PART 2I

Vulvovaginal candidiasis

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Sex Transm Infect 2006;**82**(Suppl IV):iv28–iv30. doi: 10.1136/sti.2006.023168

Vulvovaginal candidiasis (VVC) is a syndrome rather than an infection and diagnosis of VVC does not rely on laboratory or clinical criteria alone but a combination of the two. The disease spectrum ranges from ''innocent bystander,'' where symptoms are wrongly attributed to coincidental isolation of candida to complicated disease where VVC is severe, persistent, or recurrent or there is an underlying host abnormality.[1]

Who to test and treat?

Screening is not required for asymptomatic women (evidence level IV, recommendation grade C).[2 3]

Episodic VVC

Episodic VVC includes normal women with mild to moderate symptoms and no history of persistent or recurrent symptoms[1] (evidence level IV, recommendation grade C).

Symptoms suggestive of episodic VVC include external dysuria, vulval pruritus, swelling, or redness. Signs include vulval oedema, fissures, excoriation, or thick curdy discharge. The vaginal pH is usually normal[4–9] (evidence level III, recommendation grade B).

- Testing is recommended for episodic VVC whenever possible (evidence level III, recommendation grade B).[4–9]
- Treatment is clearly indicated for symptomatic women who are microscopy positive and/or those who are culture positive[4–9] (evidence level III, recommendation grade B).
- Treatment on the basis of symptoms alone is common clinical practice but results in the overtreatment of a large number of women[4–9] (evidence level III, recommendation grade B).

Complicated VVC

This includes severe episodic VVC, persistent non-*Candida albicans* infection, recurrent VVC, and those with underlying host abnormality—for example, pregnancy, HIV infection and diabetes[1] (evidence level IV, recommendation grade C).

As well as microbiological testing women with chronic symptoms need a careful history and examination. Particular attention needs to be paid to alternative diagnoses, most commonly vulval eczema/dermatitis. Possibilities otherwise include other causes of vaginal discharge—for example, recurrent bacterial vaginosis and also recurrent herpes, vulval vestibulitis syndrome, and other vulvar dermatoses[10] (evidence level III, recommendation grade B). More than one condition may occur and this may vary with time—for example, the patient may cycle between bacterial vaginosis and VVC.[11] A general examination of the skin can sometimes be very helpful (evidence level IV, recommendation grade C).

RECOMMENDED TESTS

Except in research settings samples are almost universally taken with a cotton tipped swab from the vaginal wall.

Possible uncomplicated VVC

In the context of specialist services offering a comprehensive sexual health service routine microscopy and culture is the standard of care for symptomatic women[4–9] (evidence level III, recommendation grade B).

A vaginal swab taken from the anterior fornix[12] (evidence level III, recommendation grade B).

- Gram or wet film examination[4–9] (evidence level III, recommendation grade B)
- Directly plated to solid fungal media. Speciation to *albicans*/non-*albicans* is strongly preferred[3 13–15] (evidence level III, recommendation grade B).
- Vaginal pH is not useful in the diagnosis of VVC which can coincide with bacterial vaginitis[11] (evidence level IV, recommendation grade C).

Blind[16] (evidence level III, recommendation grade B) or self taken swabs (evidence level IV, recommendation grade C) may be useful if directly taken swabs are not easily taken and if examination is not deemed necessary.

Complicated disease

Tests for individual episodes as above.

- Speciation to *albicans*/non-*albicans* is essential and should be performed to species level if a non-*albicans* species is isolated on more than one occasion[3 13–15] (evidence level III, recommendation grade B).
- Self taken swabs are useful in obtaining culture evidence of recurrent/persistent VVC. These can taken when the patient is symptomatic before treatment and can be combined with a symptom diary as part of the assessment process (evidence level IV, recommendation grade C).

RECOMMENDED SITES FOR TESTING

- If a speculum is being passed then a cotton tipped swab should be used to take a sample from the anterior fornix[12] (evidence level III, recommendation grade B).
- If speculum is not being passed then blind[16] (evidence level III, recommendation grade B) or self taken swabs may be used (evidence level IV, recommendation grade C)

PROCESSING OF SAMPLES

Microscopy should be of either a Gram stained or wet mount preparation[4–9] (evidence level III, recommendation grade B). Culture should be from a directly plated solid fungal media (evidence level III, recommendation grade B). Chromogenic agar if available enables easy identification of species and mixed species infection and is preferred for investigation for complicated VVC[17] (evidence level III, recommendation grade B).

Abbreviations: VVC, vulvovaginal candidiasis

Liquid culture media are not recommended as they do not allow semi-quantitation. Other methods of testing for candida such as latex agglutination have not made their way into routine clinical practice.[18–20] Polymerase chain reaction is currently of use only as a research tool.[21–23]

Antifungal sensitivities

There is no proved utility of antifungal sensitivity testing for complicated VVC[24] (evidence level III, recommendation grade B). It is possibly indicated for women with a chronic immunological abnormality[25] (evidence level III, recommendation grade B); or repeated isolation of a non-*albicans* yeast[26 27] (evidence level IV, recommendation grade C).

Reporting of results

Microscopy should be reported as fungal pseudohyphae and/or blastospores present or absent[4–9] (evidence level III, recommendation grade B).

Cultures should be reported as[3 13–15] (evidence level III, recommendation grade B):

- Negative
- Light growth <10 colonies per plate
- Moderate growth 10–99 colonies per plate
- Heavy growth ⩾100 colonies per plate.

Interpretation of results

In interpreting results the possibility of candida being an ''innocent bystander'' needs to be considered—that is, that symptoms from another condition are wrongly attributed to coincidental asymptomatic isolation of candida[1] (evidence level IV, recommendation grade C).

Isolation of candida is common in asymptomatic women.[2 3] Treatment is not indicated in the absence of symptoms (evidence level III, recommendation grade B).

Symptoms correlate with hyphal burden, and the presence of pseudohyphae and/or blastospores on light microscopy implies a relatively high fungal burden.[3 13–15] Microscopy is therefore relatively specific but insensitive in the diagnosis of VVC[4–9 28 29] (evidence level III, recommendation grade B). In contrast, culture is sensitive but not specific. Symptoms are not clearly associated with colony counts of <10 colonies/plate (evidence level III, recommendation grade B).

Severity of individual episodes is based on clinical and not laboratory data. Severe disease may however require more intensive treatment[30] (evidence level Ib, recommendation grade A).

Non-*albicans* species, most commonly *C glabrata*, are isolated in 5–10% of episodic VVC but cannot be distinguished from *C albicans* on clinical criteria[10 26 31] (evidence level III, recommendation grade B). They are inherently relatively azole resistant and may not respond well to conventional courses of antifungal treatment[10 26] (evidence level III, recommendation grade B).

Recurrent VVC is defined as four or more attacks of VVC in a year[1] (evidence level IV, recommendation grade C). It is usually caused by *C albicans*. Although there is evidence of persistence of infection between attacks using PCR (so called vaginal relapse) culture is negative between attacks. A diagnosis of recurrent VVC therefore requires either positive microscopy or a moderate/heavy growth of *C albicans*, when symptomatic, on at least two occasions with treatment and at least partial resolution of symptoms in between (evidence level IV, recommendation grade C).

Persistent VVC is usually caused by non-*C albicans* yeast.[1] Risk factors include underlying host abnormality and being peri-menopausal. Diagnosis of persistent/chronic non-*albicans* infection requires isolation of the same species of yeast on at least two concurrent samples and treatment on the first occasion (evidence level IV, recommendation grade C).

RECOMMENDATION FOR TEST OF CURE

Tests of cure are only indicated after the treatment of persistent non-*albicans* infection (evidence level IV, recommendation grade C). Proof of cure requires at least two negative cultures at least a week after treatment and with an interval of at least a week between cultures (evidence level IV, recommendation grade C).

STAKEHOLDER INVOLVEMENT

No stakeholders were involved in developing the guideline.

RIGOUR OF DEVELOPMENT

The Cochrane database was searched for articles on expressions ''Candidiasis'', ''Vulvovaginal''. Medline (1966–Jan 2003) was searched using expressions ''Candidiasis'', ''Vulvovaginal/di'' [Diagnosis] and ''Candidiasis'', ''Vulvovaginal'' (1990–Jan 2003). The resulting articles were hand searched and sorted. Further references were obtained from these articles. References were also obtained from Candida and *Candidosis, A Review and Bibliography* by Odds.[2] This book contains an extensive bibliography for papers predating 1988.

APPLICABILITY

The diagnosis of VVC is syndromic. Diagnostic criteria may therefore vary with the clinical setting. These guidelines are specifically written for women of reproductive age presenting to departments of genitourinary medicine or sexual health. They are written on the assumption that on-site facilities are available for microscopy with direct inoculation of culture media and incubation of microbiological samples.

In other settings the effects of transportation and the use of transport media have not been investigated but it is likely that germination and growth will occur[32] thereby increasing the sensitivity and reducing specificity. If transport media are used then slides for microscopy should be prepared before inoculation.

AUDITABLE OUTCOME MEASURES

- Proportion of symptomatic culture positive women (moderate or heavy growth) who are microscopy positive. Target: 50%
- Proportion of women with complicated VVC who have speciation performed. Target 100%
- Proportion of women dispensed antifungals with negative culture results. Target less than 30%.

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Conflict of interest: AV as no conflicts of interest. DJW has received a research grant from Astra Zeneca.

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Accepted for publication 31 August 2006

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