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BASIC RESEARCH

Oestrogen, glycogen and vaginal candidiasis

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SUMMARY

Our aim was to relate vaginal candidiasis to vaginal oestrogenisation. First, the incidence was determined (subjected to chi-square analysis) of vaginal *Candida albicans* infection in 339 consecutive dermogynaecology clinic patients aged 55 years and over, of whom 142 were using and 197 were not using oestrogen. Second, the ability of *Candida* species to utilise glycogen as a sole nutrient source was studied by performing assimilation tests using yeast nitrogen broth as a basal medium.

Of the women using oestrogen, 26% had *C. albicans* infection on initial presentation compared with 4% in the cohort not using oestrogen ($p < 0.001$). All 34 isolates of *C. albicans* assimilated glycogen. Twenty-six non-*albicans* species of *Candida* tested did not assimilate glycogen.

In this study of postmenopausal women, there was a highly significant relationship between the usage of oestrogen and the occurrence of *C. albicans* infection. The production of glycogen by oestrogen stimulated epithelial maturation provides an attractive substrate for *C. albicans*.

INTRODUCTION

Glycogen is produced by the vaginal epithelium in proportion to its oestrogenisation (Figures 1 and 2) and is the nutrient likely to be responsible for proliferation of *Candida* species when host oestrogen exceeds a certain level. Surprisingly little work has been done on this aspect of this commonest of gynaecological infections.[1,2] We have investigated the relationship between oestrogen, glycogen and candidal growth through two avenues. First, a survey of vaginal candidiasis in postmenopausal women on and off oestrogen replacement therapy. Second, the ability of *C. albicans* and some non-*albicans* species to utilise glycogen as a sole nutrient source was studied by performing assimilation tests using yeast nitrogen broth as a basal medium.[3]

MATERIAL AND METHODS

The Dermogynaecology Clinic at the Mercy Hospital for Women was established in 1989 to investigate and treat benign disorders of the vulva and vagina that previously had been found difficult to manage. From the clinic's commencement to 1998 inclusive, 339 new

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Figure 1 Mature vaginal epithelium showing progressive PAS positivity towards the surface which was proven to be glycogen by its abolition with diastase.

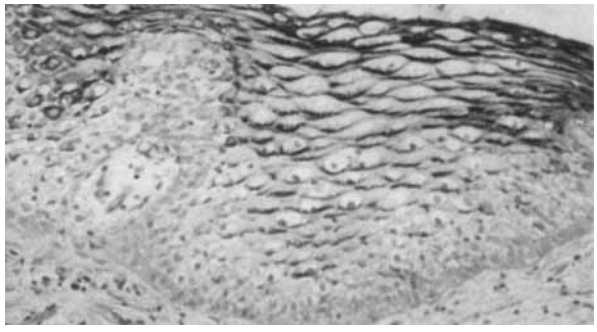
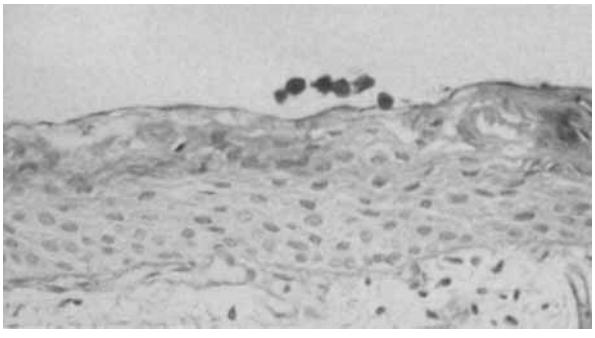


Figure 2 Atrophic vaginal epithelium stained with PAS. PAS-positive talc crystals on the surface provide a control. Note that PAS positivity is present in the epithelium but to a considerably lesser degree than in the epithelium of Figure 1.



patients aged 55 years and over were seen. Our means of investigation have been described previously.[4] Of the patients, 142 were using systemic or vaginal oestrogen on presentation and 197 were not. Chi-square testing of the incidence of symptomatic, culture positive *C. albicans* infection in each group was performed.

The laboratory arm of this report was undertaken as follows; 34 isolates of *C. albicans* and 24 isolates of non-*albicans Candida* species were incubated in yeast nitrogen broth[3] containing glucose as a positive control, glycogen as the study medium, and no sugar as a negative control.

RESULTS

The highly significant ($p < 0.001$) increased incidence of *C. albicans* infection in the cohort using oestrogen replacement is presented in Table 1. In addition, of the eight patients with *C. albicans* infection not using vaginal or systemic oestrogen, six were diabetic, one was taking tamoxifen and one had been using numerous unidentified creams (some may have been oestrogens). Two patients, only one of whom was using oestrogen, grew *Candida glabrata*. One patient grew *Candida sake* and was not using oestrogen. It is noteworthy that eight patients not using oestrogen and with negative swabs on presentation developed *C. albicans* infection after our prescription of systemic or vaginal oestrogen.

Table 1 Incidence of vaginal *Candida albicans* infection in 339 consecutive Dermogynaecology Clinic patients 55 years and over

	Using systemic or vaginal oestrogen on presentation n= 142	Not using systemic or vaginal oestrogen on presentation n= 197
C. albicans infection on initial presentation (symptomatic, culture positive)	37 (26%)	8 (4%)
No evidence *C. albicans* on initial presentation	105 (74%)	189 (96%)

Table 2 Glycogen assimilation of clinically isolated common yeasts

Species	Number of isolates	Glucose (+ve control)	Glycogen	No sugar (–ve control)
C. albicans	34	+	+	–
C. parapsilosis	10	+	–	–
C. glabrata	6	+	–	–
C. krusei	3	+	–	–
C. guilliermondii	2	+	–	–
C. tropicalis	2	+	–	–
C. lipolytica	1	+	–	–
C. lusitaniae	1	+	–	–
C. valida	1	+	–	–

Results of the assimilation tests using glycogen and controls with glucose and no sugar are presented in Table 2. All isolates of *C. albicans* assimilated glycogen but, interestingly, none of the non-*albicans* species of *Candida*.

DISCUSSION

In their comprehensive review of the epidemiology and management of candidiasis, Sobel et al[2] allude to the influence of hormonal states on this infection but do not emphasise a direct relationship between vaginal oestrogenisation and candidiasis as the evidence presented here would suggest. The clinical significance of such a relationship is great and has been discussed previously in detail.[5] In brief, it provides a likely explanation why the infection occurs only rarely between infancy and puberty; why exacerbations occur after ovulation and in pregnancy but rarely during lactation; why the oral contraceptive pill makes little difference to its incidence but depot medroxyprogesterone injections (which maintain oestrogen levels in the proliferative or postmenopausal range) reduce its incidence and, as shown in this paper, why it is not a disease of the healthy postmenopausal woman unless oestrogen is replaced.

An unexpected finding in the assimilation test results was the difference in assimilation of glycogen between *albicans* and non-*albicans* species of *Candida*. Whereas there is no doubt regarding the pathogenicity of *C. albicans*, the same cannot be said of many, if not all, non-*albicans* species of *Candida*. Further studies of non-*albicans* yeasts in yeast nitrogen broth with glycogen may provide useful information relating to their pathogenicity. This should also remind the reader of the importance of always speciating cultures positive for the *Candida* genus (and not speaking of 'yeast' or 'candidal' vaginal infection).

CONCLUSIONS

In this study of postmenopausal women there was a highly significant relationship between the usage of oestrogen and occurrence of *C. albicans* infection. The likely pathogenesis of vaginal *C. albicans* infection is production of glycogen by oestrogen-stimulated epithelial maturation providing an attractive substrate for this particular yeast.

The importance of speciating all cultures positive for the *Candida* genus is highlighted by our finding that *C. albicans* metabolised glycogen differently from non-*albicans* yeasts.

The relationship between vaginal oestrogenisation and candidiasis has considerable relevance to the clinical management of this particularly common disease.

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