9.4 Vaginal discharge 1603

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ESSENTIALS Vaginal symptoms are a frequent source of discomfort and distress for many women. Bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis are considered the most common causes in pre- menopausal women, but atrophic vaginitis and noninfectious dis- orders seem to occur more often in menopausal women. Self-diagnosis and syndromic management, although increas- ingly encouraged in many parts of the world, are fraught with in- accuracy. A proper diagnosis depends on a thorough history, examination, and readily available tests in the clinic. Ancillary tests to be considered in selective circumstances include culture for yeast, culture, or nucleic acid amplification testing for Trichomonas vaginalis, Neisseria gonorrhoeae, or Chlamydia trachomatis, and Gram stain or (rarely) maturation index. Once a proper diagnosis is obtained, appropriate treatment can be selected. Introduction Vaginal discharge, itching, burning, irritation, and odour are common causes of distress in women, yet they are frequently ig- nored or trivialized by healthcare providers. With the availability of over-the-counter antifungals, self-diagnosis and self-treatment of vaginal symptoms have become routine, but questions remain about their accuracy. Appropriate tests in the clinic and laboratory are the only reliable basis for treatment. The normal vaginal environment An understanding of the normal vaginal environment is crucial to accurate clinical assessment and interpretation of test results. The normal vaginal environment is controlled by a woman's oes- trogen status. By increasing the glycogen content of vaginal epithe- lial cells, oestrogen fosters the growth of lactobacilli, which in turn seem to inhibit the growth of other organisms. Thus, a Gram stain of vaginal secretions from a healthy woman in her reproductive years should be dominated by lactobacilli and gram-positive rods. However, vaginal cultures will yield a broad range of organisms, including skin and faecal flora (e.g. Staphylococcus epidermidis, Staph. aureus, Escherichia coli, anaerobes) and organisms, which in some situations, are considered pathogenic (e.g. Streptococcus aga- lactiae (group B streptococci), Mycoplasma hominis, Ureaplasma urealyticum, Gardnerella vaginalis, and Candida albicans). In women who are either prepubertal or postmenopausal, lactobacilli are less numerous, and other bacteria will frequently predominate. Differential diagnosis and clinical investigation Most studies suggest that infections such as bacterial vaginosis (BV) (30–35% of cases), vulvovaginal candidiasis (20–25%), and trichomoniasis (15–20%) are the most common causes of vaginal symptoms, but many miscellaneous conditions, including atrophic vaginitis, vulvar conditions (e.g. vulvodynia, lichen sclerosus, li- chen simplex), or even a physiological discharge can cause symp- toms that require assessment. A thorough evaluation will usually allow correct diagnosis. An accurate diagnosis relies on both patient history and exam- ination. Symptoms can range from discharge alone to itching, burning, irritation, dyspareunia, or malodour. Since patients may be too embarrassed to mention some of these, it is helpful to in- quire about each of them in turn. Other pertinent information is

location (vulvar, introital, or vaginal), duration, variation with menstrual cycle, association with sexual activity, and response to previous therapy. A sexual history might identify women at increased risk of a sexually transmitted infection. Pelvic examination should include inspection of the vulva and vestibule; touching the vulva and vestibule with a swab (the ‘Q-tip test’) may elicit areas of tenderness. Samples should be obtained for further evaluation. Vaginal pH testing, an amine (‘whiff’) test, and saline and 10% po- tassium hydroxide microscopy should be practised routinely. If the source of discharge is primarily the cervix, culture or nucleic acid amplification tests (NAATs) for N. gonorrhoeae and C. trachomatis should be obtained. Suspected vulvar diseases might require a bi- opsy for diagnosis. Finally, in situations where the diagnosis is not clear, definitive tests can assist in the diagnosis of bacterial vagin- osis, trichomoniasis, and vulvovaginal candidiasis (Table 9.4.1). With bacterial vaginosis and vulvovaginal candidasis specifically, 9.4 Vaginal discharge Paul Nyirjesy

Section 9 Sexually transmitted diseases 1604 NAAT is available in many settings; however, it offers no clear benefit over other tests and is frequently much more expensive. Trichomoniasis Trichomonas vaginalis is a common sexually transmitted proto- zoan, causing an estimated 180 million infections per year world- wide. Traditionally, it has been considered a minor nuisance, but it is associated statistically with an increased risk of low birth weight or preterm delivery in pregnant women and of HIV transmission in nonpregnant women. Asymptomatic men and women are the primary reservoir for infection. Affected women will complain of an abnormal purulent, frothy, or bloody discharge, itching, mal- odour, dysuria, urinary frequency, dyspareunia, and post-coital bleeding. Examination might reveal erythema and excoriations of the vulva or vagina, an abnormal discharge, and punctate haem- orrhages of the cervix (the ‘strawberry cervix’). Saline microscopy might reveal motile trichomonads, but it has limited sensitivity (22–75%). Finding many white blood cells on microscopy, a posi- tive amine test, or an elevated pH might suggest the presence of trichomoniasis, but do not prove the diagnosis. The current gold standard is culture or NAAT. Where available, antigen-based tests at the point of care are much more sensitive than microscopy and provide a more rapid answer than culture. Treatment is with nitroimidazoles, either metronidazole or tinidazole. A single dose of 2 g of either will cure more than 90% of affected cases. Alternatively, a seven-day course of 500 mg twice daily is recommended, and is recommended as initial therapy for HIV-positive women. As with other sexually transmitted infections (STIs), treatment of the partner is crucial to prevent reinfec- tion. Patients who are allergic to metronidazole should be referred for desensitization and then treated with metronidazole. In cases of treatment failure, patient compliance must first be confirmed and reinfection by her partner excluded. Since tinidazole seems to be more effective than metronidazole, higher doses of tinidazole, such as 2 g daily for seven days, can be considered. Pregnant women with trichomoniasis should receive metronidazole, as there are no data on tinidazole use in pregnancy. Bacterial vaginosis This is considered the most common cause of vaginitis, with a prevalence of 5–25%. It represents a polymicrobial infection of the vagina. The vaginal flora is markedly altered. Hydrogen peroxide- producing lactobacilli are absent, and there is an overgrowth of a wide variety of organisms, including G. vaginalis, M. hominis, Bacteroides spp., Prevotella spp., Mobiluncus spp., and many other fastidious bacteria. Bacterial vaginosis is associated with a variety of risk factors, including multiple partners, more frequent sexual intercourse, smoking, and douching. Although BV-associated bacteria can be found in male or female partners, there is no evi- dence that treating partners will decrease the risk of recurrence. In nonpregnant women, it has been associated with many conditions including pelvic inflammatory disease, infection after abortion or hysterectomy,

cervicitis, urinary tract infection, and HIV and herpes simplex virus-2 transmission. In pregnant women, studies have linked bacterial vaginosis to prematurity, preterm premature rupture of membranes, and post-partum endometritis. Although up to 50% of women are asymptomatic, affected women will note an abnormal discharge or a fishy odour, which is often worse during menses or after intercourse. Itching and ir- ritation are considered rare. The clinical criteria (Amsel's criteria) which are used to diagnose infection consist of the following: • a homogeneous grey or white discharge • a vaginal pH exceeding 4.5 • a positive amine test • more than 20% clue cells (vaginal epithelial cells stippled with bacteria) on saline microscopy Three out of the four criteria are adequate for a diagnosis. Alternatively, a Gram stain (Nugent) score, which evaluates the presence or absence of various bacterial morphotypes, can be used. Because the Nugent score is a permanent record which can be read by personnel who are blinded to patient information, it is the pre- ferred method of diagnosis in research studies. Oral or topical treatments seem equally effective. • Oral regimens, including metronidazole 500 mg twice a day for seven days, tinidazole 1 g daily for five days, or 2 g daily for two days, or clindamycin 300 mg twice daily for seven days, tend to be less expensive but might cause gastrointestinal adverse effects; metronidazole and tinidazole are incompatible with drinking alcohol. • Topical regimens, such as 0.75% metronidazole gel (one 5 g ap- plication daily for five days), 2% clindamycin standard (one 5 g application daily for seven days), or single-dose creams (one 5 g application), and 100 mg clindamycin ovules (one ovule nightly, for three doses) tend to be more expensive. In high-risk pregnant women, particularly those with prior pre- term birth, as well as nonpregnant women undergoing either hysterectomy or abortion, screening and treating for bacterial vaginosis might decrease associated morbidities. To date, low-risk pregnant women do not seem to benefit from screening and treat- ment for asymptomatic bacterial vaginosis. Apart from tinidazole, Table 9.4.1 Testing for vaginal infections Vaginal pH Amine test Microscopy Gold standard Normal ≤4.5 − Normal Bacterial vaginosis

> 4.5

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Clue cells Gram stain Trichomoniasis

> 4.5 ± Trichomonads Trichomonas culture or NAAT Vulvovaginal candidiasis ≤4.5 − Pseudohyphae, blastospores Yeast culture Atrophy 4.5 − Immature epithelial cells Maturation index

9.4 Vaginal discharge 1605 pregnant women can be treated with similar bacterial vaginosis re- gimens as nonpregnant women. Recurrence after treatment seems to occur commonly, up to 50% within six months. For patients with frequent recurrences (three or more per year), a prolonged four-month course of suppressive antibiotic therapy, such as metronidazole 0.75% gel, one 5 g appli- cator twice weekly, was associated with much lower rates of bac- terial vaginosis than a placebo group. Although probiotics have been proposed as a way to repopulate the vagina with lactobacilli, there are no conclusive data to support their use or efficacy, even in women with recurrent bacterial vaginosis. Vulvovaginal candidiasis About 75% of women will, at some time in

their lives, develop vulvovaginal candidiasis or ‘yeast infections’. C. albicans causes 90–95% of vulvovaginal candidiasis; of the many other species of yeast that are sometimes implicated, C. glabrata is thought to be the second most common. Commonly recognized risk factors for candidiasis include the use of oral contraceptives, recent use of broad-spectrum antimicrobials, pregnancy, diabetes mellitus, and immunosuppression. Being sexually active and practising oral receptive sex are associated with vulvovaginal candidiasis, but there are no data to support partner treatment. Patients with vulvovaginal candidiasis complain primarily of vulvar or vaginal pruritus, irritation, burning, dyspareunia, or abnormal discharge. The symptom of discharge is quite unreliable in predicting which women with vaginitis actually have vulvovaginal candidiasis. Examination of affected women might reveal vulvar erythema, oe- dema, excoriations, or fissures. Vaginal thrush might be present. The vaginal pH is normal. On microscopy, hyphae or blastospores may be seen, but the sensitivity is fairly low (c. 50%); thus, a simple yeast culture is recommended in women who are symptomatic but with negative microscopy. For most women with vulvovaginal candidiasis, the infection will be uncomplicated: it is sporadic, associated with relatively mild symptoms, caused by C. albicans, and is occurring in an otherwise normal host. Uncomplicated vulvovaginal candidiasis generally responds readily to any available antimycotic treatment. Topical therapies consist primarily of imidazoles, including miconazole, clotrimazole, butoconazole, and terconazole, which are available as creams or suppositories applied for 1–7 days. A single 150 mg dose of oral fluconazole seems equivalent to topical treatments. An estimated 5% will suffer complicated vulvovaginal candid- iasis, marked by either an underlying medical problem such as diabetes mellitus or HIV infection, severe symptoms, recurrent disease (four or more episodes per year), or an infection caused by a yeast other than C. albicans. Most of these women will not have any of the commonly recognized risk factors for infection. Complicated vulvovaginal candidiasis will recur within a month in at least 50% of cases, and is best managed by first obtaining a positive yeast culture to obtain information about the species of the isolate, then by more aggressive therapy and follow-up. In patients with severe vulvovaginal candidiasis, a second dose of fluconazole three days after the first, or a second week of topical therapy, im- proves the chance of complete resolution. Women with recurrent vulvovaginal candidiasis caused by C. albicans benefit from pro- longed suppressive therapy with weekly oral fluconazole (100– 200 mg) after an initial induction phase of three doses given three days apart. Finally, for C. glabrata infections, boric acid capsules (600 mg vaginally), nightly for 14 days, are often curative. Atrophic vaginitis Since women are living longer in many countries, larger propor- tions of their lives are postmenopausal. As a consequence, atro- phic vaginitis, which is caused by a lack of oestrogen, is likely to become increasingly common. Women with atrophy may present with a spectrum of complaints, including an abnormal discharge, dryness, itching, and dyspareunia. Signs of labial atrophy, vaginal pallor, or loss of rugal folds can be easily missed. The vaginal pH will usually be elevated above 4.5. On wet mount, immature epithe- lial cells, either parabasals or intermediate cells, which are rounder, smaller, and have a greater nuclear:cytoplasmic ratio can be seen. Because of its effects on vaginal flora, there might be a decreased normal flora or even a shift to cocci instead of bacilli. In the absence of contraindications, oestrogen remains the medication of choice. Topical therapy, in the form of cream, tablets, or an oestrogen ring, will give the highest local levels of oestrogen, while minimizing systemic absorption but not eliminating it. Since oestrogen tends to cause slow improvement, patients should be in- structed to adhere to treatment for at least six weeks before con- cluding that it will be ineffective. Conclusions Vaginitis is a common problem in women of all ages. Effective therapy is available for the many causes of vulvovaginal symptoms, but will depend on an accurate diagnosis. FURTHER READING Anderson MR, Klink K, Cohrssen A (2004). Evaluation of vaginal complaints. JAMA, 291, 1368–79. Centers for Disease Control and Prevention (2015).

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