

STATE OF THE ART IN DIAGNOSIS AND TREATMENT OF CUTANEOUS MYCOSES

G. Ginter and E. Rieger

ABSTRACT

The constant increase in the number and spectrum of fungal infections in dermatology is due to improved recognition as well as to an increasing population of susceptible patients. This rise in prevalence calls for improved methods of diagnosis and management. As with other microbial infections, the diagnosis of fungal disease is based on a combination of clinical observation and laboratory investigations. Laboratory methods for the diagnosis of fungal infection continue to be updated, but depend mostly on microscopic examination and cultivation of the fungus. The classification and identification of fungi is based on their morphology rather than on the nutritional and biochemical differences that are of such importance in the classification of bacteria. The development of new antifungal drugs such as the triazoles and allylamines has improved the treatment of many forms of fungal infections although problems remain. This paper reviews current laboratory diagnosis and management of fungal infections found in Europe.

KEY WORDS

dermatomycoses, diagnostic procedures, management

1. FUNDAMENTALS

1.1. THE NATURE OF FUNGI

Among the 50.000 to 250.000 known species of fungi fewer than 200 have been associated with human disease. Fungi are eukaryotic organisms that have definite cell walls and are devoid of chlorophyll. Fungi may reproduce sexually or asexually; most species are capable of both. Their nutritional requirements are simple and readily available in the dead organic material of their usual habitats.

Anatomy of Fungi: Fungi appear in two basic forms, **yeasts** and **molds**. Yeasts are typically single, small, oval cells that reproduce by simple budding. Mold colonies are made up of

filamentous strands called **hyphae**. A mass of hyphae is called a **mycelium**. Vegetative hyphae make up the body of the mold colony or **thallus**. Fertile hyphae are directed upward to form **aerial hyphae** (support the reproductive structures that produce sexual spores or asexual conidia).

Fungi **pathogenic** to humans are Fungi imperfecti (Deuteromyceta; sexual reproduction is unknown).

Mycosis is any injury to an organism by the growth of fungi into its tissue (prerequisite: predisposing factors, impairment of host defense mechanisms).

Law of specificity is invalid with respect to fungi (i.e. one type of fungus may cause various clinical pictures and vice versa)!

1.2. DYM (DHS)

DYM (DHS) System (Categorization by *Rieth*, early 1960s) is a clinically useful scheme:

D = Dermatophytes

Y = Yeasts

M = Molds

1.2.1. Dermatophytes (“Ringworm Fungi”)

Infections of the skin, hair and nails.

Classification: 3 anamorphic (asexual) genera of dermatophytes: (Table 1)

The diseases caused by these fungi are grouped under the general term **dermatophytosis = tinea**.

1.2.2. Yeasts

These are “opportunistic” or “facultative” pathogens, which convert from saprophytic to parasitic form in a predisposed host.

AXIOM: No form of yeast is physiological on or in humans. However, saprophytic forms may be present on mucous membranes, especially those of the gastrointestinal tract, *without pathological significance* (commensals). (Perhaps significant in developing immunity?)

Clinical Presentation:

Cutaneous Candidosis	(especially intertriginous areas; hair follicles; nail matrix, nail fold, nail plate)
Mucosal Candidosis	(oral cavity, esophagus, gastrointestinal tract, vagina)
Systemic Candidosis Complication	(internal organs) of pre-existing dermatoses

Classification: >60 genera (>500 species).
Clinically most important yeasts: (Table 2)

Diagnostic procedure: Biochemical differentiation [1]
(Exception: *Candida albicans* - on rice agar)

Table 1. Classification of dermatophytes.

Genus	Species
I. <i>Trichophyton</i> (worldwide approx. 30 species)	<i>rubrum</i> (most common agent) <i>mentagrophytes</i> (2nd most common agent) <i>verrucosum</i>
II. <i>Epidermophyton</i> (1 species)	<i>floccosum</i>
III. <i>Microsporum</i> (worldwide approx. 15 species)	<i>canis</i> <i>gypseum</i>

Table 2. Clinically important yeasts

Genus	Species
I. <i>Candida</i> (approx. 8 out of 100 species are facultative human pathogens)	<i>albicans</i> (most common) <i>tropicalis</i> <i>pseudotropicalis</i> <i>stellatoidea</i> <i>krusei</i> <i>parapsilosis</i> <i>guilliermondii</i> <i>glabrata</i>
II. <i>Trichosporon</i>	<i>cutaneum</i>
III. <i>Cryptococcus</i>	<i>neoformans</i>

Definition:

- Moniliasis: consigned to medical history
- Candidosis: infection due to organisms belonging to the genus *Candida*
- Candidiasis: = candidosis
- Thrush: oral candidosis

1.2.3. Molds or NDF (non dermatophytic filamentous fungi)

“Facultative” pathogens causing “opportunistic” infections in predisposed or compromised patients (convert from a saprophyte to a parasite).

Affected sites: predominantly internal organs (especially the lungs), furthermore the paranasal sinuses, rarely the skin (for example alternariosis).

Sporadic occurrence in our geographic region [Central Europe] (for example complicating a pre-existing eczema [eczema of the auditory canal] or an old burn). May act as a potent allergen (inhalatory, alimentary).

Habitat: Common soil inhabitants, dust, decomposing organic matter; outside air (“airborne fungi”); traumatic implantation of spores; nosocomial outbreaks in hospital wards (contaminated ventilation system).

Medically important molds:

- *Aspergillus* (A. fumigatus)
(A. flavus)
(A. niger)
- *Penicillium* (P. marneffeii)
- *Mucor*
- *Absidia*
- *Rhizopus*

1.3. LABORATORY DIAGNOSIS OF FUNGAL INFECTION

1.3.1. Collection of Specimens:

- skin scales (outwards from the margin of the lesion)
- hair roots, contents of plugged follicles
- nail specimens (discoloured, dystrophic or brittle parts)
- smears: sputum, oral cavity, vagina, cervix, urethra, etc.

Techniques for collection of specimens:

- Clean cutaneous and scalp lesions and nails with 70% alcohol prior to sampling.
- *Collecting specimens:*
Skin scales: use sterile instruments (autoclaved): curette, blunt scalpel, forceps, edge of a glass microscope slide.

Nail specimens: use a raspatory (bone scraper), a scalpel or scissors (deep scrapings from under the leading edge of the nail)

Hair roots: use epilation forceps; hairbrush sampling: scalp is brushed with a plastic hairbrush or scalp massage pad which is then pressed into the surface of an agar plate (sterilize in 1% chlorhexidine for 1 h, rinse in sterile water and dry before reuse).

Smears (oral cavity, vagina): prepare a slide smear using a sterile cotton swab or platinum wire loop or by scraping with a wooden spatula.

Transport of specimens:

Skin scales, nails, hair roots: in sterile glass or plastic containers; folded squares of black paper.

Smear swabs: in tubes containing liquid culture medium, inoculation onto solid culture medium.

Biopsy specimens: culture (without fixation in formaldehyde).

1.3.2. Direct Examination

Technique for immediate identification of fungal elements in skin scales, nail and hair specimens.

Processing:

- Immerse the specimen in a drop of 10% to 15% potassium hydroxide (KOH) solution (or 10% tetramethylammonium hydroxide) on a glass microscope slide for a few minutes (keratin and debris more or less dissolve, while the fungal elements remain intact and stand out from the background).
- Place a coverslip over the preparation.
- Gentle heating over an open flame reduces the time needed for the specimen to clear.
- Microscopic examination with 100-400x magnification: hyphae, mycelium, spores. Adding a drop of lactophenol with cotton blue to the preparation heightens contrast and is helpful in instructing the inexperienced.
- Stain dried slide smears and aspirations using Gram stain or methylene blue stain [1].

NOTE:

- Determination of genus and species of filamentous and yeast like fungi is impossible or not possible with certainty.
- Negative results with this technique do not rule out fungal infection!

1.3.3. Culture

Culture methods are required to determine genus and species of the fungal agent.

Processing:

- Skin, nail and hair samples can be minced to increase the surface area of the specimen. The inoculum should be spread over the surface of a tubed or bottled agar slant or streaked for isolation on plated media.

Using only gentle pressure, inoculate specimen onto culture medium in a petri dish or test tube in approximately 15 to 20 places. Use only sterile wire loops, mycological hooks, or cotton swabs. Avoid air drafts, and never completely uncover plates.

If plates are used, the lids must be sealed with either air-permeable tape or commercially available products to prevent accidental exposure to mold spores and conidia and cross-contamination.

Media in common use [2]:

- *Kimmig agar*
- *Sabouraud's dextrose agar (SAB)*: contains no added antibiotics (will support the growth of aerobic actinomycetes as well as fungi).
- *Sabouraud-BHI (SABHI) agar*: contains no added antibiotics, is more nutritional than regular SAB
- *Sabouraud's agar with antibiotics*: contains various combinations of chloramphenicol, cycloheximide, gentamicin, penicillin, or streptomycin to discourage or prevent bacterial growth

Time considerations:

- D: at least 2-3 weeks (up to 7 weeks)
- Y: 1-2 days
- M: days to weeks

Cultures should be incubated for at least four weeks before being reported as negative.

Temperature considerations:

- D: standard incubation temperature is 25° to 30°C
- Y: room temperature or 37°C incubation
- M: isolation is usually challenged at 37° and 42°C

Techniques for Examining Cultures: macroscopically and microscopically

Tease preparation culture examination:

Dig out a small portion of the mold colony with a teasing needle, taking as little agar as possible. Place the portion in a drop of lactophenol (with or without cotton blue) on a clean glass slide. Using two teasing needles, break up the mycelial mat. Place a coverslip over the preparation and examine it under the microscope for conidia, conidiogenous structures, septation, pigment, and unique morphologic features.

Disposal of examined cultures according to regulations (infectious waste).

1.3.4. Wood's Light

Wood's light is particularly useful for detection of inconspicuous scalp lesions, pityriasis versicolor, and erythrasma. This portable source is a quartz lamp emitting low frequency UV light at a wavelength of 365 nm.

Fluorescence of hair in different colors is a feature of:

- *Microsporum tinea capitis*: light bright green
- *Erythrasma*: coral red (brick red)
- *Pityriasis versicolor*: yellow to golden

1.3.5. Calcofluor White

Calcofluor is a fluorochrome with an affinity for chitin and cellulose. When added to KOH preparations, it is taken up by fungal elements, which in turn fluoresce blue-white or green when viewed with a fluorescent microscope. Yeast cells, pseudohyphae, and hyphae display a chalk-white or brilliant apple-green fluorescence, depending on the filters used [3].

Advantage: False negative diagnoses, which may result from a paucity of fungal elements in the specimen, are ruled out.

1.3.6. Histopathology

Histopathology provides the most valuable information when it reveals the presence of the organism itself. Some fungi can be identified in sections stained routinely with hematoxylin and eosin, others can only be seen when special stains are used [1,4,5]:

Reagents to demonstrate fungal elements in tissue:

- *Periodic acid-Schiff's stain (PAS)*: fungal elements appear pink
- *Methenamine-silver stain according to Grocott-Gomori*: fungal elements appear brown or black [6]

2. DIAGNOSIS AND MANAGEMENT

2.1. DERMATOPHYTOSIS (Tinea, Ringworm, Dermatophytosis)

The term dermatophytosis is used to describe infections of the skin, hair and nails due to a group of related filamentous fungi, the dermatophytes, which are also known as the ringworm fungi. The clinical presentation of these infections depends on several factors including: the site of infection, the immunological response of the host and the species of infecting fungus. In most forms of dermatophytosis, the fungus is confined to the superficial stratum corneum, nails and hair. However, deeper infection involving the dermis can occur, as in kerion, and this can result in the formation of suppurative lesions.

It is useful, for epidemiologic reasons, to classify dermatophytes according to their natural habitats: Anthropophilic species parasitize humans almost exclusively, while zoophilic species prefer lower animals, and geophilic species are soil-dwelling saprophytes. Member of all three groups are capable of producing human disease.

Diagnosis:

Direct examination:

- branching, septated filaments (mesh of hyphae = mycelium)
- the recognition of fungal hyphae and/or arthrospores during microscopic examination of clinical material gives no indication as to the species of dermatophyte involved.
- differentiation of dermatophytes from yeasts or molds is not possible by microscopic examination of the native specimen alone; culture is necessary.

Culture:

Colony morphology: The surface is a light color (whitish-yellow or beige), never gray, green, black, or dark brown. The color is more intense on the reverse (possibly pigment diffusion out from the colony). Development of downy-to-fluffy colonies or of heaped, glabrous, button-like colonies; never development of creamy colonies.

Technique for examining cultures has been described (see 1.3.3.).

2.1.1. Tinea corporis

Definition: Dermatophyte infections of the trunk, legs and arms, but excluding the groin, hands and feet.

General considerations and incidence:

Frequency: approximately 7%

Age: children and adults

Gender: male and female

Source: humans and animals. Infection with anthropophilic species (*T. rubrum*, *E. floccosum*) often follows autoinoculation from another infected body site, such as the feet. Tinea corporis due to zoophilic species (*M. canis*, *T. verrucosum*) commonly occurs following contact with infected household pets or farm animals. Human-to-human spread of infection with geophilic or zoophilic species is unusual.

Course: subacute-chronic

Duration: weeks-months-years!

Diagnosis:

Laboratory:

Native specimen: Material should be collected from the raised border of the lesion; in case of vesicles: the entire top should be submitted. Branching hyphae

Culture: Species of fungus (source of infection, appropriate treatment)

Causative agents:

- *Trichophyton rubrum* (anthropophilic)
- *Trichophyton mentagrophytes* (anthropophilic or zoophilic)
- *Trichophyton verrucosum* (zoophilic)
- *Epidermophyton floccosum* (anthropophilic)
- *Microsporum canis* (zoophilic)

Differential diagnosis:

- Nummular eczema
- Seborrheic dermatitis
- Erythema multiforme
- Lupus erythematosus
- Pityriasis rosea
- Pityriasis versicolor
- Psoriasis

Management:

a) *adjuvant measures:* thoroughly boil or disinfect laundry

b) *topical antifungal agents:* treatment of choice for localized lesions

- *imidazoles*

- *naftifine* or *terbinafine* 1%-cream once daily for 1 (-2) weeks [1,2]

- *amorolfine* cream once daily for 3 (-6) weeks [3]

NOTE: Treatment should be continued for at least 1 week after the lesions have cleared, medication should be applied at least 3 cm beyond the advancing margin of the lesion.

c) *systemic antifungal agents:*

In the case of multilocal or extensive spread, chronicity, recurrence or lack of compliance.

- *itraconazole:* 100 mg daily for 15 days [4,9]

- *terbinafine:* 250 mg daily for 2 (to 4) weeks [5,6]

- *fluconazole:* 150 mg once a week for 1-2 weeks [7], or 50 mg daily for 2-4 weeks [8]

- *griseofulvin:* 500 mg daily for 10 days or longer [9]

NOTE: Spontaneous recovery possible! Extensive lesions or non-response are possible in immunodeficient patients (e.g. HIV infection).

2.1.2. Tinea inguinalis

Definition: Dermatophyte infections of the groin and pubic region. Tinea of the groin is a highly contagious condition (minor epidemics in schools and other communities. The infection is usually transmitted via contaminated towels or the floors of bath-rooms, showers, or hotel bedrooms etc. (occurs usually between the ages of 18 and 60).

Epidemiology:

- Prevalence:* approx. 5%
Age: adolescents, adults, old age
Gender: more prevalent in men (males:females = 3:1)
Source: humans (commonly acquired from another infected area of the same individual = autoinoculation)
Course: (subacute) - chronic (seasonal improvement)
Duration: weeks - months - years

Diagnosis:

- Laboratory:* Native specimen: scales from lesion periphery. Branching hyphae
Culture: species of fungus

Etiology:

- *Trichophyton rubrum* (most often)
- *Epidermophyton floccosum* (often)
- *Trichophyton mentagrophytes*
- *Trichophyton verrucosum*

Differential diagnosis:

- Erythrasma
- Bacterial and candidal intertrigo
- Psoriasis
- Seborrheic dermatitis
- Benign familial chronic pemphigus

Management:

a) *adjuvant measures:* boil underwear

b) *topical antifungal agents:*

- imidazoles

NOTE: To prevent relapse, treatment should be continued for at least 2 weeks after disappearance of all symptoms and signs of infection.

- *naftifine* or *terbinafine* 1% cream (in D-infections!) 1 (-2) weeks [1,2]
- *amorolfine* cream once daily for 3 weeks [3]

c) *systemic antifungal agents:* if compliance is lacking or in case of extensive infection (involving the buttocks or anterior or posterior aspects of the thighs) or folliculitis.

- *itraconazole* 100 mg daily for 15 days [4,9]
- *terbinafine* 250 mg daily for 2 weeks [5,6]
- *fluconazole* 150 mg once a week for 1-2 weeks [7], or 50 mg daily for 2-4 weeks [8]

To prevent reinfection following treatment the patient should be advised to dry the groin thoroughly after bathing and to use separate towels to dry the groin and the rest of the body. The feet should be examined and treated if tinea pedis is present. Occlusive or synthetic garments should be avoided.

If the patient is obese, weight loss may be of benefit by reducing chafing and sweating.

2.1.3. Tinea capitis

Definition: Dermatophyte infections of the scalp and hair. Worldwide in distribution (most prevalent in Africa, Asia and Southern and Eastern Europe). Improved standards of hygiene and prompt eradication of sporadic infection have led to a marked decline in the incidence of tinea capitis in Western Europe and North America.

Clinical manifestations of tinea capitis are varied:

- mild scaling lesions: similar to seborrheic dermatitis
- widespread alopecia
- highly inflammatory suppurating lesion: kerion (infection with a zoophilic dermatophyte)

Epidemiology:

- Age:* children > adults
Gender: anthropophilic *Microsporum* species: males > females (6-10 years of age)
anthropophilic *Trichophyton* species: male children (under the age of 12)
Source: cattle
Course: mild to highly inflammatory
Duration: weeks to months (spontaneous remission possible after months)

Diagnosis:

Laboratory:

Native specimen:

skin scales (hyphae and arthrospores), contents of plugged follicles

hair roots: - ectothrix, endothrix, or mixed infection (except for favus, the distal portion of infected hair seldom contains any fungus; clipped hairs without roots are unsuitable for mycological investigation).

- endothrix (infected hairs are filled with arthrospores): *T. tonsurans*, *T. violaceum* (not fluorescent)
- ectothrix (the hair surface is covered with a dense mass of small (2-3 mm diameter) arthrospores): *M. canis*, *M. audouinii*, *M. ferrugineum* (brilliant green fluorescence), *T. schoenleinii* (pale dull green fluorescence)

Culture: species of fungus (NOTE: *Trichophyton verrucosum*: slow growth!)

Etiology: in Western Europe predominantly zoophilic dermatophytes!

- *Trichophyton verrucosum* (zoophilic; cattle, less often horses; 60%)

- Trichophyton mentagrophytes (var. granulosa) (zoophilic; guinea pigs, mice, hamsters; 30%)
- Trichophyton rubrum (anthropophilic; rare)
- Epidermophyton floccosum (anthropophilic)
- Microsporum canis (zoophilic; Western Europe)
- Trichophyton violaceum (anthropophilic; eastern and southern Europe, North Africa)
- Trichophyton tonsurans (anthropophilic; North America)
- Trichophyton schoenleinii (anthropophilic; sole etiological agent of favus)

Differential Diagnosis:

- Seborrheic dermatitis
- Pyoderma
- Furunculosis
- Bacterial folliculitis
- Hair loss: alopecia areata, discoid lupus erythematosus
- "dissecting cellulitis"
- Candida infection (heroin addicts)

NOTE the importance of native specimen examination to rule out a mycotic infection!

Management:

- a) adjuvant measures:
 - cut hair short!
 - antiseptic pretreatment is recommended!
 - systemic antibacterial antibiotics are usually not necessary!
 - a protective dressing is recommended initially!

NOTE:

Trichophyton infection in children: no physical exercise; patients should be kept away from school and kindergarten as long as the native specimen findings remain positive.

Anthropophilic agent: Screen all family members; ketoconazol shampoo is recommended for all family members for 1 week.

Zoophilic agent: Provide information as to the source of the infection, treat infected animals.

b) topical antifungal agents:

- wash hair with ketoconazole shampoo
- initially: polyvinylpyrrolidone-iodine complex gel
- later: naftifine gel and Sofratüill (TM) or Bactigras (TM) and protective dressing

c) systemic antifungal agents:

Mycological confirmation of the clinical diagnosis is essential before treatment is commenced. Mycological tests should be repeated 1 month after starting treatment and again before discontinuing the drug.

Children:

- *griseofulvin* 10-20 mg/kg body weight daily for several weeks (given after meal until the native specimen findings become negative; 2-3 months duration of treatment is usually

required)

- *terbinafine* 250 mg daily for 4 weeks

Children: dosage according to body weight (BW):

10-20 kg BW: 62,5 mg/day

20-40 kg BW: 125 mg/day

over 40 kg BW: 250 mg/day

(employ only in case of griseofulvin resistance, or if griseofulvin is not available)

- *itraconazole* 100 mg daily for 2-4 weeks (given after meal) [10,11]

Children: itraconazole suspension 5 mg/kg BW daily - currently (1995) in process of approval. Employ only in case of griseofulvin resistance, or if griseofulvin is not available.

- *fluconazole* (no dosage recommended 1995)

Microsporum (Gray Patch) Tinea capitis

Definition: The zoophilic *Microsporum canis* is seldom responsible for more than minor outbreaks of human infection. Household pets, such as dogs and cats, are a common source of infection, but feral cats are another prolific source of *M. canis*. *Tinea capitis* due to anthropophilic *Microsporum audouinii* is a contagious disease endemic in many countries. It is primarily a disease of children females, and most prevalent between 6 and 10 years of age. The disease seldom persists beyond the age of 16. Large outbreaks often occur in schools or other places where children are congregated.

Epidemiology:

Prevalence: epidemic and endemic by anthropophilic *M. audouinii*, endemic by *M. canis*

Age: children (up to age 14)

Gender: in males more common than in females

Source: cats (especially young and stray cats)

Course: subinflammatory

Duration: weeks - months - years (spontaneous remission in puberty at latest)

Diagnosis:

Laboratory:

Native specimen: see *Tinea capitis*

Culture: species of fungus (*M. canis*: rapid growth in a few days!)

Etiology:

- *Microsporum canis* (zoophilic)

- *Microsporum gypseum* (geophilic; infrequent)

- *Microsporum audouinii* (anthropophilic; rare; endemic in parts of Africa)

Management:

As in tinea capitis

NOTE:

-highly infectious in children - patients should be kept away from kindergarten and school until the direct microscopic examination becomes negative!

- protective dressing (cap) is recommended

- higher griseofulvin dosage in *Microsporum tinea capitis* than in *Trichophyton tinea capitis*

children: 15-25 mg/kg BW daily griseofulvin (given after meal)

duration of treatment: weeks to 2 months (until native specimen microscopy from several sites becomes negative)

- veterinary examination of cats and possibly other pets

- therapeutic resistance to griseofulvin is a possible, but rare pitfall - oral treatment with fluconazole or itraconazole is recommended [10,11]!

2.1.4. Tinea barbae (*Kerion celsi*)

Definition: Dermatophyte infections of the beard.

Epidemiology:

Age: adults (especially agricultural and slaughterhouse workers, butchers, veterinarians)

Gender: males

Source: farm, laboratory and zoo animals; hay, chaff (straw) (usually contaminated by infected mice)

Course: inflammatory

Duration: weeks - months

Diagnosis:

Laboratory: as in *Tinea capitis*!

Etiology:

- *Trichophyton verrucosum*

- *Trichophyton mentagrophytes* var. *mentagrophytes* sive *granulosa*

- *Trichophyton rubrum* (rare)

Management: as in *Tinea capitis*

2.1.5. Tinea manuum

Definition: predominantly chronic dermatophyte infection, usually unilateral, or of both hands.

Differentiate between infections of the (hairless) palm and interdigital spaces, and those of the (pilose) back of the hand.

Palmar infection: two clinical forms:

- the dyshidrotic or eczematoid form

- the hyperkeratotic form

Hand infection may be acquired as a result of contact with another person, with an animal, or with soil, either through direct contact, or via a contaminated object such as a towel or gardening tool. Autoinoculation from another site of infection can also occur. Manual work, profuse sweating and existing inflammatory conditions (such as contact eczema) are predisposing factors.

Epidemiology:

Prevalence: approx. 11%; worldwide

Age: adults

Gender: male and female

Source: humans

Course: acute (dyshidrotic form), subacute or chronic (hyperkeratotic form)

Duration: months - years (lifelong)

Diagnosis:

Laboratory:

Native specimen: skin scales, vesicle tops and contents.

Branching hyphae

Culture: species of fungus

Histopathology (PAS stain) may be necessary

NOTE:- a false negative result is possible if treatment has already been initiated: repeat direct microscopic examination after discontinuation!

- concurrent onychomycosis may be a constant source of reinfection, therefore treatment of *tinea unguium* should be considered!

Etiology:

- *Trichophyton rubrum* (80-90%)

- *Trichophyton mentagrophytes* var. *interdigitale*

- *Epidermophyton floccosum*

- *Microsporum canis*

- *Microsporum gypseum*

- *Trichophyton verrucosum*

Differential Diagnosis:

- Candidosis

- Inverse psoriasis (palmaris) (usually bilateral)

- Eczema (usually bilateral)

- Isolated atopic dermatitis of the hands

- Dyshidrotic eruptions (is usually bilateral or even symmetrical)

Management:

a) *topical antifungal agents:* Treatment for several weeks is usually recommended and should be continued for 3-4 weeks once the clinical signs and symptoms have cleared.

- imidazoles
- *naftifine* or *terbinafine* 1% cream 1-2x daily for several weeks
- *amorolfine* cream once daily for 3 (to 6) weeks
- *colorless Castellani solution* if necessary

b) systemic antifungal agents:

- *itraconazole* 100 mg daily for 4 weeks [4,9]
- *terbinafine* 250 mg daily for 2 (to 6) weeks [12]
- *fluconazole* 150 mg once a week for 1 or 2 weeks; or 50 mg/day for 2-4 weeks
- *griseofulvin*, if necessary

2.1.6. Tinea pedis (Tinea of the soles, “athlete’s foot”, epidermomycosis of the “moccasin type”)

Definition: Dermatophyte infections of the feet (interdigital spaces often involved, chronic diffuse desquamation can affect the entire sole).

Three clinical forms may be distinguished:

- acute or chronic interdigital infection
- chronic hyperkeratotic (moccasin or dry type) infection
- vesicular (inflammatory) infection

Tinea pedis is a very widespread condition that appears to be increasing in prevalence. It often begins in late childhood or young adult life and is most common between the ages of 20 and 50. Men are more frequently affected than women.

The infection is usually acquired by walking barefoot on contaminated floors. Hyphae and arthrospores of the causal dermatophytes can survive for long periods (>12 months) in human skin scales. Excessive sweating and occlusive footwear are factors that favour the development of tinea pedis.

Epidemiology:

Prevalence: 15-30% of the population in our geographic region (Central Europe), most common infectious disease of humanity worldwide. It does not occur in aboriginal people wearing no occlusive footwear!

Age: adults

Gender: more prevalent in men

Source: humans

Course: chronic

Duration: weeks - months - years - decades

Often recurrence!

Concomitant mold, candidal and/or bacterial infection is relatively common in patients with tinea pedis = secondary infection - inflammation and further maceration).

Diagnosis:

Laboratory:

Native specimen: skin scales from lesion periphery. Branching hyphae, arthrospores (sometimes appearance of characteristic yeast cells: *C. albicans*)
Culture: species of fungus

Etiology:

- *Trichophyton rubrum* (approx. 70%; chronic tinea pedis)
- *Trichophyton mentagrophytes* var. *interdigitale* (approx. 28%; more inflammatory lesions)
- *Epidermophyton floccosum* (approx. 2%)

Differential Diagnosis:

- *Candida albicans* infection (mild interdigital erosion and maceration; diabetes mellitus/hot climates)
- Gram-negative foot infection: bacterial infection (more inflammation, erosion of the skin)
- *Erythrasma* (*Corynebacterium minutissimum*)
- Inverse psoriasis
- Andrew’s bacterid
- Keratosis palmoplantaris
- Eczema, contact dermatitis

Management:

a) adjuvant measures:

- daily bathing of the feet followed by careful drying of the toes and interdigital spaces
- boil socks and stockings or wash with “myco-ex”
- wear air permeable (leather) footwear (open-toed shoes and sandals) and soft absorbent socks
- change shoes and socks frequently
- disinfect shoes
- use antifungal foot powder on the feet and inside footwear

b) topical antifungal agents:

- imidazoles
- *naftifine* or *terbinafine* 1% cream, once daily for at least 1 to 2 weeks [13,14,15,1]
- *amorolfine* cream once daily for 3 (-6) weeks [3]

c) systemic antifungal agents: If the disease is extensive, involving the sole and dorsum of the foot, or there is acute inflammation:

- *itraconazole* 100 mg daily

Tinea pedis / interdigital infection: for 2 weeks [9,16]

Tinea pedis / chronic hyperkeratotic infection (moccasin or dry type): for 4 weeks [17,4] (or 400 mg daily for 1 week)

- *terbinafine* 250 mg daily for 2 (-6) weeks (both interdigital and sole) [17,16,12]

- *fluconazole* 150 mg once a week up to 6 weeks [7], or 50 mg daily for 2-6 weeks [8]

NOTE:

- laboratory tests should be performed in any patient with foot lesions of undetermined origin
- high recurrence rate!

- concomitant onychomycosis is a constant source of reinfection - consider curative treatment to help prevent the infection from spreading!

REFERENCES

General reading:

- Thorne Crissey J, Lang H, Parish LC. Manual of Medical Mycology. London, Edinburgh, Boston, Melbourne, Paris, Berlin, Vienna: Blackwell Scientific Publications, 1995
- Kwon-Chung KJ, Bennett JE. Medical Mycology. Philadelphia, London: Lea & Febiger, 1992
- Richardson MD, Warnock DW. Fungal Infection. Diagnosis and Management. London, Edinburgh, Boston, Melbourne, Paris, Berlin, Vienna: Blackwell Scientific Publications, 1993
- Rippon JW, Fromtling RA. Cutaneous Antifungal Agents. Selected Compounds in Clinical Practice and Development. New York, Basel, Hong Kong: Marcel Dekker, 1993
- International Summit on Cutaneous Antifungal Therapy. October 21-24, 1993. San Francisco. Abstract book
- International Summit on Cutaneous Antifungal Therapy. November 10-13, 1994. Boston. Abstract book

1. Fundamentals:

1. Clark G. Staining Procedures. 3rd ed. Baltimore, Williams & Wilkins 1973.
2. Kwon-Chung KJ, Bennett JE. Medical Mycology. Lea & Febiger, Philadelphia, London 1992; Appendix B: 816-826.
3. Hageage GH Jr., Harrington BJ. Use of calcofluor white in clinical mycology. Lab Med 1984; 15: 109-112.
4. Gridley MF. A stain for fungi in tissue sections. Am J Clin Pathol 1953; 23: 303-307.
5. Luna LG. Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology. 3rd ed. New York, McGraw-Hill, 1968.
6. Grocott RG. A stain for fungi in tissue sections and smears using Gomori's methenamine-silver nitrate technique. Am J Clin Pathol 1995; 25: 975-979.

2. Diagnosis and Management:

2.1. Dermatophytosis (Tinea)

1. Kagawa S. Clinical efficacy of terbinafine in 629 Japanese patients with dermatomycosis. Clin Exp Dermatol 1989; 14: 114-115.

2. Zaias N, Berman B, Cordero CN, Hernandez A, Jacobson C, Millikan L, Rojas R, De la Rosa J, Villars V, Birnbaum JE. Efficacy of a 1-week, once-daily regimen of terbinafine 1% cream in the treatment of tinea cruris and tinea corporis. J Am Acad Dermatol 1993; 29: 646-648.
3. Nolting S, Semig G, Friedrich HK, Dietz M, Reckers-Czaschka R, Bergsträsser M, Zaug M. Vergleich von Amorolfin und Bifonazol bei der Behandlung der Dermatomykosen. Z Hautkr 1993; 68 (Suppl 1): 61-65.
4. Saul A, Bonifaz A. Itraconazole in common dermatophyte infections of the skin: Fixed treatment schedules. J Am Acad Dermatol 1990; 23: 554-558.
5. Del Palacio Hernanz A, Lopez Gomez S, Iglesias Diez L, Gonzalez Lastra F. Clinical evaluation of terbinafine (Lamisil) in dermatophytosis. J Dermatol Treatment 1990; 1 (Suppl 2): 39-40.
6. Tuezuen Y, Kotogyan A, Oguz O. Terbinafine: efficacy and safety in the treatment of dermatophytosis. Int J Dermatol 1992; 31: 720-721.
7. Montero-Gei F, Perera A. Fungal infections in normal hosts. Therapy with Fluconazole for Tinea corporis, cruris and pedis. Clin Infect Dis 1992; 14 (Suppl 1): 77-81.
8. De Cuyper C, Amblard P, Austad J, et al. Noncomparative study of Fluconazole in the treatment of patients with common fungal infections of the skin. Int J Dermatol 1992; 31 (Suppl 2): 17-20.
9. Finzi A, Cilli P. Italian multicentre trial comparing itraconazole with griseofulvin in the treatment of dermatomycoses. Preliminary results. J Eur Acad Dermatol Venereol 1992; 1 (Suppl 1): 15-18.
10. Legendre R, Esola-Macre J. Itraconazole in the treatment of tinea capitis. J Am Acad Dermatol 1990; 23: 559-560.
11. Dhondt A, Cauwenbergh G, De Doncker P. Short oral therapy in difficult- to - treat tinea infections. J Eur Acad Dermatol Venereol 1992; 1 (Suppl 1): 11-14.
12. White JE, Perkins PJ, Evans EGV. Successful 2-week treatment with terbinafine (Lamisil) for moccasin tinea pedis and tinea manuum. Br J Dermatol 1991; 125: 260-262.
13. Evans EGV., Dodman B, Williamson DM, et al. Comparison of terbinafine and clotrimazole in treating tinea pedis. Br Med J 1993; 307: 645-647.

14. Berman B, Ellis C, Leyden J, et al. Efficacy of a 1-week, twice-daily regimen of terbinafine 1% cream in the treatment of interdigital tinea pedis: Result of placebo-controlled, double-blind, multicenter trials. *J Am Acad Dermatol* 1992; 26: 956-960.
15. Evans EGV. A double-blind comparison of 1, 3, 5 and 7 day topical therapy with 1% terbinafine (Lamisil) cream in tinea pedis. *Br J Dermatol* 1992; 127 (Suppl 40): 21.
16. De Keyser P, De Backer M, Massart DL, Westelinck KJ. Two-week oral treatment of tinea pedis, comparing terbinafine (250 mg/day) with itraconazole (100 mg/day): a double-blind, multicentre study. *Br J Dermatol* 1994; 130 (Suppl 43): 22-25.
17. Hay RJ, McGregor JM, Wuite J, Ryatt KS, Ziegler C, Clayton YM. A comparison of 2 weeks of terbinafine 250 mg/day with 4 weeks of itraconazol 100 mg/day in plantar-type tinea pedis. *Br J Dermatol* 1995; 132: 604-608.

AUTHORS' ADDRESSES

Gabriele Ginter MD, Consultant Dermatologist, Dept. of Dermatology, University of Graz
Auenbruggerplatz 8, A-8036 Graz, Austria
Edgar Rieger MD, Dermatologist, same address