

03-13 Sexually transmitted infections

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330 • SEXUALLY TRANSMITTED INFECTIONS HIV testing It should always be standard practice to offer HIV testing as part of screening for sexually transmitted infection (STI) because the benefits of early diagnosis outweigh other considerations. Extensive pre-test counselling is not required in most instances, but it is important to establish efficient pathways for referral of patients at high risk for whom the clinician wishes specialist support, and for those diagnosed as HIV-positive. Clinical examination in men Inset (Perianal warts) From McMillan A, Scott GR. Sexually transmitted infections: a colour guide. Churchill Livingstone, Elsevier Ltd; 2000. (Coronal papillae, mucopus) From McMillan A, Young H, Ogilvie MM, Scott GR. Clinical practice in sexually transmissible infections. Saunders, Elsevier Inc.; 2002. Observation Rectum (Men who have sex with men practising receptive anal intercourse) Perianal area (Men who have sex with men, and heterosexual men) Urethral meatus Skin of penis (Retract prepuce if present) Genital warts Ulcers Be aware of normal anatomical features such as coronal papillae, or prominent sebaceous or para-frenal glands Pubic area Pthirus pubis (crab louse) Scrotal contents Abnormal masses or tenderness (epididymo-orchitis) • Mouth • Eyes • Joints • Skin: Rash of secondary syphilis Scabies Manifestations of HIV infection (Ch. 12) Skin around groin and scrotum Warts Tinea cruris Discharge Warts

Inguinal glands Significant enlargement

Coronal papillae Proctoscope Proctitis

A urethral swab can be submitted if the patient is unable to pass urine. Investigations for STIs in men who have sex with men • FVU, and pharyngeal and rectal swabs for combined NAAT for gonorrhoea and chlamydia • STS (repeat testing may be necessary in the event of negative test results in the first few weeks following exposure) • Serological tests for hepatitis A/B (with a view to vaccination if seronegative) • HIV test (see note) *A urethral swab can be submitted if the patient is unable to pass urine. Investigations for STIs in heterosexual males* • First-void urine (FVU) is the specimen of choice for the combined nucleic acid amplification test (NAAT) for gonorrhoea and chlamydia • Alternatively, for gonorrhoea, a urethral swab plated directly on a selective medium such as modified New York City (MNYC), or sent in an appropriate transport medium, can be cultured to allow for assessment of antimicrobial sensitivities • Serological test for syphilis (STS), e.g. enzyme immunoassay (EIA) for antitreponemal immunoglobulin G (IgG) antibody • Human immunodeficiency virus (HIV) test (see note)

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Adapted from WHO/UNAIDS, 1997. Those at particular risk from STIs • Sex workers, male and female • Clients of sex workers • Men who have sex with men • Injecting drug users (sex for money or drugs) and their partners • Frequent travellers Management goals in suspected STI • Relief of any symptoms • Screening for treatable STI that may not be causing symptoms • Tracing and treatment of sexual contacts who may also be infected • Advice to reduce risk of infection in the future Investigations for STIs in women • Self-taken vaginal swab, or clinician-obtained cervical or vaginal swab, for combined NAAT for gonorrhoea and chlamydia • Alternatively, for gonorrhoea, cervical and urethral swabs plated directly on a selective medium such as MNYC, or sent in appropriate transport medium, can be cultured to allow for assessment of antimicrobial sensitivities • Wet mount for microscopy or high vaginal swab (HVS) for culture of *Trichomonas* • STS, e.g. EIA for antitreponemal IgG antibody • HIV test (see note) Inset (Inflammation) From McMillan A, Young H, Ogilvie MM, Scott GR. Clinical practice in sexually transmissible infections. Saunders, Elsevier Inc.; 2002. Clinical examination in women Observation Vagina and cervix Abnormal discharge Warts Ulcers Inflammation In women with lower abdominal pain, bimanual examination for adnexal tenderness (pelvic inflammatory disease) Perineum and perianal skin Warts Ulcers Pubic area Abdomen Abnormal masses or tenderness Inguinal glands Significant enlargement • Mouth • Eyes • Joints • Skin: Rash of secondary syphilis Scabies Manifestations of HIV infection (Ch. 12) Inflammation

Pthirus pubis (crab louse)

Warts Labia majora and minora Ulcers Vulvitis Speculum

332 • SEXUALLY TRANSMITTED INFECTIONS focuses on genital symptoms, with reference to genital ulceration, rash, irritation, pain, swelling and urinary symptoms, especially dysuria. In men, the clinician should ask about urethral discharge, and in women, vaginal discharge, pelvic pain or dyspareunia. Enquiry about general health should include menstrual and obstetric history, cervical cytology, recent medication, especially with antimicrobial or antiviral agents, previous STI and allergy. Immunisation status for hepatitis A and B should be noted, as should information about

alcohol intake and recreational drug use. Some MSM use new psychoactive substances (NPS), formerly referred to in the UK as 'legal highs', to enhance their sexual experience. Often described as 'chemsex', this has been associated with outbreaks of infections including syphilis, LGV and hepatitis C. A detailed sexual history is imperative (Box 13.1), as this informs the clinician of the degree of risk for certain infections, as well as specific sites that should be sampled; for example, rectal samples should be taken from men who have had unprotected anal sex with other men. Sexual partners, whether male or female, and casual or regular, should be recorded. Sexual practices – insertive or receptive vaginal, anal, orogenital or oroanal – should be noted, as should choice of contraception for women, and condom use for both sexes.

STI during pregnancy Many STIs can be transmitted from mother to child in pregnancy, either transplacentally or during delivery. Possible outcomes are highlighted in Box 13.2.

STI in children The presence of an STI in a child may be indicative of sexual abuse, although vertical transmission may explain some presentations in the first 2 years. In an older child and in adolescents, STI may

Sexually transmitted infections (STIs) are a group of contagious conditions whose principal mode of transmission is by intimate sexual activity involving the moist mucous membranes of the penis, vulva, vagina, cervix, anus, rectum, mouth and pharynx, along with their adjacent skin surfaces. A wide range of infections may be sexually transmitted, including syphilis, gonorrhoea, human immunodeficiency virus (HIV), genital herpes, genital warts, chlamydia and trichomoniasis. Bacterial vaginosis and genital candidiasis are not regarded as STIs, although they are common causes of vaginal discharge in sexually active women. Chancroid, lymphogranuloma venereum (LGV) and granuloma inguinale are usually seen in tropical countries. Hepatitis viruses A, B, C and D (p. 871) may be acquired sexually, as well as by other routes. Although primarily transmitted by mosquito bite, cases of male-to-female sexual transmission of Zika virus have been described and the virus is known to persist in semen for several months (p. 247). The World Health Organization (WHO) estimates that 357 million curable STIs (*Trichomonas vaginalis*, *Chlamydia trachomatis*, gonorrhoea and syphilis) occur worldwide each year. In the UK in 2014, the most common treatable STIs diagnosed were chlamydia (220 000 cases) and gonorrhoea (nearly 40 000 cases). Genital warts are the second most common complaint seen in genitourinary medicine (GUM) departments. In addition to causing morbidity themselves, STIs may increase the risk of transmitting or acquiring HIV infection (Ch. 12). As coincident infection with more than one STI is seen frequently, GUM clinics routinely offer a full set of investigations at the patient's first visit (pp. 330–331), regardless of the reason for attendance. In other settings, less comprehensive investigation may be appropriate. The extent of the examination largely reflects the likelihood of HIV infection or syphilis. Most heterosexuals in the UK are at such low risk of these infections that routine extragenital examination is unnecessary. This is not the case in parts of the world where HIV is endemic, or for men who have sex with men (MSM) in the UK. In other words, the extent of the examination is determined by the sexual history (Box 13.1).

Approach to patients with a suspected STI Patients concerned about the possible acquisition of an STI are often anxious. Staff must be friendly, sympathetic and reassuring; they should have the ability to put patients at ease, while emphasising that clinic attendance is confidential.

Table 13.2 Possible outcomes of STI in pregnancy

Organism	Mode of transmission	Outcome for fetus/neonate	Outcome for mother
<i>Treponema pallidum</i>	Transplacental	Ranges from no effect to severe stigmata or miscarriage/stillbirth	None directly relating to the pregnancy
<i>Neisseria gonorrhoeae</i>	Intrapartum	Severe conjunctivitis	Possibility of ascending infection postpartum
<i>Chlamydia trachomatis</i>	Intrapartum	Conjunctivitis, pneumonia	Possibility of ascending infection postpartum
Herpes simplex	Usually intrapartum, but transplacental infection may occur rarely	Ranges from no effect to	

severe disseminated infection Rarely, primary infection during 2nd/3rd trimesters becomes disseminated, with high maternal mortality Human papillomaviruses Intrapartum Anogenital warts or laryngeal papillomas are very rare Warts may become more florid during pregnancy, but usually regress postpartum 13.1 How to take a sexual history • In your lifetime, have you sexual partners been male, female or both? • Do you have a regular sexual partner at present? • If yes: How long have you been together? When did you last have sex with anyone else? • If no: When did you last have sex? Was this a regular or a casual partner? • Do/did you use a condom?

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Management This depends on local epidemiology and the availability of diagnostic resources. Treatment is often presumptive, with prescription of multiple antimicrobials to cover the possibility of gonorrhoea and/or chlamydia. This is likely to include a single-dose treatment for gonorrhoea, which is desirable because it eliminates the risk of non-adherence. The recommended agents for treating gonorrhoea vary according to local antimicrobial resistance patterns (p. 340). Appropriate treatment for chlamydia (p. 340) should also be prescribed because concurrent infection is present in up to 50% of men with gonorrhoea. Non-gonococcal, non-chlamydial urethritis is treated as for chlamydia. Patients should be advised to avoid sexual contact until it is confirmed that any infection has resolved and, whenever possible, recent sexual contacts should be traced. The task of contact tracing – also called partner notification – is best performed by trained nurses based in GUM clinics; it is standard practice in the UK to treat current sexual partners of men with gonococcal or non-specific urethritis without waiting for microbiological confirmation. If symptoms clear, a routine test of cure is not necessary, but patients should be re-interviewed to confirm that there was no immediate vomiting or diarrhoea after treatment, that there has been no risk of reinfection, and that traceable partners have sought medical advice. Genital itch and/or rash Patients may present with many combinations of penile/genital symptoms, which may be acute or chronic, and infectious or non-infectious. Box 13.3 provides a guide to diagnosis. Balanitis refers to inflammation of the glans penis, often extending to the under-surface of the prepuce, in which case it is called balanoposthitis. Tight prepuce and poor hygiene may be aggravating factors. Candidiasis is sometimes associated with immune deficiency, diabetes mellitus, and the use of broad-spectrum antimicrobials, glucocorticoids or antimetabolic drugs. Local saline bathing is usually helpful, especially when no cause is found. Genital ulceration The most common cause of ulceration is genital herpes. Classically, multiple painful ulcers affect the glans, coronal sulcus or shaft of penis (Fig. 13.2), but solitary lesions occur rarely. Perianal ulcers may be seen in MSM. The diagnosis is made by gently scraping material from lesions and sending this in an appropriate transport medium for culture or detection of HSV DNA by polymerase chain reaction (PCR). Increasingly, laboratories will also test for *Treponema pallidum* by PCR. In the UK, the possibility of syphilis or any other ulcerating STI is much less likely unless the patient is an MSM and/or has had a sexual partner from a region where tropical STIs are more common. The classic lesion of primary syphilis (chancre) is single, painless and indurated; however, multiple lesions are seen rarely and anal chancres are often painful. Diagnosis is made in GUM clinics by dark-ground microscopy and/or PCR on a swab from a chancre, but in other settings by serological tests for syphilis (p. 338). Other rare infective causes seen in the UK include varicella zoster virus (p. 238) and trauma with secondary infection. Tropical STIs, such as chancroid, be the result of voluntary sexual activity. Specific issues regarding the management of STI and other infections in adolescence are discussed in Box 11.25 (p. 235). Presenting problems in men Urethral discharge In the UK the most important

causes of urethral discharge are gonorrhoea and chlamydia. In a significant minority of cases, tests for both of these infections are negative, a scenario often referred to as non-specific urethritis (NSU). Some of these cases may be caused by *Trichomonas vaginalis*, herpes simplex virus (HSV), mycoplasmas, ureaplasmas or adenoviruses. A small minority seem not to have an infectious aetiology. Gonococcal urethritis usually causes symptoms within 7 days of exposure. The discharge is typically profuse and purulent. Chlamydial urethritis has an incubation period of 1–4 weeks, and tends to result in milder symptoms than gonorrhoea; there is overlap, however, and microbiological confirmation should always be sought. Investigations A presumptive diagnosis of urethritis can be made from a Gram-stained smear of the urethral exudate (Fig. 13.1), which will demonstrate significant numbers of polymorphonuclear leucocytes (≥ 5 per high-power field). A working diagnosis of gonococcal urethritis is made if Gram-negative intracellular diplococci (GNDC) are seen; if no GNDC are seen, a label of NSU is applied. If microscopy is not available, urine samples and/or swabs should be taken and empirical antimicrobials prescribed. A first-void urine (FVU) sample should be submitted for a combined nucleic acid amplification test (NAAT) for gonorrhoea and chlamydia; a urethral swab is an alternative if the patient cannot pass urine. When gonorrhoea is suspected, a urethral swab should be sent for culture and antimicrobial sensitivities of *Neisseria gonorrhoeae*. Tests for other potential causes of urethritis are not performed routinely. A swab should also be taken from the pharynx because gonococcal infection here is not reliably eradicated by single-dose therapy. In MSM, swabs for gonorrhoea and chlamydia should be taken from the rectum. Fig. 13.1 A Gram-stained urethral smear from a man with gonococcal urethritis. Gram-negative diplococci are seen within polymorphonuclear leucocytes.

334 • SEXUALLY TRANSMITTED INFECTIONS LGV and granuloma inguinale, are described in Box 13.12 (p. 341). Inflammatory causes include Stevens–Johnson syndrome (pp. 1224 and 1254), Behçet’s disease (p. 1043) and fixed drug reactions. In older patients, malignant and pre-malignant conditions, such as squamous cell carcinoma and erythroplasia of Queyrat (intra-epidermal carcinoma), should be considered. Genital lumps The most common cause of genital ‘lumps’ is warts (p. 342). These are classically found in areas of friction during sex, such as the parafrenal skin and prepuce of the penis. Warts may also be seen in the urethral meatus, and less commonly on the shaft or around the base of the penis. Perianal warts are surprisingly common in men who do not have anal sex. The differential diagnosis includes molluscum contagiosum and skin tags. Adolescent boys may confuse normal anatomical features such as coronal papillae (p. 330), parafrenal glands or sebaceous glands (Fordyce spots) with warts. Proctitis in men who have sex with men STIs that may cause proctitis in MSM include gonorrhoea, chlamydia, herpes and syphilis. The substrains of *Chlamydia trachomatis* that cause LGV (L1–3) have been associated with outbreaks of severe proctitis in Northern Europe, including the UK. Symptoms include mucopurulent anal discharge, rectal bleeding, pain and tenesmus. Fig. 13.2 Penile herpes simplex (HSV-2) infection. 13.3 Differential diagnosis of genital itch and/or rash in men

Likely diagnosis	Acute or chronic	Itch	Pain	Discharge (non-urethral)	Specific characteristics	Diagnostic test	Treatment
Subclinical urethritis	Either \pm – \pm	Often intermittent				Gram stain and urethral swabs	As for urethral discharge
Candidiasis	Acute \square – \square	White	Post-coital			Microscopy	Antifungal cream, e.g. clotrimazole
Anaerobic (erosive) balanitis	Acute \pm – \pm	Yellow	Offensive			Clinical	Saline bathing \pm metronidazole
<i>Pthirus pubis</i> (‘crab lice’) infection	Either \square – \square					Lice and nits seen attached to pubic hairs	Can be by microscopy but usually visual
						According to local policy	– often permethrin
Lichen planus (p. 1252)	Either \pm – \pm	Violaceous papules	\pm	Wickham’s striae	Clinical	None or mild topical glucocorticoid, e.g. hydrocortisone	Lichen sclerosus
	Chronic \pm – \pm					Ivory-white plaques, scarring	

Clinical or biopsy Strong topical glucocorticoid, e.g. clobetasol Plasma cell balanitis of Zoon Chronic
 □ - ± Shiny, inflamed circumscribed areas Clinical or biopsy Strong topical glucocorticoid, e.g.
 clobetasol Dermatoses, e.g. eczema or psoriasis Either □ - - Similar to lesions elsewhere on skin
 Clinical Mild topical glucocorticoid, e.g. hydrocortisone Genital herpes Acute ± □ - Atypical ulcers
 are not uncommon Swab for HSV PCR Oral antiviral, e.g. aciclovir Circinate balanitis Either - - -
 Painless erosions with raised edges; usually as part of sexually acquired reactive arthritis (SARA, p.
 1031) Clinical Mild topical glucocorticoid, e.g. hydrocortisone (HSV PCR = herpes simplex virus
 polymerase chain reaction)

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vulvovaginal inflammation. Diagnosis is made by observing motile flagellate protozoa on a wet-mount microscopy slide of vaginal material and/or by culture. If examination reveals the discharge to be cervical in origin, the possibility of chlamydial or gonococcal infection is increased and appropriate cervical or vaginal swabs should be taken (p. 331). In addition, Gram stain of cervical and urethral material may reveal GNDC, allowing presumptive treatment for gonorrhoea to be given. If gonococcal cervicitis is suspected, swabs should also be taken from the pharynx and rectum; infections at these sites are not reliably eradicated by single-dose therapy and a test of cure will therefore be required. GUM clinics in the UK may offer sexually active women presenting with vaginal discharge an STI screen (p. 331). In other settings, such as primary care or gynaecology, testing for chlamydia and gonorrhoea may be considered in young women (< 25 years old), those who have changed partner recently, and those not using a barrier method of contraception, even if a non-STI cause of discharge is suspected clinically. Treatment of infections causing vaginal discharge is shown in Box 13.4. Examination may show mucopus and erythema with contact bleeding (p. 330). In addition to the diagnostic tests listed on page 330, a PCR test for HSV and a request for identification of the LGV substrain should be arranged if chlamydial infection is detected. Treatment is directed at the individual infections. MSM may also present with gastrointestinal symptoms from infection with organisms such as *Entamoeba histolytica* (p. 286), *Shigella* spp. (p. 265), *Campylobacter* spp. (p. 262) and *Cryptosporidium* spp. (pp. 287 and 317).

Presenting problems in women Vaginal discharge The natural vaginal discharge may vary considerably, especially under differing hormonal influences such as puberty, pregnancy or prescribed contraception. A sudden or recent change in discharge, especially if associated with alteration of colour and/ or smell, or vulval itch/irritation, is more likely than a gradual or long-standing change to indicate an infective cause. Local epidemiology is particularly important when assessing possible causes. In the UK, most cases of vaginal discharge are not sexually transmitted, being due to either candidal infection or bacterial vaginosis (BV). Worldwide, the most common treatable STI causing vaginal discharge is trichomoniasis; other possibilities include gonorrhoea and chlamydia. HSV may cause increased discharge, although vulval pain and dysuria are usually the predominant symptoms. Non-infective causes include retained tampons, malignancy and/or fistulae. Speculum examination often allows a relatively accurate diagnosis, with appropriate treatment to follow (Box 13.4). If the discharge is homogeneous and off-white in colour, vaginal pH is greater than 4.5, and Gram stain microscopy reveals scanty or absent lactobacilli with significant numbers of Gram-variable organisms, some of which may be coating vaginal squamous cells (so-called Clue cells, Fig. 13.3), the likely diagnosis is BV. If there is vulval and vaginal erythema, the discharge is curdy in nature, vaginal pH is less than 4.5, and Gram stain microscopy reveals fungal spores and pseudohyphae, the diagnosis is candidiasis. Trichomoniasis tends to cause a profuse

yellow or green discharge and is usually associated with significant vaginal discharge. Cause: Candidiasis. Clinical features: Vulval and vaginal inflammation, curdy white discharge adherent to walls of vagina, low vaginal pH. Treatment (in pregnancy seek specialist advice): Clotrimazole 1 500 mg pessary once at night and clotrimazole cream twice daily or Econazole 1 pessary 150 mg for 3 nights and econazole cream twice daily (topical creams for 7 days) or Fluconazole 2 150 mg orally stat. Trichomoniasis: Vulval and vaginal inflammation, frothy yellow/green discharge. Treatment: Metronidazole 3 400 mg twice daily orally for 5–7 days or 2 g orally as a single dose. Bacterial vaginosis: No inflammation, white homogeneous discharge. Treatment: Metronidazole 3 2 g vaginal gel 0.75% daily for 5 days. High vaginal pH: Clindamycin 1,4 vaginal cream 2% daily for 7 days. Streptococcal/staphylococcal infection: Purulent vaginal discharge. Choice of antibiotic depends on sensitivity tests. 1 Clotrimazole, econazole and clindamycin damage latex condoms and diaphragms. 2 Avoid in pregnancy and breastfeeding. 3 Avoid alcoholic drinks until 48 hours after finishing treatment. Avoid high-dose regimens in pregnancy or breastfeeding. 4 Clostridium difficile colitis has been reported with the use of clindamycin cream.

Fig. 13.3 Gram stain of a Clue cell from a patient with bacterial vaginosis. The margin of this vaginal epithelial cell is obscured by a coating of anaerobic organisms. From McMillan A, Young H, Ogilvie MM, Scott GR. Clinical practice in sexually transmissible infections. Saunders, Elsevier Inc.; 2002.

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Genital lumps The most common cause of genital ‘lumps’ is warts. These are classically found in areas of friction during sex, such as the fourchette and perineum. Perianal warts are surprisingly common in women who do not have anal sex. The differential diagnosis includes molluscum contagiosum, skin tags, and normal papillae or sebaceous glands.

Chronic vulval pain and/or itch Women may present with a range of chronic symptoms that may be intermittent or continuous (Box 13.5). Recurrent candidiasis may lead to hypersensitivity to candidal antigens, with itch and erythema becoming more prominent than increased discharge. Effective treatment may require regular oral antifungals, e.g. fluconazole 150 g once a week, plus a combined antifungal/glucocorticoid cream.

Prevention of STI Case-finding Early diagnosis and treatment facilitated by active case-finding will help to reduce the spread of infection by limiting the period of infectivity; tracing and treating sexual partners will also reduce the risk of reinfection. Unfortunately, the majority of individuals with an STI are asymptomatic and therefore unlikely to seek medical attention. Improving access to diagnosis in primary care or non-medical settings, especially through opportunistic testing, may help. However, the impact of medical intervention through improved access alone is likely to be small.

Changing behaviour The prevalence of STIs is driven largely by sexual behaviour. Primary prevention encompasses efforts to delay the onset of sexual activity and limit the number of sexual partners thereafter. Encouraging the use of barrier methods of contraception will also help to reduce the risk of transmitting or acquiring STIs.

Lower abdominal pain Pelvic inflammatory disease (PID, infection or inflammation of the Fallopian tubes and surrounding structures) is part of the extensive differential diagnosis of lower abdominal pain in women, especially those who are sexually active. The possibility of PID is increased if, in addition to acute/subacute pain, there is dyspareunia, abnormal vaginal discharge and/or bleeding. There may also be systemic features, such as fever and malaise. On examination, lower abdominal pain is usually bilateral, and vaginal examination reveals adnexal tenderness with or without cervical excitation. Unfortunately, a definitive diagnosis can only be made by laparoscopy. A pregnancy test should be performed (as well as the diagnostic tests on p. 331) because the differential diagnosis includes ectopic pregnancy. Broad-spectrum

antibiotics, including those active against gonorrhoea and chlamydia, such as ofloxacin and metronidazole, should be prescribed if PID is suspected, along with appropriate analgesia. Delaying treatment increases the likelihood of adverse sequelae, such as abscess formation, and tubal scarring that may lead to ectopic pregnancy or infertility. Hospital admission may be indicated for severe symptoms.

Genital ulceration The most common cause of ulceration is genital herpes. Classically, multiple painful ulcers affect the introitus, labia and perineum, but solitary lesions occur rarely. Inguinal lymphadenopathy and systemic features, such as fever and malaise, are more common than in men. Diagnosis is made by gently scraping material from lesions and sending this in an appropriate transport medium for culture or detection of HSV DNA by PCR. Increasingly, laboratories will also test such samples for *Treponema pallidum* by PCR. In the UK, the possibility of any other ulcerating STI is unlikely unless the patient has had a sexual partner from a region where tropical STIs are more common (see Box 13.12). Inflammatory causes include lichen sclerosus, Stevens–Johnson syndrome (pp. 1224 and 1254), Behçet’s disease (p. 1043) and fixed drug reactions. In older patients, malignant and premalignant conditions, such as squamous cell carcinoma, should be considered.

13.5 Chronic vulval pain and/or itch Likely diagnosis Itch Pain

Specific characteristics	Diagnostic test	Treatment
Candidiasis ±	Usually cyclical Microscopy (culture for yeasts other than <i>Candida albicans</i> in recurrent/refractory disease)	Oral antifungal, e.g. fluconazole 150 mg
Lichen planus ±	Violaceous papules ± Wickham’s striae	Clinical No treatment, or mild topical glucocorticoid, e.g. hydrocortisone
Lichen sclerosus ±	Ivory-white plaques, scarring ± labial resorption	Clinical or biopsy Strong topical glucocorticoid, e.g. clobetasol
Vestibulitis – □	Dyspareunia common, pain on touching erythematous area	Clinical Refer to specialist vulva clinic
Vulvodynia – □	Pain usually neuropathic in nature	Clinical Refer to specialist vulva clinic
Dermatoses, e.g. eczema or psoriasis □	Similar to lesions elsewhere on skin	Clinical Mild topical glucocorticoid, e.g. hydrocortisone
Genital herpes ± □	Atypical ulcers are not uncommon	Swab for HSV PCR Oral antiviral, e.g. aciclovir (HSV PCR = herpes simplex virus polymerase chain reaction)

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Chancres may develop on the vaginal wall and on the cervix. Extragenital chancres are found in about 10% of patients, affecting sites such as the finger, lip, tongue, tonsil, nipple, anus or rectum. Anal chancres often resemble fissures and may be painful.

Secondary syphilis This occurs 6–8 weeks after the development of the chancre, when treponemes disseminate to produce a multisystem disease. Constitutional features, such as mild fever, malaise and headache, are common. Over 75% of patients present with a rash on the trunk and limbs that may later involve the palms and soles; this is initially macular but evolves to maculopapular or papular forms, which are generalised, symmetrical and non-irritable. Scales may form on the papules later. Lesions are red, changing to a ‘gun-metal’ grey as they resolve. Without treatment, the rash may last for up to 12 weeks. Condylomata lata (papules coalescing to plaques) may develop in warm, moist sites such as the vulva or perianal area. Generalised non-tender lymphadenopathy is present in over 50% of patients. Mucosal lesions, known as mucous patches, may affect the genitalia, mouth, pharynx or larynx and are essentially modified papules, which become eroded. Rarely, confluence produces characteristic ‘snail track ulcers’ in the mouth. Other features, such as meningitis, cranial nerve palsies, anterior or posterior uveitis, hepatitis, gastritis, glomerulonephritis or periostitis, are sometimes seen. Neurological involvement may be more common in HIV-positive patients. The differential diagnosis of secondary syphilis can be extensive, but in the context of a suspected STI,

primary HIV infection is the most important alternative condition to consider (Ch. 12). Non-STI conditions that mimic the rash include psoriasis, pityriasis rosea, scabies, allergic drug reaction, erythema multiforme and pityriasis (tinea) versicolor. The clinical manifestations of secondary syphilis will resolve without treatment but relapse may occur, usually within the first year of infection. Thereafter, the disease enters the phase of latency. Latent syphilis This phase is characterised by the presence of positive syphilis serology or the diagnostic cerebrospinal fluid (CSF) abnormalities of neurosyphilis in an untreated patient with no evidence of clinical disease. It is divided into early latency (within 2 years of infection), when syphilis may be transmitted sexually, and late latency, when the patient is no longer sexually infectious. is especially important in the setting of 'sexual concurrency', where sexual relationships overlap. Unfortunately, there is contradictory evidence as to which (if any) interventions can reduce sexual activity. Knowledge alone does not translate into behaviour change, and broader issues, such as poor parental role modelling, low self-esteem, peer group pressure in the context of the increased sexualisation of our societies, gender power imbalance and homophobia, all need to be addressed. Throughout the world there is a critical need to enable women to protect themselves from undisciplined and coercive male sexual activity. Economic collapse and the turmoil of war regularly lead to situations where women are raped or must turn to prostitution to feed themselves and their children, and an inability to negotiate safe sex increases their risk of acquiring STI, including HIV. Sexually transmitted bacterial infections Syphilis Syphilis is caused by infection, through abrasions in the skin or mucous membranes, with the spirochaete *Treponema pallidum*. In adults the infection is usually sexually acquired; however, transmission by kissing, blood transfusion and percutaneous injury has been reported. Transplacental infection of the fetus can occur. The natural history of untreated syphilis is variable. Infection may remain latent throughout, or clinical features may develop at any time. The classification of syphilis is shown in Box 13.6. All infected patients should be treated. Penicillin remains the drug of choice for all stages of infection. Acquired syphilis Early syphilis Primary syphilis The incubation period is usually between 14 and 28 days, with a range of 9–90 days. The primary lesion or chancre (Fig. 13.4) develops at the site of infection, usually in the genital area. A dull red macule develops, becomes papular and then erodes to form an indurated ulcer (chancre). The draining inguinal lymph nodes may become moderately enlarged, mobile, discrete and rubbery. The chancre and the lymph nodes are both painless and non-tender, unless there is concurrent or secondary infection. Without treatment, the chancre will resolve within 2–6 weeks to leave a thin atrophic scar. 13.6 Classification of syphilis Stage Acquired Congenital Early Primary Secondary Latent Clinical and latent Late Latent Benign tertiary Cardiovascular Neurosyphilis Clinical and latent Fig. 13.4 Primary syphilis. A painless ulcer (chancre) is shown in the coronal sulcus of the penis. This is usually associated with inguinal lymphadenopathy. Courtesy of Dr P. Hay, St George's Hospital, London.

338 • SEXUALLY TRANSMITTED INFECTIONS • birth of a baby who develops signs of early congenital syphilis during the first few weeks of life (Box 13.7) • birth of a baby with latent infection who either remains well or develops congenital syphilis/stigmata later in life (see Box 13.7). Investigations in adult cases *Treponema pallidum* may be identified in serum collected from chancres, or from moist or eroded lesions in secondary syphilis using a dark-field microscope, a direct fluorescent antibody test or PCR. The serological tests for syphilis (STS) are listed in Box 13.8. These are antibody tests that almost always remain positive, even after successful treatment. Prolonged untreated infection results in higher titres that may not decline at all. Interpretation of results requires knowledge of any treatment, which may include antibiotics given coincidentally,

e.g. for skin or respiratory tract infections. Many centres use treponemal enzyme immunoassays (EIAs) for IgG and IgM antibodies to screen for syphilis. EIA for antitreponemal IgM becomes positive at approximately 2 weeks, while non-treponemal tests become positive about 4 weeks after primary syphilis. All positive results in asymptomatic patients must be confirmed by repeat tests. Biological false-positive reactions occur occasionally; these are most commonly seen with Venereal Diseases Research Laboratory (VDRL) or rapid plasma reagin (RPR) tests (when treponemal tests will be negative). Acute false-positive reactions may be associated with infections, such as infectious mononucleosis, chickenpox and malaria, and may also occur in pregnancy. Chronic false-positive reactions may be associated with autoimmune diseases. False-negative results for non-treponemal tests may be found in secondary syphilis because extremely high antibody levels can

Transmission of syphilis from a pregnant woman to her fetus, and rarely by blood transfusion, is possible for several years following infection. Late syphilis

Late latent syphilis This may persist for many years or for life. Without treatment, over 60% of patients might be expected to suffer little or no ill health. Coincidental prescription of antibiotics for other illnesses, such as respiratory tract or skin infections, may treat latent syphilis serendipitously and make the interpretation of serological test results difficult (see below). Benign tertiary syphilis This may develop between 3 and 10 years after infection but is now rarely seen in the UK. Skin, mucous membranes, bone, muscle or viscera can be involved. The characteristic feature is a chronic granulomatous lesion called a gumma, which may be single or multiple. Healing with scar formation may impair the function of the structure affected. Skin lesions may take the form of nodules or ulcers, while subcutaneous lesions may ulcerate with a gummy discharge. Healing occurs slowly, with the formation of characteristic tissue-paper scars. Mucosal lesions may occur in the mouth, pharynx, larynx or nasal septum, appearing as punched-out ulcers. Of particular importance is gummatous involvement of the tongue, healing of which may lead to leucoplakia with the attendant risk of malignant change. Gummas of the tibia, skull, clavicle and sternum have been described, as has involvement of the brain, spinal cord, liver, testis and, rarely, other organs. Resolution of active disease should follow treatment, though some tissue damage may be permanent. Paroxysmal cold haemoglobinuria (p. 950) may be seen. Cardiovascular syphilis This may present many years after initial infection. Aortitis, which may involve the aortic valve and/or the coronary ostia, is the key feature. Clinical features include aortic incompetence, angina and aortic aneurysm (p. 505). The condition typically affects the ascending aorta and sometimes the aortic arch; aneurysm of the descending aorta is rare. Treatment with penicillin will not correct anatomical damage and surgical intervention may be required. Neurosyphilis This may also take years to develop. Asymptomatic infection is associated with CSF abnormalities in the absence of clinical signs. Meningovascular disease, tabes dorsalis and general paralysis of the insane constitute the symptomatic forms (p. 1125). Neurosyphilis and cardiovascular syphilis may coexist and are sometimes referred to as quaternary syphilis. Congenital syphilis Congenital syphilis is rare where antenatal serological screening is practised. Antisyphilitic treatment in pregnancy treats the fetus, if infected, as well as the mother. Treponemal infection may give rise to a variety of outcomes after 4 months of gestation, when the fetus becomes immunocompetent:

- miscarriage or stillbirth, prematurely or at term
- birth of a syphilitic baby (a very sick baby with hepatosplenomegaly, bullous rash and perhaps pneumonia)

13.7 Clinical features of congenital syphilis

Early congenital syphilis (neonatal period)

- Maculopapular rash
- Condylomata lata
- Mucous patches
- Fissures around mouth, nose and anus
- Rhinitis with nasal discharge (snuffles)
- Hepatosplenomegaly
- Osteochondritis/periostitis
- Generalised lymphadenopathy
- Choroiditis
- Meningitis
- Anaemia/thrombocytopenia

Late congenital syphilis

- Benign tertiary syphilis

Periostitis • Paroxysmal cold haemoglobinuria • Neurosyphilis • 8th nerve deafness • Interstitial keratitis • Clutton's joints (painless effusion into knee joints) Stigmata • Hutchinson's incisors (anterior-posterior thickening with notch on narrowed cutting edge) • Mulberry molars (imperfectly formed cusps/deficient dental enamel) • High arched palate • Maxillary hypoplasia • Saddle nose (following snuffles) • Rhagades (radiating scars around mouth, nose and anus following rash) • Salt and pepper scars on retina (from choroiditis) • Corneal scars (from interstitial keratitis) • Sabre tibia (from periostitis) • Bossing of frontal and parietal bones (healed periosteal nodes)

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Pregnancy Penicillin is the treatment of choice in pregnancy. Erythromycin stearate can be given if there is penicillin hypersensitivity, but it crosses the placenta poorly; the newborn baby must therefore be treated with a course of penicillin and consideration given to retreating the mother. Some specialists recommend penicillin desensitisation for pregnant mothers so that penicillin can be given during temporary tolerance. A 10-day course of ceftriaxone is a further alternative. Babies should be treated in hospital with the help of a paediatrician. Treatment reactions • Anaphylaxis. Penicillin is a common cause; on-site facilities should be available for management (p. 75). • Jarisch-Herxheimer reaction. This is an acute febrile reaction that follows treatment and is characterised by headache, malaise and myalgia; it resolves within 24 hours. It is common in early syphilis and rare in late syphilis. Fetal distress or premature labour can occur in pregnancy. The reaction may also cause worsening of neurological (cerebral artery occlusion) or ophthalmic (uveitis, optic neuritis) disease, myocardial ischaemia (inflammation of the coronary ostia) and laryngeal stenosis (swelling of a gumma). Prednisolone 40–60 mg daily for 3 days is recommended to prevent the reaction in patients with these forms of the disease; antisyphilitic treatment can be started 24 hours after introducing glucocorticoids. In high-risk situations it is wise to initiate therapy in hospital. • Procaine reaction. Fear of impending death occurs immediately after the accidental intravenous injection of procaine penicillin and may be associated with hallucinations or fits. Symptoms are short-lived, but verbal assurance and sometimes physical restraint are needed. The reaction can be prevented by aspiration before intramuscular injection to ensure the needle is not in a blood vessel. Gonorrhoea Gonorrhoea is caused by infection with *Neisseria gonorrhoeae* and may involve columnar epithelium in the lower genital tract, rectum, pharynx and eyes. Transmission is usually the result of vaginal, anal or oral sex. Gonococcal conjunctivitis may be caused by accidental infection from contaminated fingers. Untreated mothers may infect babies during delivery, resulting in ophthalmia neonatorum (Fig. 13.5). Infection of children beyond the neonatal period usually indicates sexual abuse. Clinical features The incubation period is usually 2–10 days. In men the anterior urethra is commonly infected, causing urethral discharge and dysuria, but symptoms are absent in about 10% of cases. Examination will usually show a mucopurulent or purulent urethral discharge. Rectal infection in MSM is usually asymptomatic but may present with anal discomfort, discharge or rectal bleeding. Proctoscopy may reveal either no abnormality, or clinical evidence of proctitis (p. 334) such as inflamed rectal mucosa and mucopus. In women, the urethra, paraurethral glands/ducts, Bartholin's glands/ducts or endocervical canal may be infected. The rectum may also be involved either due to contamination from a urogenital site or as a result of anal sex. Occasionally, the rectum is the prevent the formation of the antibody-antigen lattice necessary for the visualisation of the flocculation reaction (the prozone phenomenon). In benign tertiary and cardiovascular syphilis, examination of CSF should be considered because asymptomatic neurological disease may coexist. The CSF should also be

examined in patients with clinical signs of neurosyphilis (p. 1125) and in both early and late congenital syphilis. Positive STS may be found in patients who are being investigated for neurological disease, especially dementia. In many instances, the serology reflects previous infection unrelated to the presenting complaint, especially when titres are low. Examination of CSF is occasionally necessary. Chest X-ray, electrocardiogram (ECG) and echocardiogram are useful in the investigation of cardiovascular syphilis. Biopsy may be required to diagnose gumma. Endemic treponematoses, such as yaws, endemic (nonvenereal) syphilis (bejel) and pinta (pp. 253 and 254), are caused by treponemes that are morphologically indistinguishable from *T. pallidum* and cannot be differentiated by serological tests. A VDRL or RPR test may help to elucidate the correct diagnosis because adults with late yaws usually have low titres. Investigations in suspected congenital syphilis Passively transferred maternal antibodies from an adequately treated mother may give rise to positive serological tests in her baby. In this situation, non-treponemal tests should become negative within 3–6 months of birth. A positive EIA test for antitreponemal IgM suggests early congenital syphilis. A diagnosis of congenital syphilis mandates investigation of the mother, her partner and any siblings. Management Penicillin is the drug of choice. Currently, a single dose of 2.4 megaunits of intramuscular benzathine benzylpenicillin is recommended for early syphilis (< 2 years' duration), with three doses at weekly intervals being recommended in late syphilis. A 14-day course of procaine penicillin is recommended for the treatment of neurosyphilis, supplemented by a 3-day course of prednisolone (see below). Doxycycline is indicated for patients allergic to penicillin, except in pregnancy (see below). Azithromycin is less favoured due to the potential for resistance. All patients must be followed up to ensure cure, and partner notification is of particular importance. Resolution of clinical signs in early syphilis with declining titres for non-treponemal tests, usually to undetectable levels within 6 months for primary syphilis and 12–18 months for secondary syphilis, is an indicator of successful treatment. Specific treponemal antibody tests may remain positive for life. In patients who have had syphilis for many years there may be little serological response following treatment.

13.8 Serological tests for syphilis

Non-treponemal (non-specific) tests • Venereal Diseases Research Laboratory (VDRL) test • Rapid plasma reagin (RPR) test

Treponemal (specific) antibody tests • Treponemal antigen-based enzyme immunoassay (EIA) for IgG and IgM • Treponema pallidum haemagglutination assay (TPHA) • *T. pallidum* particle agglutination assay (TPPA) • Fluorescent treponemal antibody-absorbed (FTA-ABS) test

340 • SEXUALLY TRANSMITTED INFECTIONS be seen as soon as possible. Delay in treatment may lead to complications (Box 13.10). Chlamydial infection Chlamydial infection in men Chlamydia is transmitted and presents in a similar way to gonorrhoea; however, urethral symptoms are usually milder and may be absent in over 50% of cases. Conjunctivitis is also milder than in gonorrhoea; pharyngitis does not occur. The incubation period varies from 1 week to a few months. Without treatment, symptoms may resolve but the patient remains infectious for several months. Complications, such as epididymo-orchitis and sexually acquired reactive arthritis (SARA, p. 1031), are rare. Sexually transmitted pathogens, such as chlamydia or gonococci, are usually responsible for epididymo-orchitis in men aged less than 35 years, whereas bacteria such as Gram-negative enteric organisms are more commonly implicated in older men. Treatments for chlamydia are listed in Box 13.11. NSU is treated identically. The partner(s) of men with chlamydia should be treated, even if laboratory tests for chlamydia are negative. Investigation is not mandatory but serves a useful epidemiological purpose; moreover, positive results encourage further attempts at contact-tracing. Chlamydial infection in women The cervix and urethra are commonly involved. Infection is asymptomatic in about 80% of patients but may cause intermenstrual and/or post-coital

bleeding, dysuria or vaginal discharge. Lower abdominal pain and dyspareunia are features of PID. Examination may reveal mucopurulent cervicitis, contact only site infected. About 80% of women who have gonorrhoea are asymptomatic. There may be vaginal discharge or dysuria but these symptoms are often due to additional infections, such as chlamydia (see below), trichomoniasis or candidiasis, making full investigation essential (p. 331). Lower abdominal pain, dyspareunia and intermenstrual bleeding may be indicative of PID. Clinical examination may show no abnormality, or pus may be expressed from urethra, paraurethral ducts or Bartholin's ducts. The cervix may be inflamed, with mucopurulent discharge and contact bleeding. Pharyngeal gonorrhoea is the result of receptive orogenital sex and is usually symptomless. Gonococcal conjunctivitis is an uncommon complication, presenting with purulent discharge from the eye(s), severe inflammation of the conjunctivae and oedema of the eyelids, pain and photophobia. Gonococcal ophthalmia neonatorum presents similarly with purulent conjunctivitis and oedema of the eyelids. Conjunctivitis must be treated urgently to prevent corneal damage. Disseminated gonococcal infection (DGI) is seen rarely, and typically affects women with asymptomatic genital infection. Symptoms include arthritis of one or more joints, pustular skin lesions, tenosynovitis and fever. Gonococcal endocarditis has been described. Investigations Gram-negative diplococci may be seen on microscopy of smears from infected sites (see Fig. 13.1). Pharyngeal smears are difficult to analyse due to the presence of other diplococci, so the diagnosis must be confirmed by culture or NAAT. Management of adults Emerging resistance is making it increasingly difficult to cure gonorrhoea with a single oral dose of antimicrobials, and recommended treatment in the UK has changed to intramuscular ceftriaxone 500 mg given with an oral dose of azithromycin 1 g, in the hope that combination therapy will slow down the development of cephalosporin resistance. The alternatives listed in Box 13.9 are less likely to be effective. Longer courses of antibiotics are required for complicated infection. The partner(s) of patients with gonorrhoea should Fig. 13.5

Gonococcal ophthalmia neonatorum. From McMillan A, Scott GR. Sexually transmitted infections: a colour guide. Churchill Livingstone, Elsevier Ltd; 2000. 13.10 Complications of delayed therapy in gonorrhoea • Acute prostatitis • Epididymo-orchitis • Bartholin's gland abscess • Pelvic inflammatory disease (may lead to infertility or ectopic pregnancy) • Disseminated gonococcal infection 1Contraindicated in pregnancy and breastfeeding. 2If prevalence of quinolone resistance for *Neisseria gonorrhoeae* is < 5%. 3May be available only in specialist clinics. 13.9 Treatment of uncomplicated anogenital gonorrhoea Uncomplicated infection • Ceftriaxone 500 mg IM plus azithromycin 1 g orally or • Cefixime 400 mg stat or • Ciprofloxacin 500 mg orally stat^{1,2} or • Ofloxacin 400 mg orally stat^{1,2} Pregnancy and breastfeeding • Ceftriaxone 500 mg plus azithromycin 1 g IM stat or • Spectinomycin 2 g IM stat³ Pharyngeal gonorrhoea • Ceftriaxone 500 mg IM plus azithromycin 1 g stat or • Ciprofloxacin 500 mg^{1,2} orally stat or • Ofloxacin 400 mg^{1,2} orally stat

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bleeding from the cervix, evidence of PID or no obvious clinical signs. Treatment options are listed in Box 13.11. The patient's male partner(s) should be investigated and treated. Many infections clear spontaneously but others persist. PID, with the risk of tubal damage and subsequent infertility or ectopic pregnancy, is a rare but important long-term complication. Other complications include perihepatitis, chronic pelvic pain, conjunctivitis and SARA (p. 1031). Perinatal transmission may lead to ophthalmia neonatorum and/or pneumonia in the neonate. Other sexually transmitted bacterial infections Chancroid, granuloma inguinale and LGV as causes of genital ulcers in the

tropics are described in Box 13.12. LGV is also a cause of proctitis in MSM (p. 334).

13.11 Treatment of chlamydial infection

Standard regimens • Azithromycin 1 g orally as a single dose¹ or • Doxycycline 100 mg twice daily orally for 7 days²

Alternative regimens • Erythromycin 500 mg four times daily orally for 7 days or 500 mg twice daily for 2 weeks or • Ofloxacin 200 mg twice daily orally for 7 days²

¹Safety in pregnancy and breastfeeding has not been fully established. ²Contraindicated in pregnancy and breastfeeding.

13.12 Salient features of lymphogranuloma venereum, chancroid and granuloma inguinale (Donovanosis)

Infection and distribution Organism Incubation period Genital lesion Lymph nodes Diagnosis Management

Lymphogranuloma venereum (LGV) E/W Africa, India, SE Asia, S America, Caribbean *Chlamydia trachomatis* types L1, 2, 3 3–30 days Small, transient, painless ulcer, vesicle, papule; often unnoticed Tender, usually unilateral, matted, suppurative bubo; inguinal/femoral nodes involved¹ Serological tests for L1–3 serotypes; swab from ulcer or bubo pus for *Chlamydia* Doxycycline² twice daily orally for 21 days or Erythromycin 500 mg four times daily orally

Chancroid Africa, Asia, Central and S America *Haemophilus ducreyi* (short Gram-negative bacillus) 3–10 days Single or multiple painful ulcers with ragged undermined edges As above but unilocular, suppurative bubo; inguinal nodes involved in ~50% Microscopy and culture of scrapings from ulcer or pus from bubo Azithromycin³ 1 g orally once or Ceftriaxone 250 mg IM once or Ciprofloxacin² 500 mg twice daily orally for 3 days

Granuloma inguinale Australia, India, Caribbean, S Africa, S America, Papua New Guinea *Klebsiella granulomatis* (Donovan bodies) 3–40 days Ulcers or hypertrophic granulomatous lesions; usually painless⁴ Initial swelling of inguinal nodes, then spread of infection to form abscess or ulceration through adjacent skin Microscopy of cellular material for intracellular bipolar-staining Donovan bodies Azithromycin³ 1 g weekly orally or 500 mg daily orally or Doxycycline² 100 mg twice daily orally or Ceftriaxone 1 g IM daily N.B. Partners of patients with LGV, chancroid and granuloma inguinale should be investigated and treated, even if asymptomatic. ¹The genito-ano-rectal syndrome is a late manifestation of LGV. ²Doxycycline and ciprofloxacin are contraindicated in pregnancy and breastfeeding. ³The safety of azithromycin in pregnancy and breastfeeding has not been fully assessed. ⁴Mother-to-baby transmission of granuloma inguinale may rarely occur.

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Genital herpes simplex Infection with herpes simplex virus type 1 (HSV-1) or type 2 (HSV-2) produces a wide spectrum of clinical problems (p. 247), and may facilitate HIV transmission. Infection is usually acquired sexually (vaginal, anal, orogenital or oroanal), but perinatal transmission to the neonate may also occur. Primary infection at the site of HSV entry, which may be symptomatic or asymptomatic, establishes latency in local sensory ganglia. Recurrences, either symptomatic or asymptomatic viral shedding, are a consequence of HSV reactivation. The first symptomatic episode is usually the most severe. Although HSV-1 is classically associated with orolabial herpes and HSV-2 with anogenital herpes, HSV-1 now accounts for more than 50% of anogenital infections in the UK. Clinical features The first symptomatic episode presents with irritable vesicles that soon rupture to form small, tender ulcers on the external genitalia (Fig. 13.6 and see Fig. 13.2). Lesions at other sites (e.g. urethra, vagina, cervix, perianal area, anus or rectum) may cause dysuria, urethral or vaginal discharge, or anal, perianal or rectal pain. Constitutional symptoms, such as fever, headache and malaise, are common. Inguinal lymph nodes become enlarged and tender, and there may be nerve root pain in the 2nd and 3rd sacral dermatomes. Extragenital lesions may develop at other sites, such as the buttock, finger or eye, due to auto-inoculation. Oropharyngeal infection may result from orogenital sex. Complications, such

342 • SEXUALLY TRANSMITTED INFECTIONS Analgesia may be required and saline bathing can be soothing. Treatment may be continued for longer than 5 days if new lesions develop. Occasionally, intravenous therapy may be indicated if oral therapy is poorly tolerated or aseptic meningitis occurs. Catheterisation via the suprapubic route is advisable for urinary retention due to autonomic neuropathy because the transurethral route may introduce HSV into the bladder. Recurrent genital herpes Symptomatic recurrences are usually mild and may require no specific treatment other than saline bathing. For more severe episodes, patient-initiated treatment at onset, with one of the following 5-day oral regimens, should reduce the duration of the recurrence: • aciclovir 200 mg five times daily • famciclovir 125–250 mg twice daily • valaciclovir 500 mg twice daily. In a few patients, treatment started at the onset of prodromal symptoms may abort recurrence. Suppressing therapy may be required for patients with frequent recurrences, especially if these are experienced at intervals of less than 4 weeks. Treatment should be given for a minimum of 1 year before stopping to assess recurrence rate. About 20% of patients will experience reduced attack rates thereafter, but for those whose recurrences remain unchanged, resumption of suppressive therapy is justified. Aciclovir 400 mg twice daily is most commonly prescribed. Management in pregnancy If her partner is known to be infected with HSV, a pregnant woman with no previous anogenital herpes should be advised to protect herself during sexual intercourse because the risk of disseminated infection is increased in pregnancy. Consistent condom use during pregnancy may reduce transmission of HSV. Genital herpes acquired during the first or second trimester of pregnancy is treated with aciclovir as clinically indicated. Although aciclovir is not licensed for use in pregnancy in the UK, there is considerable clinical evidence to support its safety. Third-trimester acquisition of infection has been associated with life-threatening haematogenous dissemination and should be treated with aciclovir. Vaginal delivery should be routine in women who are symptomless in late pregnancy. Caesarean section is sometimes considered if there is a recurrence at the beginning of labour, although the risk of neonatal herpes through vaginal transmission is very low. Caesarean section is often recommended if primary infection occurs after 34 weeks because the risk of viral shedding is very high in labour. Human papillomavirus and anogenital warts Human papillomavirus (HPV) DNA typing has demonstrated over 90 genotypes (p. 1238), of which HPV-6, HPV-11, HPV-16 and HPV-18 most commonly infect the genital tract through sexual transmission. It is important to differentiate between the benign genotypes (HPV-6 and 11) that cause anogenital warts, and genotypes such as 16 and 18 that are associated with dysplastic conditions and cancers of the genital tract but are not a cause of benign warts. All genotypes usually result in subclinical infection of the genital tract rather than clinically obvious lesions affecting penis, vulva, vagina, cervix, perineum or anus. as urinary retention due to autonomic neuropathy, and aseptic meningitis, are occasionally seen. First episodes usually heal within 2–4 weeks without treatment; recurrences are usually milder and of shorter duration than the initial attack. They occur more often in HSV-2 infection and their frequency tends to decrease with time. Prodromal symptoms, such as irritation or burning at the subsequent site of recurrence, or neuralgic pain affecting buttocks, legs or hips are commonly seen. The first symptomatic episode may be a recurrence of a previously undiagnosed primary infection. Recurrent episodes of asymptomatic viral shedding are important in the transmission of HSV. Diagnosis Swabs are taken from vesicular fluid or ulcers for detection of DNA by PCR, or tissue culture and typing as either HSV-1 or 2. Electron microscopy of such material will give only a presumptive diagnosis, as herpes group viruses appear similar. Type-specific antibody tests are available but are not sufficiently accurate for general use. Management First episode The following 5-day oral regimens should be started within 5 days of the beginning of the episode, or while lesions are still forming: • aciclovir

400 mg three times daily • valaciclovir 500 mg twice daily. Famciclovir 250 mg three times daily or aciclovir 200 mg five times daily is an alternative. Fig. 13.6 Herpetic ulceration of the vulva. From McMillan A, Scott GR. Sexually transmitted infections: a colour guide. Churchill Livingstone, Elsevier Ltd; 2000.

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• Surgical removal may be used to excise refractory warts, especially pedunculated perianal lesions, under local or general anaesthesia. Molluscum contagiosum Infection by molluscum contagiosum virus, both sexual and non-sexual, produces flesh-coloured, umbilicated, hemispherical papules usually up to 5 mm in diameter after an incubation period of 3–12 weeks (Fig. 13.7). Larger lesions may be seen in HIV infection (p. 306). Lesions are often multiple and, once established in an individual, may spread by auto-inoculation. They are found on the genitalia, lower abdomen and upper thighs when sexually acquired. Facial lesions are highly suggestive of underlying HIV infection. Diagnosis is made clinically or very rarely by electron microscopy. Typically, lesions persist for several months before spontaneous resolution occurs. Treatment regimens are therefore cosmetic; they include cryotherapy, hyfrecation, topical applications of 0.15% podophyllotoxin cream (contraindicated in pregnancy) or expression of the central core. Clinical features Anogenital warts caused by HPV may be single or multiple, exophytic, papular or flat. Perianal warts (p. 330), while being more common in MSM, are also found in heterosexual men and in women. Rarely, a giant condyloma (Buschke–Löwenstein tumour) develops, with local tissue destruction. Atypical warts should be biopsied. In pregnancy, warts may dramatically increase in size and number, making treatment difficult. Rarely, they are large enough to obstruct labour and, in this case, delivery by caesarean section will be required. Uncommonly, perinatal transmission of HPV leads to anogenital warts, or possibly laryngeal papillomas, in the neonate. Management The use of condoms can help prevent the transmission of HPV to non-infected partners, but HPV may affect parts of the genital area not protected by condoms. Vaccination against HPV infection has been introduced and is in routine use in many countries. There are three types of vaccine: • A bivalent vaccine offers protection against HPV types 16 and 18, which account for approximately 75% of cervical cancers in the UK. • A quadrivalent vaccine offers additional protection against HPV types 6 and 11, which account for over 90% of genital warts. • A nonavalent vaccine protects against five additional high-risk types (31, 33, 45, 52 and 58). All vaccines have been shown to be highly effective in the prevention of cervical intra-epithelial neoplasia in young women, and the quadrivalent and nonavalent vaccines have also been demonstrated to be highly effective in protecting against HPV-associated genital warts. It is currently recommended that HPV vaccination should be administered prior to the onset of sexual activity, typically at age 11–13, in a course of three injections. In the UK, only girls are offered vaccination, but it is possible that vaccination will be extended to MSM in whom HPV transmission is associated with an increased risk of anal cancer. As no vaccine protects against all oncogenic types of HPV, cervical screening programmes will still be necessary. A variety of treatments are available for established disease, including the following: • Podophyllotoxin, 0.5% solution or 0.15% cream (contraindicated in pregnancy), applied twice daily for 3 days, followed by 4 days' rest, for up to 4 weeks, is suitable for home treatment of external warts. • Imiquimod cream (contraindicated in pregnancy), applied 3 times weekly (and washed off after 6–10 hours) for up to 16 weeks, is also suitable for home treatment of external warts. • Catephen (an extract of the green tea plant, *Camellia sinensis*) is applied by the patient three times daily for up to 16 weeks. • Cryotherapy using liquid nitrogen to freeze warty tissue is

suitable for external and internal warts but often requires repeated clinic visits. • Hyfrecation – electrofulguration that causes superficial charring – is suitable for external and internal warts. Hyfrecation results in smoke plume, which contains HPV DNA and has the potential to cause respiratory infection in the operator/patient. Masks should be worn during the procedure and adequate extraction of fumes should be provided. Fig. 13.7 Molluscum contagiosum of the shaft of the penis. From McMillan A, Scott GR. Sexually transmitted infections: a colour guide. Churchill Livingstone, Elsevier Ltd; 2000. Viral hepatitis The hepatitis viruses A–D (p. 871) may be sexually transmitted: • Hepatitis A (HAV). Insertive oroanal sex, insertive digital sex, insertive anal sex and multiple sexual partners have been linked with HAV transmission in MSM. HAV transmission in heterosexual men and women is also possible through oroanal sex. • Hepatitis B (HBV). Insertive oroanal sex, anal sex and multiple sexual partners are linked with HBV infection in MSM. Heterosexual transmission of HBV is well documented and commercial sex workers are at particular risk. Hepatitis D (HDV) may also be sexually transmitted. • Hepatitis C (HCV). Sexual transmission of HCV is well documented in MSM but less so in heterosexuals. Sexual transmission is less efficient than for HBV.

344 • SEXUALLY TRANSMITTED INFECTIONS Further information Books and journal articles Pattman R, Sankar N, Elawad B, et al. (eds). Oxford handbook of genitourinary medicine, HIV, and sexual health. Oxford: Oxford University Press; 2010. Rogstad KE (ed.). ABC of sexually transmitted infections, 6th edn. Oxford: Wiley–Blackwell; 2011. Website bashh.org/guidelines British Association for Sexual Health and HIV; updates on treatment of all STIs. The sexual partner(s) of patients with HAV and HBV should be seen as soon as possible and offered immunisation where appropriate. Patients with HAV should abstain from all forms of unprotected sex until non-infectious. Those with HBV should likewise abstain from unprotected sex until they are non-infectious or until their partners have been vaccinated successfully. No active or passive immunisation is available for protection against HCV but the consistent use of condoms is likely to protect susceptible partners. Active immunisation against HAV and HBV should be offered to susceptible people at risk of infection. Many STI clinics offer HAV immunisation to MSM along with routine HBV immunisation; a combined HAV and HBV vaccine is available.

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