Primary Care Management Protocols for Genital Ulceration and Urethritis

Andrew Murray

Summary
Information in medical textbooks is usually presented in a format determined by the subject matter and generally not in the manner most useful for clinical decision-making in primary care. The author repackages, for the clinician's use, information regarding genital ulceration and urethritis.

KEYWORDS: Problem Solving; Information Systems; Physicians, Family; Genital Diseases, Female; Genital Diseases, Male; Urethritis; Primary Health Care.

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A primary care clinician who needs some assessment or management information in order to deal with a patient with a certain problem often finds that the textbook chapters or review articles on the subject contain much unnecessary information. At the same time the information and perspectives that he does need are often not to be found in these sources. The reason for this is that the specialists who compile these sources of information have different perspectives of what information is necessary and they cannot adequately perceive the information needs of the primary care clinician.

An additional problem is that the disease and its complications are dealt with as a single clinical problem and the information is then presented in a way that is not applied. The clinician has to spend valuable time assessing which items of information apply to the problem. The traditional format of etiology, symptoms, signs, complications, special investigations and management, is followed, without much thought about the problem solving process that the clinician has to go through.

The following is an attempt to present an information source relating to different sexually transmitted diseases in a format where application of the information is more in line with the primary care clinician's problem-solving process. The first block of information is a summary of the assessment and management information, it explains the usual situation. The information that follows either expands that initial body of information or explains certain aspects of it. As one who is particularly interested in the repacking of information for our needs as primary care clinicians I would appreciate feedback on the usefulness or otherwise of this presentation.
## Assessment and Management of Genital Ulceration

### Protocol

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Management</th>
</tr>
</thead>
</table>
| **Syphilis**: Incubation period — 3-4 weeks  
— painless solitary raised indurated ulcer with regular margin and serous base (ulcers are often atypical)  
— bilateral discrete rubbery painless inguinal glands (usually atypical). | **Syphilis**: Always treat partner regardless of presence of symptoms — always educate patient about the disease, its complications and the need to change sexual behaviour — always do syphilis serology and follow patient up. Syphilis — primary and secondary — Benzathine penicillin 2,4 μg im into 2 sites (4ml/buttock) at 1 visit. |

| **Chancroid**: Incubation period — less than 1 week  
— multiple painful non-indurated ulcers with purulent bases which bleed easily and with ragged edges surrounded by a raised red margin (the ulcers are often atypical).  
— Inguinal glands — only present in 50%— often typical-enlarged painful matted red — usually unilateral but also bilateral — inguinal and at times also femoral (may cause groove sign) — abscess — sinus or ulcer. | **Chancroid**: Erythromycin 500mg three times/day for 5 days — aspirate inguinal abscesses — insert needle through healthy skin — may have to repeat aspiration every few (2-3) days. |

| **Herpes**: Primary episode much worse than recurrences and often associated with constitutional symptoms (fever and malaise) and lymphadenopathy.  
— Ulcer-prodrome of burning/itchy sensation — group of small (1-3mm) vesicles — forms painful superficial ulcers with a grey slough and erythematous halo — lesions coalesce and become crusted — may be localised or extensive — it may become secondarily infected — the cervix is often involved — may cause serous vaginal discharge.  
— Inguinal glands — transient, slightly painful and bilaterally enlarged. | **Herpes**: Acyclovir 200mg per os five times/day for 5 days — only for women with a primary episode who present during first week  
— Cotrimoxazole 160/800mg two times/day for 10 days.  
— Keep lesions dry and clean. |

| **LGV**: Incubation period — 3 weeks  
— Ulcer — often remains unnoticed — usually small with raised edges, painless and transient — it may have a purulent base.  
— Inguinal glands — present in 80%— often typical — enlarged painful matted red — usually unilateral but also bilateral — inguinal and at times also femoral (may cause groove sign) — abscess — sinus or ulcer. Constitutional symptoms may be present — also backache (pelvic adenitis). | **LGV**: Minocycline 100 mg twice/day for 2-3 weeks.  
— Aspirate inguinal abscesses — as for chancroid. |

| **Granuloma Inguinale**: Incubation period — indeterminate  
— Ulcer — raised, painless beefy red and velvety (granulomatous), indurated and with rolled edges — often satellite lesions which coalesce.  
— Inguinal glands — not involved but pseudobubos may form due to subcutaneous spread — may cause tissue destruction.  
— Scabies, Erosive Balanitis, Candida, Epithelioma, Tuberculosis etc. | **Granuloma Inguinale**: Minocycline 100 mg twice/day for 2-3 weeks. If diagnosis remains uncertain — treat for both syphilis and chancroid. |
### Assessment:

**Primary Syphilis — Treponema Pallidum**
- Incubation period — relatively long — usually 3-4 weeks (9-90 days)
- Ulcer (chancre) — macule to papule to a painless solitary raised indurated ulcer with a regular margin and a serous base — the features are often atypical or painful, multiple, non-indurated ulcers with purulent or bleeding base. If untreated it heals without a scar after 3-8 weeks.
- Inguinal glands — bilateral discrete rubbery and painless — the features are usually typical.
- Secondary syphilis — the onset is 6-8 weeks after the appearance of the chancre which is often (30%) still present — features include constitutional symptoms, generalized lymphadenopathy and mucocutaneous lesions (condylomata lata, skin rash which is usually macular but can be quite atypical).

**Chancroid — Haemophilus Ducreyi**
- Male:female ratio = 20:1
- Incubation period — short — usually less than one week.
- Ulcer — papules — pustules — multiple painful non-indurated ulcers with purulent bases which bleed easily and with ragged edges surrounded by a raised red margin — the ulcers are often atypical (eg single ulcers) and may be confused with herpes, syphilis or LGV.
- Inguinal glands — only present in 50% — often typical — enlarged painful matted red — usually unilateral but also bilateral — inguinal and at times also femoral (may cause groove sign) — abscess — sinus or ulcer.

### Management:

**Primary Syphilis — Treponema Pallidum**
- Treatment — stat dose preferred as compliance is then not a problem.
- Benzathine penicillin 2.4 mu imi into 2 sites (4 mu in each buttock) at single visit.
- If penicillin sensitive — give multidose treatment for 15 days eg: md
  - Erythromycin stearate 500 mg 4 times/day or tetracycline 500 mg 4 times/day or minocycline 100 mg 2 times/day.
- Routine treatment of all ulcers with penicillin is not advisable: — Make a specific (clinical) diagnosis if possible and treat appropriately.
- If the features are atypical, then treat for syphilis and other probable conditions (usually chancroid).
- Confirm the diagnosis serologically — RPR with a titre of ≥1:16 or a combination of a flow RPR titre (≤1:8) and a positive TPHA.
- Patient education guidelines:
  - About sexually transmitted infections and the need to change sexual behaviour.
  - The complications — congenital syphilis and tertiary syphilis (cardiovascular and neurosyphilis).
  - The importance of investigation and treatment of the contact(s) in order to prevent complications, reinfection and infection of contacts.
  - The necessity of follow-up serology after three months, especially if patients were treated with multidose therapy.

**Chancroid — Haemophilus Ducreyi**
- Treatment — it is not sensitive to penicillin — produces beta-lactamase.
- Erythromycin 500 mg three times/day for 5 days or
- Cotrimoxazole 160/800 mg two times/day for 10 days or
- Minomycin 100 mg two times/day for 10 days.
- If unable to distinguish from:
  - Syphilis — add benzathine penicillin or from
  - Herpes — prescribe cotrimoxazole for 10 days or from
  - LGV — erythromycin 500 mg four times/day or minocycline 100 mg twice/day for 14 days.
- Aspirate inguinal abscesses to prevent sinus or ulcer formation — insert needle through healthy skin — may have to repeat aspiration every few days.
DIAGNOSIS — usually clinical — it is a common disease — for definitive diagnosis do a culture (take a swab from the ulcer — plate it directly on the specific chancroid medium — place in a candle jar — incubate within 2 hours). Microscopy is not sensitive and no serological test is available.

- Treat sexual partner — women may have asymptomatic cervical ulcer or endocervicitis.
- Syphilis serology — mixed infections occur and the chancre may be masked.
- Patient education — explain that it is a STD and of the necessity of treatment of the sexual contacts — prevents reinfection.

Genital Herpes — Herpes Simplex Virus — usually Type 2 but also Type 1:

- Severity varies much — primary episodes are more severe (pain and duration of lesions) than recurrent episodes especially in women and in homosexuals with peri-anal lesions.
- Incubation period — relatively short — one week (2-20 days).
- Prodrome — itching or burning sensation — duration 1-2 days — followed in the initial episode by headache, fever, muscle aches and swollen glands.
- Ulcer — localised erythema — group of small (1-3 mm) vesicles which is transient (lasts 6-7 days) — forms painful superficial ulcers with a grey slough and erythematous halo (lasts 6-7 days) — lesions coalesce and become crusted — heals without scar after a week — it may become secondarily infected with delayed healing (3 weeks) — duration is much less with recurrent episodes (10 days versus 20 days) — may be localised or extensive and the cervix is often involved — may cause vaginal discharge.
- Inguinal glands — transient, slightly painful and bilaterally enlarged — especially during primary episode.
- May have history of:
  - Precipitating factors — emotional or physical stress, fever, sexual intercourse, certain stages of the menstrual cycle.
  - Recurrences — at regular frequent intervals or only infrequently.

DIAGNOSIS — usually clinical — definitive diagnosis is indicated in antenatal patients and when diagnosis is in doubt
- Viral isolation — take a swab as early during the course of the local lesion as possible — preferably during the vesicle stage — exert firm pressure on lesion while taking the swab — shake swab in virus transport medium to dislodge viruses — discard swab — place specimen bottle in ice and send to laboratory as soon as possible (within hours) — results may only be available after ten days (this may present a problem in antenatal screening). Transport medium lasts months if kept in refrigerator — colour should be pink if in good condition.
- Pap smears are usually sensitive and specific enough and results are...
immediately available — useful in follow-up of ante-natal patients.
— serology is of little value — raised IgM indicates reactivation but IgG
remains positive and cross reactivity occurs between HSV 1 and HSV 2.

| **Lymphogranuloma Venereum — Chlamydia Trachomatis Serotypes**
<table>
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<tr>
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<td><strong>Incubation period</strong> — relatively long — 3 weeks (1-6 weeks)</td>
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| **Primary lesion (ulcer)** often remains unnoticed and patient may present
| with inguinal lymphadenopathy and at times constitutional symptoms. |
| **Ulcer** — usually small with raised edges, painless and transient — it may
| have a purulent base — may be confused with chancroid. |
| **Inguinal glands** — present in 80% and often typical — onset gradual
| — enlarged painful matted red — usually unilateral but also bilateral
| — inguinal and at times also femoral (may cause groove sign) — abscess —
| sinus or ulcer. Pelvic adenitis in women may cause backache. |
| **Constitutional symptoms** (fever, malaise, headache) may accompany
| adenitis. |

**DIAGNOSIS** — usually clinical — the condition is endemic in Swaziland and
adjoining areas — for definitive diagnosis:
— culture — take a swab made from dacron from the ulcer or urethra (not
from aspirate of abscess) — shake swab in chlamidial transport medium
— discard swab — send as soon as possible to laboratory — could keep
specimen overnight at 4°C — a complement fixation test and micro-IF
serology is also useful.

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<td><strong>Incubation period</strong> — indeterminate — possibly 1-4 weeks.</td>
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| **Low infectivity, not common, presents late and largely restricted to
| lower socio-economic groups. |
| **Ulcer** — small painless papule — ulcerates and enlarges by
| subcutaneous spread — raised, painless, beefy red and velvety
| (granulomatous), indurated and with rolled edges — often satellite lesions
| which coalesce — may become secondarily infected — heals with a scar. |
| **Inguinal glands** — not involved but pseudobubos may form due to
| subcutaneous spread — may cause much tissue destruction. |
| **Constitutional symptoms** are absent. |

**DIAGNOSIS** — usually clinical — for definitive diagnosis do microscopy for
Donovan bodies — take a scraping of the base of the lesion — make a smear
on a slide — do not fix — send to lab for Giemsa stain. No serological tests
or culture available.

| **Lymphogranuloma Venereum — Chlamydia Trachomatis Serotypes**
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| — Aspirate inguinal abscesses to prevent sinus or ulcer formation — insert
| needle through healthy skin — may have to repeat aspiration every few
| days. |
| — Discuss — the need to treat sexual partner and
| — the problem of compliance with 14 day treatment and of complications
| such as gross destruction of perineal tissue. |

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| If severe infection — add — Streptomycin 1 gm/day for ten days.
FURTHER EXPANDED INFORMATION

SYPHILIS — regard all ulcers as possibly syphilitic (even if the features seem typical of another condition) until serologically proven otherwise (note that serology may be negative at time of presentation) — chancres are often atypical and features may be changed by a mixed infection.

SYPHILIS SEROLOGY

SeroDiagnosis

AVAILABLE TESTS
— non-specific (non-treponemal) tests — RPR or VDRL
— sensitive but not specific although high titres (≥1:16) are almost always due to syphilis.
— specific (treponemal) tests — TPHA or FTA ABS (IgM & IgG).

INTERPRETATION OF THE RPR AND TPHA TESTS
— A positive RPR with a titre of ≥ 1:26 is serological evidence of primary or secondary syphilis — the RPR becomes positive ~4 weeks after infection and this titre is almost always diagnostic of active infection — confirm the diagnosis with TPHA test if the RPR titre is ≥1:8 as low RPR titres may be false positive (due to many different factors — see below).
— Tests may be negative early during clinical course when the chancre is already present — retesting after adequate treatment is not indicated as treatment will stop further antibody production and serological tests will therefore stay negative.
— If the RPR titre is low (≤1:18) and TPHA is positive and there are not clinical features of primary or secondary syphilis, then it should be considered that the patient has late latent syphilis (treat as for tertiary syphilis) unless there is reliable historical evidence that the duration of infection is less than two years in which case the condition is that of early latent syphilis (treat as for primary syphilis).
— If the RPR is negative and the TPHA is positive it indicates that the patient has had syphilis but was cured — TPHA remains positive permanently.
— False positive RPR tests may have to be investigated as it may be due to SLE, rheumatoid arthritis, cirrhosis, hepatitis, psoriasis, leprosy, active pulmonary tuberculosis, malaria and various viral infections.

EVALUATION OF RESPONSE TO TREATMENT
— consider with multidose regime.
— Adequate treatment during primary and secondary stages will reduce or eliminate the reactivity of RPR (FTA IgG and TPHA remains positive).
— If treated during primary stage — RPR — non-reactive after 6-12 months. If treated during secondary stage — RPR — non-reactive after 12-18 months.

ASSESSMENT AND MANAGEMENT OF URETHRITIS

PROTOCOL

Assessment

Early symptoms and signs
Have a high index of suspicion as symptoms may be very mild — 10% are asymptomatic.
— History of penile discharge and dysuria.
— On milking urethra scanty discharge may only just be noticeable or even absent.

Minimal criteria
— Evidence of urethra discharge (history, inspection, microscopy, culture)
— Sexual partner with diagnosis of cervicitis or PID.

Management

Antibiotic treatment
— Should always be effective against both N. gonorrhoea and C. trachomatis
— Procin pen 4,8 mu imi stat plus Probenicid 1 gm per os plus
— Minocycline or doxycycline 100 mg twice daily or tetracycline 250 mg 6 hourly for at least 7 days (preferably 10 days) starting the following morning (penicillin is bacteriocidal and tetracycline is bacteriostatic).
— If allergic to penicillin — minocycline or doxycycline 100 mg twice daily or tetracycline 500 mg four times daily for 7-10 days.
— If urethritis is complicated by eg epididymo-orchitis, peri-urethral infection or prostatitis — extend duration of treatment
— Minocycline or doxycycline 100 mg twice daily or tetracycline 500 mg four times daily for 10-14 days.
— If patient cannot tolerate tetracyclines — use erythromycin at same doses.

Patient education guidelines
— How he contracted the disease.
— The complications in both male and especially female and the fact that the incidence of complications increases with the number of recurrences.
— The importance of compliance — give detailed instructions.
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— The need to abstain from coitus until both partners' treatment is completed in order to prevent reinfection unless both are on simultaneous treatment.
— The necessity of treating the partner as soon as possible regardless of whether she has symptoms (or signs on examination) of cervicitis or PID as many (50%) of infected females are asymptomatic.
— The need for him (or his partner) to change sex behaviour — eg faithful in marriage — discuss implications of having multiple partners.
— The importance of follow-up especially if any symptoms persist (PGU)

Persistance or recurrence of urethritis after adequate treatment
— Reinfection by the same (untreated or inadequately treated) partner or by another partner — always examine and treat the partner(s).
— Poor compliance — find the reason eg poor communication and understanding, extended multidose oral medication or drug side-effects.
— Organism not sensitive to prescribed antibiotic eg
— U. urealyticum not sensitive to tetracycline — prescribe erythromycin.
— Beta-lactamase producing N. gonorrhoea (10%) — Spectinomycin 2g imi stat
— Trichomonas vaginalis — metronidazole 2g stat.
— Candida albicans — ketoconazole per os and imidazole cream on penis.
— Herpes genitalis and other intra-urethral ulcers. Always do a culture and sensitivity on persistent or recurrent infections as well as microscopy of wet mounts to search for trichomonas and candida.
— Descending infection from lower urinary tract due to urethral stricture.
— Concomitant pharyngeal and/or rectal gonococcal infection — not common — consider taking swabs for culture — most urethritis regimens excluding spectinomycin are effective in curing these infections.

FURTHER EXPANDED INFORMATION
Assessment and Management Rationale
ASSUME AND TREAT ALL CASES OF URETHRITIS AS A MIXED INFECTION OF N. GONORRHOEA AND C. TRACHOMATIS
— Urethritis may be caused by N. gonorrhoea, C. trachomatis, Ureaplasma urealyticum, Candida albicans, Trichomonas vaginalis and intra-urethral ulcers such as Herpes genitalis.
— Mixed infections of N. gonorrhoea and non-gonococcal organisms (NGU) are common (20%). Chlamidia trachomatis is usually the cause of NGU (60%)
— Clinical features may give some indication which organism is involved but are too unreliable to base management decisions on.
— Definitive diagnosis of N. gonorrhoea (gram stain or culture) does not exclude presence of C. trachomatis.
— Laboratory facilities for the diagnosis of C. trachomatis are not available to most clinicians
— Complications in males and females of infections caused by N. gonorrhoea and NGU (usually C. trachomatis) are equally common and equally severe.

DO A CULTURE AND SENSITIVITY ON ALL CASES WITH PERSISTENT URETHRITIS TO ESTABLISH IF N. GONORRHOEA IS THE ORGANISM INVOLVED AND IF IT IS RESISTANT ESPECIALLY TO PENICILLIN
The pattern of resistance to antibiotics is constantly changing.
— N. gonorrhoea may produce beta-lactamase (PPNG — Penicillinase Producing N. Gonorrhoea) which inactivates penicillin — 15% of isolates in South Africa. Some non-PPNG strains are also resistant to penicillin.
— Some strains are resistant to tetracycline (TRNG) and some are resistant to spectinomycin (these have not been isolated in RSA).

DRUG SENSITIVITIES OF THE OTHER ORGANISMS
— C. trachomatis, U. urealyticum and M. hominis — specific diagnosis is difficult and not necessary for clinical purposes — all are usually sensitive to minocycline, doxycycline and tetracyclines. U. urealyticum may be resistant to tetracycline — prescribe erythromycin if NGU does not respond to tetracycline.
— T. vaginalis — metronidazole — usually 2 g stat for both partners — if infection recurs prescribe 400 mg three times/day for 5 days.
— C. albicans — ketoconazole 400 mg (2x 200 mg tabs) with a meal, once a day for five days as well as imidazole cream for both partners.
— Intra-urethral ulcers — see genital ulcer protocol:
— Herpes — will probably have a history of recurrent episodes — no treatment is curative,
— Most of the other agents causing genital ulcers will respond to an extended regime of minocycline or tetracycline.

CLINICAL FEATURES OF GONOCOCCAL AND NON-GONOCOCCAL URETHRITIS — USUALLY ATYPICAL AND USUALLY NOT CLINICALLY USEFUL

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<thead>
<tr>
<th></th>
<th>N. gonorrhoea</th>
<th>C. trachomatis</th>
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<tbody>
<tr>
<td>Relative prevalence</td>
<td>60-80%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Incubation period</td>
<td>1-10 days (-21 days)</td>
<td>7-21 days</td>
</tr>
<tr>
<td>Onset</td>
<td>Sudden</td>
<td>Gradual</td>
</tr>
<tr>
<td>Symptoms and signs</td>
<td>Florid — profuse purulent discharge</td>
<td>Macopurulent discharge</td>
</tr>
<tr>
<td>Microscopy</td>
<td>Diagnostic in 95%</td>
<td>Not diagnostic, only pus cells</td>
</tr>
</tbody>
</table>

GRAM STAIN
The presence of Gram-negative intracellular diplococci does not exclude a mixed infection with for example C. trachomatis. It does however establish the diagnosis and also a basis for evaluation of the response to treatment. If N. gonorrhoea is present and does not respond to procain penicillin it may be because the organism produces beta lactamase. It is also useful when phimosis or ulcers on the glans make it difficult to exclude the presence of gonococcal urethritis.

TECHNIQUE
— Make a thin smear and fix (heating the glass slide in a spirit lamp — move it a few times slowly through the flame).
— CRYSTAL VIOLET — 30 seconds (stains all organisms dark purple)
— Wash with water (slow running tap water for 5 seconds)
— LUGOLS IODINE — 30 seconds (dye-iodine complex is
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formed)
— Wash with water
— ACETONE IODINE — 30 seconds (decolourizes only the Gram-negative bacteria)
— Wash with water
— CARBOL FUCHSIN — 30 seconds (counterstain Gram-negative bacteria red)
— Dry — blot carefully with blotting paper or paper towel. Examine under oil immersion (X100 magnification) for Gram-negative (red) intracellular diplococci. One may screen the slide first under high power magnification (X40) to identify possibly affected leucocytes.

CULTURE OF N. GONORRHOEA
If penicillin resistance is suspected, do a culture to establish the diagnosis and drug sensitivity. Innoculation of material should, if laboratory facilities are available, be made directly from the patient on to a selective medium. The culture should be sent in a CO₂ candle jar to the laboratory to be incubated within an hour or two. If this is not possible the swab should be sent to the laboratory in Stuarts transport medium. Again it is important that the specimen reaches the laboratory as soon as possible.

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