Primary Care Management Protocols for Genital Ulceration and Urethritis

Andrew Murray

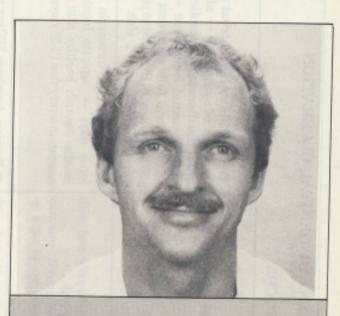
Summary
Information in medical textbooks
is usually presented in a format
determined by the subject matter
and generally not in the manner
most useful for clinical decisionmaking in primary care. The
author repackages, for the
clinician's use, information
regarding genital ulceration and
urethritis.

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

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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



Curriculum Vitae

Andrew Murray obtained his MBChB at the University of Stellenbosch in 1974. He did his internship at the Tygerberg hospital and spent the next four years doing hospital jobs in Ladysmith Natal, Tygerberg and Worcester. After three and a half years in private general practice in the Strand he joined the Dept of Family Medicine at Medunsa in 1983.

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 aetiolgy, 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

Management Assessment Syphilis: Incubation period — 3-4 weeks Syphilis: Always treat partner regardless of painless solitary raised indurated ulcer with regular margin and serous base (the ulcers presence of symptoms - always educate patient are often atypical) about the disease, it complications and the need to bilateral discrete rubbery painless inguinal glands (usually atypical). change sexual behaviour - always do syphilis serology and follow patient up. Syphilis - primary and secondary - Benzathine penicillin 2,4 mu imi into 2 sites (4ml/buttock) at 1 visit. Chancroid: Incubation period — less than 1 week · Chancroid: Erythromycin 500mg three times/day - multiple painful non-indurated ulcers with purulent bases which bleed easily and with for 5 days - aspirate inguinal abscesses - insert needle through healthy skin - may have to repeat 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 aspiration every few (2-3) days. unilateral but also bilateral - inguinal and at times also femoral (may cause groove sign) abscess - sinus or ulcer. · Herpes: Primary episode much worse than recurrences and often associated with · Herpes: Acyclovir 200mg per os five times/day for constitutional symptoms (fever and malaise) and lymphadenopathy. 5 days - only for women with a primary episode who Ulcer-prodrome of burning/itchy sensation — group of small (1-3mm) vescicles — forms present during first week. painful superficial ulcers with a grey slough and erythematous halo - lesions coalesce and - Cotrimoxazole 160/800mg two times/day for 10 become crusted - may be localised or extensive - it may become secondarily infected days. the cervix is often involved - may cause serous vaginal discharge. Keep lesions dry and clean. Inguinal glands — transient, slightly painful and bilaterally enlarged. ■LGV: Incubation period — 3 weeks • LGV: Minocycline 100 mg twice/day for 2-3 weeks. Ulcer — often remains unnoticed — usually small with raised edges, painless and transient – Aspirate inguinal abscesses — as for chancroid. 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). • Granuloma Inguinale: Minocycline 100 mg • Granuloma Inguinale: Incubation period — indeterminate Ulcer — raised, painless beefy red and velvety (granulomatous), indurated and with twice/day for 2-3 weeks. If diagnosis remains rolled edges - often satellite lesions which coalesce. uncertain - treat for both syphilis and chancroid. Inguinal glands — not involved but pseudobubos may form due to subcutaneous spread may cause tissue destruction. Scabies, Erosive Balanitis, Candida, Epithelioma, Tuberculosis etc.

Primary Care Management Protocols for Genital Ulceration and Urethritis

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 eg 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 (condylomota lata, skin rash which is usually macular but can be quite atypical).

DIAGNOSIS is usually clinical but confirmation with serology is necessary because the clinical features are at times atypical and the complications are serious. Darkfield microscopy — diagnostic if done by experienced person.

Chancroid — Haemophilis 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 bilalateral — 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 (4mℓ 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 adviseable: Make a specific (clinical) diagnosis if possible and treat appropriately.
- If the features are atypical, then treat for syphilis and other probable conditiofns (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.

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- 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 — Haemophilis 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 contrimoxazole 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 virusses 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 ante-natal 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

● Genital Herpes — Herpes Simples Virus — usually Type 2 but also Type

- Treatment no cure is available antiviral drugs are only useful (in decreasing pain and duration of lesions and period of viral shedding) if used early (within the first week) in the primary episode of women:
- Acyclovir 200 mg per os five times/day for 5 days.
 It is usually not indicated in males as the infection is usually mild. Acyclovir is effective for prevention of recurrent episodes if used continuously and this may be considered in consultation with a venereologist.
- Cotrimoxazole 160/800mg two times/day for 10 days to prevent secondary infection.
- Keep lesions dry and clean.
- No intercourse during active phase.
- Discuss:
- the recurrent nature of the disease usually 6-8 times per year but it may not occur again or only very infrequently.
- the importance of informing the doctor in case of pregnancy because of the high incidence of severe neontal infection (causing brain damage or death) if vaginal delivery takes place during the active phase (the patient may be asymptomatic) — examine the patient weekly from 36 weeks (inspection, pap smear and viral studies) and do a ceasarian section if viral shedding is present.

continued

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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 L1, L2 and L3

- Incubation period relatively long 3 weeks (1-6 weeks)
- Primary lesion (ulcer) often remains unnoticed and patient may present with inguinal lymphadenopathy and at times constitutional symtpoms.
- 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 bilalateral 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.

Lymphogranuloma Venereum — Chlamydia Trachomatis Serotypes L1, L2 and L3

- Treatment for 14-21 days with:
- Tetracycline 500mg four times/day or
- Minocycline or doxycycline 100 mg twice/day or
- Erythromycin 500 mg four times/day.
- 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 s of compliance with 14 day treatment and of complications such as gross destruction of perineal tissue.

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Granuloma Inguinale — Calymmabacterium Granulomatis

- Incubation period indeterminate possibly 1-4 weeks.
- 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.

Granuloma Inguinale — Calymmabacterium Granulomatis

- Treatment for 14-21 days with:
- Tetracycline 500 mg four times/day or
- Minocycline or doxycycline 100 mg twice/day or
- Erythromycin 500 mg four times/day

If severe infection — add — Streptyomycin 1 gm/day for ten days.

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FURTHER EXPANDED INFORMATION

PREVALENCE — SA is a blend of developed and developing world.

 Developed countries — herpes very common — syphilis less common and then mostly among homosexuals — other STD ulcers occur infrequently.

 Developing countries — syphilis and chancroid is common — herpes, LGV, granuloma inguinale is less common (LGV and GI — endemic in some regions).

DIAGNOSIS — the majority of diagnoses are clinical — it is possible to make specific diagnosis in most cases of genital ulceration but laboratory facilities required to do this are not available to most clinicians — the only rapidly performed diagnostic test for syphilis (darkfield microscopy) is only useful in experienced hands.

CLINICAL DIAGNOSIS — is often difficult because:

clinical features are often atypical,

- mixed infections occur and one infection may mask the other.
- lesions may not be visible when subpreputial infection cause phimosis,
- secondary infection may change or obscure clinical features.

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.

TREATMENT IF DIAGNOSIS REMAINS OBSCURE — always include treatment of syphilis — treat also any other probable condition — treatment for syphilis and chancroid will cure ≥80% of ulcers.

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;
- Procain 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 doxycyline 100 mg twice daily or tetracycline 500 mg four times daily for 7-10 days
- If urethritis is complicated by eg epididimo-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 symtpoms (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. urealiticum not sensitive to tetracycline prescribe erythromycin.
- Beta-lactamase producing N. gonorrhoea (10%)
 Spectinomycin 2g imi stat
- Trichomonas vaginalis metronidazole 2 g 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.
- Concommitant 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

Relative prevalence
Incubation period
Onset
Symptoms and signs
Microscopy
N. gonorrhoea
60-80%
1-10 days (-21 d
Sudden
Sudden
Florid — profus
purulent dischar
Diagnostic in 95

N. gonorrhoea
60-80%
1-10 days (-21 days)
Sudden
Florid — profuse
purulent discharge
Diagnostic in 95%
C. trachomatis
20-30%
7-21 days
Gradual
Mucopurulent
discharge
Not diagnostic, only
pus cells

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 Gramnegative 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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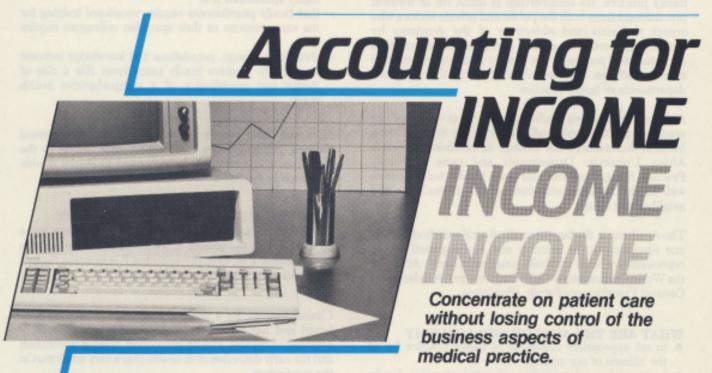
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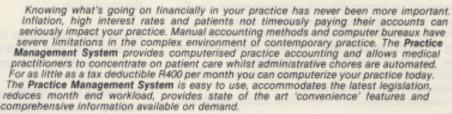
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