Dermatomycoses: from head to toe

Five kingdoms of living world

- Planta
- Animalia
- Fungi (eukaryotes - dermatophytes, yeast-like, moulds)
- Protista (protozoa, algae, tripanosomes, etc.)
- Monera (prokaryotes, bacteria).

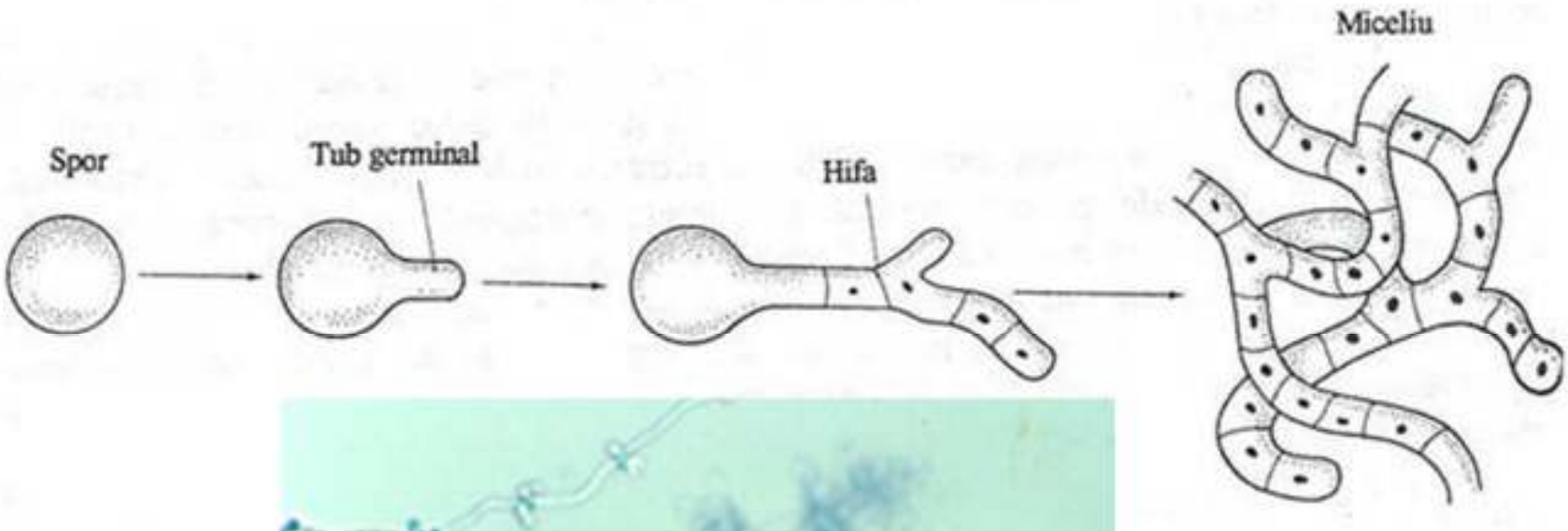
PROLOGUE: A BIOLOGICAL GUIDE

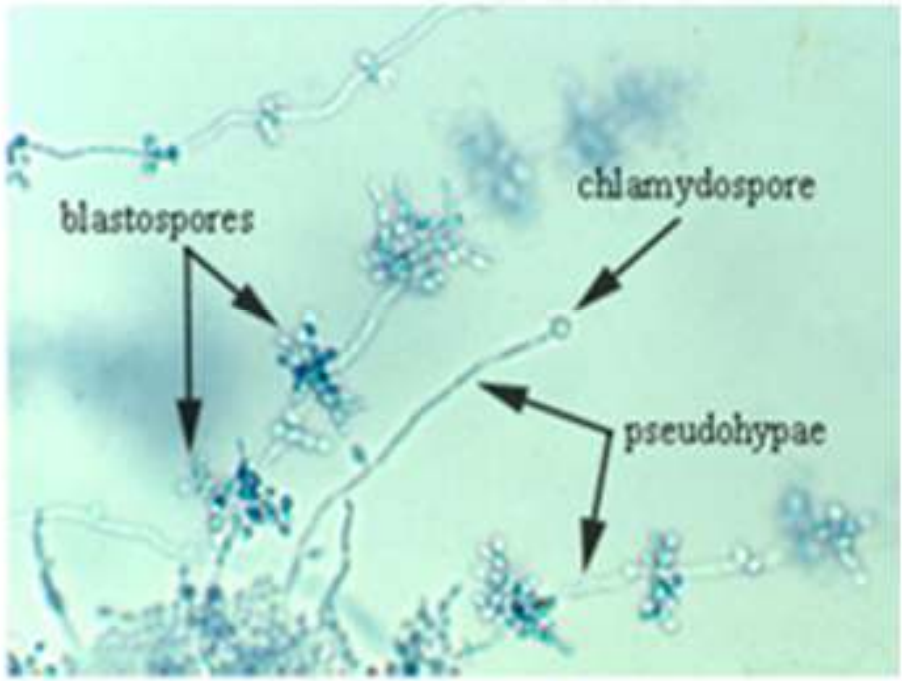
- Fungi are everywhere.
- There are some 1.500.000 known species.
- About 200 species a pathogenic for humans.
- Eukaryotic cells (contain nuclei and organelles)
- Heterotrophic - fungi lack chlorophyll and are therefore not photosynthetic like plants and algae
- Saprophytes (living on dead organic matter) or parasites (utilizing living tissue).
- Rigid cell walls (have chitin not murein like bacteria) and are therefore non-motile, like plants.

FORM AND REPRODUCTION

- Fungal cells are eukaryotes with a single set of genetic material (haploid).
  - **multicellular (dermatophytes), reproduction through sporulation**, adult cells are separated completely and form filamentous structures (hiphae); the totality of hyphae = micelium (thalus): Microsporum*, Trichophyton, Epidermophyton.*
  - **unicellular (yeast-like), reproduction through budding**, resulting daughter cells incomplete separated, forming pseudohyphae and pseudomicellium: *Cryptococcus neoformans; Candida spp*.
  - **dimorphic (moulds, micromicetes**), two growing forms: filamentous as in multicellular fungi at 22ºC (saprophytic phase) and yeast-like at 37ºC (parasitic phase): *Aspergilus, Blastomyces, Coccidioides, Histoplasma capsulatum, etc.*

Dermatophyte cycle: spores-hyphae-micelium-spores
Yeast cycle: blastospores-pseudomicelium-chlamydospores blastospores





CLASSIFICATION OF THE FUNGI

- A definitive classification is not possible until the perfect stage has been identified and described. The classification is arranged in six groups (see table), three of which are relevant to disorders in human beings.
- The last group, Fungi Imperfecti, is a group with no identified sexual reproduction and whose perfect stage is therefore unknown.
- The actinomycetes are gram-positive bacteria which cause, inter alia, pseudomycoses.

CLASSIFICATION OF THE FUNGI

CLASS	SUBCLASS	ORDER	GENUS
1. Archimycetes	nonpathogenic in human beings		
2. Myxomycetes	nonpathogenic in human beings		
3. Phytomycetes	Oomycetes		
	Zygomycetes	Mucorales	*Mucor*
		Entomophthorales	*Basidiobolus*
4. Ascomycetes	Hemiascomycetidae		*Candida*
			Cryptococcus
	Euascomycetidae	Plectomycetes	*Dermatophytes*
			Aspergillus
		Pyrenomycetes	*Claviceps Purpurae*
		Discomycetes	*Piedraia Hortai*
5. Basidiomycetes	nonpathogenic in human beings		
6. Adelomycetes	all human pathogenic fungi not included in the Phytomycetes or Ascomycetes		
Actinomycetes			*Mycobacterium*
			Actinomycetes
			Nocardia

FUNGAL PATHOGENICITY

- The two major **physiologic barriers** to fungal growth within the human body are **temperature and redox potential**. Most fungi are mesophilic (10-20^{o}C) and can not grow at 37^{o}C. Similarly, most fungi are saprophytic and their enzymatic pathways function more efficiently at the redox potential of non-living substrates than at the relatively more reduced state of living metabolizing tissue.
- In addition, the body has a highly efficient set of cellular defences to combat fungal proliferation.
- Thus, the basic mechanism of fungal pathogenicity is its ability to adapt to the tissue environment and to withstand the lytic activity of the host's cellular defenses.
- In general, the development of human mycoses is related primarily to the immunological status of the host and environmental exposure (warm and moist conditions), rather than to the infecting organism.

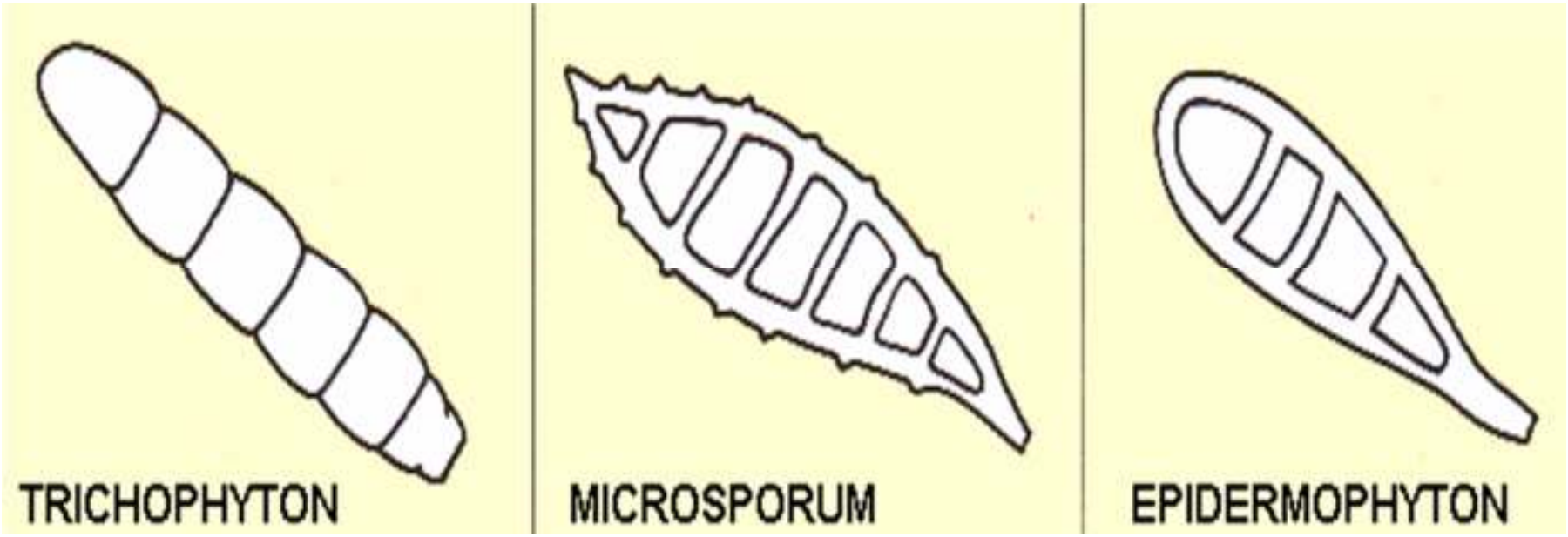
DERMATOMYCOSES – DEFINITION AND CHARACTERISTICS

- **Dermatomycoses** are infections of the skin, hair or nails by fungi.
- The principal causative agents are **dermatophytes,** which are subdivided into three groups (genera):
  - ✓ Trichophyton: thin-walled, smooth, four to six septa
  - ✓ Microsporum: thick-walled, with projections five to more septa
  - ✓ Epidermophyton: thick-walled, oval shaped four or fewer septa
- Besides the dermatophytes**, yeasts** are also capable of causing skin disorders - **Candida spp. and Pityrosporum.**
- Infections are increasingly being caused by species of fungus which are classified neither as yeasts nor dermatophytes – **moulds**. An example of this is **Scopulariopsis brevicaulis**, which can occur in nails.

Etiological classification of dermatomycoses

- Dermatophytons of 3 genera: Trichophyton, Microsporum and Epidermophyton
- Keratophytons of some yeast species: Pityrosporum ovale, Pityrosporum orbiculare, Malassezia furfur.
- Candida genus (Candida albicans and non-albicans spp).
- Pseudofungi (Corynebacterium minutissimum, Actinomyces israelii, etc).
- Moulds (Scopulariopsis, Aspergillus, Penicillium, etc.)

DERMATOPHYTES - CLASSIFICATION



DERMATOPHYTES – THEIR HOST

- On the basis of the original host, a distinction is made between
- anthropophilic,
- zoophilic (zooantropophilic)
- geophilic

- Zoophilic dermatophytes in human beings frequently evoke a more intense inflammatory reaction than an infection by anthropophilic species.
- Dermatophytes have a preference for growth in and around the hair, in the horny layer of skin, in the moist, warm folds of the skin, or just under the nails.
- Keratinophilia is a major characteristic of dermatophytes; they only grow in the dead, horny layer of the skin, hair and nails.

3 dermatophyte genera: species and diseases

- ***Trichophyton***

  T.violaceum, T.tonsurans (antropophilic trichophyton superficial Tinea); **T.verrucosum, T.gypseum** (zooantropophilic trichophyton deep Tinea); T.schoenleini (favus); **T.rubrum** (rubromycosis)**; T. menthagrophytes var. interdigitale (**Tinea plantaris).

- ***Microsporum***

  M.ferrugineum, M.audoini (antropophilic microsporum Tinea); **M.canis, M.nanum (**zooantropophilic microsporum Tinea).

- ***Epidermophyton***

  E.floccosum (Tinea cruris).

Factors which are conducive to the development of a dermatomycoses

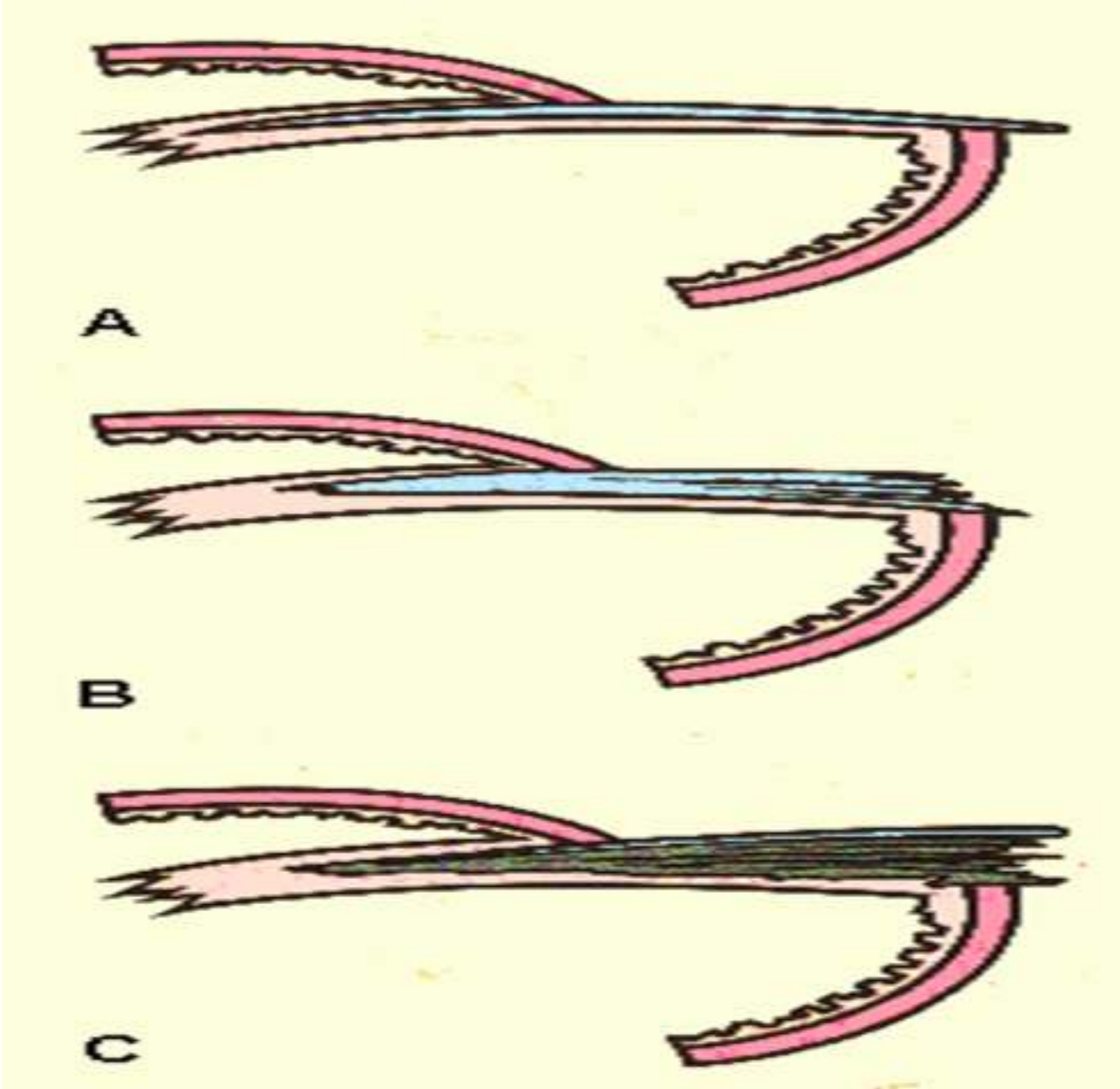
- FREQUENT WASHING WITH SOAP AND INADEQUATE RINSING
- USE OF DISINFECTANTS
- MOIST SKIN, EXACERBATED BY WEARING CLOTHES OF SYNTHETIC FIBRES
- MECHANICAL IRRITATION

DERMATOPHYTES – THEIR ANIMAL HOST

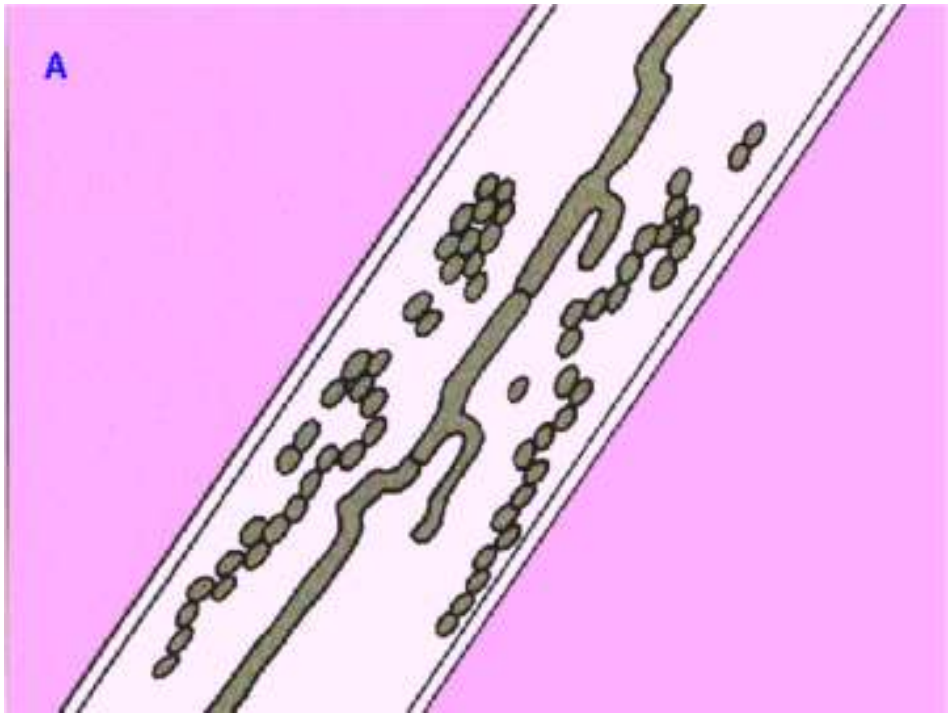
	Host	Affinity for human beings
Microsporum canis	cat, dog	+ + +
Microsporum equinum	horse	+
Microsporum nanum	pig	+ / -
Microsporum persicolor	field vole	+
Trichophyton equinum	horse	+
Trichophyton erinacei	Western hedgehog	+ +
Trichophyton gallinae	birds	+ / -
Trichophyton mentagrophytes	rodents	+ +
Trichophyton quinckeanum	mouse	+ +
Trichiphyton simii	apes, birds	+ +
Trichophyton verrucosum	cattle	+ + +

DERMATOPHYTES AND THE SKIN

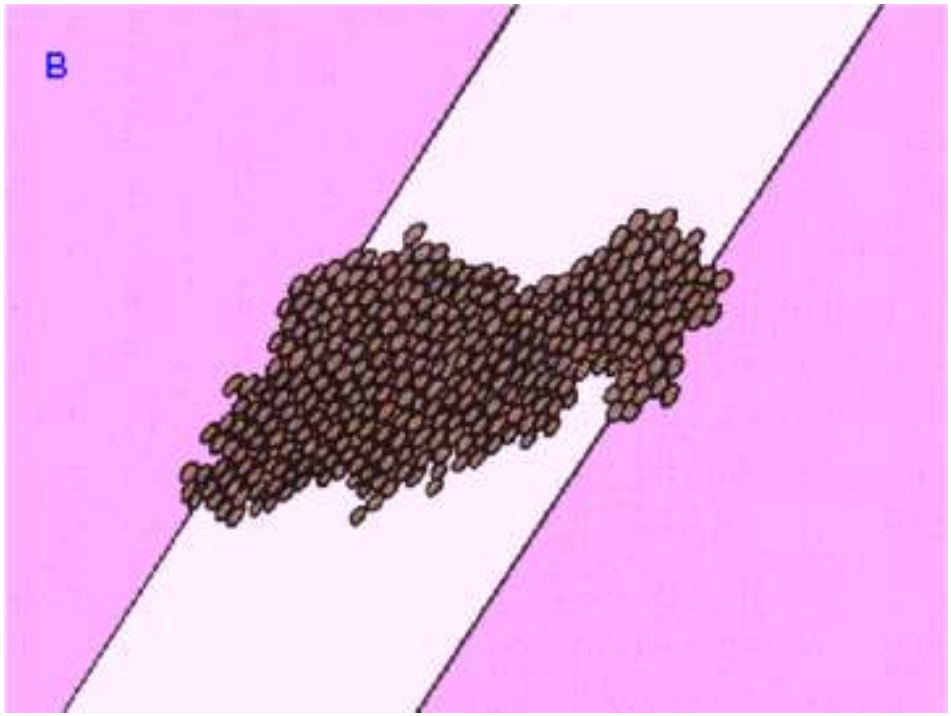
DERMATOPHYTES AND THE NAILS



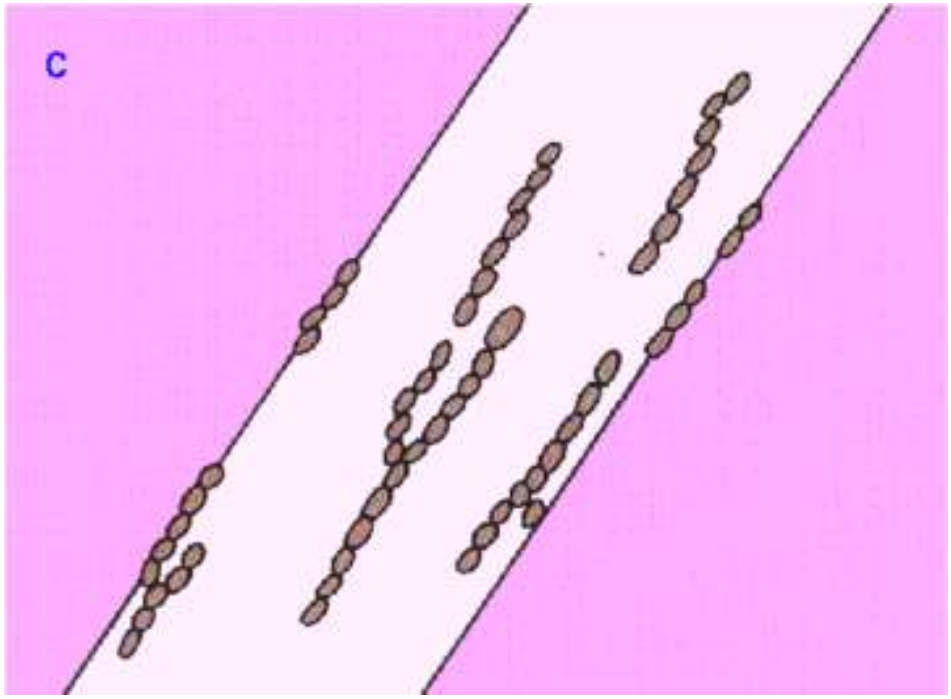
Endothrix spore growth



Small-spored ectothrix growth



Large-spored ectothrix growth



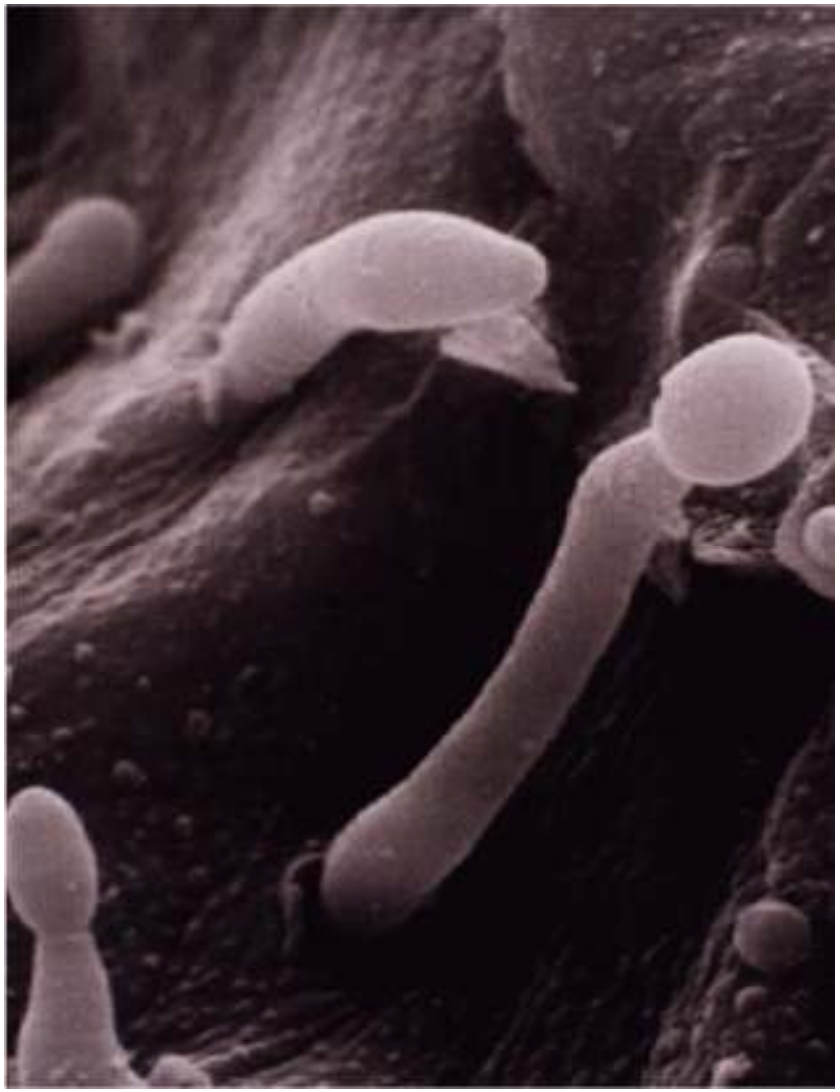
Summary of the different forms of growth of dermatophytes in hair

Endothrix		*Trichophyton tonsurans* *Trichophyton soudanense* *Trichophyton violaceum*
Ectothrix	small-spored	*Microsporum canis* *Microsporum ferrugineum* *Microsporum audouinii*
	large-spored	*Trichophyton verrucosum* *Trichophyton mentagrophytes* *Microsporum gypseum*
Favus		*Trichiphyton schoenleinii*

YEASTS

- The two major species of yeast capable of causing skin infections are Candida albicans and Pityrosporum ovale.
- The most striking property of these yeasts is that they are commonly part of the normal flora - real opportunists.
- Particular importance attaches to predisposing factors.
- There are various predisposing factors which are conducive to the transition from commensal to pathogenic; a moist skin, a high pH and the presence of sugars and certain amino acids create a favourable climate for Candida.

Pseudohyphae of C.albicans (in vaginal mucosa of rat)



PITYROSPORUM

- It is **a lipophilic yeast** which only grows when oil, glycerin or glyceryl monostearate is added to the culture medium. Pityrosporum is chiefly found as a **commensal** on areas of the skin containing a relatively large number of sebaceous glands.
- The yeast can assume various morphological forms. Until quite recently this led to the assumption that **Pityrosporum ovale, Pityrosporum orbiculare and Malassezia** were three different organisms. Now, however, it is known that they are different forms of growth of one and the same yeast: **P. ovale**.
- It has recently been established that P. ovale also plays a role in **seborrhoeic dermatitis**. Patients with this infection have a high concentration of P. ovale on the skin, as a result of which inflammatory reactions occur. **Dandruff** is regarded as a form of seborrhoeic dermatitis.

DERMATOMYCOSES - CLASSIFICATION

- Dermatomycoses can be classified in various ways. The simplest of all would seem to be a systematic arrangement **on the basis of the causative agents**. In a classification of this nature, the disorders are designated by reference to the individual genus: **trichophytosis, epidermophytosis, microsporosis, candidosis (candidiasis) and pityrosporosis.**
- A classification focused more **on the epidemiology and method of dissemination** is one that is based on the original host of the various fungi. This produces such terms as **anthropophilic, zoophilic and possibly geophilic** agents: fungi which therefore have human beings, an animal or the soil as their primary habitat.
- Closer to actual practice is a classification **on the basis of the clinical picture**, designated, for example, by the severity of the inflammation: **mild, moderate or severe.**
- The most widely used classification is largely **based on the site of the clinical picture**. As mentioned earlier, the largest group of dermatomycoses consists of disorders which are caused by dermatophytes - **TINEA**.

DERMATOMYCOSES

DERMATOPHYTE INFECTIONS

- Tinea capitis
- Tinea barbae
- Tinea corporis
- Tinea cruris
- Tinea pedis interdigitalis
- Tinea pedis plantaris
- Tinea manus palmaris
- Tinea inguium

YEAST INFECTIONS

- Candidose
- Pityrosporose

Dermatophytoses = Tinea

There are **5 Dermatophytoses** by etiology:

- **Epidermophytosis,**
- **Rubromycosis,**
- **Trichophytosis,**
- **Microsporosis,**
- **Favus**

There are **5 Tinea** by site (WHO ICD-10)

- **Tinea pedis et Tinea manum** (soles and palms);
- **Tinea cruris** (inguinal fold)
- **Tinea corporis** (glabrous skin);
- ***Tinea unguium*** (nails)*;*
- ***Tinea capitis, Tinea barbae*** (scalp, face, beard, moustaches)

REFERENCE SYSTEM FOR THE DERMATOMYCOSES

Dermatophyte infections	tinea capitis	microsporosis
		trichophytosis
		favus
		kerion
	tinea barbae tinea corporis tinea cruris tinea pedis interdigitalis tinea pedis plantaris tinea manus palmaris tinea unguium	
Yeast infections	candidosis	Candida-perionyxis
	pityrosporosis	pityriasis versicolor
		pityrosporum-folliculitus

Clinical presentation – general rule

Usually,

the esential **primary lesion** in dermatomycoses is **erythema** and the **secondary** are **scales**, that means **erythemato-scuamous eruption**; in exudative forms primary can also be vesiculous and in infiltrative forms can be nodular, thus other secondary lesions can be erosive or ulcerative.

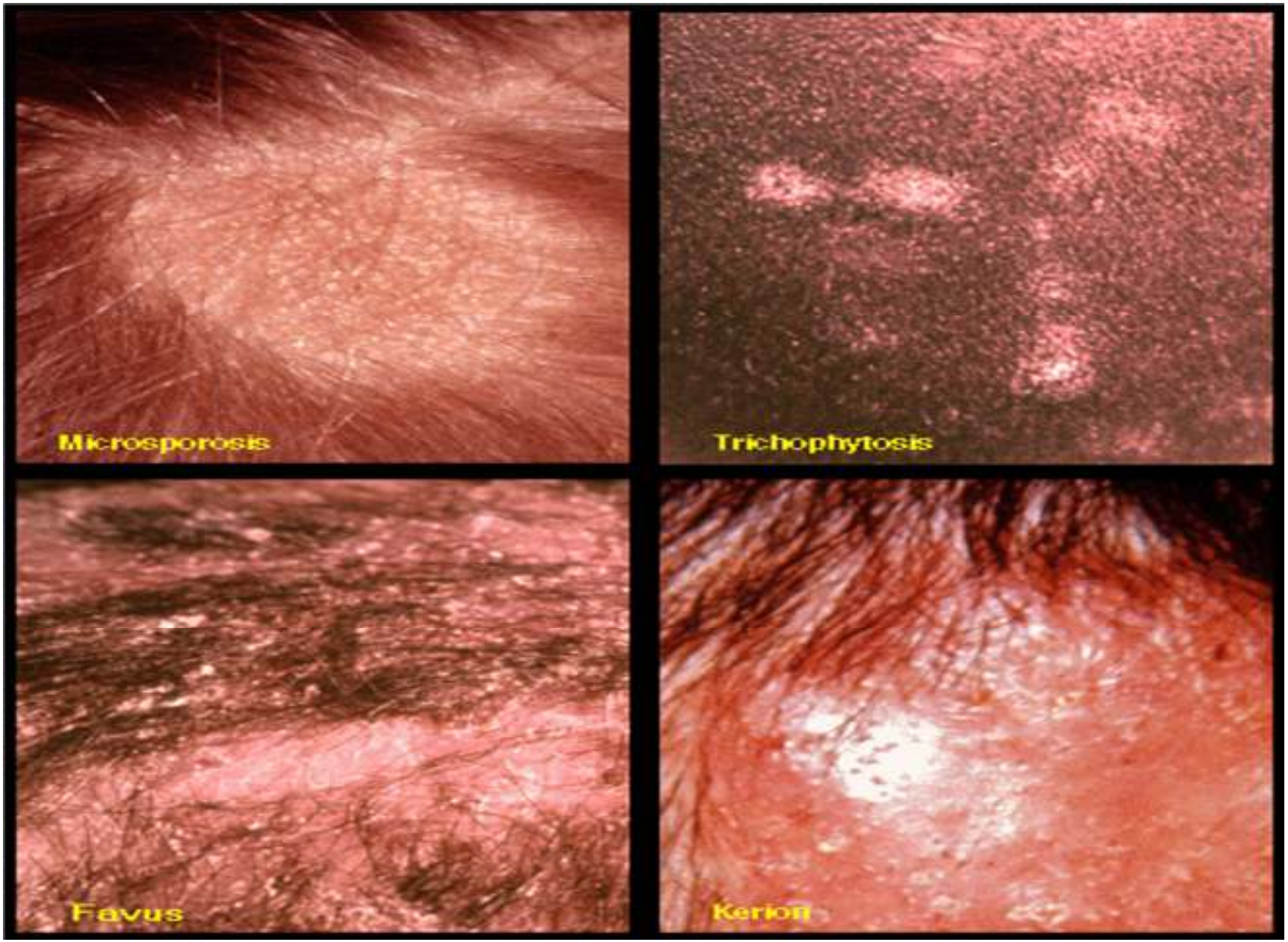
TINEA CAPITIS

In tinea capitis, also called ringworm of the scalp, the lesions are typically ring-shaped and the skin and hair are infected. The hairs break off and leave bald patches.

Four subgroups of tinea capitis can be distinguished:

- - Microsporosis
- - Trichophytosis (herpes tonsurans)
- - Favus
- - Kerion

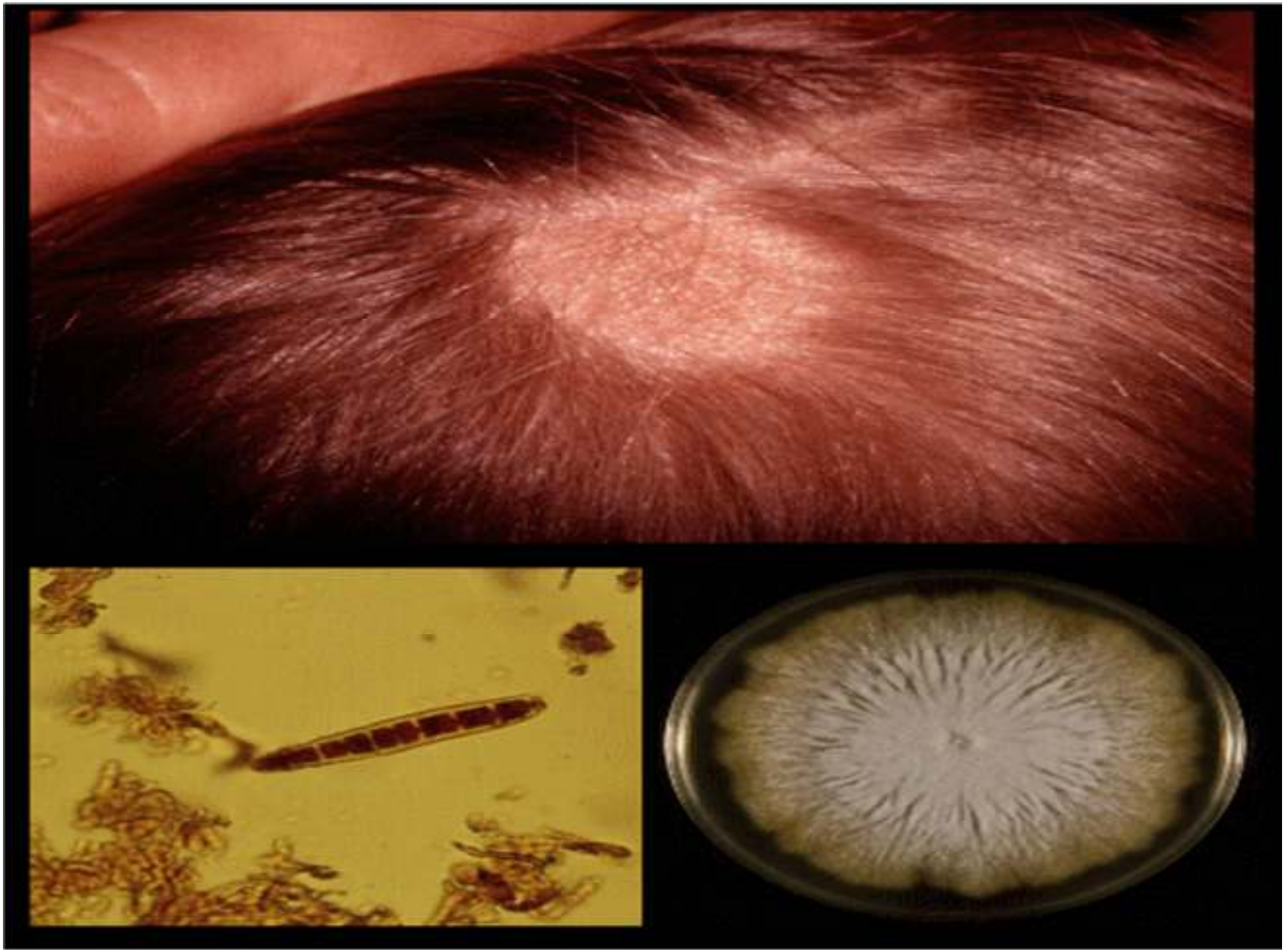
TINEA CAPITIS



Microsporum
Tinea capitis

- **Zooantropophilic (M.canis, M.nanum):** erythema, 1-3 foci, of 3-5 cm diameter, scuamous, round, with sharp limits; the hairs shafts cut-off uniformly at 5-8 mm from the skin level.
- **Antropophilic (M.ferrugineum, M.audoini):** multiple erythematous foci with smaller diameter, scaling is less, the hairs shafts cut-off nonuniformly at 5-8 mm from the skin level.

Zooantropophilic Microsporum Tinea capitis



Tinea capitis: antropophilic micrsoporum (M.ferrugineum)

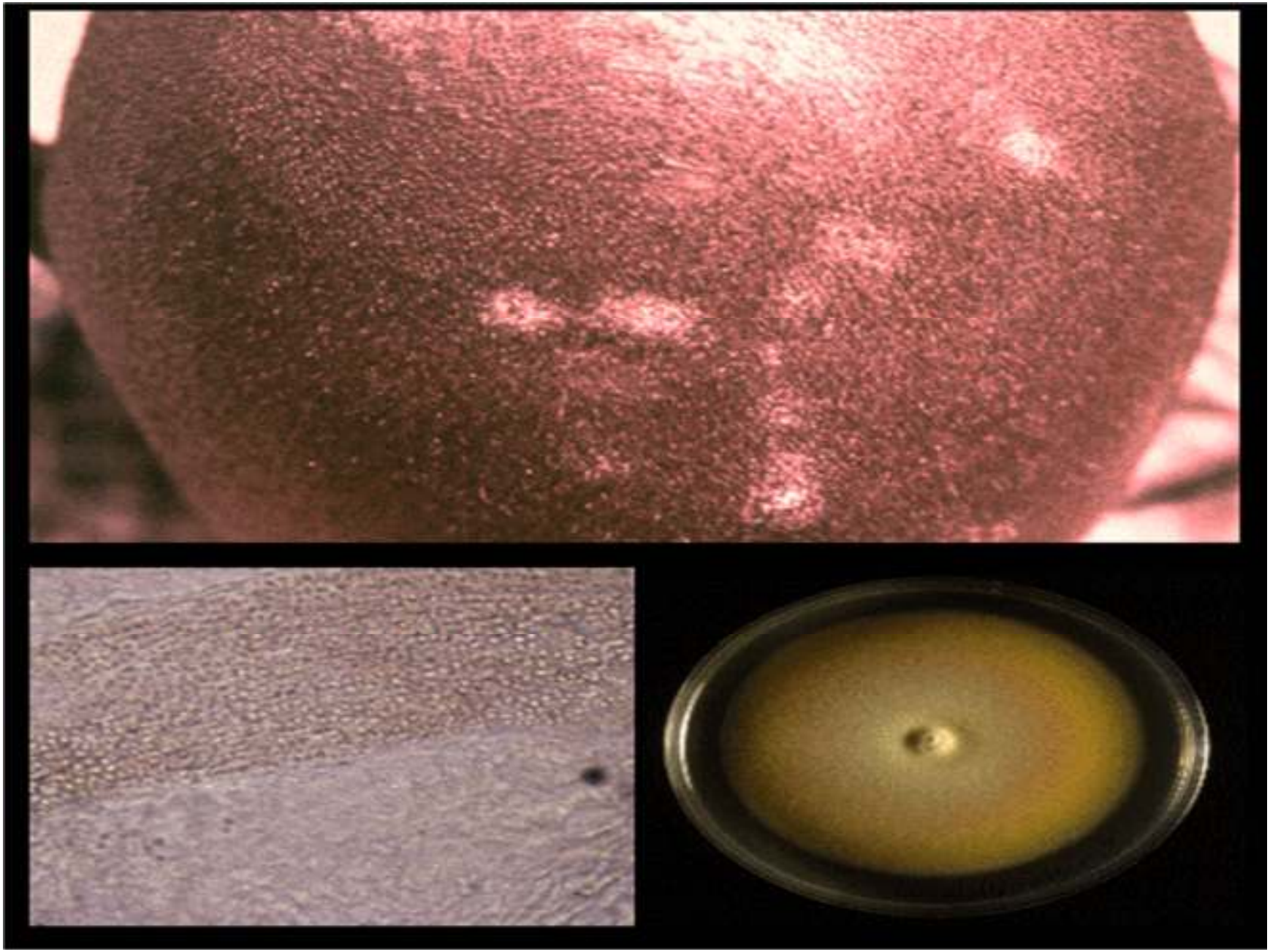
Tinea faceis: antropophilic microsporum

TRICHOPHYTOSIS

- Children are especially prone to attack by trichophytosis or herpes tonsurans, in adults - usually females;
- The major causative agents of herpes tonsurans are **Trichophyton tonsurans** and **T. violaceum.**

- Clinical presentation:
  - Children form: multiple, small erythematous patches with tiny adherent scales, hair shafts are broken at 1-3 mm from skin surface spontaneous healing can occur after puberty.
  - Adult female chronic form: black dots, comedo-like, broken off hairs at the surface of the skin and are only visible as a small stub, some atrophy and occult scaling.

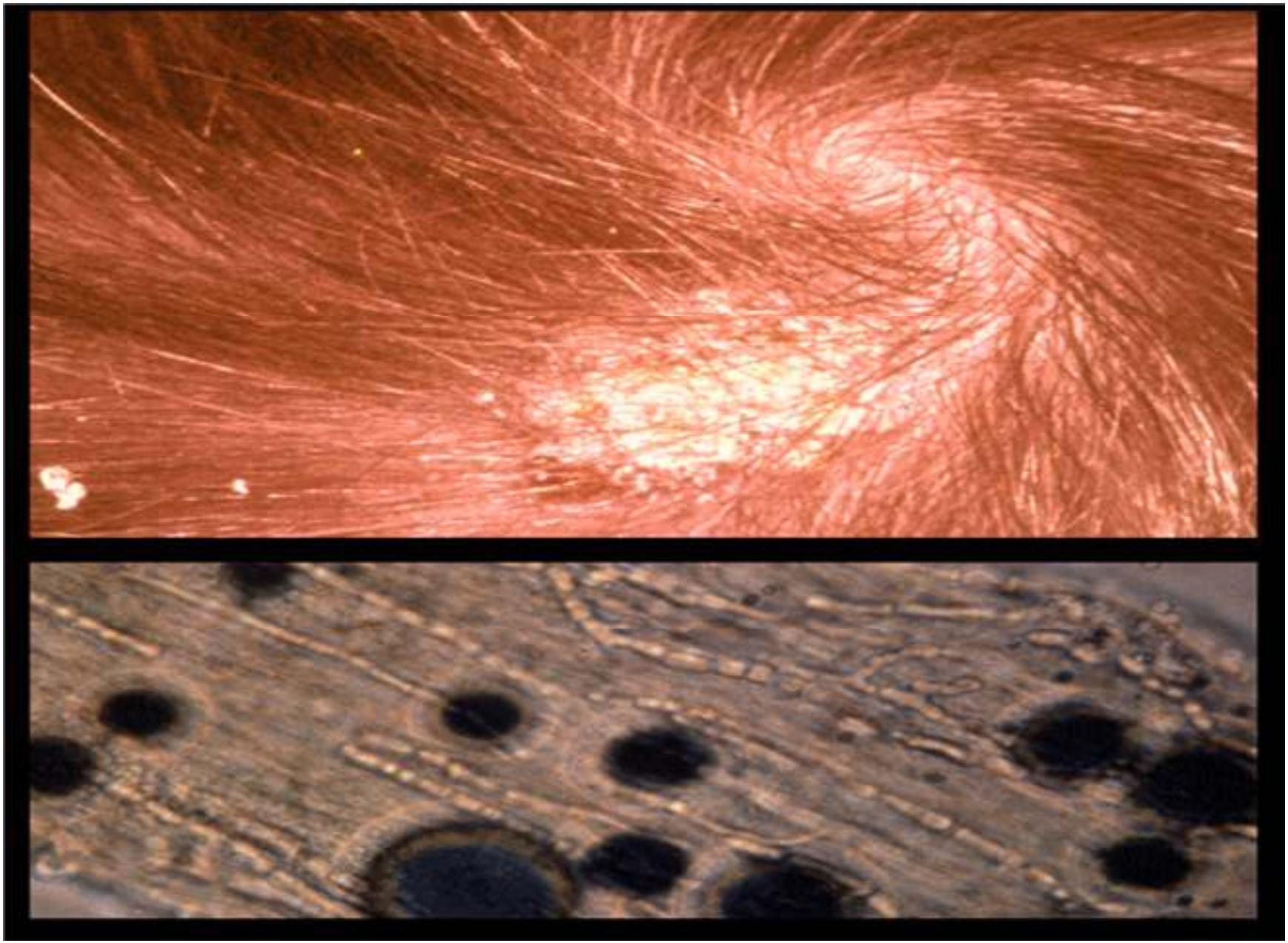
TRICHOPHYTOSIS



FAVUS

- Favus is caused by Trichophyton schoenleinii
- Three clinical forms: scutular (typical), impetiginous and pityriasiform
- Begins as a red scaling patch on the scalp which develops until it covers an area several centimetres in diameter.
- The next stage is the formation of scutula: yellow, cup-shaped crusts with a diameter of one to two centimetres.
- A salient feature is that the hairs are not broken off from the beginning, but the hairs lose their gloss and are arranged on the scalp in irregular tufts.
- As the patch increases in size, total and irreversible hair loss occurs in the central region.
- The 'mouse smell' is mentioned in all textbooks.
- The impetiginous form of favus is characterized by moist crusts with underlying accumulations of pus.
- The pityriasiform (scaling) form is dominated by erythema and scales.

FAVUS



KERION

- Kerion occurs at all ages. The causative agents of this disorder are **Trichophyton verrucosum** or **T.** mentagrophytes var. **gypseum**.
- Kerion begins as an erythematous annular patch which gradually elevates itself above the surrounding skin. It is clearly circumscribed, while the slightly nodular surface is covered with pustules. Pus is released when pressure is applied **(honeycomb sign)**. It is associated with occasional pain. A kerion infection is not restricted to the scalp. Infections of this nature are also possible in the beard area.
- If left untreated, the condition will persist for several weeks or months. Then the symptoms will gradually diminish. An atrophic scar may remain after healing, while the sustained hair loss will not be fully replaced. However, superinfections can seriously complicate this relatively benign process.

KERION

Kerion Celsi

TINEA BARBAE

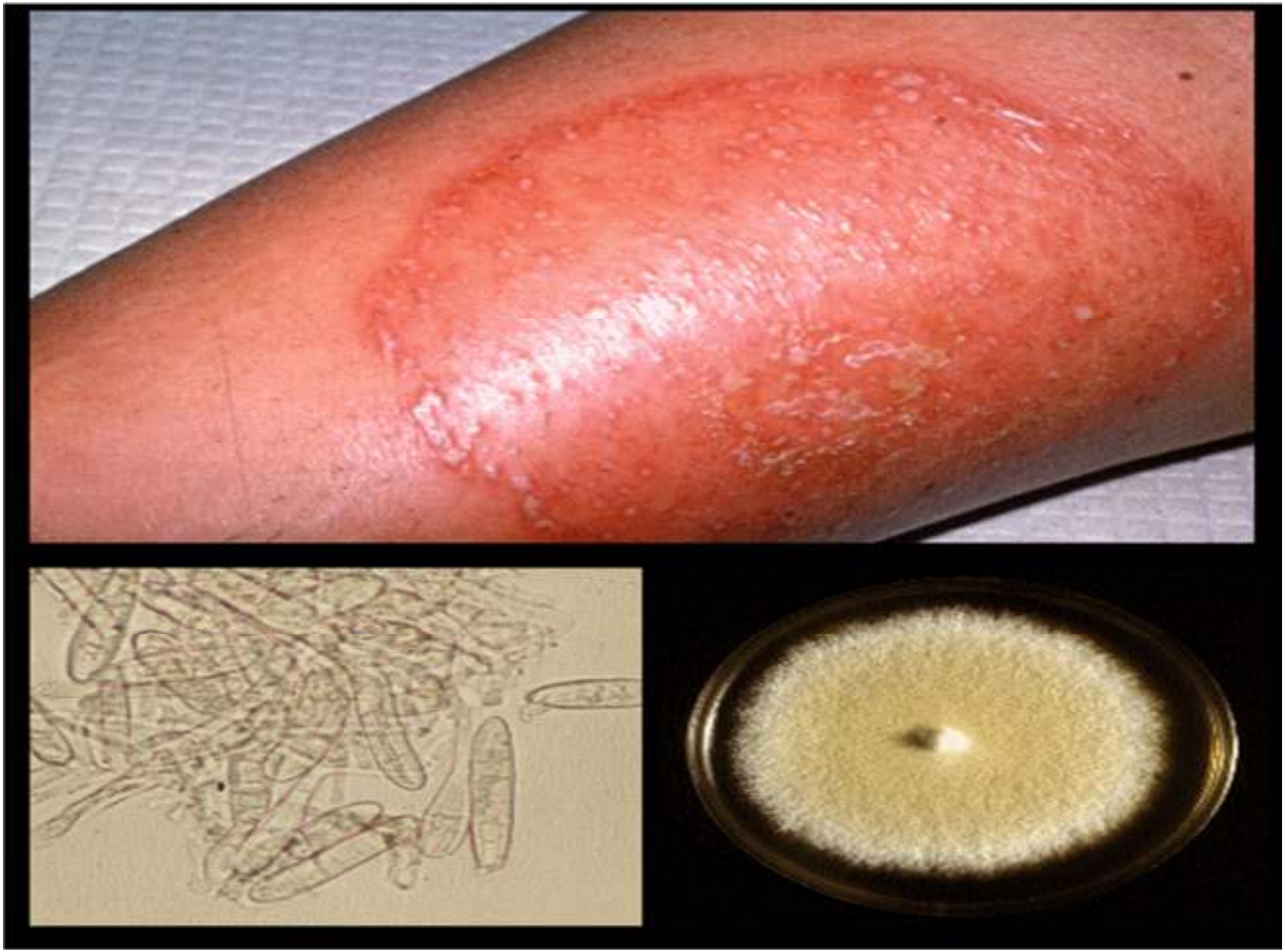
- **T. gypseum** (mice) **or T. verrucosum (cows)**.
- Tinea barbae is also called trichophyte (parasitic) sycosis.
- Tinea barbae and tinea capitis are one and the same infection.
- Kerion also occurs in association with tinea barbae.
- The infection can last for months and there is a real risk of bacterial superinfection.

TINEA BARBAE

TINEA CORPORIS

- Every dermatophyte can be the causative agent of tinea corporis: Microsporum spp., Trichophyton spp. and Epidermophyton floccosum.
- Tinea corporis, formerly called herpes circinatus, is a tinea or ringworm disorder of glabrous skin.
- Annular scaling erythematous patches, slowly expanding edge with inflammation which is frequently somewhat elevated.
- The lesions are clearly circumscribed and vesicles may also occur.
- The patient may also complain of itch and a burning sensation.
- The lesion spreads peripherally and tends to heal in the centre.
- After several months, depending in part on the species of fungus involved, spontaneous healing can occur.
- Chronic infections are also possible, however, and T. rubrum infections are notoriously obstinate.

TINEA CORPORIS

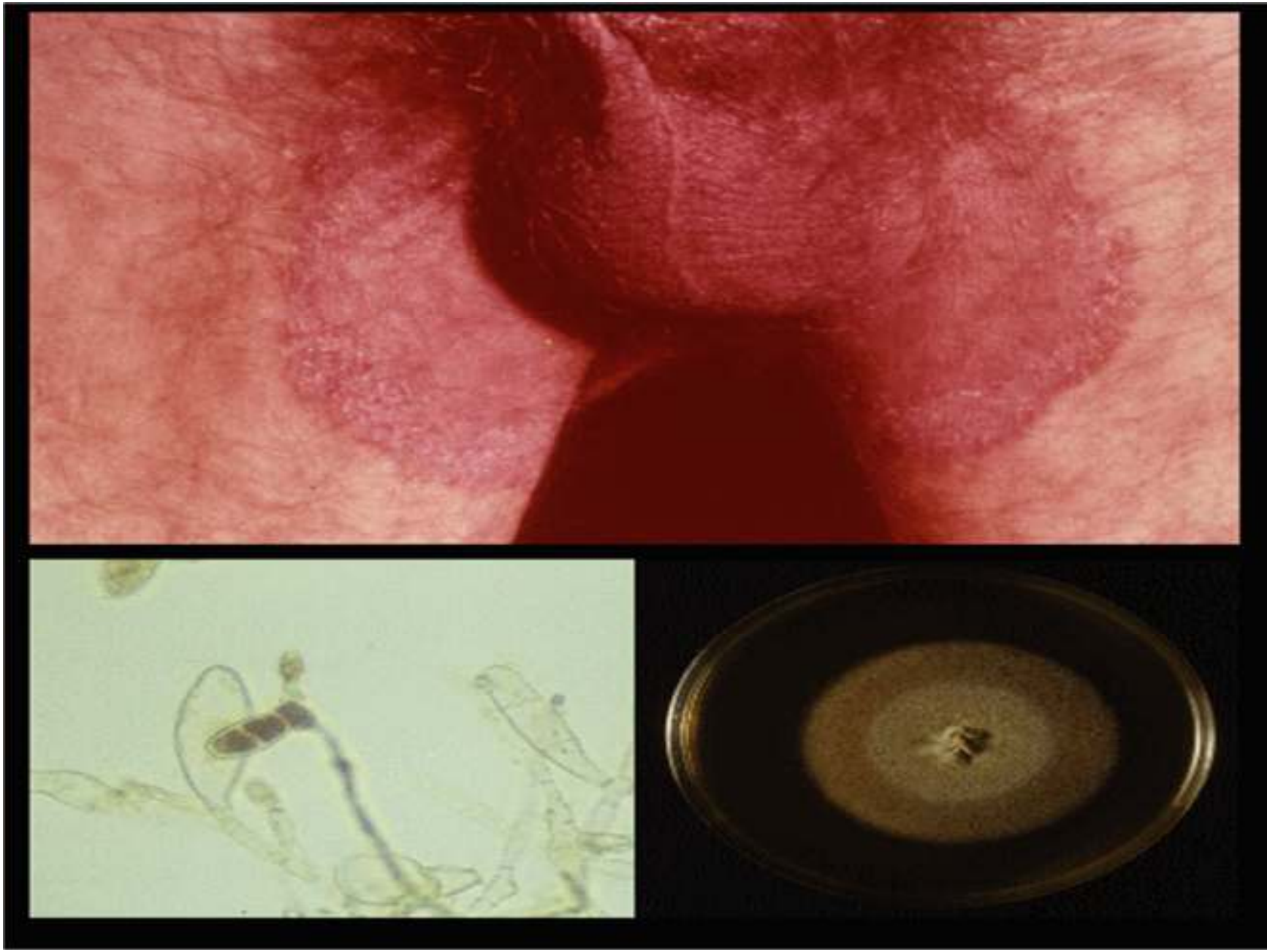


TINEA CORPORIS

TINEA CRURIS

- Caused by **Epidermophyton floccosum** or **Trichophyton rubrum**.
- Tinea cruris is more common in men than in women, probably because the male population is also more susceptible to tinea pedis.
- Tinea cruris begins with arcuate erythematous plaques in the perineal fold which spread to the thighs.
- Itch and a burning sensation are the patient's major complaints.
- Scaling is not always present and vesicles are rare.
- The scrotum may also be affected, while T. rubrum can spread to the anal region and the abdomen.

TINEA CRURIS



TINEA CRURIS

TINEA PEDIS PLANTARIS AND TINEA MANUS PALMARIS

- The causative agents are the same as in tinea pedis. The relevant fungi are therefore **Trichophyton mentagrophytes var. interdigitale, T. rubrum and Epidermophyton floccosum.**
- Athlete's foot
- Dermatophyte infections of the palm and sole show erythematosquamous eruption.
- These are frequently attended by deeper, brownish pustules.
- After they have broken, they dry up with considerable scaling.
- The course of the infection is quite often chronic.

TINEA PEDIS PLANTARIS AND TINEA MANUS PALMARIS

Tinea pedis et Tinea manum clinical forms

- Dyshidrotic vesiculous form
- Scuamous hyperkeratotic form
- Intertriginous (interdigitalis) form

Tinea pedis, dyshidrotic form

Tinea pedis, dyshidrotic form

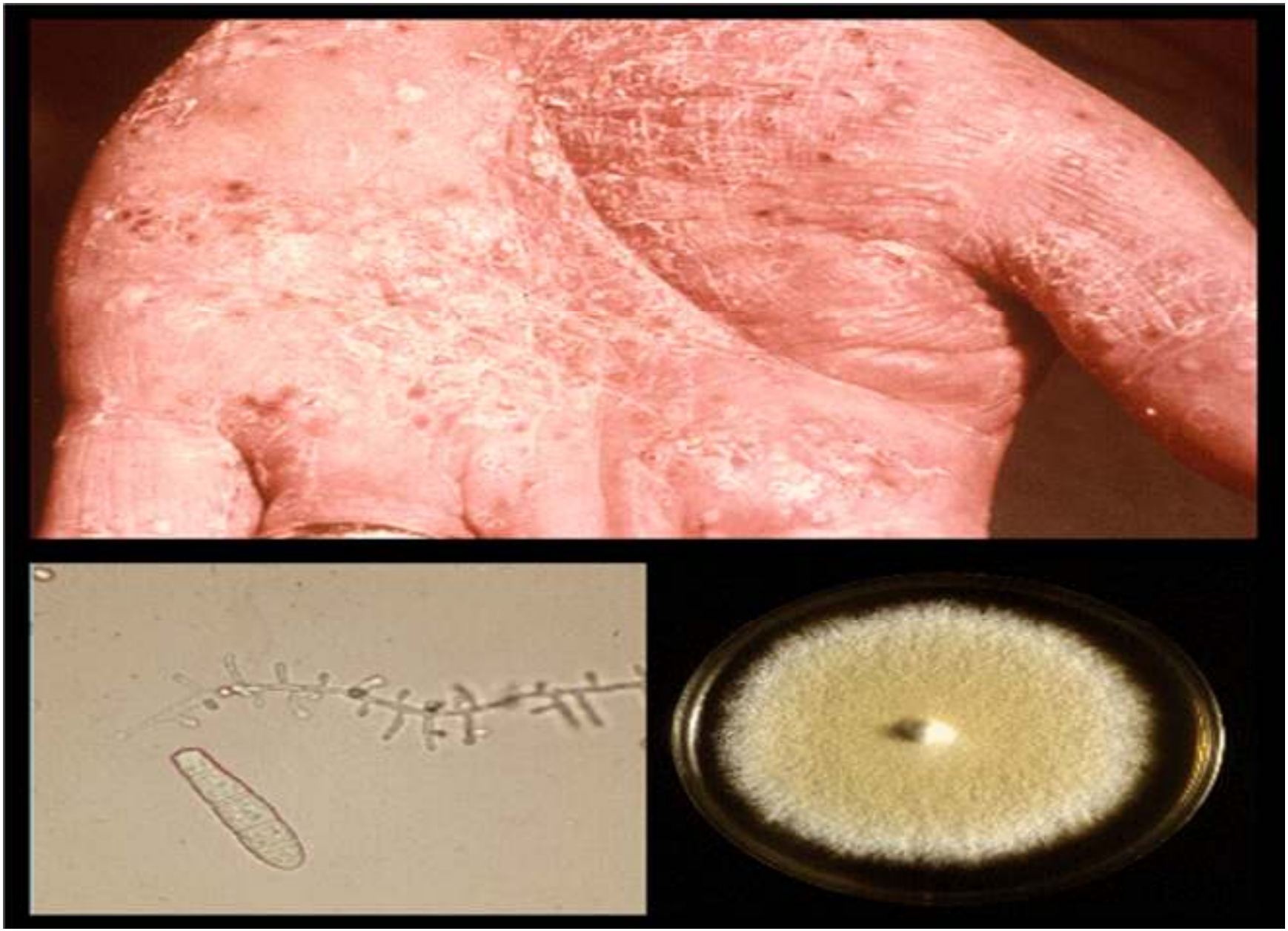
Tinea pedis, hyperkeratotic form

Tinea pedis, hyperkeratotic form

Tinea pedis, hyperkeratotic form

Tinea pedis, intertriginous form

TINEA MANUS PALMARIS



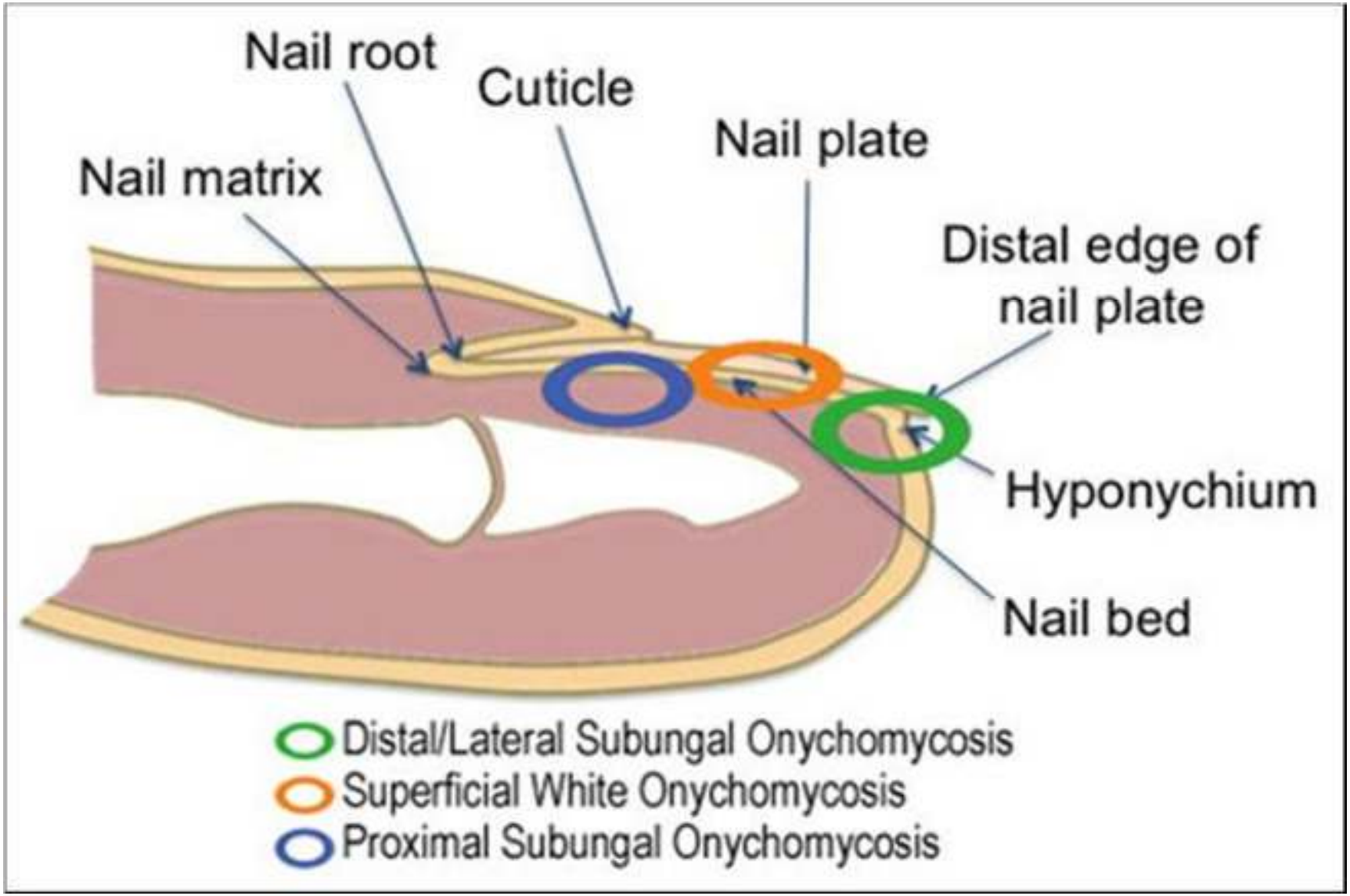
TINEA MANUS PALMARIS

Tinea manus

TINEA UNGUIUM

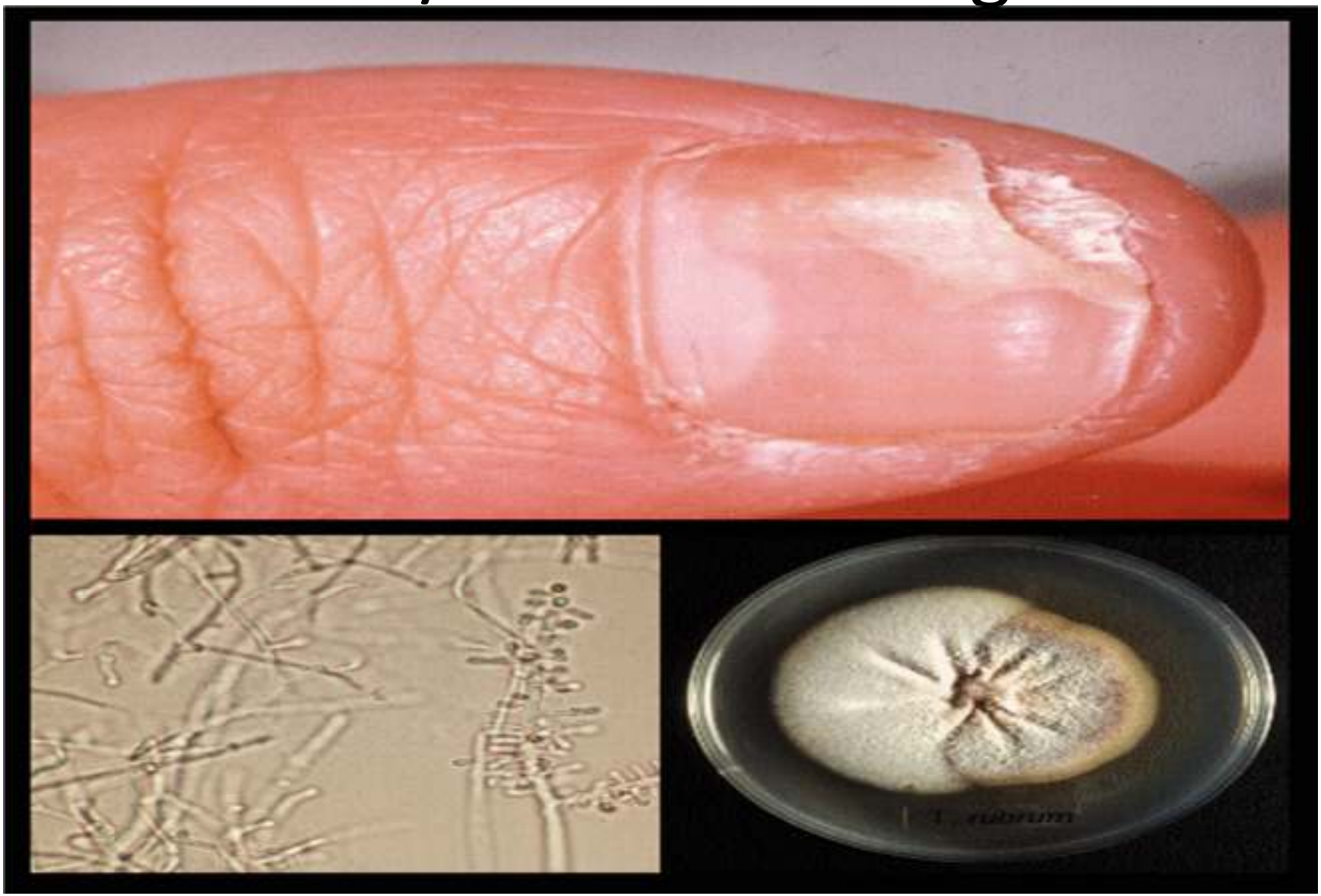
- The principal agent is **Trichophyton rubrum**, however, **Epidermophyton floccosum, Trichophyton menthagrophytes, T.tonsurans** and **T.schoenleinii** can also be the causative agent.
- Atrophy (onycholysis), discoloration and subungual hyperkeratosis.
- Three clinical forms: **normotrophic, hypertrophic and atrophic**
- Onychomycosis may be the patient's only disorder, but in many cases the skin is also affected (tinea pedis).
- The initial lesion is small and consists merely of a discoloured spot (yellow or white). As it grows towards the base of the nail, this is attended by more discoloration (brown or black) and the nail is raised.
- The nail becomes brittle and friable. Onycholysis can occur and the entire nail plate can be destroyed. Although it usually starts with just one nail, after some time other nails are also frequently infected.

Tinea unguium clinical forms



Tinea unghium:
distal/lateral subungual onychomycosis

Tinea unghium: distală/laterală subunghială



Tinea unghium:
superficial white onychomycosis

Tinea unghium:
proximal subungual onychomycosis

CANDIDOSIS

- Candida albicans is the most widely known and most pathogenic species of yeast.
- C. albicans is normally present as a commensal in human beings, especially in the gastrointestinal tract and also in the vagina.
- Candida infections are most often found in the large and small flexure lines; this is frequently referred to as intertrigo.
- Erythema, which has a quite dark red colour, and exudation occur deep in the crease or fold, on the apposed surfaces of the skin.
- The skin is severely macerated and erosions may develop.
- Small 'islands off the coast', or satellite lesions, and pustulation may also be present.
- The patient often experiences itch and a burning pain.
-

Candidosis

Candidosis of mucous membranes

- Oral candidiasis (stomatitis)
- Angular cheilitis
- Cheilitis
- Vulvo-vaginitis
- Urethritis and balano-posthitis .

Candidosis of the skin

- Intertrigo
- Paronychia and onychia
- Erythroderma

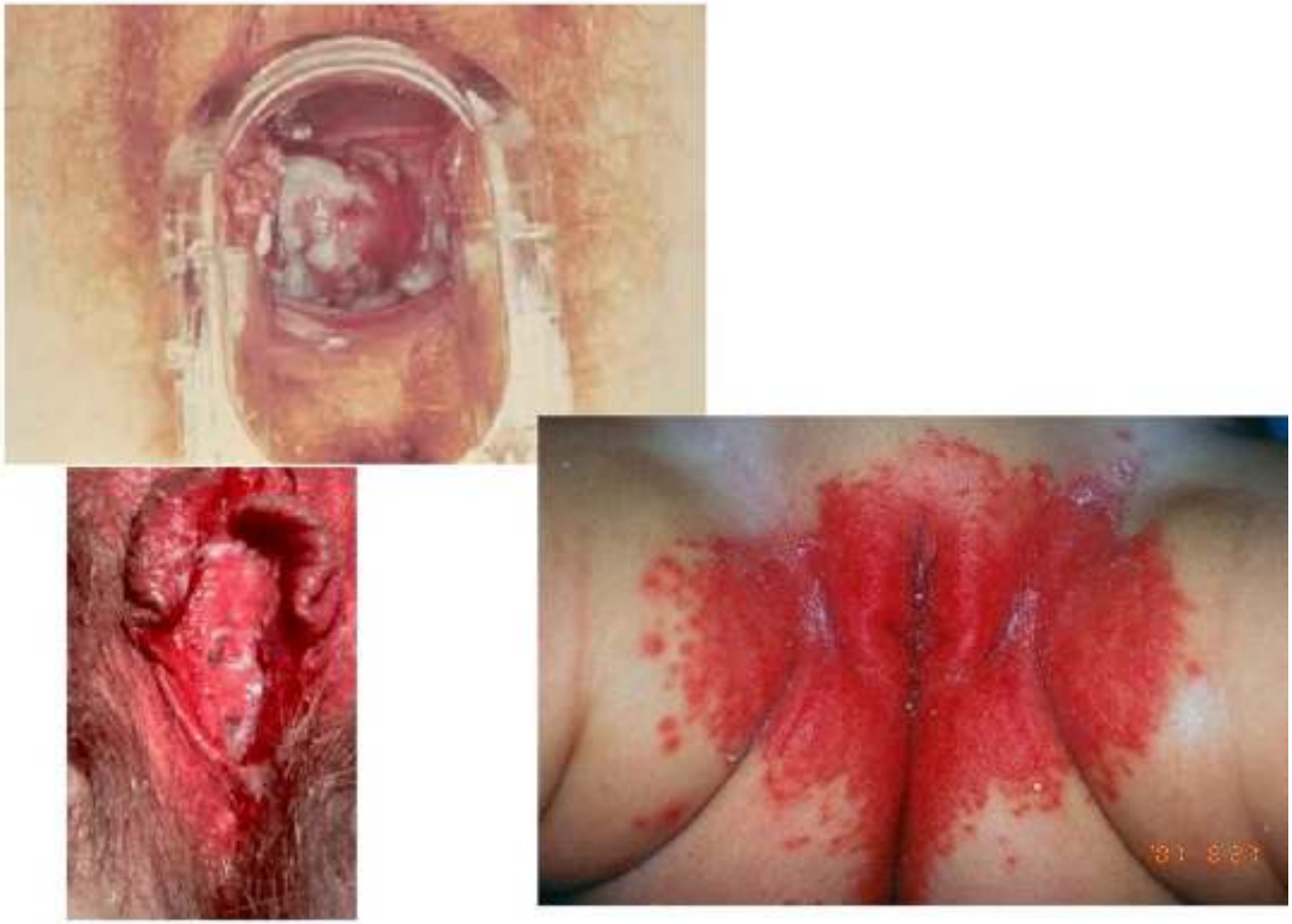
Chronic muco-cutaneous candidosis

- Oral chronic
- Endocrine
- Diffuse chronic
- Granulomatous.

Visceral (systemic) candidosis

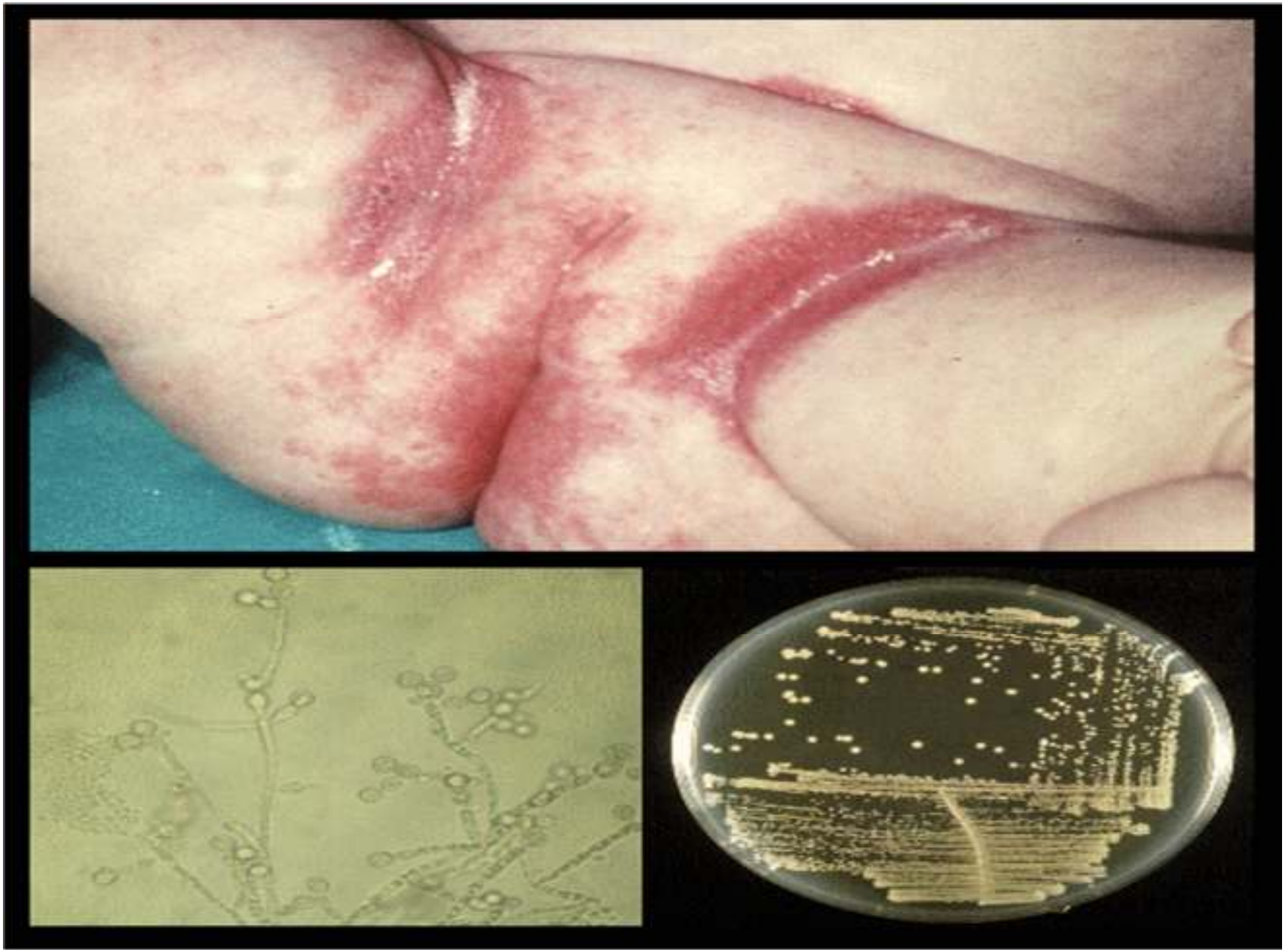
Oral candidosis / angular cheilitis

Candida vulvo-vaginitis



Candida balanoposthitis

Candida intertrigo

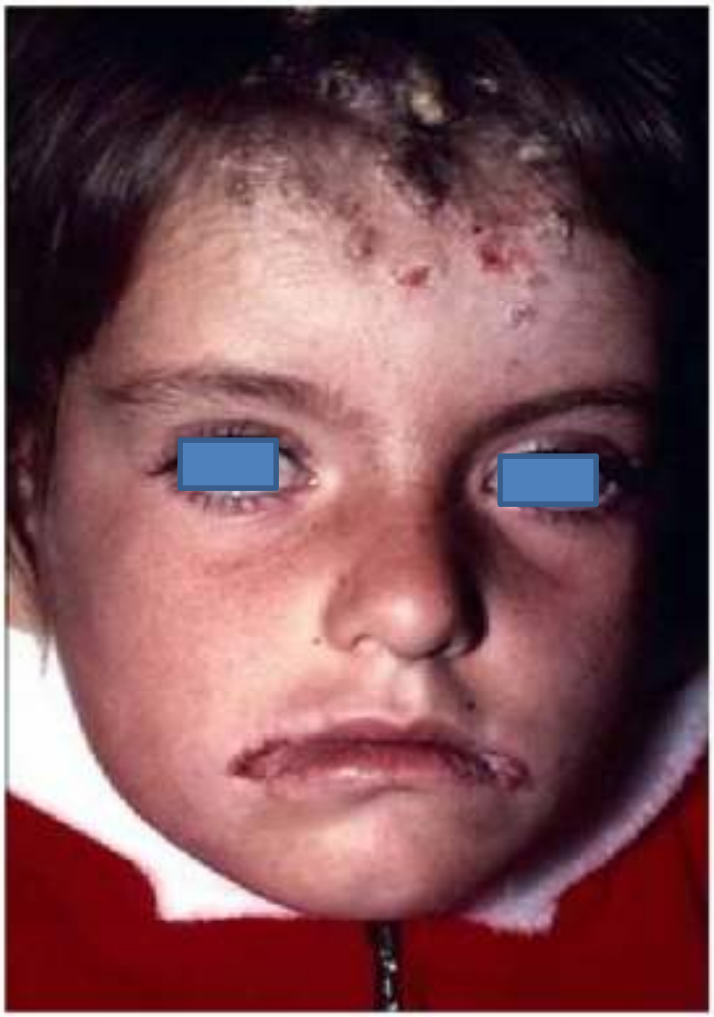


Candida intertrigo

Candida paronychia and onychia

Candida paronychia and onychia

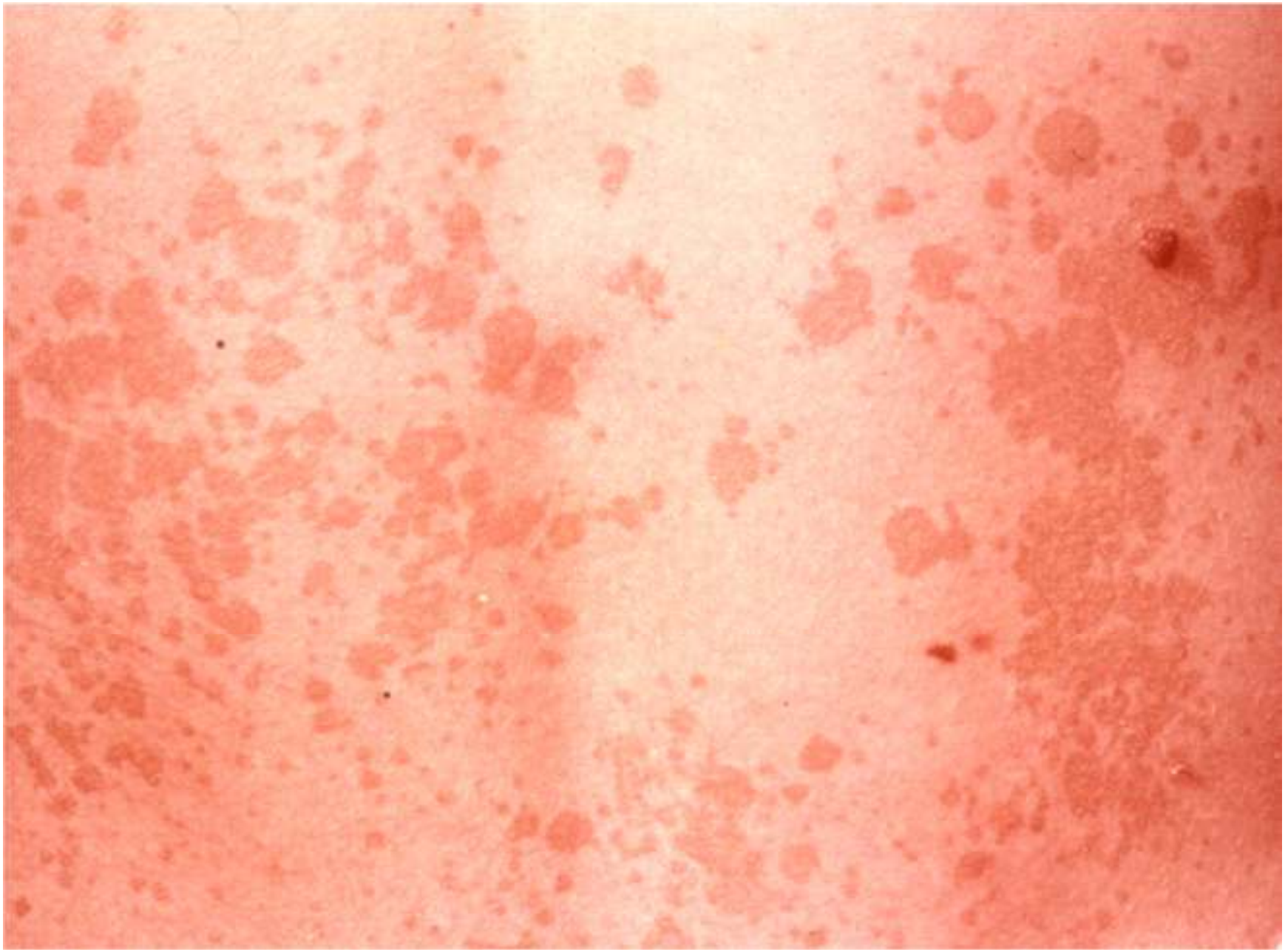
Granulomatous candidiasis



PITYRIASIS VERSICOLOR

- Pityrosporum ovale, Pityrosporum orbiculare, Malassezia furfur – the same agent
- Is dependent upon oil or fat for its growth. This yeast species is always present on the skin of human beings as a commensal, especially in ear wax, on the scalp and at other sites where many sebaceous glands are present.
- Pityriasis versicolor is a disorder which is particularly noticeably because of the discoloration of the skin.
- By comparison with untanned skin the patches are darker, but on tanned skin they are lighter. The colour can vary from yellow to brown, red or whitish.
- After some time the patches coalesce.
- A second major characteristic is the very fine scaling, which is sometimes only apparent after scraping with a spatula. 'Pityron' is Greek for 'bran'.
- Patients are usually not so susceptible to itch or inflammation.
- Positive Balzer (iodine) sign.

PITYRIASIS VERSICOLOR



PITYRIASIS VERSICOLOR

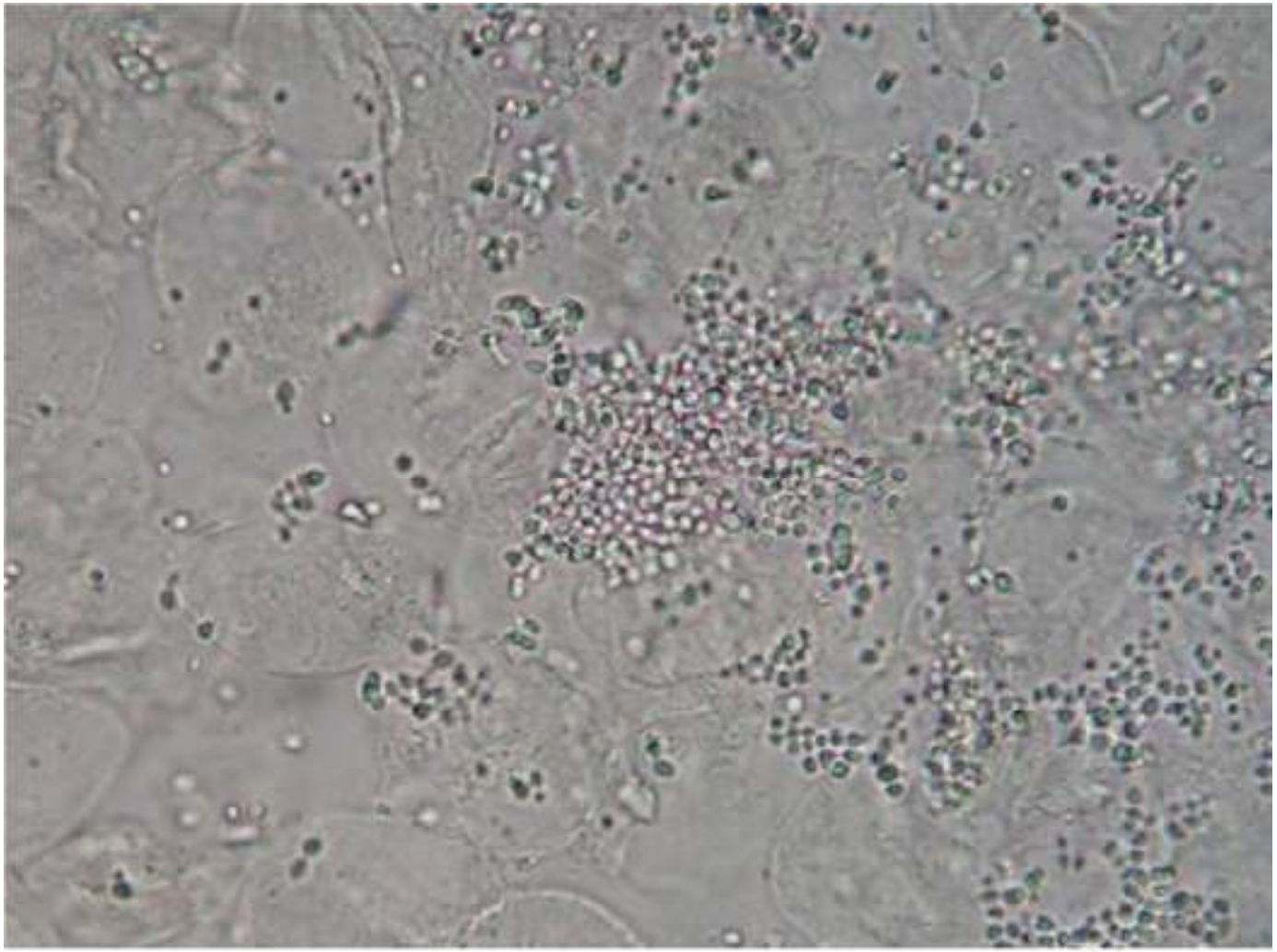
PITYRIASIS VERSICOLOR

Iodine Balzer test

LAB in mycology

- Direct microscopy (KOH 20%)
- Culture on selective media (2-4 weeks)
- Wood's lamp examination (fluorescence)
- Histopathology = PAS staining

Candida albicans:
celule levurice înmugurite



Sampling - scraping the edge of the lesion for microscopic examination

Trichophyton mentagrophytes

Trichophyton rubrum

Epidermophyton floccosum

Aspergillus fumigatus

Culture on selective media

- Disclose the fungus implied
- **Sabouraud media** – classic for growing fungi :
  - glucose 4 g,
  - peptone 1g,
  - agar 2 g,
  - distilled water 100 ml.
- Mycograma – to reveal drug resistance.

Culture: a) T.rubrum; b) E.floccosum; c) T.mentagrophytes; d) M.canis

WOOD's lamp

Fluorescence with Wood's light

Microsporum canis	bright yellowish green
Microsporum audouinii	bright yellowish green
Trichophyton schoenleinii (favus)	pale green
Pityrosporum (pityriasis versicolor)	yellowish brown
Corynebacterium (erythrasma)	coral-red

Main systemic antifungals

- **Poliens:**
  - Amphotericine B (1956)
  - Nystatine (1951)
- **Miscellaneous:**
  - Flucytosine (1957)
  - Grizeofulvine (1958)
  - Potassium iodide (1811)
- **Azoles:**
  - Imidazole – Myconazole (1969); Ketokonazole (1977)
  - Triazoles – Itraconazole (1980); Fluconazole (1982)
- **Alilamines:**
  - Terbinafine
- **Morfolines:**
  - Amorolfine (1989)

Local treatment

1. Local antifungals: sulfur ointment 5-10%, iodine solution 2-5%, Castellani solution, methylen blue solution 2%, clotrimazole, miconazole, econazole, ketokonazole (nizoral), natamycin (pimafucin), ciclopiroxolamine (ciclopirox, batrafen), terbinafine (lamisil), bifonazole (micospor), naftifine (exoderil).
2. Keratolytics (in fungal hyperkeratosis): salicylic acid ointment 3-5-10-20%, Arievich ointment (lactic/salicylic acid), Whitefield ointment (benzoic/salicylic acid).
3. Keratoplastics (in fungal infiltrates): ichthyol ointment 10%, tar ointment 3-5%, naftalan ointment 3-5%.
4. Wet to dry lotions with antiseptics (in fungal exudates):

   d-Alibur sol., ethacridine lactate sol., potassium permanganate sol., furacilin sol., tannin sol.

ANTIMYCOTICS

	TOPICAL	ORAL	DERMATOPHYTES	YEASTS
gentian violet	+			+
Whitfield's ointment	+		+	+
tolnaftate	+		+	
undecylenic acid	+		+	
nystatin	+			+
natamycin	+			+
amphotericin B	+			+
griseofulvin		+	+	
miconazole	+		+	+
econazole	+		+	+
isoconazole	+		+	+
clotrimazole	+		+	+
ketoconazole	+	+	+	+
bifonazole	+		+	+
terconazole	+			+
itraconazole		+	+	+
fluconazole		+		+
terbinafine		+	+	