Original Article

# Prevalence of *Chlamydia trachomatis* in Genito-urinary Medicine Clinic, Hospital Kuala Lumpur: A 5-year Retrospective Analysis

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**Abstract**

**Background** *Chlamydia trachomatis* is the most common bacterial sexually transmitted infection worldwide. It is the commonest cause of non-gonococcal urethritis in men and can cause serious complications in the female reproductive tract if left untreated.

**Objective** The aim of this study is to establish the prevalence of *Chlamydia trachomatis* infection in symptomatic patients attending the GUM Clinic in HKL.

**Method** A retrospective study involving 596 patients seen from January 2001 to December 2005 was performed. Relevant demographics and test results were obtained from the case notes and the Chlamydia test log books.

**Results** A total of 549 patients were tested for *C. trachomatis* during this period and had the test results available for analysis. 366 were males and 183 were females with a ratio of 2:1. The prevalence of *C. trachomatis* infection was 23.5% (n=86) for male patients and 17.5% (n=32) for female patients with the highest prevalence in the group aged 15-19 years in both sexes. The highest prevalence was found in Malays in both sexes, probably reflecting the racial composition of the GUM Clinic attendees rather than a true peak prevalence in this population.

**Conclusion** The high prevalence rates in this study were expected as we were only screening symptomatic patients. The need for routine screening in the sexually active population aged less than 30 years should also be considered to assess the prevalence of *C. trachomatis* infection in the general population in this country.

**Keywords** chlamydia; prevalence; non-gonococcal urethritis

## Introduction

*Chlamydia trachomatis* is the most common bacterial sexually transmitted infection in many parts of the world, with estimated new cases of more than 90 million people worldwide[1]. In women, infection most commonly presents as cervicitis. Left untreated, it may cause serious sequelae in the female reproductive tract such as pelvic inflammatory disease, ectopic pregnancy, chronic pelvic pain and tubal infertility. Chlamydial infection in men may cause urethritis, epididymitis and prostatitis and may be associated with infertility but rarely cause complications. In the majority of patients however, infection remains asymptomatic. Chlamydial infection has been shown to increase both the transmission and acquisition rates for HIV infection[2]. Early effective treatment is therefore of paramount importance.

Estimates of prevalence vary enormously among different populations in countries across the world depending on the populations studied. Overall, healthcare settings have higher prevalence estimates than population-based studies[3]. In general, chlamydial prevalence is higher in sexually active adolescent women and those attending sexually transmitted disease centres, ranging from 10% to 40%[4]. A systematic review of estimates in various populations in the UK revealed that in female patients, the highest estimates were in those under 20 year old from the GUM clinics[3]. Although prevalence data in men are limited, the growing numbers of research in this area have shown that the prevalence of infection in men is also considerable[3, 5-6].

Despite the importance of chlamydial genital infection, data on its prevalence in Malaysia is still scarce. A few prevalence surveys conducted in selected female populations showed variable rates with the highest prevalence in those with pelvic inflammatory disease[7-8]. Little information is available regarding the prevalence of *C. trachomatis* infection among patients attending a GUM clinic. The only previous published data on GUM clinic attendees showed that *C. trachomatis* caused urethritis in approximately 8% of

symptomatic heterosexual male patients[9]. In this study, we sought to estimate the prevalence of *Chlamydia trachomatis* infection in symptomatic male and female patients attending the GUM clinic at Hospital Kuala Lumpur.

## Method

A retrospective study involving 596 patients who were tested for *C. trachomatis* from January 2001 to December 2005 was carried out. These patients presented with either a urethral or vaginal discharge and microscopy showed at least 5 pus cells per high power field with a negative culture for Gonorrhoea. 47 patients had to be excluded from the study as the Chlamydia test results were not available. Patients' demographic details and test results were obtained from the case notes and the Chlamydia test logbooks. All male and female patients had their respective urethral and endocervical swabs sent for direct fluorescent antibody (DFA) test (MicroTrak Chlamydia trachomatis Direct Specimen Test, Trinity Biotech, Ireland) for Chlamydia antigen detection.

## Results

A total of 549 patients were available for analysis in this study. 366(67%) patients were males and 183 (33%) females. More than half of the patients were Malays (58%) followed by Indians (25%), Chinese (13%) and others (4%) who were either Bangladeshi or Indonesian immigrant workers. More than 70% of patients were in the 20-40 age group.

86(23.5%) of male patients tested positive for Chlamydia as compared to 32(17.5%) female patients. In the male patients, the prevalence of Chlamydia infection was highest in two age groups, the 15-19 (30.6%) and 30-39 (30.8%) years. The prevalence also did not seem to decline with age, remaining high even in the oldest age group **(Figure 1)**.

In contrast, the highest prevalence in the female patients was in the youngest age group of 15-19 years (38.9%). There appears to be a declining trend in prevalence with increasing age **(Figure 2)**.

The annual trend of chlamydial prevalence shows a rising trend towards the end of the five year study period for both sexes **(Figure 3)**.

In both male and female patients, the prevalence of Chlamydia infection was highest in Malays at 24.7% and 20% respectively **(Figure 4)**. However female patients from the minority ethnic group (all Indonesians) had an equally high prevalence as the Malays **(Figure 4)**.

**Figure 1.** *C. trachomatis* prevalence by age group in male patients

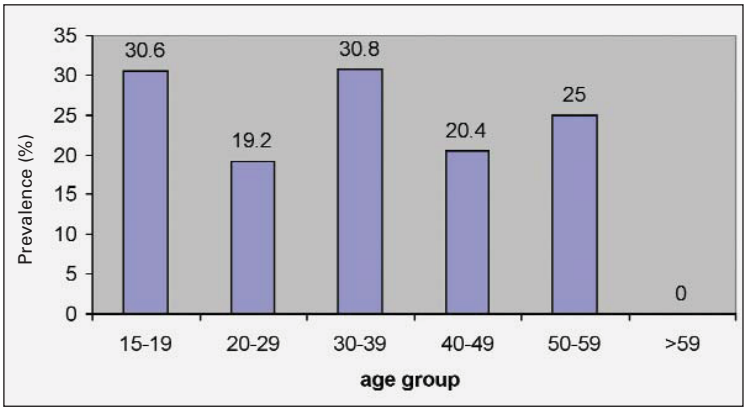



**Figure 2.** *C. trachomatis* prevalence by age group in female patients

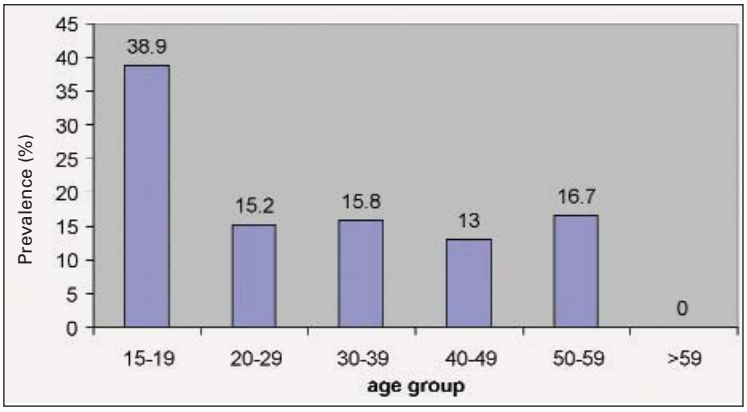


**Figure 3.** Annual prevalence of *C. trachomatis* infection, GUM clinic HKL

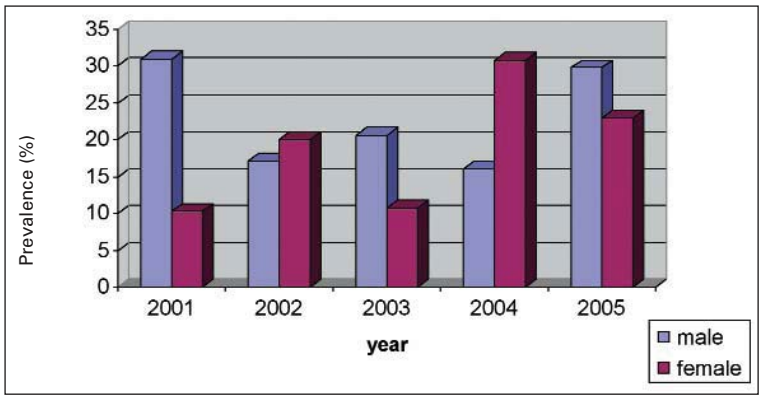
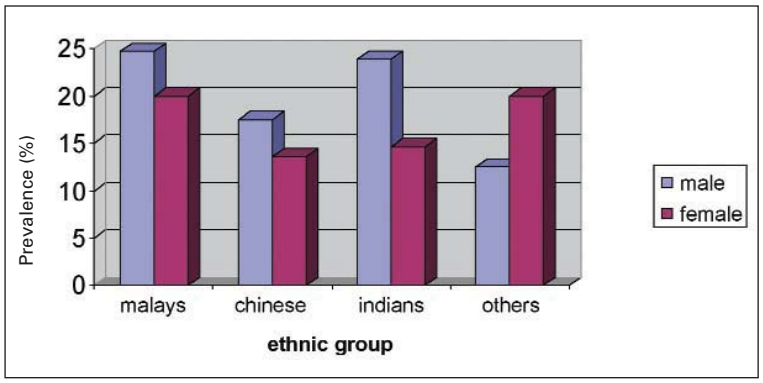



**Figure 4.** Racial distribution of *C. trachomatis* infection, GUM clinic HKL




## Discussion

The prevalence of Chlamydia trachomatis in both male and female attendees at the GUM clinic was very high. This was expected as we were only screening symptomatic patients from a sexually transmitted disease clinic population. **Table 1** shows a comparison of Chlamydia prevalence between different female populations previously studied in this country.

It is interesting to note that male patients had a higher prevalence as opposed to female patients, in contrast to previous studies. However, this gender difference may not necessarily reflect a true difference in the epidemiology of C.trachomatis infection in this country. This is probably due to a higher attendance rates of male patients in the GUM clinic as compared to the female patients. Female patients are more likely to present themselves to a gynaecological clinic when faced with symptoms. This finding is consistent with studies conducted in STD clinic patients in European countries like Sweden and Slovenia where a relatively larger proportion of male as opposed to female cases has been reported[10-11].

**Table 1.**

| | Prevalence (%) | n | Test method |
|---|---|---|---|
| GUM clinic HKL | 17.5 | 549 | DFA |
| Females with PID[8] | 22.7 | 88 | PCR |
| Sex workers[8] | 6.3 | 208 | PCR |
| ANC attendees[7] | 1.6 | 1070 | PCR |

The prevalence pattern in female patients in this study appears to conform to what is already well known about Chlamydia genital infection where it is commonest in those below 20 years of age and declines with increasing age. Sexually active young adults are more susceptible to genital chlamydial infections because of greater exposure to high-risk social behaviour. Male patients however do not seem to follow the same pattern. The prevalence peaked at two age groups, the youngest (less than 20 years old) and those in their thirties and did not decrease with increasing age. Whether this could reflect differences in sexual behaviour pattern between the two sexes in this country as they get older is a contention and should be studied further.

Among the various ethnic groups in this country, Chlamydia seems to be most prevalent in Malays in both sexes. This does not necessarily mean that the Malays were more afflicted with the infection compared to other races as the Malays form the largest racial group attending the GUM clinic. The differences in prevalences among the races appear to reflect the racial composition of patients attending the GUM clinic rather than a true racial difference.

As this is a retrospective study, inherent limitations such as missing test results (n=47) and missing data are unavoidable. Nevertheless this could skew the data and hence some degree of caution should be exercised in interpreting the findings in this study.

Despite these limitations, our findings are comparable to other studies in *C. trachomatis* infection in the South East Asia region **(Table 2)**.

**Table 2.**

| Country | Prevalence (%) | |
|---|---|---|
| | Male | Female |
| Malaysia (this study) | 23.5 | 17.5 |
| Singapore[12] | NA | 17.0 |
| Thailand[13] | 16.1 | NA |

* 1 BP patient and 3 pemphigus patients defaulted follow-up before treatment was instituted.

## Conclusion

The results of this study strongly support the implementation of testing for *C. trachomatis* infection among symptomatic men and women who attend GUM clinics in Malaysia. More resources should be allocated to enable implementation of routine screening in all patients as more than 70% of both male and female patients are asymptomatic at the time of infection. Effective screening, contact tracing and treatment of patients and the sexual partners are imperative to reduce the prevalence of *C. trachomatis* genital infection and the burden of untreated disease. The need for routine screening in the sexually active population aged less than 30 years should also be considered to assess the prevalence of *C. trachomatis* infection in the general population in this country.

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Case Report

# A Case of acne scarring treated with Fractional Photothermolysis

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Acne is a disorder of the pilosebaceous follicle that affects up to 80% of people in their teens and twenties and up to 10% of the older adults. While many are left without any permanent sequelae, some result in disfiguring acne scars. We report a case of depressed acne scars which improved with fractional resurfacing erbium glass 1550nm laser (Fraxel laser).

## Case Report

This is a 35-year-old Chinese man who presented with multiple acne scars. He has no known medical illness and is not taking any medication (including isotretinoin) currently. He has not undergone any laser procedure prior to this.

There were multiple ice-picked and saucer-shaped (depressed fibrotic) acne scars over his face, predominantly over his bilateral cheeks and temporal region.

The treatment plan consisted of a few sessions of full face Fraxel laser resurfacing, with an interval of 1 month between each session. The laser settings were stepped up according to the patient's response. Initial treatment level was:

8mJ / 1000 MTZ
10 mJ / 1000 MTZ
Total energy: 3.0 kJ

The subsequent treatment level was stepped up to:

8 mJ / 500 MTZ
15 mJ / 500 MTZ
20 mJ / 500 MTZ
25 mJ / 250 MTZ (spot treatment to ice-pick scars)
Total energy: 5.0 kJ

Both treatments were tolerated well, with minimal downtime. After the 2 sessions of Fraxel laser, his acne scars became less prominent and shallower. Please refer to the before-and-after photographs attached.

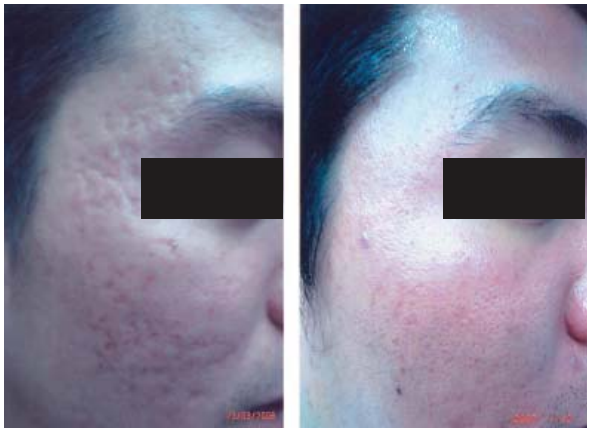

**Figure 1.** (A) Before treatment (B) Marked improvement after 2 sessions of Fraxel laser

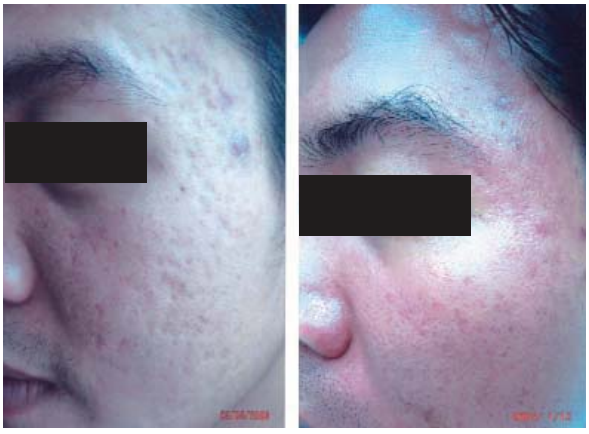

**Figure 2.** (A) Before treatment B) Marked improvement after 2 sessions of Fraxel laser

## Discussion

Acne scarring affects 30% of patients with moderate to severe acne vulgaris. It is particularly common in acne conglobata and acne fulminans. To reduce the incidence of scarring, acne is best treated early. There are various treatments available for acne scars, such as chemical peel, dermabrasion, laser (resurfacing), dermal fillers, punch grafting and subcision therapy.

Fractional photothermolysis is a novel technology designed to create a network of microscopic intradermal zones of thermal injury in the dermis and overlying epidermis with islands of spared, normal tissue, using focused beams of infrared laser energy (1550nm). Fractional photothermolysis (Fraxel laser treatment; Reliant Technologies; Palo Alto; California) is currently approved by the US Food and Drug Administration for the treatment of periorbital rhytids and dyspigmentation. The Fraxel laser is a 30watt, diode pumped, 1,550nm erbium fiber laser that targets water as its chromophore. It is a safe and gradual laser procedure that stimulates the body to replace aged and photo-damaged skin, even on delicate skin areas, such as the neck, chest and hands.

Utilizing the concept of fractional treatment, 70-100um wide and 250-800um deep, microthermal zones of tissue coagulation are produced. Tissue is not vaporized and the stratum corneum remains intact. The epidermal coagulated tissue is expelled and replaced by keratinocyte migration. When there is a significant damage to the basement membrane zone, the dermal contents are also expelled as microscopic epidermal and dermal necrotic debris. Zone of collagen denaturation in the dermis cause upregulation of the inflammatory cascade, which leads to collagen remodeling and new collagen formation.

The mid-infrared wavelength of the Fraxel laser allows deeper penetration into the tissue without the injury observed with traditional ablative laser (such as lengthy downtime, severe pain and prolonged edema). The reported complications are post-inflammatory hyperpigmentation (up to 20%), hypopigmentation, infection and scarring.

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Case Report

# Sweet's Syndrome with extracutaneous involvement

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Sweet's syndrome was first described by Dr. Robert Douglas Sweet in 1964[1]. It was originally described as an 'acute febrile neutrophilic dermatosis'[1]. There are primarily three subtypes of Sweet's syndrome, ie. classical Sweet's syndrome, malignancy-associated Sweet's syndrome and drug-induced Sweet's syndrome. We are reporting a case of classical Sweet's syndrome in a 47-year-old man.

## Case Report

A 47-year-old Chinese man was presented to University Malaya Medical Centre in March 2003 with a 2-month history of fever, headache, swelling of the left side of his neck together with skin lesions on both hands. He did not have any symptoms suggestive of an underlying systemic or regional infection and denied any ingestion of drugs, supplements or traditional medication. There was no significant past medical history and a systemic review was normal. Physical examination revealed that he was febrile with a temperature of 38°C. There was a tender, firm lymphadenopathy measuring 4 to 5cm at the left cervical region together with painful plaques and pustules on both hands. The rest of the systemic examinations were normal. Our differential diagnoses for his skin lesions included pyoderma gangrenosum, Sweet's syndrome or granulomatous vasculitis with pyrexia of unknown origin.

Investigations showed leukocytosis (32.5*109 /L) with neutrophilia (85%) and thrombocytosis (554*109 /L) in the full blood count. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were raised [CRP-15.2mg/dl, ESR-121 mm/hour], but renal function test, liver function test, hormonal studies, tumour markers, connective tissue screening (ANF, ANCA, C3, C4) and retroviral screening were normal.

Cultures of blood, urine, sputum and skin swab and biopsy for bacteria, fungus and mycobacteria cultures were all negative.

Chest x-ray was normal. Computer tomography (CT) of his neck, thorax, abdomen and pelvis showed multiple left cervical lymphadenopathy, most likely due to an infective or inflammatory process. Cervical lymph node biopsies performed at three different occasions were consistent with reactive hyperplasia. Skin biopsy histopathology showed marked edema of papillary dermis. The upper dermis was infiltrated with neutrophils and a few eosinophils. Histiocytes containing nuclear debris were present. There were no granuloma and no evidence of malignancy. The findings were consistent with a diagnosis of 'acute febrile neutrophilic dermatitis'. Bone marrow aspiration and trephine biopsy showed a reactive marrow with no evidence of infiltration by malignancy.

The patient was diagnosed to have classical / idiopathic Sweet's syndrome without any underlying malignancy. He was treated with oral indomethacin 50mg three times a day, but this was discontinued due to angioedema. Commencement of oral prednisolone 30mg daily led to a gradual resolution of fever, skin lesions and lymphadenopathy. As the prednisolone was tapered to a dose of 7.5mg daily, he had a relapse with fever and lymphadenopathy. A repeat of the investigations showed similar findings as previously. The dose of oral prednisolone was increased to 30mg daily and oral azathioprine 50mg daily was supplemented as a steroid sparing immunosuppressant. He remained relatively well for 2 years on a low dose of prednisolone and azathioprine. In mid 2005, both his medications were stopped as he was in remission.

However, less than a year later, in March 2006, he presented to UMMC with fever, right neck swelling and painful plaques on his neck and extremities. Physical examination revealed that he was febrile with tender right cervical lymphadenopathy and multiple erythematous plaques and pustules on the neck and extremities **(Figure 1)**.

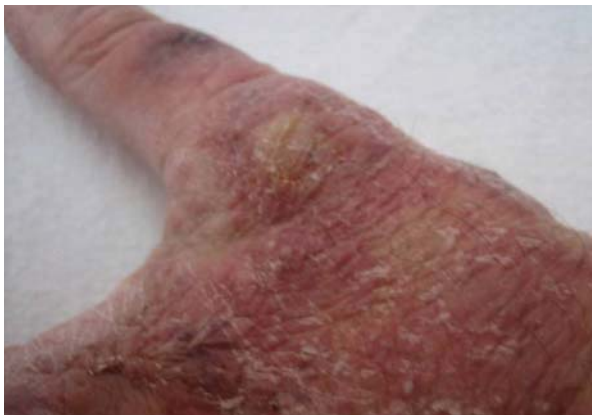


**Figure 1.**

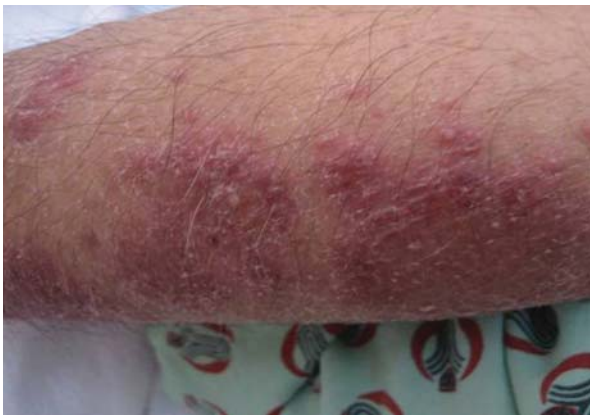


**Figure 2**

Investigations showed leukocytosis (29.8*109/L) with neutrophilia (89%), elevated CRP of 13.3 mg/dl and ESR of 66 mm/hour. Repeat of all blood investigations and cultures of urine, sputum and skin swabs were negative. However, computer tomography (CT) of thorax and pelvis were normal. An abdominal CT however showed multiple hypodense lesions in the spleen, and a biopsy showed the splenic tissues extensively infiltrated with small clusters of neutrophils. No organisms were cultured from the tissue. A repeat skin biopsy showed evidence of focal spongiosis with perivascular infiltrates composed of a mixture of neutrophils and chronic inflammatory cells which was compatible with a 'febrile neutrophilic dermatitis' histopathology.

Oral prednisolone was recommenced at 30mg daily with gradual tapering and discontinued in January 2007. On his recent follow-up in April 2007, he was in remission and did not require any medication.

## Discussion

Sweet's syndrome was first described by Dr. Robert Douglas Sweet in 1964 as an 'acute febrile neutrophilic dermatosis'. The syndrome is characterized by pyrexia, elevated neutrophil count, painful red papules, nodules and plaques and an infiltrate consisting predominantly of mature neutrophils diffusely distributed in the upper dermis[1]. Epidemiological studies of Sweet's syndrome did not reveal any racial predilection and it affects primarily the adult population. The peak incidence of Sweet's syndrome is between the fourth to seventh decade[2]. There are primarily three subtypes of Sweet's syndrome[3] : classical Sweet's syndrome, malignancy-associated Sweet's syndrome and drug-induced Sweet's syndrome[5]. The classical / idiopathic Sweet's syndrome has a greater female predominance especially those in the third to fifth decade[4]. This form of Sweet's syndrome can be preceded by an upper respiratory tract or gastrointestinal infection or associated with inflammatory bowel disease[4].

The specific pathogenesis of Sweet's syndrome is unknown. Chromosomal anomalies have been reported in a few patients with hematological malignancy-associated Sweet's syndrome. Abnormality of chromosome 3q has been described in three Sweet's syndrome patients with hematological malignancy. Sweet's syndrome has also been linked to a form of hypersensitivity reaction to bacterial, viral or tumour antigen as evident by the characteristics of skin lesions and also excellent response of signs and symptoms to systemic corticosteroids[1]. It has been postulated that the hypersensitivity reaction in turn leads to cytokine stimulation with subsequent neutrophilic activation[2]. Cytokines which may potentially play a role in the pathogenesis of Sweet's syndrome include granulocyte colony stimulating factor (GCSF), granulocyte macrophage colony stimulating factor (GMCSF), interferon-gamma, interleukin-1, interleukin-3, interleukin-6 and interleukin-8[4]. These are supported by the significant elevation of serum interleukin-1-alpha, interleukin-1-beta, interleukin-2 and interferon-gamma in patients with Sweet's syndrome.

| | |
|---|---|
| **Major criteria** | • Abrupt onset of painful erythematous plaques or nodules |
| | • Histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis |
| **Minor criteria** | • Pyrexia > 38'C |
| | • Association with an underlying haematologic or visceral malignancy, inflammatory disease, or pregnancy, or preceded by an upper respiratory or gastrointestinal infection or vaccination |
| | • Excellent response to treatment with systemic corticosteroids or potassium iodide |
| | • Abnormal laboratory values at presentation (3 of 4): ESR >20mm/hour, positive CRP, >8,000 leukocytes >70% neutrophils |

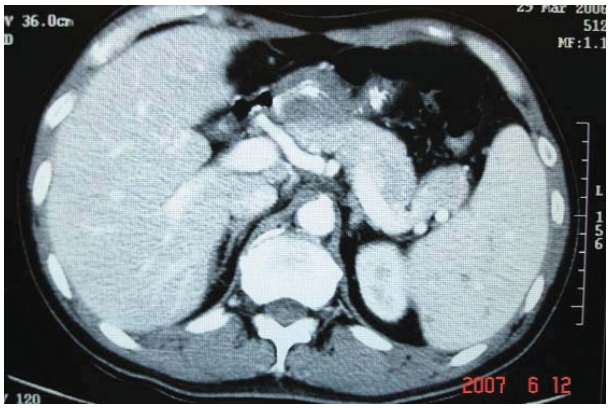
** Both major criteria and 2 of the 4 minor criteria are required to establish a diagnosis of classical Sweet's syndrome.*

Su and Liu proposed a diagnostic criteria for Sweet's syndrome in 1986 shown in the diagram above.

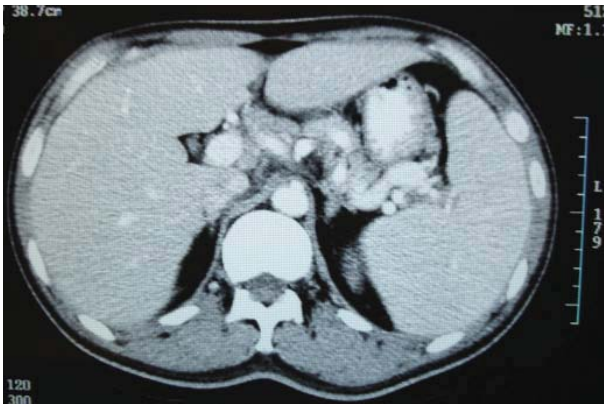
Our patient has fulfilled both the major and three out of four of the minor criteria: pyrexia >38°C, excellent response to systemic corticosteroids, raised ESR, positive CRP, leukocytosis and neutrophilia.

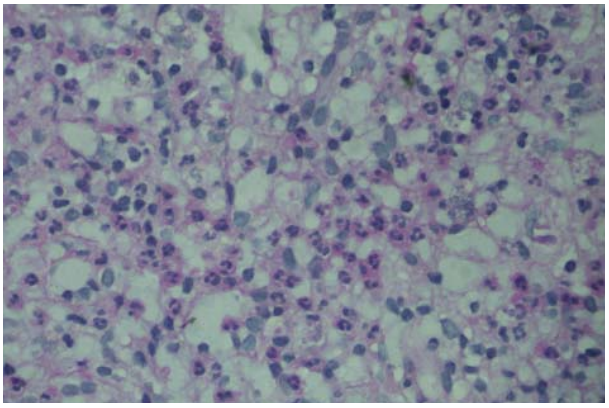
In addition, this patient also presented with extracutaneous manifestation as evidenced by the aseptic splenic abscess. These hypodense lesions in the spleen resolved completely within 3 months of treatment initiation with corticosteroids, which is in keeping with the natural history of this disease **(Figure 2)**. So far in the literature search, extracutaneous involvement of bone, lungs, liver, kidneys heart, eyes and joints have been described. Nevertheless, there is only one case of Sweet's syndrome with aseptic splenic lesions reported in a case of Sneddon-Wilkinson's disease[7] .

Systemic corticosteroids remain the gold standard for the treatment of classical Sweet's syndrome. Systemic steroids provide prompt relief of cutaneous and systemic symptoms. The dosage of prednisolone used is usually 1mg/kg/day with gradual tapering within 4 - 6 weeks. Nevertheless, some patients may require a longer duration of treatment or even daily pulse intravenous treatment during acute presentation, followed by tapering of oral dose of corticosteroid or another immunosuppressant agent to achieve optimal disease control[4].



Multiple hypodense splenic lesions.


Hypodense lesions completely resolved after initiation of steroids therapy



Splenic tissues extensively infiltrated with small clusters of neutrophils.

Other pharmacotherapeutic agents which have been found to have therapeutic efficacy include potassium iodide, colchicine, indomethacin, dapsone, clofazimine, cyclosphosphamide and cyclosporine[4, 6, 7].

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Case Report

# Cutis Marmorata Telangiectatica Congenita in a 3-month-old infant

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Cutis marmorata telangiectatica congenita (CMCT) is an uncommonly reported, sporadic, congenital cutaneous disorder with persistent cutis marmorata, telangiectasia, and phlebectasia. It may be associated with a variety of other congenital anomalies, including but not limited to undergrowth or overgrowth of an involved extremity. We report a case of a baby with CMCT.

## Case Report

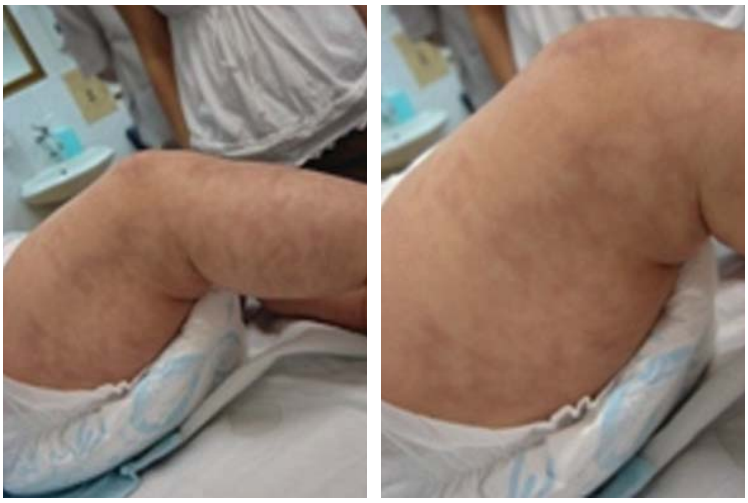
A 3-month-old male baby presented with an erythematous rash on the right thigh and leg since birth and had gradually faded over the months. He was the only child in the family and had been otherwise well and healthy. Antenatal and postnatal histories were normal. There was no maternal family history of similar problem and the mother is a single parent with no past medical history. An ultrasound scan of the abdomen by a private pediatrician showed normal kidneys.

On examination, there was a reticulate erythema on the right thigh and leg **(Figure. 1)**. A lighter similar rash was seen on the right side of the abdomen. The right leg was slightly smaller than the left. Other physical examination and the developmental assessment for his age were normal. A diagnosis of cutis marmorata telangiectatica congenita wascongenita was made based on the clinical findings. His mother was not keen on further evaluation of the associated limb asymmetry. On follow up he showed further improvement of his condition.

## Discussion

Cutis marmorata telangiectatica congenital (CMTC) is a congenital cutaneous vascular phenomenon presenting with reticulate, mottled blue-violet discoloration at birth or early infancy. It was first described in 1922 by the Dutch pediatrician, Van Lohuizen. It has been known less commonly as congenital generalised phleblectasia, naevus vascularis reticularis, congenital livedo reticularis and Van Lohuizens Syndrome.

**Figure 1.** Reticulate erythema on the right thigh and leg



The pathophysiology of CMTC remains unclear, and the cause may be multifactorial. Various theories have been suggested including an unknown environmental factor[1], autosomal dominant inheritance and elevated maternal serum human chorionic gonadotrophin hormone levels during pregnancy[2]. Most cases occur sporadically, although rare cases occur in families. There have been only two reports in the literature describing autosomal dominant inheritance of CMCT within a family[3]. Several case reports show a female preponderance or equal sex incidence.

The distribution can be localized (often unilateral) as in this case, or generalised, although never involving the whole body. There is a full spectrum of severity ranging from faint reticular, patchy skin changes to ulceration and scarring. Capillary malformations (ie, nevus flammeus), capillary and cavernous hemangioma, atrophy or hypertrophy of the affected extremity, macrocephaly[4] (macrocephaly cutis marmorata telangiectatica congenita syndrome), and glaucoma[5] may also be associated with CMCT.

Diagnosis is clinical. Biopsies are not necessary as histology findings are non-specific and non-diagnostic. Microscopic findings include dilated veins and capillaries, or increased number of vessels.

It is important to differentiate CMTC from other skin conditions presenting with a reticulate dermatosis. These include:

a) Physiological cutis marmorata with a symmetrical pattern, which is transient in nature, appearing with cold and disappearing with re-warming. It is common in young infants.
b) Portwine stain with a reticulate pattern may create confusion. It may co-exist with CMTC.
c) Neonatal lupus erythematosus. A serology test should be done if there is neonatal heart block and/ or a maternal history of lupus.
d) Brockenheimer's diseases: a rare progressive deep venous malformation that begins in childhood and carries a poor prognosis.
d) Klippel-Trenaunay Syndrome with vascular lesions associated with asymmetrical hypertrophy of soft tissue or bones.
e) Bluish mottled skin may also be seen in Down's Syndrome, homocystinuria, and Lange Syndrome but the other co-existing clinical features of these conditions will differentiate them from CMTC.

The prognosis of CMTC is good. Skin lesions usually improve, especially during the patient's first 2 years of life with spontaneous resolution by adolescence or early adulthood. This phenomenon is attributed to skin maturation. No treatment is needed unless associated anomalies (eg, glaucoma, hypospadias, syndactyly, cranial abnormalities, limb asymmetry) require treatment. In these cases, consultation with an orthopaedic surgeon and/or neurosurgeon may be necessary for evaluation of associated anomalies. Consultation with an ophthalmologist may be necessary because glaucoma has been reported in association with CMTC. However, all patients with glaucoma have periocular skin changes around the affected eye. Therefore, ophthalmologic evaluation is less indicated in this setting.

CTMC is a rare benign congenital vascular abnormality presenting with reticulate discoloration involving varying extent of the body. Diagnosis is clinical and made by exclusion of other differential diagnoses. A careful examination should be made for associated abnormalities. CMTC has a favorable prognosis with partial or complete resolution during adolescence and therefore needs no specific therapy.

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Case Report

# Uveitis: A presenting sign of both secondary syphilis and HIV Infection

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## Introduction

Uveitis is a well-documented presentation of syphilis with or without concomitant HIV infection[1,2]. Syphilitic uveitis occurs most frequently during secondary and tertiary phases of the infection and its prevalence has declined in tandem with the decline in syphilis prevalence during the early phase of the HIV epidemic. However, during the past 5 years, there has been a resurgence of syphilis and an increased number of patients with ocular syphilis has been reported[3,4]. Early diagnosis of ocular syphilis which is highly amenable to simple antibiotic treatment can prevent blindness. Unfortunately, the ocular manifestations of syphilis are indistinguishable from that of other causes. Hence, a high index of suspicion is necessary to diagnose syphilitic uveitis. Awareness and recognition of concurrent syphilitic skin involvement, often mistaken for psoriasis, can aid in the diagnosis. We describe a patient whose ocular syphilis was diagnosed and treated promptly because of the presence of a palmoplantar rash.

## Case Report

A 69-year-old Chinese gentleman presented with a 2- week history of left eye pain and photophobia. He was diagnosed to have bilateral panuveitis for which he was admitted to our hospital for further management. A palmoplantar rash was noted and he was referred to us for possible palmoplantar psoriasis. He gave a 1-month history of scaly skin lesions that affected both his palms and soles but denied any previous skin problem including genital rash and ulcer. He had intermittent arthralgia affecting his knees and ankles. He has been separated from his wife for the past 20 years but had a regular sexual partner for 10 years when he was younger. He is retired but used to work as a general worker in the logging industry. His last sexual exposure was 3 years ago when he had unprotected genital sex with a commercial sex worker.

Physical examination revealed multiple erythematous scaly plaques on his palms and soles **(Figure 1, 2, 3)**. Ocular examination revealed bilateral injected eyes with a best-corrected visual acuity of perception to light for his left eye and 6/60 for his right eye. Right eye had dense vitritis with focal retinochoroiditis and hyperaemic disc. Left eye had cataractous lens with seclusio pupillae and poor fundal view. Intraocular pressures of both eyes were normal. Neurological examination was unremarkable.

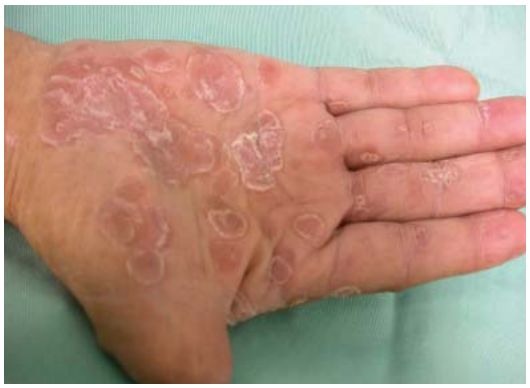

**Figure 1:** Erythematous scaly plaques on right palm

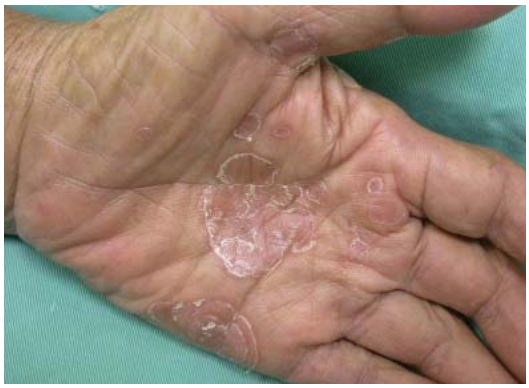

**Figure 2:** Erythematous scaly plaques on left palm

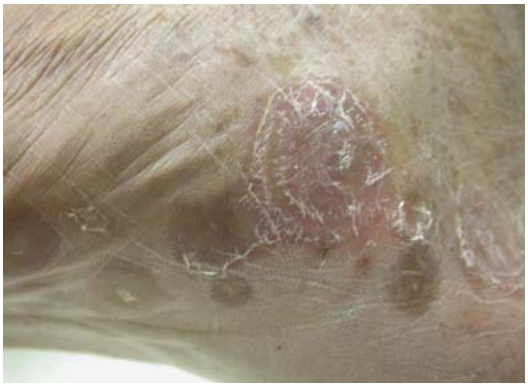

**Figure 3:** Erythematous scaly plaques on right sole

Cardiovascular examination revealed a pansystolic murmur, grade 3/6 over the left sternal edge radiating to the whole chest wall with no evidence of heart failure. There was no hepatosplenomegaly or palpable lymph nodes.

Both serum Treponema pallidum particle agglutination test (TPPA) and Rapid plasma reagin test (RPR ) were positive. Serum RPR titer was 1:64. Lumbar puncture revealed a clear and colourless cerebrospinal fluid (CSF) with positive CSF-VDRL, a pleocytosis of predominantly neutrophils (>10 cells per high power field with 70% polymorph) and a raised CSF protein of 64 g/L with normal glucose level. He was also found to be HIV positive with a CD 4 count of 433 cells/μL. His CD4 to CD8 ratio was 0.34.

Chest radiography showed cardiomegaly with enlarged right ventricle and atrium. Echocardiography showed minimal pericardial effusion with severe tricuspid regurgitation and tricuspid valve prolapse. Right atrium and ventricle were dilated with paradoxical septal motion. Ejection fraction was 70%.

The patient was given intravenous crystalline penicillin 4 mega units 4 hourly (24 mega units daily) for 2 weeks. He was referred to our infectious disease specialist and cardiologist for further management of his retroviral infection and heart problem. He responded well to treatment.

On his last follow-up, 6 months post-treatment, his skin was clear with a RPR titer of 1:8. The best corrected vision for his right and left eye improved to 6/12 and 6/36 respectively. The panuveitis resolved leaving behind extensive posterior synechiae of the left pupil. He rejected a request for a repeat CSF analysis.

## Discussion

Uveitis is a well-documented although rare clinical presentation of syphilis. It is however, the commonest ocular presentation of this ever-present sexually transmitted spirochaetal infection, accounting for 2.5% to 4.3% of cases1. Common ocular manifestations of syphilitic uveitis include granulomatous iridocyclitis, non-granulomatous iridocyclitis, panuveitis and keratouveitis. Several reports on ocular syphilis in HIV patients suggest that ocular involvement may be more common in this group of patients[1,2,5].

Several studies have linked syphilis with HIV seroconversion 6,7. The majority of the studies showed an increased likelihood of HIV seroprevalence in persons with syphilis compared to similar populations without syphilis. In a review of several studies done in the United States, the median HIV seroprevalence in patients with syphilis was 27.5% for men and 12.4% for women whereas the median HIV seroprevalence in persons without syphilis was 4.5 and 2.7 for men and women, respectively.

Secondary syphilis is a systemic disease and patients can present with signs and symptoms referable to any system. These include hepatitis, nephrotic syndrome, uveitis or neurosyphilis but the commonest presentation of secondary syphilis is a non-irritating generalized maculopapular eruption involving the palms and soles[8]. In our patient, the presence of a palmoplantar rash helped us to clinch the diagnosis of syphilis which led to the detection of a concomitant HIV infection. We routinely screen all our patients with STDs for retroviral infection because of the high prevalence of HIV infection in these patients. Syphilis does not appear to be a more common cause of uveitis in HIV-infected patients as compared to cytomegalovirus, herpes simplex virus and toxoplasmosis which still remain important culprits[1]. However, early treatment of ocular syphilis can prevent blindness, making it a worthwhile effort to screen all patients with uveitis for syphilis.

Ocular syphilis is more common in HIV-infected patients, and, it may be more severe and associated with a higher prevalence of neurosyphilis making HIV screening particularly important in syphilitic uveitis[1,2,5]. Our patient had severe panuveitis with dense vitritis similar to that described by Kuo et al probably because of the concomitant HIV infection[5]. The positive CSF-VDRL with CSF pleocytosis and a raised CSF protein satisfy the criteria for the diagnosis of neurosyphilis but HIV patients often have pleocytosis and raised proteins in their CSF making these diagnostic parameters less helpful[9]. It is important to rule out neurosyphilis in HIV patients because of reports of more severe disease, treatment failure and reactivation. Centre for Disease Control, Atlanta recommends lumbar puncture for all HIV-infected patients with late latent syphilis or syphilis of unknown duration. A recent study showed that neurosyphilis is commoner in patients with a serum RPR titer of 1:32 and suggested performing a lumbar puncture only for those with signs and symptoms suggestive of neurosyphilis or those with a serum RPR titer of 1:32[9]. We routinely perform lumbar puncture for all patients with ocular syphilis but treat all ocular syphilis with intravenous crystalline penicillin regardless of CSF findings and use

abnormal CSF findings to monitor treatment of associated neurosyphilis. Our patient responded very well to crystalline penicillin with marked improvement in his vision. The best corrected visual acuity improved from only perception to light to 6/36 for his left eye and from 6/60 to 6/12 for his right eye.

## Conclusion

During the past 5 years, there has been a resurgence of syphilis with an increasing number of ocular syphilis being reported as an initial presentation. Diagnosis of ocular syphilis requires a high index of suspicion since the ocular manifestations are non-specific. The presence of a palmoplantar rash with uveitis is highly suggestive of syphilis but even without skin manifestation, it is prudent to screen all patients with uveitis for syphilis which can lead to blindness if left untreated or treated late. All patients with STDs particularly syphilis should be screened for HIV infection and all patients with ocular syphilis should be assessed for neurosyphilis and treated as neurosyphilis regardless of CSF findings.

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Case Report

# Kaposi's Sarcoma in a 35-year-old homosexual

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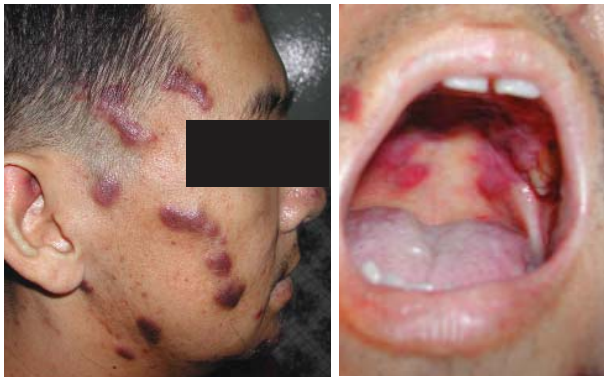
Kaposi's sarcoma (KS) is strongly associated with Human Herpes Virus 8 (HHV8) and Human Immunodeficiency Virus infection (HIV). It was the first malignancy to be linked with Acquired Immunodeficiency Syndrome (AIDS) and it is still the most commonly encountered malignancy associated with HIV. We report a case of Kaposi's sarcoma in a homosexual man.

## Case Report

A 35-year-old Chinese homosexual first presented in November 2004 with prolonged fever for 2 months, which was associated with shortness of breath and significant weight loss. He was noted to have multiple painless, non pruritic, purplish plaque-like lesion, involving the face and trunk for past 4 months.

On examination, he had multiple firm discrete violaceous plaques and nodules scattered over the hard palate, trunk and face **(Figure 1)**. Systemic examination revealed oral thrush, hepatosplenomegaly, multiple cervical and inguinal lymph nodes.

**Figure 1.** Multiple dark red plaque and nodules over face, scalp and hard palate

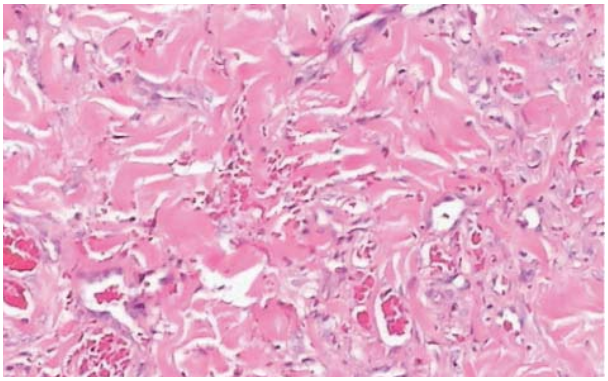


Laboratory investigations showed normochromic anaemia, high erythrocyte sedimentation rate (ESR) and deranged liver function test. Serological tests for syphilis, hepatitis B and C were non reactive. Sputum culture, acid fast bacilli (AFB) smear and AFB culture were negative.

Chest x-ray and Computed Tomography of the thorax showed mediastinal and abdominal lymphadenopathy, ascites and pleural effusion. The Enzyme-Linked Immunosorbent Assay (ELISA) screening test was positive for HIV-1 and the Western blot confirmed the diagnosis. The CD4 count was 60 cells/μL. Punch biopsy from a skin nodule and lymph node biopsy confirmed Kaposi's sarcoma **(Figure 2)**.

He was started on PCP prophylaxis and Highly Active Antiretroviral Therapy (HAART - Indinavir / Ritonavir / Efavirenz). The skin lesions responded well to HAART. Unfortunately, patient defaulted treatment and succumbed to disease after 12 months of the diagnosis.

**Figure 2.** (skin histopathology slide of x10) : Skin slide showed underlying dermis showing angiosarcomatous component which composed of numerous slit like congested vascular channels. Extravasation of red blood cells are noted. Immunohistochemical stains for Factor VIII antigen is positive.



## Discussion

HIV disease presentation has dramatically changed since the introduction of antiretroviral therapy (ART). ART has reduced both the morbidity and the mortality associated with HIV[1]. However, HIV-infected individuals still have an increased risk of developing a malignancy compared with the general population[2]. Kaposi's sarcoma is the most common HIV-related malignancy.

Kaposi's sarcoma is first described by Dr Moritz Kaposi in 1872. HIV-associated or Epidemic Kaposi's sarcoma is an aggressive form of the disease. Kaposi's sarcoma is one of the AIDS defining skin diseases. It is strongly linked to HHV 8 and male homosexual behavior. It is characterized by few or widespread multifocal brown violaceous or dark red colour patches, papules, plaques and/or deep skin nodules. Typically, the lesions are bilateral, symmetrically distributed along the lines of skin cleavage, involving the extremities. These lesions may involve the skin, mucosal membranes, lymph nodes and visceral organs such as the gastrointestinal tract, lungs, liver and spleen.

The mucocutaneous Kaposi's sarcoma lesions are usually asymptomatic, it may be single or multiple and sometimes appear simultaneously or sequentially. The skin lesions can appear over the face, trunk or extremities, particularly behind the ears and the earlobes. Oropharyngeal lesions are seen over the hard and soft palate, gingival and buccal membrane.

If left untreated, the median survival is 18 months. But with the introduction of ART, there is a marked decline in the incidence (30-50%), morbidity, and mortality (81%)[3]. Currently, ART is the first-line therapy for Kaposi's sarcoma in patients with low CD4 counts and/or high viral loads. First-line treatment for Kaposi's sarcoma in patients with CD4 counts greater than 350 cells / μL is unclear[4].

In aggressive disease, liposomal doxorubicin or daunorubicin are the first-line chemotherapeutic agents. Paclitaxel is a safe and effective alternative monotherapy, with response rates ranging from 59% to 71%. Other agents used alone or in combination include vinca alkaloids[5], bleomycin[6] and Granulocyte Macrophage Colony Stimulating Factor (GM-CSF). Less commonly used systemic approaches include interferon alpha, thalidomide, systemic retinoids, and human chorionic gonadotrophin.

There are many options for local treatment which include radiotherapy, electron beam therapy, photodynamic therapy, liquid nitrogen, intralesional vinca alkaloids, intralesional interferon alpha and the others.

Prognosis of Kaposi's sarcoma depends on the extent of the disease (tumour burden), the presence or absence of systemic B symptoms (fever, weight loss >10%) and the presence of opportunistic infections[7].

Despite the marked reduction in morbidity and mortality from HIV with the introduction of ART, the excess malignancy in this population has not reduced. New challenges like drug resistance, treatment complications and increased incidence of malignancies have been noted in this group of patients who are now living longer.

## Acknowledgement

We are most grateful to the infectious disease team, surgical team and pathologist from Penang Hospital for co managing Mr. L.

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Case Report

# Extramammary Paget's Disease in an elderly man

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## Introduction

Extramammary Paget's disease (EMPD) is a rare form of adenocarcinoma observed in areas with numerous apocrine or eccrine glands. It is presumed to be a variant of epithelial carcinoma, with potential to develop from or to be the cause of an underlying adenocarcinoma. The clinical manifestation of EMPD is varied. The lesions appear as a solitary patch with an eczematous surface and well-defined borders. Differential diagnoses include Bowen's disease, psoriasis, leukoplakia, superficial fungal infection and eczematous dermatoses. Definitive diagnosis requires biopsy of the lesion and immunohistochemical staining. In most cases of non invasive or minimally invasive EMPD, surgical resection with clear margins and careful follow up is recommended, since the recurrence rates is high.

## Case report

A 66-year-old male Chinese retired timber worker presented with reddish skin lesions on his left groin of 3 years duration. The skin lesions initially started as a small reddish patch, which gradually increased in size. They were occasionally itchy. He experienced no bowel or urinary disturbances. He consulted general practitioners and was treated for eczema and fungal infection, without improvement.

Examination revealed a large erythematous plaque with a warty surface, with some areas of atrophy and telangiectasia over the left groin and scrotal skin measuring 8 x 7 cm in size **(Figure 1)**. His regional lymph nodes were not enlarged and he had no organomegaly.

Our clinical diagnosis was Bowen's Disease with a differential diagnosis of Extramammary Paget's Disease. The skin histology showed clusters of intraepithelial large tumour cells displaying ovoid, pleomorphic nucleoli and vacuolated cytoplasm. Mitoses are visible **(Figure 2 & 3)**. There were chronic inflammatory cells in the dermis. The tumour cells were stained positive with Carcinoembryonic Antigen (CEA) **(Figure 4)** and Periodic Acid Schiff (PAS.)

**Figure 1.** Erythematous plaque with a warty surface, some areas of atrophy and telangiectasia over the left groin and scrotal skin

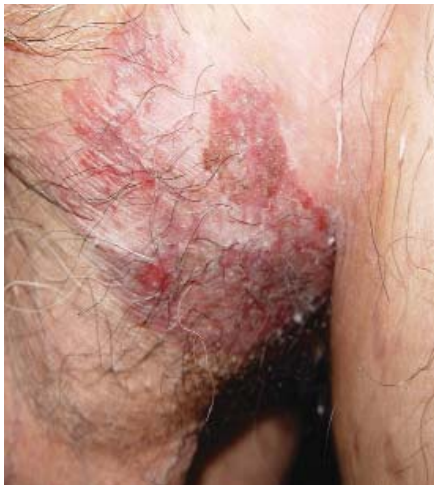


**Figure 2.** Clusters of Paget's cells with abundant cytoplasm and prominent nucleolus

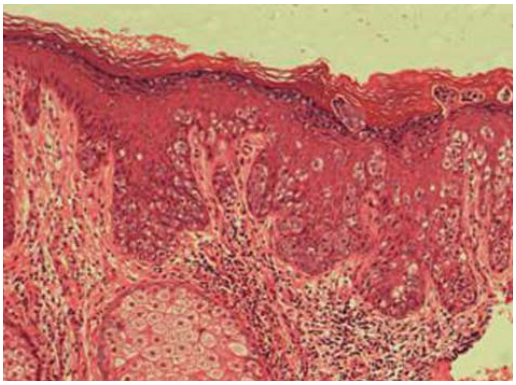


**Figure 3.** Multiple Paget's cells with vacuolated cytoplasm

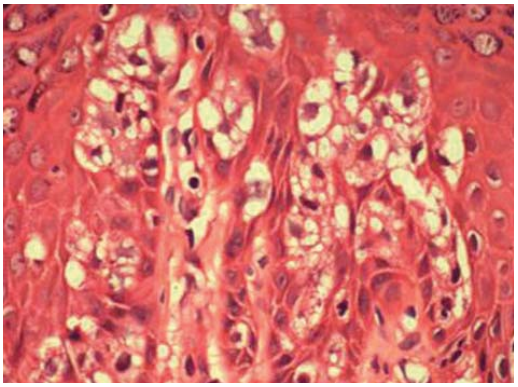
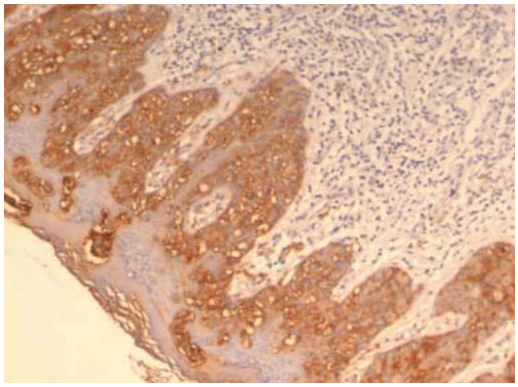


**Figure 4.** The Paget's cells were stained positive with CEA



The tumour cells showed diastase resistant cytoplasm with prominent hyperchromatic nucleus.

Immunohistochemical stains for cytokeratin 20 (CK 20) and Human Melanoma, Black 45 (HMB 45) were negative. Colonoscopy and cystoscopy examination were normal. This was performed to exclude adenocarcinoma of gastrointestinal tract and urethra respectively.

He was referred to the urologist and plastic surgeon for wide excisionwide excision of the lesion. The histology of the excised lesion was consistent with EMPD, with excision margin free of tumour.

## Discussion

Extramammary Paget's disease (EMPD) is a rare form of adenocarcinoma observed in areas with numerous apocrine or eccrine glands. This tumour was first described by Crocker in 1889. The clinical lesions and histological changes are similar to Paget's disease of the Breast.

Three patterns of EMPD have been described:

1. An in situ epithelial form without associated carcinoma
2. An epithelial form with associated adnexal carcinoma
3. A form associated with visceral malignancy of either genitourinary or the gastrointestinal tract.

Seventy seven percent of patients with EMPD are women. It is most common in postmonopausal Caucasian women, especially in the 6th and 7th decades[1]. The common sites are the vulva, perianal, scrotal and penile regions. Rarely, lesions affecting the thighs, buttocks, axillae, eyelids and external ear canal have been reported[2].

Clinically, EMPD presents as an erythematous plaque with a velvety surface, sometimes with exudation and crusting, or scaling. Pruritus is common. Occasionally the skin lesions show hyperpigmentation, hypopigmentation, ulceration and leukoplakia.

Long-standing lesions may be modified by repeated trauma, excoriation or superimposed infection.

Our patient presented with itchy skin lesion on the left groin for 3 years and was treated as eczema and fungal infection by various general practitioner with no improvement. The clinical lesions of extramammary Paget's disease can mimic other dermatoses such as eczema, tinea cruris, candida intertrigo, Bowen's disease, flexural psoriasis, erythrasma, lichen sclerosis, and superficial spreading amelanotic melanoma. The diagnosis could be easily missed if diagnosis was not considered and biopsy not performed. Hence, any eczematous or thickened lesions where apocrine glands are encountered, and which does not resolve with appropriate therapy should arouse the suspicion of Paget's disease.

EMPD is often associated with underlying malignancy. We had investigated our patient for associated malignancy and he did not have other associated malignancy. Various reports have shown different percentages of associated malignancy over different durations of follow up. One case series reported a prevalence rate of 59%[3] and two others found a visceral malignancy prevalence rates of 86%[4] and 50%[5] respectively. Twenty five percent of EMPD is associated with adnexal adenocarcinoma of the dermis. Twenty nine percent of the patients had concurrent or subsequent internal malignancy[1]. Penile and scrotal Paget's is associated with adenocarcinoma of the male genitourinary tract. Perianal Paget's disease has an association with colorectal carcinoma. Vulval Paget's is associated with endometrial, endocervical, vaginal, urethral and bladder carcinoma.

Paget's cells are large, with abundant pale cytoplasm with large nuclei and absent intercellular bridges. The cells are dispersed between keratinocytes. They form clusters, glandular structures or solid nests, and extrude into adnexal structures. Chronic inflammatory cells are found in the dermis.

Paget's cell cytoplasm is positive with PAS and diastase resistant which suggest the cells are glandular in origin. Most cases of EMPD are strongly positive for CEA, especially those without an associated cancer. Cytokeratin 20 is found in cases of EMPD with an underlying carcinoma. HMB45 does not react with Paget's cells in mammary or extramammary PD (to differentiate Paget's disease from melanoma)

The differential histological diagnosis includes pagetoidincludes pagetoid Bowen's disease and pagetoid superficial spreading melanoma. Bowen's disease can show a pagetoid pattern of epidermal involvement but the infiltrating atypical cells are squamous in origin. Intracellular mucin, signet cells and glandular structures are present in Paget's disease but absent in Bowen's disease. In cases where morphological features of glandular differentiation are absent, immunohistochemical staining (Cam5.2, Epithelial Membrane Antigen (EMA), CEA positive in Paget's disease) will usually resolve the problem[7].

The cells of Paget's and melanoma both contain melanin granules. Reactive epidermal atypia is common in Paget's but rare in melanoma. S100 and HMB45 are positive in melanoma. HMB45 does not label Paget's cells. However, S100 is positive in 25% of mammary Paget's and occasionally positive in EMPD[7].

Treatment of EMPD includes wide surgical excision and split skin graft, Moh's micrographic surgery, radiation, curettage, laser, cryosurgery, and topical 5 florouracil (5-FU)[5,6].

Local recurrence is high (33%)[8] and usually requires a wider local excision. With no underlying malignancy, EMPD has a high local recurrence despite adequate excision. Multifocal involvement and difficulty in clinical delineation of cutaneous margins are major factors in relapse. With underlying malignancy, the prognosis is poor. Helwig and Graham reported a mortality rate of 83%[3]. Therefore, close long term follow up of all patents with EMPD is important to look for recurrence and development of associated malignancy.

## Conclusions

EMPD is a rare, slow growing adenocarcinoma. The clinical presentation resembles eczema, psoriasis, fungal infection, and Bowen's disease. This tumour is often misdiagnosed and topical steroids or antifungal medication prescribed. Any eczematous or thickened lesions where apocrine glands are encountered, and which does not resolve with appropriate therapy should arouse the suspicion of Paget's disease. Long term follow-up is required to detect recurrence and the development of an associated cancer.

## Acknowledgement

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Case Report

# Chronic Arsenicism - a forgotten entity?

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## Introduction

Arsenicism is now rare but is still a relevant disease as arsenic is present in the environment and occupational setting. Moreover, it is preventable and warrants long-term follow-up for cutaneous and internal carcinoma.

## Case Report

A 66-year-old Chinese man was referred to us with hyperkeratotic papules on palms and soles, on the background of cryptogenic cirrhosis Child's B, complicated by several episodes of hepatic encephalopathy. Cirrhosis work-up was negative, including hepatitis A IgM, hepatitis B surface antigen, hepatitis C IgG, caeruloplasmin, copper and iron levels, smooth muscle antibody, anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, anti-double-stranded DNA antibody, rheumatoid factor and alphafeto protein. Computerised tomography of the abdomen showed decompensated liver cirrhosis with portal hypertension and no hepatoma.

He had pancytopaenia (Hb 9.8 g/dL, WBC $1.3x10^3/\mu L$, platelet $83x10^3/\mu L$). Bone marrow aspirate features were suggestive of early myelodysplastic syndrome. The rest of the investigations were negative (vitamin B12, folate, acute leukaemia, T cell CD4 and T cell CD8 panels). He was immobile from peripheral neuropathy and declined any further tests.

He had a significant history of drinking well-water during his teenage years but did not consume traditional Chinese medicine (TCM) or arsenic-containing medications. He worked as a plumber and a contractor. He had no history of asthma or skin problems.

Clinically, he had signs of chronic arsenic poisoning, viz hypopigmented macules on the background of generalised hyperpigmentation, diffuse alopecia, palmoplantar punctate hyperkeratosis **(Figure 1)**, Mee's lines **(Figure 2)** and bilateral ankle oedema. Skin biopsy showed features consistent with arsenic keratosis. **(Figure 3)**

## Discussion

Our patient has chronic arsenicism, complicated by cirrhosis, pancytopaenia and peripheral neuropathy.

Arsenic is a ubiquitous metal found in naturally contaminated drinking water and landfill in some areas of the world[1, 2], Chinese proprietary medicines[3] and in occupational settings, including agricultural chemicals, mining, carpentry and manufacture of gallium arsenide computer microchips[4].

**Figure 1.** Photograph shows hyperkeratotic papules on the index finger, middle and ring fingers - 'arsenical keratosis'

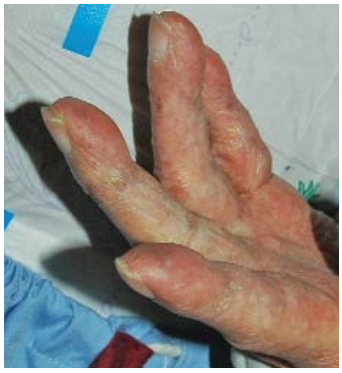


**Figure 2.** Photograph shows transverse white lines on nails - 'Mee's lines'

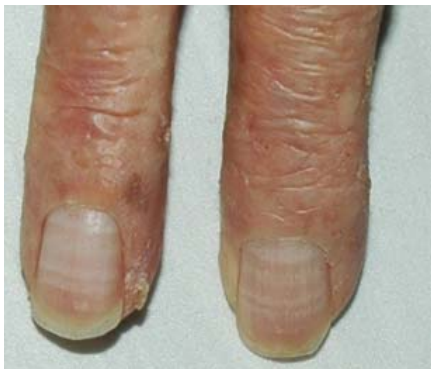
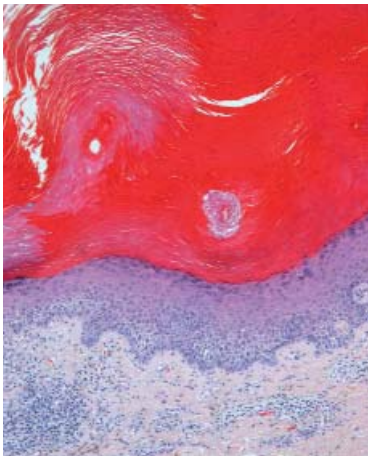


**Figure 3.** H&E stain of a section of skin. 10x magnification. Epidermis shows marked hyperkeratosis with focal parakeratosis and mild spongiosis. Mild parabasal and basal cell dysplasia. Superficial dermis shows moderate superficial perivascular infiltrates of lymphocytes, eosinophils and plasma cells. No elastotic changes.



In acute exposure (medicinal, homicidal, suicidal), the patients present with nausea, vomiting, diarrhoea, fatigue, facial oedema and acute renal failure. If survived, they often develop peripheral polyneuropathy, shedding of hair and nails and cutaneous signs of chronic arsenic poisoning.

Chronic arsenicism, in our local context, is due primarily to inorganic arsenic in traditional chinese medicine (TCM)[5]. There is symmetrical mottled hyperpigmentation on the upper chest, axillae, nipples, groin, arms, legs, palms, soles and pressure points, which may become generalised, with superimposed hypopigmented macules, described as 'raindrops on a dusty road'. Alopecia, nasal perforation, peripheral neuropathy, encephalopathy, haematologic abnormalities, hypertension, chronic lung disease, cirrhosis, diabetes mellitus, oedema of legs, digital cyanosis and necrosis of the legs (black foot disease) may occur[6].

There is a risk of developing cutaneous malignancy (basal cell carcinoma (BCC), Bowen's disease (squamous cell carcinoma in situ), squamous cell carcinoma (SCC)) from arsenical ketasoses (ArKs) and internal cancers (lung, stomach, colon, liver, kidney, bladder and hematopoietic system)[1, 2]. The current WHO and US Environmental Protection Agency sets a maximum arsenic contaminant limit at 0.05mg/L[7], although at this level, some carcinoma may still develop.

ArKs are precancerous[6,8] punctate, yellow, corn-like, easier-felt-than-seen papules (2-5 mm), which may become large, discrete confluent elevations (>5 mm) with a nodular, wart-like or horny appearance. They typically appear several years after the first exposure, symmetrically distributed on palms (thenar and hypothenar eminences, lateral aspects of fingers, dorsal aspects of interphalangeal joints) and weight-bearing plantar surface, and occasionally on the trunk, proximal extremities, eyelids, penis and scrotum.

Arsenic-induced BCC are multiple, randomly scattered, primarily on the trunk and in hair-bearing regions. Arsenical Bowen's disease appear initially as skin-coloured to red papules. The papules may enlarge and become keratotic. The crust, when removed, reveals a red, oozing and papillomatous base. Arsenic-related SCC can arise de novo or from malignant transformation of ArKs and Bowen's disease[3]. A diagnosis of ArKs and chronic arsenicism should be considered when numerous characteristic keratoses are seen on the palms and soles or when multiple lesions of BCC, Bowen's disease or SCC are found on an individual, especially in sun-protected areas of the body.

Chelation therapy with Dimercaprol (British anti-lewisite; BAL) is the mainstay in acute arsenicism. ArKs can be treated by cryotherapy, curettage, topical chemotherapy (5FU[9]), topical immunomodulator (5% imiquimod[10]), oral acitretin[11] and photodynamic therapy. Vitamin E and selenium, which works by impeding the carcinogenic effects of DNA damage, shows promise as potential treatments for these skin lesions[12, 13].

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Case Report

# Atypical Presentation of Genital Herpes in an HIV Infected Man

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Herpes simplex virus (HSV) infection is one of the common opportunistic viral infections that may occur in human immunodeficiency virus (HIV) - infected patients. The natural history of HSV infection is often altered in this group of patients. Characteristically, genital herpes presents with multiple painful vesicles and erosions in immunocompetent patients. However, clinical presentations in immunocompromised patients are frequently severe and atypical which may lead to a delay in diagnosis and treatment. Genital herpes enhances transmission of HIV infection and hence early detection of this condition is important to reduce transmission of HIV and HSV.

## Case Report

A 50-year-old, single, heterosexual Chinese man, diagnosed with HIV infection since 2006 was referred for evaluation of non-healing ulcerated perianal nodules & plaques of 6 months duration. The lesions started as vesicles which slowly evolved over months. They were not painful but associated with mild pruritus. There was a persistent foul smelling serous discharge from the lesions. He had no fever, urinary symptoms or urethral discharge. He was started on HAART since March 2006 with zidovudine, lamivudine and nevirapine and at the time of evaluation, his CD4+ T-cell count was 15/mm$^3$. He was also on co-trimoxazole for prophylaxis against *pneumocystis carinii* pneumonia. He admitted to a history of unprotected casual sex but denied abusing any illicit drug. He had been treated with several courses of antibiotics from various doctors prior to presentation without any improvement. Incision and drainage was also done but the lesions persisted.

On examination, there were ulcerated nodules on his suprapubic region and a verrucous nodular lesion at the perianal region with surrounding vesicles **(Figure 1a)**. Swabs for Gram stain demonstrated a few Gram positive cocci but bacterial culture was negative. Screening for gonorrhea and syphilis were negative. Tzanck smear examination revealed multinucleated giant cells. A skin biopsy for histopathological examination showed pseudoepitheliomatous hyperplasia of the epidermis with intraepithelial vesicles **(Figure 2)** and the presence of multinucleated cells with viral inclusion bodies **(Figure 3)**. Skin biopsy specimen for fungal culture was negative. He was diagnosed to have verrucous genital herpes.

**Figure 1.** (a) Initial verrucous ulcerated nodules at perianal region with surrounding vesicles. (b) All lesions resolved with post-inflammatory dyspigmentation after 6 months of therapy

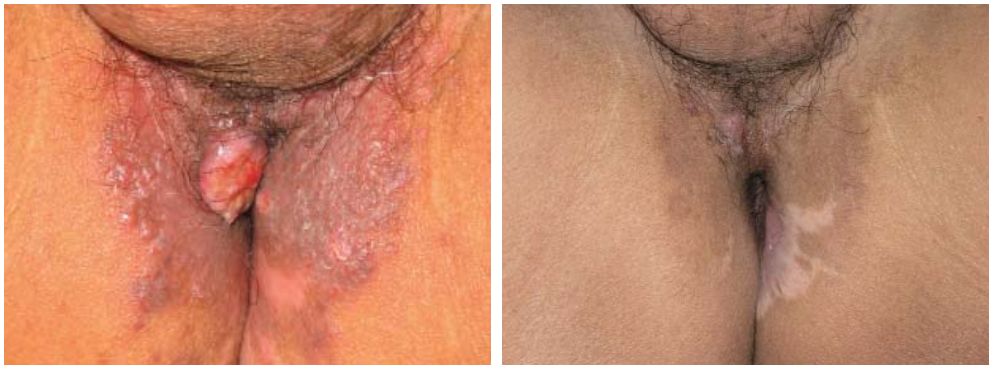


**Figure 2.**

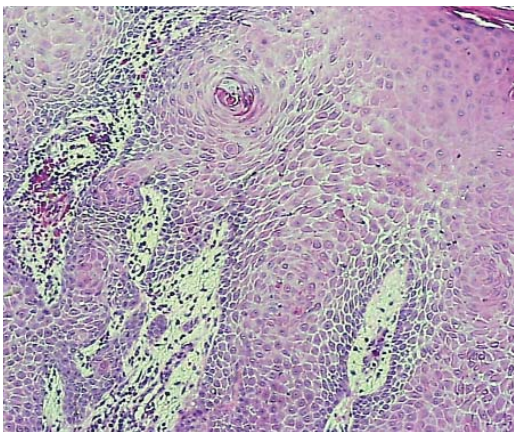
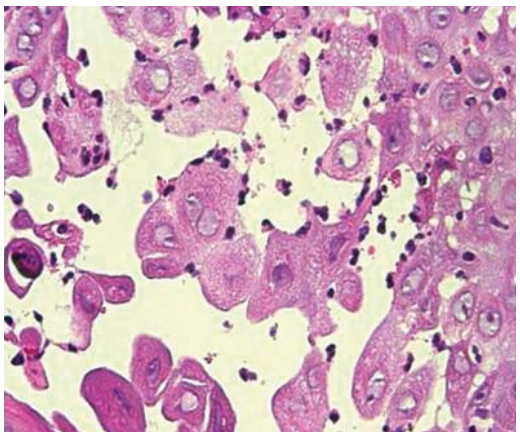


**Figure 3.**



He was started on oral acyclovir 200mg 5 times per day for 5 days initially but without much improvement. Acyclovir was then increased to 400mg 5 times per day for another 2 weeks. There was significant improvement of the lesion after 2 weeks of treatment. The drug was subsequently tapered to 400mg 4 times per day for the next 3 months with almost complete resolution of his lesions. This was followed by suppressive therapy at a dose of 400mg 3 times per day and he remained clear of any lesions 6 months later **(Figure 1b)**.

## Discussion

Immunocompromised persons such as HIV-infected patients often experience a severe, chronic and atypical form of lesion in both primary and reactivated HSV infections as compared to immunocompetent patients. This can result in a delay in diagnosis and treatment among these patients. As in our case, the patient's condition was undiagnosed for 6 months, causing him much distress. Although HSV infection is typically painful, the relatively painless nature of his lesions added to more confusion. Verrucous genital lesions are usually caused by infection with human papillomavirus (HPV) although concomitant infection with more than one organism can result in verrucous lesions in patients with acquired immunodeficiency syndrome (AIDS)[1]. There have been several case reports of genital herpes presenting as verrucous lesions in HIV-infected patients. Carrasco et al reported a 28-year-old HIV-positive man who presented with hyperkeratotic, verrucous or exophytic plaques on his scrotum that were due to herpes simplex infection[2]. Tong et al described a 32-year-old HIV-positive man who presented with a verrucous lesion of the intergluteal cleft that clinically resembled condyloma acuminata or verrucous carcinoma[1]. Type 2 HSV was isolated when lesional tissue was cultured and cultures for other viruses, fungi and acid-fast bacilli were all negative.., It is postulated that immune dysfunction secondary to HIV, mediated by T-helper type 2 cytokines results in epidermal hyperplasia[2]. Furthermore, the chronicity of the lesion also predispose to the atypical presentation.

Nodules are another atypical presentation of genital herpes as reported in the literature. Emanuela et al reported a case of a man with AIDS who presented with perianal nodules, which clinically resembled squamous cell carcinoma[3]. The diagnosis of herpes was confirmed by histopathology of the biopsy specimen and nested PCR analysis. Besides verrucous and nodular lesions, there have also been reports of atypical presentation of genital herpes in the form of an indolent penile ulcer as reported by Tayal el al[4]. The case was atypical in that the lesion was large, single, painless and not associated with lymphadenopathy. The diagnosis was confirmed by histopathology and immunochemistry using polyclonal antibodies directed against both HSV types 1 and 2.

Acyclovir, valaciclovir and famciclovir are all recognized as appropriate treatment for primary or recurrent genital herpes in HIV-infected patients. Antiviral therapy should be continued until all mucocutaneous lesions have dried and crusted. Increased dosages of acyclovir, valaciclovir and famciclovir, above those recommended for immunocompetent individuals, may be required[5]. Acyclovir at a dose of 400 mg given five times daily has been used to treat HSV in immunocompromised patients[2]. As in our case, the patient responded to treatment only after doubling the dose of acyclovir. It has been reported that hyperkeratotic herpes infection is associated with acyclovir resistance[1]. Fortunately, our patient proved to be sensitive to acyclovir although the duration of therapy was longer for disease resolution. In general, long term suppressive therapy is recommended in a HIV-infected patient with a CD4+ T-cell count of < 100/mm$^3$ and who suffer severe and protracted HSV outbreaks. It is also indicated in a HIV-infected patient with a CD4+ T-cell count in any range but experiences frequent recurrences (more than 6 episodes per year). Acyclovir, valaciclovir and famciclovir all appear useful for the treatment and suppression of HSV in immunocompromised persons. In cases that do not respond to increased doses of these antiviral therapies, susceptibility testing of HSV cultures should be performed if the test is available.

In cases with confirmed or presumed acyclovir resistance, intravenous foscarnet or topical cidofovir have been successfully used[2].

There is a close relationship between HSV and HIV infection. In HIV-seropositive individuals, genital herpes lesions may not only be the source of transmission of HSV, but may also be a focus of shedding of HIV due to the infected CD4+ cells infiltrating the herpetic lesions. Furthermore genital ulceration during HSV infection provides increased available surface area for the exchange of infected fluids which facilitates HIV transmission[5]. In addition, the plasma HIV load increases to a median of 3.4 times during an acute outbreak of HSV infection and this will accelerate progression of HIV[5]. Studies have shown that by reducing or attenuating the occurrences of HSV outbreaks, acyclovir therapy may help reduce the deleterious effects of these infections. These studies suggest that chronic suppressive acyclovir therapy prolongs survival in AIDS patients with a prolonged history of HSV infection[2]. Resistance does not appear to be increased or induced by chronic suppressive therapy with these antiviral agents[2].

In summary, genital herpes can present in an atypical manner among immunocompromised patients. HSV infection should be considered in the differential diagnosis of chronic verrucous genital papules, nodules or plaques in HIV-seropositive persons. When in doubt, a biopsy and culture for all potential organisms should be performed. Antiviral therapy with acyclovir, famciclovir or valaciclovir are all useful but dose requirement and treatment duration may be higher and more prolonged than in immunocompetent patients to ensure successful therapy. Early detection and treatment of genital herpes among HIV-infected patient will not only reduce transmission of HSV but also HIV infection.

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Case Report

# Purpura Fulminans in an army trainee

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Purpura fulminans is a condition characterized by haemorrhagic tendencies and usually associated with septicaemia or a previous history of infection. It was first described by Guelliot in 1884 as an acute disease with features of hypotension, disseminated intravascular coagulation and purpura leading to necrosis.

## Case Report

A 20-year-old female army trainee presented with a 2-day history of spiking fever, chills, rigors, vomiting, diarrhea, abdominal pain and numbness of all limbs. She was admitted to Hospital Tuanku Ja'afar with a Glasgow Coma Scale (GCS) of 11/15. She was subsequently intubated and ventilated and admitted to ICU for respiratory distress and a low GCS.

She was treated for septicaemic shock as well as disseminated intravascular coagulation with our DIVC regime consisting of 6 units of cryoprecipitate, 6 units of fresh frozen plasma and 2 units of platelet. She was treated with IV antibiotics and was supplemented with intravenous fluid support and ionotropes. Within the next 24 hours she was noted to have well demarcated purplish red macular patches on an erythematous base over the trunk, limbs and face which later transformed into gangrenous lesions over the right lower limb especially on the 2nd to 5th toes up to the shin **(Figure 1)**. A referral was made to our department for her acute skin changes. A provisional diagnosis of generalized purpura secondary to DIVC was made initially and subsequently changed to purpura fulminans. The patient was referred to the orthopaedic team in view of her gangrenous wound and underwent two wound debridements under general anaesthesia. She was put on multiple antibiotics for various different organisms from the culture and sensitivity report.

Her creatinine on admission was 180umol/L. The clotting profile was also found to be deranged but normalized after the DIVC regime. X-ray of both ankles did not reveal any osteomyelitic changes.

**Figure 1.** Hemorrhagic and ecchymosed purplish well demarcated lesions with signs of necrosis over the patellar region bilaterally on the lower limbs

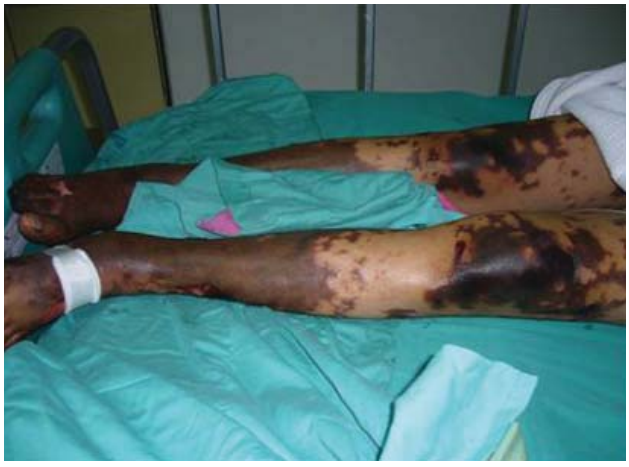
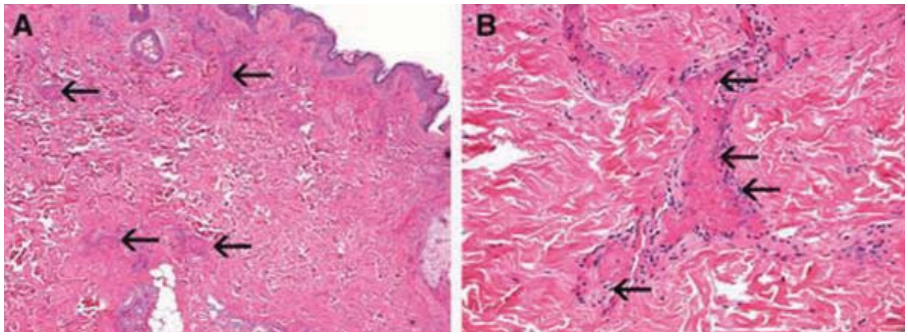


**Figure 2.** Thrombosis of venules and capillaries are visible in both superficial and deep dermis (arrows)




A skin biopsy performed revealed the presence of a scanty and unremarkable epidermis. The main changes involved the vessels in the subcutaneous tissue and adnexae. Inflammation, necrosis and fibrinoid deposits were seen involving these structures consistant with disseminated intravascular coagulation. Immunofluorescense studies and connective tissue screen were negative. The final diagnosis was purpura fulminans based on clinical & histological features **(Figure 2)**.

Her coagulation profile normalized and her general condition improved with the prompt and aggressive management. However her limbs were gangrenous and she had lost most of her sensation over her lower limbs especially her right lower limb. She was referred to University Hospital for fasciotomy and reconstruction under the orthopedic team.

## Discussion

Purpura fulminans is an acute onset haemorrhagic condition with a high morbidity and mortality rate. It presents with extensive multiple ecchymotic (purplish, violaceous) purpuric lesions throughout the body. It is associated with fever, hypotension as well as disseminated intravascular coagulation.

There are 3 different categories of classification[2,4]. (1) Inherited or acquired abnormalities of protein C or other coagulation systems. (2) Acute infectious Purpura Fulminans (commonest cause is Gram negative microorganism) and (3) Idiopathic.

Purpura fulminans is commonly associated with meningococcal sepsis which usually has a poor prognosis[1]. It usually presents with an acute onset of cutaneous haemorrhage and necrosis secondary to vascular thrombosis and DIVC.

There is often pain followed by petechiae. Ecchymosis develops and evolves into painful indurated, well demarcated purple papules with erythematous borders. These lesions then progress into necrosis with formation of bullae and vesicles. Gangrenous necrosis follows with extension into the subcutaneous tissue and occasionally involves the muscle and bone as in our patient.

Management of purpura fulminans should be prompt and aggressive with treatment of the underlying cause, which is more commonly due to meningococcal septicaemia[3] as in our patient. Prompt resuscitation with fluids, broad spectrum antibiotic therapy bearing in mind gram negative organisms in particular and inotropic support if the patient is haemodynamically compromised[5]. The triggered DIVC must be corrected appropriately and ventilatory support with a team of efficient intensive care unit staff is important.

It must be mentioned here that purpura fulminans due to Staphylococcus .aureus infection has symptoms identical to those of fulminant meningococcemia but requires additional treatment against methicillin resistant Staphylococcal aureus.

## Acknowledgements

I would like to thank the Director General of Health, Ministry of Health, Malaysia, for allowing me to publish this article.

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Commentary

# Therapeutic advances in reducing risk of genital herpes transmission

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Anogenital herpes is the commonest cause of sexually transmitted genital ulcers worldwide, including Malaysia[1], and is mainly caused by HSV type 2 although the incidence of HSV type 1 is increasing[2]. The disease may have an overall negative impact on the individual, the community and the nation. This consists of not only the physical impact of the disease on the individual and the life-threatening encephalopathy if transmitted to an infant around birth[3], but also the psychosocial and financial implications. More importantly, it has been shown to enhance the transmission and acquisition of HIV infection[4]. Studies of adolescent sexual culture have shown a trend towards a younger age at first intercourse, but age at first marriage is unchanged resulting in an expanded "risk window" during which young people may have many sexual partners, which may further compound the negative impact.

In order to treat and prevent the transmission of the disease and prevent any outbreak of HIV infection, numerous advances have been made although the ultimate strategy is still far from sight. Over the last 20 years, we have had specific antiviral agents (acyclovir, valacyclovir, famciclovir) to treat the acute episode as well as reduce the frequency of relapse. Recently, antiviral therapy was shown to reduce the frequency and degree of viral shedding from the genital mucosal surfaces[5-6]. This prompted a study to determine whether a reduction in viral shedding would result in a reduction in transmission of the disease. In this landmark study[7], a randomized, double-blind, placebo-controlled of 1484 immunocompetent, monogamous, HSV-2 discordant couples, partners with HSV-2 received either 500mg of valacyclovir once daily or placebo for 8 months. The incidence of clinically symptomatic HSV-2 infection (genital herpes) in susceptible partners was reduced by 75% with the use of valacyclovir. Overall, the acquisition of HSV-2 infection (defined via laboratory-confirmed symptoms or seroconversion) by susceptible, HSV-2 seronegative heterosexual partners was reduced by 48%. Among the source partners, valacyclovir significantly reduced the frequency at which HSV DNA was detected in samples of genital secretions (2.9% compared with 10.8% days in the placebo group; $p<0.001$). However, transmission can still occur in people prescribed antiviral therapy. Therefore, infected individuals and their partners should be counseled to use safer sex practices, including the use of condoms.

These encouraging data have raised more questions as to whether the clinical effects would be similar for other antiviral drugs in the same class and for the management of genital HSV infection, particularly with regards to prevention of transmission, in different patient populations. More research is required to provide answers to these important questions.

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# Understanding towards leprosy: a ground level survey among public & medical personnel in Penang Hospital

Although leprosy is one of the oldest diseases of mankind, many people remain unaware of the significance of the early symptoms of leprosy and the importance of early diagnosis and treatment[1]. When people do recognize the possibility of leprosy, they are subjected to the traditional fears and stigma associated with the disease[2].

Although multi-drug therapy (MDT) is well established as the effective cure and is widely available, an important minority of patients continue to delay in presentation. Those who delay have an increased risk of nerve impairment[3] or disability[4,5].

The aim of the study was to determine the level of awareness of leprosy among the public and medical personnel in Penang Hospital and to gather data and explore individual's treatment preference and the beliefs and attitudes towards leprosy.

A survey was carried out over a 2-month period (May - June 2006) in the Dermatology Clinic, Penang Hospital where randomly selected individuals were interviewed and answered a survey questionnaire in 3 languages (Malay, English and Mandarin) . Public is defined as patients who visited the skin clinic during May - June 2006 (excluding the diagnosed leprosy cases, age < 12 years old, illiterate or ill patients).

Medical personnel is defined as staff nurses and medical assistants working in Penang Hospital excluding skin clinic staff. A total of 800 respondents (400 public; 400 medical personnel) were interviewed. 20.5% of public and 10.3% of medical personnel never heard of the disease leprosy or "kusta". 19.2% of public and 10.2% of medical personnel thought that leprosy did not exist in Malaysia. Only 58.8% of public and 78.0% of medical personnel recognized the signs and symptoms of leprosy Majority of respondents equate deformities to leprosy. Most of the respondents failed to recognize the subtle signs of leprosy. Majority of respondents still thought that leprosy was an incurable disease Only 41.8% of public and 68.0% of medical personnel chose to consult a doctor as their first priority **(Figure 1)**. The medical personnel's knowledge on leprosy, although inadequate was better than the public (P<0.0001).

Since the introduction of Multiple Drug Therapy (MDT) in 1982 by WHO, the prevalence of leprosy has declined steadily. MDT was started in Malaysia since 1985. Malaysia has achieved elimination status with prevalence < 1 per 10,000 & incidence rate of < 1 per 100,000 populations in 1994. Thus, Malaysia has achieved WHO's target for control earlier than expected.

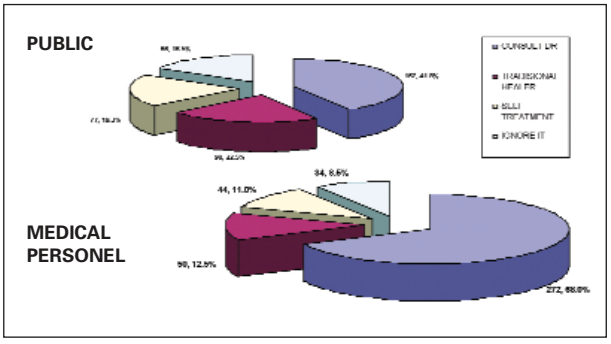
However, recently for the past 3 years, there has been an increase in incidence rate. It may be partly contributed by poor awareness among the health care provider and the public (In our series, 19.2% of public and 10.2% of medical personnel thought that leprosy did not exist in Malaysia) and an increase of immigrants into our country.

The clinical diagnosis of leprosy is frequently missed or misdiagnosed. As shown in our series, only 58.8% of public and 78.0% of medical personnel recognized the signs and symptoms of leprosy. Being a great imitator, leprosy has a wide spectrum of clinical manifestations ranging from simple dermatological and neurological to that of ophthalmological, orthopaedic, rhinological or dental presentations[4-6]. In our series, 84.5% of respondents equated deformities to leprosy. They failed to recognize the subtle sign of leprosy. Only 63.1% and 57.0% of respondents knew that patients may present with skin lesions and neuropathy. It is often considered too formidable or difficult to diagnose and treat as most doctors have scanty knowledge of the disease. They often have misperception that leprosy is incurable. In our series, only 43.0% of respondents knew that leprosy was a curable disease

A high index of suspicion is needed to make a correct diagnosis. Medical personnel should always consider leprosy as a possible cause of peripheral neuropathy or neuropathic ulcers[6].

It was very interesting to note that, 50.2% of public and 32.0% medical personnel preferred to seek alternative treatment before they choose to consult the doctors. Misbeliefs about leprosy, low level of awareness to modern treatment, stigma[2,7] and the influence of traditional healers are important factors associated with this issue[8].

**Figure 1.** What would you do, if you suspect yourself having leprosy?



To achieve the aim of "Malaysia without leprosy", the level of awareness towards the disease need to be improved. There are 2 guiding principles to achieve the mission: (1) High index of suspicion to diagnose and (2) to treat leprosy early & promptly[5].

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