EXPERIMENTS ON THE BIOLOGY OF FUNGOUS INFECTIONS OF THE FEET*

STANLEY A. ROSENTHAL, PH.D. AND RUDOLF L. BAER, M.D.

Several years ago (1, 2) we conducted studies attempting to deliberately produce tinea pedis by immersing the healthy (fungus-free) feet of volunteer subjects in suspensions of living dermatophytes for 30 minutes. The source of these fungi was either fragmented cultures of dermatophytes or the foot bath water of persons with mycologically proven, clinically active tinea pedis. Among 68 subjects thus exposed, not a single case of acute tinea pedis was observed during the 6 weeks of observation following the exposure, although a transient, asymptomatic infection was apparently induced in about one half of these subjects.

The studies referred to above appeared to simulate naturally occurring conditions more closely than did the technics used by earlier investigators (3, 4, 5) who induced experimental superficial fungous infections of the feet by maceration and occlusion of the interdigital spaces. We concluded from the results of our studies that mere exposure of healthy feet to fungi was not sufficient to induce clinical disease.

The demonstration of pathogenic fungi on clinically healthy skin (6) strongly suggested that these organisms maintain themselves without producing disease, perhaps for considerable periods of time. Clinical disease might well result under altered conditions of host-parasite relationship.

Strauss and Kligman (7) demonstrated that in many persons with a fungous infection of the foot, a normal interdigital space would become infected as evidenced by a KOH positive examination if the webs or the entire foot were occluded. In persons with normal feet, however, experimental infections were most difficult to induce. Prolonged wetness of the inoculated site was essential to an experimental infection and the clinical infection healed when occlusion was stopped. Their most successful method, resulting in a 55% rate of infection, was to place moist, fungous-contaminated filter paper between the toes which were then kept under occlusive conditions.

The studies to be reported here are further attempts to deliberately induce fungous infections of the feet in human volunteers by methods which more closely resemble those encountered under natural conditions. We were particularly interested in evaluating the role of trauma in the occurrence of experimental fungous disease of the feet.

GENERAL METHOD

a) Selection of Subjects: The subjects were, for the most part, young adults. The feet of each subject had mycological examinations twice at weekly intervals. Scales were obtained from all toe webs and from the sole of each foot, and were combined for inoculation onto Sabouraud medium containing antibiotics (8) and for microscopic examination. The finding of dermatophytes, either by culture or on microscopic examination, eliminated the subject from further participation in the experiment.

b) Preparation of Subjects: The subjects can be divided into 3 groups on the basis of the preparation of their feet preceding fungous exposure: a) no deliberate traumatization of the feet, b) "mild" traumatization of the feet (no frank blistering); and c) "severe" traumatization of the feet (frank blistering).

With 104 subjects (groups b and c), foot sites (2nd toe web and/or sole of 1 or both feet) were exposed to cantharidin* or croton oil†. The vesicant agents were applied either once or twice at 24 hour intervals, before the subjects were exposed to fungi. In 28 subjects these vesicant agents were applied without any prior damage to the skin sites. In 76 subjects the application of cantharidin to the toe web and sole areas was preceded by vigorous scraping of the areas with a scalpel moistened with 10% KOH, to remove some of the horny layer. This scraping was done with sufficient intensity to produce mild erythema and slight discomfort. While this was done in a uniform manner.

* Cantharone, Ingram Pharmaceutical Co. (7 mg cantharidin/cc in acetone-flexible collodion base.)
† Croton Oil, N.F. VII., Magnus, Mabee and Reynard, Inc.
ner, it must as assumed that the intensity of the scrapings and consequently the amount of horny layer removed varied to some extent from site to site.

Removing some of the horny layer before application of cantharidin had a marked effect on the production of blisters. This observation will be discussed below.

c) Exposure to dermatophytes: All subjects were maintained in an environmentally controlled room at 37°C and 85% relative humidity for 2 hours, during the last 30 minutes of which the feet were placed in a foot bath containing large numbers of dermatophytes. The inocula were prepared by scraping the growth from Sabouraud agar cultures and fragmenting the organisms in a homogenizer. Known volumes of this stock suspension were added to 1 liter of foot bath water. Viable counts were made by the pour plate method. The depth of the foot bath was ample to cover the soles and the toe webs. The volunteer subjects were exposed to strains of T. mentagrophytes, T. rubrum, or, in a few instances, E. floccosum.

After the deliberate exposure to dermatophytes, the subjects were instructed to put on their regular footwear and to go about their normal daily activities. No restrictions were placed on frequency of bathing, types of footwear used, etc., but the subjects were told not to use any ointments, powders, cosmetics or other material except soap on their feet until the study was completed.

d) Follow-up examinations: Each subject was examined clinically and mycologically at approximately weekly intervals for a minimum of 6 weeks following a fungous exposure. At each visit materials were taken separately from each 2nd toe web and from each sole site for microscopic and cultural examination. In addition, whenever possible the subjects were reexamined several months after the deliberate fungous exposure.

On the basis of the findings in clinical and mycologic examinations after exposure, our subjects were placed into one of 5 categories:

1. Persistent clinical (symptomatic) infection: Demonstration of pathogenic fungi from areas showing clinical evidence of fungous disease (erythema, scaling, vesicles, papules, etc.) over 4 or more weeks.

2. Persistent asymptomatic infection: Repeated demonstration of dermatophytes over 4 or more weeks by microscopic examination and/or culture in the absence of visible clinical changes ("healthy carrier state").

3. Transient clinical (symptomatic) infection: A brief (1-3 weeks) appearance of clinical and mycologic signs of fungous infection.

4. Transient asymptomatic infection: The microscopic or cultural demonstration of fungi on 1 or 2 occasions in the absence of clinical signs of infection.

5. No infection (no "take"): No clinical or mycologic evidence of fungous infection of the feet.

### TABLE I

<table>
<thead>
<tr>
<th>Blistering after application of cantharidin</th>
<th>Soles</th>
<th>Toe webs</th>
</tr>
</thead>
<tbody>
<tr>
<td>No scalpel scraping before application of vesicant agent</td>
<td>0/28*</td>
<td>1/3</td>
</tr>
<tr>
<td>Scalpel scraping before application of vesicant agent</td>
<td>91/118 (77%)</td>
<td>104/118 (88%)</td>
</tr>
</tbody>
</table>

* Including 7 sites treated with croton oil.

**RESULTS**

Production of blisters on the soles and toe webs

With 21 subjects, cantharidin was placed on the clinically normal soles, and with 3 of these subjects this material was also placed in the 2nd toe web. Croton oil was placed on the soles of 7 subjects. After 24 hours there was no evidence of visible blistering at any of the sole sites and at only 1 of the toe web sites.

With 76 subjects the sole and toe webs were vigorously scraped with a scalpel before application of cantharidin. Seventy-one of these 76 subjects blistered at 1 to 4 sites after 1 or 2 daily applications of cantharidin. Most blisters appeared after the first application. The relative susceptibility to blistering of the soles and toe webs is shown in Table I.

Effects of experimental fungous exposure in 23 subjects with no deliberate trauma to the feet

These 23 subjects were exposed to suspensions of T. rubrum or T. mentagrophytes ranging in concentration from 1,100 to 200,000 viable organisms per ml with a median count of 27,000 and an average count of 38,000.

In none of the 23 subjects were there any clinical signs of fungous infection and only 1 subject showed a transient asymptomatic infection (microscopically positive on one occasion).

Thirteen of the 23 subjects were available for reexamination 2 to 6 months after their last clinical and mycologic examination. None of these 13 subjects reported the development of any lesions on the feet in the interim, and all,
including the 1 subject who had had a transient asymptomatic infection, were clinically normal and mycologically negative.

Effects of experimental fungous exposure in 33 subjects after non-blistering trauma

Since these 33 subjects showed no frank blisters after application of the vesicant agents, the 2nd toe web and the sole of each foot were vigorously scraped with a scalpel before immersion in the fungus-contaminated foot baths. The concentration of viable dermatophyte elements (T. rubrum or T. mentagrophytes) in the foot baths ranged from 4,200 to 295,000 per ml, with a median count of 24,600 and an average count of 67,800.

Only one of the 33 subjects developed clinical signs of fungous infection. This T. mentagrophytes infection occurred in a toe web area. Ten subjects showed a transient asymptomatic infection, in 9 by the microscopic demonstration of fungi (once in 8 subjects, and twice in one subject) and by a positive culture in another subject. With 22 subjects there was no clinical or mycologic evidence of fungous infection of the feet during the 6 week or longer examination period following exposure.

Ten to 13 months after deliberate exposure to fungi 22 of the 33 non-blistered subjects were reexamined. Five of these subjects had previously shown a transient asymptomatic infection during the 6 week post-exposure examination period. None of these 5 reported any signs of tinea pedis during the interval since the last examination and all were clinically normal and microscopically negative for fungi at the time of reexamination. One subject, however, yielded a culture of T. rubrum from a toe web site. He had been exposed to this species 10 months previously, but fungi had never before been demonstrated in scrapings from this site. Sixteen subjects, clinically normal and mycologically negative during the 6 weekly post-exposure examinations were clinically normal and mycologically negative upon reexamination and reported no signs of tinea pedis during the 10 to 13 months period between examinations.

Effects of experimental fungous exposure in 71 subjects after blistering trauma

In 70 of these subjects a vigorous scraping with a scalpel had preceded the application of cantharidin to a 1 cm area site on one or both soles and to a small area in one or both second toe webs. One subject developed a blister in a toe web site without preliminary scraping. The blisters were opened with a scalpel, and the blister fluid drained without debridement, just before immersion in the foot bath. The concentration of viable dermatophyte elements in these foot baths (T. rubrum, T. mentagrophytes or E. floccosum) ranged from 550 to 275,000 per ml, with a median count of 75,000 and an average count of 85,000.

Of the 71 blistered subjects who were exposed to fungi, 26 (37%) developed persistent or transient clinical or persistent asymptomatic infection, 11 (15%) developed a transient asymptomatic infection, while 34 (48%) developed no clinical or mycologic evidence of fungous infection.

The 26 subjects who developed clinical infections or persistent asymptomatic infections had a total of 78 blistered sites. Twenty-four of these subjects developed clinical lesions and only 2 remained persistent asymptomatic carriers for 19 and 22 weeks respectively, when the experiment was terminated.

The 11 subjects who showed a transient asymptomatic infection had a total of 35 blistered sites. Eight of the 11 subjects each had this transient asymptomatic infection on 1 blistered site, 1 subject had it on 2 blistered sites, while 2 subjects had it on a traumatized site that had not been blistered while the previously blistered sites were mycologically negative. The 34 subjects who failed to show any signs of infection had a total of 88 blistered sites.

The following are some of the observations made in the 24 clinically infected subjects:

a) Clinical incubation time: The time from deliberate exposure to the first appearance of definite clinical signs of infection in the 24 clinically infected subjects is given in Fig. 1. With 15 of these subjects, first clinical signs appeared within 10 weeks, and in the majority within 4 weeks after exposure. With 9 subjects the clinical incubation time was more prolonged, ranging from 14 to 38 weeks after exposure.

In every instance, clinical disease occurred at a site (sole or 2nd toe web) which had been previously traumatized by the formation of a cantharidin blister. In no instance was there
clinical infection at a non-blistered site although the entire foot was exposed to the same inoculum. It is also important to note that in every instance the causative species which was isolated from the lesions was the same species used for deliberate exposure.

b) Clinical signs: The clinical signs of tinea pedis produced in our subjects ranged widely, from non-pruritic areas of slight scaling and erythema to extremely pruritic lesions showing varying degrees of fissuring, vesicles, bullae, crusting, etc. It was not possible to correlate any particular clinical characteristics with either T. rubrum or T. mentagrophytes infections.

c) Duration of clinical disease: After clinical lesions had developed, we urged our subjects to allow the disease to continue without medication so that the course of the infection could be observed. This gave us an opportunity to observe fifteen of the subjects weekly until the lesions had spontaneously resolved. Fig. 2 shows the wide variations in duration of clinical disease, ranging from 2 to 26 weeks with a median duration of 6 weeks.

It is of interest that a subject whose lesions healed spontaneously in 4 weeks became a healthy carrier at the previously involved site. She returned to our laboratory 30 weeks after her spontaneous clinical cure with new lesions at the previous site of involvement.

Eight subjects requested antimycotic therapy.
The duration of their disease before institution of therapy ranged from 2 to 12 weeks with a median time of 5 weeks. One subject was lost from observation while he still had clinically active lesions.

d) Site of infection: The 26 subjects who showed clinical or persistent asymptomatic infections had received a total of 78 blisters, 39 on the sole and 39 in the 2nd toe web. The incidence of infection on these blistered sites is tabulated in Table II. The difference in infection rates between the blistered toe web and sole sites is not statistically significant (P < .05) but the difference in the infection rate between blistered and non-blistered sites is significant (P > .01). The one persistent asymptomatic infection at a non-blistered site occurred in an individual who also had clinical lesions at a blistered toe web site.

e) Demonstration of local resistance: In 14 of the 26 subjects, 4 blisters were produced (on each sole and in each 2nd toe web) before exposure to dermatophytes, and clinical disease was produced in 12 of these subjects. However, in not a single subject was clinical disease produced at all 4 blistered sites. With 8 subjects lesions developed at only 1 of the 4 sites, with 2 subjects at 2 sites and with 2 subjects at 3 sites. Other blistered sites in these 12 subjects did not show clinical disease although 4 sites in 2 subjects showed a persistent asymptomatic infection and 7 sites in 6 subjects showed a transient asymptomatic infection. Nineteen blistered sites in 9 subjects were not infected, either clinically or mycologically.

f) Role of species of dermatophyte in producing experimental infections: Of the 71 blister-
tered subjects 29 were exposed to *T. rubrum*, 39 were exposed to *T. mentagrophytes* and 3 were exposed to *E. floccosum*. The infection rates in these 71 subjects are presented in Table III. The difference in infection rates between *T. rubrum* and *T. mentagrophytes* is not statistically significant (*P* < .05). Differences in pathogenicity between strains were not studied since a single strain of each of these species was used in most instances.

g) Relative susceptibility of male and female subjects to experimental fungous infection of the feet: Of the 71 blistered subjects who were deliberately exposed to fungi, 32 were female and 39 were male. The infection rates in these 2 groups are compared in Table IV, which indicates that both groups were equally susceptible.

h) Effect of season on experimental infections: Thirty-nine blistered subjects were deliberately exposed to dermatophytes during the cold (October–March) months and 32 during the hot (April–September) months of the year. The infection rates for these 2 periods of exposure are presented in Table V, which indicates that the season during which exposure took place did not significantly influence the development of experimental fungous infection of the feet.

Nineteen of the 71 blistered subjects were re-examined 4–11 months after exposure or after spontaneous cure of an experimental infection. Of 13 subjects who had been exposed but failed to show any mycologic evidence of fungous dis-

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**TABLE III**

<table>
<thead>
<tr>
<th>Species</th>
<th>Total No. of subjects exposed</th>
<th>Type of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>Transient</td>
</tr>
<tr>
<td></td>
<td>Asymptomatic Infection only</td>
<td>Infection*</td>
</tr>
<tr>
<td><em>T. rubrum</em></td>
<td>29</td>
<td>17 (59%)</td>
</tr>
<tr>
<td><em>T. mentagrophytes</em></td>
<td>39</td>
<td>14 (36%)</td>
</tr>
<tr>
<td><em>E. floccosum</em></td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

* Including persistent clinical, transient clinical and persistent asymptomatic infections.

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**TABLE IV**

Infection rates in 39 male and 32 female subjects

<table>
<thead>
<tr>
<th>Infection*</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient asymptomatic infection</td>
<td>5 (13%)</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>No infection</td>
<td>19 (49%)</td>
<td>15 (47%)</td>
</tr>
</tbody>
</table>

* Including persistent clinical, transient clinical and persistent asymptomatic infections.

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**TABLE V**

Effect of season on experimental fungous infection

<table>
<thead>
<tr>
<th>Season during which exposure took place</th>
<th>Infection*</th>
<th>Transient asymptomatic infection</th>
<th>No infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>April–September (32 subjects)</td>
<td>14 (44%)</td>
<td>5 (15%)</td>
<td>13 (41%)</td>
</tr>
<tr>
<td>October–March (39 subjects)</td>
<td>12 (31%)</td>
<td>6 (15%)</td>
<td>21 (54%)</td>
</tr>
</tbody>
</table>

* Including persistent clinical, transient clinical and persistent asymptomatic infections.

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Discussion on the results and the implications of the study.
Five subjects, who had been experimentally infected but whose lesions spontaneously healed were reexamined 4—11 months after their spontaneous cure. All were clinically normal and mycologically negative on reexamination.

DISCUSSION

Perhaps the most significant finding in this study is the important role of blistering trauma in engendering clinical and asymptomatic experimental infections. Among 23 subjects who did not receive deliberate trauma before exposure there were no clinical infections and only 1 transient asymptomatic infection. Thirty-three other persons were "lightly" traumatized on a total of 132 foot sites. This was accomplished by the application of doses of cantharidin or croton oil which did not result in the production of clinically visible blisters. An added insult to these non-blistered sites was a vigorous scraping with a scalpel immediately preceding the immersion in the fungus-contaminated foot baths. Only 1 of these 33 subjects developed a persistent clinical infection at one site. There were 10 additional subjects in the "lightly" traumatized group who showed transient, asymptomatic infections for a total of 11 (33%) infections.

Among the 71 subjects who received severe trauma to the feet (from 1 to 4 blisters) before deliberate fungous exposure there was an infection rate of 52% (26 subjects with clinical infections or persistent asymptomatic infections plus 11 subjects with transient asymptomatic infections). There is not only a difference in total infection rate between the mildly and severely traumatized subjects but also a very striking difference in the kind of infections which occurred in these two groups (1 of 33 (3%) clinical infections in the mildly traumatized group and 26 of 71 (37%) clinical or persistent asymptomatic infections in the blistered group). There is little doubt that blistering in some way strongly favored the establishment of the fungi in the skin. It appears quite likely that some of the subjects showing transient asymptomatic infections in our "mildly" traumatized group might have developed more persistent or clinically apparent fungous infection if they had been blistered before the exposure to the fungus-contaminated foot baths.

The demonstration of 26 infections (omitting those who showed only a transient, asymptomatic infection) in the blistered group is an indication of the value of the technic used by us in inducing experimental fungous infection and disease of the feet in man. Although our infection rate of 37% is not as high as that obtained by others (7), our technic did not involve any occlusive procedures after exposure.

Another important finding is the failure to engender symmetrically situated clinical infections. Twelve of the 26 infected subjects had been blistered on 4 sites, yet none developed clinical disease on all 4 sites. Only 2 subjects showed persistent infections on 3 of the blistered sites, 2 at 2 sites and the others only at 1 of the 4 sites.

It is possible that this is accounted for by differences in the intensity of the trauma to the various sites. Although the same concentration of cantharidin was applied to all sites, the amount of horny layer removed with a scalpel before application of the vesicant agent could not be accurately controlled. Another possible explanation is that there is a difference in susceptibility even in symmetrically situated sites. It is a well known clinical observation that tinea pedis may occur and recur in a certain area on the feet with neighboring areas remaining entirely unaffected. We have also observed, in unpublished experiments, that symmetrical sites on the back and forearm usually differ in their capacity to blister when negative pressure (suction) is applied.

The observation that the soles are as susceptible to experimental infection as the toe webs is interesting. One might have guessed that the moist, intertriginous areas of the toe webs would be more conducive to fungal growth than the apparently drier, more exposed, plantar area. However, the much larger quantity of horny layer on the soles could well counterbalance this factor.

Another finding and one which merits more extensive investigation, is the long delayed development in 9 of our subjects of clinical fungous disease at sites which had remained clinically normal for 14—38 weeks after exposure. Four of these subjects had been asymptomatic healthy carriers for 14—24 weeks at sites which eventually showed clinical manifestations. With these 4 subjects it is obvious that the delicate balance between the pathogenicity of the fungus
and the host's resistance, in equilibrium for some
time, finally swung in favor of the parasite.

The events in the other 5 subjects with a very
prolonged clinical incubation time are less
easily explained. Four of these subjects were
mycologically negative throughout the 6 or
more week period following exposure, while the
5th subject became mycologically negative (for
3 successive weeks) after having had an asym-
tomatic infection up to the 8th week following
exposure. These 5 subjects were discharged
from the experiment but returned 9 to 30 weeks
later with clinical fungous disease at a previous
blistered site. The fact that a fungous infection
now existed was confirmed by repeated labora-
tory examinations.

It would seem almost certain that fungi were
present at or near the sites which subsequently
showed clinical infection, although they could
not be detected in repeated microscopic exami-
nations and cultures carried out by experienced
mycologists. To our knowledge, none of the
dermatophytes have been demonstrated to exist
in a phase similar to pleuropneumonia-like
forms described for certain bacteria. The search
for such a phase among these fungi is urgently
required. Of particular interest in this connec-
tion is the recent report (9) of the isolation of
"protoplasts" from a patient with Candida
tropicalis endocarditis. Treatment with ampho-
tericin B resulted in negative blood cultures for
C. tropicalis but the disease persisted. Culture
of blood on osmotically controlled thioglycollate
medium resulted in the growth of microorgan-
isms which at first consisted of small coccoid
to rod forms but which, over 103 days of incu-
bation, developed into budding yeast forms
which were identified as C. tropicalis.

Our various infection groups (persistent or
transient clinical infection, persistent or tran-
sient asymptomatic infection or no infection)
may be explained as follows: Viable fungal ele-
ments are introduced into the skin through the
defect (blister) where they are covered with the
serum coagulum. The depth of the deposition of
these organisms would depend on the severity of
the trauma. Once within the site, these fungi can
either die or survive. If they survive, it may be
for only a short period of time or they may sur-
vive indefinitely. The fungi within the defect
would be covered and would escape detection
when mycologic scrapings were done during a
certain period of time after exposure. As the
outward flow of the skin cells progressed, the
fungi would be carried along until they ap-
proached the surface of the skin. The length of
time required for this would depend on at least
two factors: the original depth of inoculation
and the rate of skin growth at a particular site.
If the fungi die after being introduced into the
traumatized site, the subject would remain
clinically normal and mycologically negative by
death and perhaps dissolution of fungi. If
growth of the inoculum in the skin was only
temporary, fungi might be seen only on 1 or 2
occasions (transient asymptomatic infection). If
fungi persisted and grew in equilibrium with
the human host, one would have a repeated
appearance of fungi without clinical signs of in-
fec tion (persistent asymptomatic infection). If
the host parasite equilibrium was altered in
favor of the parasite one would have clinical
disease, either persistent or transient, depending
on the balance of power at any one time. The
possibility of an asymptomatic infection occur-
ring with the fungi existing in an as yet undis-
covered atypical phase has already been men-
tioned. We have always seen typical fungi
(filaments and arthrospores) at clinically in-
volved sites.

The question arises as to what would have
happened if there had been a control group of
subjects whose feet were blistered but without
deliberate exposure to fungi. One might suppose
that blistering trauma followed by a natural ex-
posure to dermatophytes might have lead to
fungous infection or disease. Could we be at-
tributing some of these "natural" infections to
our experimental exposure? This possibility ap-
pears remote, since, without exception, only
that species of fungus which was used for de-
liberate exposure (either T. rubrum or T.
mentagrophytes) was reisolated from the in-
fected sites in our subjects. Indeed on the basis
of these studies, the combination of blistering
trauma plus adequate exposure to fungi has
been so effective in engendering fungous infec-
tions that one might well suspect that the com-
bination of these factors forms part of the
mechanism by which tinea pedis is contracted
under natural conditions.

Our results suggest that T. mentagrophytes
and T. rubrum are equally pathogenic in ex-
perimental infections. The fact that T. rubrum
is a much more frequent cause of tinea pedis than *T. mentagrophytes* in New York City as well as in other parts of the world is likely to be due to factors other than differences in pathogenicity.

**SUMMARY**

Clinical or persistent asymptomatic fungous infections of the feet have been induced in 37% of 71 human volunteer subjects without the use of occlusive procedures following exposure. Severe (blistering) trauma immediately before exposure appeared to be an important factor in the occurrence of experimental infections of the feet since infections occurred only rarely in non-blistered sites. The clinical incubation time and the duration of the induced lesions varied widely among individual subjects. A clinical and, in some instances, also a mycologic incubation time of 3 months or more in some of the volunteers suggests the possibility that dermatophytes may exist in a protoplast-like phase.

Male and female subjects were equally susceptible to experimental infection. Sites on the toe webs and on the soles also were equally susceptible. No difference in pathogenicity could be demonstrated between *T. rubrum* and *T. mentagrophytes*. The infection rates in subjects exposed during the cold months (October-March and the warm months (April-September) were not statistically different.

**REFERENCES**