From:
The Department of Prosthetic Dentistry
The Royal Dental College,
Aarhus,
Denmark

DENTURE STOMATITIS
II. THE EFFECT OF ANTIFUNGAL AND PROSTHETIC TREATMENT

by
E. BUDTZ-JØRGENSEN
U. BERTRAM

INTRODUCTION

Much controversy has existed as to which therapeutic measures would be appropriate in the treatment of denture stomatitis. Investigators believing trauma to be the significant etiological factor have advocated the construction of new, well-fitting dentures (*Nyquist*, 1952) and the use of tissue conditioners (*Lytle*, 1957; *Ampil*, 1966; *Gonzales*, 1966). *Cahn* (1936), *Lyon* and *Chick* (1957) and *Cawson* (1963) have reported a beneficial effect from antifungal therapy in treating patients with denture stomatitis. *Turrell* (1966) proved to »his own satisfaction» that leaving the dentures out for two weeks would result in resolution of the inflamed tissue whether the cause was trauma or candida infection. *Spreng* (1945, 1963) who believed in allergy to denture base materials as a significant etiological factor in denture stomatitis has reported an anti-inflammatory effect of gold-foiling the denture base and has advocated a shift to another denture base material in cases of denture stomatitis.

Most investigators have agreed that the treatment of choice in cases of granular inflammation (papillary hyperplasia) is surgical removal, (*Hecht*, 1939; *Waite*, 1961; *Guernsey*, 1965). Yet *Lyon* and *Chick* (1957) and *Roland et al.* (1958) reported an anti-inflammatory effect of antifungal therapy in cases of granular inflammation, even though the papillary outgrowths persisted.

Received for publication, October 24, 1969.

The present investigation was carried out to study the therapeutic effect of both chemotherapy and prosthetic treatment in denture stomatitis, i.e.,

1) in case of localized simple, generalized simple and granular inflammation;

2) in cases of denture stomatitis associated with either traumatic or presumably non-traumatic dentures;

3) in cases of verifiable and non-verifiable candida infection.

This was done by studying the anti-inflammatory effect of:

I) antifungal therapy

II) removing trauma to the palatal mucosa by occlusal equilibration, by relining the dentures with tissue conditioners, and by the construction of new, well-fitting dentures.

MATERIAL AND METHODS

The present investigation included 58 patients with full dentures and denture stomatitis. As controls, there were 58 cases with full dentures but without denture stomatitis, equal to the experimental group in age and sex distribution. The patients with denture stomatitis were divided into two treatment groups, designated A and P. Group A comprised 36 patients who received antifungal therapy while the 22 patients in group P received prosthetic treatment. The distribution according to sex and age in the two treatment groups is recorded in Table I.

Twenty-two patients in the denture stomatitis group complained of burning and itching pain from the palatal as well as the glossal mucous membrane. Nineteen of these patients were placed in group A in order to study the effect of antifungal therapy on oral symptoms. In group P all 22 patients

Table I.

Distribution after age and sex in the nystatin group (antifungal therapy; group A) and the prosthetic group (prosthetic treatment: tissue conditioning, occlusal equilibration, new dentures; group P)

		Age of patients							Mean
		25–34	35–44	45–54	55–64	65–74	75–84	Total	age
Nystatin	Women	2	1	9	10	3		27	55.0
group	Men			4	3	2		9	56.8
Prosthetic	Women	1	2	1	5	3	3	15	61.0
group	Men			1	3	3		7	61.5
Total		3	3	15	21	13	3	58	57.7

Table II.

Patient distribution after inflammatory types present in the nystatin group and the prosthetic group

Type of inflammation	Simple localized	Simple generalized	Granular	Total
Nystatin group	6	17	13	36
Prosthetic group	7	5	10	22

had dentures with unbalanced occlusion. One half (18) of the patients in group A had traumatic dentures, i.e., dentures with unbalanced occlusion, while the other half had presumably non-traumatic dentures, i.e., 7 cases with balanced occlusion and 11 cases, fully edentulous, that only wore a maxillary denture. The distribution after inflammatory types and accompanying symptoms and signs present in the two treatment groups is recorded in Tables II and III.

Clinical treatment

Antifungal therapy (Group A). Nystatin (Mycostatin® SQUIBB) tablets, each containing 500.000 units, were given three times a day for 14 days. The tablets were allowed to dissolve in the mouth, while the dentures were placed in a glass of water. The patients were instructed not to alter their denture-wearing habits.

Prosthetic treatment (Group P). In order to eliminate or reduce possible trauma to the palatal mucosa the maxillary and mandibular dentures were

Table III.

Patient distribution after accompanying signs and symptoms present in the nystatin group and the prosthetic group

	Accompanying signs and symptoms						
	S+CH+Gl	S+Ch	S+Gl	S	Ch+Gl	Ch	Gl
Nystatin group	6		7	6	1	4	3
Prosthetic group		1	1	1	1	1	3
Total	6	1	8	7	2	5	6

S: subjective symptoms; Gl: Glossitis; Ch: angular cheilitis

rebased two times with tissue conditioner (Coe-Comfort, Coe Laboratories, Inc., Chichago, Ill.) at an interval of 3—4 days. If necessary, occlusal equilibration was performed to obtain a balanced occlusion. After the treatment with Coe-Comfort was finished new dentures were constructed with the final impression being taken in zinc-oxide-eugenol paste. The teeth were set in balanced occlusion and articulation, acrylic teeth being used for the mandibular denture and porcelain teeth for the maxillary denture. The new dentures were remounted on an adjustable articulator to secure a balanced occlusion.

Methods of examination

The effect of treatment (antifungal or prosthetic) was studied:

1) *Clinically.* By means of photographs of the inflamed areas of the palate, the tongue, and the angles of the mouth. The photographs were taken under standardized conditions before, during, and after treatment. The following clinical index of the anti-inflammatory effect of treatment was used:

a) excellent effect — no inflammation

b) fair effect — decreased inflammation

c) no effect — no change in inflammation.

2) *By cultivation.* Maxillary alginate impressions were taken and poured in Sabouraud's agar before, during, and after treatment according to the method described in the first part of this study (*Budtz-Jørgensen & Bertram*, 1970). The agar models were incubated at 37° for 72 hours and were evaluated for the quantity and location of yeast colonies. Possible colonies were examined for Candida albicans by tube formation in human serum before any treatment was instituted. Yeasts other than Candida albicans were identified by fermentation tests.

3) *By smears.* Scrapings were taken from the inflamed areas, i.e., the palate, the tongue and the angles of the mouth, before, during and after treatment and were fixed in ether/alkohol 1:1 and stained according to the P.A.S.-method with haematoxylin as counterstain. By direct microscopic examination the smears were evaluated for occurrence of leucocytes and hyphal structures, differentiating quantitatively between no hyphae, single hyphae and mycelium. The following index of the anti-inflammatory effect of treatment determined by smears was used:

a) excellent effect — absence of leucocytes following treatment

b) fair effect — leucocytes in decreased quantity following treatment

c) no effect — no or minor changes in the quantity of leucocytes following treatment.

Table IV.

Methods of examination performed at the various attendances in the nystatin group

		Before nystatin	During nystatin	After nystatin	1 week after nystatin	1 month after nystatin
Photo	Palate	+	+	+	+	+
	Tongue	+	+	+	+	+
	Angles of the mouth	+	+	+	+	+
Smear	Palate	+	+	+	+	+
	Tongue	+	+	+	+	+
	Angles of th mouth	+	+	+	+	+
Cultivation		+			+	+
Impression (gran. inflam.)		+	+	+	+	+

Table V.

Methods of examination performed at the various attendances in the prosthetic group

		Before Coe-Comfort	3 days with Coe-Comfort	6 days with Coe-Comfort	1 month with new denture
Photo	Palate	+	+	+	+
	Tongue	+			+
	Angles of the mouth	+			+
Smear	Palate	+	+	+	+
	Tongue	+			+
	Angles of the mouth	+	+	+	+
Cultivation		+	+	+	+
Impression (gran. inflam.)		+	+	+	+

4) *By plaster models.* In cases of granular inflammation maxillary alginate impressions were taken and poured in plaster before, during and after treatment. The possible changes in the surface architecture of the palatal mucosa in the individual patient were compared by visual examination of the plaster models.

The methods of examination performed at the various attendances in both treatment groups are recorded in Tables IV and V. The 58 controls had previously been investigated for occurrence of yeast-like fungi by cultivation and by direct smear-technique (Part I).

RESULTS

I. Effect of antifungal therapy

Of the 36 patients in group A, 15 patients revealed mycelium and 9 patients single hyphae in smears from the palate before treatment. Twelve patients did not show any hyphal structures. Thirty-three patients (92 %) were positive for yeast-like fungi by cultivation. Twenty-nine patients showed Candida albicans whereas 4 patients showed other yeast-like fungi.

After having taken nystatin tablets for one week definite clinical improvement was seen in 26 patients accompanied by a striking reduction in the quantity of leucocytes as determined by smears; hyphal structures were found only in two patients. After two weeks of antifungal therapy further improvement was apparent by clinical examination and by examination of palatal smears in the same 26 patients who initially had responded to nystatin; hyphal structures were never seen in palatal smears. The cases of glossitis and angular cheilitis showed definite improvement when examined both clinically and by smear-technique, except for two cases of median rhomboidean glossitis and one case of angular cheilitis.

As the mere sucking of tablets might have a stimulating and cleaning effect on the palatal mucosa and thus lead to reduced inflammation, the final result of antifungal therapy was not evaluated until one week after the nystatin tablets had been withdrawn. The sucking of tablets might also result in a reduction in the quantity of leucocytes, as determined by smears, even if the inflammation clinically was unchanged.

Clinical effect of antifungal therapy. The effect of antifungal therapy was evaluated clinically one week after withdrawal of nystatin and was correlated to the quantity of hyphal structures present in the pre-treatment smears (Fig. 1 a). Yeast-like fungi were isolated by cultivation in 5 cases; in no cases were hyphal structures recognized in palatal smears. Definite improvement was seen in 26 patients. It was obvious that a positive result of antifungal

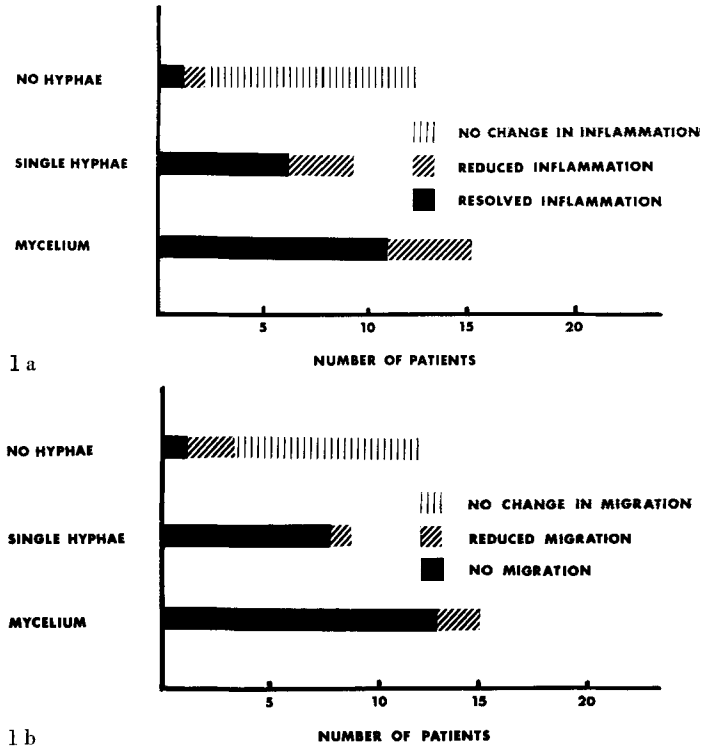


Fig. 1 a, b. The relationship between the therapeutical effect of antifungal therapy in patients showing no hyphae, single hyphae or mycelium in pre-treatment palatal smears. a) Evaluated clinically one week after treatment with nystatin tablets was terminated. b) Deter mined by palatal smears, i.e., decrease in degree of leucocyte-migration, one week after treatment with nystatin tablets was terminated.

therapy was dependent on the presence of hyphal structures in the pre-treatment smears; yet it is remarkable that a clinical effect was seen in 9 patients who showed single hyphae in pre-treatment palatal smears and in 2 patients who never showed any hyphal structures.

A statistically significant correlation was found between the yield of yeast colonies by cultivation and the therapeutic effect of antifungal therapy, ($P<0.01$) (Table VI).

The 6 patients with localized simple inflammation did not reveal hyphal structures in pre-treatment palatal smears and the inflammatory condition did not improve following antifungal therapy. Among the patients with a generalized simple and a granular inflammation (30 patients), however, definite improvement of the inflammatory condition was seen in 26 patients (Fig. 2 a).

Table VI.

The relationship between the anti-inflammatory effect of antifungal therapy and the yield of yeast colonies by cultivation before antifungal therapy

Effect of nystatin	Quantity of yeast colonies 0–10	10–25	>25
Excellent	1	6	11
Fair	2	4	2
Poor	8	1	1
Total	11	11	14
$\chi^2 = 18.5$	4 DF	$0.001 < P < 0.01$	

* The chi-square test ($\chi^2 = \sum \frac{(E-O)^2}{E}$) was used for testing the agreement between the values observed and the values expected. Values of ≤ 0.05 were accepted as statistically significant

A more dramatic therapeutic effect of antifungal therapy was recognized among the 18 patients with presumably non-traumatic dentures than among the 18 patients with traumatic dentures (Table VII). In 6 patients with traumatic dentures small, circumscribed, probably traumatic lesions were revealed following antifungal therapy, after the diffuse erythema had disappeared.

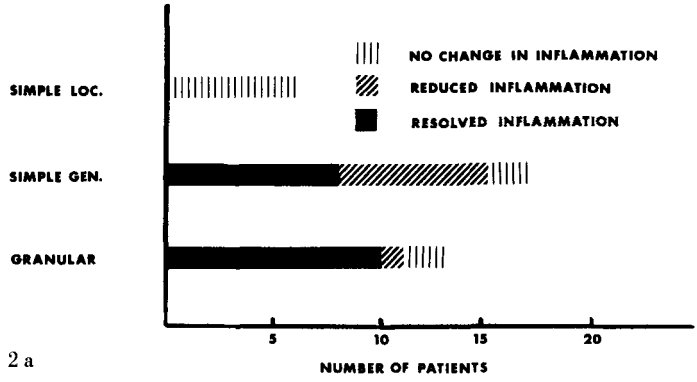
The clinical effect of nystatin treatment in a patient with a generalized simple and in a patient with a granular inflammation is illustrated in Figs. 3 and 4.

Effect of antifungal therapy determined by smears. A clear correlation was found between clinical improvement and reduction in the quantity of

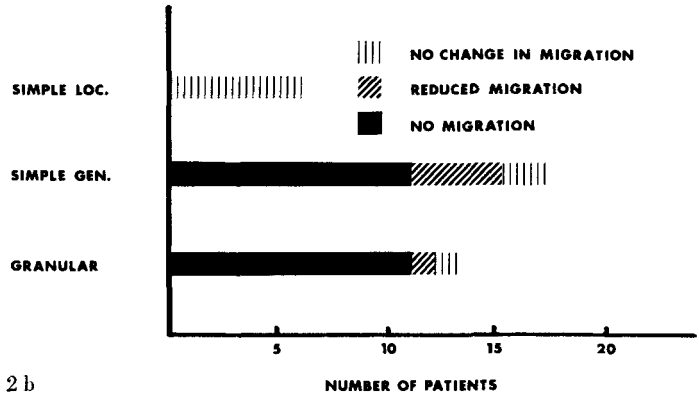
Table VII.

Comparison of the anti-inflammatory effect of antifungal therapy in patients with traumatic and non-traumatic dentures.

Denture function	Effect of nystatin Excellent	Fair	Poor	Total
Non-traumatic dentures	14	2	2	18
Traumatic dentures	4	6	8	18



2 a



2 b

Fig. 2 a, b. The relationship between the therapeutical effect of antifungal therapy it patients showing localized simple, generalized simple or granular inflammation before treatment.a) Evaluated clinically one week after treatment with nystatin tablets was terminated. b) Determined by palatal smears, i.e., decrease in degree of leucocyte-migration, one week after treatment with nystatin tablets was terminated.

leucocytes in palatal smears (Fig. 2 b). Determined by smears the result was excellent in 22 patients, fair in 5 patients, whereas 9 patients did not show any improvement. Improvement was recognized in 3 patients who did not show hyphal structures in pre-treatment smears (Fig. 1 b).

Effect of antifungal therapy evaluated by maxillary casts. In 13 patients in group A with granular inflammation an attempt was made to demonstrate the effect of antifungal therapy by using maxillary casts. In comparing pre-treatment casts with casts made one week after nystatin had been withdrawn only minor changes of the surface architecture were observed. No patients showed regression of the papillary hyperplasia following antifungal therapy and in some patients the crevices between the papilloferous outgrowths even seemed to have increased in depth.

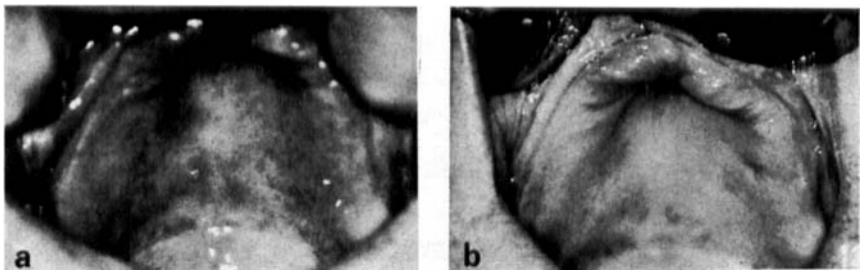


Fig. 3 a, b. The therapeutic effect of antifungal therapy in a patient showing a generalized simple inflammation of the maxillary denture-bearing tissues. a) Before treatment. b) One week following withdrawal of nystatin.

Effect of antifungal therapy on symptoms and accompanying signs. In group A 19 patients complained of burning and itching pain from the oral mucous membranes. Fifteen of these revealed mycelium in smears from the palate and/or the tongue, 2 patients revealed single hyphae whereas 2 patients did not show any hyphal structures. One week following withdrawal of nystatin the 17 patients that showed hyphal structures in pre-treatment oral smears were symptomless while the symptoms had persisted in the two patients who did no initially show hyphae.

Seventeen patients in group A showed glossitis, i.e., 15 patients with localized or generalized inflammation of the dorsal surface of the tongue with more or less marked atrophy of the filiform papillae and 2 patients with median rhomboidean glossitis. In all patients glossal pre-treatment smears revealed mycelium and leucocyte-infiltration. Following antifungal therapy the inflamed lesions had disappeared in 15 patients and the glossal smears showed no hyphal structures and only very few leucocytes. In the

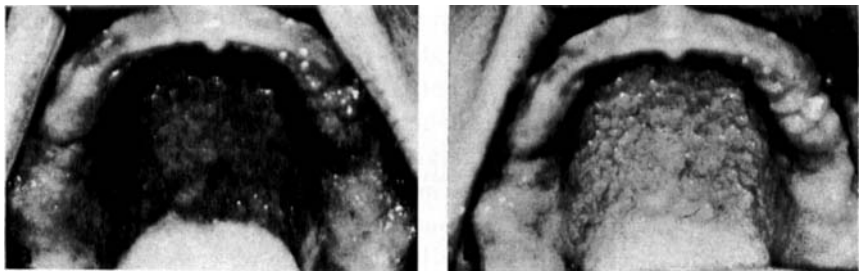


Fig. 4 a, b. The therapeutic effect of antifungal therapy in a patient showing a granular inflammation with spontaneous bleeding of the maxillary denture-bearing tissues. a) Before treatment. b) One week following withdrawal of nystatin. The palatal mucosa is clinically not inflamed, yet the granulations have persisted.

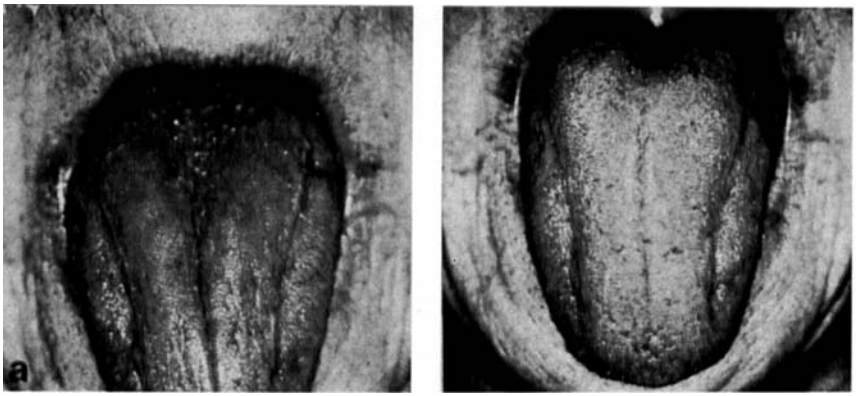


Fig. 5 a, b. The beneficial effect of antifungal therapy in a patient with a generalized atrophic glossitis. a) Before treatment. b) One week following withdrawal of nystatin. The dorsal surface of the tongue now appears clinically normal.

2 patients of median rhomboidean glossitis the inflammation persisted and mycelium was found persistently in smears during and after antifungal therapy. Fig. 5 is an illustration of the beneficial effect of antifungal therapy in a case of severe generalized atrophic glossitis.

Twelve patients in group A revealed angular cheilitis. In 11 of these mycelium was found in smears from the angles of the mouth and they all showed improvement or complete healing following antifungal therapy. One case of angular cheilitis, without hyphal structures isolated in smears from the angles of the mouth, did not respond to antifungal therapy.

Incidence of relapse. Before antifungal therapy, yeast-like fungi were isolated by cultivation in 33 patients (92 %) in group A. One month after nystatin had been withdrawn yeast-like fungi were isolated by cultivation in 25 patients (69 %) with the yeast colonies being nearly localized to the inflamed areas in 22 patients. Twenty-nine patients (80 %) showed denture stomatitis, yet, in most of the patients that had responded to nystatin the degree of inflammation was reduced as compared to the pre-treatment situation. Compared to the situation one week after nystatin had been withdrawn an increased degree of inflammation (relapse) was recognized in 14 patients one month after nystatin had been withdrawn out of 26 patients who had responded to antifungal therapy.

All 14 patients with relapse showed yeast-like fungi by cultivation and in 10 patients hyphal structures were isolated by palatal scrapings (Table VIII). Fifteen patients showed unchanged inflammation as compared to the the post-treatment situation. Of these, 7 showed yeast-like fungi by cultivation,

Table VIII.

The relationship between the incidence of relapse of denture stomatitis one month following withdrawal of nystatin and the re-appearance of yeast-like fungi in smears and by cultivation

	Clinically	Hyphal structures	Yeasts by cultivation
Relapse	14	10	14
No inflammation	7	0	3
Unchanged inflammation	15	1	7

whereas hyphal structures were isolated only in 1 patient. Seven patients showed no inflammation of the palatal mucosa; none of these yielded hyphal structures in smears, whereas 3 showed yeast-like fungi by cultivation.

Among the patients with unchanged inflammation compared with the post-treatment situation, 13 had traumatic dentures and only 2 presumably non-traumatic dentures (Table IX). Of the 14 patients with relapse, 5 had traumatic dentures, 9 non-traumatic dentures. The seven patients with not inflamed palatal mucosa had presumably non-traumatic dentures.

One month after nystatin had been withdrawn 8 patients were complaining of relapse of subjective symptoms. They all showed hyphal structures in smears from the palate and/or the tongue. In 2 patients relapse of the glossitis was seen and in 1 patient angular cheilitis had reappeared.

II. Effect of prosthetic treatment

Of the 22 patients in group P 19 patients (86 %) were positive for Candida albicans by cultivation. Eleven patients showed a verifiable candida infec-

Table IX.

Distribution of patients with traumatic and non-traumatic dentures respectively in the group of patients with relapse of inflammation and in the group of patients with unchanged/no inflammation one month following withdrawal of nystatin

	Non-traumatic dentures	Traumatic dentures
Rellapse	9	5
No inflammation	7	0
Unchanged inflammation	2	13

tion, i.e., 9 patients revealed mycelium, 2 single hyphae in palatal smears usually associated with a significant leucocyte-infiltration. Eleven patients did not show any hyphal structures in palatal smears and the leucocyte-infiltration appeared sparse.

Effect of tissue conditioning and occlusal equilibration. The effect of Coe-Comfort and occlusal equilibration on denture stomatitis was evaluated clinically, by smears and by cultivation of yeast-like fungi after 3 and 6 days with Coe-Comfort in the maxillary and the mandibular denture.

After 3 days, reduced inflammation was recognized in 6 patients who did not show hyphal structures in the pre-treatment palatal smears. Determined by palatal smears only insignificant changes in degree of leucocyte-infiltration were observed. Yeast-like fungi were isolated by cultivation and in smears in approximately the same quantities in the patients who were positive for candida before treatment.

After 6 days' treatment with Coe-Comfort the inflammatory condition had improved in 10 out of the 11 patients who did not show hyphal structures in palatal smears prior to treatment (Fig. 6). The palatal smears now showed leucocytes in reduced and very small quantities; hyphal structures were never seen. Reduced inflammation was recognized only in 1 out of the 11 patients with a verifiable candida infection prior to treatment (Fig. 6); these patients continued to yield hyphal structures and leucocytes in palatal smears in approximately unchanged quantities. Yeast-like fungi were isolated by cultivation in the same quantities in the 19 patients who had been positive for Candida albicans prior to treatment.

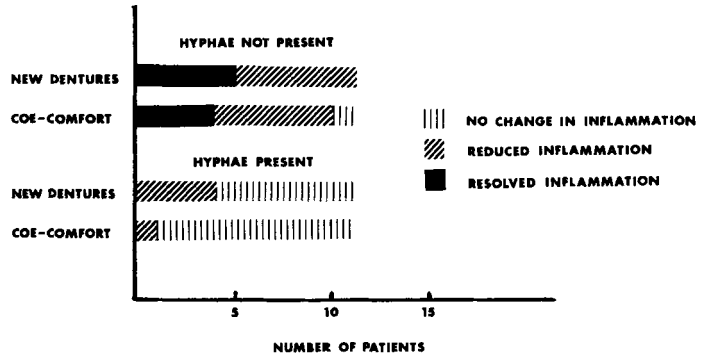


Fig. 6. The therapeutical effect of prosthetic treatment evaluated clinically in patients with verifiable candida infection (hyphal structures present in palatal smears) and non-verifiable candida infection (hyphal structures not present). Effect of tissue conditioning evaluated after 6days' treatment with Coe-Comfort. Effect of new dentures evaluated after one month.

Effect of new dentures The effect of the new dentures on denture stomatitis was evaluated clinically, by smears and by cultivation of yeast-like fungi after the patients had used the dentures for 1 month.

In the 11 patients without hyphal structures in the pre-treatment smears the inflammatory lesions had disappeared in 5 patients and the degree of inflammation had decreased in 6 patients. Among the 11 patients with a verifiable candida infection prior to treatment the degree of inflammation had decreased in 4 patients and was unchanged in 7 patients (Fig. 6). The beneficial effect of the new dentures was most pronounced among the 7 patients with a localized simple inflammation, (in 4 patients the inflammation had disappeared, in 3 patients the inflammation had decreased).

Determined by palatal smears the anti-inflammatory effect of the new dentures was in accordance with the clinical evaluation except for 1 patient who showed decreased inflammation by clinical evaluation, but no change in inflammation as determined by smears. Of the 11 patients with a verifiable candida infection prior to prosthetic treatment hyphal structures were isolated in smears in 7 patients, whereas 4 patients did not show hyphal structures. These 4 patients showed reduced inflammation clinically.

Among a total of 15 patients with reduced or resolved inflammation following prosthetic treatment, 5 patients did not show any yeast colonies by cultivation, and in 6 patients yeast colonies were cultured in decreased and very small quantities compared to the pre-treatment culturing. In 4 of the patients with reduced inflammation yeast colonies were cultured in approximately unchanged quantities. In the 7 patients with a verifiable candida infection and unchanged degree of inflammation following prosthetic treatment yeast colonies were cultured in the same or even increased quantities.

The accompanying signs and symptoms persisted following prosthetic treatment, whether they were pain, glossitis, or angular cheilitis.

Determined by visual inspection of the plaster models the 10 cases of granular inflammation did not show any change in surface architecture following prosthetic treatment, including 4 cases of clinically decreased inflammation.

DISCUSSION

It is usually accepted that Candida albicans in the mycelial phase is a parasite, but a saprophyte in the blastospore phase. The isolation of hyphal structures in smears, therefore, is an indication of candida infection, whereas the mere isolation of Candida albicans by cultivation is considered an unreliable proof of candida infection (*Kozinn & Taschdijan,* 1962; *Cawson,* 1965). The verification of a candida infection accordingly is accomplished

by isolating hyphal structures by a palatal scraping. It was a significant finding in this study that the effect of antifungal therapy was seen almost exclusively in patients who revealed hyphal structures in palatal smears, i.e., patients with a granular or generalized simple inflammation of the palatal mucosa. Moreover, the accompanying signs and symptoms, i.e., pain, glossitis, and angular cheilitis, specifically associated with the granular and generalized simple inflammation, usually cleared up following antifungal therapy. Finally, a beneficial effect of prosthetic treatment was primarily seen in patients without a verifiable candida infection.

By isolating candida for cultivation, using the impression method, it was possible to locate the yeast colonies in the inflamed areas, and a significant correlation between degree of inflammation and the quantity of yeast colonies was established (*Budtz-Jørgensen & Bertram*, 1970). In this study a correlation was found between the quantity of yeast colonies found by cultivation before treatment and the therapeutical effect of antifungal therapy. Accordingly, it does not seem unrealistic to consider the quantitative determination of yeast colonies by cultivation, using the impression method, a useful adjunct to the smear-technique in establishing evidence of candida infection.

Candida infection of the oral mucous membranes has previously been found associated with heavy leucocyte-migration (*Jepsen & Winther*, 1965). In this study leucocytes were usually present in abundance in the pre-treatment smears which revealed single hyphae or mycelium, in that respect differing from cases of denture stomatitis, which did not reveal hyphal structures. The therapeutic effect of antifungal therapy was illustrated by a striking reduction in quantity of leucocytes in the post-treatment palatal smears, as well as in the glossal and angular smears.

The fact that a therapeutic effect of antifungal therapy was seen even in patients who revealed single hyphae and no actual mycelium in pre-treatment palatal smears may be due to an error of method in smear-sampling. In this study a metal spatula was used for smear-sampling instead of a glass-slide, as advocated by *Cawson* (1966); hence, the smears comprised material collected from a rather limited, and perhaps not representative, area. Yet other possible explanations exist:

1) Literature has given evidence that Candida albicans is one of the most allergenic micro-organisms and that delayed hypersensitivity to Candida albicans is very common in the adult population (*Blamutier & Touteé*, 1960; *Charpin et al.*, 1960; *Rimbaud et al.*, 1960; *Holti*, 1966). The presence of a hypersensitivity to candida may explain that a therapeutical effect of antifungal therapy was seen in patients who only showed rather few yeast-like fungi in palatal smears and by cultivation.

2) It might be the tissue surface of the maxillary denture rather than the oral mucosa that is harboring the candida. Evidence of this hypothesis has been produced by *Cahn* (1936), who reported an anti-inflammatory effect of disinfecting the dentures, and by *Lyon* and *Chick* (1957), *Cawson* (1965) and *Wilton* (1968), who obtained an equal or even higher yield of candida from the dentures than from the oral mucosa, partly by smear-technique, partly by cultivation. *Spreng* (1945, 1963) and *Nyquist* (1952) reported an anti-inflammatory effect of lining the denture base with gold foil. *Spreng* used this finding as a diagnostic criteria of an allergic-type of denture stomatits, whereas *Nyquist* thought the gold foil might reduce the trauma inflicted on the oral mucosa or eliminate a possible suction effect of surface pores of the dentures. Presuming candida to be the actual etiological factor of denture stomatitis, gold foil may have therapeutical significance by its oligodynamic effect and by disrupting any contact between a microporous, infected denture base and the palatal mucosa.

An impressive therapeutical effect of antifungal therapy was seen in patients with a granular inflammation of the palatal mucosa. Although the hyperplasia persisted the inflammation resolved in 10 out of 13 patients. These lesions have usually been ascribed to badly fitting dentures and trauma (*Nyquist*, 1952; *Guernsey*, 1965; *Lambson*, 1966; *Fairchild*, 1967), candida infection being a complicating factor, (*Turrell*, 1966; *Cawson*, 1966). The high incidence of resolved inflammation, evaluated clinically and by smears, and the fact that the granular inflammation usually is located in the central part of the hard palate, an area deprived from the free flow of saliva and hence perhaps offering a good environment for the growth of yeast-like fungi, may indicate that Candida albicans plays an active role in the pathogenesis of the palatal hyperplasia.

A rather high incidence of relapse of denture stomatitis occurred in patients who initially were responsive to antifungal therapy. This may be explained by the fact that no precautions were taken to disinfect the dentures during antifungal therapy; accordingly, the palatal mucosa may have been reinfected by the dentures after nystatin had been withdrawn. The fact that yeast-like fungi were isolated by cultivation and in palatal smears in most of the patients showing relapse adds further proof for the significance of candida infection in denture stomatitis. It was an interesting finding that the incidence of relapse of glossitis and angular cheilitis was insignificant compared to that of denture stomatitis. This may indicate that the infection with candida starts in the palate from where it gradually spreads to involve other parts of the oral mucosa.

The role of trauma in denture stomatitis was illustrated, first, by the anti-

inflammatory effect of prosthetic treatment, secondly, by the fact that after the diffuse erythema had disappeared following antifungal therapy circumscribed lesions remained in some of the patients with traumatic dentures.

Tissue conditioning and occlusal equilibration was not followed by any significant change in the number of yeast colonies isolated by cultivation. Yeast-like fungi, cultured in the patients who were clinically responsive to treatment with Coe-Comfort, were probably in the non-pathogen blastospore phase as hyphal structures were never isolated in palatal smears in these patients. *Gibbons* (1965) and *Woelfell* (1968) reported a contamination of tissue conditioner with candida. Silicone denture material was found to provide a satisfactory habitat for the propagation of yeast-like fungi. It is, therefore, not surprising to find that yeast-like fungi were cultured in approximately the same quantities following tissue conditioning.

Among the patients without candida infection the construction of new dentures resulted in further decrease of the inflammatory degree and a reduction in the quantity of yeast-like fungi isolated by cultivation. The reduction in quantity of yeast colonies could be caused by a change in the ecologic environment as trauma of the palatal mucosa has been partly or completely removed.

Among the patients with verifiable candida infection the new dentures did not give rise to significant change in quantity of yeast colonies found by cultivation, even though decreased inflammation was seen in 4 patients. It is rather intriguing that hyphal structures were not isolated in palatal smears in the 4 patients that showed decreased inflammation following prosthetic treatment.

The following may be concluded:

1) Hyphal structures present in a direct palatal smear are an indication of candida infection: Patients who showed generalized simple inflammation or granular inflammation of the maxillary denture-bearing mucosa consistently revealed hyphal structures in palatal smears and were responsive to antifungal therapy without modification of their dentures.

2) The smear-technique is an unreliable method for a quantitative determination of candida infection: The severity of the inflammatory reaction and the terapeutical effect of antifungal therapy were unrelated to the quantity of hyphae present in a direct palatal smear.

3) The isolation of candida for cultivation is an unreliable method for establishing evidence of candida infection: By cultivation it is not possible to determine whether candida are present in the parasitical, mycelial phase or in the saprophytical blastospore phase.

4) The impression-technique for culturing candida, used as an adjunct to the smear-technique, is a reliable method for a quantitative determination of candida infection: It has been possible to establish a statistically significant correlation between the severity of the inflammatory reaction and the yield of candida by cultivation (*Part I*). In this study a statistically significant correlation was found between the yield of candida isolated by cultivation and the therapeutic effect of antifungal therapy.

5) Trauma is a predisposing factor to candida growth in the palate: Using the impression method candida were found located in the circumscribed, traumatic lesions of the palate (Part I). By removing trauma, the lesions were completely or partly abolished and a concomitant reduction in candida was seen by cultivation.

6) The significance of trauma as a direct, predisposing factor to candida infection in the palatal mucosa has not been established: Examination of direct smears from traumatic lesions usually did not show hyphal structures; on the other hand, a candida-induced inflammation might well be present under a presumably non-traumatic denture (Part I). Prosthetic treatment usually did not have therapeutical effect in candida-induced denture stomatitis.

THERAPEUTICAL GUIDELINES

The treatment of choice, antifungal or prosthetic, is entirely dependent on whether an oral candidiasis is verifiable. The verification of candida infection of the palatal mucosa is accomplished by a smear. In order to cover a representative area of the inflamed mucosa a glass-slide ought to be used for smear-sampling.

1) *The localized simple inflammation* These cases were found associated with traumatic dentures (Part I) and it was significant that they responded to prosthetic treatment, but not to antifungal therapy. Accordingly, smear-sampling is not necessary, as candida infection is very unlikely. The indicated treatment is occlusal equilibration, tissue conditioning and if necessary the construction of a new set of well-fitting and well-functioning dentures. It is important to change the conditioner regularily, as these materials are suitable media for candida growth. It is important to treat cases of localized simple inflammation as the traumatic inflammatory lesions predispose to candida growth and may eventually develop into a more widespread candida infection of the oral mucous membranes.

2) *The genralized simple inflammation* The treatment of choice is antifungal therapy after a verification of candida infection has been accomplished by a palatal smear. One nystatin tablet, taken three times a day for 10—14 days, should be sufficient but it may be necessary to continue the antifungal therapy up to 4 weeks. It is probably important to disinfect the dentures during the night and while the patient is sucking the tablets, in order to avoid the risk of re-infecting the patient by the dentures. Denture cleansers based on a chelating agent with a mixture of enzymes were found to be effective in dealing with Candida albicans, *MacCallum et. al.* (1968). Antifungal therapy has to be completed before a new set of dentures are constructed.

3) *The granular inflammation* Cases of granular inflammation were responsive to antifungal therapy. Although the inflammation usually disappeared the palatal hyperplasia persisted. The crevices between the palatal hyperplasia probably predispose to candida growth and candida infection. The palatal hyperplasia ought to be radically eradicated following antifungal therapy.

SUMMARY

An attempt was made to determine the relative significance of antifungal therapy and prosthetic treatment upon denture stomatitis. Candida infection was verified by isolating hyphal structures in palatal, glossal, and angular smears. Furthermore, yeast-like fungi were isolated for cultivation by using the impression method described in Part I (*Budtz-Jørgensen & Bertram*, 1970).

A therapeutic effect of antifungal therapy, evaluated both clinically and by smears, was seen in patients who revealed hyphal structures in pre-treatment palatal smears, i.e., cases of generalized simple or granular inflammation. Moreover, the accompanying signs and symptoms, i.e., pain, glossitis and angular cheilitis, usually cleared up following antifungal therapy.

A statistically significant correlation was found between the yield of Candida albicans by cultivation and the therapeutic effect of antifungal therapy. It was concluded that the quantitative determination of yeast-like fungi by cultivation is a reliable adjunct to the smear-technique in establishing the etiological significance of candida in denture stomatitis.

It was discussed why a therapeutic effect of antifungal therapy was seen in patients who only revealed few hyphal structures in palatal smears.

A therapeutic effect of prosthetic treatment (occlusal equilibration, tissue conditioning and the construction of new dentures) was noticed primarily in patients with non-verifiable candida infection.

Finally, therapeutical guidelines are given for the treatment of denture stomatitis.

RÉSUMÉ

STOMATITE PROTHÉTIQUE

II. EFFET DU TRAITEMENT ANTIFUNGIQUE ET DU TRAITEMENT PROTHÉTIQUE

Cette étude a été entreprise dans le but d'essayer de déterminer la signification relative du traitement prothétique et du traitement antifungique dans les cas de stomatite prothétique. L'infection à Candida a été vérifiée par isolement de structures filamenteuses dans les frottis du palais, de la langue et de la commissure. D'autre part, les champignons levuriformes ont été isolés pour la culture en utilisant la méthode de l'empreinte décrite dans la partie I de cette étude (*Budtz-Jørgensen & Bertram*, 1970).

Avec le traitement antifungique, on a constaté un effet anti-inflammatoire, évalué tant par examen clinique que par frottis, chez les patients dont les frottis du palais avant traitement présentaient des structures filamenteuses, c'est-à-dire dans les cas d'inflammation généralisée simple ou granuleuse.

De plus, les symptômes subjectifs et objectifs concomitants, c'est-à-dire douleur, glossite et cheilite angulaire, se dissipaient habituellement après le traitement antifungique.

Une corrélation statistiquement significative a été trouvée entre la production de Candida albicans par culture et l'effet anti-inflammatoire du traitement antifungique. Les auteurs en concluent que la détermination quantitative des champignons levuriformes par culture apporte un complément de valeur sûre à la méthode des frottis lorsqu'on veut évaluer l'importance étiologique des candida dans la stomatite prothétique.

Les auteurs discutent la raison pour laquelle on constatait un effet anti-inflammatoire du traitement antifungique chez des patients dont les frottis du palais n'avaient présenté qu'un petit nombre de structures filamenteuses.

Avec le traitement prothétique (rétablissement de l'équilibre occlusal, préparation des tissus et construction de nouvelles prothèses), on a essentiellement constaté un effet anti-inflammatoire chez les patients pour qui l'infection à candida n'avait pu être vérifiée.

Les auteurs terminent en indiquant quelques règles thérapeutiques pour guider le traitement de la stomatite prothétique.

ZUSAMMENFASSUNG

STOMATITIS PROTHETICA

II. DER EFFEKT ANTIMYKOTISCHER UND PROTHETISCHER BEHANDLUNG

Es wurde versucht, die relative Bedeutung antimykotischer und prothetischer Behandlung der Stomatitis prothetica zu bestimmen. Soormykose wurde durch den Nachweis von Pilzfäden in palatinalen, glossalen und angularen Abstrichen bestätigt. Ausserdem wurden Pilze, mittels der in Teil I (Budtz-Jørgensen & Bertram, 1970) beschriebenen Abdruck-Technik, kulturell nachgewiesen.

Ein therapeutischer Effekt bei antimykotischer Behandlung, sowohl klinisch als durch Abstriche bewiesen, konnte bei den Patienten beobachtet werden, die Pilzfäden in palatinalen Abstrichen vor der Behandlung auswiesen; das heisst, bei den Fällen mit generalisierten, einfachen oder granulären Entzündungen. Die begleitenden Symptome wie Schmerzen, Glossitis und Rhagaden waren gewöhnlich nach antimykotischer Behandlung verschwunden.

Es wurde eine statitistisch signifikante Korrelation zwischen der Quantität von kulturell nachgewiesenen Pilzen und dem Effekt antimykotischer Behandlung gefunden. Es wurde bestätigt, dass der quantitative kulturelle

Nachweis von Pilzen neben der Abstrich-Technik ein zuverlässiges Hilfsmittel ist, mit dem man die ätiologische Bedeutung der Pilze bei Stomatitis prothetika beweisen kann.

Weiters wurde darüber diskutiert, warum ein anti-inflammatorischer Effekt antimykotischer Behandlung bei den Patienten entstand, die nur einzelne Hyphen in palatinalen Abstrichen gezeigt haben.

Ein therapeutischer Effekt prothetischer Behandlung (Okklusionskorrektion, Unterfütterung mit Silikonabformmaterialen und Konstruktion der neuen Prothesen) wurde zuerst in der Patientengruppe mit nicht-verifizierter Candida-Infektion beobachtet.

Schliesslich wurden therapeutische Richtlinien für die Behandlung der Stomatitis prothetica gegeben.

REFERENCES

Ampil, J. P., 1966: Tissue reaction to tissue conditioner J. Phillipp. dent. Ass., *19:* 20—22.

Blamutier, J. & F. Touteé, 1966: Étude statistique de l'allergie a Candida albicans. Press. méd. *74:* 2531—33.

Budtz-Jorgensen, E. & U. Bertram, 1970: Denture stomatitis. I. The etiology in relation to trauma and infection. Acta odont. scand. *28:* 71—92.

Cahn, L. R., 1936: The denture sore mouth. Ann. Dent. *3:* 33—36.

Cawson, R. A., 1963: Denture sore mouth and angular cheilitis. Brit. dent. J. *115:* 441—449.

—»— 1965: Symposium denture sore mouth. The role of Candida. Dent. Practit. *16:* 138—42.

—»— 1966: Chronic oral candidosis. In: Symposium on candida infection. Ed. H. I. Winner & R. Hurley. E. and S. Livingstone. Edinburgh and London.

Charpin, J., A. Zafiropoulo & M. Blanc, 1960: Allergies respiratoire dues a Candida albicans. Path. et Biol. *8:* 319—322.

Fairchild, J. M., 1967: Inflammatory papillary hyperplasia of the palate. J. prosth. Dent. *17:* 232—237.

Gibbons, P., 1965: Clinical and bacteriological findings in patients wearing Silastic 390 soft liner. J. Mich. dent. Ass. *47:* 65.

Gonzalez & W. R. Laney, 1966: Resilient materials for denture prosthesis. J. prosth. Dent. *16:* 438—444.

Guernsey, L. H., 1965: Reactive inflammatory papillary hyperplasia of the palate. Oral Surg., Oral Med. & Oral Path. *20:* 814—827.

Hecht, S. S., 1939: Chronic irritation of the epithelial tissues of the mouth associated with dentures. Amer. J. Orthodont. & Oral Surg. *25:* 574—585.

Holti, G., 1966: Candida allergy. In: Symposium on candida infection. Ed. H. I. Winther & R. Hurley. E. and S. Livingstone. Edingburgh and London.

Jepsen, A. & E. Winther, 1965: Mycotic infection in oral leukoplakia. Acta odont. scand. *23:* 239—256.

Kozinn, P. J. & C. L. Taschdjian, 1962: Enteric candidiasis: Diagnosis and clinical considerations. Pediatrics. *30:* 71—85.

Lambson, G. O., 1966: Papillary hyperplasia of the palate. J. prosth. Dent. *16:* 636—645.
Lehner, T., 1967: Oral candidosis. Dent. Practit. *17:* 709—716.
Lyon, D. G. & A. O. Chick, 1957: Denture sore mouth and angular cheilitis. Dent. Practit. *7:* 212—217.
Lytle, R. B., 1957: The management of abused oral tissues in complete denture construction. J. prosth. Dent. *7:* 27—42.
MacCallum, M., G. D. Stafford, W. T. MacCulloch & E. C. Combe, 1968: Which cleanser? Dent. Practit. *19:* 83—89.
Nyquist, G., 1952: Denture sore mouth. Acta odont. scand. *10:* suppl. 9.
Rimbaud, P., H. Harnat, C. Bessière, J. A. Rioux & J. M. Bastide, 1960: Contribution a l'étude séro-immunologique de la candidose expérimentale du lapin. Path. et Biol. *8:* 329—335.
Roland, N., E. V. Zegarelli, A. H. Kutscher & H. Silvers, 1958: Monilial denture sore mouth and angular stomatitis treated with Amphotericin and 9,21-difluoro-21-desoxyhydrocortizone (FFF). N. Y. St. dent. J. *24:* 358—363.
Spreng, M., 1945: Die Prothese und die lebenden Gewebe. J. A. Barth. Basel.
—»— 1963: Allergie und Zahnmedizin. 2nd. ed. J. A. Barth. Leipzig.
Turrell, A. S. W., 1966: Ætiology of inflamed upper denture-bearing tissues. Brit. dent. J. *118:* 542—546.
Waite, D. E, 1961: Inflammatory papillary hyperplasia J. oral Surg. Anaesth. *19:* 219—214.
Wilton, J. M. A., 1968: Personal communication.
Woelfel, J. B., 1968: Evaluation of upper dentures lined with resilient silicone rubber. J. amer. dent. Ass. *76:* 582—590.

Address:
The Department of Prosthetic Dentistry,
The Royal Dental College,
Aarhus, Denmark