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RELATIONSHIP OF *CANDIDA ALBICANS* IN THE GENITAL AND ANORECTAL TRACTS*

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The terms Monilia and Moniliasis, still widely used to denote thrush infections, are taxonomically incorrect. The name Monilia, first used by John Hill (1748–52), now applies to certain fruit-rotting fungi. The generic name *Candida*, in use since 1923, was informally agreed upon at the III Microbiological Congress in New York in 1939, and was finally adopted at the VIII International Botanical Congress in Paris in 1954. A memorandum of the Medical Research Council in 1958 describes it as a "designation now generally accepted" (Med. Res. Coun. Memo. No. 23, 1958). *Candida albicans* is its principal but not the sole pathogenic member.

There is convincing evidence that other species of *Candida* frequently cause disease in man. Hurley and Morris (1964) review this evidence and correlate the presence of certain species of yeast-like fungi other than *C. albicans* with superficial disease of the vagina; Hurley (1965) considers the tendency to regard *C. albicans* as the only member of the genus *Candida* causing human disease or experimental disease in animals a "regrettable misconception".

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It has been known for a long time that *Candida* species are found as saprophytes in the female genital and alimentary tracts. It is also accepted by several workers that the intestinal reservoir of *Candida* is probably one of the main sources, or possibly the main source, of infection in candidial vulvovaginitis (de Sousa and van Uden, 1960). Yet, while there exist many excellent studies concerning the incidence of *Candida* in the bowel and genito-urinary tract, it appears that no specific investigation of their mutual relationship has been undertaken.

In the last few years (probably because of the wide use of antibiotics) thrush is said to have ousted *Trichomonas vaginalis* in the United States of America as the principal cause of inflammatory lesions of the female genital tract (Pace and Schantz, 1957). Figures from Guy's Hospital since 1962 confirm this statement.

Table I shows the incidence of asymptomatic candidiasis of the vagina. In Great Britain it varies from 4·6 to 7·6 per cent. Somewhat higher figures are found in American and Italian studies. The incidence of *Candida* is yet higher in the genital tracts of pregnant women and in diabetics.

TABLE I*

INCIDENCE OF ASYMPTOMATIC *CANDIDA ALBICANS* IN THE VAGINA

Authors	Date	Place	No. and Types of Patients	*Candida albicans* Present	
				No.	Percentage
Dawkins, Edwards, and Riddell	1953	Great Britain	500 Family Planning Clinic	38	7·6
Mackenzie	1961	Edinburgh	150 Hospital Patients	13 Yeasts 7 *C. alb.*	8·7 4·6
Clark and Solomons	1959	U.S.A.	277 Non-Pregnant 739 Pregnant	45 202	16·2 27·3
Grasset, Senèze, and Gauthier ..	1954	France	424 Leucorrhoea	—	1
Giunchi	1958	Italy	Normal Pregnant	— —	13·7 35·9

* Modified after Winner and Hurley (1964)

The occurrence of *Candida albicans* in faeces (see Table II) shows an almost identical prevalence (27 per cent.) in two recent studies in Great Britain, and a somewhat wider range (16·9 to 37·7 per cent.) in the United States. Much higher figures are found in hot climates and in countries with lower standards of sanitation. A series in Mexico yielded 40 per cent.; another, in Baghdad, 70 per cent. (Akrawi, 1960). A very high proportion of persons recently treated with antibiotics have *Candida* in the alimentary tract: 85 per cent. in a series in Argentina and 86 per cent. in a similar study in Brazil (Silveira and Correia, 1960).

Present Study

Material and Methods

150 female patients attending the Venereal Diseases Department at Guy's Hospital were studied. Women who were pregnant or who had recently been treated with broad-spectrum antibiotics, corticosteroids, or cytotoxic agents were excluded as such drugs may enhance candidiasis. Diagnosis was based on clinical symptoms and the finding of *Candida albicans* in stained smears and cultures of the vaginal secretions and faeces.

Gram-stained smears accompanied by wet films were examined immediately. Vaginal and cervical secretions were plated on chocolate agar (McLeod) and incubated at 37°C. for 48 hrs. Coverslips on the surfaces of the inoculated media to promote anaerobiasis were used on some subcultures.

All faecal specimens were cultured at least twice on Sabouraud's medium and incubated at 37°C.; again coverslips were used on some subcultures.

A few doubtful cultures were confirmed or identified by fermentation tests. Cultural examination is considered essential as the error in the diagnosis of vaginal candidiasis by stained and wet-film technique combined with "clinical impression" is sometimes as great as 60 per cent. (O'Brien, 1964).

Results

43 of the 150 patients studied were found to have vulvovaginal candidiasis; three more had blastospores in the vagina but had no clinical symptoms and were therefore not treated. 21 of the 43 patients (48 per cent.) treated for infection with *Candida* were found to have *Candida albicans* in the faeces (Table III). Five other patients had other members of the *Candida* group but not *C. albicans*. A further more recent, series of over 220 patients (not included in this study) yielded an almost identical figure (48·2 per cent.).

TABLE III

OCCURRENCE OF *CANDIDA ALBICANS* IN FAECES IN PATIENTS WITH GENITAL CONDITIONS

Sex	Findings	No. of Cases
Female	Yeasts and *C. albicans*	26
	C. albicans only	21 (48 per cent.)
	Total	43
Male	Consorts examined	6
	C. albicans	2 (33 per cent.)

The average incidence of *Candida albicans* in the faeces in Great Britain is 27 per cent.; the higher incidence of 48 per cent. found among patients with vaginal candidiasis suggests that the intestinal pool may be an important source of infection in women with this condition.

Treatment

This usually consisted of two Nystatin pessaries inserted nightly for 10 to 15 days, combined with oral Nystatin, 0·5 M.U. three times a day for 7 days if *Candida* was found in the alimentary tract.

Local treatment had to be repeated in eight patients and three had more than two combined

TABLE II*

OCCURRENCE OF *CANDIDA ALBICANS* IN FAECES

Authors	Date	Place	Series	No. of Cases	Percentage with	
					All Yeasts	*C. albicans*
Mackenzie	1961	Edinburgh	Hospital Patients	103	34	27
Artagaveytia-Allende and García-Zorrón	1956	Mexico	Healthy Subjects	80	—	40
Winner	1960	London	Hospital Patients	239	—	27·2
Schnoor	1939	U.S.A.	Healthy Subjects	314	33·1	16·9
Felsenfeld	1944	U.S.A.	Newly admitted patients	300	—	19·3
			Chronically institutionalized	600	—	37·7
Symposium ..	1957	Argentine	Children treated with antibiotics	—	—	85·2
			Untreated children	—	—	56·3

*Modified after Winner and Hurley (1964).

courses, including local ointment and change of pessaries. One had to be treated with gentian violet. There were no failures and all patients eventually became free from infection with *Candida*.

The criterion of cure was the absence of *Candida* in two consecutive smears and cultures taken not earlier than 4 weeks after treatment. Equally, absence of *Candida* in two consecutive samples of faeces was considered proof of successful oral treatment.

Consorts

Only four of the 28 male consorts investigated had candidial balanitis; two suffered from candidial urethritis. In one of the latter the fungus was also cultured from midstream urine. Nineteen further male consorts were found to be suffering from other genital infection (see Table IV). Fifteen had non-specific urethritis, four had gonococcal urethritis. Only three of the 28 male consorts examined had no genital disorder at all. The surprising amount of male non-specific urethritis which came to light seemed to be large enough to justify further investigation.

TABLE IV

INCIDENCE OF *CANDIDA ALBICANS* IN 150 FEMALE AND 28 MALE CONSORTS

Sex	Findings	
Female	Total examined	150
	No. with genital *Candida* ..	46 (30 per cent.)
	No. with other simultaneous infection	7
Male	Total examined	28
	No. with *Candida*	6
	No. with other genital infection	19

Discussion

There could be several interpretations of these results. Different investigators since Stoecklin (1898) have suggested that the pathogenicity of the thrush fungus might be modified by the presence and interaction of bacilli. Winner and Hurley (1964) point out that this observation of Stoecklin foreshadowed the modern work on the inter-relationship between micro-organisms. There is, for instance, evidence of a natural balance in the "normal" buccal cavity, and possibly also in the vagina, between *Candida albicans* and lactobacilli, the former providing a growth factor—a member of the vitamin B group—for the latter (Wilson and Goaz, 1959); the lactobacilli in turn inhibit the multiplication and activity of *Candida albicans* by the production of lactic acid. A similar relationship has been observed between yeasts and staphylococci (Virtanen, 1951), and yeasts and lactobacilli (Young, Krasner, and Yudkofsky, 1956; Guillot, 1958).

Other studies demonstrated a growth factor for *Mycobacterium tuberculosis* in the polysaccharide fraction of cell-free extracts of *C. albicans*. This fraction stimulated in particular the growth of tubercle bacilli which had been inhibited by streptomycin. Both the living cells of *C. albicans* and the extracted polysaccharide enhanced the evolution of experimental tuberculosis in mice (Mankiewicz and Liivak, 1960). A special cultural method for the detection of tuberculosis has been developed in America, by making use of the observation that *Mycobacterium tuberculosis* will alter a selective dye, so as to prevent its lethal action on *Candida albicans* (Mankiewicz, 1957), and this has been confirmed by Kawamori, Kawai, and Asahara (1961); Yamabayashi (1958) showed that *Candida albicans* contained a substance that enhanced the virulence of *Proteus vulgaris* and *Pseudomonas aeruginosa*.

Similarly, it is possible that the male consorts in our series might, by their promiscuity, have infected their partners and thereby changed the pathogenicity of the saprophytic yeasts present in the urogenitary tracts of the women. Or the females might have had in their vaginal flora certain bacteria or viruses which by themselves, or enhanced through the presence of *Candida*, produced a non-specific urethritis in the male.

Recent microbiological investigations have elucidated the mechanism by which the viral component of mixed infections enhances the pathogenic effects of the bacterial component.

The viral component apparently suppresses some cellular defence mechanism (Buddingh, 1963). This would explain a certain success of antibiotic treatment in viral infections. Buddingh (1965) thinks that "Early therapy apparently catches the bacterial infection at the right moment, when multiplication is most rapid"; he emphasizes that this process in combined infections is in no sense a "one-way" reaction. "Just as the virus increases bacterial virulence, the bacteria exert a marked inhibitory, though not completely suppressive, effect on the virus.... Implicit in this observation is the likelihood that antiviral agents may very well be derived from bacterial factors very much as antibacterials have been derived from fungi."

Another possibility is an allergic response to toxins liberated by *Candida*. Maibach and Kligman (1962), who succeeded in producing experimental dermatitis by both live and dead suspensions of *Candida*, claim that there exists a very strong bond between the cells and such toxins. Winner (1966)

lists amongst features noted in experimental *Candida* infection in animals ". . . superimposition of allergy and failure of antibodies to protect". He states that derangements of immunity mechanisms are common features in human and animal candidial disease. Forman (1965) has observed several cases of balanitis and balano-posthitis, caused, in his opinion, by an allergic reaction to *Candida*.

Summary

Thrush appears now to be the principal cause of vulvovaginitis. Of 150 female patients who attended the Venereal Diseases Department at Guy's Hospital, 46 were found to harbour *Candida albicans* in the genito-urinary tract, and 43 of these were suffering from candidial vulvovaginitis and received treatment. This represents an incidence of 28·8 per cent. as compared with findings of 4·5 to 7·5 per cent. asymptomatic carriers of *Candida albicans* in recent British studies.

48 per cent. of patients with candidial vulvovaginitis also had *Candida* in the alimentary tract. A further series of over 200 patients (not included in this study) yielded an almost identical figure, 48·2 per cent. This compares with 27 per cent. of a hospital population found to be carriers in Great Britain, and these figures indicate that the intestinal reservoir is probably a major source of vulvovaginal infection.

A comparatively large number of the male consorts of these patients suffered from non-specific urethritis. This suggests that candidial vulvovaginitis may be an important aetiological factor in urethritis of doubtful causation in the male.

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REFERENCES

Akrawi, Y. Y. (1960). *J. Fac. med. Baghdad*, **2,** 63.
Artagaveytia-Allende, R. C., and Garcia-Zorron, N. (1956). *Ciencia (Méx)*, **16,** 212.
Buddingh, G. H. (1963). *Amer. J. Path.*, **43,** 407.
—— (1965). *Antibiotic News*, **1,** (2), 1.
Clark, D. H., and Solomons, E. (1959). *Amer. J. Obstet. Gynec.*, **78,** 1314.
Dawkins, S. M., Edwards, J. M. B., and Riddell, R. W. (1953). *Lancet*, **2,** 1230.
De Sousa, H. M., and Van Uden, N. (1960). *Amer. J. Obstet. Gynec.*, **80,** 1096.
Felsenfeld, O. (1944). *Amer. J. med. Sci.*, **207,** 60.
Forman, L. (1965). Personal communication.
Giunchi, G. (1958). *Sci. med. ital. (Engl. Ed.)*, 2 ser., **6,** 580.
Grasset, J., Senèze, J., and Gauthier, R. (1954). *Bull. Féd. Soc. Gynéc. Obstét. franç.*, **6,** 181.
Guillot, N. (1958) *Ann. Inst. Pasteur.*, **95,** 194.
Hill, J. (1748–52). "A General Natural History: or New and Accurate Descriptions of the Animals, Vegetables, and Minerals of the Different Parts of the World" (3 vols). Osborne, London.
Hurley, R. (May, 1965). Personal communication.
—— and Morris, E. D. (1964). *J. Obstet. Gynaec. Brit. Cwlth.*, **71,** 692.
Kawamori, T., Kawai, J., and Asahara, Y. "Studies in Candidiasis in Japan". Tokyo.
Mackenzie, D. W. R. (1961). *Sabouraudia*, **1,** 8.
Maibach, H. I., and Kligman, A. M. (1962). *Arch. Derm. (Chicago)*, **85,** 233.
Mankiewicz, E. (1957). *Amer. Rev. Tuberc.*, **75,** 836.
—— and Liivak, M. (1960). *Nature (Lond.)*, **187,** 250.
O'Brien, J. R. (1964). *Canad. med. Ass. J.*, **90,** 1073.
Pace, H. R., and Schantz, S. I. (1957). *Monogr. on Ther.*, **2,** 29.
Schnoor, T. G. (1939). *Amer. J. trop. Med.*, **19,** 163.
Silveira, J. S., and Correia, J. U. (1960). *Hospital (Rio de J.)*, **58,** 333.
Stoecklin, H. de (1898). *Arch. Méd. exp.*, **10,** 1.
Symposium on Moniliasis (1957). *Rev. Asoc. med. argent.*, **71,** 2.
Virtanen, I. (1951). *Ann. Med. exp. Fenn.*, **29,** 352.
Wilson, T. E., and Goaz, P. W. (1959). *J. dent. Res.*, **38,** 1044.
Winner, H. I. (1960). Unpublished data on the incidence of *Candida albicans* in sputum and faeces.
—— (1966) "Squibb Symposium on *Candida albicans*". London. (In the press).
—— and Hurley, R. (1964). "Candida Albicans", 1st ed., pp. 34 and 39; and Tables 10 and 11, pp. 125 and 135. Churchill, London.
Yamabayashi, H. (1958). *Med. J. Osaka Univ.*, **9,** 11.
Young, G., Krasner, R. I., and Yudkofsky, P. L. (1956). *J. Bact.*, **72,** 525.

Le rapport entre le *Candida albicans* et les voies génitales ano-rectales

RÉSUMÉ

Le muguet semble maintenant être la cause principale de la vulvo-vaginite. 46 des 150 patientes qui ont rendu visite au dispensaire anti-vénérien de Guy's Hospital avaient les voies uro-génitales infectées par le *Candida albicans*, et 43 des 46 souffraient de vulvo-vaginite causée par le *Candida albicans* et ont été traitées. Cela représente un taux de 28,8 pour cent comparé au taux de 4,5 à 7,5 pour cent de porteuses de *Candida albicans* sans symptômes dans les récentes études britanniques.

48 pour cent des patientes souffrant de vulvo-vaginite avaient aussi une infection du canal alimentaire par le *Candida albicans*. Dans une autre série de plus de 220 malades (hors de cette étude) 48·2 pour cent furent infectes, tandis que 27 pour cent de la population hospitalière est porteuse en Grande Bretagne; ces chiffres indiquent que le réservoir intestinal est probablement la source principale de l'infection vulvo-vaginale.

En comparison un grand nombre des conjoints de ces patientes souffraient d'urétrite non-gonococcique. Cela suggère que la vulvo-vaginite causée par le *Candida albicans* peut être un important facteur étiologique de l'urétrite d'origine douteuse chez l'homme.