it might merely represent a mechanical sequence of basal lamina rupture without specific significance. In tumours it might represent an invasion mechanism in the preliminary stages of tumour growth (5–9).

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Immunological Studies in Chronic Mucocutaneous Candidiasis before and after Ketoconazole Treatment

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Immune functions were studied in eight patients with chronic mucocutaneous candidiasis representing a broad clinical spectrum of this disease. Clinical improvement after ketoconazole for 6 months was not associated with amelioration of cutaneous delayed hypersensitivity to Candida antigen or the in vitro lymphocyte responses to Candida antigen of T-cell mitogens. *Key words: Polyendocrine deficiency syndrome; Immune function.*

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Chronic mucocutaneous candidiasis (CMC) is a rare condition with persistent *C. albicans* infections of the skin, mucous membranes and nails. It is often associated with autoimmune or endocrine disorder. It has been surmised that a defective host defence, particular-

ly the cell-mediated immunity, predisposes to the infection. This is supported by regression of lesions in a few patients after immunological reconstitution (1). On the other hand, the immune response to chronic fungal infections may be modified by the infection itself, which may induce T suppressor cells or inhibitory serum substances (2, 3). The onset of immunological defects after yeast infection in some patients is in accordance with this interpretation, as are sparse reports of normalization of immune reponses to Candida antigen after treatment therapy with antifungal antibiotics (4, 5).

This issue can now be clarified by repeating the immunological studies after eradication of the infection with a new orally-active antifungal agent, ketoconazole (6). The findings are contradictory, however. It should be noted that many reports only concern one or a few patients. Reversal of negative delayed skin hypersensitivity to Candida antigen occurred only in some cases after ketoconazole treatment (6). The in vitro lymphocyte transformation to Candida antigen and production of macrophage inhibition factor remained abnormal in some patients and was normalized in others (6, 7). We therefore collected 8 patients with CMC and investigated whether there was any change in specific and non-specific immune responses after ketaconazole therapy.

PATIENTS AND METHODS

Patients

Clinical details of the 8 patients are presented in Table I. The clinical findings are reported in detail elsewhere (8). Ketoconazole was administered in a dose of 200 mg once daily except in one patient (O. H.) with pernicious anaemia, who received 400 mg/d.

Methods

The immunological investigations were performed before treatment and repeated after 6 months of ketoconzole therapy.

Skin tests. Delayed hypersensitivity reactions were measured 48 hours after an intradermal injection of 0.1 ml of 1 : 100 dilution of *C. albicans* antigen (Hollister-Stier Laboratories, USA). An induration of >5 mm was considered a positive reaction.

In vitro lymphocyte stimulation. Lymphocytes were exposed to Candida antigen and the mitogens phytohemagglutinin (PHA) and concanavalin A (Con A) at predetermined opitmal concentrations according to a standard method (9). The results were expressed as the ratio between the counts per minute obtained from a patient with CMC and the corresponding mean value from healthy controls analysed with each patient. A ratio below 0.6 was considered abnormally low, based on the results from 50 healthy blood donors.

Immune complexes. Circulating immune complexes in serum were demonstrated by incubating serum samples from CMC patients with polymorphonuclear leukocytes (PMN) from healthy blood donors (10). Six of 224 sera (3%) from healthy blood donors showed a positive PMN phagocytosis test when positivity was scored as more than 5% of PMN's having ≥5 positive granules.

RESULTS

Clinical investigations

Clinical findings are presented in Table I. Before treatment clinical and mycological signs of *C. albicans* infection were found in the mouths of all eight patients, on the skin in two cases and in finger and/or toe nails in 7 cases. After receiving ketoconzole for 6 months, one patient was cleared of infection (O. H.). The remaining 7 were all cleared of oral and skin infections including paronychiae, but there was still discrete mycotic involvement of a few nails.

Immunological investigations

The results from the pretreatment immunological investigations are presented in Table II. Absence of cutaneous delayed hypersensitivity to Candida antigen occurred in 5 patients (62%), and the results were unaltered after treatment with ketoconazole for 6 months.

The lymphocytes failed to respond adequately to Candida antigen and mitogens in one patient (C. D.). His delayed skin test with Candida was negative. In four patients the lymphocytes were normally stimulated in vitro, yet there were no delayed skin reaction to Candida. Candida antigen elicited skin reactions in two patients but the lymphocyte response to Candida in vitro was inhibited, although normal proliferative responses were obtained with PHA and Con-A. No immunological defect was observed in one patient (L. B.). The lymphocyte reactivity was unchanged after 6 months of ketoconazole therapy.

A raised level of circulating immune complexes was demonstrated only initially in one patient (13%). He was still positive at the follow-up examination 6 months later and another patient was also positive at that time.

DISCUSSION

This study demonstrates that the defect in cell-mediated immune responses occurring in patients with CMC is heterogenous (1). There was a profound clinical improvement after 6 months of ketoconazole therapy suggesting a marked reduction of the antigen load. However, there was no restoration of lymphocyte reactivity in vivo or in vitro. The divergent results in the literature may be explained by the heterogenous nature of CMC, selection of patients, the small number of cases studied and the use of different laboratory

Table I. *Clinical details of 8 patients with chronic mucocutaneous candidiasis*

Pat.	Sex	Age at onset (yrs)	Duration at treatment (yrs)	Associated diseases
C. D.	M	3	14	Pubertas tarda Retarded growth
L. B.	M	8	26	–
A. R.	F	8	20	–
M. K.	M	5	5	Hypothyroidism Alopecia Hypoparathyroidism Hypoadrenocorticism
E. Å.	M	15	39	Hypothyroidism Dermatophytosis
M. W.	M	5	11	–
J. W.	M	5	8	–
O. H.	M	20	29	Pernicious anaemia Dermatophytosis

Table II. *Pretreatment immunological findings in 8 patients with chronic mucocutaneous candidiasis*

	Delayed skin test (Candida) Negative/tested	In vitro lymphocyte stimulation (subnormal/tested)			Circulating immune complexes (positive/tested)
		Candida antigen	PHA	Con-A	
No. of patients	5/8	3/8	1/8	1/8	1/8

methods. It has been reported that ketoconazole inhibits the lymphocyte response in vitro to PHA in concentrations corresponding to those obtained in vivo (11). This effect was not found in this study.

Our findings support a primary disturbance of cell-mediated immune functions in CMC.

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A Method for Testing the Effect of Pressure-relieving Materials in the Prevention of Pressure Ulcers

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Karlsmark T, Kristensen JK. A method for testing the effect of pressure-relieving materials in the prevention of pressure ulcers. Acta Derm Venereol (Stockh) 1987; 67: 260–263.

A method is described by which the effect of pressure and relief of pressure on blood flow in cutaneous and subcutaneous tissue can be evaluated. Five normal persons were placed supine on a transparent polyacrylate board and blood flow in the skin overlying the sacral area was measured. Cutaneous blood flow was measured by the laser-Doppler technique and subcutaneous blood flow was measured by the ^{133}Xenon washout technique using atraumatic application. Blood flow was measured by both techniques before and after relief of pressure, using the antipressure material Comfeel® Pressure Relieving Dressing (in the following referred to as Comfeel PRD) consisting of a foamy plastic material with an adjustable central opening.

With this material, it was possible to obtain relief of pressure which was shown as a significant increase in blood flow measured by both methods. It is suggested that the methods described should be used to test other materials as well. (Received July 8, 1986.)

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