Tropical Genital Ulcer Disease

BASHH
Module 1: epidemiology of STIs and Bacterial infections
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Learning Objectives

1. Understand the epidemiology of Genital Ulcer Disease (GUD)
2. Understand the implications for aetiology and differential diagnosis of GUD in different settings
3. Describe the management of GUD in resource poor settings
4. Understand the strengths and weaknesses of syndromic management of GUD
5. Explore the implications for sexual health clinicians in the UK
Case study

• 22 year old male undergraduate student
• Presents to central London Sexual Health Clinic
• 7 day history of genital ulcer
• Moderate pain
• LSI 12 days ago UPVI and UPOI with RFP
• No other SI over past 3 months
• No other partners for over a year
• No male partners
• No PMH or DH of note

With your neighbour discuss

• What is the DDx?
• What is the most likely diagnosis?
• What else do you want to know?
• What tests will you do
Primary Genital herpes

- Commonest cause of genital ulceration in the UK
- Incubation period 4 days (2-12 days)
- Primary episode can last 2 weeks
- Primary episode is usually painful and associated with systemic symptoms
Further probing

- He has been on his year off
- RFP also a student on her year off – both white British from the SE
- He travelled around SE Asia with his RFP and then they parted ways
- She went to Malawi, Zimbabwe, and South Africa
- He travelled through Southeast Asia down to the Pacific islands and Papua New Guinea
- Took intermittent Doxycycline for malaria prophylaxis
- Then met up two weeks ago and had UPSI
- On direct questioning
  - Did not pay for sex,
  - No other SI with anyone including oral sex

With your partners ..

- What else enters the DDx?
- What will you test for?
- How will you manage this case?
Differential diagnosis

- Genital herpes (1 or 2)
- Primary Syphilis
- **Chancroid**
- **Donovanosis**
- LGV
- Other aetiologies
  - Non STI viruses e.g. EBV, VZV, CMV
  - TB
  - Behcet's
  - Trauma
  - Fixed drug eruption
  - Carcinoma
  - Dermatological conditions

What will aid your diagnosis

- Epidemiology
- Clinical manifestations
Estimates of the number of people (in millions) with prevalent HSV-2 infection in 2012, by age, sex and WHO region.


https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0114989
Estimated prevalence (and 95% UI) of chlamydia, gonorrhoea, trichomoniasis, and syphilis in women and men aged 15–49 years by WHO region, based on 2005–2012 data.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0143304
Epidemiology of Chancroid

- Very sensitive to antibiotics
- Need high rates of partner exchange to sustain
- Epidemics in western Europe and N. America USA which declined before antibiotics and faster than syphilis
  - Attributed to female empowerment and reduced male migration => change in nature of sex work
  - 1995 < 1 in 250 ulcers UK were Chancroid, donovanosis or LGV
- Rapid declines in Thailand, Kenya, and Senegal
  - Attributed to Sex Work interventions, better STI treatment access and circumcision

Prevalence and Associations of Genital Ulcer and Urethral Pathogens in Men Presenting With Genital Ulcer Syndrome to Primary Health Care Clinics in South Africa

David A. Lewis, FRCP(UK), PhD,*† Etienne Müller, PhD,* Lisa Steele, PhD,‡ Mayia Sternberg, PhD,§ Frans Radebe, MSc,* Michael Lyall, MB, ChB,*‡ Ronald C. Ballard, PhD,* and Gabriela Paz-Bailey, MD, PhD‡§

613 men with GUD:
- Genital HSV = most common, 73.6%
  (HSV2 = 98.2%)
- Syphilis = most common bacterial cause (4.9%),
  **Chancroid (10 cases, 1.6%)**
- LGV (8 cases, 1.3%).
200 men with GUD:
HSV-2, 28%; T. pallidum, 11.5%; C. trachomatis, 3%; HSV-1, 0.5%;
and H. ducreyi, 0%.
First case of chancroid in 14 years at the largest STI clinic in Paris, France

Sébastien Fouéré¹, François Lassau¹, Clotilde Rousseau³, Martine Bagot¹ and Michel Janier¹

Abstract
We report the first case of chancroid seen at our clinic in 14 years. It was diagnosed by nucleic acid amplification test in a male patient returning from Madagascar. Although the disease is considered on the verge of disappearance even in tropical countries, its real potential for reemergence — due to new strains of Haemophilus ducreyi, underreporting and a lack of widespread use of molecular testing — could be underestimated.

Chancroid – desperate patient makes own diagnosis

P Barnes and M Chauhan

Abstract
We report a case of chancroid in a white heterosexual man in the United Kingdom. This patient was seen by four separate health services over a period of five weeks with excruciatingly painful penile ulcers. Despite several negative herpes simplex virus polymerase chain reaction tests and a self-diagnosis of chancroid, he was repeatedly offered multiple courses of aciclovir. This case highlights the need for awareness of alternative diagnoses in persistent cases of genital ulcer disease.
CHANCROID
Aetiology

• *Haemophilus ducreyi* (gram negative bacteria)

• Fastidious organism difficult to isolate

• Requires supplemented chocolate agar and 5% CO$_2$ for growth

CLINICAL MANIFESTATIONS

• Incubation period 5-7 days

• A papule develops initially but goes on to erode into a painful, soft, and non-indurated ulcer with necrotic base
  – → *soft chancre*

• 50% of patients will develop painful local adenopathy which may suppurate or rupture
Chancroid ulcers
Chancroid Male - regional adenopathy

Clinical features in men
Clinical features in men
Clinical features in men
Clinical features in men
Clinical features in men
Clinical features in women

• The usual sites of infection are:

• Labia minora
• Fourchette

• Sometimes,
  – Vaginal wall
  – Cervix
Clinical features in women
C, D) Skin ulcers in children from Papua New Guinea

Diagnosis

- PCR has improved diagnostic sensitivity for chancroid
- No FDA approved commercial PCR
- Culture has been shown to be 75% sensitive in comparison to M-PCR
Chancroid - gram stain of *H. ducreyi*

Chancroid and HIV

Chancroid is a significant risk factor for HIV seroconversion

HIV+ individuals may have:

- increased numbers of ulcers
- longer ulcer healing times
- atypical ulcer appearances
Other management

• Single dose azithromycin or ceftriaxone
  – Ciprofloxacin and erythromycin are alternatives – use for 3 days

• Partner notification-
  – Give epidemiological treatment

• Abstain from sex until complete healing

Donovanosis
Epidemiology of Donovanosis

- Rare in Western Europe and North America

- Endemic in pockets e.g. parts of India, Papua New Guinea, the Caribbean, central Australia and southern Africa

- Low infectivity but long incubation

- Reduced in circumcision

Donovanosis (Granuloma inguinale)

Aetiology

- Intracellular gram negative bacteria *Klebsiella granulomatis* (previously called *Calyymmatobacterium granulomatis*)

- Chronic, progressively destructive bacterial infection of the genital region
Donovanosis - other terminology

- Granuloma inguinale
- Granuloma venereum
- Lymphogranuloma inguinale
- Granuloma genito-inguinale
- Granuloma contagiosa
- Granuloma Donovani
- Granuloma inguinale Tropicum
- Ulcerating granuloma of the pudenda
- Serpiginous ulceration of the groin
- Infective granuloma
- Chronic venereal sores
- Ulcerating sclerosing granuloma
- Granuloma venereum genito-inguinale

Donovanosis – clinical features

- 50-day incubation period
- Painless
- Slowly progressive
- Ulcerative lesions
- Highly vascular – beefy red and contact bleeding
- No lymphadenopathy
- But Sub cutaneous granulomas (pseudobuboes)
- Extranodal dissemination in 10% of cases
Clinical Features: variants

- Ulcerogranulomatous- classical lesion- beefy red ulcer- bleeds to the touch
- Hypertrophic
- Necrotic
- Sclerotic

Clinical Features: sites of infection

- Genital in 90%
- Inguinal 10%
- Extragenital - lip, gums, palate
- Haematogenous spread to liver, bone
- Pregnancy: lesions progress more rapidly
Clinical features in men

• The usual sites of infection are:
  - Prepuce
  - Coronal sulcus
  - Frenulum
  - Glans

Typical beefy red donovanosis penile ulcer.

O’Farrell N Sex Transm Infect 2002;78:452-457
Hypertrophic donovanosis ulcer with a regular margin.

Clinical features in men
Clinical features in men

Clinical features in men

 Globalskinmeds.com
Dr. Tabua, Chief Medical Officer from Port Moresby, PNG

Courtesy CDC/Joe Miller
malignant transformation
Autoamputation

Extranagenital lesions

Dr. Tabua, Chief Medical Officer from Port Moresby, PNG
Clinical features in women

• The usual sites of infection are

• Labia minora
• Fourchette

• Sometimes,
  – Vaginal wall
  – Cervix

Fig. 7.6.9.1 Characteristic serpiginous ulcer in female patient with long-standing donovanosis.

J. Richens
Oxford Textbook of Medicine: Intracellular klebsiella infections (donovanosis and rhinoscleroma)
Untreated

- Genital elephantiasis
- Vaginal, urethral and anal stenosis
- Malignancy

Donovanosis and squamous cell carcinoma: The relationship conundrum!
Arora AK et al

Diagnosis

• Difficult to culture

• Visualise dark staining **Donovan bodies** on Giemsa or Leishman stain of tissues
  – crush prep

• Silver stain of biopsy

• PCR tests available but none FDA approved
Treatment

- No RCTs
- Prolonged
  - Azithromycin 500mg daily for three weeks
  - Azithromycin 1g weekly for three weeks
  - Doxycycline 100 mg BD for three weeks or more
  - Erythromycin and Septrin are alternatives
  - Gentamicin
- Until lesions heal
- No evidence for empirical treatment of partners
- Partners should be followed up for 60 days after contact

Donovanosis and HIV

- HIV acquisition associated with long-standing ulcers
- Ulcers take longer to heal in HIV-positive subjects
Indications for syphilis treatment:
- RPR positive; and
- Patient has not been treated for syphilis recently.

Treat for HSV2 where prevalence is 30% or higher, or adapt to local conditions.

- Patient complains of a genital sore or ulcer
  - Take history and examine
    - Only vesicles present?
      - Yes
        - TREAT FOR HSV2
          - TREAT FOR SYPHILIS IF INDICATED
            - Educate and counsel
              - Promote condom use and provide condoms
              - Offer HIV counselling and testing if both facilities are available
            - TREAT FOR HSV2
              - TREAT FOR SYPHILIS AND CHANCROID
            - TREAT FOR HSV2
            - TREAT FOR SYPHILIS IF INDICATED
        - No
          - Sore or ulcer present?
            - Yes
              - TREAT FOR SYPHILIS
                - TREAT FOR HSV2
              - Educate and counsel
                - Promote condom use and provide condoms
                - Offer HIV counselling and testing if both facilities are available
            - No
              - Ulcer(s) healed?
                - Yes
                  - Continue treatment for a further 7 days
                - No
                  - Ulcer(s) improving?
                    - Yes
                      - Refer
                    - No
                      - Educate and counsel
                        - Promote condom use and provide condoms
                        - Offer HIV counselling and testing if both facilities are available
                        - Ask patient to return in 7 days

Indications for syphilis treatment:
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- Patient has not been treated for syphilis recently.

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Why Syndromic Management?

Syndromic management is based on identification of consistent groups of symptoms, easily recognized signs (syndromes) AND the provision of treatment that will deal with the majority OR most serious of organisms responsible for syndrome.

Few low and middle income countries health facilities have laboratory equipment or skills for aetiological diagnosis of STIs.

Thus the syndromic approach to STI management was born, to overcome these constraints & challenges!

Why the Syndromic Management?

<table>
<thead>
<tr>
<th>Etiologic</th>
<th>Clinical</th>
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<tr>
<td>• Testing facilities not available</td>
<td>• Specialist training</td>
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<tr>
<td>• Testing facilities at other sites</td>
<td>• High clinical skill</td>
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<tr>
<td>• Expensive</td>
<td>• Mixed infections overlooked</td>
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<tr>
<td>• Time consuming</td>
<td>• Signs &amp; symptoms not specific</td>
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<tr>
<td>• Immediate treatment</td>
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<td>• Mixed infections overlooked</td>
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Why Syndromic Management?

Bogaerts et al. (1995) in Rwanda compared sensitivity of 3 approaches for patients with genital ulcers:
1. treated for chancroid AND syphilis without lab tests
   • Correctly managed 99%
2. Choice of treatment based on lab test for syphilis
   • Correctly managed 82.1%
3. Treatment indicated on clinical diagnosis alone without laboratory tests
   • Correctly managed 38.3%

Conclusion: A simple syndromic approach should be used for case management.

Why Syndromic Management?

**Correct diagnosis**

Using the syndromic approach:
• 70% of genital ulcers correctly diagnosed
  (Dangor et al. 1990).
• 40% chancroid & 24% syphilis correctly diagnosed
  Nairobi, Kenya

**Cure rates**

Studies from Zambia and Côte d’Ivoire report cure rates of:
87–97% for vaginal discharge
92–97% for male urethral discharge
82–100% for female GUD
69–100% for male GUD.

(La Ruche et al. 1995; Hanson et al. 1996)
### Why Syndromic Management?

**Impact on HIV**

**Mwanza Intervention Trial:** Communities randomly allocated to receive improved STI case management

- 42% reduction in HIV incidence (Grosskurth et al. 1995)
- 30–50% reduction active syphilis and symptomatic male urethral discharge prevalence (Mayaud et al. 1996).

Syndromic management achieved clinically assessed cure rates of:

- 91% in Abidjan (La Ruche et al. 1995)
- 96–98% in Mwanza (Mwijarabi & Mayaud 1997).

**Cost**

- With other approaches atypical clinical features, false negative results or mixed infections may be inadequately managed.

- Patients may return for further investigation, suffer prolonged morbidity and re-treated

  - **AT FURTHER COST**

- The cost per patient cured by the concomitant syndromic approach may be cheaper (Islam et al. 1994).

### Changing WHO recommendations on syndromic management:

[Advisory Group Meeting reviews and updates STI treatment recommendations in the light of recent developments.](#)

<table>
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<tr>
<th>Year</th>
<th>Recommendations</th>
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<td>1991</td>
<td>WHO recommends comprehensive management of STIs within context of HIV and STI control, prevention and care programmes</td>
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<td>1996</td>
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<tr>
<td>2001</td>
<td>New guidelines included syndromic management of genital ulcer disease and vaginal discharge due to new findings. E.g. HSV2 identified as main cause of genital ulcers</td>
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<td>2004</td>
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| 2016 | Updated due to concerns of resistance
(1) Strategy towards ending STIs by 2030
(2) STI guidelines as individual infections
Moving away from syndromic approach! |
HOW CAN WE IMPROVE?

How can we improve?

• Add things to the algorithm – to improve predictive value, sensitivity and specificity
  1. Risk assessment
  2. Some tests
  3. Point of care tests

• Presumptive treatment in high prevalence groups
Back to case

• What would you do?

Back to case

• Herpes is common ➔ Treat for herpes
• PCR for HSV 1-2 and syphilis

• Herpes 2 positive and syphilis negative
• Responded to presumptive herpes treatment

• If had not responded would have done PCR for chancroid
Learning Objectives

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4. Understand the strengths and weaknesses of syndromic management of GUD
5. Explore the implications for sexual health clinicians in the UK