

TREATMENT OF PITYRIASIS CAPITIS (DANDRUFF) WITH ECONAZOLE NITRATE

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Abstract. 63 patients of both sexes with pityriasis sicca or steatoides were examined for presence of *Pityrosporum ovale* on the scalp. Only those cases in which very numerous yeasts were seen in all squamæ present in the preparation were considered positive. According to the severity or duration of pityriasis, 60% of the patients in this population represented severe cases and 38% refractory cases. A solution of econazole nitrate was applied as a spray, morning and evening, for a period of 10 to 20 days (mean). The overall assessment of the clinical effects of econazole nitrate indicated 56 favourable results, with complete disappearance of objective clinical signs in 47 cases; the course of pruritus proceeded roughly parallel with that of the objective signs. The mycological checking of the clinical results, performed at least 7 days after the conclusion of therapy, disclosed 6 failures and 57 successes. In 17 patients, the microscopic examination of squamæ was complemented by culture before and after treatment: in all cases, the culture, positive before econazole nitrate therapy, became negative after treatment, thus confirming the results of direct examination. These data suggest that *Pityrosporum ovale* plays a pathogenetic part in pityriasis simplex capitis.

Key words: Econazole nitrate; Pityriasis simplex capitis; *Pityrosporum ovale*

Pityriasis simplex of the scalp is an extremely common condition in which a yeast already described by Sabouraud (1904), Malassez's spore (1874), erroneously named "bottle bacillus" by Unna (1891), and commonly known at present as *Pityrosporum ovale*, is found, sometimes in abundance (1). It is a fungus composed of frequently budding ovoid or, more rarely, minute spherical yeast-like elements, measuring 0.25 to 5 μm in major diameter. It never takes on filamentous forms. This fungus usually lives on the human scalp, and occurs on the scalp beside any pityriasic state. Consequently

many authors consider it a harmless saprophyte playing no part in the aetiology of pityriasis capitis.

However, it may be wondered whether, as commonly observed with *Candida albicans*, *Pityrosporum ovale* may not develop pathogenicity on some terrains, through proliferation of its population. In addition, it is known to be capable of infesting the follicular canal and it could then play a part in the inflammatory process of acne through its lipolytic activity (2).

We therefore considered that the results of an antifungal therapy might provide an argument in favour of the aetiological role of this fungus in pityriasic states, insofar as its disappearance would be associated with that of dandruff.

The antifungal agent we used was 1-[2,4 dichloro- β (*p*-chlorobenzoyloxy)-phenetyl]-imidazole nitrate, whose international non-proprietary name is econazole nitrate (Pevaryl®; Cilag-Chemie). Its spectrum of activity covers dermatophytes, moulds, dimorphic fungi and yeasts (3).

MATERIALS AND METHODS

63 patients, 21 males and 42 females, ranging in age from 13 to 64, were included in this trial. 54 patients were affected with pityriasis sicca and 9 with pityriasis steatoides. In three-quarters of the cases (47 patients), dandruff was accompanied by often severe pruritus.

Seven patients were unable to give precise information about the duration of the condition, but it was always of very long standing. In the remaining 56 cases, the dermatosis had been present from 1 month to 40 years, and for at least 1-2 years in 41 of them.

As for the severity of the pityriasis, rated from 1+ to 4+, the condition was mild or moderate in 25 patients and severe in 38 (Table I).

In summary, 60% of the patients in this population represented severe cases, and 38% refractory cases. Most

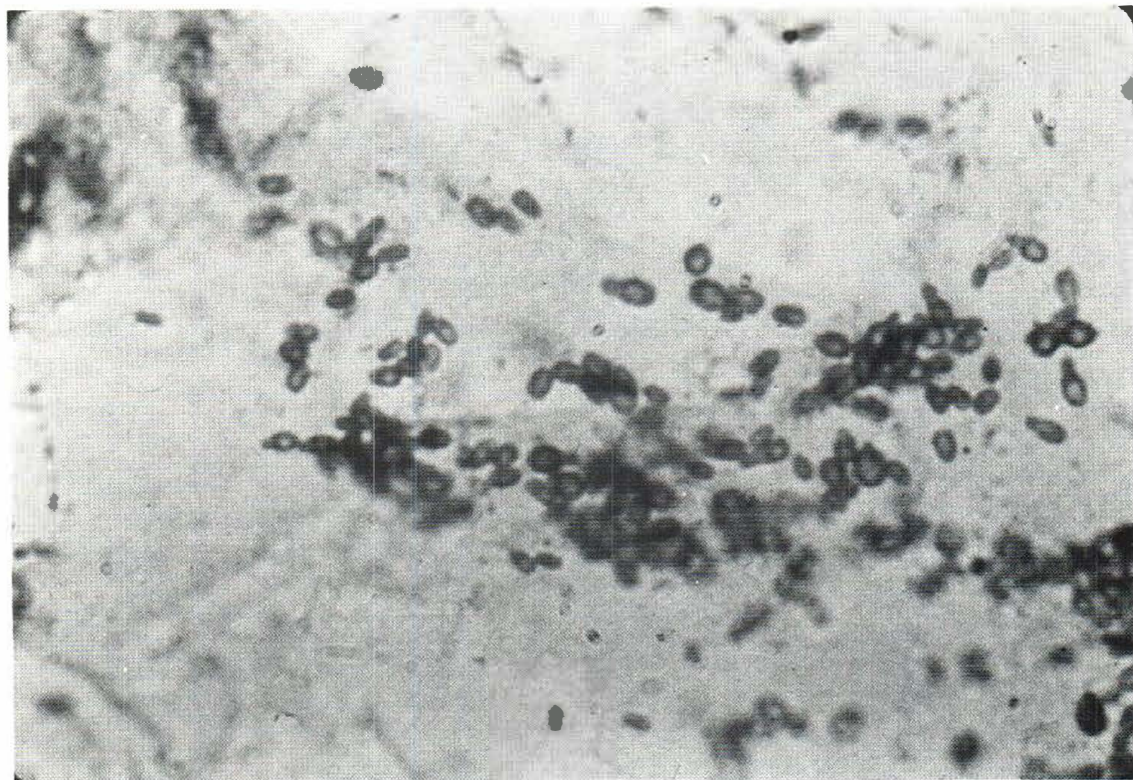


Fig. 1. *Pityrosporum ovale* agglomerates within the dandruff.

patients had previously treated themselves with various dandruff shampoos, without material result; in addition, 12 of them had tried various medications: selenium disulfure (Selsun; Abbot Laboratories) (6 cases) with a single favourable result followed by recurrence, amphotericine B (Fungizone; Squibb Laboratories) (2 cases) with favourable effects followed by recurrence, betamethasone dipropionate (Diprosone; Schering Laboratories) (1 case) and fluocinolone acetonid (Synalar; Syntex Laboratories) (1 case) without result, hydroxyquinolin (1 case) with improvement followed by recurrence, polysulphide (1 case) with aggravation.

In all patients, econazole nitrate was applied morning and evening for an average period of 10 to 20 days as a spray containing 1% of active ingredient, used like a hair-spray, though endeavouring to achieve maximum penetration to the scalp through the hair. In practice, the patients were advised to raise their hair "the wrong way" while spraying. In a number of cases, the treatment was prolonged beyond 3 weeks.

In all cases, a sample of dandruff was taken before commencing the treatment, by scraping the scalp with Brocq's curette (Drapier S. A., Paris); the samples thus obtained were stored in sterile Petri dishes. This sampling was repeated under the same conditions at the end of treatment.

The dandruff samples, fixed on slides with the help of a spray (of hair-spray type), were then stained with

fast periodic acid-Schiff (PAS) staining (filtered sulphurous fuchsin, Gurr Laboratories, London).

The positive samples showed yeasts agglomerated in packets within the squamæ. They displayed the variable forms described above (Fig. 1). Only those cases in which very numerous yeasts were present in all squamæ present in the preparation were considered positive. The presence of a few isolated yeasts was regarded as devoid of significance.

Direct examination was complemented in a number of cases by culture on Sabouraud's medium with chloramphenicol and sterile olive oil added (Chapeautot per-

Table 1. *Distribution according to the severity of pityriasis*

Severity	No.
Fine scattered dandruff without plaque formation	7
Desquamation in limited plaques (temporal and/or occipital and/or frontal)	18
Fine desquamation involving the greater part of or the whole scalp	37
Thickened squamæ with appearance of Alibert's amiantaceous pseudotinea	1

Table II. *Clinical results*

0=failure, 1=slight improvement, 2=marked improvement, 3=complete cure

Score	Duration of treatment (weeks)											Overall results
	1-1.5	2	3	4	5	6	7	8	9	10	12	
0				1		1		1			1	4
1	1		2									3
2	3	1	2	2	1							9
3	12	12	8	6	2	5	1	1				47
Total according to duration	16	13	12	9	3	6	1	2			1	63

tone 30 g, agar 20 g, chloramphenicol 0.5 g, distilled water 1000 ml; Pasteur Institute, Paris). The growth of the colonies is fairly rapid, taking ca. 8-10 days: the colonies obtained are of yeast-like appearance, brownish in colour. On microscopic examination, the cultured yeasts showed the same size and forms as observed *in vivo*.

RESULTS

1. *Clinical results* (Table II)

The overall assessment of the clinical effects of econazole nitrate indicated 56 favourable results (88.9%), with complete disappearance of the objective clinical signs in 47 cases (74.6%).

The effects on pruritus were roughly the same as those on the cutaneous symptoms: of 44 cases in which its course could be recorded, it disappeared totally in 34 cases and almost totally in 1, while it remained unchanged in 7 cases (the 4 failures and 3 slight results in the series). It also persisted, though attenuated, in 2 much improved patients. Some results were obtained quite rapidly: eruption and pruritus disappeared within 3 days in one case and within 4 days in another. But it was often difficult to obtain precise statements from the patients about the actual rapidity of the results. Thus the relationship between the result and the time after which it was obtained, as indicated in Table II, corresponds to the condition of the scalp as observed at the follow-up examination, which had to be put off for up to 12 weeks in the case of the least co-operative patients. However, 41 patients (i.e. two-thirds of the population) were seen again after 1-3 weeks, as scheduled in the protocol. These 41 cases contained 32 (68%) of the 47 complete cures and 6 (66%) of the 9 significant improvements recorded.

The permanence of the results could be noted in only 13 cases, from 7 days to 4 months after the end of treatment (Table III). On the other hand, 7 relapses were observed after the end of treatment (Table III). In one of these patients, the resumption of treatment restored the situation within 15 days, which was confirmed by an additional mycological examination. It must be added that no regard was taken as to whether the pityriasis capitis was of "sicca" or "steatoides" type.

2. *Mycological results*

The mycological checking of the clinical results was scheduled to take place 7 days after the end of treatment. Actually, this schedule was adhered to in only 17 cases. In the remaining 46 cases, it varied from 10 to 90 days (Table IV). This lack of discipline in some patients finally had the advantage of showing that the mycological result could remain stable long after the end of the course of treatment.

The examination disclosed 6 mycological failures (9.5%) and 57 successes (90.5%). The latter number exceeds that of the clinical successes. Indeed, in a case classified as a clinical failure after 4 weeks' treatment, the sample taken 15 days after the end of econazole nitrate applications showed no *Pityrosporum ovale*. The 6 post-treatment samples in which the squamæ remained heavily infested with parasites corresponded to the other 3 cases classified as clinical failures (0) and to the 3 cases classified as "slight" results (1). In 17 patients, the microscopical examination of squamæ was complemented by culture before and after treatment. In all these cases, the culture, positive before econazole nitrate therapy, became negative after treatment, thus confirming the results of direct examination.

We deemed it interesting, in connection with this work, to study the sensitivity to econazole and various other antifungal agents, of a strain of *Pityro-*

Table III. *Permanence of the results*

<i>No relapses (checking on 13 patients only)</i>							
Time after the end of treatment (days)	7	14	21	30	50	75	120
Number of patients	1	4	4	1	1	1	1
<i>Relapses</i>							
Time after the end of treatment (days)	21	30	42	50	84	120	
Number of patients	1	2	1	1	1	1	

Table IV. Direct examination after treatment

Result of direct examination	Time after the end of treatment (days)								Total
	7	10-12	15	20	30	40	60	90	
Negative samples	16	16	16	6	—	2	1	—	57
Positive samples	1	—	—	1	1	1	1	1	6
Total	17	16	16	7	1	3	2	1	63

sporum ovale isolated from a patient with pityriasis capitis in this series and to compare it with that of a strain of *Pityrosporum orbiculare* isolated from a patient with pityriasis versicolor. The results obtained are summarized in Table V. It can be seen that econazole and amphotericin B inhibited the two strains identically, starting from a concentration of 1 µg/ml medium. A slight difference was noted with nystatin, which inhibited *Pityrosporum ovale* from a concentration of 1 µg/ml, while it inhibited *Pityrosporum orbiculare* (pityriasis versicolor) only from 10 µg/ml. Griseofulvin proved totally ineffective at all concentrations studied. As to 5-fluorocytosine, it proved active only at high concentrations, which can be explained by the fact that the medium used contained antimetabolites.

COMMENTS

The high rate of clinical (89%) and mycological success (90%) obtained with econazole nitrate in pityriasis capitis, a condition rightly considered specially obstinate, reflects both the antifungal effectiveness of the product and the acceptability of its pharmaceutical form: it does not stain the hair and is very well tolerated and its simplicity of handling certainly plays a part in the results obtained.

Furthermore, without claiming the results of this therapeutic trial to be conclusive, they do seem to establish a causal relationship between fungal infestation and dermatological disorders: in 6 cases in which the treatment had little or no effect, the fungus remained in abundance, while in 2 cases, cured clinically and mycologically, a relapse confirmed by microscopic examination was accompanied by marked reinfestation. On the other hand, in a single case, the disappearance of yeasts was not associated with a regression of clinical symp-

Table V. Sensitivity of *Pityrosporum* to various antifungal agents

Antifungal agent	Strain of <i>Pityrosporum</i>	Concentration, µg/ml ^a			
		0	1	10	100
Econazole (Base)	P.o. 1543	+	○	○	○
	P.v. 1556	+	○	○	○
Amphotericin B	P.o. 1543	+	○	○	○
	P.v. 1556	+	○	○	○
Nystatin	P.o. 1543	+	○	○	○
	P.v. 1556	+	+	○	○
Griseofulvin	P.o. 1543	+	+	+	+
	P.v. 1556	+	+	+	+
5-Fluorocytosin	P.o. 1543	+	+	+	○
	P.v. 1556	+	+	+	○

^a Sabouraud's agar medium covered with a layer of peanut oil.

+ = growth, ○ = no growth. P.o. 1543 = strain isolated from pityriasis capitis, P.v. 1556 = strain isolated from pityriasis versicolor.

toms while, in 56 of the 57 cases in which Econazole nitrate treatment resulted in mycological sterilization of the scalp, pityriasis disappeared, most often completely.

Thus, in the case of pityriasis capitis, *Pityrosporum ovale* would appear not to be the saprophyte which it usually seems to be, but the agent responsible for the cutaneous disorders that disappear with it.

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