

Donovanosis – recent papers

Gavin Hart MD, MPH

This bibliography provides a comprehensive listing of publications since the beginning of 1992. Previous segments were published in Venereology 1993;6:103-8; Venereology 1995; 8:43-7; Venereology 1995; 8:257-62; Venereology 1997; 10:53-9 and Venereology 1998; 11:46-8

A hat trick of ulcerating pathogens in a single genital lesion

Samuel M, Aderogba K, Dutt N, Lambert JS, Taylor C. Int J STD & AIDS. 2007; 18(1):65-6
We report on a patient from a London clinic, (a Jamaican heterosexual man known to have herpes) who has donovanosis and syphilis in a single genital ulcer. The case highlights the importance of careful clinical examination of genital ulcers.

Methods of specimen collection for the diagnosis of STIs.

Kaimal S, Thappa DM. Indian Journal of Dermatology, Venereology & Leprology 2007; 73(2):129-32

Granuloma inguinale: a case report. [Review] [22 refs]

Rashid RM, Janjua SA, Khachemoune A. Dermatology Online Journal. 2006; 12(7):14
Granuloma inguinale is common in certain regions of the world, however, it is rarely reported in the United States. It is the result of infection by *Calymmatobacterium granulomati*, although current literature proposes to re-classify this organism as *Klebsiella granulomati*. Here we report a case of granuloma inguinale, review the literature, and discuss historical context, treatment options, and differential diagnosis.

Donovanosis (granuloma inguinale).

Richens J. Sex Transm Inf. 2006; 82 Suppl 4:iv21-2
A segment of the UK national screening and testing guidelines for all sexually transmitted diseases.

Genital ulcers caused by sexually transmitted diseases: current therapies, diagnosis and their relevance in HIV pandemy. [Portuguese]

Da Costa JB, Domingues D, Castro R, Exposto F. Acta Medica Portuguesa. 2006; 19(4):335-42
The sexual transmitted pathogens associated with genital ulcers are *Treponema pallidum*, *Haemophilus ducreyi*, *Calymmatobacterium granulomatis*, *Chlamydia trachomatis* and *Herpes simplex virus* type 1 or 2. Although geographic differences still exist, herpetic infections prevalence is growing worldwide as the most frequent ulcerative sexual transmitted disease. The failure of the many different used guidelines in achieving a sustained reduction in the number of new cases, in particular the WHO syndromic management, leads into an over treatment of bacterial agents and missing of viral agents. This situation is also associated with poor efficacy and wasting of economical resources. Ulcerative and non-ulcerative sexual transmitted diseases are important in the world HIV pandemy because they promote HIV transmission and are also associated with the disease evolution. Portugal had until recently the highest incidence of HIV infection in Europe and that points out to importance of treating and control of both ulcerative and non-ulcerative sexual transmitted diseases in order.

Evolution of venereology in India. [Review] [43 refs]

Thappa DM. Indian Journal of Dermatology, Venereology & Leprology 2006; 72(3):187-96
Discusses the terminology and origins of STDs generally, and the history of individual STDs, including AIDS, with special reference to India. It also describes academic developments and health service delivery issues in India.

Donovanosis (inguinal granuloma). [French]

Caumes E, Janier M, Dupin N' et al. Annales de Dermatologie et de Venereologie. 2006; 133:2S35

Genital ulcer disease in central Australia: predictors of testing and outcomes

Wilkey JE, Fethers KA, Latif AS, Kaldor JM. Sexual Health. 2006; 3(2):119-22
OBJECTIVES: To identify factors associated with the uptake and outcome of testing for infectious causes of genital ulcer disease (GUD) in central Australia. METHODS: Prospective investigation of GUD cases in central Australia from February 2002 to August 2003. Data were collected from primary health care clinics in remote indigenous communities of Central Australia. RESULTS: During the study period, 134 cases of GUD were reported and investigated. Of these cases, 71 (53%) were in women (age range 14-75, median 28) and 63 (47%) in men (14-63, median 28). Testing for syphilis was undertaken for 111 (82.8%) cases, 75 (56%) were tested for herpes simplex virus infection, and 82 (61.2%) for donovanosis. Testing for at least one of the three sexually transmissible pathogens of interest was undertaken in 128 (95.5%) cases, while 99 (73.9%) were tested for two pathogens and 41 (30.6%) for all three agents. Of subjects tested, 19.8% had

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new syphilis infection, 51% had herpes simplex virus infection and 7% had donovanosis. In 19 of 41 (46.3%) subjects fully investigated no cause for genital ulceration was found. **CONCLUSION:** This study provides the first quantitative description of GUD diagnosis in central Australia. Logistic constraints limited the systematic application of diagnostic tests. Current treatment protocols may need to be reassessed in light of the higher than expected detection of genital herpes as a cause of GUD.

Vulvar donovanosis as pseudo-elephantiasis [Portuguese]

Silva BB, Costa PV, Dias HK, Batista SM. *Revista Da Associacao Medica Brasileira.* 2006; 52(1):11

Detection and discrimination of herpes simplex viruses, *Haemophilus ducreyi*, *Treponema pallidum*, and *Calymmatobacterium (Klebsiella) granulomatis* from genital ulcers. [erratum appears in *Clin Infect Dis.* 2006 ;43(2):270]. Mackay IM, Harnett G, Jeffreys N, et al. *Clin Inf Dis.* 2006; 42(10):1431-8

BACKGROUND: Genital ulcer disease (GUD) is commonly caused by pathogens for which suitable therapies exist, but clinical and laboratory diagnoses may be problematic. This collaborative project was undertaken to address the need for a rapid, economical, and sensitive approach to the detection and diagnosis of GUD using noninvasive techniques to sample genital ulcers. **METHODS:** The genital ulcer disease multiplex polymerase chain reaction (GUMP) was developed as an inhouse nucleic acid amplification technique targeting serious causes of GUD, namely, herpes simplex viruses (HSVs), *H. ducreyi*, *Treponema pallidum*, and *Klebsiella* species. In addition, the GUMP assay included an endogenous internal control. Amplification products from GUMP were detected by enzyme linked amplicon hybridization assay (ELAHA). **RESULTS:** GUMP-ELAHA was sensitive and specific in detecting a target microbe in 34.3% of specimens, including 1 detection of HSV-1, three detections of HSV-2, and 18 detections of *T. pallidum*. No *H. ducreyi* has been detected in Australia since 1998, and none was detected here. No *Calymmatobacterium (Klebsiella) granulomatis* was detected in the study, but there were 3 detections during ongoing diagnostic use of GUMP-ELAHA in 2004 and 2005. The presence of *C. granulomatis* was confirmed by restriction enzyme digestion and nucleotide sequencing of the 16S rRNA gene for phylogenetic analysis. **CONCLUSIONS:** GUMP-ELAHA permitted comprehensive detection of common and rare causes of GUD and incorporated noninvasive sampling techniques. Data obtained by using GUMP-ELAHA will aid specific treatment of GUD and better define the prevalence of each microbe among at-risk populations with a view to the eradication of chancroid and donovanosis in Australia.

Genital elephantiasis and sexually transmitted infections - revisited. [Review,66 refs]

Gupta S, Ajith C, Kanwar AJ, et al. *Int J STD & AIDS.* 2006; 17(3):157-65

Genital elephantiasis is an important medical problem in the tropics. It usually affects young and productive age group, and is associated with physical disability and extreme mental anguish. The majority of cases are due to filariasis; however, a small but significant proportion of patients develop genital elephantiasis due to bacterial sexually transmitted infections (STIs), mainly lymphogranuloma venereum (LGV) and donovanosis. STI-related genital elephantiasis should be differentiated from elephantiasis due to other causes, including filariasis, tuberculosis, haematological malignancies, iatrogenic, or dermatological diseases. Laboratory investigations like microscopy of tissue smear and nucleic acid amplification test for donovanosis, and serology and polymerase chain reaction for LGV may help in the diagnosis, but in endemic areas, in the absence of laboratory facilities, diagnosis largely depends on clinical characteristics. The causative agent of LGV, *Chlamydia trachomatis* serovar L1-L3, is a lymphotropic organism which leads to the development of thrombolympangitis and perilympangitis, and lymphadenitis. Long-standing oedema, fibrosis and lymphogranulomatous infiltration result in the final picture of elephantiasis. Elephantiasis in donovanosis is mainly due to constriction of the lymphatics which are trapped in the chronic granulomatous inflammatory response generated by the causative agent, *Calymmatobacterium (Klebsiella) granulomatis*. The LGV-associated genital elephantiasis should be treated with a prolonged course of doxycycline given orally, while donovanosis should be treated with azithromycin or trimethoprim-sulphamethoxazole combination given for a minimum of three weeks. Genital elephantiasis is not completely reversible with medical therapy alone and often needs to be reduced surgically.

Bilateral psoas abscess in a case of granuloma inguinale.

West W, Fletcher H, Hanchard B, et al. *West Indian Med J.* 2005;54(5):343-5

The authors present a case of disseminated granuloma inguinale with bilateral psoas abscesses. Infection with *calymmatobacterium granulomatis* is usually localized to the genital organs but rarely may be disseminated. A search of the literature revealed that only two cases of psoas abscesses due to *Calymmatobacterium granulomatis* were previously reported.

Sentinel surveillance of sexually transmitted infections in South Africa: A review.

Johnson L. Coetzee DJ. Dorrington RE. Sex Transm Inf. 2005;81(4): 287-293

Objectives: To review studies of sexually transmitted infection (STI) prevalence in South Africa between 1985 and 2003 in selected sentinel populations. To examine how STI prevalence varies between populations and to identify the limitations of the existing data. Methods: Studies of the prevalence of syphilis, chancroid, granuloma inguinale, lymphogranuloma venereum, gonorrhoea, chlamydia, trichomoniasis, bacterial vaginosis, candidiasis, and herpes simplex virus type 2 (HSV-2) were considered. Results were included if they related to women attending antenatal clinics or family planning clinics, commercial sex workers, individuals in the general population (household surveys), patients with STIs, patients with genital ulcer disease (GUD), or men with urethritis. Results: High STI prevalence rates have been measured, particularly in the case of HSV-2, trichomoniasis, bacterial vaginosis and candidiasis. The aetiological profile of GUD appears to be changing, with more GUD caused by HSV-2 and less caused by chancroid. The prevalence of gonorrhoea and syphilis is highest in 'high risk' groups such as sex workers and offenders of STI clinics, but chlamydia and trichomoniasis prevalence levels are not significantly higher in these groups than in women attending antenatal clinics. Conclusions: The prevalence of STIs in South Africa is high, although there is extensive variability between regions. There is a need for STI prevalence data that are more nationally representative and that can be used to monitor prevalence trends more reliably.

Factors affecting sexual transmission of HIV-1: Current evidence and implications for prevention.

Chan DJ. Current HIV Research. 2005;3(3):223-241

The predominant mode of HIV-1 transmission globally is from sexual practices. The risk of HIV-1 transmission by sexual means is a function of infectivity, susceptibility and mode of transmission (type of sexual practice). In addition, transmission may be significantly increased or decreased by factors relating to the HIV-1 per se, sexual behaviour, other sexually transmissible infections (STIs), antiretroviral therapy (ART), spermicidal microbicides and HIV-1 vaccines, the host immune system, genital anatomy and nutritional deficiencies. Current research into the factors affecting sexual transmission of HIV-1 appears to benefit developed nations more than developing nations because of structured public health systems and the capacity to translate research findings into prevention strategies. A redistribution of global aid funding would do much to alleviate the pandemic in developed countries.

Genital ulcer disease and human immunodeficiency virus: A focus.[117 refs]

Sardana K. Sehgal VN. Int J Dermatol. 2005;4(5): 391-405

Recent conceptual and empiric work has underlined the reciprocal relationship (epidemiological synergy) between HIV infection and other STDs, whereby each may alter the transmission and manifestations of the other, resulting in a potentially explosive mutually reinforcing spiral of infection. Evidence supporting the role of GUD in facilitating HIV transmission has come from three types of study, namely biological plausibility, sero-conversion and interventional trials.

Ulcerative lesions.

Keck JW. Clinics in Family Practice. 2005; 7(1 SPEC. ISS): 13-30

Genital ulcer disease remains a worldwide problem with geographic variability in pathogen prevalence. A syndromic approach is recommended, taking into account clinical presentation, local prevalence data, and available laboratory testing. Treatment recommendations are well published, and management decisions should take into account local susceptibility data. Clinicians should be aware of the special considerations for patients who are pregnant, immunocompromised, or HIV-seropositive. Evaluation and treatment of sexual partners is important in controlling outbreaks of this disease. Finally, given the role genital ulceration plays in the transmission of HIV, counseling and testing for this disease is recommended in all patients diagnosed with genital ulcer disease.

Changing patterns of sexually transmitted infections in India.

Sharma VK. Khandpur S. National Medical Journal of India. 2004;17(6): 310-319

Sexually transmitted infections (STIs) are more dynamic than other diseases prevailing in the community. Their epidemiological profile varies from country to country and from one region to another within a country, depending upon ethnographic, demographic, socioeconomic and health factors. The clinical pattern is also a result of the interaction among pathogens, the behaviours that transmit them and the effectiveness of preventive and control interventions. We reviewed the changing patterns of different STIs (excluding HIV

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infection) In India and their various risk factors. A MEDLINE search was undertaken using the key words 'sexually transmitted infections, epidemiology, India'. Related articles were also searched. In addition, a manual search for many Indian articles, published in journals that are not indexed was also carried out. Wherever possible, the full article was reviewed. If the full article could not be traced, the abstract was used. Most of the published data are institution based. There is a paucity of community-based data, except for information obtained from high risk groups such as commercial sex workers, truck drivers, hotel workers and drug abusers. From the literature search undertaken, it was observed that during the 1960s and 1970s, bacterial infections including syphilis, chancroid and gonorrhoea were the major STIs, while viral infections caused by herpes simplex virus and human papillomavirus were so rare that they merited publication as case reports. Since the 1980s, the spread of human immunodeficiency virus (HIV) with subsequent behavioural (sexual and healthcare) change, the indiscriminate and prophylactic use of over-the-counter broad-spectrum antibiotics, upgradation of health services at the primary level and the success of 'syndromic' approach of treatment, has resulted in major changes in epidemiological patterns. As in developed countries, there has been a rise in viral and chlamydial infections and a relative fall in the incidence of traditional infections. This has forced a reappraisal of the importance of sexual and healthcare behaviours, since the control of incurable viral STIs depends to a great extent on societal efforts at primary prevention and counselling rather than their early diagnosis and treatment, which is an effective strategy against curable bacterial STIs.

Selected sexually transmitted diseases and their relationship to HIV. [Review,120 refs]

Wu JJ, Huang DB, Pang KR, Tying SK. *Clinics in Dermatology*. 2004; 22(6):499-508

Although sexually transmitted diseases (STDs) are underreported and underrecognized, they are a major source of morbidity, mortality, and represent a major socioeconomic cost in developing and industrialized nations. Individuals who develop STDs are often coinfecting with human immunodeficiency virus (HIV). Coinfection with HIV both facilitates the natural history of STDs and worsens the clinical picture. The objective of this article is to provide a review to the practicing clinician on the epidemiology, clinical manifestations, methods of diagnosis, and treatment for four cutaneous STDs--chancroid, genital herpes, granuloma inguinale, and lymphogranuloma venereum--in coinfecting HIV patients.

Facial and oral aspects of some venereal and tropical diseases. [Review,19 refs]

Ramos-E-Silva M. *Acta Dermatovenerologica Croatica*. 2004;12(3):173-80

Diseases of the tropical areas include some venereal diseases, and they are still very prevalent in some countries; Brazil is one of them. Very few cases are originated in large cities, as Rio de Janeiro, but at the University Hospital of the Federal University of Rio de Janeiro we also see those patients who come from the interior of the State of Rio de Janeiro or from other states to seek medical care at better equipped hospitals for this type of investigation and therapy. Venereal and tropical dermatoses have many different cutaneous manifestations and may affect skin in several locations. The face is one of the affected areas especially when the disease has a predilection for cartilage, oral and/or nasal mucosa. Alterations observed on the skin of the face and on the mucosa of the mouth of some tropical diseases, such as leprosy, leishmaniasis, paracoccidioidomycosis, donovanosis, and syphilis, as they are observed in Brazil, are presented and discussed in this article.

Short treatment of donovanosis with azithromycine

Clyti E, Couppie P, Strobel M, et al. *Annales de Dermatologie et de Venereologie*. 2004; 131(5):461-464

Introduction. Azithromycine is recommended in the treatment of donovanosis with a 7-day treatment cycle. We report the efficacy of a single cure of 1 gram in two patients. Observations. Four patients, presenting with donovanosis, were treated with azithromycine according to 2 regimens. The first used 500 mg/d the molecule during 1 week, the second used azithromycine in single cure of 1 gram. The latter led to the complete cure of 2 patients. Discussion. Many antibiotics are used in the treatment of donovanosis. Since 1996, Australian authors have used l'azithromycine in this indication. A single dose of this molecule appears effective in recent and confined donovanosis.

Donovanosis in developed countries: neglected or misdiagnosed disease?[comment].

Morrone A, Toma L, Franco G, Latini O. *Int J STD & AIDS*. 2003;14(4):288-9

Oral donovanosis

Veeranna S, Raghu TY. *Int J STD & AIDS*. 2002; 13(12):855-6

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A 23-year-old male presented with oral ulcers. Tissue smear showed Donovan bodies. The patient was treated with oral tetracycline.

Donovanosis. [Review, 69 refs]

O'Farrell N. *Sex Transm Inf* 2002; 78(6):452-7

Donovanosis, a chronic cause of genital ulceration, has recently been the subject of renewed interest after a long period of relative obscurity. The causative organism, *Calymmatobacterium granulomatis*, has been cultured for the first time in many years and a polymerase chain reaction diagnostic using a colorimetric detection system has been developed. Phylogenetic analysis confirms close similarities with the genus *Klebsiella* and a proposal made that *C granulomatis* be reclassified as *Klebsiella granulomatis* comb nov. Azithromycin has emerged as the drug of choice and should be used if the diagnosis is confirmed or suspected. In donovanosis endemic areas, syndromic management protocols for genital ulceration may need to be adapted locally. A significant donovanosis epidemic was reported in Durban from 1988-97 but the current status of this epidemic is unclear. The donovanosis elimination programme among Aboriginals in Australia appears successful and is a model that could be adopted in other donovanosis endemic areas. Overall, the incidence of donovanosis seems to be decreasing. Increased attention would undoubtedly be paid to donovanosis if policy makers recognised more readily the importance of genital ulcers in fuelling the HIV epidemic.

Disseminated donovanosis (granuloma inguinale) with osteomyelitis of both wrists.

Fletcher HM, Rattray CA, Hanchard B, et al. *West Indian Med J* 2002; 51(3):194-6

Donovanosis is a sexually transmitted infection which presents with genital ulceration and inguinal lymphadenopathy. Rarely, it presents with extra-genital manifestations. We present a case of disseminated donovanosis with cervical ulceration, massive pelvic lymphadenopathy, osteomyelitis of the wrists and septic arthritis of the knees and right elbow. A 23-year-old gravida two presented with wasting, oedema, ascites, bilateral iliac lymphadenopathy, anaemia and a large ulcer of the cervix uteri. Two months later in the outpatient clinic, she was much improved but still had post-coital bleeding and a hyperaemic cervix, suggestive of persistent infection. The course of antibiotics was therefore repeated. Histopathological examination of a specimen from colposcopic biopsy of the cervix uteri revealed granuloma inguinale. She improved after several courses of antibiotics, blood transfusion, surgical debridement and aspiration of affected joints.

Sexually transmitted diseases: microbiology and management. [Review, 105 refs]

Birley H, Duerden B, Hart CA, et al. *J Med Microbiol* 2002; 51(10):793-807

Donovanosis: increased incidence in our setting as a result of imported cases from endemic areas.

[Spanish] Bernal Ruiz AI, Gonzalez Ruiz A, Gutierrez Rodriguez C, Garcia Munoz M. *Anales de Medicina Interna*. 2002; 19(2):103-4

Donovanosis in India: declining fast?[comment].

Gupta S, Kumar B. *Int J STD & AIDS* 2002; 13(4):277

Dispute the statements of a recent paper by indicating that though the prevalence of donovanosis had declined in the north of India, the prevalence remained high at about 5% of STD clinic attenders on the east coast. Furthermore the decline in the north began before HIV prevention measures were introduced suggesting that these were not the reason for the decline. Comment on: *Int J STD AIDS*. 2001;12(7):423-7;

An uncommon cause of a destructive vulval lesion.

van der Griend B, Rane A, Green E. *Aust NZ J Obstet Gynaecol* 2001; 41(4):459-60

We present a case of a 39-year-old woman with a vulval lesion, which macroscopically looked consistent with a fungating squamous cell carcinoma of the vulva. However, further investigations demonstrated a less common cause for this presentation.

European guideline for the management of tropical genito-ulcerative diseases

Roest RW, van der Meijden WI. *Int J STD & AIDS* 2001; 12 Suppl 3:78-83

Trovofloxacin for the treatment of chronic granuloma inguinale

Hsu SL, Chia JK. *Sex Transm Inf* 2001; 77(2):137

Dorsal perforation of prepuce: a common end point of severe ulcerative genital diseases?

Gupta S, Kumar B. *Sex Transm Inf* 2000; 76:210-2

Severe ulcerative genital diseases can cause destruction of the prepuce, glans, or sometimes of the whole penis (phagedena). We observed a characteristic pattern of partial destruction of the prepuce as a result of a wide variety of ulcerative genital diseases. Five patients, two with severe genital herpes, one with hidradenitis suppurativa, and two with donovanosis presented with perforation on the dorsal surface of the prepuce. In four of them, the glans protruded through the defect and in one, the defect was not large enough to allow protrusion of the glans. In two patients, the preputial sac was obliterated. The relatively decreased blood supply of the prepuce is the probable explanation for perforation at this selective site.

A colorimetric detection system for *Calymmatobacterium granulomatis*

Carter JS, Kemp DJ. *Sex Transm Inf* 2000;76:134-6

OBJECTIVE: To incorporate the first polymerase chain reaction (PCR) assay for *Calymmatobacterium granulomatis* into a colorimetric detection system for use in routine diagnostic laboratories. **METHODS:** A capture oligonucleotide specific for the *Klebsiella* *phoE* gene was covalently linked to tosyl activated magnetic beads. Biotinylated *phoE* PCR products obtained from 14 positive specimens from patients with donovanosis and isolates of *Klebsiella pneumoniae*, *K rhinoscleromatis*, and *K ozaenae* were cleaved with *HaeIII* for the purpose of differentiation, captured by the prepared beads, and subjected to standard EIA detection methodology. Eight samples from unrelated genital conditions underwent the same procedure. It was anticipated from the sequence data that the biotinylated fragment would be cleaved from the capture oligonucleotide target region in the three *Klebsiella phoE* products (that is, a negative colorimetric result) while the entire fragment of interest would remain intact in the positive *C granulomatis phoE* products (that is, a positive colorimetric result). **RESULTS:** All 14 positive specimens from patients with donovanosis gave strong colorimetric readings with this detection system. Isolates of *K pneumoniae*, *K rhinoscleromatis*, *K ozaenae*, and the eight specimens from unrelated genital conditions were negative. **CONCLUSION:** The successful development of a colorimetric detection system for *C granulomatis* incorporating two levels of specificity enables the molecular diagnosis of this condition to be undertaken by routine diagnostic laboratories. This should have an important role in the Australian government's campaign to eradicate donovanosis by 2003 though the test still needs to undergo trials and be validated using a larger number of samples from geographically diverse parts of the world in order to ascertain the generalisability of the methodology.

Donovanosis causing cervical lymphadenopathy in a five-month-old boy

Bowden FJ, Bright A, Rode JW, et al. *Ped Inf Dis J* 2000;19(2):167-9

Describes perinatal transmission from a mother with extensive untreated donovanosis. The child presented with cervical lymphadenopathy and chronic suppurative otitis media, and was successfully treated with oral azithromycin suspension, 10 mg/kg daily for 14 days.

Transepithelial elimination of cutaneous vulval granuloma inguinale

Ramdial PK, Kharsany AB, Reddy R, et al. *J Cutaneous Pathol* 2000; 27(10):493-9

BACKGROUND: Transepithelial elimination (TEE), a distinct and well-known entity, is a process during which the skin eradicates undesirable or irritative dermal substances through intact epidermis or follicular epithelium by passive or active means. Although TEE is being described in an increasing number and range of pathological processes, to date, TEE of granuloma inguinale (GI) remains unrecorded in the English-language literature. The aims of this study were: 1) To appraise the light microscopic and ultrastructural morphological epidermal changes that are associated with TEE of cutaneous vulval GI; and 2) To determine the role of intra-epidermal leucocytes and histiocytes in the pathogenesis of TEE of vulval GI. **METHODS:** This is a retrospective 9-year histopathological review of all cases diagnosed and coded as vulval granuloma inguinale in the Department of Anatomical Pathology, Nelson R. Mandela School of Medicine, University of Natal, Durban, South Africa. Ultrastructural evaluation was performed on selected cases using a Jeol transmission electron microscope. **RESULTS:** Of 53 skin biopsies from 47 patients with vulval GI, 43 were suitable for the study. The age range of patients was 15-40 years (mean age=22 years). There were eleven papular, twelve nodular, seven verrucous and thirteen ulcerative lesions. Donovan bodies within macrophages, free-lying Donovan bodies and dense aggregates of neutrophils and plasma cells were seen in the dermis of all biopsies. There was consistent overlying pseudoepitheliomatous hyperplasia. The dermal inflammatory infiltrate hugged the dermo-epidermal junction and appeared entrapped between elongated and acanthotic epidermal rete ridges and pegs. Transepidermal neutrophil microabscesses, histiocytes containing Donovan bodies and neutrophilic and histiocytic fragmentation were present. A variable number of free-lying and intra-histiocytic Donovan bodies and neutrophils were present on the surface of the epidermis. On ultrastructural investigation epidermal spongiosis, intracellular oedema, free-lying, intra-

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neutrophilic and intra-histiocytic Donovan bodies, and intact and degenerating neutrophils and histiocytes were evident between keratinocytes. The degenerative histiocytes demonstrated marked vacuolation, mitochondrial swelling and bacilli within phagolysosomal vacuoles, bound by intact or disrupted limiting membranes. **CONCLUSION:** The inflammatory infiltrate at the epitheliomesenchymal interface, pseudoepitheliomatous hyperplasia, intra-epidermal accumulation and disintegration of neutrophils and histiocytes, and the associated release of lytic enzymes, play important contributory roles in TEE of GI. TEE of infectious agents is a poorly recognised mechanism of spread of infectious diseases and represents a public health hazard. In cutaneous vulval GI, TEE is highlighted as a hitherto unrecognised, potential method of spread of *Calymmatobacterium granulomatis*.

[Painless ulcer of the penis. Granuloma inguinale tropicum] [German]

Fuessl HS. MMW Fortschritte der Medizin 2000; 142(8):43-4

Phylogenetic analysis of *Calymmatobacterium granulomatis* based on 16S rRNA gene sequences

Kharsany AB, Hoosen AA, Kiepiela P, et al. J Med Microbiol 1999; 48(9):841-7

Calymmatobacterium granulomatis is the aetiological agent of granuloma inguinale - a chronic granulomatous genital infection - and is morphologically similar to members of the genus *Klebsiella*. This study determined the 16S rRNA gene sequence of *C. granulomatis* and the taxonomic position of the organism in relation to the genus *Klebsiella*. Genomic DNA was extracted from *C. granulomatis*-infected monocytes and from frozen and formalin-fixed paraffin wax-embedded tissue biopsy specimens from patients with histologically proven granuloma inguinale. The 16S rDNA was amplified by PCR with broad range oligonucleotide primers. The amplified DNA fragments were cloned into pMOS vector, digested with Bam HI and Pst I restriction endonucleases, hybridised with a gram-negative bacterial probe (DL04), sequenced in both directions by the automated ALF DNA sequencer, verified on an ABI Prism 377 automated sequencer and analysed with DNASIS and MEGA software packages. Sequence analysis revealed DNA homology of 99% in *C. granulomatis* from the different sources, supporting the belief that the bacteria in the culture and the biopsy specimens belonged to the same species, although there was some diversity within the species. Phylogenetically, the strains were closely related to the genera *Klebsiella* and *Enterobacter* with similarities of 95% and 94% respectively. *C. granulomatis* is a unique species, distinct from other related organisms belonging to the gamma subclass of Proteobacteria.

Treating donovanosis

Bowden FJ. Skov SJ. Aust Fam Physician. 1999; 28(11):1103-4

A letter critical of a case study appearing in: Aust Fam Physician. 1999 Jun;28(6):605

National guideline for the management of donovanosis (granuloma inguinale).

Clinical Effectiveness Group (Association of Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases).

Sex Transm Inf 1999; 75 Suppl 1:S38-9

Phylogenetic evidence for reclassification of *Calymmatobacterium granulomatis* as *Klebsiella granulomatis* comb. nov.

Carter JS, Bowden FJ, Bastian I, et al. Int J System Bacteriol 1999; 49 Pt 4:1695-700

By sequencing a total of 2089 bp of the 16S rRNA and *phoE* genes it was demonstrated that *Calymmatobacterium granulomatis* (the causative organism of donovanosis) shows a high level of identity with *Klebsiella* species pathogenic to humans (*Klebsiella pneumoniae*, *Klebsiella rhinoscleromatis*). It is proposed that *C. granulomatis* should be reclassified as *Klebsiella granulomatis* comb. nov. An emended description of the genus *Klebsiella* is given.

Diagnostic polymerase chain reaction for donovanosis

Carter J, Bowden FJ, Sriprakash KS. et al. Clin Inf Dis 1999; 28(5):1168-9

A brief report describing diagnosis, using 11 DNA extracts, using amplification of a 700-bp region of the *Klebsiella phoE* gene, encompassing the two unique base changes of *C. granulomatis*.

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Donovanosis. [Review, 23 refs]

Hart CA, Rao SK. J Med Microbiol 1999; 48(8):707-9

Intrapelvic donovanosis presenting as a psoas abscess in two patients.

Mein J, Russell C, Knox J, et al. SexTransm Inf 1999; 75(1):75-6.

Describes 2 cases of psoas abscess (confirmed histologically) in HIV negative aboriginal women.

[Granuloma inguinale (donovanosis)]. [Review, 15 refs] [Japanese]

Kojima H. Ryoikibetsu Shokogun Shirizu 1999; (25 Pt 3):14-7

Granuloma inguinale (donovanosis) presenting as a neck mass in an infant

Govender D. Hadley GP. Donnellan R. Pediatric Surgery International. 1999; 15(2):129-31

A case of granuloma inguinale (GI) presenting as a lateral neck mass in a 4-month-old, HIV-positive infant is described. The histological features of the mass were typical of GI, with numerous macrophages containing intracellular organisms with a "closed-safety-pin" appearance. This is a rare occurrence, and the mode of transmission of infection is discussed. An awareness of GI in infants by both clinicians and pathologists is important to prevent morbidity and allow for prompt institution of appropriate treatment.

Missing the diagnosis of donovanosis in northern Australia

Mein JK, Anstey NM, Bowden FJ. Med J Aust 1999; 170(1):48

A letter emphasising the importance of extragenital infection, citing cases of 7 month old infant admitted with cervical adenopathy and failure to thrive, 8 year old girl with granuloma of tooth socket, women undergoing hysterectomy for cervical cancer, granulomatous lesion detected on vaginal examination, perinephric abscess, and psoas abscesses.

Ultrastructure of Calymmatobacterium granulomatis: comparison of culture with tissue biopsy specimens

Kharsany AB, Hoosen AA, Naicker T, et al. J Med Microbiol 1998; 47(12):1069-73

The ultrastructural features of cells of *Calymmatobacterium granulomatis* from monocyte co-cultures and tissue biopsy specimens were compared. In cultures the bacteria were mainly extracellular, i.e., not within membrane-bound vacuoles. The bacterial body was surrounded by a uniformly extensive homogeneous layer with a relatively high electron density. This layer varied considerably in tissue biopsy specimens, having either homogeneously electron-dense or delicate web-like structures with varying density and thickness. In tissue specimens the bacteria were located predominantly within vacuoles of varying sizes in the cytoplasm of the macrophages and, occasionally, extracellularly within the intercellular spaces of the stroma. The bacterial cytoplasm contained ribosomes scattered throughout with electron-dense granules located peripherally. The trilaminar cell-wall structure was typical of a gram-negative organism, comprising an outer membrane, a middle electron-opaque layer and an inner plasma membrane. Surface structures such as fimbriae, flagella and bacteriophages were not identified in specimens from either source.

Extragenital donovanosis of the foot

Rao MV, Thappa DM, Jaisankar TJ, et al. Sex Transm Inf 1998; 74(4):298-9

An extremely rare case of primary extragenital donovanosis affecting the dorsa of right foot is reported. Clinical and histopathological features of the disease are described and the rarity, absence of genital lesions, and consequent difficulty in diagnosis are discussed.

Is the eradication of donovanosis possible in Australia?

Bowden FJ, Savage J. Aust N Z J Public Health 1998; 22(1):7-9

The authors advocate the use of azithromycin to treat donovanosis. They cite the statement by The Commonwealth Minister of Health and Family Services, Dr. Michael Wooldridge, "Our aim is to eradicate.. (donovanosis)..from Australia by 2003, within 5 years", and list elements to be included in a successful eradication program: support from affected communities, central coordination of a national program, local coordination by suitably qualified health staff, good educational materials and programs, standardised protocols for diagnosis and management, freely available medications and diagnostics, better epidemiological data, ongoing research.

Extragenital donovanosis in a patient with AIDS

Sanders CJ. Sex Transm Inf 1998; 74(2):142-3

A case of extragenital donovanosis in a patient with AIDS is reported from Zimbabwe. Despite the rarity of donovanosis in Zimbabwe it is important that health workers are familiar with this disease since donovanosis increases the risk of HIV transmission and appropriate treatment is often successful even in patients with severe immunodeficiency.

Disseminated donovanosis (granuloma inguinale) causing spinal cord compression: case report and review of donovanosis involving bone. [Review, 36 refs]

Paterson DL. Clin Inf Dis 1998; 26(2):379-83

Donovanosis is a genital ulcer disease that occasionally has extragenital manifestations. This report describes a case of disseminated donovanosis in a 54-year-old woman from northern Australia who had subsequent thoracic vertebral osteomyelitis and spinal cord compression. Malignancy and vertebral tuberculosis were the major differential diagnoses. The patient had no genital lesions at the time of diagnosis of extragenital donovanosis but had undergone a hysterectomy, thus raising the possibility of prior disease of the uterine cervix (most previous cases have been associated with primary cervical disease). Despite treatment with doxycycline, she had no significant neurological improvement. Donovanosis disseminated to bone has been reported in 18 cases in the last 55 years. Awareness of donovanosis in the differential diagnosis of osteomyelitis and prompt pelvic examinations enabling early diagnosis of occult cervical disease are the most important measures in preventing morbidity and mortality due to disseminated donovanosis.

Surgical treatment of granuloma inguinale

Bozbor A, Erbil Y, Berber E, et al. *Br J Dermatol* 1998; 138(6):1079-81

Granuloma inguinale is an indolent, progressive, ulcerative and granulomatous skin disease caused by *Calymmatobacterium granulomatis*. It is generally treated with antibiotics. However, long-standing and complicated disease requires surgical treatment. Two patients with extensive and multiple perianal fistulas and abscesses unresponsive to medical treatment were managed with radical surgical resection. The first patient healed by primary intention, but a diverting colostomy was made for the second patient and the tissue defect was closed with a rotation flap. Follow-up at 4 years revealed the disappearance of the symptoms and the absence of recurrence in both patients.

Clinico-epidemiologic features of granuloma inguinale in the era of acquired immune deficiency ,
Shroff HJ, et al. *Sex Transm Dis* 1998; 25(4):196-200

BACKGROUND AND OBJECTIVES: Granuloma Inguinale (GI) is an endemic sexually transmitted disease (STD) in India. With increasing prevalence of human immunodeficiency virus (HIV) among patients with STD at a clinic in Mumbai, a study was conducted to determine clinico-epidemiologic features of GI and HIV. **GOAL:** To determine possible interaction between GI and HIV. **STUDY DESIGN:** Prospective follow-up of 21 consecutive cases (GI in HIV-seropositive individuals) and 29 controls (GI in HIV-seronegative individuals) to determine time to heal. All cases and controls received a standard treatment regimen of erythromycin, 2 g po daily, under supervision until healing occurred. **RESULTS:** Although GI ulcers at recruitment were not significantly larger among HIV-seropositive individuals as compared with those seen among HIV-seronegative individuals (mean size 4.4 cm² vs. 3.6 sq²; odds ratio [OR] 1.22, confidence interval [CI] .95, 0.63, 2.40; p = 0.52), the former took longer time to heal completely (mean 25.7 days vs. 16.8 days; OR 1.82, CI .95, 0.99, 3.36; p = 0.03) and tended to produce greater tissue destruction (as included in results). **CONCLUSION:** These findings are important because slow-healing GI ulcers with underlying HIV infection, which may be caused by their interaction, will lead to increased transmission of both the infections.

Disseminated granuloma inguinale secondary to cervical infection

Cliff S, Wilson A, Wansborough-Jones M, et al. *J Inf* 1998;36(1):129-30

Granuloma inguinale and HIV: a unique presentation and novel treatment regimen

Manders SM, Baxter JD. *J Amer Acad Dermatol* 1997;37(3 Pt 1):494-6

A case report of a 20-year-old United States man with penile ulcer for 5 months. He had been unsuccessfully treated with doxycycline, erythromycin, ceftriaxone and cephalexin. He tested positive for HIV-1, and showed intracytoplasmic inclusions in histiocytes on a Giemsa stained biopsy. Trimethoprim-sulphamethoxazole produced substantial improvement over 2 months. The addition of ofloxacin (400 mg daily) produced clinical cure in 5 months.

Culture of the causative organism of donovanosis (*Calymmatobacterium granulomatis*) in HEp-2 cells

Carter J, Hutton S, Sriprakash KS, et al. *J Clin Microbiol* 1997; 35(11):2915-7

We report successful culture of *Calymmatobacterium granulomatis* by standard cell culture methods. Swabs were obtained from lesions in three patients with a clinical diagnosis of donovanosis. For two patients, there was histological confirmation of the disease (i.e., the presence of Donovan bodies in Giemsa-stained smears). Specimens were inoculated onto cycloheximide-treated HEp-2 cell monolayers in RPMI 1640 medium (supplemented with fetal calf serum, NaHCO₃, vancomycin hydrochloride, and benzylpenicillin). At 48 h, organisms resembling Donovan bodies were identified in monolayer cultures from all three specimens. The organisms appeared as pleomorphic bacilli with characteristic bipolar staining and "safety pin" appearance. Using a PCR designed to differentiate *C. granulomatis* from the *Klebsiella* species (which have a high degree of molecular homology), we were able to demonstrate that the cultured organisms produced a PCR product identical to that obtained from the original swab specimens. It is now possible to test in vitro susceptibility of *C. granulomatis* to antibiotics and to provide a ready source of DNA and antigenic material to enable the development of serological tests and, possibly in the future, a vaccine.

Failure of trimethoprim in the treatment of donovanosis

Birchistle K, Greig J, Hay P. *Genitourin Med* 1997; 73(3):224-5

Describes a case of failed trimethoprim treatment for 3 weeks, successfully treated with 6 week course of doxycycline.

Bowden FJ, Savage J Comment in: *Sex Transm Infect.* 1998 ;74(1):78-9 on the difficulty of compliance with long durations of doxycycline and recommend use of azithromycin.

Granuloma inguinale (donovanosis): an unusual cause of otitis media and mastoiditis in children

Govender D, Naidoo K, Chetty R. *Amer J Clin Pathol* 1997;108(5):510-4

Granuloma inguinale (donovanosis) is seen predominantly in adults (it rarely occurs in children) and mainly affects genital skin and mucosa. Infection occurs at other skin and mucosal sites, and hematogenous dissemination to bone also has been described. The infection responds dramatically to appropriate antibiotic treatment. We present two cases of granuloma inguinale occurring in children (8 months and 5 months of age) causing mastoiditis and external ear discharges. A temporal lobe abscess also developed in the 8-month-old child. Subsequent computed tomography scans showed marked improvement in the brain lesion after treatment. The second child had a polypoid mass in the middle ear that on biopsy showed the features of granuloma inguinale. The mother of this child had biopsy-proven granuloma inguinale of the uterine cervix. These cases indicate that granuloma inguinale can be transmitted during vaginal delivery, and careful cleansing of neonates born to infected mothers is recommended.

Donovanosis: treatment with azithromycin

Morles CA, Hernandez I, Ferreiro MC. *Int J STD & AIDS* 1997; 8(1):54-6

In June 1994 a man with perianal donovanosis for 6 months was treated with azithromycin 1 g stat followed by 500 mg daily for a further 4 days. The lesion had completely resolved after 1 week. Previous treatment with several doses of crystalline penicillin did not stop progression of the lesion.

Comment on this article by Bowden FJ, Savage J. *Donovanosis: treatment with azithromycin.* *Int J STD & AIDS* 1998; 9:61-2

Disputes that Morles et al were the first to use azithromycin as they had been using it since 1994 and cite 3 publications from 1995-1996 in support.

Dr Morles replied that his patient had been treated on 28 June 1994, and the findings were presented to a scientific meeting on 23-26 November 1994.

The dark side to Donovanosis: color, climate, race and racism in American South venereology.

[Review, 129 refs]

Hammar L. *Journal of Medical Humanities* 1997; 18(1):29-57

Medical experimentation on humans with "classic" sexually transmitted diseases (e.g., syphilis, gonorrhea) is not generally well known, but experimentation with others such as Granuloma inguinale, or Donovanosis, is even less so. Endemic to non-existent here, hyper-epidemic there, between 1880 and 1950 Donovanosis was linguistically and morally "constructed" as a disease of poor, sexually profligate, tropical, darkly-skinned persons. It was also experimentally produced on and in African-American patients in many charity hospitals in the American South. This essay analyzes Donovanosis literature of the period that heavily featured skin color, climate and tropicity, venereal sin, and racial susceptibility. It then recounts the history of human experimentation with it, and explains both its linguistic construction and its biomedical experimental history in terms of "disease narratives" produced not only by but for venereologists.