L., Cadman, L., Austin, J., Ho, L., Terry, G., Liddle, S., Dina, R., McCarthy, J., Buckley, H., et al. (2010). Performance of the Abbott RealTime high-risk HPV test in women with abnormal cervical cytology smears. J Med Virol 82, 1186-1191.

Davey, E., d'Assuncao, J., Irwig, L., Macaskill, P., Chan, S. F., Richards, A., and Farnsworth, A. (2007). Accuracy of reading liquid based cytology slides using the ThinPrep Imager compared with conventional cytology: prospective study. BMJ 335, 31.

Davis-Devine, S., Day, S. J., and Freund, G. G. (2005). Test performance comparison of inform HPV and hybrid capture 2 high-risk HPV DNA tests using the SurePath liquid-based Pap test as the collection method. Am J Clin Pathol 124, 24-30.

Day, S. P., Hudson, A., Mast, A., Sander, T., Curtis, M., Olson, S., Chehak, L., Quigley, N., Ledford, J., Yen-Lieberman, B., et al. (2009). Analytical performance of the Investigational Use Only Cervista HPV HR test as determined by a multi-center study. J Clin Virol 45 Suppl 1, S63-72.

de Sanjose, S., Diaz, M., Castellsague, X., Clifford, G., Bruni, L., Munoz, N., and Bosch, F. X. (2007). Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis 7, 453-459.

Dziura, B., Quinn, S., and Richard, K. (2006). Performance of an imaging system vs. manual screening in the detection of squamous intraepithelial lesions of the uterine cervix. Acta Cytol 50, 309-311.

Gath, D. H., Hallam, N., Mynors-Wallis, L., Day, A., and Bond, S. A. (1995). Emotional reactions in women attending a UK colposcopy clinic. J Epidemiol Community Health 49, 79-83.

Gay, J. D., Donaldson, L. D., and Goellner, J. R. (1985). False-negative results in cervical cytologic studies. Acta Cytol 29, 1043-1046.

Guo, M., Gong, Y., Deavers, M., Silva, E. G., Jan, Y. J., Cogdell, D. E., Luthra, R., Lin, E., Lai, H. C., Zhang, W., and Sneige, N. (2008). Evaluation of a commercialized in situ hybridization assay for detecting human papillomavirus DNA in tissue specimens from patients with cervical intraepithelial neoplasia and cervical carcinoma. J Clin Microbiol 46, 274-280.

Gutman, S. (2000). Labeling liquid-based systems: FDA clarification. J Reprod Med 45, 969-970.

Heider, A., Austin, R. M., and Zhao, C. (2011). HPV test results stratify risk for histopathologic follow-up findings of high-grade cervical intra-epithelial neoplasia in women with low-grade squamous intra-epithelial lesion Pap results. Acta Cytol 55, 48-53.

Hutchinson, M. L., Isenstein, L. M., Goodman, A., Hurley, A. A., Douglass, K. L., Mui, K. K., Patten, F. W., and Zahniser, D. J. (1994). Homogeneous sampling accounts for the increased diagnostic accuracy using the ThinPrep Processor. Am J Clin Pathol 101, 215-219.

IARC (2007). Monograph on Human Papillomaviruses. IARC 90, 47-178.

Kelly, D., Kincaid, E., Fansler, Z., Rosenthal, D. L., and Clark, D. P. (2006). Detection of cervical high-grade squamous intraepithelial lesions from cytologic samples using a novel immunocytochemical assay (ProEx C). Cancer 108, 494-500.

Keyhani-Rofagha, S., and Vesey-Shecket, M. (2002). Diagnostic value, feasibility, and validity of preparing cell blocks from fluid-based gynecologic cytology specimens. Cancer 96, 204-209.

Kinney, W., Stoler, M. H., and Castle, P. E. (2010). Special commentary: patient safety and the next generation of HPV DNA tests. Am J Clin Pathol 134, 193-199.

Klaes, R., Friedrich, T., Spitkovsky, D., Ridder, R., Rudy, W., Petry, U., Dallenbach-Hellweg, G., Schmidt, D., and von Knebel Doeberitz, M. (2001). Overexpression of p16(INK4A) as a specific marker for dysplastic and neoplastic epithelial cells of the cervix uteri. Int J Cancer 92, 276-284.

Kong, C. S., Balzer, B. L., Troxell, M. L., Patterson, B. K., and Longacre, T. A. (2007). p16INK4A immunohistochemistry is superior to HPV in situ hybridization for the detection of high-risk HPV in atypical squamous metaplasia. Am J Surg Pathol 31, 33-43.

Kwan, T. T., Chan, K. K., Yip, A. M., Tam, K. F., Cheung, A. N., Lo, S. S., Lee, P. W., and Ngan, H. Y. (2009). Acceptability of human papillomavirus vaccination among Chinese women: concerns and implications. BJOG 116, 501-510.

Kwan, T. T., Chan, K. K., Yip, A. M., Tam, K. F., Cheung, A. N., Young, P. M., Lee, P. W., and Ngan, H. Y. (2008). Barriers and facilitators to human papillomavirus vaccination among Chinese adolescent girls in Hong Kong: a qualitative-quantitative study. Sex Transm Infect 84, 227-232.

Kwan, T. T., Cheung, A. N., Lo, S. S., Lee, P. W., Tam, K. F., Chan, K. K., and Ngan, H. Y. (2011). Psychological burden of testing positive for high-risk human papillomavirus on women with atypical cervical cytology: a prospective study. Acta Obstet Gynecol Scand 90, 445-451.

Kwan, T. T., Lo, S. S., Tam, K. F., Chan, K. K., and Ngan, H. Y. (2012). Assessment of knowledge and stigmatizing attitudes related to human papillomavirus among Hong Kong Chinese healthcare providers. Int J Gynaecol Obstet 116, 52-56.

Laverty, C. R., Thurloe, J. K., Redman, N. L., and Farnsworth, A. (1995). An Australian trial of ThinPrep: a new cytopreparatory technique. Cytopathology 6, 140-148.

Lee, K. R., Ashfaq, R., Birdsong, G. G., Corkill, M. E., McIntosh, K. M., and Inhorn, S. L. (1997). Comparison of conventional Papanicolaou smears and a fluid-based, thin-layer system for cervical cancer screening. Obstet Gynecol 90, 278-284.

Lee, P. W., Kwan, T. T., Tam, K. F., Chan, K. K., Young, P. M., Lo, S. S., Cheung, A. N., and Ngan, H. Y. (2007). Beliefs about cervical cancer and human papillomavirus (HPV) and acceptability of HPV vaccination among Chinese women in Hong Kong. Prev Med 45, 130-134.

Linder, J., and Zahniser, D. (1998). ThinPrep Papanicolaou testing to reduce false-negative cervical cytology. Arch Pathol Lab Med 122, 139-144.

Liu, S. S., Leung, R. C., Chan, K. K., Cheung, A. N., and Ngan, H. Y. (2010). Evaluation of a newly developed GenoArray human papillomavirus (HPV) genotyping assay and comparison with the Roche Linear Array HPV genotyping assay. J Clin Microbiol 48, 758-764.

Liu, S. S., Tsang, P. C., Chan, K. Y., Cheung, A. N., Chan, K. K., Leung, R. C., and Ngan, H. Y. (2008). Distribution of six oncogenic types of human papillomavirus and type 16 integration analysis in Chinese women with cervical precancerous lesions and carcinomas. Tumour Biol 29, 105-113.

Loghavi, S., Walts, A. E., and Bose, S. (2012). CINtec(R) plus dual immunostain: A triage tool for cervical pap smears with atypical squamous cells of undetermined significance and low grade squamous intraepithelial lesion. Diagn Cytopathol.

Lozano, R. (2007). Comparison of computer-assisted and manual screening of cervical cytology. Gynecol Oncol 104, 134-138.

Maissi, E., Marteau, T. M., Hankins, M., Moss, S., Legood, R., and Gray, A. (2004). Psychological impact of human papillomavirus testing in women with borderline or mildly dyskaryotic cervical smear test results: cross sectional questionnaire study. BMJ 328, 1293.

McGoogan, E., and Reith, A. (1996). Would monolayers provide more representative samples and improved preparations for cervical screening? Overview and evaluation of systems available. Acta Cytol 40, 107-119.

Miller, F. S., Nagel, L. E., and Kenny-Moynihan, M. B. (2007). Implementation of the ThinPrep imaging system in a high-volume metropolitan laboratory. Diagn Cytopathol 35, 213-217.

Ngan, H. Y., Cheung, A. N., Liu, S. S., Liu, K. L., and Tsao, S. W. (2002). Telomerase assay and HPV 16/18 typing as adjunct to conventional cytological cervical cancer screening. Tumour Biol 23, 87-92.

Ngan, H. Y., Cheung, A. N., Liu, S. S., Yip, P. S., and Tsao, S. W. (1999a). Abnormal expression or mutation of TP53 and HPV in vulvar cancer. Eur J Cancer 35, 481-484.

Ngan, H. Y., Liu, S. S., Yu, H., Liu, K. L., and Cheung, A. N. (1999b). Proto-oncogenes and p53 protein expression in normal cervical stratified squamous epithelium and cervical intra-epithelial neoplasia. Eur J Cancer 35, 1546-1550.

Ngan, H. Y., Liu, V. W., and Liu, S. S. (1999c). Risk of cervical cancer is not increased in Chinese carrying homozygous arginine at codon 72 of p53. Br J Cancer 80, 1828-1829.

Ngan, H. Y. S., Tam, K. F., Cheung, T. H., Li, W. H., Wong, A. W. Y., Wong, G., Leung, J., Cheung, A. N., Lam, S. Y., and Ip, P. (2008). Guidelines on the Management of Abnormal Cervical Cytology. In, (HKCOG).

Nucci, M. R., and Crum, C. P. (2007). Redefining early cervical neoplasia: recent progress. Adv Anat Pathol 14, 1-10.

Peyton, C. L., Schiffman, M., Lorincz, A. T., Hunt, W. C., Mielzynska, I., Bratti, C., Eaton, S., Hildesheim, A., Morera, L. A., Rodriguez, A. C., et al. (1998). Comparison of PCR- and hybrid capture-based human papillomavirus detection systems using multiple cervical specimen collection strategies. J Clin Microbiol 36, 3248-3254.

Pirotta, M., Ung, L., Stein, A., Conway, E. L., Mast, T. C., Fairley, C. K., and Garland, S. (2009). The psychosocial burden of human papillomavirus related disease and screening interventions. Sex Transm Infect 85, 508-513.

Pitts, M. K., Dyson, S. J., Rosenthal, D. A., and Garland, S. M. (2007). Knowledge and awareness of human papillomavirus (HPV): attitudes towards HPV vaccination among a representative sample of women in Victoria, Australia. Sex Health 4, 177-180.

Ratnam, S., Coutlee, F., Fontaine, D., Bentley, J., Escott, N., Ghatage, P., Gadag, V., Holloway, G., Bartellas, E., Kum, N., et al. (2010). Clinical performance of the PreTect HPV-Proofer E6/E7 mRNA assay in comparison with that of the Hybrid Capture 2 test for identification of women at risk of cervical cancer. J Clin Microbiol 48, 2779-2785.

Ratnam, S., Coutlee, F., Fontaine, D., Bentley, J., Escott, N., Ghatage, P., Gadag, V., Holloway, G., Bartellas, E., Kum, N., et al. (2011). Aptima HPV E6/E7 mRNA test is as sensitive as Hybrid Capture 2 Assay but more specific at detecting cervical precancer and cancer. J Clin Microbiol 49, 557-564.

Rodriguez, A. C., Schiffman, M., Herrero, R., Hildesheim, A., Bratti, C., Sherman, M. E., Solomon, D., Guillen, D., Alfaro, M., Morales, J., et al. (2010). Longitudinal study of human papillomavirus persistence and cervical intraepithelial neoplasia grade 2/3: critical role of duration of infection. J Natl Cancer Inst 102, 315-324.

Sasieni, P., Castanon, A., and Parkin, D. M. (2009). How many cervical cancers are prevented by treatment of screen-detected disease in young women? Int J Cancer 124, 461-464.

Schiffman, M. (2007). Integration of human papillomavirus vaccination, cytology, and human papillomavirus testing. Cancer 111, 145-153.

Schorge, J. O., Hossein Saboorian, M., Hynan, L., and Ashfaq, R. (2002). ThinPrep detection of cervical and endometrial adenocarcinoma: a retrospective cohort study. Cancer 96, 338-343.

Sherman, M. E., Schiffman, M. H., Lorincz, A. T., Herrero, R., Hutchinson, M. L., Bratti, C., Zahniser, D., Morales, J., Hildesheim, A., Helgesen, K., et al. (1997). Cervical specimens collected in liquid buffer are suitable for both cytologic screening and ancillary human papillomavirus testing. Cancer 81, 89-97.

Smith, H. O., Tiffany, M. F., Qualls, C. R., and Key, C. R. (2000). The rising incidence of adenocarcinoma relative to squamous cell carcinoma of the uterine cervix in the United States--a 24-year population-based study. Gynecol Oncol 78, 97-105.

Solomon, D., Davey, D., Kurman, R., Moriarty, A., O'Connor, D., Prey, M., Raab, S., Sherman, M., Wilbur, D., Wright, T., Jr., and Young, N. (2002). The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA 287, 2114-2119.

Solomon, D., Schiffman, M., and Tarone, R. (2001). Comparison of three management strategies for patients with atypical squamous cells of undetermined significance: baseline results from a randomized trial. J Natl Cancer Inst 93, 293-299.

Stevens, M. P., Garland, S. M., Rudland, E., Tan, J., Quinn, M. A., and Tabrizi, S. N. (2007). Comparison of the Digene Hybrid Capture 2 assay and Roche AMPLICOR and LINEAR ARRAY human papillomavirus (HPV) tests in detecting high-risk HPV genotypes in specimens from women with previous abnormal Pap smear results. J Clin Microbiol 45, 2130-2137.

Stevens, M. P., Garland, S. M., and Tabrizi, S. N. (2006). Human papillomavirus genotyping using a modified linear array detection protocol. J Virol Methods 135, 124-126.

Stoler, M. H., Wright, T. C., Jr., Sharma, A., Apple, R., Gutekunst, K., and Wright, T. L. (2011). High-risk human papillomavirus testing in women with ASC-US cytology: results from the ATHENA HPV study. Am J Clin Pathol 135, 468-475.

Tabrizi, S. N., Taylor, N., McCullough, M. J., Phillips, G., Wark, J., Gertig, D., Petersen, R. W., Saville, M., and Garland, S. M. (2010). Human papillomavirus genotype detection from archival papanicolaou-stained cervical tests. Cancer cytopathology 118, 482-489.

Tam, K. F., Cheung, A. N., Liu, K. L., Ng, T. Y., Pun, T. C., Chan, Y. M., Wong, L. C., Ng, A. W., and Ngan, H. Y. (2003). A retrospective review on atypical glandular cells of undetermined significance (AGUS) using the Bethesda 2001 classification. Gynecol Oncol 91, 603-607.

Tay, S. K., Ngan, H. Y., Chu, T. Y., Cheung, A. N., and Tay, E. H. (2008). Epidemiology of human papillomavirus infection and cervical cancer and future perspectives in Hong Kong, Singapore and Taiwan. Vaccine 26 Suppl 12, M60-70.

Wang, X., Khoo, U. S., Xue, W. C., and Cheung, A. N. (2002). Cervical and peritoneal fluid cytology of uterine sarcomas. Acta Cytol 46, 465-469.

Wentzensen, N., Bergeron, C., Cas, F., Eschenbach, D., Vinokurova, S., and von Knebel Doeberitz, M. (2005). Evaluation of a nuclear score for p16INK4a-stained cervical squamous cells in liquid-based cytology samples. Cancer 105, 461-467.

Wentzensen, N., Bergeron, C., Cas, F., Vinokurova, S., and von Knebel Doeberitz, M. (2007). Triage of women with ASCUS and LSIL cytology: use of qualitative assessment of p16INK4a positive cells to identify patients with high-grade cervical intraepithelial neoplasia. Cancer 111, 58-66.

Wilbur, D. C. (2003). Cervical cytology automation: an update for 2003. The end of the quest nears? Clin Lab Med 23, 755-774.

Wilbur, D. C., Cibas, E. S., Merritt, S., James, L. P., Berger, B. M., and Bonfiglio, T. A. (1994). ThinPrep Processor. Clinical trials demonstrate an increased detection rate of abnormal cervical cytologic specimens. Am J Clin Pathol 101, 209-214.

Wong, O. G., Lo, C. K., Chow, J. N., Tsun, O. K., Szeto, E., Liu, S. S., Ngan, H. Y., and Cheung, A. N. (2012). Comparison of the GenoFlow human papillomavirus (HPV) test and the Linear Array assay for HPV screening in an Asian population. J Clin Microbiol 50, 1691-1697.

Wong, O. G., Lo, C. K., Szeto, E., and Cheung, A. N. (2011). Efficacy of Abbott RealTime High Risk HPV test in evaluation of atypical squamous cells of undetermined significance from an Asian screening population. J Clin Virol 51, 136-138.

Workshop (1989). The 1988 Bethesda System for reporting cervical/vaginal cytologic diagnoses: developed and approved at the National Cancer Institute workshop in Bethesda, MD, December 12-13, 1988. Diagn Cytopathol 5, 331-334.

Wright, T. C., Jr., Massad, L. S., Dunton, C. J., Spitzer, M., Wilkinson, E. J., and Solomon, D. (2007). 2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests. Am J Obstet Gynecol 197, 346-355.

Yip, Y. C., Ngai, K. L., Vong, H. T., Tzang, L. C., Ji, S., Yang, M., and Chan, P. K. (2010). Prevalence and genotype distribution of cervical human papillomavirus infection in Macao. J Med Virol 82, 1724-1729.

Zhao, C., Elishaev, E., Yuan, K. H., Yu, J., and Austin, R. M. (2007). Very low human Papillomavirus DNA prevalence in mature women with negative computer-imaged liquid-based Pap tests. Cancer 111, 292-297.

zur Hausen, H. (1994). Molecular pathogenesis of cancer of the cervix and its causation by specific human papillomavirus types. Curr Top Microbiol Immunol 186, 131-156.

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*Compared to culture (symptomatic patients)
**Compared to wet mount (symptomatic and asymptomatic patients)

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References

1 BD Affirm™ VPIII Microbial Identification Test [package insert]. Sparks, MD: BD Diagnostics; 2010.
2 Owen MK, Clenney TL. Management of vaginitis. *Am Fam Physician* 2004;70:2125-2132.
3 Lowe NK, Neal JL, Ryan-Wenger NA. Accuracy of the clinical diagnosis of vaginitis compared with a DNA probe laboratory standard. *Obstet Gynecol* 2009;113:89-95.

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"Even under research conditions that provided clinicians with sufficient time and materials to conduct a thorough and standardized clinical evaluation, the diagnosis … remains difficult."

Lowe NK, Neal JL, Ryan-Wenger NA. Accuracy of the clinical diagnosis of vaginitis compared with a DNA probe laboratory standard. *Obstet Gynecol* 2009;113:89-95.[3]

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Dermatological Quiz

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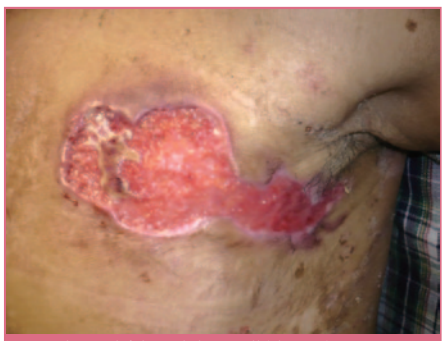

Fig. 6: Ulcer on left lateral chest wall (close-up)

This 55 year-old man noticed a red painful lesion developed over his left lateral chest wall for a few weeks which rapidly increased in size and broke down into this large painful ulcer (Fig. 6) with purulent discharge. He had history of Crohn's disease followed up regularly by gastroenterologists. He had seen various doctors and tried different topical treatments and oral antibiotics with no improvement. Skin biopsy showed diffuse neutrophils at the base of the ulceration and non-specific tissue necrosis with surrounding mononuclear cell infiltrates at the ulcer edge. Special stains and tissue culture for bacterial, mycobacterial, fungal and viral agents were all negative.

Imaging:

1. What is your clinical diagnosis or differential diagnoses?
2. How will you manage this man?

(See P. 44 for answers)

PRESS RELEASE Oct. 18, 2012
THE FEDERATION OF MEDICIAL SOCIETIES OF HONG KONG

In response to the recent serious medical incident and related public discussion, the Federation of Medical Societies of Hong Kong would like to make the following announcements:

1. The monitoring of cosmetic business in relation to medical related procedures
In the best interests of consumers and patients, there must be a clear line drawn between cosmetic business and cosmetic medicine. Cosmetic business is commercial activity subject to consumer safety protection regulations. Cosmetic medicine involves many medical specialties. This is a form of medical treatment provided by doctors. Only registered medical practitioners or registered dentists are allowed to provide cosmetic treatments appropriate to their specialties, level of training and experience. For patient safety protection, any doctors with misconducts or providing services below the expected standards will be subjected to disciplinary actions by the regulatory professional bodies.

The following are some relevant suggestions regarding this aspect:

a. Define in detail what process or treatment should not be carried out by commercial business entities, including cosmetic business, in the absence of registered doctors.
b. Continuous and regular monitoring of cosmetic business.
c. More education to the public on potential risk and dangers related to cosmetic treatment, so that citizens can make a fully informed choice of their own.
d. Monitoring of advertisement in beauty business especially its genuineness.

2. The monitoring of use of experimental procedures, and blood and pharmaceutical Products
All clinical procedures of experimental nature, or of a high risk/benefit ratio, which are not yet evidence based or clinically proven, should only be performed with prior approval by appropriate ethical review board and written informed consent of the patients. The procedure needs to be supported with independent expert opinion, and carried out only by professionals with accredited training in the field. Procedures involving blood products and any pharmaceutical products should always be performed with the highest level of infection control, safety measures and other aspects of care in mind.

In line with other developed countries, the Hong Kong SAR Government should set up guidelines to regulate the use of human cellular products including the use of stem cells and ex-vivo expanded immune cells.

3. The doctors' professional conduct
From the ancient days more than 2000 years ago in Greece with the Hippocratic Oath, to the modern days of Declaration of Geneva and code of good practice by various international professional bodies and medical councils, doctors have always been required to follow a very strict conduct.

Doctors should always put their patients' health as the first consideration, to do them good and do no harm. Doctors should respect their patients and their privacy, and safeguard the professional dignity and professionalism. Doctors should not permit consideration of factors such as ethnic origin, nationality, political affiliation, social standing or any other factors to intervene between their duties and their patients. Such factors would also include financial advantages.

Doctors should always remind ourselves of these principles and code of conduct. Our patients place their health and lives in doctors' hands, and doctors shoulder a huge responsibility. With an ever-evolving modern world of medicine and technology, medical professionals will continue to face ethical issues and moral challenges. It is of utmost importance that the medical professionals should abide by the well laid out professional conduct, and as the old Chinese saying goes, treat your patients like treating your own children.

The Federation of Medical Societies of Hong Kong was established in 1965, and currently has a membership of 131 professional societies. Founding members are Hong Kong Medical Association and British Medical Association (Hong Kong Branch). Member societies include doctors, dentists, nursing, pharmaceutical and allied health professionals. The Federation of Medical Societies of Hong Kong endeavours to provide the leadership and mechanism whereby the activities of member societies can be coordinated to promote professional interests, achieve fraternity and to advance common ideals of the medical and health professions of Hong Kong.

The press statement is issued by the Executive Committee of Federation of Medical Societies of Hong Kong and with support from the following member societies:

以上聲明由香港醫學組織聯會的執行委員會及下列各學會聯同發出：

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香港麻醉科學會

FMSHK Press Conference on Oct 18th

Recent medical beauty treatment incidents have drawn public attention. In response to the serious nature and the related public and professional concerns, the Federation of Medical Societies of Hong Kong has collected member societies' feedback and held a press conference on 18 October 2012, presenting a statement with suggestions and recommendations on this issue. The statement is supported as at to date by 45 member societies. (The Press Release is on Page 35)

With support of the media, the summary was reported in television news and 14 local newspapers. We hope that the reflected opinion would help reinforce the professionalism amongst our medical and health colleagues, and serve as a useful reference for the government in planning and consulting for future measures and directions.


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Central & Western Health Festival 2012/2013

The HKFMS Foundation Limited is delighted to continue the support and participation for the annual Central and Western Health Festival. This year, the Festival was successfully held on 3-4 November in the Sheung Wan Sports Centre. In the two-day Festival, over 2,400 citizens joined the Foundation activities, namely 3 health talks, occupational therapy game booths, dental checks and eye tests. We would like to express our sincere thanks to the following speakers and member societies, namely Dr. Priscilla WONG of the Hong Kong Society of Rheumatology, Dr. Siu-keung LAM of the Hong Kong Society for Colposcopy and Cervical Pathology, Dr. Tai-nin CHAU of the Hong Kong Association for the Study of Liver Diseases; the Hong Kong Society of Professional Optometrists, the Hong Kong Occupational Therapy Association and Dr. Sai-kwing CHAN, Second Vice-President of the Federation. We would also like to thank the following sponsors for their gifts and support: Abbott Medical Optics, Colgate, Culture Homes, Hong Wo Pharmaceutical, International Medical, Mekim, Oral-B and Skyview Optical.

Six Sigma Seminar

On 30th October the Federation co-organised a free seminar with the Six Sigma Institute for the member societies of our Federation. The speaker, Dr KC CHAN, shared the successful experiences of deploying Lean Six Sigma in Health Care and introduced the appropriate management tools for medical organisations. The seminar was successfully conducted with positive feedback from the audience, representing participation from 29 member societies. The Federation hopes the seminar could help disseminate the notion of customer focus in the workplace of medical industry, with the ultimate objective to enhance effectiveness and efficiency within limited resources. Feedback and suggestions to the FMSHK secretariat for organising further training courses on health management are welcome.

Photo Exhibition of the Project of Photog-buddy

Photog-buddy is a project of personal development for a group of bereaved teenagers aged 13 to 19, co-organised by the HKFMS Foundation Limited and Togetherness. This is part of an ongoing charity project for bereaved children supported by the HKFMS Foundation. Through 8 weeks of learning photography techniques and joining outdoor practices, participants were emotionally guided to build a healthy personality and to reform their spiritual direction. The workshop, which consisted of eight 3-hour sessions (2pm to 5pm on Saturdays), has been successfully completed in July and August. Voluntary tutors taught photography techniques and self-expression skill as well as tips to define self-oriented themes on photography. Therefore, the bereaved teenagers could leave the past behind, cherish the present and look forward to the future.

The exhibition was held at the Gallery, HKICC Lee Shau Kee School of Creativity on 18-21 October, aimed at encouraging public awareness on caring those adolescents, thereby assisting them to overcome their psychological barriers. It was our honour to have various distinguished guests to officiate the celebration ceremony on 20 October. The participated teenagers were given much encouragement for their growth and positive changes, and guests were also touched by the appreciation and efforts from the bereaved children. Through the numerous creative artworks and the photographs displayed during the exhibition, the awareness of the public on the needs of the bereaved children was enhanced. The HKFMS Foundation looks forward to collaborate further with various partners to promote this worthy cause, in helping the bereaved youngsters to brave their adversity and become the future pillars of our society.

(From left to right: Mr. Dickie HUNG & Mr. Danny CHO, workshop tutors, Ms. Dorothy WONG, Representative of Hospice Care, Ms. Flori LAM, Council Member of Hong Kong Pain Society, Mr. Benjamin LEE, Hon. Treasurer of the Foundation, Dr. Raymond LO, President of the Foundation, Ms. Christina SUN, CEO of Togetherness, Dr. Chun-key LAW, President of Hong Kong College of Radiologists, Ms. Joyce CHENG, Hospital Ward Manager of the Sha Tin Hospital, Dr. Po-wan KO, Hon. Secretary of The Hong Kong Paediatric Society and Ms. Pearl TSE, Ex-CEO of Togetherness)

New Members

HONG KONG SOCIETY OF PAEDIATRIC RESPIROLOGY

c/o Department of Paediatrics, Kwong Wah Hospital, 25 Waterloo Road, Yaumatei, Kowloon, HK.
Tel.: 3517 5055 Fax: 3517 5164 Home page: http://www.hkspr.org

The Hong Kong Society of Paediatric Respirology was founded in 1997 with the mission of promoting the development of paediatric respirology and critical care. Under the leadership of our previous presidents Dr So Kwan-tong and Dr Alfred Tam and our current president Dr Daniel Ng, the Society has established our present leading position in Hong Kong and Asia. We hold regular clinical meetings and our annual scientific meetings are always well attended. We have developed guidelines on asthma, sleep disorders and recurrent wheeze in children. We have frequent exchanges with our sister societies in China Mainland and Taiwan. There are three main areas that we will be focusing on in the coming years, i.e. research, training, and accreditation. These are important in the future development of paediatric respirology as a recognizsed subspecialty in Hong Kong.

Chow Pok-yu
Honorary Secretary

The Hong Kong Association for Child and Adolescent Psychology and Psychiatry

The Hong Kong Association for Child and Adolescent Psychology and Psychiatry was founded in 1988. Membership of the Association spans across a wide range of professional fields such as child psychiatrists, child psychologists, child psychiatric nurses, occupational therapists and psychiatric social workers working with children and adolescents. It is also extended to any person, who by his / her profession, works for the mental health of children and adolescents as well as to any student who is currently undertaking training in courses related to child and adolescent mental health.

The objectives of the Association are to (1) promote and advocate for better mental health of children and adolescents, (2) promote a better understanding of child and adolescent mental health among the public, (3) promote professional standards of all kinds of professionals working on the mental health of children and adolescents, and (4) cooperate with similar organisations in Hong Kong and other countries with a view to improve the mental health of children and adolescents.

In the past few years, the Association had focused in organising scientific meetings/ conferences/ seminars on a variety of interesting topics. In future, we look forward to more collaboration opportunities with members of The Federation of Medical Societies of Hong Kong and other professional bodies.

Members of the executive committee:

Chairman	Dr. S F Hung Honorary Consultant, Kwai Chung Hospital
Vice-Chairman	Professor Patrick W L Leung Professor, Department of Psychology, Chinese University of Hong Kong
Hon. Secretary	Dr. C P Tang Consultant, Kwai Chung Hospital
Hon. Treasurer	Dr. Y K Lee Associate Consultant, Department of Psychiatry, United Christian Hospital
Committee Member	Professor Ernest S L Luk Adjunct Professor, Department of Psychiatry, Chinese University of Hong Kong
Committee Member	Professor Kelly Y C Lai Associate Professor, Department of Psychiatry, Chinese University of Hong Kong
Committee Member	Dr. T P Ho Honorary Clinical Associate Professor, Department of Psychiatry, Hong Kong University
Committee Member	Dr. Phyllis K L Chan Consultant, Department of Psychiatry, Queen Mary Hospital
Committee Member	Dr. C C Lee Consultant, Kwai Chung Hospital
Committee Member	Dr. T S Lai Private Psychiatrist

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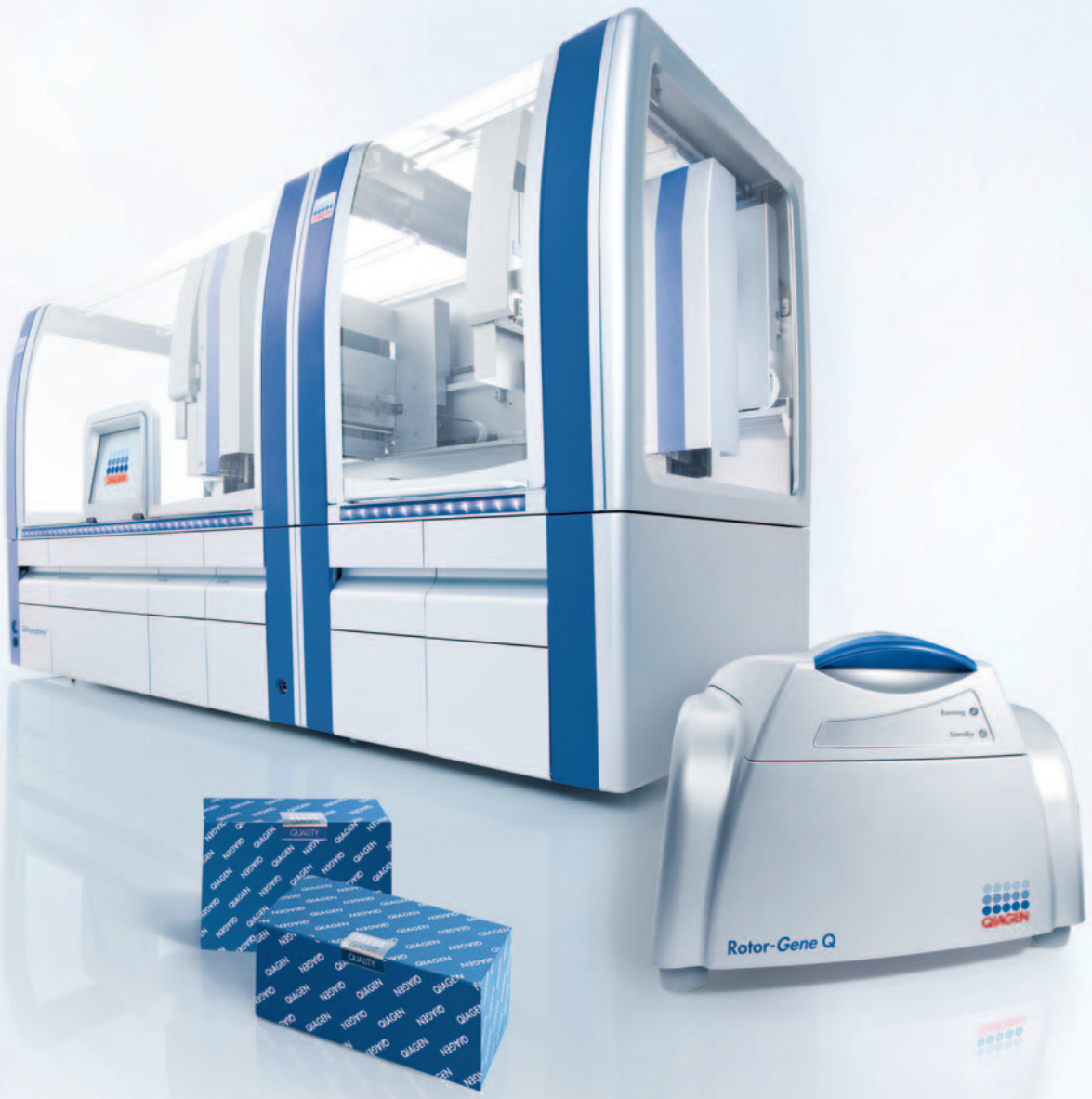

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Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						* 19th Annual Scientific Meeting- Radiation Oncology in Neurosurgical Practice **1**
* HKMA CME– Laser Forum 2012 (Certificate Course- Frontiers in Laser Surgery and Safety) * HKMA CME – Laser Forum 2012 (Seminar on Cosmetic Surgery) * 2012 Paediatric Update No.3 – Paediatric Neurology * Joint Professional Volleyball Tournament 2012 * HKMA Tennis Tournament 2012 **2**	**3**	* HKMA Shatin Doctors Network - The Management Landscape of Atopic Dermatitis * HKMA CME - The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 5) * FMSHK Officers' Meeting * HKMA Council Meeting **4**	* HKMA Shatin Doctors Network– Practical Approach to Common Facial Skin Diseases **5**	* HKMA NTW Community Network-Latest Development in Modern Oral Contraceptives * HKMA CME - The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 5) **6**	* HKMA Shatin Doctors Network – The unique role of dopamine and nor-adrenaline in treatment of depression **7**	* Refresher Course for Health Care Providers 2012/2013 **8**
* HKMAPS Photo Sharing * HKMA Tennis Tournament 2012 **9**	**10**	* HKMA Kowloon West Community Network - Lecture Series on Allergic Diseases (Session 3) - Asthma and Allergic Rhinitis in Paediatrics **11**	* Hong Kong Neurosurgical Society Monthly Academic Meeting –Flow regulator: development of shunt valves * HKMA CME – Certificate Course for GPs 2012 **12**	* HKMA Kowloon East Community Network-Advance Treatment in Low Back Pain * HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2012– Review and Updates on Refractive Error **13**	* HKMA Yau Tsim Mong Community Network - BPH Management: Not Only Focus on Prostate? * HKMA Shatin Doctors Network - Achieving Glycemic Control in Patients with Type 2 Diabetes **14**	**15**
* Joint Professional Volleyball Tournament 2012 * HKMA Tennis Tournament 2012 **16**	**17**	* HKMA Tai Po Community Network - Common Pitfalls in Management of Breast Disease **18**	* HKMA Central, Western & Southern Community Network - Chronic Hepatitis B: Review and Treatment * HKMA Shatin Doctors Network - Review and Update on GERD **19**	* HKMA CME – Certificate Course for GPs 2012 * FMSHK Executive Committee Meeting **20**	**21**	**22**
* HKMA Tennis Tournament 2012 **23**	**24**	**25**	**26**	**27**	**28**	* HKMA Hong Kong East Community Network – Latest Update in GERD Treatment **29**
* HKMA Tennis Tournament 2012 **30**	* FMSHK Annual Dinner 2012 * HKMA Annual Ball 2012 **31**					

Date / Time	Function	Enquiry / Remarks
1 SAT 9:00 am	**19th Annual Scientific Meeting- Radiation Oncology in Neurosurgical Practice** Organiser: Hong Kong Neurosurgical Society, Speaker: Dr. Reinhard E Wurm, Venue: Langham Hotel, 8 Peking Road, TST	Ms. Shirley MA Tel: 2468 5402
2 SUN 9:00 am	**HKMA CME– Laser Forum 2012 (Certificate Course- Frontiers in Laser Surgery and Safety)** Organisers: HK Surgical Laser Assn, Hong Kong Association of Cosmetic Surgery, Hong Kong Medical Association, Hong Kong Dental Association & Association of Hong Kong Nursing Staff, Chairmen: Dr. Johnny Wong, Dr. Chow Pak Chin, Dr. Wong Wai Hong & Dr. Chow Ka Yuen, Leo, Speakers: Dr. Seto S K Ryan, Dr. Johnny Wong, Dr. Chen Ngan Ivan, Dr. Cheng Chak Kwan, Arthur, Dr. Chong Kam Lung, Kelvin, Dr. Chan Wai Man; Mr. Au Tat Lun, Alun, Dr. Chan Pui Yin, Nicola, Dr. Hui Shiu Kee & Dr. Wong Mon Ching, Venue: Lecture Theatre, Mezz Floor, Hospital Authority, 147B Argyle Road, Kowloon	Dr. Or Chi Kong Tel: 2911 0022 5 CME points
	HKMA CME – Laser Forum 2012 (Seminar on Cosmetic Surgery) Organisers: HK Surgical Laser Assn, Hong Kong Association of Cosmetic Surgery, Hong Kong Medical Association, Hong Kong Dental Association & Association of Hong Kong Nursing Staff, Chairmen: Dr. Or Chi Kong & Dr. Ying Shun Yuen, Clement, Speakers: Dr. Lam Chuk Kwan, Stephanie, Dr. Ho Wai Sun, Wilson, Dr. Hsieh Cheung Philip, Dr. Kwan Kin Hung & Dr. Ho Wai Sun, Wilson, Venue: Seminar Room, Mezz Floor, Hospital Authority, 147B Argyle Road, Kowloon	Dr. Or Chi Kong Tel: 2911 0022 2.5 CME points
	2012 Paediatric Update No.3 – Paediatric Neurology Organiser: Hong Kong College of Paediatricians, Chairmen: Dr. Sik Nin Wong & Dr. Shun Ping Wu, Speakers; Dr. Shun Ping Wu, Dr. Sheila Wong, Dr. Louis CK Ma & Dr. Sophelia Chan, Venue: Pao Yue Kong Auditorium, G/F, HK Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong	Hong Kong College of Paediatricians Tel: 2871 8773 3 CME points (Category A)
7:00 pm	**Joint Professional Volleyball Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Sun Yat Sen Memorial Park Sports Centre	Miss Phoebe WONG Tel: 2527 8285
8:00 pm	**HKMA Tennis Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club	Miss Phoebe WONG Tel: 2527 8285
4 TUE 1:00 pm	**HKMA Shatin Doctors Network - The Management Landscape of Atopic Dermatitis** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. LO Kuen Kong, Venue: Jasmine Room, Level 2, Royal Park Hotel, Shatin, Hong Kong	Ms. Wendy CHENG Tel: 2824 0333 1 CME point
1:30 pm	**HKMA CME - The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 5)** Organisers: Hong Kong Medical Association & Department of Health, Speaker: Prof. Stanley HUI/ Mr. Sam WONG, Venue: Chiu Chow Garden, Shops 001-003, 1/F, Uptown Plaza, Tai Po, NT	HKMA CME Dept. Tel: 2527 8452 2 CME points
8:00 pm	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
8:00 pm	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association, Chairman: Dr. TSE Hung Hing, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Christine WONG Tel: 2527 8285
5 WED 1:15 pm	**HKMA Shatin Doctors Network– Practical Approach to Common Facial Skin Diseases** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. KU Lap Shing, Simon, Venue: Star Seafood Floating Restaurant, Shatin	Ms. Sandy LEE Tel: 2377 9801 1.5 CME points
6 THU 1:00 pm	**HKMA NTW Community Network-Latest Development in Modern Oral Contraceptives** Organiser: HKMA NTW Community Network, Chairman: Dr. WONG Yu Man, James, Speaker: Dr. KUN Ka Yan, Venue: Maxim's Palace, Tuen Mun	Mr. Alan LAW Tel: 2527 8285
1:30 pm	**HKMA CME - The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 5)** Organiser: The Hong Kong Medical Association, Speaker: Prof. Stanley HUI/ Mr. Sam WONG, Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, HK	HKMA CME Dept. Tel: 2527 8452 2 CME points
7 FRI 1:00 pm	**HKMA Shatin Doctors Network – The unique role of dopamine and nor-adrenaline in treatment of depression** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. LAI Tai Sum, Tony, Venue: Lei Garden Restaurant, 6/F, New Town Plaza Phase 1	Mr. Chris PAU Tel: 9736 7830 2 CME points
8 SAT 2:30 pm	**Refresher Course for Health Care Providers 2012/2013** Organisers: Hong Kong Medical Association, HK College of Family Physicians & HA-Our Lady of Maryknoll Hospital, Speaker: Dr. Hui Pak Kwan, Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon	Ms. Clara Tsang Tel: 2354 2440 2 CME points
9 SUN 2:00 pm	**HKMAPS Photo Sharing** Organiser: Hong Kong Medical Association, Speaker: Dr. Amy Pang, Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, HK	Ms. Nadia HO Tel: 2527 8285
8:00 pm	**HKMA Tennis Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club	Miss Phoebe WONG Tel: 2527 8285
11 TUE 1:00 pm	**HKMA Kowloon West Community Network - Lecture Series on Allergic Diseases (Session 3) - Asthma and Allergic Rhinitis in Paediatrics** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. LEUNG Gin Pang, Speaker: Dr. LEE Qun Ui, Venue: Crystal Room I-III, 30/F, Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, NT	Miss Candice TONG Tel: 2527 8285 1 CME point
12 WED 7:30 pm	**Hong Kong Neurosurgical Society Monthly Academic Meeting – flow Regulator: Development of Shunt Valves** Organiser: Hong Kong Neurosurgical Society, Chairman: Dr. Wilson Ho, Speaker: Dr. Wong Ping Hong, Derek, Venue: Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital	Dr. Gilberto LEUNG Tel: 2255 3368 1.5 CME points
1:00 pm	**HKMA CME – Certificate Course for GPs 2012** Organiser: The Hong Kong Medical Association, Venue: TKO	Mr. Alan LAW Tel: 2527 8285

Date / Time	Function	Enquiry / Remarks
13 THU 1:00 pm	**HKMA Kowloon East Community Network- Advance Treatment in Low Back Pain** Organiser: HKMA-KLN East Community Network, Chairman: Dr. AU Ka Kui, Gary, Speaker: Dr. Sun Kin Wai, Kelvin, Venue: Lei Garden Restaurant, Shop No. L5-8, APM Millennium City 5, 418 Kwun Tong Road, Kwun Tong	Mr. Alan LAW Tel: 2527 8285 1 CME point
2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2012– Review and Updates on Refractive Error** Organiser: The Hong Kong Medical Association, Speaker: Dr. Fan Shu Ping, Dorothy, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 1 CME point
14 FRI 1:00 pm	**HKMA Yau Tsim Mong Community Network - BPH Management: Not Only Focus on Prostate?** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. LAM Tzit Yuen, David, Speaker: Dr. SO Chun, Venue: Eaton Smart,. Hong Kong, YMT	Miss Candice TONG Tel: 2527 8285 1 CME point
1:30 pm	**HKMA Shatin Doctors Network - Achieving Glycemic Control in Patients with Type 2 Diabetes** Organiser: HKMA-Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. CHEUGN Fu Keung, Venue: Royal Park Hotel, Shatin	Mr. Jas CHEUNG Tel: 9455 9816 1 CME point
16 SUN 6:00 pm	**Joint Professional Volleyball Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Sun Yat Sen Memorial Park Sports Centre	Miss Phoebe WONG Tel: 2527 8285
8:00 pm	**HKMA Tennis Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club	Miss Phoebe WONG Tel: 2527 8285
18 TUE 1:45 pm	**HKMA Tai Po Community Network - Common Pitfalls in Management of Breast Disease** Organiser: HKMA-Tai Po Community Network, Speaker: Dr. Ho Nga Sze, Venue: Chiuchow Garden Restaurant, 1/F Uptown Plaza, Tai Po	Ms. Joyce Tel: 2664 3808 1 CME point
19 WED 1:00 pm	**HKMA Central, Western & Southern Community Network - Chronic Hepatitis B: Review and Treatment** Organiser: HKMA-Central, Western & Southern Community Network, Chairman: Dr. YIK Ping Yin, Speaker: Dr. Wong Chun Yu, Benjamin, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Mr. Alan LAW Tel: 2527 8285 1 CME point
1:30 pm	**HKMA Shatin Doctors Network - Review and Update on GERD** Organiser: HKMA-Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. SZE Wan Chee, Venue: Jasmine Room, Level 2, Royal Park Hotel, Shatin	Ms. Cindy LUI Tel: 2969 5202 1.5 CME points
20 THU 1:00 pm	**HKMA CME – Certificate Course for GPs 2012** Organiser: Hong Kong Medical Association, HA-United Christian Hospital & HK College of Family Physicians, Chairman: Dr. Leung Man Fuk, Speaker: Dr. Lin Shek Ying, Venue: East Ocean Seafood Restaurant, Shop 137, 1/F, Metro City Plaza 3, Mau Yip Road, Tseung Kwan O, Kowloon	Mr. Alan LAW Tel: 2527 8285 1 CME point
8:00 pm	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
23 SUN 8:00 pm	**HKMA Tennis Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club	Miss Phoebe WONG Tel: 2527 8285
29 SAT 1:00 pm	**HKMA Hong Kong East Community Network – Latest Update in GERD Treatment** Organiser: HKMA Hong Kong East Community Network, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Miss Candice TONG Tel: 2527 8285
30 SUN 8:00 pm	**HKMA Tennis Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club	Miss Phoebe WONG Tel: 2527 8285
31 MON 7:00 pm	**FMSHK Annual Dinner 2012** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Run Run Shaw Hall, the Hong Kong Academy of Medicine Jockey Club Building	Ms. Nancy CHAN Tel: 2527 8898
8:00 pm	**HKMA Annual Ball 2012** Organiser: The Hong Kong Medical Association, Venue: Grand Ballroom, Conrad Hong Kong	Ms. Candy YUEN Tel: 2527 8285

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Answer to Dermatological Quiz

1. This middle aged man developed this rapidly enlarging ulcer over a few weeks. The ulcer showed an erythematous violaceous slightly undermined edge over a purulent granulomatous base with yellowish discharge. Together with the history of inflammatory bowel disease and the lack of response to antibiotics, the clinical diagnosis of pyoderma gangrenosum (PG) should be considered. Differential diagnoses should include chronic ulcer due to infections (e.g caused by streptococcal infection, rarely due to deep mycoses such as chromoblastomycosis, or atypical and typical mycobacterial infection), vasculitis (such as cutaneous polyarteritis nodosa, granulomatous vasculitis such as Wegener's granulomatosis), autoimmune connective tissue disease (such as Behcet's disease), and malignancy (such as squamous cell carcinoma). The diagnosis of PG is by exclusion of other differential diagnoses, usually by repeated cultures and skin biopsies. In our patient, the histological finding and culture results helped to rule out these differential diagnoses.

2. Pyoderma gangrenosum is commonly associated with inflammatory bowel diseases (as shown in our patient, 20-30%), arthritis (such as rheumatoid arthritis, 20%) and haematological diseases (such as acute and chronic myelogenous leukaemia and monoclonal gammopathy, up to 15%). Thorough work up of gastrointestinal studies, haematological studies, and radiological studies as guided by symptoms are indicated to exclude these associations. Oral prednisolone (0.5-1mg/kg as tailored to the disease severity) gives most predictable effective response. Steroid sparing agents such as cyclosporine and thalidomide can be considered for refractory disease that requires prolonged high doses of systemic steroid. For individuals with concomitant Crohn's disease, such as our patient, infliximab has been used with success.

Dr. Ka-ho LAU
MBBS(HK), FRCP(Edin, Glasg), FHKCP, FHKAM(Med)
Yaumatei Dermatology Clinic, Social Hygiene Service

預防子宮頸癌新突破

9歲或以上女性[1]，無論長幼，都應主動預防
提高抗體水平，對抗HPV致癌病毒
引致的癌前病變[2]

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1. Bivalent HPV Vaccine - Hong Kong Full Prescribing Information 2011. 2. CDC. The Pink book. http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/hpv.pdf. Accessed on 25 October 2012. 3. Australian Government Department of Health and Ageing Cervical Screening Program. http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/hpv. Accessed on 25 October 2012. 4. UK Department of Health. The Green book. http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_087787.pdf. Accessed on 25 October2012.

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Reference:1. Dexilant prescribing information (DEX051 HK1 TT, HK Branch). 2. Wittbrodt ET et al., Clin Exp Gastroenterol 2009;2:117-28. 3. Fass R et al., Aliment Pharmacol Ther 2009;29:1261-72. 4. Sharma P et al., Aliment Pharmacol Ther 2009;29:731-41. 5. Metz DC et al., Aliment Pharmacol Ther 2009;29:742-54. 6. Howden CW et al., Aliment Pharmacol Ther 2009;30:895-07. 7. Lee RD et al., Aliment Pharmacol Ther 2009;29:824-33. 8. Lee RD et al., Aliment Pharmacol Ther 2010;31:1001-11.

For further information, consult full prescribing information.

* 96% of patient on Dexlansoprazole 60mg achieved 24-h heartburn-free days[6]

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