The treatment of *Candida* vaginitis and vulvitis

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SYNOPSIS

Vulvovaginitis may have an infectious cause, a non-infectious cause or a combination of both. A vaginal swab is usually needed to establish the diagnosis even though *Candida albicans* is the commonest infectious cause. Treatment of vulvovaginitis may require modification of the vaginal environment. Specific treatment for *C. albicans* involves inserting an antifungal drug into the vagina when the patient is symptomatic. Patients with recurring infections may need long-term prophylaxis with an oral antifungal drug. The diagnosis must be reviewed if patients do not respond to treatment.

Index words: candidiasis, antifungal drugs.

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Introduction

Candida albicans is the commonest cause of vulvitis and vaginitis. However, it is not the only cause and the clinician must be aware of the common conditions which produce similar symptoms (Table 1). Vaginal swabs and vulval biopsy are the most useful tools for differentiating these conditions.

Myths, traps and sexual sequelae

Candida reaches the vagina via oral ingestion. It is not sexually transmitted. It is therefore unnecessary to recommend treatment of the male partner unless he has candidal balanitis or another form of cutaneous candidiasis in the genital area.

C. albicans infection is an oestrogen dependent disorder. It therefore seldom occurs in healthy children, women who are breastfeeding or postmenopausal women unless they are on relatively high doses of oestrogen replacement. The infection almost always occurs within the insensitive vaginal lumen. The resultant 'burning' of the sensitive vulval epithelium is caused by the yeast's metabolites (seldom by infection of the vulval skin). Treatment must be directed to the vaginal source of the infection. Applying antifungal preparations to the vulva will not only be ineffective but will also worsen the contact dermatitis which is a feature of the complaint.

Mixed pathology is common in the vulval area. The commonest combination is vulval dermatitis exacerbated by bouts of candidiasis. Swabbing as often as necessary is the only means of selecting the appropriate treatment. The inappropriate use of antifungal applications can make the dermatitis worse as these products are relatively toxic to genital epithelium.

Candida species other than albicans are being diagnosed with increasing frequency. Examples are *Candida glabrata*, *krusei*, *parapsilosis* and *tropicalis*. These non-albicans yeasts are relatively non-pathogenic and rarely, if ever, require treatment. This is fortunate, because they are generally resistant to the usual antifungal drugs, and the over-the-counter availability of these treatments is probably why these yeasts are being selected out and appearing more often. This is also why pathologists must identify the species in all cultures positive for Candida.

Any woman who has genital discomfort for longer than, say, six months may develop impairment of sexual arousal. Dyspareunia can result from a combination of coital physical, chemical and biological trauma.

Recurrent candidiasis is an undoubted problem and the vast majority of sufferers are healthy women. I am unaware of any dietary regimen, so-called 'natural products' or lifestyle modification (other than prolongation of breastfeeding) which makes any significant difference to the incidence of this complaint. The vast majority of these patients will not be diabetic. Glucose tolerance testing is indicated in the more difficult cases and always in the postmenopausal woman with *C. albicans* infection if she is not receiving hormone replacement therapy.

General principles of treatment

Health professionals

The importance of having a vaginal swab taken before starting any treatment needs to be particularly emphasised to the patient. If the patient does not respond as you would expect to your first treatment, stop everything and think again. Is your diagnosis correct? There is no place for the empirical use of vaginal antifungals if the patient does not get a complete and prolonged response to a one week course.

Patients' personal care

Inflamed epithelium is hypersensitive to chemical and physical trauma, therefore special care needs to be taken and only normal saline can be guaranteed safe for washing. Most patients will benefit from avoiding soap and other cleansing agents and bathing the area with normal saline (salt, two teaspoons to the litre) applied with cotton wool and gently patted dry with a soft towel. For the same reason, patients should be advised not to use home remedies, over-the-counter preparations and non-prescribed medication. In the sexually active, the avoidance of artificial lubricants should be discussed.

Table 1
Vulvovaginal inflammatory conditions

More common infections	*Non-infectious conditions*
Fungal Candidiasis Tinea cruris or versicolor Viral Herpes simplex Bacterial Gram positive cocci *Staphylococcus aureus* Folliculitis Furuncles Abscess Streptococci Erysipelas Gram negative cocci Gonococcal vulvovaginitis Gram negative bacilli Donovanosis Chancroid Spirochaetes Syphilis Mixed and non-specific Bartholinitis Parasites Trichomoniasis Pediculosis pubis Scabies	Spongiotic disorders (characterised by intraepidermal oedema) Irritant contact dermatitis Allergic contact dermatitis Atopic dermatitis (eczema) Psoriasiform disorders Psoriasis Lichen simplex chronicus Lichenoid reactions (epidermal basal layer damage) Lichen sclerosus Erosive lichen planus Erosive vaginitis Plasma cell vulvitis Lupus erythematosus Drug eruption Vesicobullous disorders Including pemphigus, erythema multiforme, pemphigoid, herpes gestationalis and dermatitis herpetiformis Granulomatous disorders Including Crohn's disease and sarcoidosis Vasculopathic disorders Including Behcet's disease and urticaria

Note: Bacterial vaginosis (Gardnerella infection) does not produce vaginitis.
Streptococci and coliforms are not vaginal pathogens

Treatment of *C. albicans* infection

Many preparations are effective in the treatment of candidiasis. A vaginal imidazole, inserted nightly for one week, is recommended as the standard treatment for candidal vulvovaginitis.

Treatment of recurrent candidiasis

There is no generally agreed definition of recurrent candidiasis. However, the infection may be deemed recurrent if there is a proven recurrence less than six months after a similar episode has been successfully treated. Unless further measures are undertaken, experience suggests that recurrences, at an unacceptable frequency, are likely.

Laboratory confirmation of each suspected infection is an integral part of the management. The woman should be advised to have a vaginal swab taken whenever she suspects a recurrence.

There are several strategies for the prevention of recurrent infection. One week of a vaginal imidazole is still the treatment of choice when clinical (proven) infection occurs.

Alteration of the vaginal environment

This may be accomplished by a change of contraception to depot medroxyprogesterone acetate (which provides oestrogen-free ovulation suppression). For women taking hormone replacement therapy a lower dose of oestrogen can be used.

Long-term vaginal therapy

The nightly insertion of one million units of nystatin in a vaginal cream, tablet or pessary (including during menstruation) can virtually be guaranteed to keep a woman free of candidiasis without producing any significant discharge during the day. This therapy should continue for six months in the more troublesome cases. It is the treatment of choice for pregnant women who have had more than one proven infection during the pregnancy. This prophylaxis should not be stopped until the onset of labour.

Long-term oral therapy

Ketoconazole, fluconazole and itraconazole are effective oral anticandidal drugs available in Australia. They do not attain a concentration in vaginal secretions which is sufficient for them to be recommended as the sole treatment for clinical infection but they are definitely effective for prophylaxis. There is evidence that fluconazole is the most effective and least toxic but, at the usual dosage of 100 mg orally twice weekly (for prophylaxis), the patient will pay almost $40 a week.

Ketoconazole 200 mg orally daily is over 80% effective in preventing recurrences, but reports of hepatotoxicity and occasionally other adverse effects reduce its attractiveness. Sometimes recurrences will occur unless the dosage is raised to 200 mg twice daily. Ketoconazole requires an authority prescription if it is supplied by the Pharmaceutical Benefits Scheme. Six months continuous treatment is recommended.

Treat each recurrence thoroughly

Many women, given ready access to microbiological diagnosis and safe in the knowledge that they can get rapid treatment for each recurrence, will settle on just that – medication with each proven recurrence. In the event of multiple recurrences I would recommend 14 days continuous use (including during

menstruation) of a vaginal imidazole cream and a simultaneous course of ketoconazole 200 mg twice daily for five days. In many cases this regimen will reduce the frequency of recurrences.

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Self-test questions

The following statements are either true or false (answers on page 75)

5. Not all species of Candida found in the vagina need treatment with antifungal drugs.
6. Genital candidiasis rarely occurs in healthy postmenopausal women unless they are taking hormone replacement therapy.

Your questions to the PBAC

I am writing to express my concern with respect to the February decision of the Pharmaceutical Benefits Advisory Committee (PBAC) to list bupropion. Even in my small town we have been inundated by requests for the drug, from smokers of all types. This has been spurred on by both word of mouth and continued media coverage. Making an assessment of the relevance of the drug to that particular person has been all but impossible, with people fearful that if they do not get in quick they will not get the bargain price. To be honest it has been almost like a firesale at the local department store, with the hysteria to match.

It has been impossible to get through to the Health Insurance Commission for more relevant and urgent authority prescriptions because the staff are busy processing requests for bupropion. I am deeply concerned at the cost to taxpayers of this PBAC-induced mayhem, and what benefit there will be to Australian consumers.

Discussions I have had with patients reveal poor compliance with the drug. No associated rehabilitation program was offered in conjunction with the release of this drug, and there are no local resources to provide one on a mass scale.

All in all, this has got to be the poorest effort at listing of a drug by the PBAC that I have ever seen, and has put most general practitioners in an awkward position of having to decide how to respond to mass hysteria and pressure.

Dr Ewen McPhee

General Practitioner

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PBAC response

At its September 2000 meeting the PBAC recommended that bupropion be listed as an authority required pharmaceutical benefit for use within a comprehensive treatment program, as short-term adjunctive therapy for nicotine dependence with the goal of maintaining abstinence. The recommended listing provided for only one application per patient per year and prohibited the authorisation of increased maximum quantities or repeats.

In making its recommendations, the PBAC considers the effectiveness, cost-effectiveness and clinical place of a product compared to other products. Where there is no alternative as was the case for bupropion, the PBAC compares the product with standard medical care and considers the benefits the new product will provide compared to the cost of achieving those benefits. The PBAC also took into account the comparative performance of bupropion and nicotine replacement therapy.

The PBAC considered treatment with bupropion to be clinically and cost-effective where compared to standard therapy and nicotine replacement therapy. The PBAC is of the view that the large number of Australians currently seeking this therapy is an encouraging indication that many smokers want to stop smoking, and that listing this treatment on the Pharmaceutical Benefits Scheme is entirely appropriate. Furthermore, the Commonwealth Government has a role in promoting the cessation of smoking as this is a public health issue.

In relation to the comprehensive treatment program requirement of the authority listing for bupropion, this need not necessarily be a formal rehabilitation program, and in fact may be limited to counselling by the prescribing practitioner. The manufacturer of bupropion advises that a comprehensive motivational support program in smoking cessation, developed by the company, was in place when the medication was first released, as a private prescription, in November 2000. Patient enrolment in the program may be initiated by the prescribing doctor, a pharmacist or the patient in response to a package insert outlining the program and relevant contact details. Encouragement for patients to access the well established national *QUIT* program is also appropriate as a source of motivational support.

The Health Insurance Commission (HIC) appreciates the frustration prescribers may have felt as they experienced difficulties in getting through to obtain telephone authorities when calls unexpectedly nearly doubled when bupropion was listed on 1 February 2001. The HIC responded by re-allocating staff from other areas and in some states, additional staff were recruited to assist during the period of high demand, which has since eased significantly.

Correction

One of the letters published in 'Your questions to the PBAC' (Aust Prescr 2001;24:7) mentioned celecoxib as a general benefit on the Pharmaceutical Benefits Scheme (PBS). This is incorrect. Celecoxib is listed on the PBS as a restricted benefit for chronic arthropathies (including osteoarthritis) with an inflammatory component.