

ONYCHOMYCOSIS CAUSED BY ASPERGILLUS TERREUS*

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The etiologic agents of onychomycosis are many and varied. In addition to the several species of Trichophyton, Syringospora (Candida, Monilia) and Epidermophyton floccosum, a number of species of genera, rarely considered to be pathogenic, have been implicated in nail infections. Included among the latter are such genera as Penicillium, Scopulariopsis, Aspergillus, Hyalopus, Cephalosporium and Sterigmatocystis, fungi usually considered to be the weeds of mycology and as such are often found as contaminants in cultures made from nail lesions. One should, therefore, view with uncertainty, reports of cases blaming these organisms for producing lesions solely on the basis of growing the fungus in culture. The proof of the ability of the organism to produce the unguinal infection should rest on the demonstration of the fungus in the infected nail and its cultivation on artificial mediums. Because of their ability to grow in most substrata with the reproduction of their cultural characteristics such as irregular hyphae or filaments, conidia and conidiophores, it is difficult to apply Koch's postulates as proof of the pathogenicity of such organisms.

The Aspergilli have been singled out particularly in the past few years as being guilty of a greater number of onychomycoses than had been previously suspected. In the routine examination and cultivation of infected nails at the Barnard Free Skin and Cancer Hospital, Aspergilli, in addition to other molds, have frequently developed in cultures. In the absence of positive microscopic findings in the potassium hydroxide preparations (30 per cent), these organisms were considered to be contaminants. The need for careful examination of these preparations should be stressed since it is quite possible that they may be overlooked in too cursory an examination. On the other hand, every case of unguinal lesion resulting in a culture of Aspergillus should not be diagnosed as an aspergillosis without adequate proof.

A review of the pertinent literature has revealed that there are at least 11 species of Aspergillus which have been found in onychomycoses either alone or in combination with other known pathogens. These are listed in Table 1. The addition of the organism described in this paper makes a total of 12 species of Aspergillus which may cause unguinal lesions.

Aspergillus terreus Thom is a fairly common mold in the environment. It has been reported as present in numerous countries of Europe, South America, Asia, Africa and in many states of the United States. It is found chiefly in the soil, and Negroni and Negri (11) isolated it four times from the soil in Buenos Aires, Argentina. MacKinnon (12) reported the organism from the soil, moist leather, and in tubes of media exposed to the air of Montevideo, Uruguay. In

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the role of a pathogen it has been reported as causing lesions on the hand and forearm of a Nebraska cornhusker (13). *A. terreus* has been demonstrated by MacKinnon (12) in epidermal desquamations of the auditory canal of a woman. The fungus was not pathogenic to pigeons either by subcutaneous or intravenous inoculations. Intraperitoneal injections of rabbits were negative whereas subcutaneous inoculations resulted in nodules and abscesses which became reabsorbed. Intravenous inoculations with massive doses of *A. terreus* developed numerous granulating areas in the lungs which contained caseous pus and fungous spores.

The following case is presented as the first onychomycosis to be reported due to *A. terreus*.

TABLE 1
Aspergilli isolated from onychomycoses

| NO. | ASPERGILLUS CULTURED | POTASSIUM HYDROXIDE PREPARATION | YEAR | AUTHORS (REF.) |
|-----|--|---------------------------------|------|--|
| 1 | <i>A. unguis</i> (Weill & Gaudin) Dodge | Positive | 1919 | Weill & Gaudin (1) |
| 2 | <i>A. Gratioti</i> Sartory | Positive | 1920 | Sartory, A. (2) |
| 3 | <i>A. Jeanselmei</i> Ota | Positive | 1923 | Ota (3) |
| 4 | <i>A. diplocystis</i> (Sartory, Sartory, Hufschmitt & Meyer) Dodge | Positive | 1930 | Sartory, A., Sartory, R., Hufschmitt & Meyer (4) |
| 5 | <i>A. onychophylus</i> Greco & Bigatti | Positive | 1934 | Greco & Bigatti (5) |
| 6 | <i>A. fumigatus</i> Fresenius | Positive | 1940 | Sartory, A. & Sartory, R. (6) |
| 7 | <i>A. flavus</i> Link | Positive | 1941 | Bereston & Keil (7) |
| 8 | <i>A. Sydowi</i> (Bainier & Sartory) Thom & Church | Positive | 1942 | Negroni (8) |
| 9 | <i>A. versicolor</i> (Vuillemin) Tiraboschi | ? | 1942 | Negroni (8) |
| 10 | <i>A. nidulans</i> (Eidam) Lindt | Positive | 1945 | Bereston & Waring (9) |
| 11 | <i>A. glaucus</i> Link | Positive | 1946 | Bereston & Waring (10) |
| 12 | <i>A. terreus</i> Thom | Positive | 1948 | Moore & Weiss |

REPORT OF A CASE

L. M., a 47 year old dentist, was first seen in the office on January 30, 1948 complaining of an eruption over his skin which he stated had been present approximately 15 years.

His general physical examination was negative and he had no other complaints. He presented large circinate and gyrate patches, yellowish-red in color, chiefly in and inferior to the right axilla. These lesions apparently began in the axilla and slowly spread from that point to involve the adjoining portion of the trunk anteriorly, inferiorly and posteriorly. A mild seborrheic dermatitis involved the margins of the eyelids. Cultures and smears were made from the patches of dermatitis in the axillary region. The smears showed large staphylococci while the cultures developed growths of both *Staphylococcus aureus* and *S. albus*.

Examination of the toenails disclosed them to be somewhat hypertrophic, especially under the free margins, with definite brittleness. The nail tissue was loose and crumbling in places. Vertical striations were present but not pronounced. The nail of the large toe on the left foot was especially affected with a chalky white involvement of approximately one-third of the nail, extending to the right lateral margin (Fig. 1).

Scrapings and cultures were made from this toenail. Filaments, spores and conidiophores were identified in the scrapings as belonging to an *Aspergillus*. Cultures developed many small cononies of a fungus which was identified as *A. terreus* Thom.

MYCOLOGY

When first seen on January 30, 1948 the nail of the large toe on the left foot appeared chalky white in color, simulating a leukonychia trichophytica. Scrap-



FIG. 1. ONYCHOMYCOSIS OF THE TOENAIL OF THE LEFT FOOT SHOWING LEUKONYCHIA

ings and cultures were made of the soft friable material on the under surface of the nail. The scrapings were mounted in 30 per cent potassium hydroxide, heated gently and then observed microscopically. At first, fungi were not visible. After several hours of clearing and when crystals had begun to develop, there were observed opaque areas in the mounts which revealed numerous fine, branching filaments (Fig. 2:1) and masses of spores surrounding conidiophores of the *Aspergillus* type (Fig. 2:2). These structures became more apparent on the following day. On the third day, the scrapings planted on Sabouraud's glucose agar developed hyaline to white filamentous growths which became buff to tan and then light cinnamon color with age. Microscopically, the colonies were growths of an *Aspergillus*.

The patient was seen next on February 27, 1948. The nail had become soft and more brittle as a result of treatment. Cultures and potassium hydroxide mounts were made again from the scrapings on the under surface of the nail. The preparations revealed irregular, somewhat thickened cells in branched

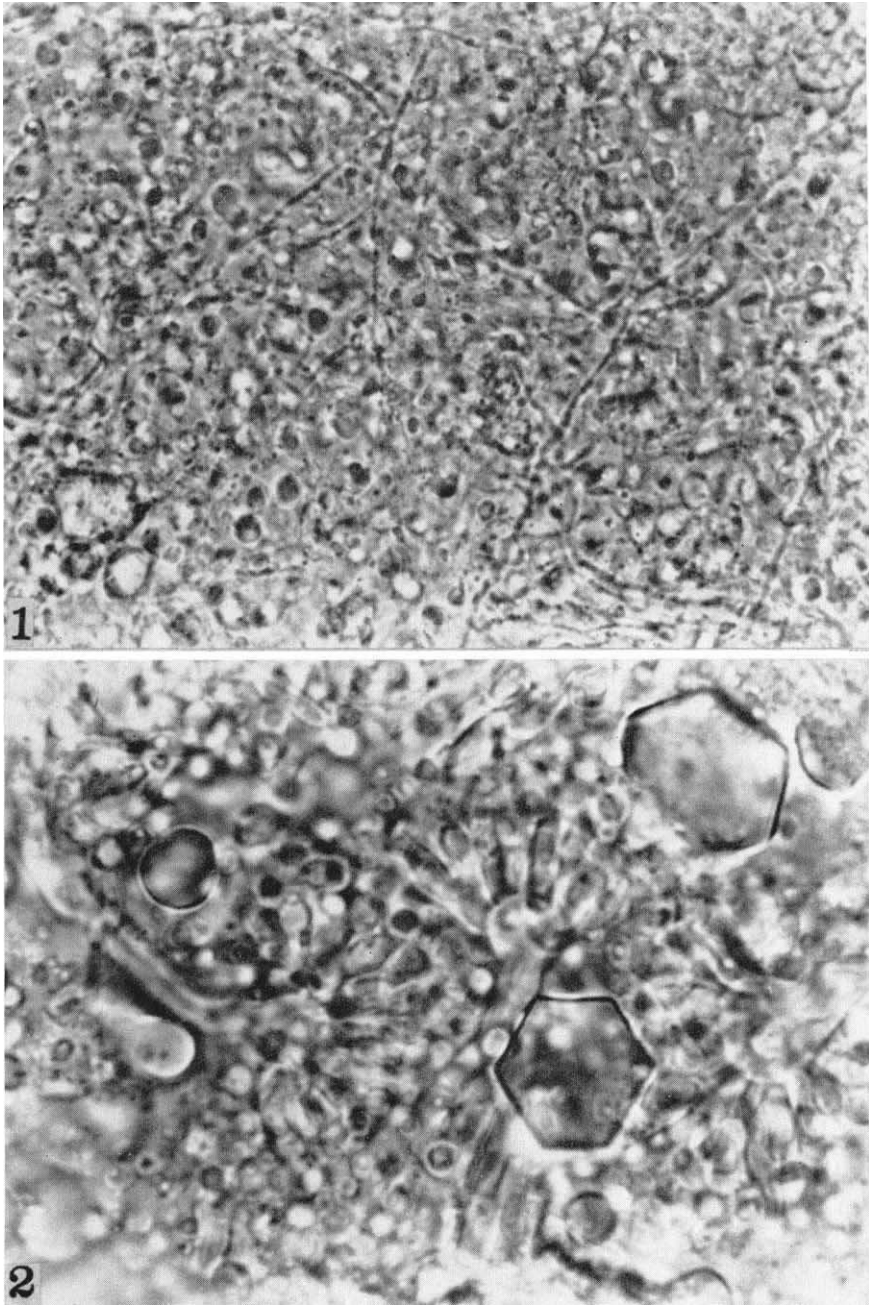


FIG. 2. POTASSIUM HYDROXIDE PREPARATIONS MADE ON JANUARY 30, 1948 OF SCRAPINGS FROM ONYCHOMYCOSIS

1. Mount showing fine, branching filaments. $\times 970$. 2. Mount showing conidia and conidiophores of *Aspergillus*. $\times 1960$.

hyphae. The cells appeared as segments in some instances, broader at one end than at the other (Fig. 3: 1-2). The terminal portions of many of these irregular filaments showed a morphology strongly reminiscent of the favic chandeliers.

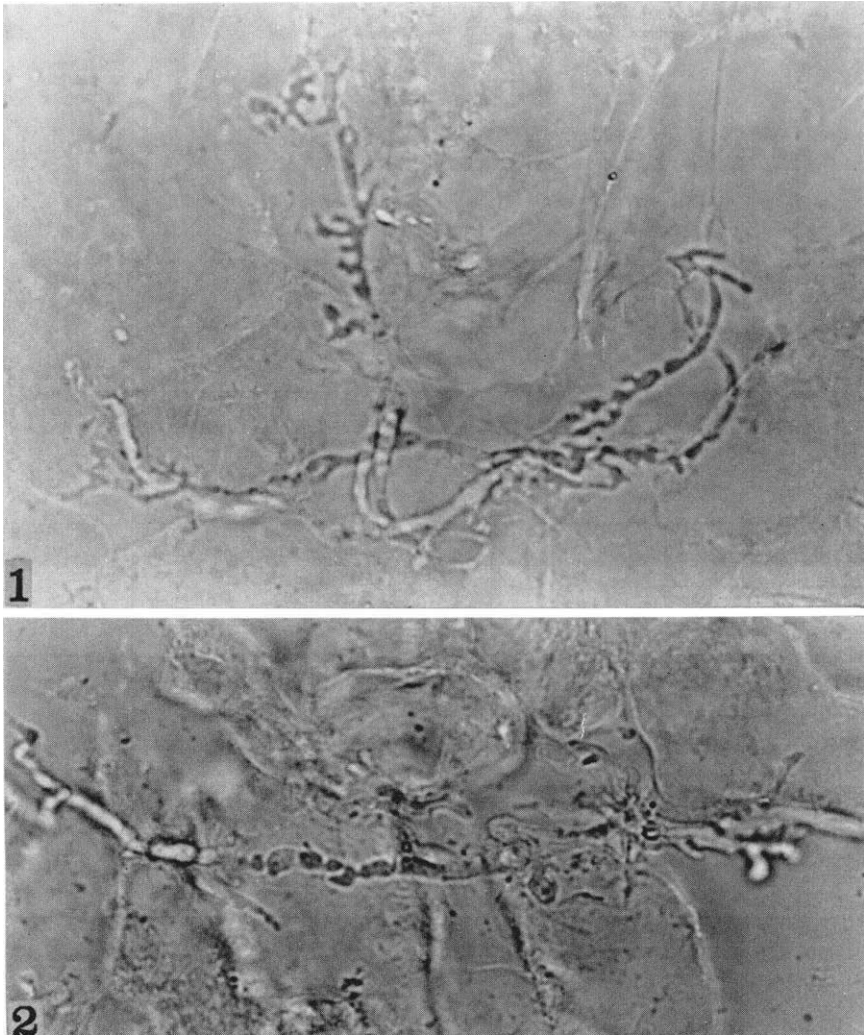


FIG. 3. POTASSIUM HYDROXIDE PREPARATIONS MADE ON FEBRUARY 27, 1948
AFTER TREATMENT

1. Irregular branching filaments showing sclerotic, swollen cells and formations suggestive of favic chandeliers. $\times 1140$. 2. Thick, irregular filaments with sclerotic cells. $\times 1140$.

Conidiophores were not observed in several mounts of the material. A similar Aspergillus was again obtained in the cultures.

On Czapek's agar, the young subcultures showed a pinkish-cinnamon powdery

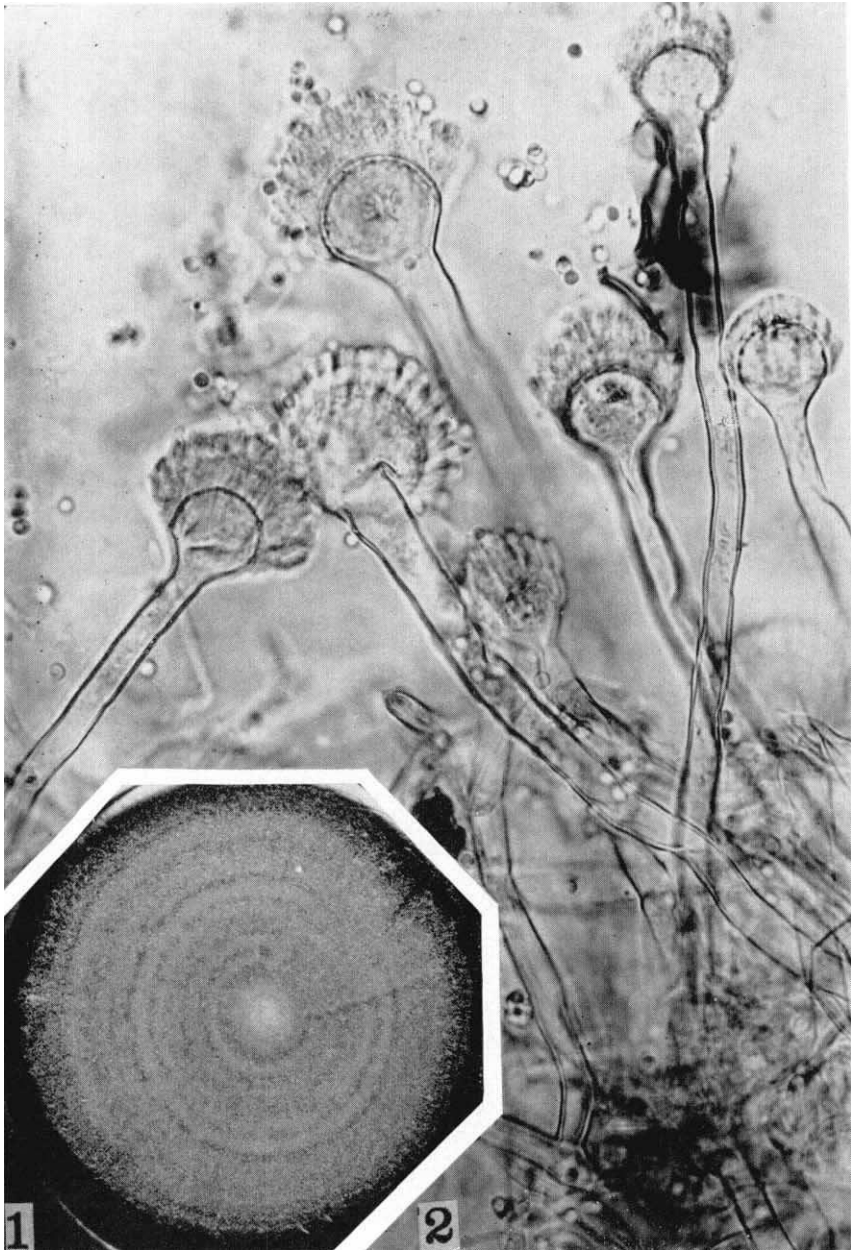


FIG. 4

1. *Aspergillus terreus* grown on Sabouraud's glucose agar, 35 day old culture. Four-fifths actual size; 2. Conidiophores of *A. terreus* grown on Czapek's agar. $\times 860$ this is gal. 1x

surface with a light to sulfur-yellow central area. The reverse of the colony was a light, somewhat dirty yellow color with a pinkish or primrose central area.

The colony attained a diameter of approximately 4 centimeters in 11 days. On Sabouraud's glucose agar, growth was more rapid, attaining a diameter of 6 centimeters in 11 days. The colony color was a slightly darker pinkish-cinnamon. The reverse of the colony was dark yellow with the pigment diffusing into the agar. The reverse of the colony also showed concentric rings of growth.

Older colonies—35 days—had a diameter of approximately 7 centimeters on Czapek's agar and showed a tendency to form a deeper cinnamon color with areas of floccosity. The reverse of the colony showed zones of dirty yellow and others of brown color. On Sabouraud's glucose agar (Fig. 4: 1) the colony covered the Petri dish with a widespread floccose condition over the surface. The growth was cinnamon in color with a dark brown pigmentation of the agar.

Microscopically, the diagnostic structures are the conidiophores (Fig. 4: 2). These spore-bearers measure approximately 150 microns in length, some 100 to 125 microns, and others measure up to approximately 250 microns. They measure 5 to 8 microns in diameter, are somewhat tortuous, with smooth walls, chiefly nonseptate, occasionally with septa, and terminate in a swollen structure, the vesicle. The vesicles measure approximately 15 microns in diameter, some smaller and others up to approximately 24 microns. The vesicles bear on their upper, rounded, dome-like surface closely packed phialides in two series, the primary phialides measuring approximately 7.5 by 2.5 microns and the secondary phialides approximately 6 by 2.5 microns. The spore-bearing heads, when not broken up, formed a compact, columnar arrangement with the conidia in long chains. The conidia are smooth, chiefly globose or spherical to ellipsoid, measuring approximately 2.5 microns in diameter. Cleistothecia or ascocarps were not observed in the cultures. An examination of the floccose growth on Sabouraud's glucose agar revealed intertwined masses of hyphae described as "rope-like". In summary, the gross and microscopic characteristics of the fungus grown on Czapek's and Sabouraud's glucose agars are compatible with those of *Aspergillus terreus* Thom.

DISCUSSION

Onychomycosis caused by *Epidermophyton floccosum*, the various fungi of *Trichophyton*, *Achorion* (*Trichophyton*) and *Syringospora* (*Monilia*, *Candida*) present numerous characteristics depending upon the particular organism involved. In general, the infectious process may begin laterally, at the distal or at the proximal end. The nail may become lusterless and discolored, producing a yellowish, whitish-yellow or brownish color and rarely a leukonychia. Pitting and the formation of striations invariably becomes evident and these are usually accompanied by thickening, more pronounced with *Syringospora* infections. In some instances the nail plate becomes separated from the underlying tissue, is raised, thin and brittle. The nails develop a brittleness and friability. This is especially pronounced in the toenails. Invariably there is an accompanying accumulation of a soft caseous material underneath the free margins of the nails and there may result a hardened, sponge-like formation. The fungi may often

be best demonstrated in the cheesy substance. Involvement of the paronychia tissue is not common except in those cases caused by yeast-like organisms.

Nails affected by the so-called weeds of mycology may show many of the characteristics just described. In those cases resulting from an infection with an *Aspergillus*, Bereston and Waring (10) have set down several criteria to characterize aspergillosis of the nails. These include "thickening, brittleness, greenish or yellowish discoloration, vertical striations and crumbling of the distal portion of the infected nail". The case presented here had some thickening, brittleness, crumbling of the distal portion of the nail and striations which were not pronounced. Instead of the greenish or yellowish discoloration, there was a leukonychia resembling leukonychia trichophytica.

To definitely establish a diagnosis of aspergillosis of the nails, one should not depend entirely on the clinical features which by themselves may be misleading. Certainly, the present case would fit in clinically more with a *Trichophyton* rather than an *Aspergillus* infection. The ultimate proof of the diagnosis should, we feel, depend upon the demonstration of the fungus in samples of the nail, usually in the friable or cheesy material just beneath the nail plate at the free margin. In such instances one should be able to find either the characteristic conidia, conidiophores and filaments in the untreated case or the irregular, thickened hyphae in the treated case.

It is generally agreed that the treatment of onychomycosis is not very successful. Roentgen ray therapy is palliative at best. Some success has been obtained with the long continued use of bichloride of mercury (1:1,000) in water as soaks. Alcoholic mercury lotion in the same dilution has proven better in some instances. Iodine crystals (2 per cent) in alcohol or benzene, various soaks and numerous commercial preparations have also been used but in no case can a single remedy be used effectively without the adjunct either of other preparations or physical means for combating the infection. Avulsion of the infected nail has been done in those cases where *Trichophyton purpureum* (*T. rubrum*) has been the agent. Although this produced an apparent clinical cure, the infection again became evident in most instances when the nail finally grew out, in spite of the continued use of fungicides following avulsion. The patient presented here used a solution containing bichloride of mercury (1:500), resorcin (5 per cent) in ethyl alcohol (70 per cent) for his nail infection and a similar lotion with the bichloride of mercury in a dilution of 1:1,000 for his skin lesions. When last seen in March, 1948, the skin lesions and the nail infection had improved considerably.

SUMMARY

A case of onychomycosis is presented in which the etiologic agent was *Aspergillus terreus* Thom. The patient had skin lesions which were not proven to be due to this fungus, but were possibly those of seborrheic dermatitis. The fungus was demonstrated in potassium hydroxide preparations of the toenail and was grown in culture. The infected nail resembled tinea unguium, particularly leukonychia trichophytica. The known species of *Aspergillus* causing ony-

chomycosis have been listed. It is apparent that many species of *Aspergillus* may cause onychomycosis.

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