GRISEOFULVIN THERAPY OF DERMATOMYCOSES*

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Concerning a general glance at griseofulvin therapy, I would like to make a ew remarks, without however, going into statistical details and special details. Mycology is not a new branch of medical science. However, recent advance in antibiotic research has given added importance to mycology, with the result that mycological research is being carried out in variovs sections of medical science in many countries. At this lecture, I would like to mention the antibiotic therapy of mycoses in dermatoiogic clinic. My desire may be filled if my talks may be even only a little useful for general practioners including skin-clinicians.

Trichophyton-disease is one of the most common skin diseases of outpatients encountered in different countries. Various external remedies have been tried for

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its treatment. In spite of proper use of these remedies, however, re-ocurrence as a result of incomplete cure, development of dermatitis caused by irritation of the remedy locally used, and unsuccessful topical treatment because of deepseated lesion have been observed in not less number of cases. Therefore, clinicians are anxious for the appearance of oral remedy, definitely effective and without the defects above mentioned.

Griseofulvin, a new antibiotic, is just one remedy that may meet those demands. As for this antibiotic, it should be borne in mind that already in 1939: Oxford, Raistrick and Simonart isolated griseofulvin from a Penicillium, and later in 1958, Gentles reported on the effectiveness of this new antibiotic in the case of experimental dermatomyceses. Following this, Williams, Riehl, Blank, Sulzberger, Memmesheimer, Reiss and Desai etc. made an evaluation of griseofulvin. Later a similar evaluation was made by other investigaters of different countries. Thus, the modern therapy of dermatomycoses centres around griseofuivin therapy. There is now no question of the effectiveness of this antibiotic in some, but not all, cases.

Regarding the effectiveness of griseofulvin in the treatment of various types of tinea superficialis, as usual, immediate effect appears in trichophytia superficialis while a relatively long time is required for the treatment of nail-mycoses. Also, as *Sulzberger* and Goldfarb pointed out and as we know from our personal experience, it proved very difficult in curing keratotic type-lesions of tinea pedis. Some slides show some cases of griseofulvin effect observed at my clinic.

According to *Blank* and *Roth*, Trichophton ruburm is most susceptible to griseofulvin, followed by Trichophyton mentagrophytes, Trichophyton megnini and Microsporum. The fact that the effect of griseofulvin varies accroding to the species, strongly suggests the necessity of exact determination of causative organism in the beginning of the treatment, in connection with the fact that Candida albicans is unsusceptible to griseofulvin.

Concerning dosage of griseofulvin, 1.0 g may be considered the standard daily dosage, in accordance with the direction of Blank etc. However, according to our experience of some Japanese, even 0.5-0.7 g. per day was enough to prove sufficient effectiveness in many cases of tinea superficialis. In most cases, average duration of the administration and total doses of griseofulvin are as shown in Table.

TABLE I

Duration of treatment in days and total doses given, in respect of disease types

	Tinea maculosa et vesiculosa	Tinea pedis (vesiculating)	Tinea cruris	Total
Average duration of treatment in days	10.3	13.6	13.7	12.1
Average total doses (g)	9.2	12.3	12.9	11.0

TABLE 2

Duration of treatment in days and total doses given, in respect of etiological organism

	Tr. rubrum	Tr. mentagrophytes	Tr. interdigitale	Total
Average duration of treatment in days	11.2	15.0	10.5	12.1
Average total doses (g)	10.3	13.5	9.4	11,0

In regard to the side effects of griseofulvin, slight gastrointestinal disorder, headache and eruptions (urticaria, erythema multiforme etc.) have been reported and there are, at present, not many cases of severe type of the side effects. During 1959, 1960 and 1961, we have not yet met with severe cases of such side effects, but it is noted dysidrotic eruption on the palms was seen in five cases. Slide shows these cases and dysidrotic type.

TABLE 3

Five cases of "Trivhophytid ? occurring during griseofulvin-therapy

Case No.	Skin manifectation	Species of fungi	Daily dosage (g)	Duration (Days)	"Trichophytid"
1	Tinea corporis	Tr.ruburm	1.0	13	Dysidrotic eruptions on palms
2	Tinea pedis	Tr.interdig	1.0	9	,,
3	Tinea pedis	Tr.interdig.	0.75–1.5	14	,,
4	Tinea cruris	Tr interdig.	0.75	9	,,
5	Tinea pedis	Tr.ruburm.	0.75	3	,,

Clinically the dysidrotic type can be considered as "trichophytid" or griseofulvin exanthema. I regard such "id" cases as interesting from the viewpoint of comparative immunobiology of mycoses with tuberculoses, because, as is well known, tuberculid occasionally occurrs during the chemotherapy of tuberculosis.

I would like to make a short talk concerning critical follow up of girseofulvin therapy. This talk is based on personal cases of tinea superficialis due to Trichophyton ruburm and Trichophyton mentagrophytes (but not the keratotic type or nail mycoses). These cases were treated with griseofulvin and observed at our clinic during 1959, 1960 and 1961. These are cases in which tinea lesion had appeared in the previous year. Three slides show a case of such reoccurrence. Slide Shows tinea superficialis on the knee before griseofulvin therapy (September in 1959). Slide shows the healing of the tinea following griseofulvin therapy (October in 1959). Slide shows the reoccurrence of the tinea in August in 1960 at almest the same site where the tinea lesion existed in 1959. Concerning

the daily doses of griseofulvin in these cases of the reoccurrence, good results were obtained by the administration of 1.0g per day or of 0.75g per day. However, the number of days needed for griseofulvin therapy of these cases differed in 1959, 1960 and 1961. Namely, in some of these cases, the length of time needed for griseofulvin therapy was approximately the same in each of the 3 years. However, other cases proved more difficult to heal, and a greater length of time was necessary for therapy in each succeeding year. As one case of these cases, I would like to take up a case of dysidrotic type of tinea pedis due to Trichophyton ruburm. In this case, the duration of griseofulvin therapy was 20 days in 1960 and 84 days in 1961. The appearance of such a case suggests the possibility of dermatophytes resistant to griseofulvin. In practice, I have not yet met species of dermatophytes resistant to Griseofulvin. However, it is quite possible that the problems of fungi resistent to griseofulvin may be met in the future. Also, in connection with the limitation of this antibiotic therpay, the importance of the immunologic aspect of dermatomycoses must be stressed.

As above mentioned, I referred to only a general information of griseofulvin therapy of dermatomycoses and a critical follow up of this therapy.

In conclusion, I wish to express my deep gratitude and many thanks to the audience for their attentive and eager co-operation.

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