Sexually Transmitted Infection Workshop 2004

Reported by PT Chan 陳寶德, LS Chiu 趙麗珊

Date: 21 November, 2004
Venue: Lecture Theatre, G/F, CHP Building
Organiser: Centre for Health Protection; Infectious Disease Control Training Centre, Hospital Authority; The Hong Kong Society of Dermatology and Venereology

Management of genital wart virus infection

Speaker: Dr. R. Basu Roy
Honorary Consultant Physician, Royal Bournemouth and Christchurch Hospitals, NHS Trust, United Kingdom

Anogenital wart is a very common sexually transmitted infection (STI). The aetiology is human papilloma virus (HPV). It is almost always transmitted by sexual contact. Approximately one percent of sexually active adults (15-49 years old) develop genital warts. The highest rate of HPV infection is in women under 25 years old. The prevalence is even higher in those who are immuno-suppressed such as renal transplant patients who are reported to be up to 40%. HPV infection has an incubation period of one to eight months with a mean of 3.1 months. Warty lesions can be found anywhere in the genital area including vulva, cervix, vagina, penis, anus and intra-anal sites. Non-genital areas such as conjunctiva, oral, nasal and laryngeal sites are also possible sites of infection. Although autoinfection from hands to genital area and anal area is possible in children, sexual abuse should always be suspected in such cases.

There are numerous types of HPV among which more than 20 types can infect the genital tract. The most common types are 6 and 11 (90% of the genital wart), but they are rarely associated with squamous cell carcinoma. Types 16 and 18 are less common but they are strongly associated with cervical dysplasia. Co-factors of malignant transformation include hormonal factors such as long term use of contraceptive pills, immuno-compromised patients, and smoking. Intercourse at an early age and the number of sexual partners also increase the risk of cancer. Diagnosis of genital wart is often made by clinical inspection. Application of 5% acetic acid can help to make the diagnosis. The HPV infected area will be stained whitish in colour.

Treatment of wart can neither eradicate nor affect the natural history of HPV. It does not decrease the infectivity and does not prevent the development of cervical cancer. Therefore, the decision for treatment is based on patient's symptom and psychology.

There are various options for treating genital wart. First is the use of cytodestructive drugs. These include podophyllotoxin which offers 54-65% cure rate in three to six months. However, it will cause severe toxicity on excessive applications. Imiquimod, an immune modulator, can be applied to the lesion three times per week for a maximum of 16 weeks. Side effects include local itching, erythema and erosion. Both drugs can be applied by patient. Podophyllin resin offers a cure rate of 43% at three months and 56% at six months. However, there is significant toxicity from systemic

absorption. 5-Fluorouracil (5FU) is a pyrimidine antagonist which offers a cure rate of 33-70% after daily application of eight weeks. The side effect is painful ulceration. It can be used for treatment of intrameatal and intravaginal warts (2.5 grams of cream for five consecutive nights and as an adjunct to laser therapy to minimise recurrence). Trichloroacetic acid (TCAA) works as a caustic agent and is a 50% solution in ethanol. It destroys wart by chemical coagulation of proteins. It can be used during pregnancy. However, it is extremely erosive to skin. Careful protection of the surrounding skin such as the use of petroleum jelly or sodium bicarbonate is needed. The above three kinds of drugs should be administered by trained health care workers. The second method of treatment is surgery. Removal of wart can be done by excision, diathermy, scissor, curettage, cryosurgery or laser (CO_2) surgery. Other treatment such as topical or intra-lesion interferon, immunomodulatory approaches and autogenous vaccine therapy have also been tried but are very rarely use due to the cost and systemic side effects.

Though removal of the wart cannot prevent further recurrence, transmission of HPV and development of cervical cancer, it can alleviate the anxiety of some patients. Therefore, it is important to have a thorough discussion with patient about the pros and cons of initiating treatment. It is also important to exclude other STI as well. Contact tracing is necessary. Cytology screening (Pap smear) should be encouraged.

A conservative approach is used in pregnancy as warts tend to regress after delivery and most of the commonly used cytodestructive topical agents are contraindicated. Removal is only recommended if the warts obstruct delivery or cause much symptom. Potential harm of genital wart to newborns includes laryngeal papillomatosis which is usually caused by HPV type 6 and 11.

In conclusion, genital wart is a common sexually transmitted infection caused by HPV infection. Some strains of HPV are strongly associated with squamous cell carcinoma. Treatment of genital wart is only for symptomatic relief (both physical and psychological).

Learning points:

Anogenital wart is a common sexually transmitted infection caused by human papilloma virus. Type 16 and 18 are associated with squamous cell carcinoma. Treatment of wart does not decrease infectivity and does not prevent malignancy.

The consequences of untreated sexually transmitted infections in women

Speaker: Dr. I. Ahmed-Jushuf
Consultant Physician in Sexual Health, Nottingham City Hospital, United Kingdom

It was estimated by the WHO that there were 340 millions new sexually transmitted infections (STI) cases in 1999. Apart from causing disease and death, STI also facilitates transmission of HIV by ten times. It can have consequences for partners and newborns as well.

Pelvic inflammatory disease (PID) is a serious consequence of STI as it is associated with long term complications including Fitz-Hugh-Curtis Syndrome (20%), ectopic pregnancy (20%), infertility (20%), menstrual disorder, dyspareunia and neonatal infection. Its symptoms are sometimes non-specific and careful history taking is needed to identify the risk factors. Common signs and symptoms include lower abdominal pain, dyspareunia, inter-menstrual bleeding, abnormal vaginal discharge, adnexial tenderness, cervical motion tenderness and fever. Risk indicators are age < 30 years old, multiple partners, past history of STI, insertion of intrauterine device < six weeks, post-partum endometritis, recent pelvic procedure and bacterial vaginosis. Causative organisms include *Neisseria gonorrhoeae, Chlamydia trachomatis* and anaerobes. Treatment can be either ofloxacin

400 mg twice daily and metronidazole 400 mg twice daily for two weeks or a stat dose of intramuscular injection of 250 mg ceftriaxone/ 2 gram of cefoxitin, with oral probenecid 1 gram, followed by 100 mg doxycycline twice per day and 400 mg metronidazole twice per day for two weeks. Besides drug treatment, it is important to perform contact tracing and treat the partners as well. Follow up should be arranged to look for any long term complications.

STI in pregnancy was also discussed. Syphilis can be transmitted to neonates leading to congenital syphilis. Multi-organ failures are observed in the first two years of life including rash, haemorrhagic rhinitis, periostitis, osteochondritis, nephrotic syndrome, cranial nerve palsy and thrombocytopenia. Treatment of genital herpes with oral acyclovir is only recommended for primary *herpes simplex* virus infection in the third trimester of pregnancy. Caesarean section is indicated if lesions present during labour. Treatment of mother and baby with oral acyclovir is indicated if vaginal delivery is unavoidable. Special considerations should be made in treating genital warts during pregnancy as several common topical agents like podophyllin and 5-fluorouracil are contraindicated. Cryotherapy and TCAA are safe in pregnancy. Caesarean section is only indicated if the wart obstructs the birth canal. Finally, mother-to-child transmission of human immunodeficiency virus is up to 40% without intervention. Transmission rate can be reduced to less than one percent with timely HAART (highly active antiretroviral therapy) and caesarean section.

Learning points:

STI can cause significant morbidity to patients as well as their partners and newborns. One of the serious consequences is pelvic inflammatory disease. The choice of a treatment regimen for PID should be based on its local epidemiology and the local antimicrobial sensitivity patterns. Early identification and appropriate treatment of STI can minimise their adverse effects.

Sentinel syndromic sexually transmitted infection surveillance in private clinics in Hong Kong

Speaker: Dr. K.T. Chan
Acting Senior Medical and Health Officer, Special Preventive Program, Centre for Health Protection

Sexually transmitted infections (STI) are important disease entities as they cause significant disease burden and facilitate transmission of human immunodeficiency virus (HIV) in the community. Currently, information on STI in Hong Kong is reflected by data from public Social Hygiene Clinics, behaviour surveillance study which is carried out yearly and STI/HIV survey (with contribution from the private sector as well) which is carried out every five years. STI surveillance comprises several elements, including studies on aetiology of STI syndromes and bacterial resistance that are important in individual patient care, as well as collection of prevalence data on STI in order to improve program management. Individual STI syndromes are of different values in monitoring STI incidence. For example, urethral discharge in man is a good measure of the incidence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infection as they often have acute, symptomatic presentations and are relatively specific for infection with STI pathogens. In contrast, vaginal discharge is a weak indicator of STI infections as there are many other non-STI causes for this symptom. In female, endocervical gonorrhoea or chlamydia infection is a good measure of STI prevalence as these diagnostic tests are specific for active, untreated infection and these infections can be asymptomatic in women.

Sentinel syndromic sexually transmitted infection surveillance involves collection of patients' data from five groups of doctors serving different territories in Hong Kong: dermatologists, gynaecologists, group practitioners, general practitioners and doctors in Social Hygiene Clinics. The information collected includes age

of patient, gender, syndromic STI diagnosis, laboratory test performed and behaviour on condom use. The survey is carried out over one week period in every quarter of the year. Preliminary findings of the survey show that most STI are diagnosed by doctors in Social Hygiene Clinics, private dermatologists and general practitioners, with the highest number of STI diagnosed per day seen in Social Hygiene Clinics. Only a small percentage of patients seen for STI are below the age of 20. The syndromes of STI most frequently detected in Social Hygiene Clinics are genital growth, followed by genital discharge (urethral and vaginal) and genital ulcer. On the other hand, in the private sector, the most common syndrome is genital discharge (urethral and vaginal), followed by genital ulcer and genital growth. There is a trend of decreasing condom use as age of patients increases and in male patients aged greater than 50 years old, with up to 60% never use condom. Moreover, less than 30% of patients attending private practitioners have been tested for syphilis and HIV serology. In the long run, regular sharing of collected STI information and reinforcing further collaboration on sentinel STI surveillance in the private sector may produce more representative data for monitoring of STI prevalence and patients' behaviour.

Learning points:

Sentinel syndromic sexually transmitted infection surveillance in private clinics can complement data from the public sector to give a more representative data on STI in Hong Kong. Each STI syndrome has different value in monitoring STI incidence and prevalence.

Overview of genital ulcer disease

Speaker: Dr. I. Ahmed-Jushuf
Consultant Physician in Sexual Health, Nottingham City Hospital, United Kingdom

There are five sexually transmitted infections that can give rise to genital ulcer, namely, syphilis, herpes simplex, chancroid, lymphogranuloma venereum (LGV) and donovanosis. The prevalence of different pathogens in genital ulcer syndrome varies from one country to another. Syphilis can be divided into early (including primary, secondary and early latent syphilis) and late (including late latent and tertiary syphilis) stages. The diagnosis of primary syphilis is suspected when the typical indurated, painless chancre with a clean base is seen. A chancre can occur at genitalia, mouth or fingers or elsewhere depending on the site of inoculation. In the early stage, dark ground examination for spirochete may help in diagnosis. Serology is also useful to confirm the diagnosis but it takes time to develop an antibody response. Penicillin injection remains the most effective treatment for syphilis. When it is contraindicated, alternative drugs such as doxycycline, oxytetracycline, erythromycin, azithromycin and ceftriaxone can be tried.

Herpes simplex (HSV) is a common cause of genital ulcer in the Western countries. It presents as multiple vesicles or painful superficial erosions. The diagnosis is confirmed by viral culture. Antibody to HSV is present in a high percentage of sexually active subjects in Western countries and is unable to tell whether HSV is the cause of the current genital ulcer. Primary herpes simplex is frequently more symptomatic than recurrent herpes. Moreover, complications such as urinary retention, meningism and constitutional symptoms are seen more frequently in primary herpes simplex infection. Antiviral agents, including acyclovir, valaciclovir or famciclovir, can be used in first episode genital herpes. Genital hygiene and topical analgesics are also useful. Acute retention of urine may either be due to neurological involvement or due to pain in passing

urine. Adequate topical or systemic analgesics should be tried in the first place. If it fails, suprapubic catheter should be inserted. The speaker warns against urethral catheterisation as this may introduce ascending herpes infection. Psychological support and counselling is also important in newly diagnosed herpes simplex. For recurrent herpes, usually only topical analgesic is necessary as the symptoms tend to be transient and less severe. In patients with extremely painful recurrences, especially if the recurrences are too often (greater than six times per year), suppressive antiviral therapy can be considered. In immunosuppressed cases, such as HIV positive patients, a longer course of oral antiviral agent may be necessary.

Chancroid is due to infection by *Haemophilus ducreyi*. It is a prevalent cause of genital ulcer in Africa, Caribbean and Southwest Asia. The diagnosis is suspected when multiple 'dirty' ulcers and enlarged regional lymph nodes (buboes) are seen. Gram-stained smears from the ulcer may show gram-negative coccobacilli forming the characteristic shoal of fish appearance in about 50% of cases. Culture has a sensitivity of 70-80% but a special culture medium is needed. Polymerase chain reaction is a new tool in the diagnosis of chancroid but is not widely available. Ciprofloxacin, erythromycin, azithromycin, spectinomycin and ceftriaxone are antibiotics of choice in the treatment of chancroid.

LGV is caused by *Chlamydia trachomatis* types L1 to L3. It accounts for up to 10% of genital ulcer syndrome in India, Africa, Papua New Guinea and Caribbean. Men usually present with acute LGV, whereas women usually present with late stage disease. The primary stage is usually transient and is characterised by painless, self-healing and non-indurated ulcer. This is followed by lymphadenitis of the inguinal, femoral or even iliac nodes. Genitoanorectal syndrome occurs in later stage of disease and can be manifested as proctocolitis, perirectal abscess or fistulas, strictures of urethra or rectum, and genital elephantiasis secondary to lymphatic obstruction. The diagnosis can be confirmed by culture, complement fixation test, fluorescence antibody test or polymerase chain reaction. The Frei intradermal test is now abandoned. Doxycycline or erythromycin can be used for the treatment of LGV.

Donovanosis is due to infection by *Calymmato-bacterium granulomatis*. It is mostly found in Papua New Guinea, Southeast India, Caribbean, South America, Australia and South Africa. Clinical presentation is that of a non-healing ulcer with a clean, beef red base and some degree of fibrosis or scarring may be seen. It is often diagnosed on skin biopsy with Donovan bodies seen histologically. Polymerase chain reaction and serological tests are not commercially available. Cotrimoxazole, doxycycline, erythromycin, azithromycin, gentamicin, norfloxacin are antibiotics that can be used in donovanosis.

Learning points:

Syphilis, herpes simplex, chancroid, lymphogranuloma venereum and donovanosis are five sexually transmitted causes of genital ulcer. Their relative importance and prevalence vary in different countries.

Management of urethral and vaginal discharge

Speaker: Dr. R. Basu Roy
Honorary Consultant Physician, Royal Bournemouth and Christchurch Hospitals, NHS Trust, United Kingdom

Sexually transmitted infections (STI) are important as they can lead to multiple complications. In men, they may lead to infertility, urethral stricture and facilitate HIV infection. In women, besides facilitation of HIV transmission, they can cause pelvic inflammatory disease, infertility, ectopic pregnancy, fetal loss, neonatal pneumonia/ conjunctivitis and cervical cancer. The main

feature of syndromic approach is that main infectious causes are grouped according to syndromes and all important causes for that syndrome are treated. The advantages of syndromic approach include complete STI care offered at first visit, treatment more readily accessible, and emphasis on patient education, partner notification and sexual health promotion. However, the inherent problems of such an approach include oversimplification of disease management, a possible wastage of drugs, and promotion of antibiotic resistance by overtreating all possible causes at the same time.

Urethritis can be caused by *Neisseria gonorrhoeae, Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma genitalis, Trichomonas vaginalis, Candida species* and *herpes simplex virus*. In up to 20-30% of cases, no microorganism can be identified. The vulnerable factors for urethritis are patients' age below 25 years, frequent partner change, contact with commercial sex workers and drug abuse. In physical examination of a patient with urethral discharge syndrome, it is also necessary to check for inguinal lymphadenopathy, examine the testis, epididymis, spermatic cord and look for rashes or ulcers. Syndromic management of urethral discharge covers both *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. The appropriate choice of drugs will be guided by local knowledge on resistance patterns. Untreated urethritis can lead to epididymo-orchitis, seronegative reactive arthritis, Reiter's syndrome and chronic recurrent non-gonococcal urethritis.

The commonest pathogens causing acute epididymo-orchitis in patients aged below 35 years are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Other causes include enteric organisms following urethral catheterisation. It can also occur in 12-19% of men with Behcet's disease. The differential diagnosis includes testicular torsion, abscess, obstructed inguinal hernia, tumour, tuberculosis or fungal epididymo-orchitis. For STI causes and male aged below 35 years, ceftriaxone injection, followed by doxycycline for 10 to 14 days is suggested. For non-STI causes and men aged above 35 years, ofloxacin or ciprofloxacin for 10 to 14 days can be used. Again the choice of antibiotics depends on local resistance patterns.

Acute prostatitis can be secondary to infection by gram-negative organisms (e.g. *E. coli, Proteus species, Klebsiella species*), enterococci, *Staphylococcus aureus* and rarely by *Bacteroides*. It manifests as symptoms of urinary tract infection, low back pain, penile/rectal pain, fever, arthralgia and myalgia. Physical examination may show pyrexia, tachycardia and tender prostate. Mid-stream urine, blood culture and prostatic massage are often needed in investigating patients with acute prostatitis. Ciprofloxacin, ofloxacin, cotrimoxazole or trimethoprim for 28 days can be used in treating acute prostatitis. Intravenous cephalosporin may be necessary for more severe cases.

Chronic prostatitis can be secondary to infection by *E. coli, Staphylococcus aureus* or *Streptococcus faecalis*. Some chronic prostatitis cases are not induced by bacteria, causing chronic pelvic pain syndrome and prostatodynia. Patients with chronic prostatitis can present with pain over the perineum, lower abdomen, penis, testis, rectum and lower back. They may also have pain on ejaculation. Prostatic massage can be helpful in diagnosing prostatitis and to achieve optimal results, patient should not take any antibiotics in the previous one month, and should not ejaculate within two days prior to the procedure. Transrectal ultrasound and blood test for prostatic specific antigen may also be useful in investigating patients with symptoms of chronic prostatitis. For bacterial chronic prostatitis, doxycycline, trimethoprim or cotrimoxazole for 28 days can be used. For abacterial chronic prostatitis, depending on the underlying causes, terazocin, alfuzocin, non-steroidal anti-inflammatory drugs or diazepam may be used.

Vaginal discharge has multiple causes besides infection. It can be physiological, related to oral or injectable contraception and intrauterine contraceptive device. It may also be secondary to cervical ectopy, polyps, fibroids, estrogen deficiency, foreign bodies, trauma, fistula, malignancies or dermatological diseases. Vaginal infections that cause abnormal discharge include candidiasis, bacterial vaginosis or trichomoniasis. Various antifungal agents either in pessary or oral forms can be used for candidiasis. Metronidazole is effective for trichomoniasis and bacterial vaginosis. There are two important cervical infections leading to vaginal discharge, namely, gonorrhoea and chlamydia. The latter agent has its incidence doubled in the United Kingdom in the past decade and can be asymptomatic in females. Early recognition, patient education and partner treatment are essential in reducing the morbidity and complications of these STI.

Learning points:

Syndromic approach to STI management has its own merits and limitations. Choice of antibiotics has to be based on local resistance patterns.