CHAPTER 25

SEXUALLY TRANSMITTED INFECTIONS

SEXUALLY TRANSMITTED INFECTIONS MANAGED AT SECONDARY LEVEL OF CARE

These guidelines apply to patients who are referred from primary healthcare centres for further investigation and management of **persistent** STI symptoms or syndromes that have not improved or resolved and are still present 7 days after administration of standard first-line syndromic therapy.

25.1 MALE URETHRITIS SYNDROME (MUS)

A64 + N34.1

Male urethritis/ visible urethral discharge that persists despite appropriate syndromic management should be investigated for suspected ceftriaxone-resistant gonorrhea. Referral letter from PHC should include all relevant information (including HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» It is essential to confirm ceftriaxone-resistant gonorrhea.
» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.
» Genital specimen collection and test requests (to confirm presence of any STI pathogens and if *Neisseria gonorrhoeae* present, and determine ceftriaxone susceptibility):
  – *Materials:* Two Dacron swabs (wire shaft, slender tip); Amies transport medium (all obtained from local NHLS laboratory).
    > Urethral swab 1: Gently insert 2cm into the urethral meatus, and rotate for 5-10 seconds. Place this swab immediately into Amies transport medium.
    > Test request: Transport on ice to local NHLS laboratory as soon as possible, preferably within 24 hours for *Neisseria gonorrhoeae* culture and sensitivity testing. (Contact laboratory for directions on transport of specimens).
    > Presumptive diagnosis: Persistent urethritis due to possible ceftriaxone-resistant gonorrhea.
    > Urethral swab 2: Gently insert 2cm into urethral meatus, and rotate for 5-10 seconds. Place in a sterile universal container or tube, cut off the wire shaft and close the container.

> *Test request:* transport on ice to NICD STI reference laboratory as soon as possible for PCR genital discharge pathogens.
> Presumptive diagnosis: Persistent urethritis due to possible ceftriaxone-resistant gonorrhea.

MEDICINE TREATMENT

Persistent urethral discharge after 7 days confirmed on examination, pending results:

- Ceftriaxone, IM, 1 000 mg immediately as a single dose.
  - Dissolve ceftriaxone 1 g in 3.6 mL lidocaine 1% without adrenaline (epinephrine).

LoE: III[i]

AND

LoE: III[ii]

- Azithromycin, oral, 2 g as a single dose.

LoE: III[iii]

Severe penicillin allergy: Z88.0

- Gentamicin, IM, 6 mg/kg, IM as a single dose. (See Appendix II for guidance on prescribing).

AND

LoE: III[iv]

- Azithromycin, oral, 2 g as a single dose.

Ask patient to return in two weeks for follow-up of laboratory results and further clinical evaluation. Treat accordingly.

25.2 VAGINAL DISCHARGE SYNDROME (VDS)

B37.3/N76.0/N89.8

Abnormal vaginal discharge that persists despite appropriate syndromic management should be investigated. Referral letter from PHC should include all relevant information (including HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.
» Genital specimen collection and test requests (to confirm presence of STI pathogens and if *Neisseria gonorrhoeae* is present, and determine ceftriaxone susceptibility):
  – *Materials:* One cotton-tip swab (plastic shaft); two Dacron swabs (plastic shaft, slender tip); Amies transport medium (all obtained from local NHLS laboratory). Insert speculum to visualize cervix.
  – *Endocervical swab 1:* Gently insert Dacron swab 2cm into the endocervical canal, and rotate for 5-10 seconds. Place this swab immediately into Amies transport medium.

  - > *Test request:* Transport on ice to local NHLS laboratory as soon as possible, preferably within 24 hours for *Neisseria gonorrhoeae* culture & sensitivity testing.
  - > *Presumptive diagnosis:* Persistent cervicitis due to possible ceftriaxone-resistant gonorrhea.
- *Endocervical swab 2*: Gently insert Dacron swab 2cm into the endocervical canal, and rotate for 5-10 seconds. Place in sterile universal container or tube, break off plastic shaft and close the container.
  - > *Test request:* Transport on ice to NICD STI Reference laboratory as soon as possible for PCR genital discharge pathogens.
  - > *Presumptive diagnosis:* Persistent cervicitis/vaginal discharge due to possible ceftriaxone-resistant gonorrhea.
- *Vaginal swab1*: Gently insert cotton-tip swab into the vagina and then dip swab in the poster fornix fluid. Place swab in sterile universal container or tube, break off plastic shaft and close the container.
  - > *Test request:* Transport to local NHLS laboratory as soon as possible for M/C/S - for bacterial vaginosis; *Candid*a culture and sensitivity testing.
  - > *Presumptive diagnosis:* Persistent vaginal discharge due to bacterial vaginosis or candidiasis.

MEDICINE TREATMENT

Persistent cervicitis confirmed on speculum examination, pending results:

- Ceftriaxone, IM, 1 g immediately as a single dose.
  - o Dissolve ceftriaxone 1 g in 3.6 mL lidocaine 1% without adrenaline (epinephrine). *LoE: III[v]*

AND *LoE: III[vi]*

- Azithromycin, oral, 2 g as a single dose.

If metronidazole, oral was not given at PHC prior to referral administer:

- Metronidazole, oral, 2 g as a single dose. *LoE: III[vii]*

Severe penicillin allergy: Z88.0

- Gentamicin, IM, 6 mg/kg, IM as a single dose. (See Appendix II for guidance on prescribing).

AND *LoE: III[viii]*

- Azithromycin, oral, 2 g as a single dose.

If metronidazole, oral was not given at PHC prior to referral administer:

- Metronidazole, oral, 2 g as a single dose. *LoE: III[ix]*

Ask patient to return in two weeks for follow-up of laboratory results and further clinical evaluation. Treat accordingly.

25.3 GENITAL ULCER SYNDROME (GUS)

A60.9/A51.0

Genital ulcer disease that persists despite appropriate syndromic management should be investigated. Referral letter from PHC should include all relevant information (including HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.
» Genital specimen collection and test requests:
  – Materials: Two cotton-tip swabs (plastic shaft); one Dacron swab (wire shaft); glass slide, slide box (all obtained from local NHLS laboratory)
  – Cotton swab 1: Prior to taking specimen, roll a cotton-tip swab across the lesion gently to remove exudates from secondary infection and/ or debris in a way that minimizes bleeding. Discard cotton swab.
  – Cotton swab 2: Roll a second cotton-tip swab over the base of the ulcer, including the ulcer edges. Make a thin smear by rolling evenly over the centre of a labelled-glass slide to the size of a R2 coin. Air dry slide and place in slide box. Discard cotton swab.
  – Dacron swab: Collect material from base of ulcer lesion; place swab in sterile universal container or tube and cut off wire shaft. Close container.
    > *Test request:* Transport glass slide and Dacron swab on ice to NICD STI Reference laboratory as soon as possible for microscopy for Donovanosis and PCR genital ulcer pathogens.
    > *Presumptive diagnosis:* Persistent genital ulcer disease
» Venous blood specimen: 5 mL in serum separator tube for syphilis serology – send to local NHLS laboratory.

MEDICINE TREATMENT

Ask patient to return in two weeks for follow-up of laboratory results and further clinical evaluation. Treat accordingly, but note that syphilis does not require re-treatment if benzathine penicillin was used to treat GUS.

If the syndromic treatment at PHC used doxycycline instead of benzathine penicillin and syphilis is detected on PCR, treat with:

- Benzathine benzylpenicillin, IM, 2.4 MU immediately as a single dose.
  - Dissolve benzathine benzylpenicillin, IM, 2.4 MU in 6 mL lidocaine 1% without adrenaline (epinephrine).

LoE: III^{x}

Recurrent herpes

For frequent recurrences of herpes simplex (i.e. ≥4 episodes of clinically apparent reactivations per year), suppressive antiviral therapy may be considered.

- Antiviral (active against herpes simplex) e.g.: LoE: II[xi]
- Aciclovir, oral, 400 mg 12 hourly.
  - Review annually for ongoing suppressive therapy.

LoE: III[xii]

REFERRAL

If ulcer PCR results for STI pathogens are inconclusive and genital ulceration persists, refer to specialist for genital ulcer biopsy and histopathological examination to exclude a non-infectious cause, which includes cancer.

25.4 BUBO

A58

Buboes that persist despite appropriate syndromic management should be investigated. Referral letter from PHC should include all relevant information (i.e. HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.

» Genital specimen collection and test requests:
  Materials: One Dacron swab (wire shaft); 21-gauge sterile needle and syringe; two sterile universal containers or tubes (all obtained from local NHLS laboratory).

  1. If genital ulcer is present:

  – Dacron swab: Collect material from base of ulcer lesion; place swab in sterile universal container or tube and cut off wire shaft. Close container.
    > *Test request:* Transport Dacron swab on ice to NICD STI reference laboratory as soon as possible for PCR for chancroid and LGV.

  2. If genital ulcer is absent:

  – After topical disinfection, insert 21-gauge needle into bubo and aspirate pus into syringe. Transport pus in two sterile tubes/ containers to laboratory.
    > *Test request:* send one tube on ice to NICD STI reference laboratory as soon as possible for PCR for chancroid and Lymphogranuloma Venereum (LGV).
    > *Test request:* send one tube to local NHLS laboratory for bacterial M/C/S.
  – *Presumptive diagnosis:* Persistent bubo unresponsive to syndromic management.

MEDICINE TREATMENT

- Doxycycline 100 mg, oral 12 hourly for 21 days.

LoE: III[xiii]

Note: Follow-up until there is complete resolution of symptoms. Fluctuant buboes may require frequent needle aspiration to prevent rupture – review every 72 hours, as necessary.

For laboratory-confirmed diagnosis of LGV:

- Doxycycline 100 mg, oral 12 hourly for more than 21 days may be required for complete resolution of disease.

LoE: III[xiv]

References:

[i] Ceftriaxone (1000mg - MUS): Fifer H, Natarajan U, Jones L, Alexander S, Hughes G, Golparian D, Unemo M. Failure of Dual Antimicrobial Therapy in Treatment of Gonorrhea. NEJM 2016. 374;25: 2504-2506.

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[ii] Lidocaine 1%:MCC registered package inserts of Kocef® 250 mg, 500 mg, 1 g; Rociject® 500 mg, 1 g; Oframax® 250 mg, 1 g.

[iii] Azithromycin (2000mg - MUS): Bignell C, Unemo M; European STI Guidelines Editorial Board. 2012 European guideline on the diagnosis and treatment of gonorrhoea in adults. Int J STD AIDS.2013 Feb;24(2):85-92. https://www.ncbi.nlm.nih.gov/pubmed/24400344

[iv] Gentamicin, IM + azithromycin, oral: Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5;64(RR-03):1-137. Erratum in: MMWR Recomm Rep. 2015 Aug 28;64(33):924.https://www.ncbi.nlm.nih.gov/pubmed/26042815

[v] Ceftriaxone, IM + azithromycin: World Health Organisation: WHO guidelines for the treatment of *Neisseria gonorrhoeae*, 2016. http://apps.who.int/iris/bitstream/10665/246114/1/9789241549691-eng.pdf

[vi] Lidocaine 1%:MCC registered package inserts of Kocef® 250 mg, 500 mg, 1 g; Rociject® 500 mg, 1 g; Oframax® 250 mg, 1 g.

[vii] Metronidazole: Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5;64(RR-03):1-137. Erratum in: MMWR Recomm Rep. 2015 Aug 28;64(33):924.https://www.ncbi.nlm.nih.gov/pubmed/26042815

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[ix] Metronidazole: Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5;64(RR-03):1-137. Erratum in: MMWR Recomm Rep. 2015 Aug 28;64(33):924.https://www.ncbi.nlm.nih.gov/pubmed/26042815

[x] Benzathine benzylpencillin (GUS): World Health Organization. [ix]WHO guidelines for the treatment of Treponema pallidum (syphilis), 2016. http://www.who.int/reproductivehealth/publications/rtis/syphilis-treatment-guidelines/en/

[xi] Antiviral therapy, oral (recurrent herpes simplex): Le Cleach L, Trinquart L, Do G, Maruani A, Lebrun-Vignes B, Ravaud P, Chosidow O. Oral antiviral therapy for prevention of genital herpes outbreaks in immunocompetent and nonpregnant patients. Cochrane Database Syst Rev. 2014 Aug 3;(8):CD009036. https://www.ncbi.nlm.nih.gov/pubmed/25086573

[xii] Antiviral therapy, oral (recurrent herpes simplex): Workowski KA, Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5;64(RR-03):1-137. Erratum in: MMWR Recomm Rep. 2015 Aug 28;64(33):924. https://www.ncbi.nlm.nih.gov/pubmed/26042815

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[xiii] Doxycyline (21 days: Bubo): de Vries HJ, Smelov V, Middelburg JG, Pleijster J, Speksnijder AG, Morré SA. Delayed microbial cure of lymphogranuloma venereum proctitis with doxycycline treatment. Clin Infect Dis. 2009 Mar 1;48(5):e53-6. https://www.ncbi.nlm.nih.gov/pubmed/19191633

[xiv] Doxycyline (> 21 days: Bubo): Oud EV, de Vrieze NH, de Meij A, de Vries HJ. Pitfalls in the diagnosis and management of inguinal lymphogranuloma venereum: important lessons from a case series. Sex Transm Infect. 2014 Jun;90(4):279-82. https://www.ncbi.nlm.nih.gov/pubmed/24787368