
In The Name Of GOD

Dermatophytoses

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Introduction

- Three genera of fungi:
  - *Microsporum*
  - *Trichophyton*
  - *Epidermophyton*
- Alike in physiology, morphology, and pathogenicity
- Unique ability to invade and multiply in keratinized tissue
- Ten species of dermatophyto
- described since ancient time
- But Sabouraud categorize and classified

DERMATOPHYTES ISOLATED WORLDWIDE		
		Thallus (macroscopic) appearance* and/or microscopic findings
Most common		
Trichophyton	*mentagrophytes* (previously *mentagrophytes* var. *mentagrophytes*)	Granular front, buff reverse; pencil-shaped macroconidia, clusters of round microconidia, spiral hyphae
	interdigitale (previously *mentagrophytes* var. *interdigitale*)	Downy front, buff reverse; see above
	rubrum	White wooly front, venous blood reverse; pencil-shaped macroconidia, teardrop-shaped microconidia
	tonsurans	Granular front, mahogany reverse; pencil-shaped macroconidia, microconidia of varying sizes
	verrucosum	Convoluted, cream to gray, compact; chains of chlamydospores at 37°C
	violaceum	Creamy, waxy, becomes violet
Microsporum	*canis*	White wooly front, orange reverse; multi-celled, spindle-shaped macroconidia with thick walls and rough surface
	ferrugineum	Folded red–orange (rust-colored) front
	gypseum	Cinnamon–tan granular front; multi-celled, cucumber-shaped macroconidia with thin walls
Epidermophyton	*floccosum*	Khaki green, suede to granular; beaver tail-shaped macroconidia; no microconidia

Table 77.6 Dermatophytes isolated worldwide.

DERMATOPHYTES ISOLATED WORLDWIDE		
		Thallus (macroscopic) appearance* and/or microscopic findings
Less common		
Trichophyton	*ajelloi*	Powdery surface, resembles *Microsporum* spp.
	concentricum	Glabrous colonies; antler-like hyphae
	equinum	Club-shaped macroconidia
	gourvilii	Waxy, pink to red front
	megninii	Pink, felt-like front with red reverse
	schoenleinii	Glabrous; antler- and nailhead-like hyphae; rat-tail-like macroconidia (media often fissured)
	simii	Club-shaped macroconidia in clusters
	soudanense	Yellow to apricot front with fringed border
	terrestre	Cream to yellow granular surface
	yaoundei	Glabrous, chocolate-brown front
Microsporum	*amazonicum*	Multi-celled, spindle-shaped, macroconidia with large inclusions
	audouinii	Flat, tan front with salmon reverse; pectinate (comb-like) hyphae
	cookei	Oval, thick-walled macroconidia
	equinum	One- to four-celled macroconidia resembling *M. canis*
	fulvum	Bullet-shaped macroconidia with spiral hyphae
	gallinae	Diffusable pink–red pigment
	nanum	Two-celled macroconidia
	persicolor	Pink to red front and reverse, resembles *T. mentagrophytes*
	praecox	Powdery front with yellow–orange reverse
	racemosum	Cream-colored powdery front
	vanbreuseghemii	Largest macroconidia
*On Sabouraud's agar.		

Table 77.6 Dermatophytes isolated worldwide. *Adapted from ref 85.*

Epidemiology

- Some are restricted geographically
  - *T. concentricum:* South America and equator
- Some are worldwide:
  - *Trichophyton rubrum*
- Change in geography:
  - Human travel and migration
  - Antifungal therapy
  - Socioeconomic status, occupation, air conditioning, and use of footwear, tropical environment

TYPES OF DERMATOPHYTES BASED ON MODE OF TRANSMISSION		
Category	**Mode of transmission**	**Typical clinical features**
Anthropophilic	Human to human	Mild to non-inflammatory, chronic
Zoophilic	Animal to human	Intense inflammation (pustules and vesicles possible), acute
Geophilic	Soil to human or animal	Moderate inflammation

Table 77.7 Types of dermatophytes based on mode of transmission.

Epidemiology…

- Tinea pedis, tinea cruris, and tinea unguium more in Men
- Most commonly post pubertal except tinea capitis
- Risk factors for infection in childhood
  - household exposure to tinea capitis or tinea pedis
  - Contaminated hats, brush, and shoes
  - Down syndrome
  - Chronic mucocutaneous candidiasis
  - Immunodeficiency disease
  - HIV

Pathogenesis

Fungal factors:

- Contact and adherence of infectious elements of fungus (arthroconidia) to skin
- Produce keratineases to break keratin and allow invasion and penetration to stratum corneum
- Mannans especially in *T. rubrum* decrease epidermal proliferation and reduce likelihood of fungus sloughed off before invasion
- Preference of cooler temperature at skin surface of fungus

Host factors:

- Protease inhibitor limit extent of invasion
- Sebum inhibitory effect on dermatophytes
- Macerated skin encourage invasion
- Serum factors that inhibit fungus growth (globulins, ferritin, metal chelators)
- Host immune response
- Skin disorders like ichthyoses that affect skin barrier function

Clinical features

Tinea corporis

- Dermatophytosis of trunk and extremities, except hair, nail, groin, palms and soles
- Restricted in stratum corneum of exposed skin
- T. rubrum most common
- T. mentagrophytes second

COMMON DERMATOPHYTES THAT CAUSE TINEA CORPORIS	
Dermatophyte	Clinical features
Anthropophilic	
Trichophyton rubrum	Commonly harbored by hair follicles; may produce concentric rings; can recur; causative organism in nodular perifolliculitis (Majocchi granuloma) and most common cause of tinea corporis
T. tonsurans	Commonly seen in adults who care for children with tinea capitis caused by this organism
Epidermophyton floccosum	Generally restricted to groin, feet; responsible for eczema marginatum
T. concentricum	Responsible for tinea imbricata; infections typically chronic
T. interdigitale (previously *T. mentagrophytes* var. *interdigitale*)	Causes interdigital tinea pedis, tinea cruris, and onychomycosis
Zoophilic	
T. mentagrophytes (previously *T. mentagrophytes* var. *mentagrophytes*)	May be associated with dermatophytid reaction; causes inflammatory tinea pedis and tinea barbae; associated with exposure to small mammals
Microsporum canis	Associated with pet exposure (cat or dog)
T. verrucosum	May mimic bacterial furunculosis; associated with exposure to cattle
Geophilic	
M. gypseum	Frequently associated with outdoor/ occupational exposure; lesions may be inflammatory or bullous

Table 77.8 Common dermatophytes that cause tinea corporis.

Tinea corporis…

- Transmission:
  - human-to-human autoinoculation (tinea capitis or pedis)
  - animal-to-human: domestic animals
  - soil-to-human

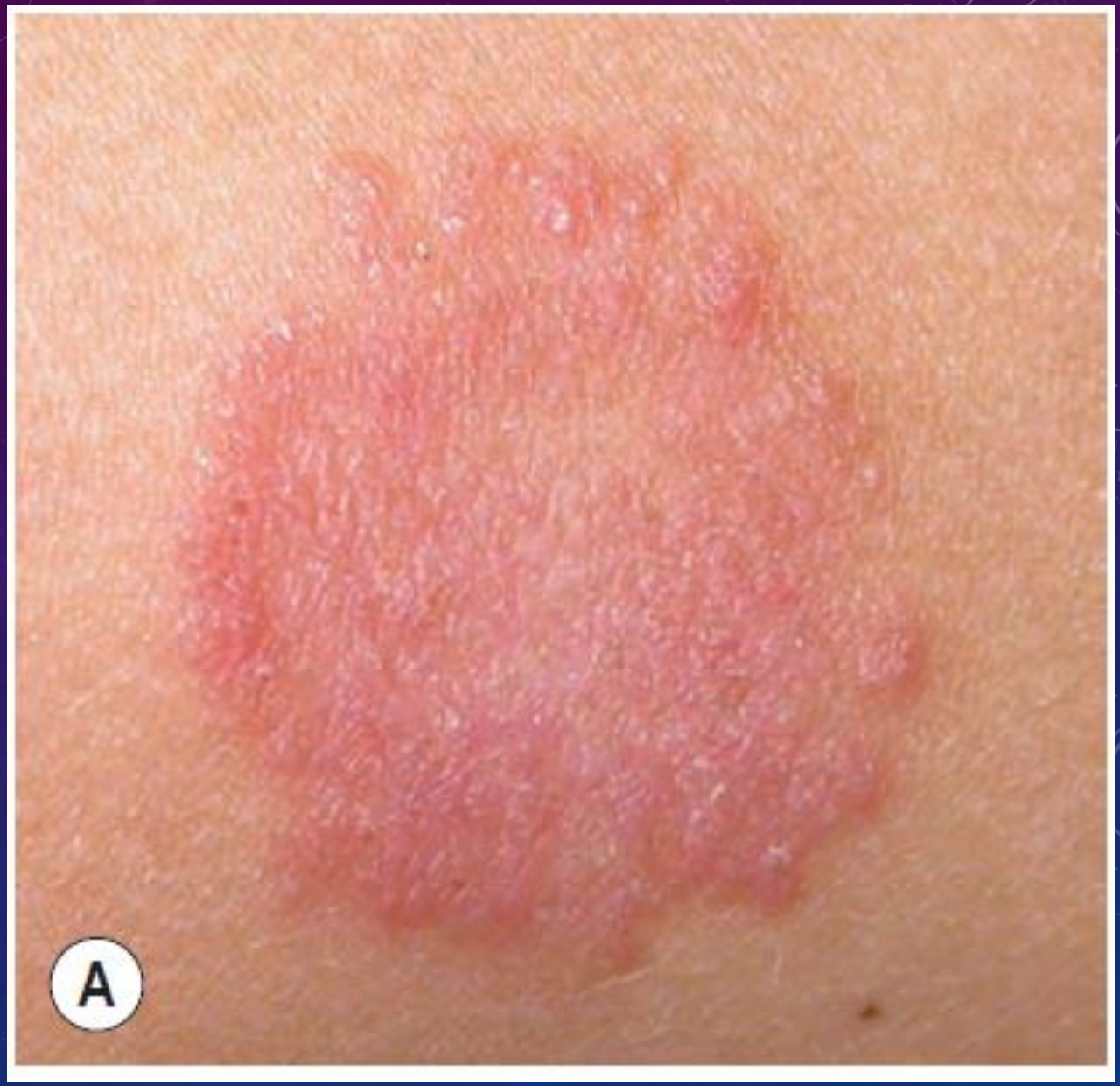
- Sources:
  - Occupational (military) and recreational exposure (gymnasiums, locker rooms, wrestling) and contact with contaminated furniture

Tinea corporis…

- Incubation: 1 - 3 weeks
- Typical form spreads centrifugally from a part of skin invasion with central clearing
  - Form annular, arcuate, circinate, concentric, and oval
  - Scale is present except in use of topical steroid (incognito)
  - Pustules of active border is suggestive
- Vesicular, granulomatous and verrucous sometimes
- Tinea profunda: excessive inflammatory response to dermatophyte, analogous to kerion

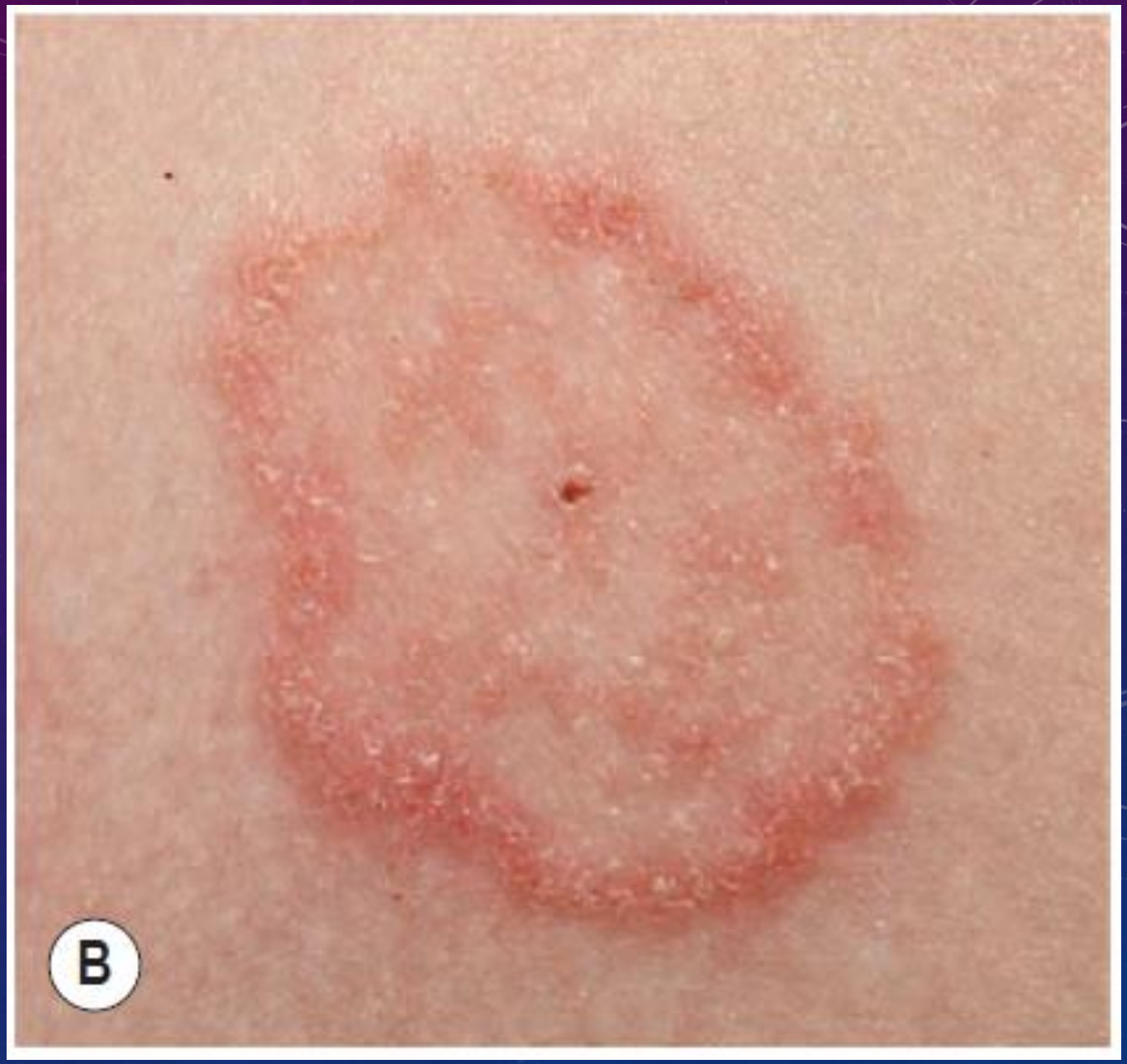
Tinea corporis…

- Nodular perifolliculitis:
  - Follicular papulopustules or granulomatous nodules deep folliculitis with disruption of follicular wall
  - Seen in women have tinea pedis or onychomycosis and shaving
- May be extensive and vegetative and prolonged granulomatous in immunosuppression
- *Tinea imbricata*
  - *T. concentricum*
  - *In south* America and equatorial
  - Chronic
  - Concentric annular ring like erythema gyratum repens
- Hair follicle serve as reservoirs for infection, hairier body area are more resistant
- Pruritic and burning



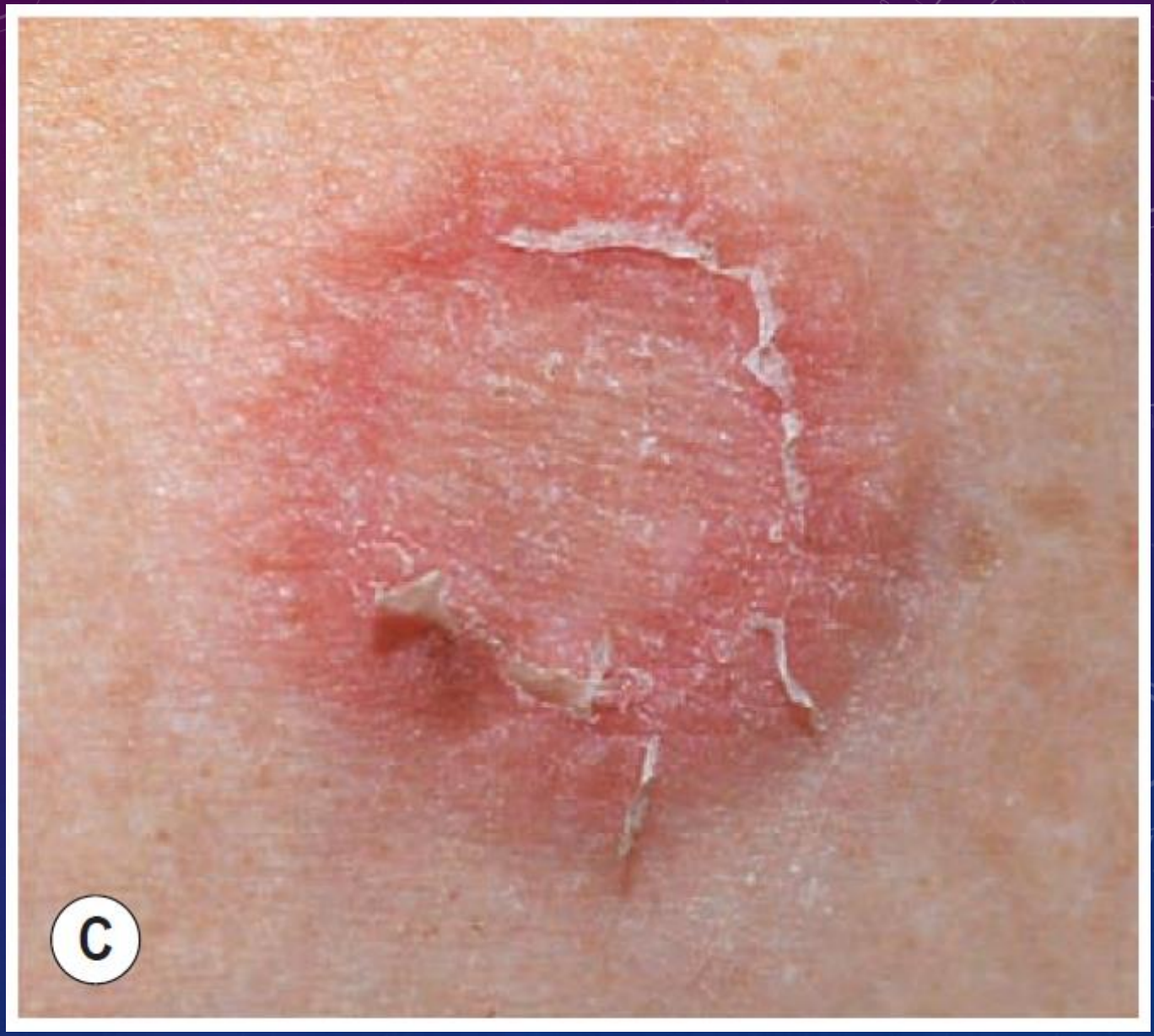
Tinea corporis

- **A .** There is a subtle annular configuration with a border composed of individual, slightly scaly papules.



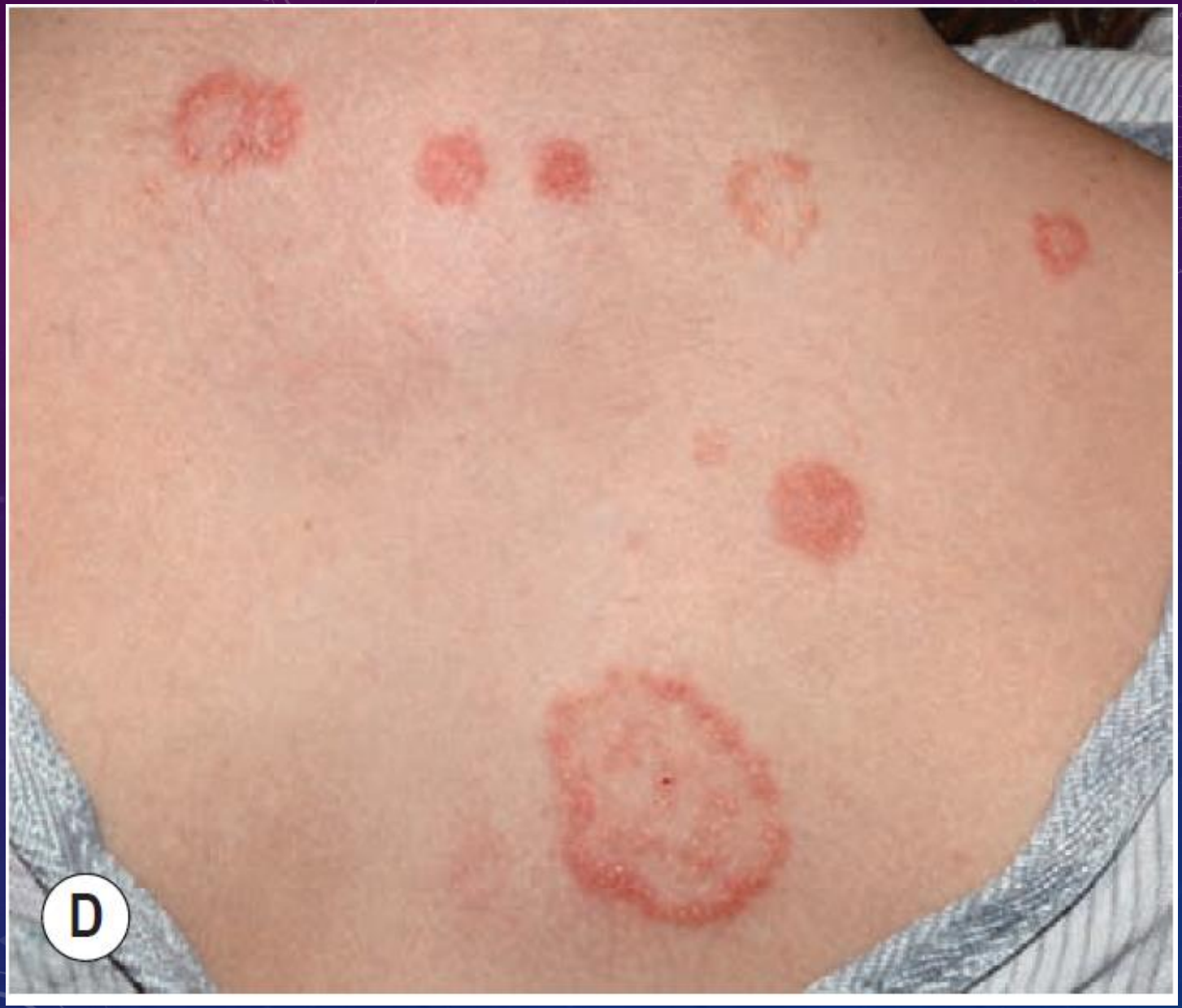
Tinea corporis

B. Classic annular lesion with a scaly raised border and central clearing.



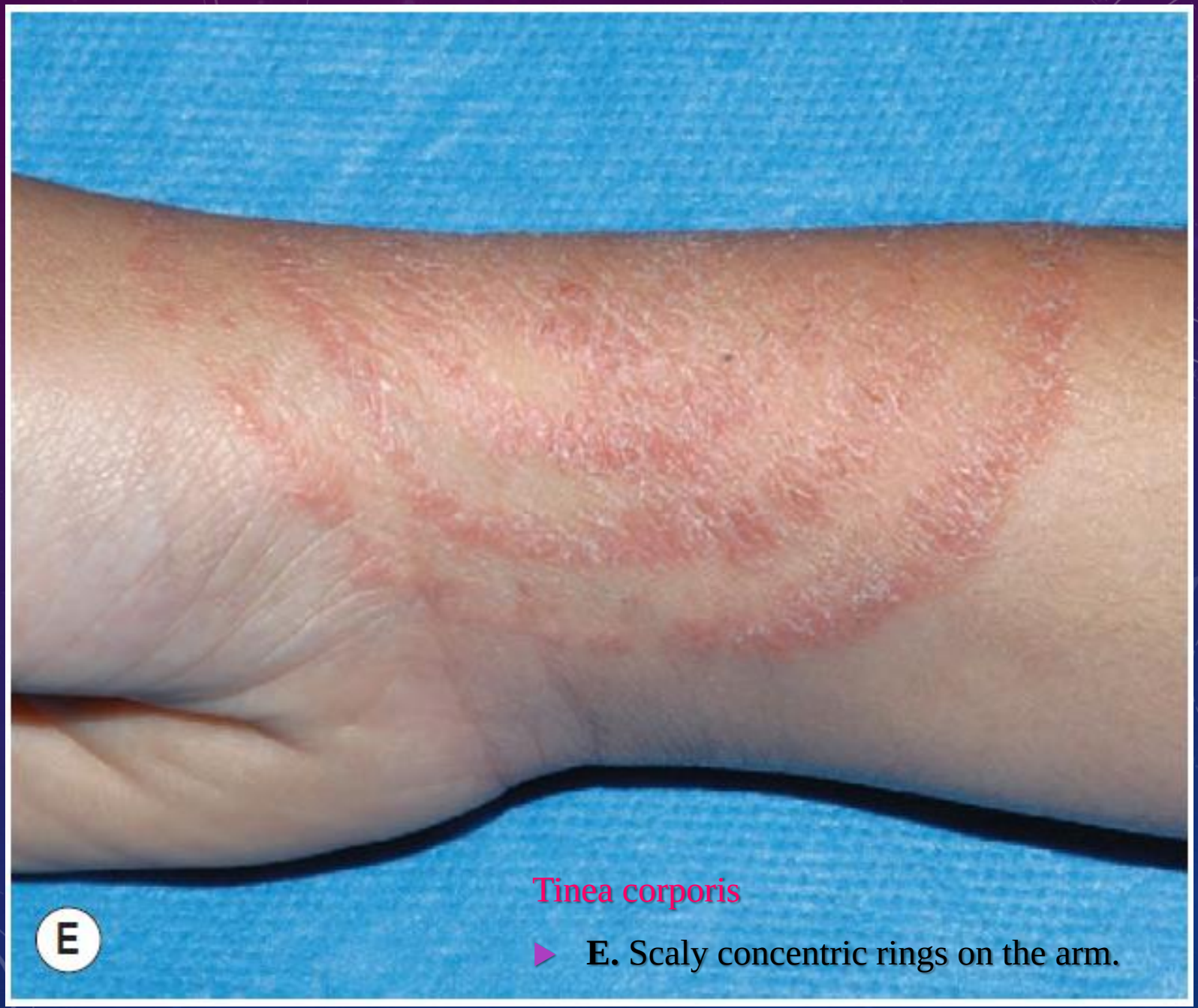
Tinea corporis.

- **C.** Annular lesion with trailing scale reminiscent of erythema annulare centrifugum.



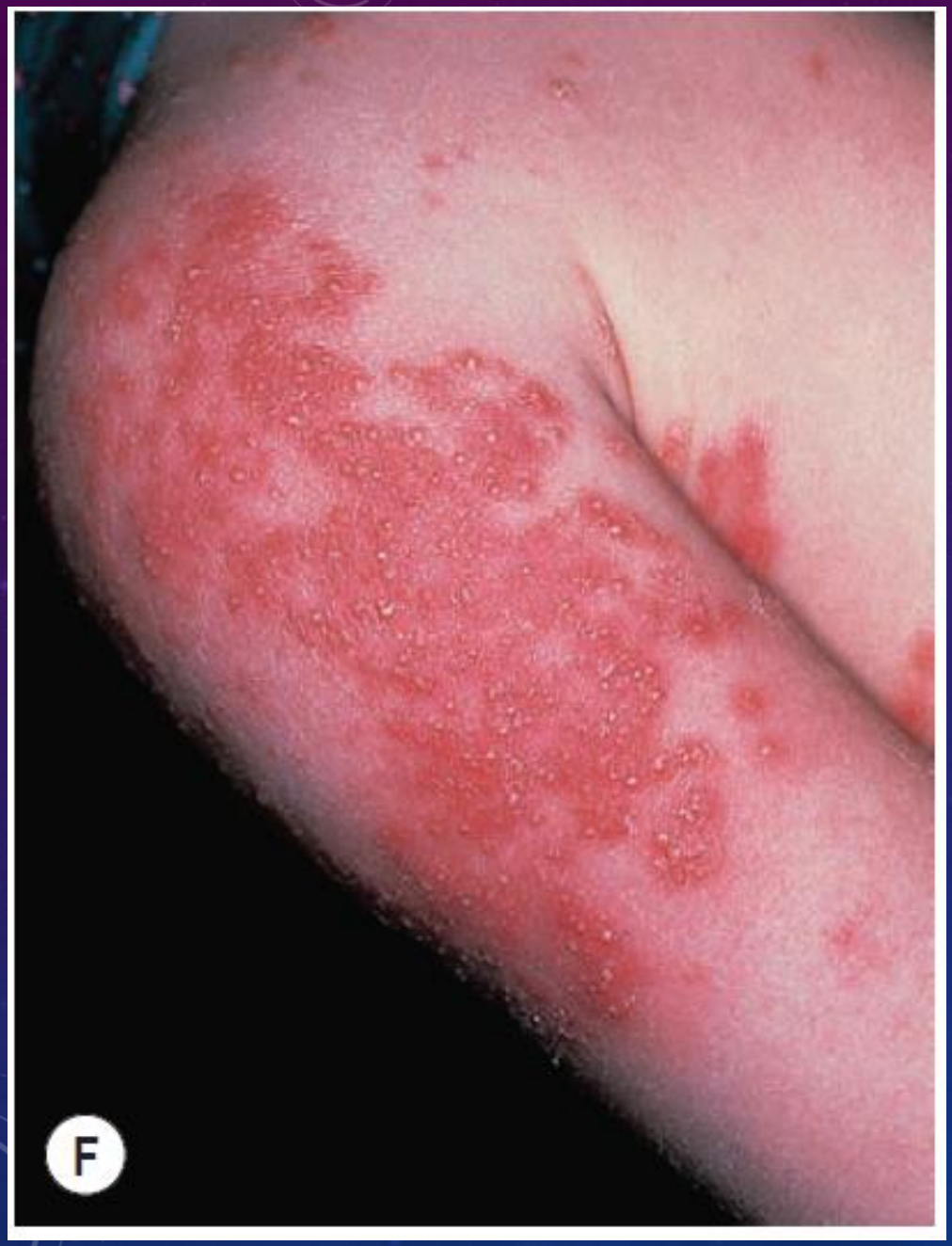
Tinea corporis.

D. Multiple annular and circinate lesions of various sizes on the upper back.



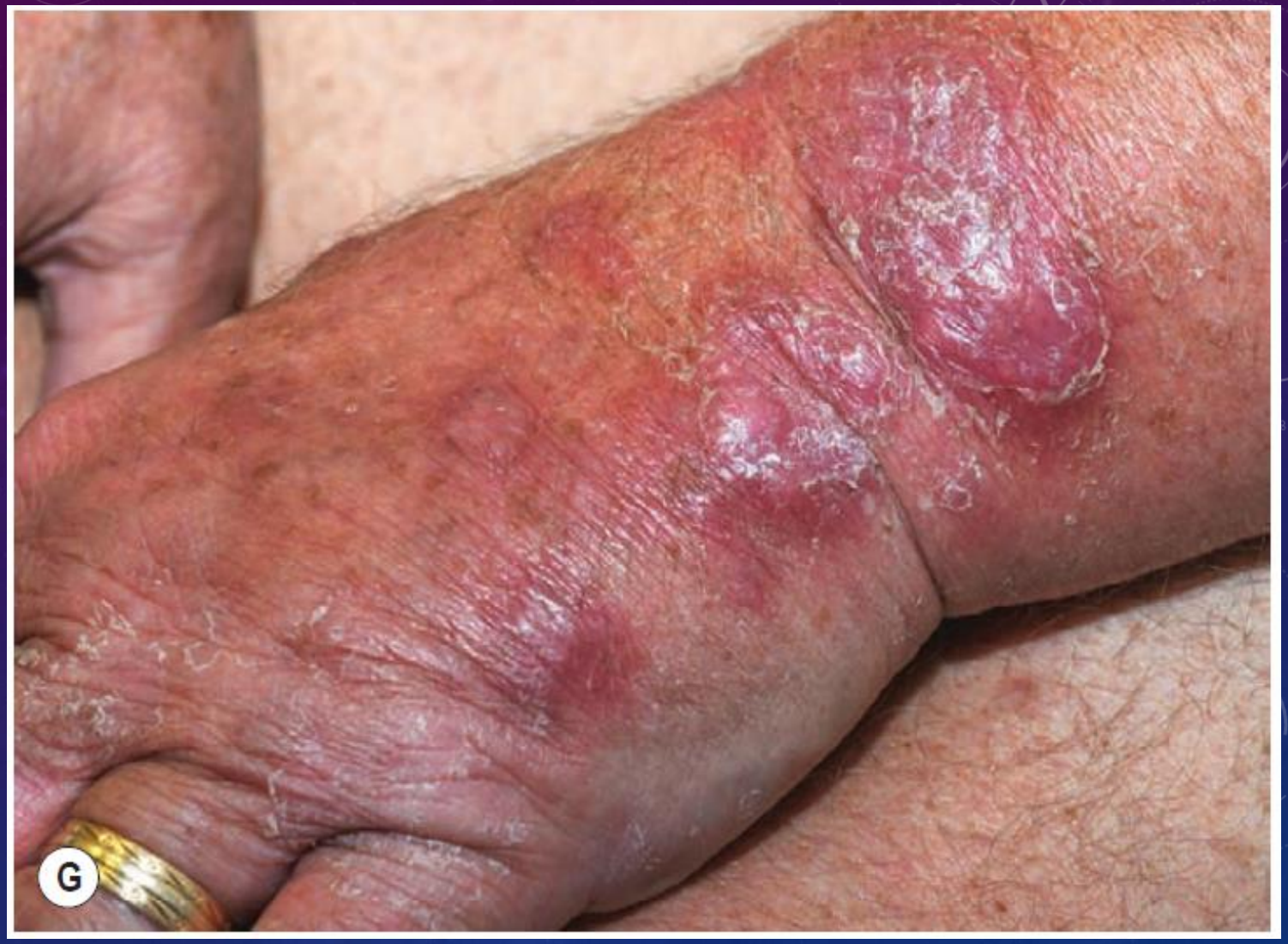
Tinea corporis

- **E.** Scaly concentric rings on the arm.



Tinea corporis.

- **F.** Pustules within multiple figurate lesions on the upper arm.



Tinea corporis.

- **G** Inflammatory nodules on the dorsal hand and a thick granulomatous plaque on the distal forearm (tinea profunda). There is associated scale, including on the digits, and a few of the papulonodules are follicular (Majocchi granuloma).

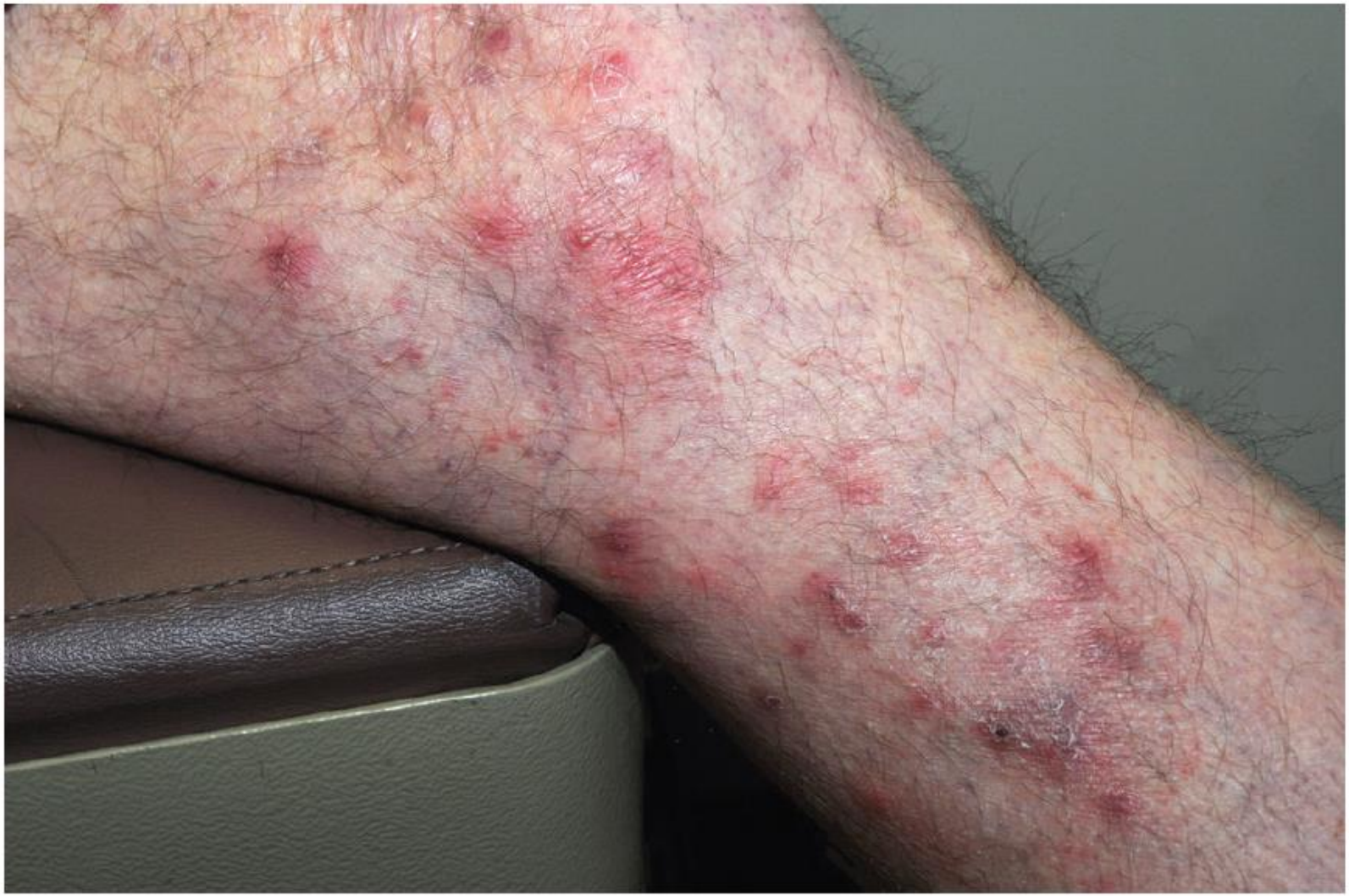


Fig. 77.7 Nodular perifolliculitis (Majocchi granuloma). Perifollicular inflammation and follicular pustules on the leg due to *Trichophyton rubrum*. A few of the lowermost papules have a granulomatous appearance. *Courtesy, Kalman Watsky, MD.*

Clinical features

Tinea cruris

- Inner aspect of upper thigh and inguinal area, extension to buttocks and abdomen
- Most common Epidermophyton floccosum, T. rubrum, and T. mentagrophytes
- Most in men
  - Scrotum provides a warm and moist environment
  - More likely to have tinea pedis and onychomycosis
- Obesity, Hyper hydrosis, having tinea pedis and contact to clothing of it
- Sharply demarcated with raised, erythematous, scaly advancing border with pustule or vesicles

Tinea cruris…

- Circinate and serpiginous mostly unilateral
- Anthropophilic species (T. rubrum) , tend to chronic with licheninfection
- Zoophilic form (T. mentagrophytes), cause acute infection and prominent inflammation with pustule and vesicle
- Scrotum spared , if involved candidiasis should be considered
- Measure for prevent of recurrences:
  - Loose clothing, drying thoroughly after bath, use topical powders, weight reduction, laundering contaminated clothing and treating tinea pedis

TINEA CRURIS: COMMON CAUSATIVE PATHOGENS	
Dermatophyte	**Clinical features**
Trichophyton rubrum	• Most common cause of tinea cruris • Infection tends to be chronic • Fungus not viable in scale (e.g. on furniture, rugs, linens) for long periods of time • Frequent extension to buttocks, waist, and thighs
Epidermophyton floccosum	• Commonly associated with "epidemics" of tinea cruris in locker rooms or dormitories • Infection is acute (rarely chronic) • Arthroconidia are viable in scale (e.g. on furniture, rugs, linens) for long periods of time • Infection rarely extends beyond groin region • Causative agent of "eczema marginatum" (well-demarcated borders with multiple small vesicles or, sometimes, vesiculopustules)
T. mentagrophytes (previously *T. mentagrophytes* var. *mentagrophytes*)	• Infection tends to be more severe and acute, with intense inflammation and pustule formation • May rapidly spread to the trunk and lower extremities, causing a severe inflammatory condition • Often acquired from animal dander

Table 77.10 Tinea cruris: common causative pathogens.

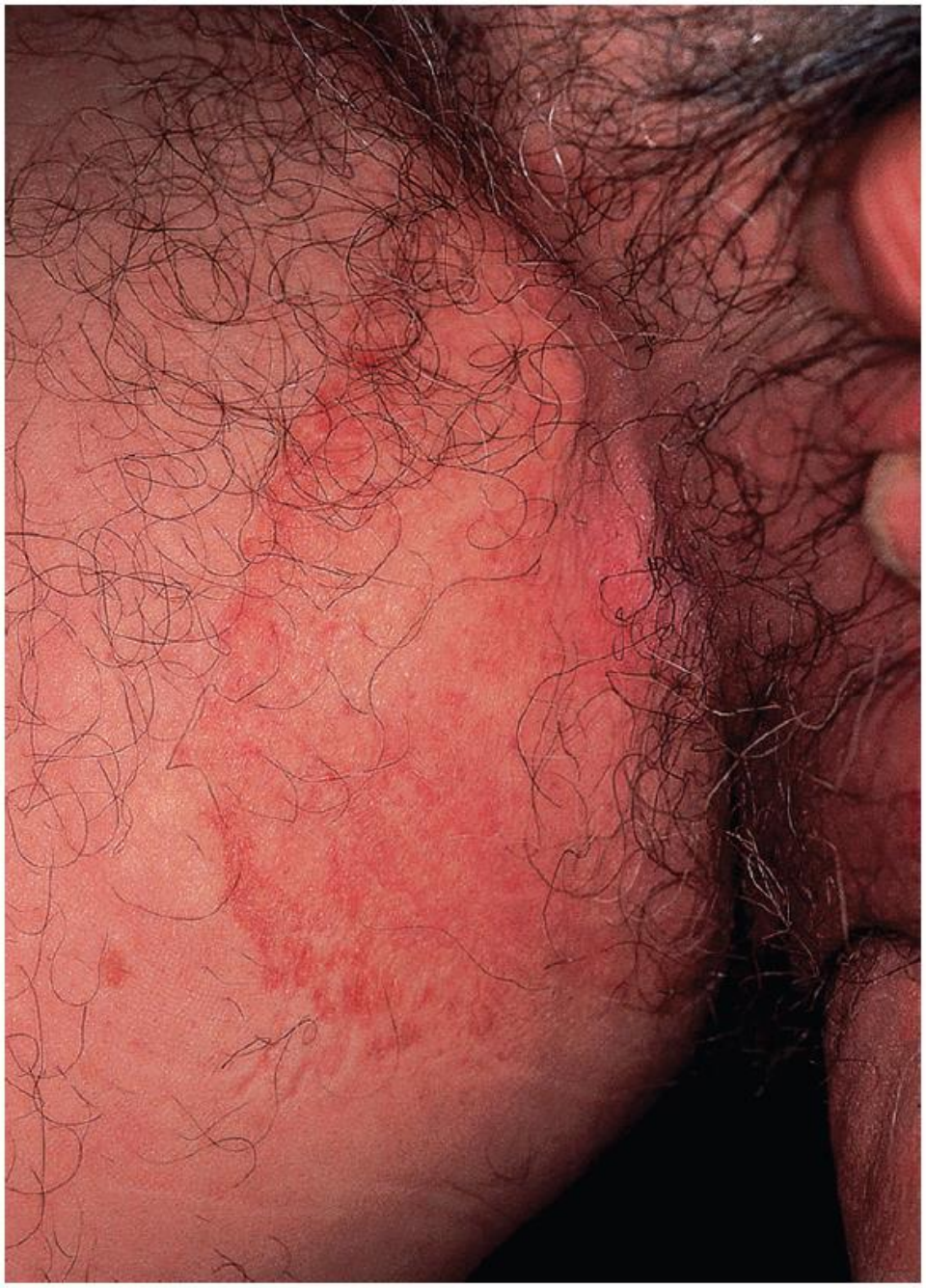


Fig. 77.8 Tinea cruris. A thin, "broken-up" erythematous plaque with an arciform papular border on the upper inner thigh.

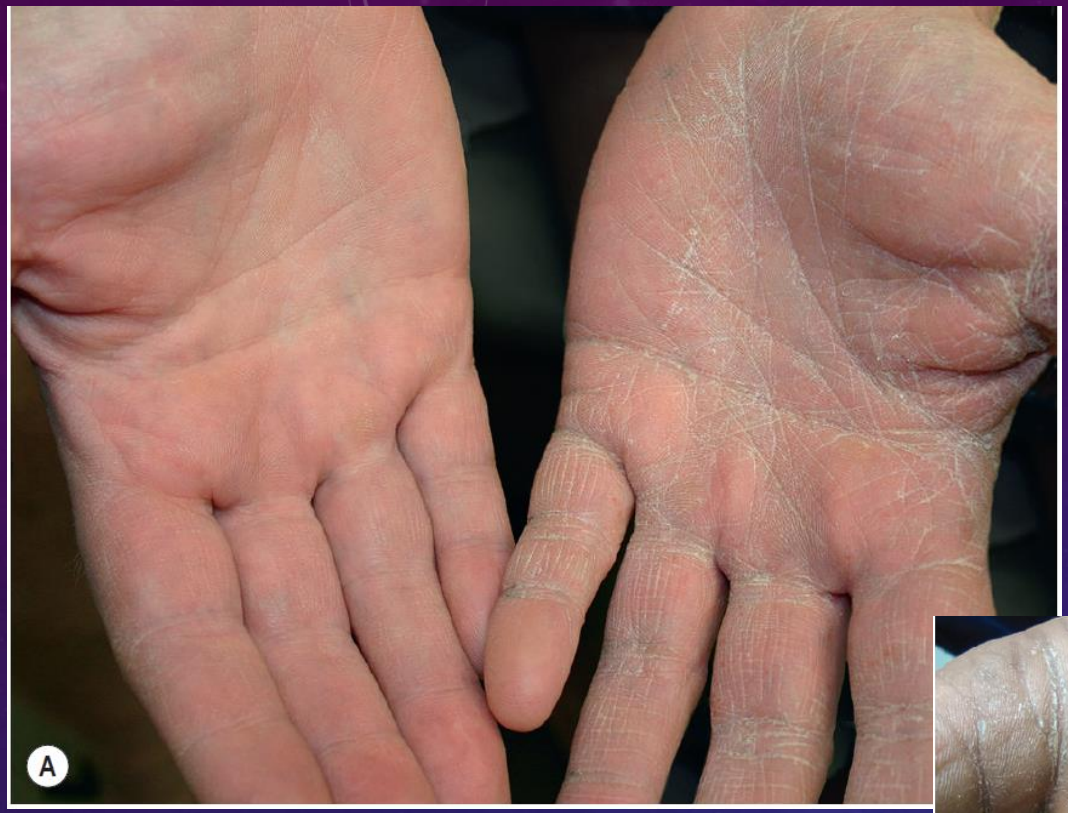
Clinical features

Tinea manuum

- Infection of palm and interdigital spaces are distinct tinea manuum
- Dorsal aspect of hand involvement is part of tinea corporis
- Because of lack of sebaceous glands of palm
- T. rubrum, T. mentagrophytes, and E. floccosum
- Two non dermatophyte fungi
  - *Neoscytalidium dimidiatum*
  - *N. Hyalinum*
- Moccasin-type tinea pedis is present and similar in chronicity and Hyperkeratosis

Tinea manuum…

- Non-inflammatory and unilateral (two feet and one hand)
- Hyperkeratosis of palm, digit, and creases (not responding to emollient)
- Tinea unguium of involved hand but not all finger
- Other presentations: exfoliative, vesicular, and papular
- Differential diagnosis
  - Dermatophytid reaction, psoriasis and dermatitis



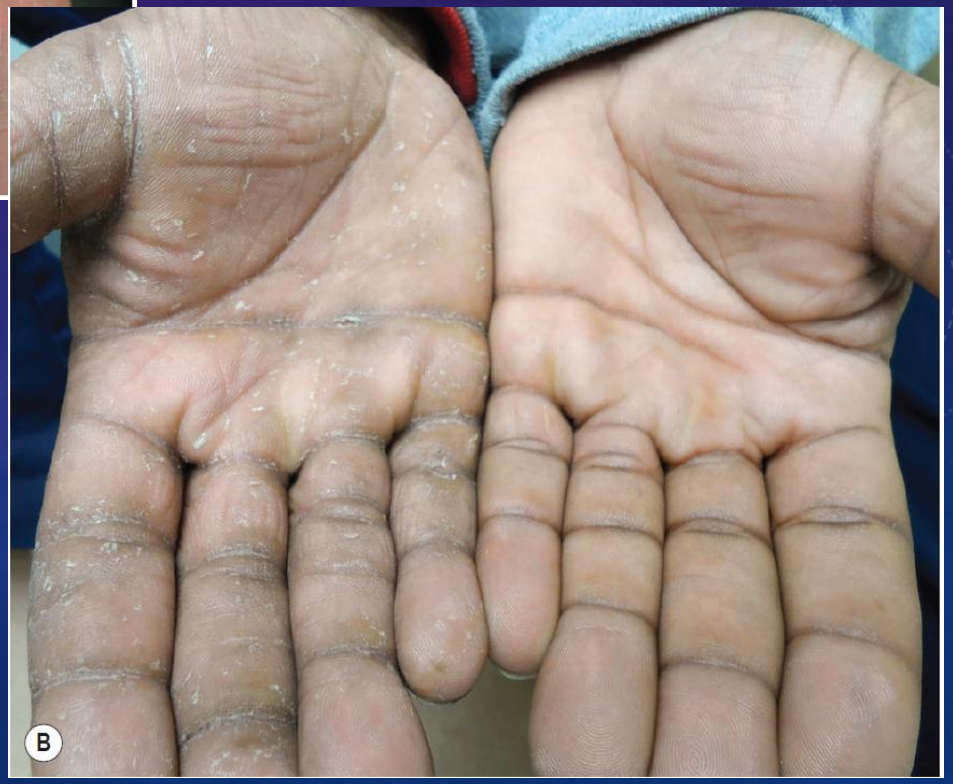


Fig. 77.9 Tinea manuum.
A. Diffuse scaling of the palm of one hand, with accentuation in the creases.
B. Multiple collarettes of scale reminiscent of keratolysis exfoliativa on one palm.

Clinical features

Tinea barbae

- Bearded areas face and neck of men
- Acquired from animal and zoophilic
- Commonly T. mentagrophytes and T. verrucosum
- Microsporum canis and T. rubrum uncommon
- *T. schoenleinii, T. violaceum*, and *T. megninii* are endemic in some area

Tinea barbae…

- Incidence lower with use of disposable razors and disinfectants
- First form:
  - Severe and intense inflammation and multiple follicular pustules
  - Abscesses, sinus tracts, bacterial superinfection, kerion-like boggy plaque with constitutional symptoms like malaise fever lymphadenopathy and scarring alopecia
- Second form:
  - Mostly T. rubrum, superficial, less inflammatory, like tinea corporis
  - Reversible Alopecia

Tinea barbae…

- Differential diagnosis
  - Bacterial folliculitis, viral (herpes simplex & zoster), acne, cervicofacial actinomycosis, and dental sinus

- Spontaneous resolution when fall out all infected hairs

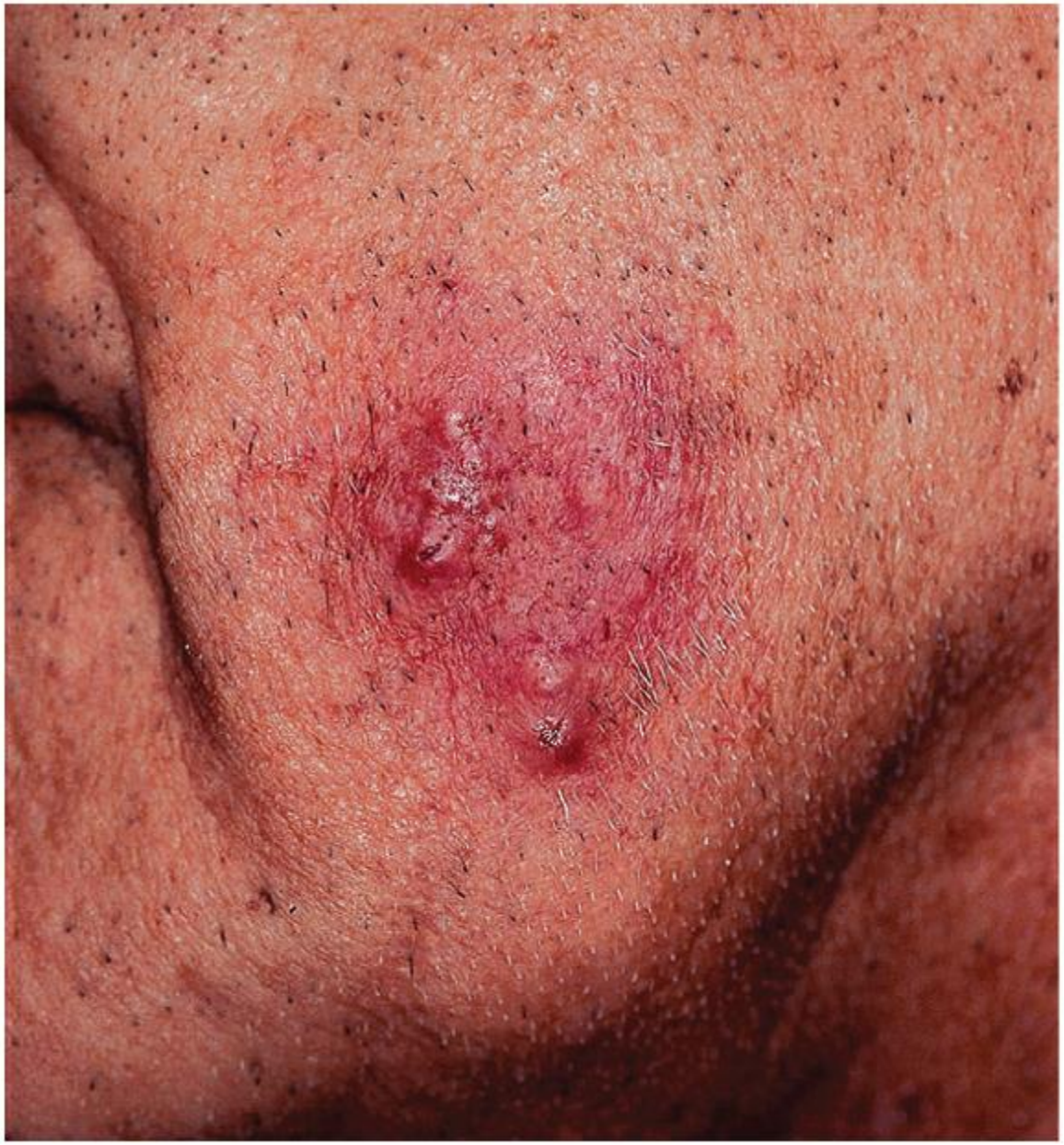
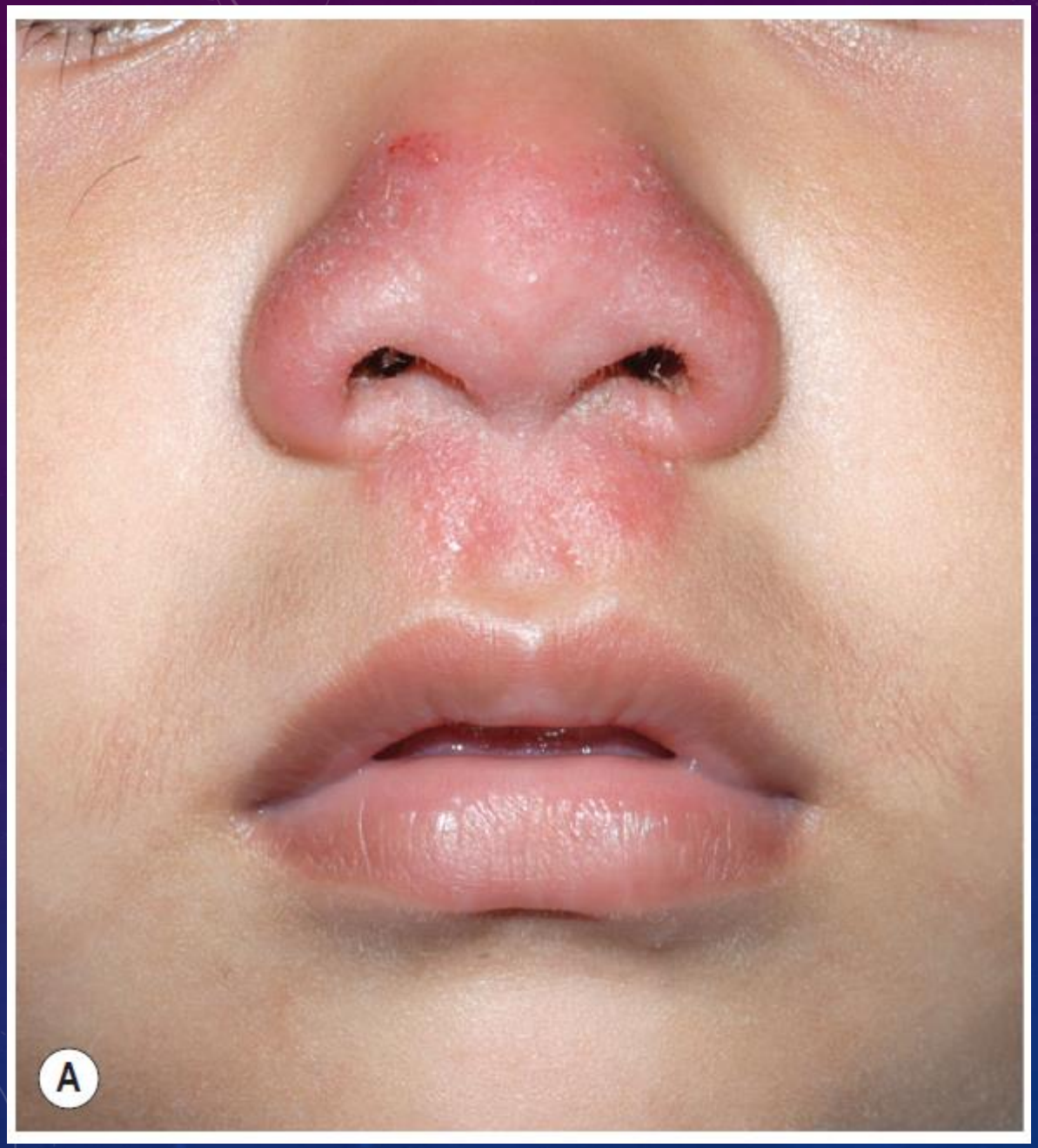


Fig. 77.10 Superficial form of tinea barbae due to *Trichophyton rubrum*. Several follicular pustules are evident.
Courtesy, Jean L Bolognia, MD.

Clinical features

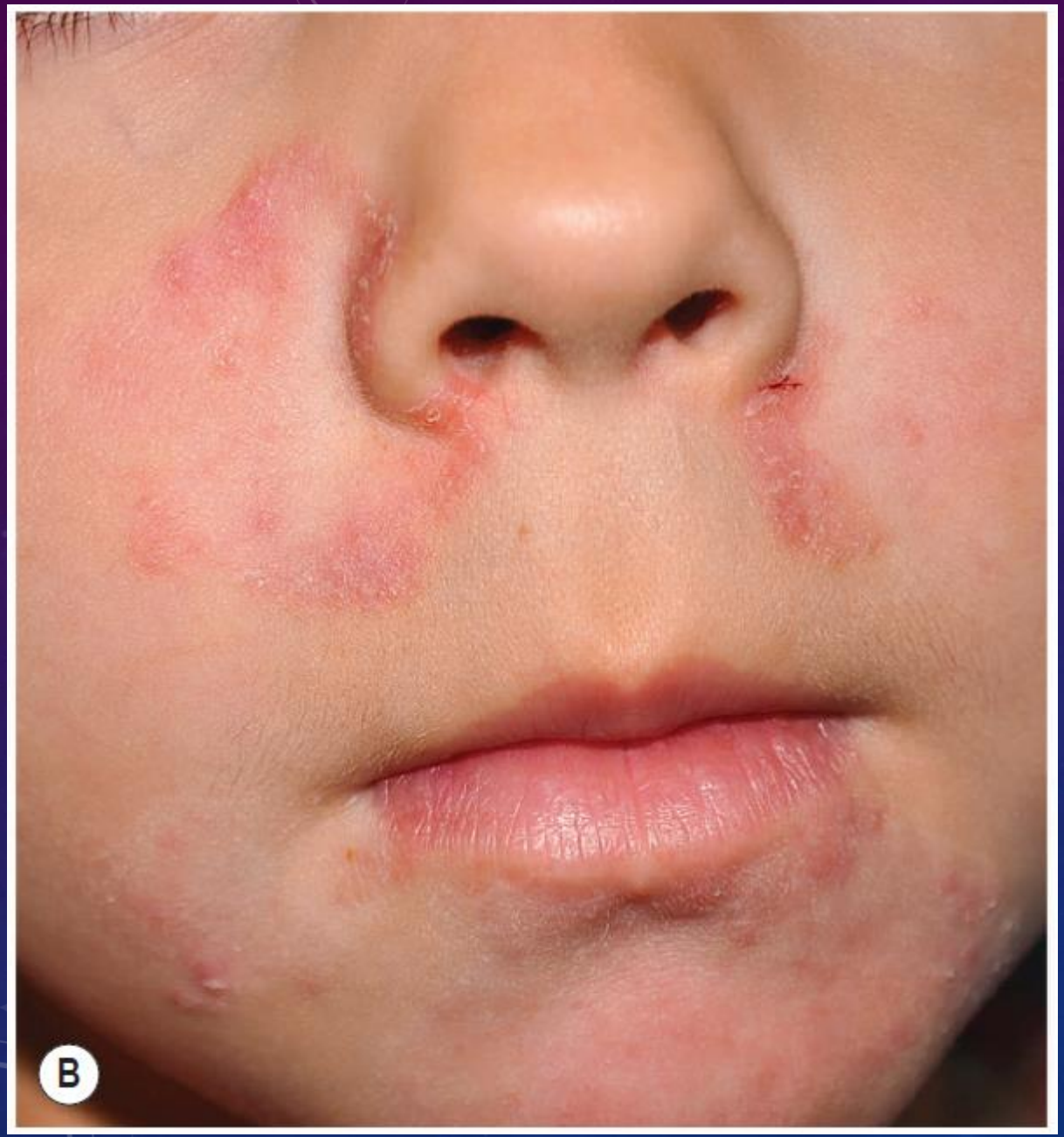
Tinea faciei

- Some have classic features
- Others more difficult to diagnose



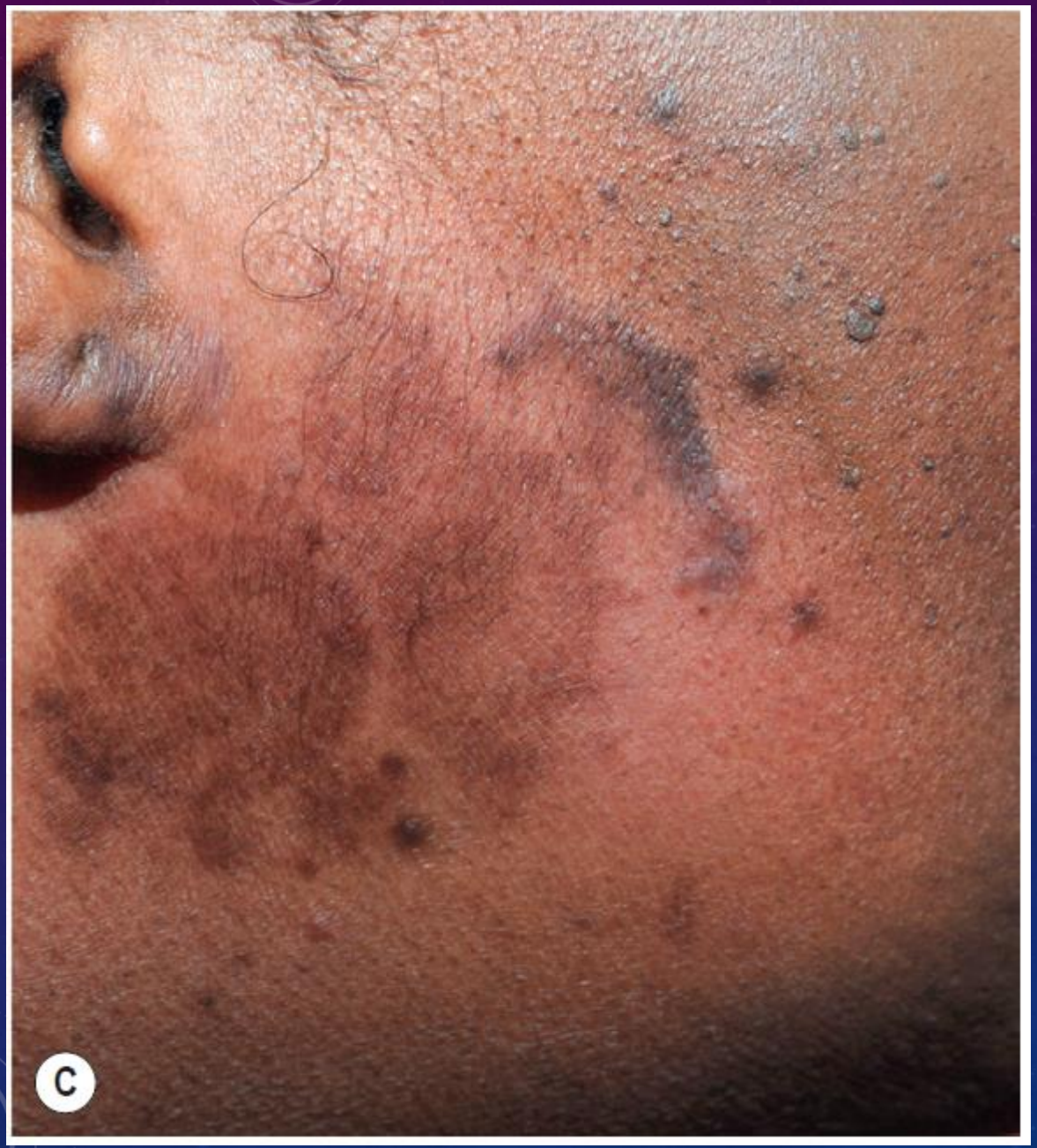
Tinea faciei

- **A** Erythema and scale on the nose and philtrum of a young child. The location and lack of central clearing may lead to the misdiagnosis of dermatitis with secondary impetiginization.



Tinea faciei

- **B** Child with pink papules, a few tiny pustules, and thin annular and arcuate scaly plaques in a perinasal and perioral distribution. These clinical findings could be mistaken for periorificial dermatitis.



Tinea faciei

- **C.** Hyperpigmented lesions with subtle arcuate and annular configurations in a woman with darkly pigmented skin. There is minimal scale following the use of topical corticosteroids (“tinea incognito”). The clue to the application of topical corticosteroids is the relative hypopigmentation as compared with the more medial cheek.

Clinical features

Tinea capitis

- Common in children
- In US & Europe *Trichophyton tonsurans* and *Microsporum canis 1st & 2end* , Some countries *M. canis or T. violaceum is* common cause
- Dermoscopy: “comma”, “corkscrew”, and dystrophic broken hairs
- Posterior cervical and posterior auricular lymphadenopathy
- Factor in severity of tinea
  - Host immune response
  - pathogenicity of organism
- Range from non-inflammatory scaling like seborrheic dermatitis to severe pustular reaction with alopecia
- Alopecia with or without scale is most common form (focal or entire scalp)

Tinea capitis…

kerion form

- Advanced disease and exaggerated host response
- Boggy purulent plaque with abscess formation and alopecia
- Systemically ill with extensive lymphadenopathy
- Hair usually return, but the longer infection more likely alopecia persist
- Misdiagnose as bacterial abscess and treated with antibiotics and incision
  - Worsen and increase likelihood of scarring alopecia

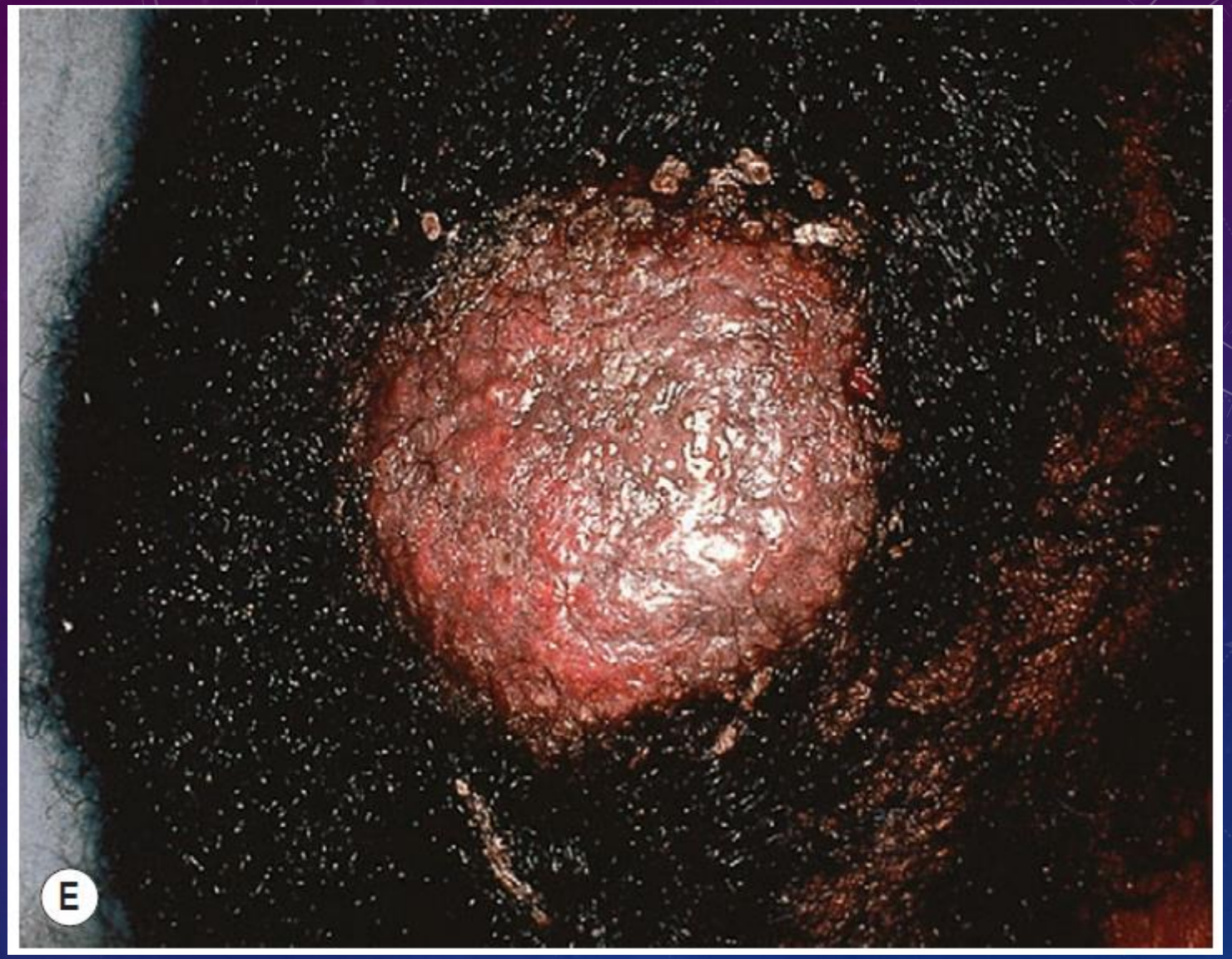


Fig. 77.12 Tinea capitis. The range of clinical presentations of tinea capitis due to *Trichophyton tonsurans*, from mild scalp scaling (**A**) to patchy alopecia with black dots (**B**) or scale (**C**) to large areas of alopecia with pustules and scale-crust (**D**). ***Kerion formation due to T. tonsurans (E) .*** Microscopic examination of involved hairs demonstrates an endothrix pattern (KOH–chlorazol black stain) **(F)**. Histologic examination shows arthroconidia and hyphae within hair shafts to the level of Adamson's fringe (limit of the zone of keratinization; inset) (**G)**.

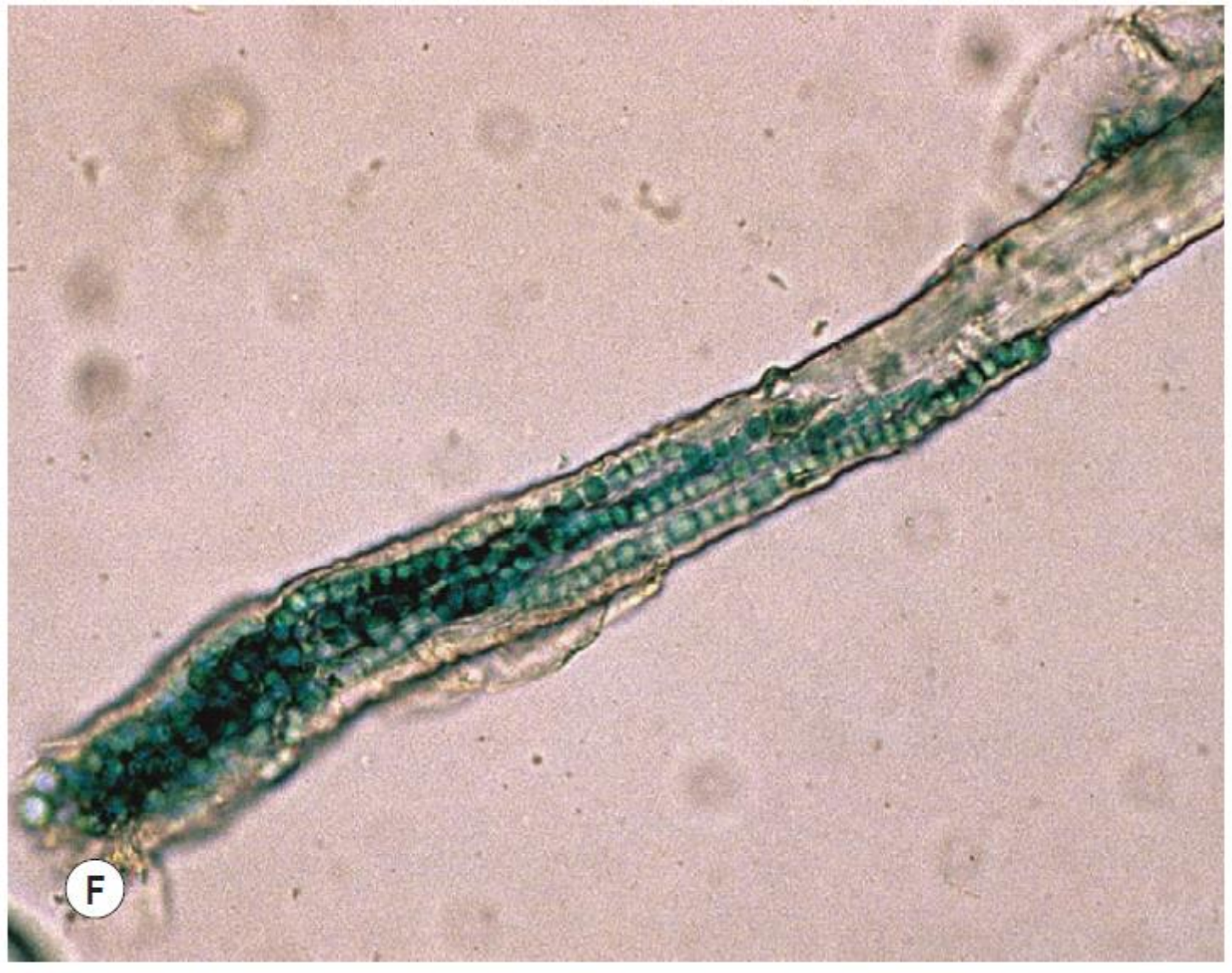
Tinea capitis…

carrier state

- *Due to T. tonsurans,* no sign in scalp only positive culture
- Typically occur in adults exposed to infected children
- Contagious and should treat with antifungal

Tinea capitis…

- Three Patterns of Infection:
  1) Endothrix
     - Anthropophilic fungi, *Trichophyton* , non-fluorescent, arthroconidia within hair shaft
     - Scaling to “black dots” with patch alopecia and kerion
     - *T. tonsurans* and *T. violaceum* are important causes
  2) Ectothrix
     - Arthroconidia formed from fragmented hyphae outside hair shaft
     - Cuticle destruction, fluorescent (Microsporum) or non-fluorescent (Trichophyton)
     - Patchy, scaly alopecia to kerion



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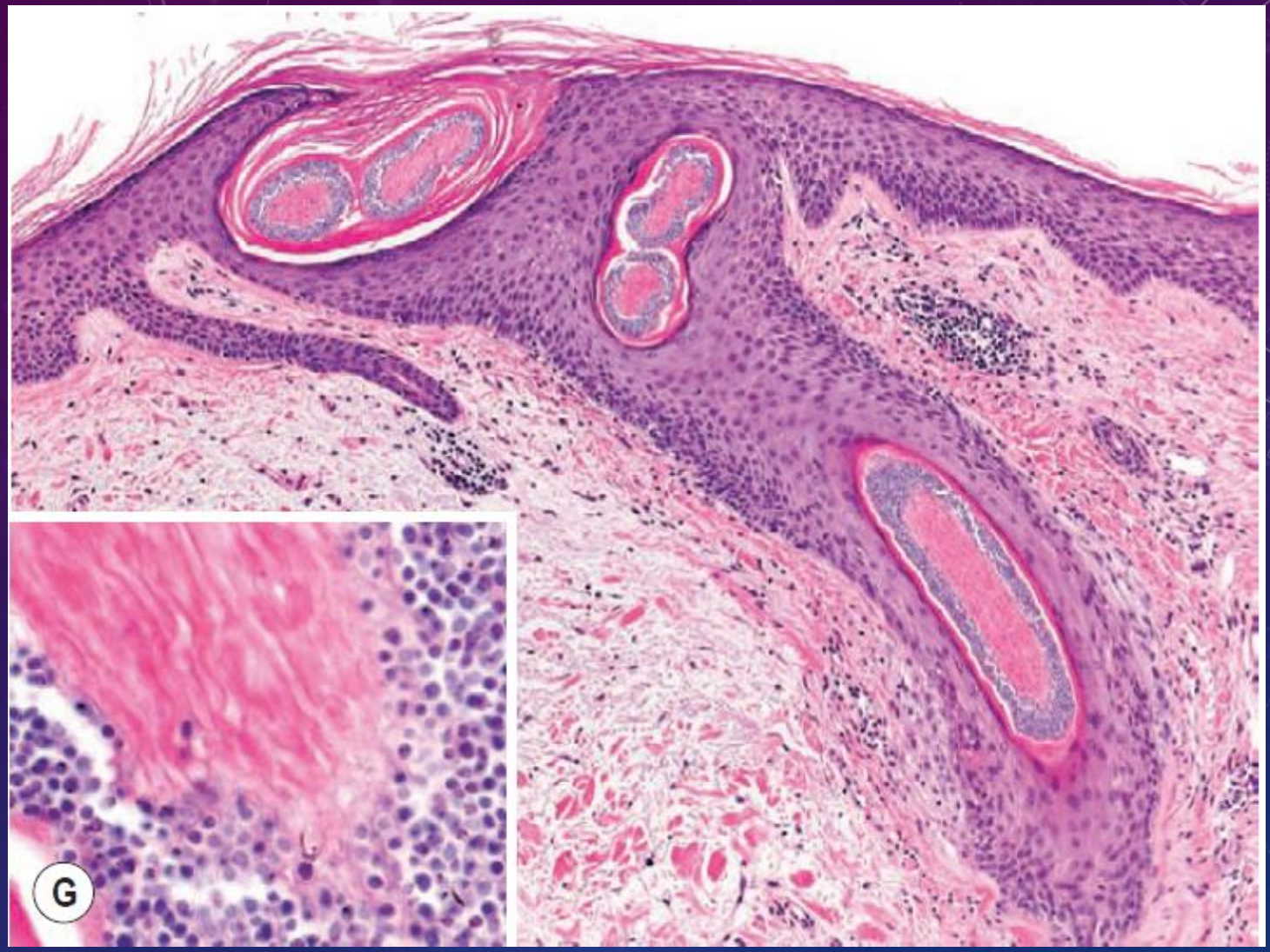

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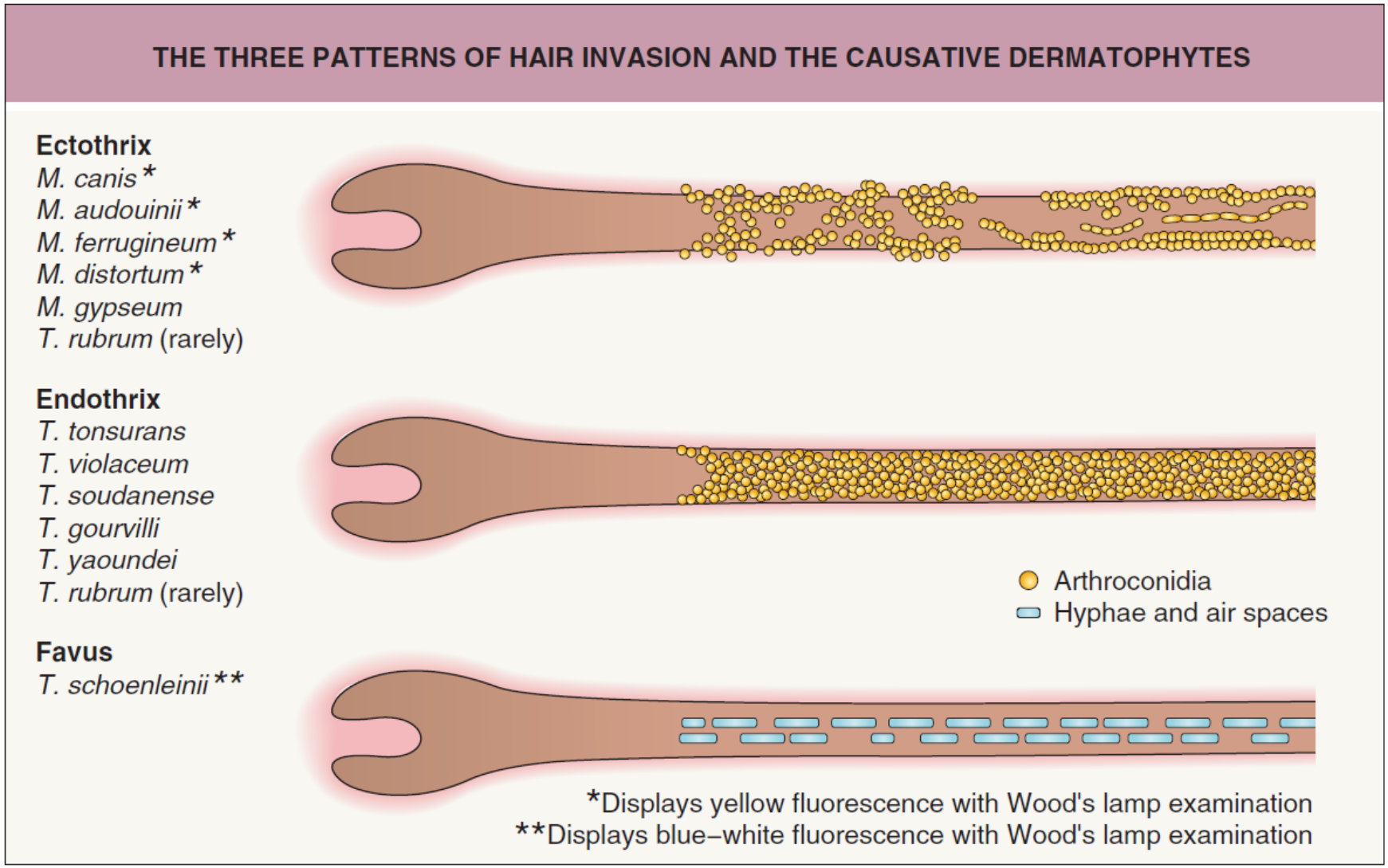


Fig. 77.13 The three patterns of hair invasion and the causative dermatophytes.

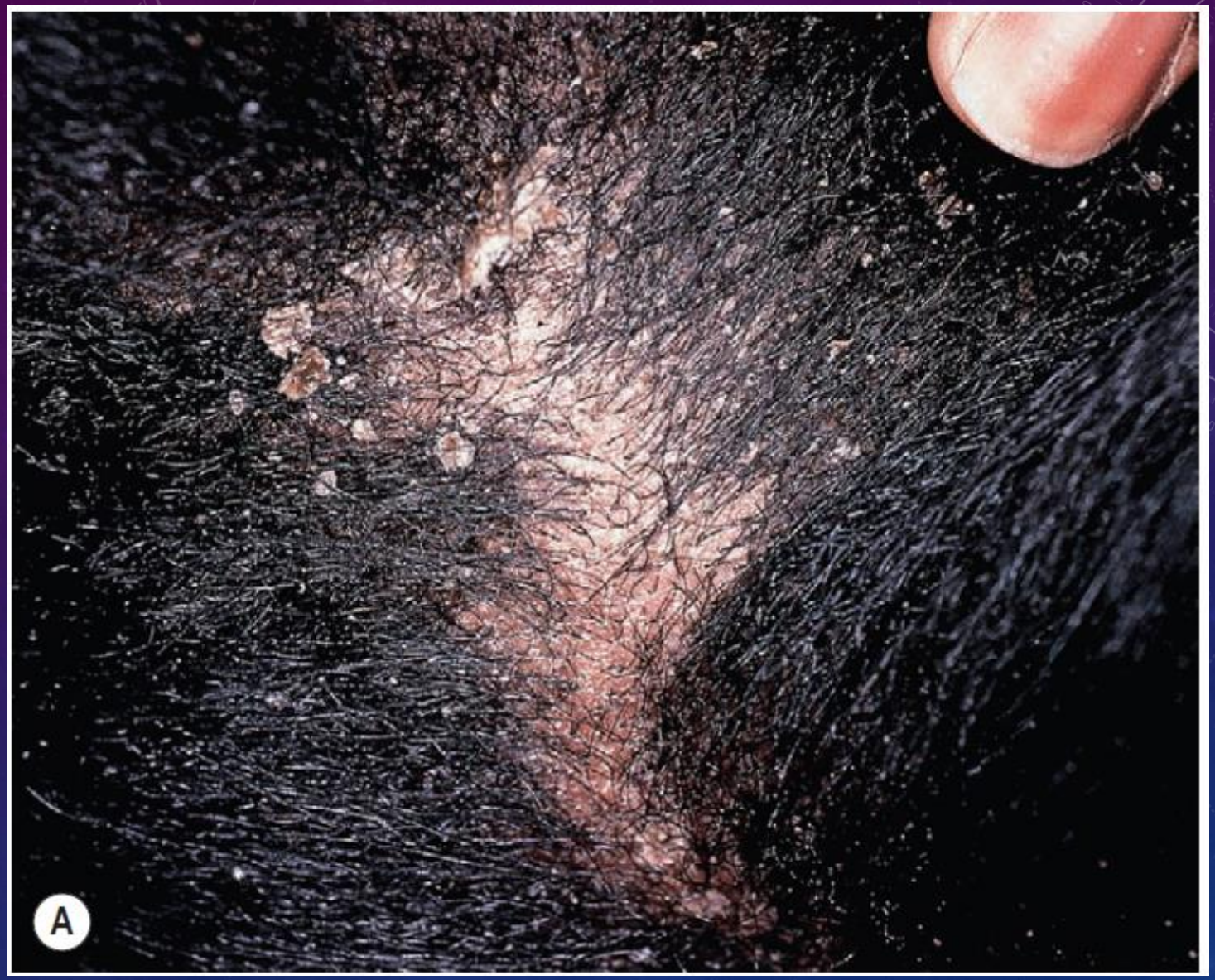


Fig. 77.12 Tinea capitis. ***The range of clinical presentations of tinea capitis due to Trichophyton tonsurans, from mild scalp scaling (A)*** to patchy alopecia with black dots (**B**) or scale (**C**) to large areas of alopecia with pustules and scale-crust (**D**). **E** Kerion formation due to *T. tonsurans.* **F** Microscopic examination of involved hairs demonstrates an endothrix pattern (KOH–chlorazol black stain). **G** Histologic examination shows arthroconidia and hyphae within hair shafts to the level of Adamson's fringe (limit of the zone of keratinization; inset).

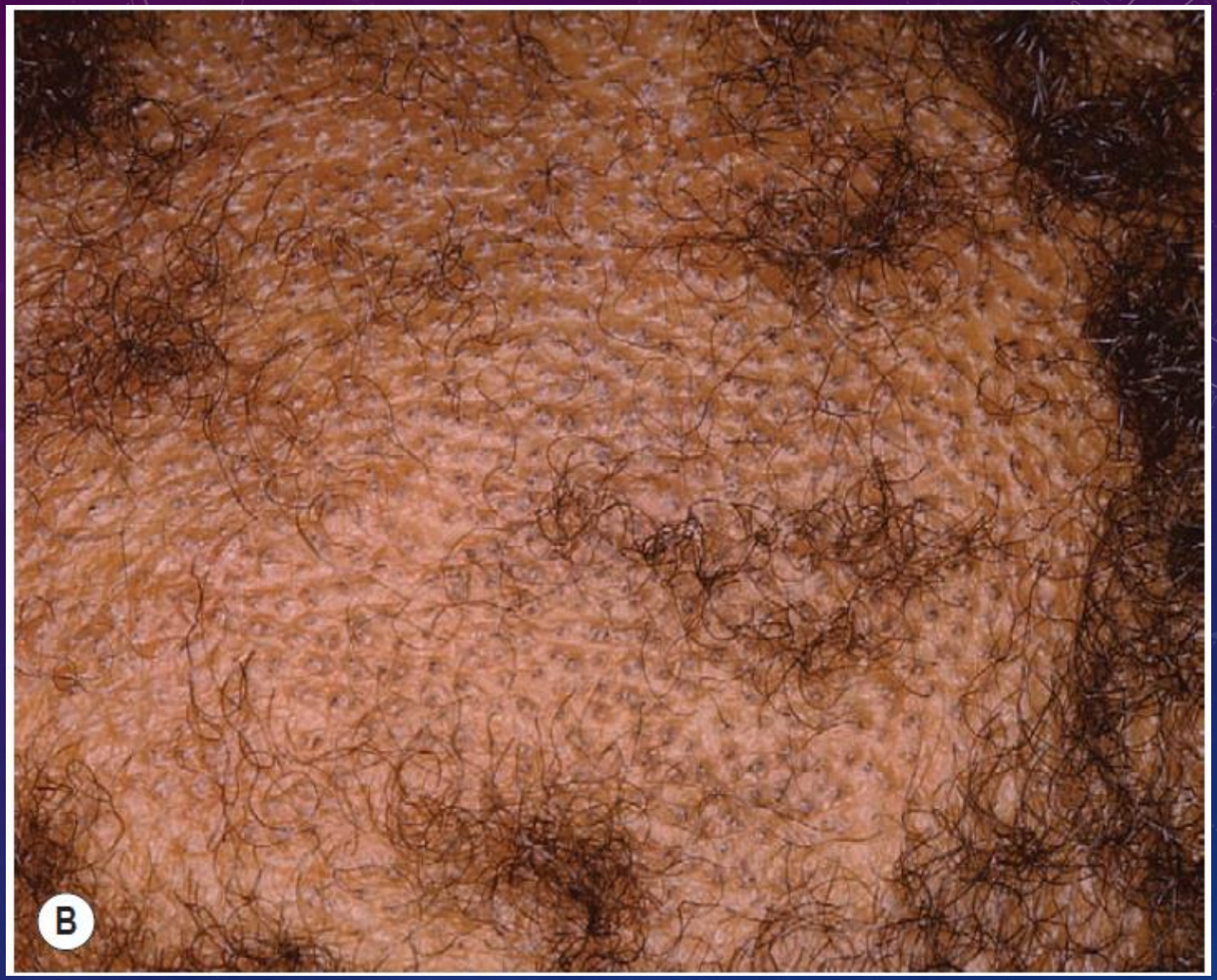
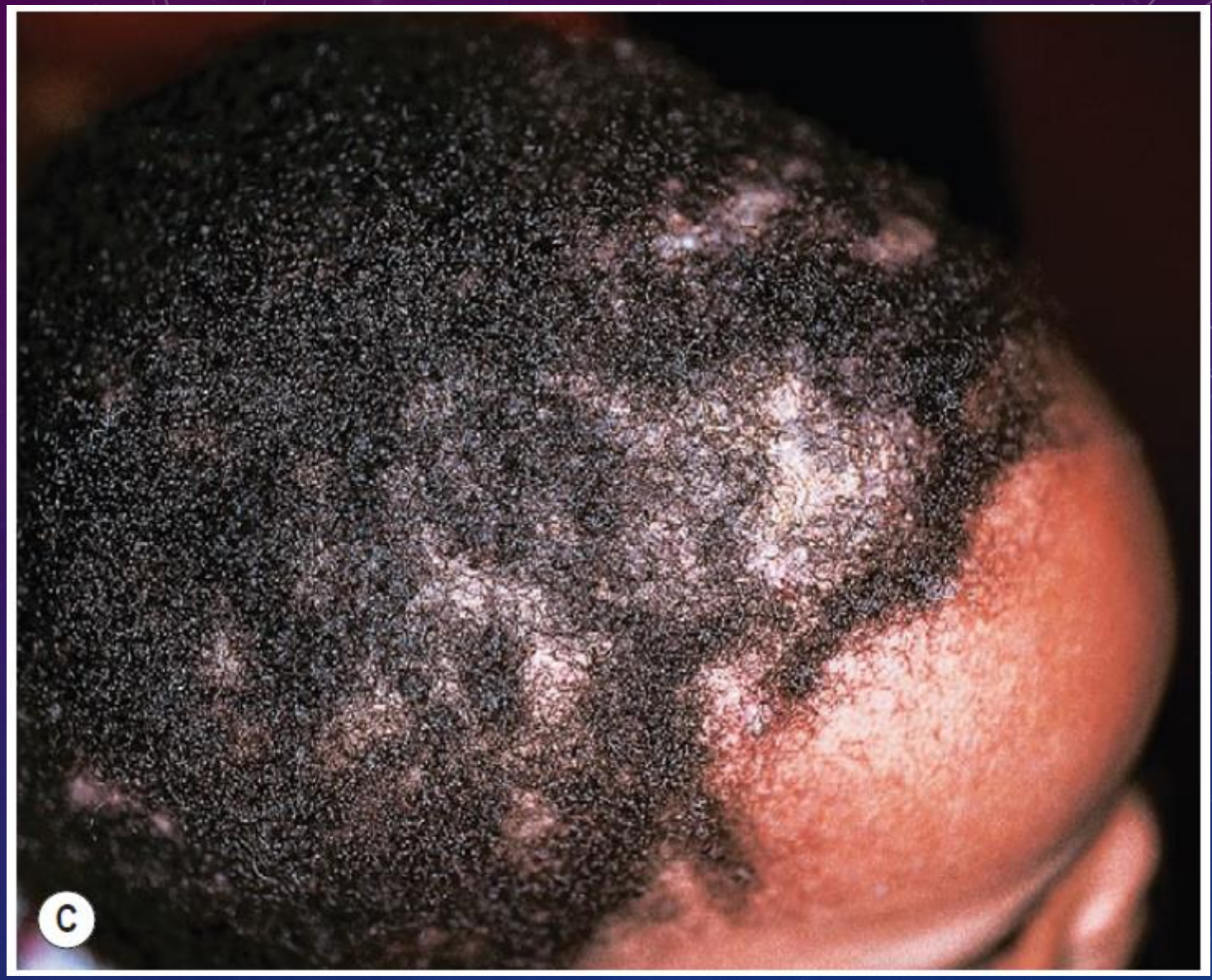


Fig. 77.12 Tinea capitis. The range of clinical presentations of tinea capitis due to *Trichophyton tonsurans*, from mild scalp scaling (**A**) ***to patchy alopecia with black dots (B)*** or scale (**C**) to large areas of alopecia with pustules and scale-crust (**D**). **E** Kerion formation due to *T. tonsurans.* **F** Microscopic examination of involved hairs demonstrates an endothrix pattern (KOH–chlorazol black stain). **G** Histologic examination shows arthroconidia and hyphae within hair shafts to the level of Adamson's fringe (limit of the zone of keratinization; inset).



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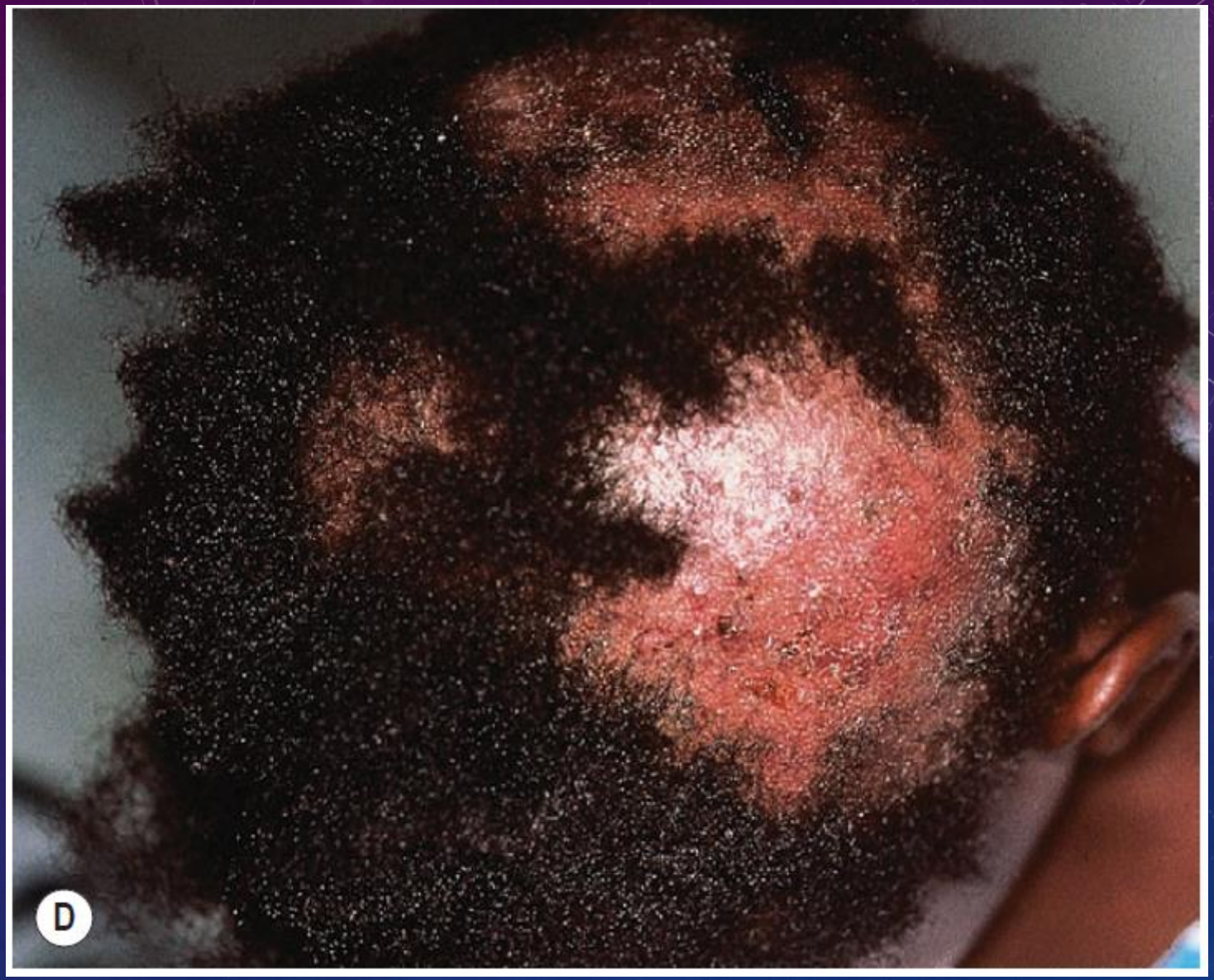

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Tinea capitis…

3) Favus

- most severe form of tinea capitis
- *T. schoenleinii* mostly
- Hyphae and air spaces are within hair shaft
- bluish-white fluorescence in Wood's light
- thick yellow crust composed of hyphae and skin debris ("scutula")
- Scarring alopecia in chronic infections

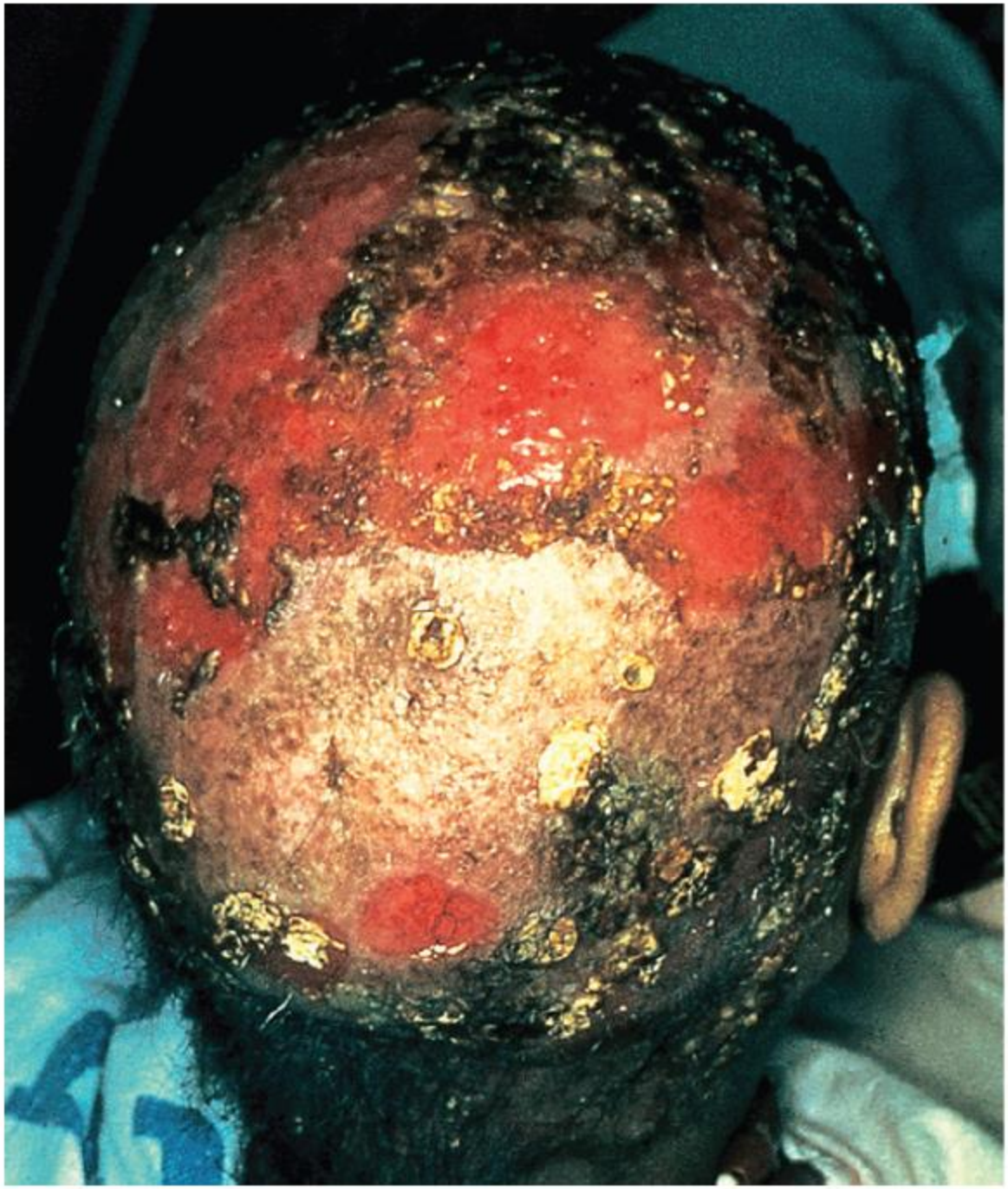


Fig. 77.14 Favus due to *Trichophyton schoenleinii*. Scarring alopecia with erosions and several scutula on the occipital scalp. The latter represent masses of keratin plus fungi.

Courtesy, Israel Dvoretzky, MD.

Tinea capitis…

- In alopecia (especially in children) dermatophytos should consider
- Oral therapy
- Preventative measures
  - Examine family member of affected person
  - antifungal shampoo for household contact

Clinical features

Tinea Pedis

- Dermatophytosis of sole and interdigital web spaces of feet
- Dorsal aspect of foot → tinea corporis
- Most common location of dermatophyte infections
- More in adult than child and both sexes
- Lack of sebaceous gland and moist occlusive environment in shoes
- Barefoot in locker room, gyms, public places

Tinea Pedis…

- *T. rubrum*, *T. interdigitale* , *T. mentagrophytes* , *E. floccosum*, and *T. tonsurans* (in children)

- Non-dermatophyte pathogens:
  - *Neoscytalidium dimidiatum* and *N. Hyalinum* (moccasin and interdigital types)
  - *Candida* (interdigital type)

Tinea Pedis…

Four type

1) Moccasin
2) Interdigital
3) Inflammatory
4) Ulcerative

THE FOUR MAJOR TYPES OF "TINEA PEDIS" CAUSED BY DERMATOPHYTES AND NON-DERMATOPHYTES			
Type	**Causative organism**	**Clinical features**	**Treatment considerations**
Moccasin	*Trichophyton rubrum* *Epidermophyton floccosum* *Neoscytalidium hyalinum* *N. dimidiatum*	Diffuse hyperkeratosis, erythema scaling and fissures on one or both plantar surfaces; frequently chronic and difficult to cure*; occasionally associated with immune deficiency	Topical antifungal plus product with urea or lactic acid; may require oral antifungal therapy
Interdigital	*T. interdigitale* (previously *mentagrophytes* var. *interdigitale*) *T. rubrum* *E. floccosum* *N. hyalinum* *N. dimidiatum* *Candida* spp. *Fusarium* spp.	Most common type; erythema, scaling, fissures and maceration in the web spaces; the two lateral web spaces are most commonly affected; "dermatophytosis complex" (fungal infection followed by bacterial invasion†) can develop; pruritus common; may extend to dorsum and sole of foot	Topical antifungal; may require topical or oral antibiotic if superimposed bacterial infection
Inflammatory (vesicular)	*T. mentagrophytes* (previously *T. mentagrophytes* var. *mentagrophytes*)	Vesicles and bullae on the medial foot; often associated with a dermatophytid reaction‡	Topical antifungal usually sufficient
Ulcerative	*T. rubrum* *T. interdigitale* (previously *T. mentagrophytes* var. *interdigitale*) *E. floccosum*	Typically an exacerbation of interdigital tinea pedis; ulcers and erosions in the web spaces; commonly secondarily infected with bacteria; seen in immunocompromised and diabetic patients	Topical antifungal; may require topical or oral antibiotics if secondary bacterial infection (common)

Dermatophytes Non-dermatophytes

*Because of the thickness of stratum corneum on plantar surfaces and the inability of *T. rubrum* to elicit a sufficient immune response to eliminate the fungus[21].

†Often *Pseudomonas, Proteus* spp., or *Staphylococcus aureus.*

‡Reaction to fungal elements presenting as a dyshidrotic-like eruption on the fingers and palms (culture negative for fungus).

Table 77.11 The four major types of "tinea pedis" caused by dermatophytes and non-dermatophytes.

Tinea Pedis…

- Complicated with bacterial superinfection: "dermatophytosis complex"
- Osteomyelitis, dermatophytid reactions, cellulitis (in patients with edema, HTN, harvested saphenous veins)
- Oral antifungal therapy in DM , immune deficiency and moccasin

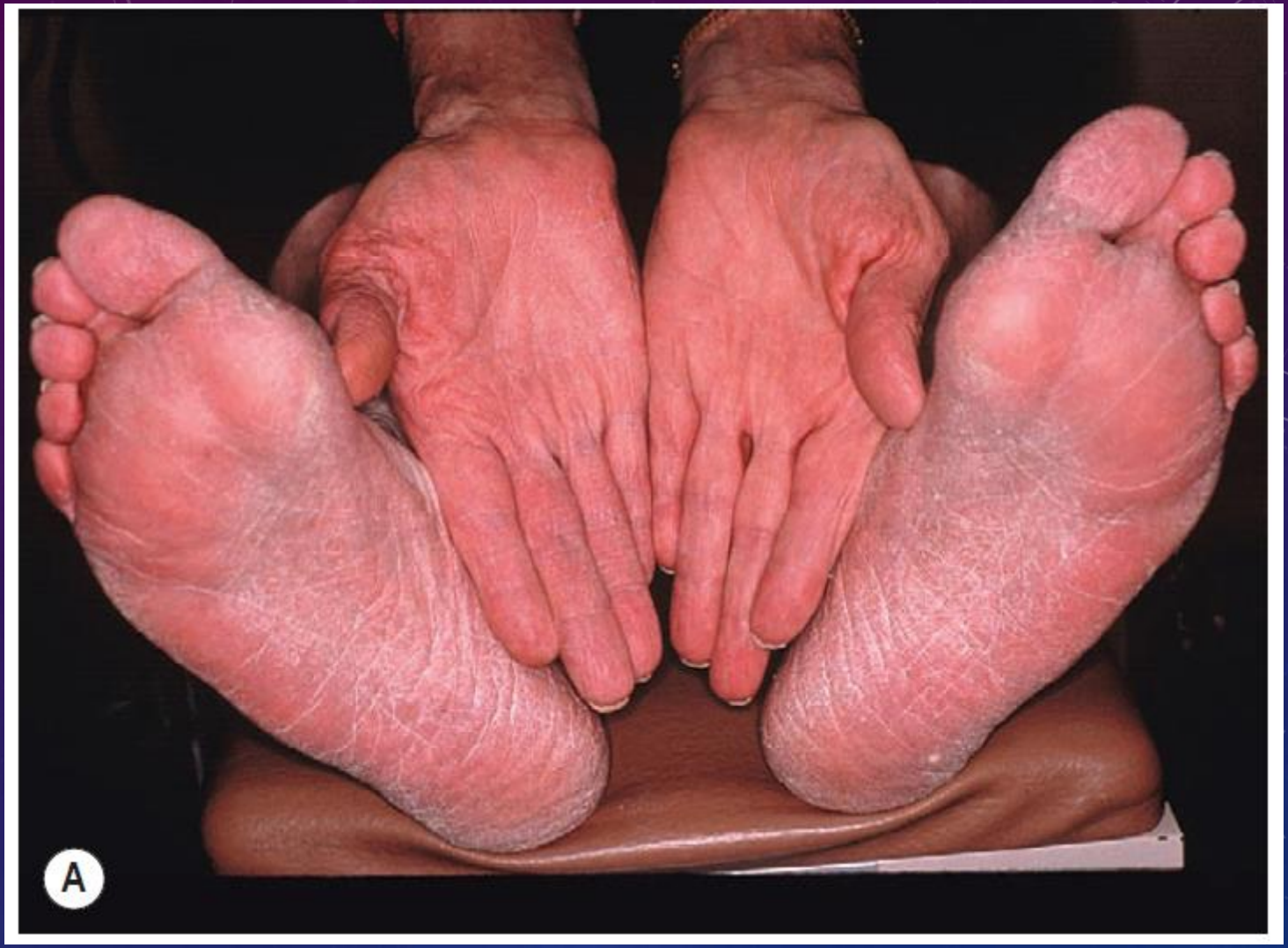
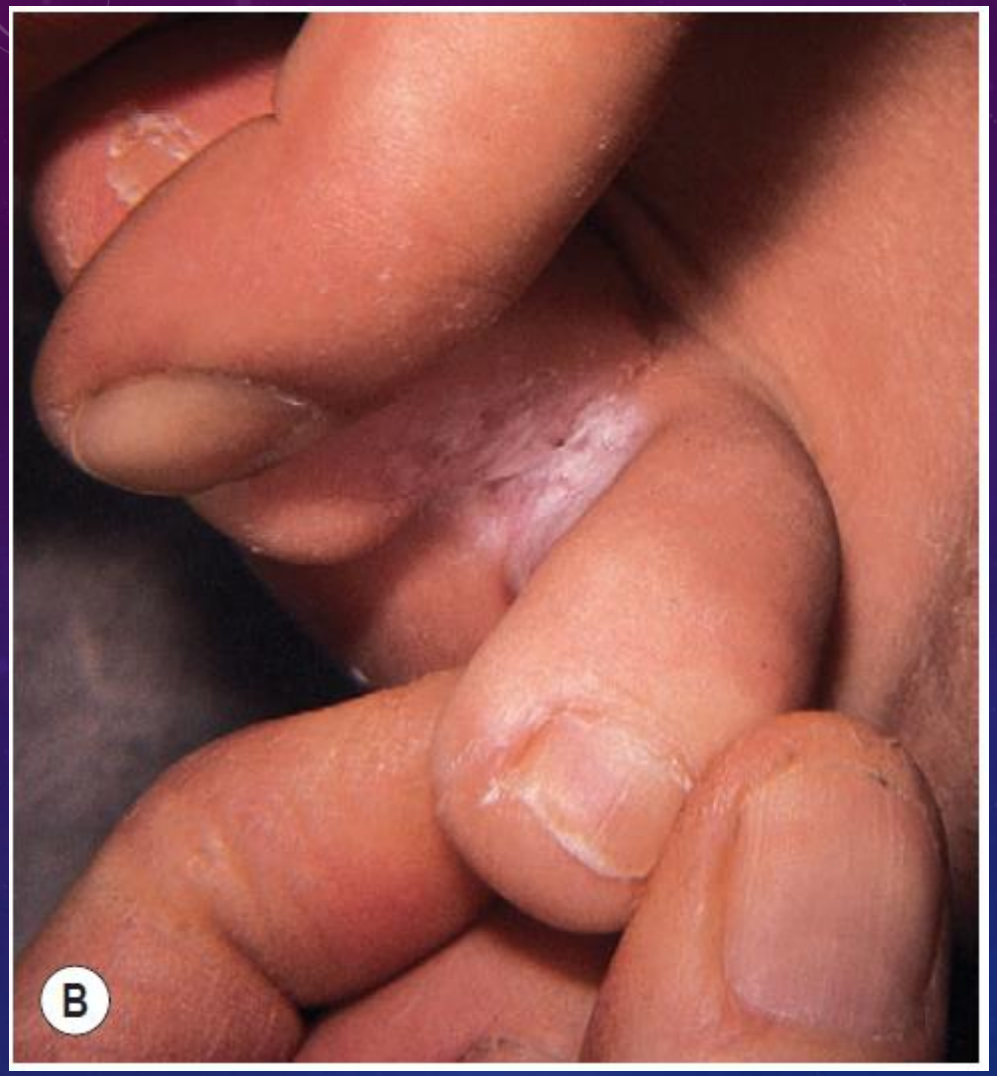


Fig. 77.15 Tinea pedis. **A** Diffuse scaling on both feet (moccasin type) as well as on the right hand, representing “one hand–two feet” tinea. **B** Maceration between the third and fourth toes in the interdigital form. **C** Erythema, scale-crust, and bullae in the inflammatory form. **D** Extension of tinea pedis onto the dorsal foot in a serpiginous configuration of erythema and papules. Scale is minimal due to the patient’s use of a potent topical corticosteroid for presumed dermatitis.



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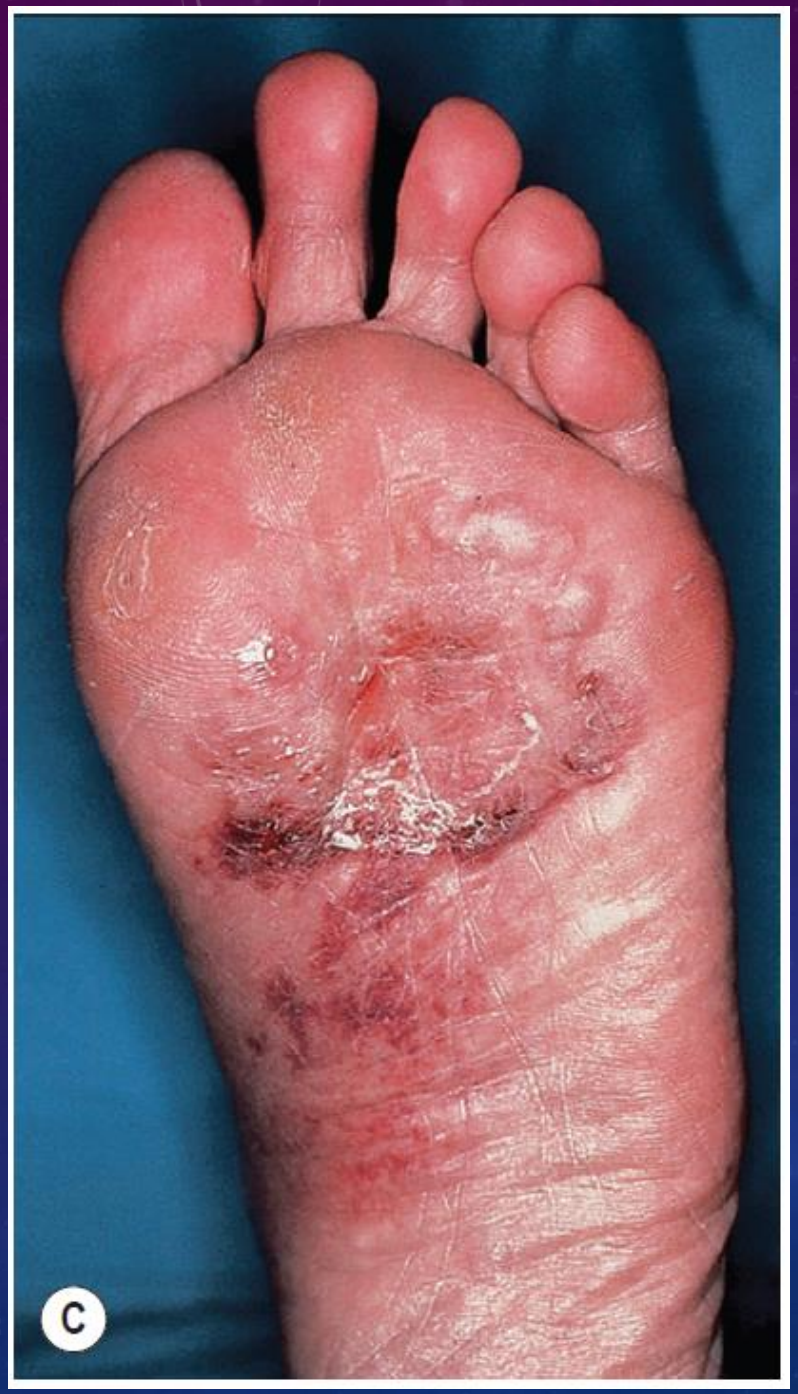

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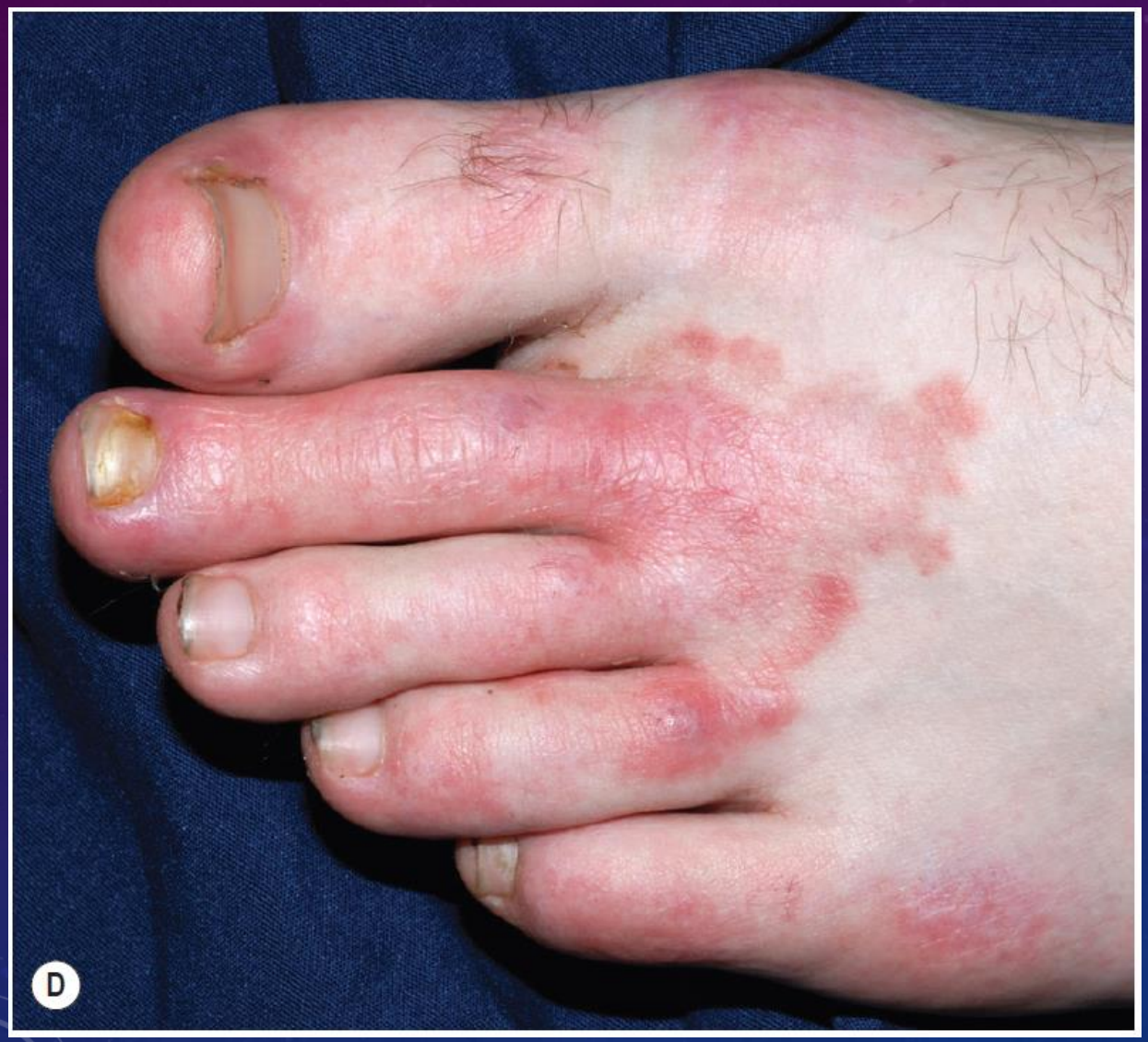

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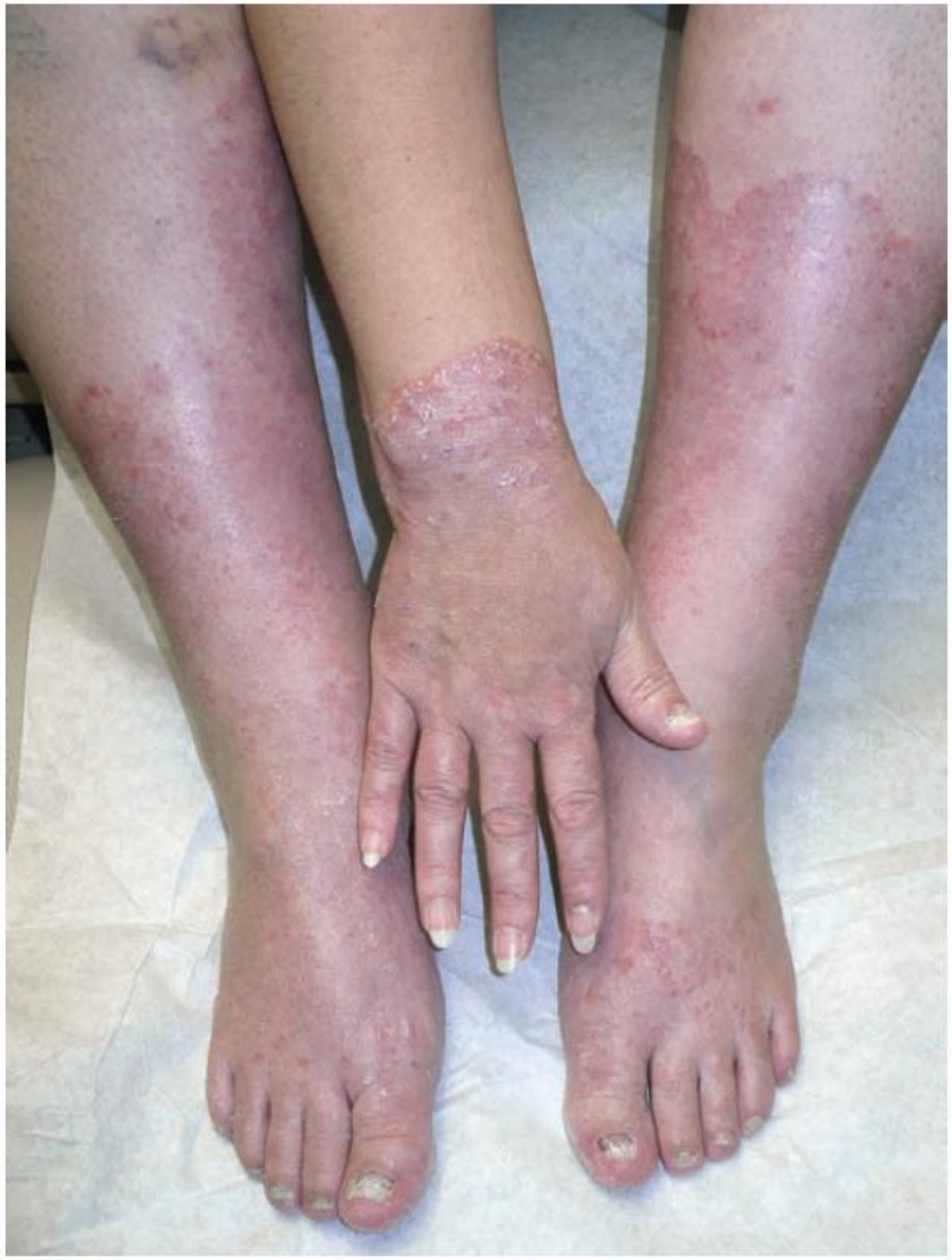


Fig. 77.16 Extensive tinea corporis emanating from tinea manuum and tinea pedis. Note the confluent involvement, serpiginous scaly borders, and associated tinea unguium of the toenails and one fingernail.

Clinical features

Tinea Unguium

- *Dermatophytosis → 90%*
  - *T. rubrum, T. interdigitale, E. floccosum* and *T. tonsurans* (in children)

- Non- *Dermatophytosis → 10%*
  - *Fusarium* spp (deeper invasion of nail plate)
  - *Candida*

Four type

1) *Distal/lateral subungual:* invasion via hyponychium (most common)
   - hyperkeratosis nail bed
   - yellowish and thickening distal of nail plate
   - onycholysis
   - further proximal invasion
   - dystrophic pattern

Tinea Unguium…

2) *Superficial white:* direct penetration into dorsal surface of nail plate
   - Discrete white patch, transverse striate band, origination from proximal fold and deeper invasion of nail plate

3) *Proximal subungual:* invasion under proximal nail fold (ID patient)

4) *Mixed pattern:* ≥2 of the above pattern

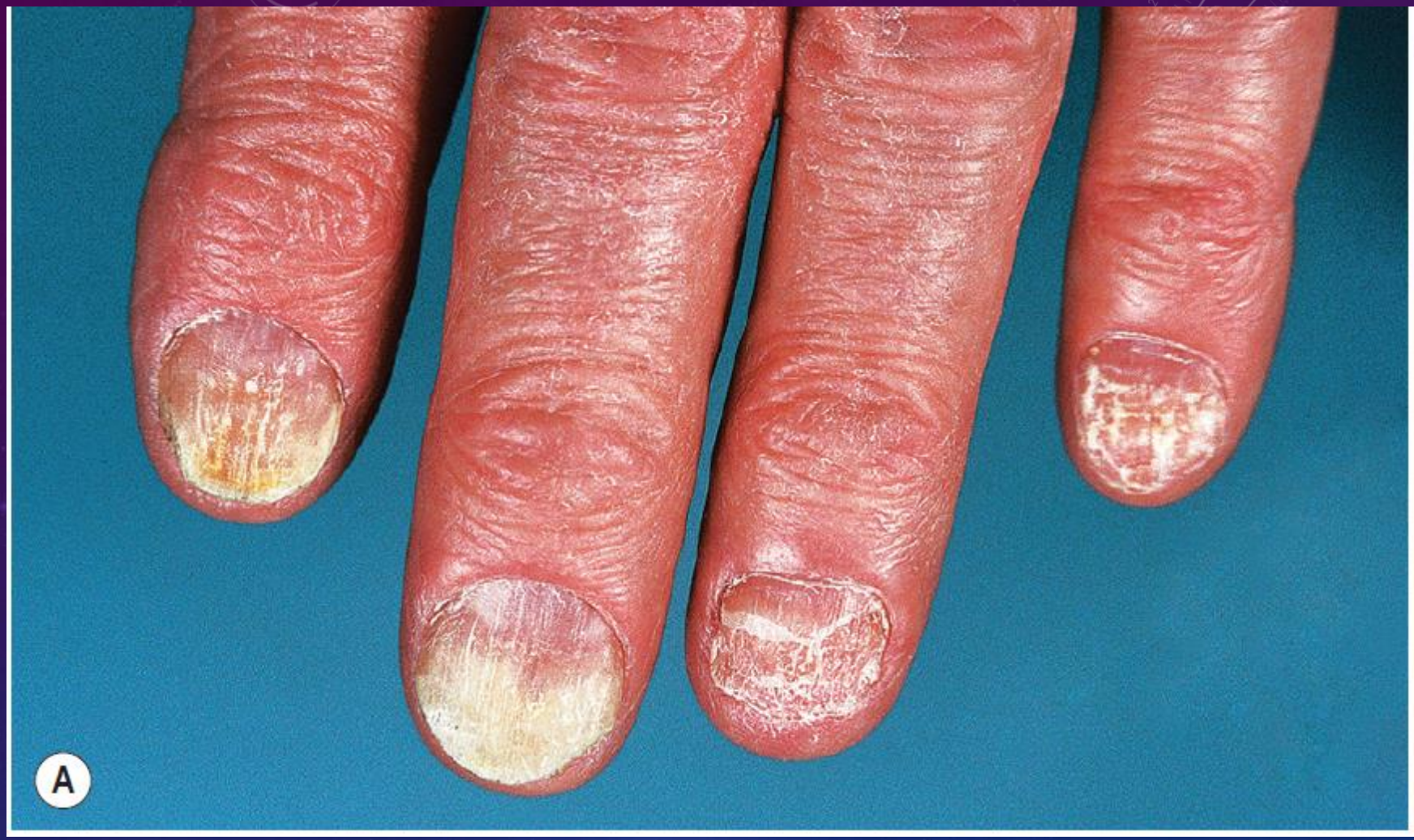
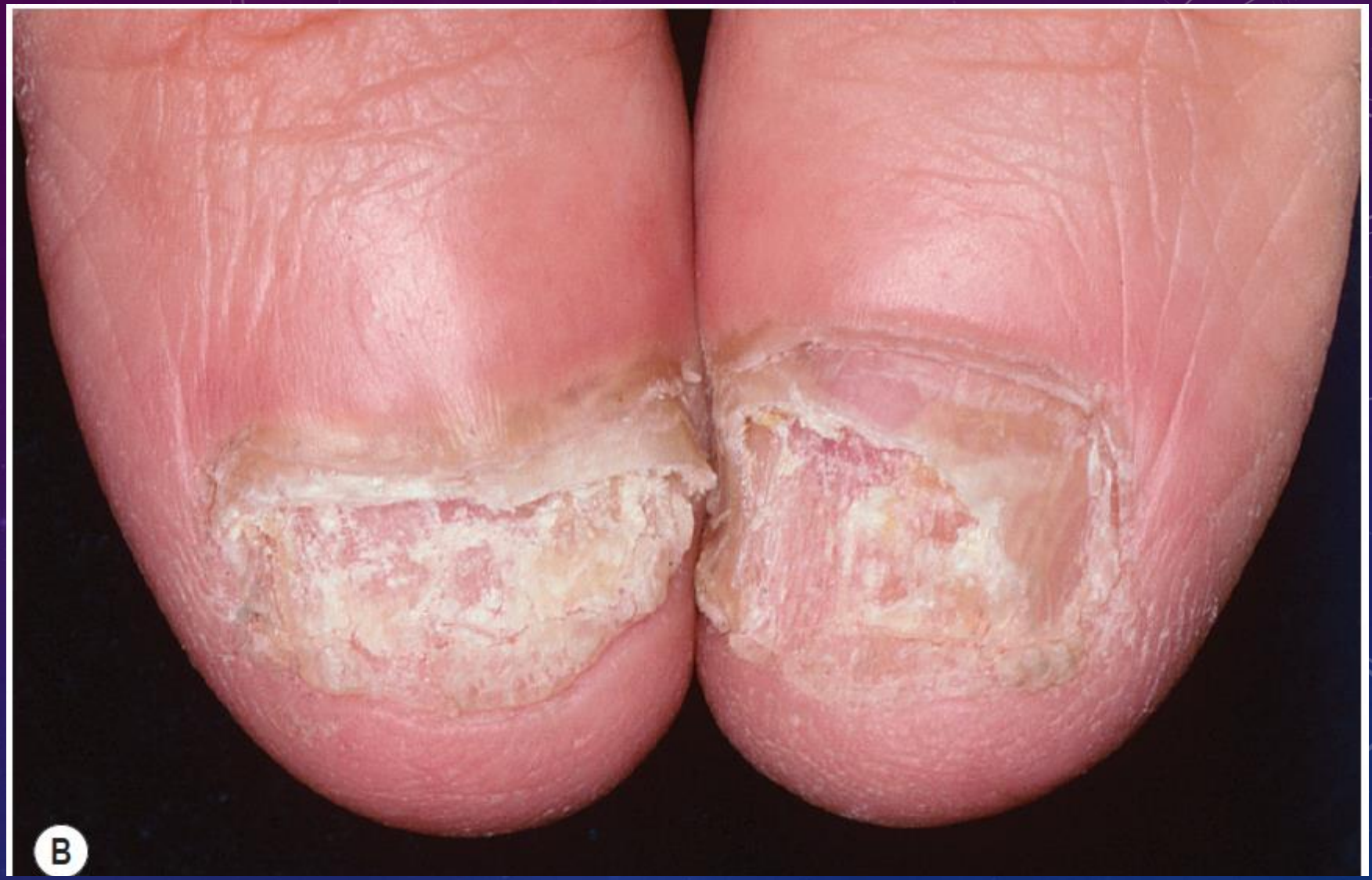


Fig. 77.17 Tinea unguium. Onycholysis, yellowing, crumbling and thickening of the fingernails (**A**), thumb nails (**B**), and toenails (**C**) in the distal/lateral subungual variant. **D** White discoloration of the toenail in the superficial white variant. **E** Hyphae within a formalin-fixed, PAS-stained nail plate.



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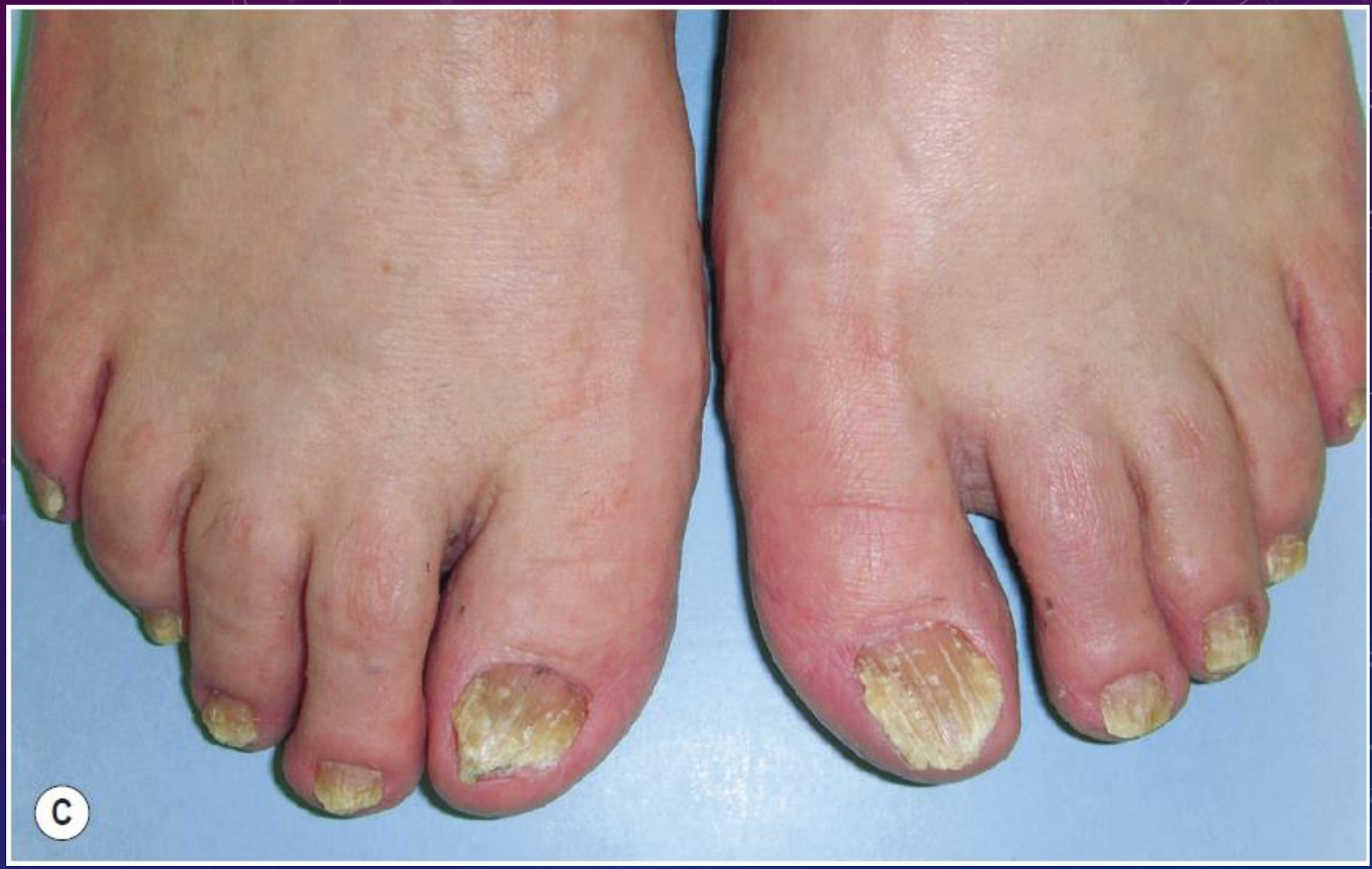

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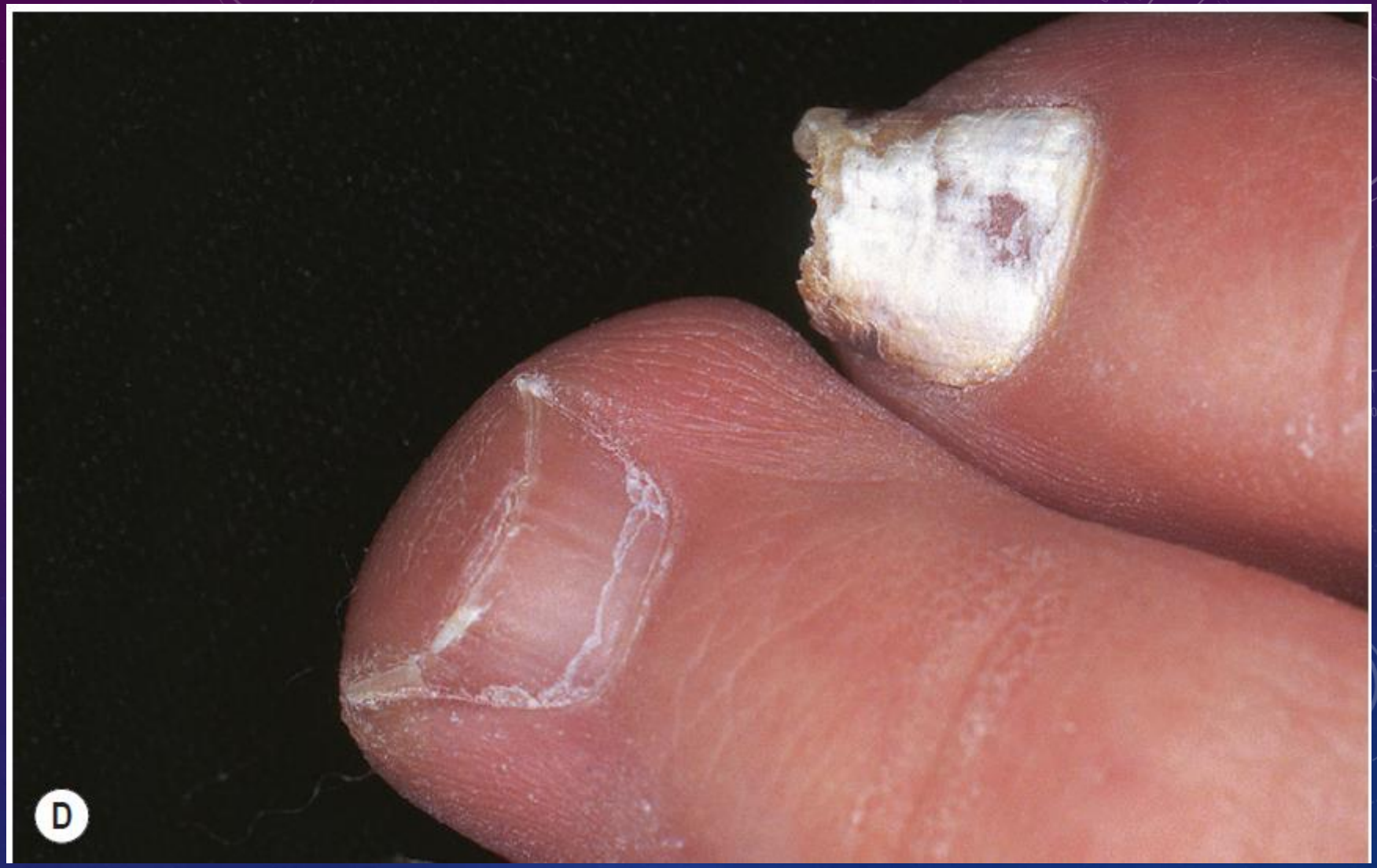

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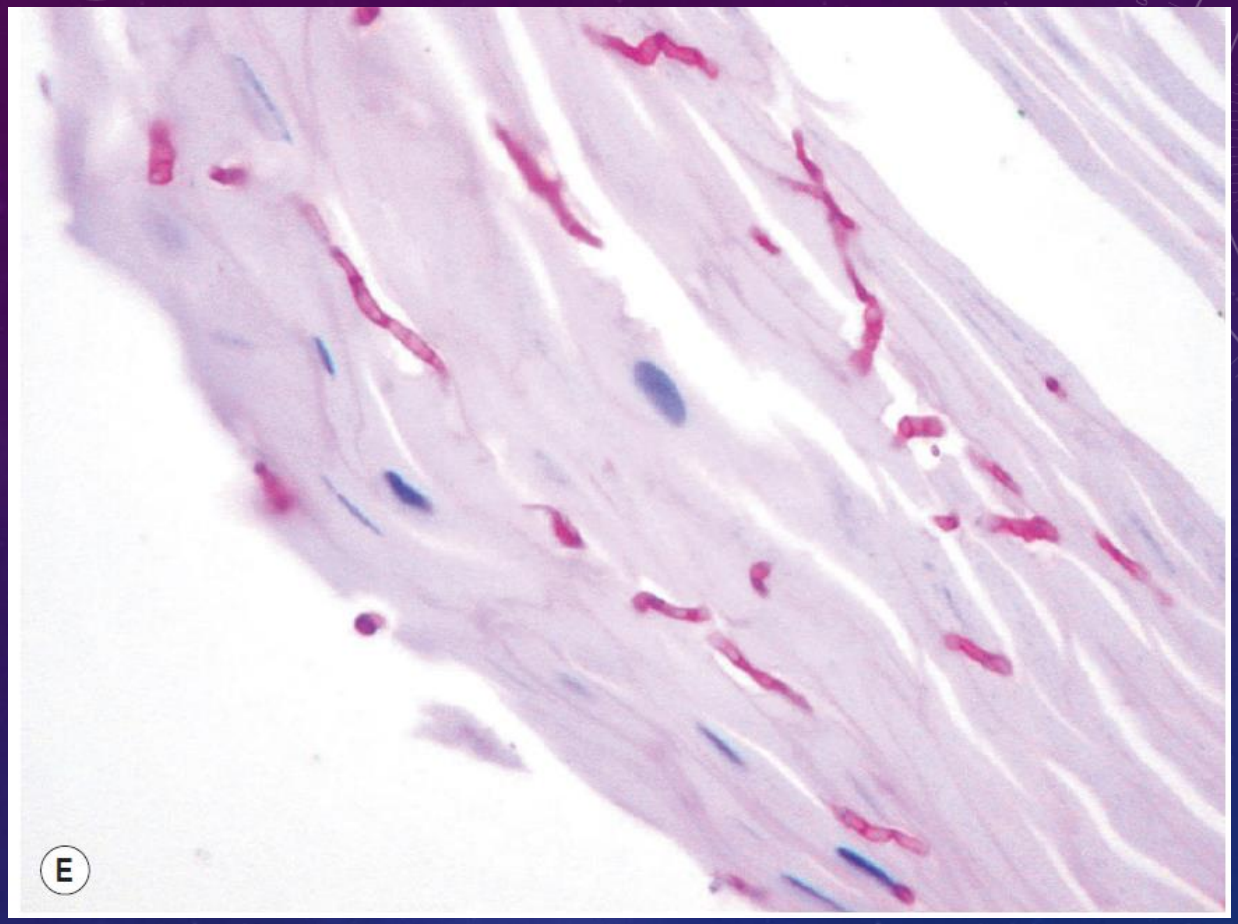
Tinea Unguium…

- Challenging: difficulties in diagnosis, long treatment, side effect of medication, and frequent recurrences
- Complication: discomfort and pain in trimming of nail, running and cellulitis in DM, immunocompromised
- Men more than women, associated with tinea pedis
- Toenail more than finger nail, single nail can occur but mostly multiple nail on one or both hands or feet



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Tinea Unguium…

- *T. rubrum*: invasive in children and ID
- 50% or more of nail dystrophy are onychomycosis
- Candida nail infection
  - Chronic paronychia
  - Fingernails are usually with ridging, yellow and onycholysis
  - Common in less than 3 years

Inverse dermatophytosis

- Proliferation of fungail in dermis
- Chronic dermatophytosis mostly *T. rubrum*
- Primary or secondary immunodeficiency
- Hematogenous spread
- Tend or ulcerative or draining dermal and subcutaneous nodules
- Surgical excision and systemic antifungal

Differential diagnosis

- Many other conditions can mimic
- KOH examination and culture are necessary
- KOH preparations→ Guidelines in fig 77.18
- Culture in media with cycloheximide and DTM
- But non-dermatophyte do not grow there *Scopulariopsis, Aspergillus, Cryptococcus n, Candida ,…*

Differential diagnosis…

- General lab characters for identification
  - Colonial (color, topography, texture):
  - Morphology
  - Conidia examination micro or macro conidia and shape, cell wall texture
  - Growth rate and biochemical test
  - Arthroconidia and chlamydoconidia
  - Hyphal patterns (spiral, pectinate, antler, racquet, and nodular bodies)

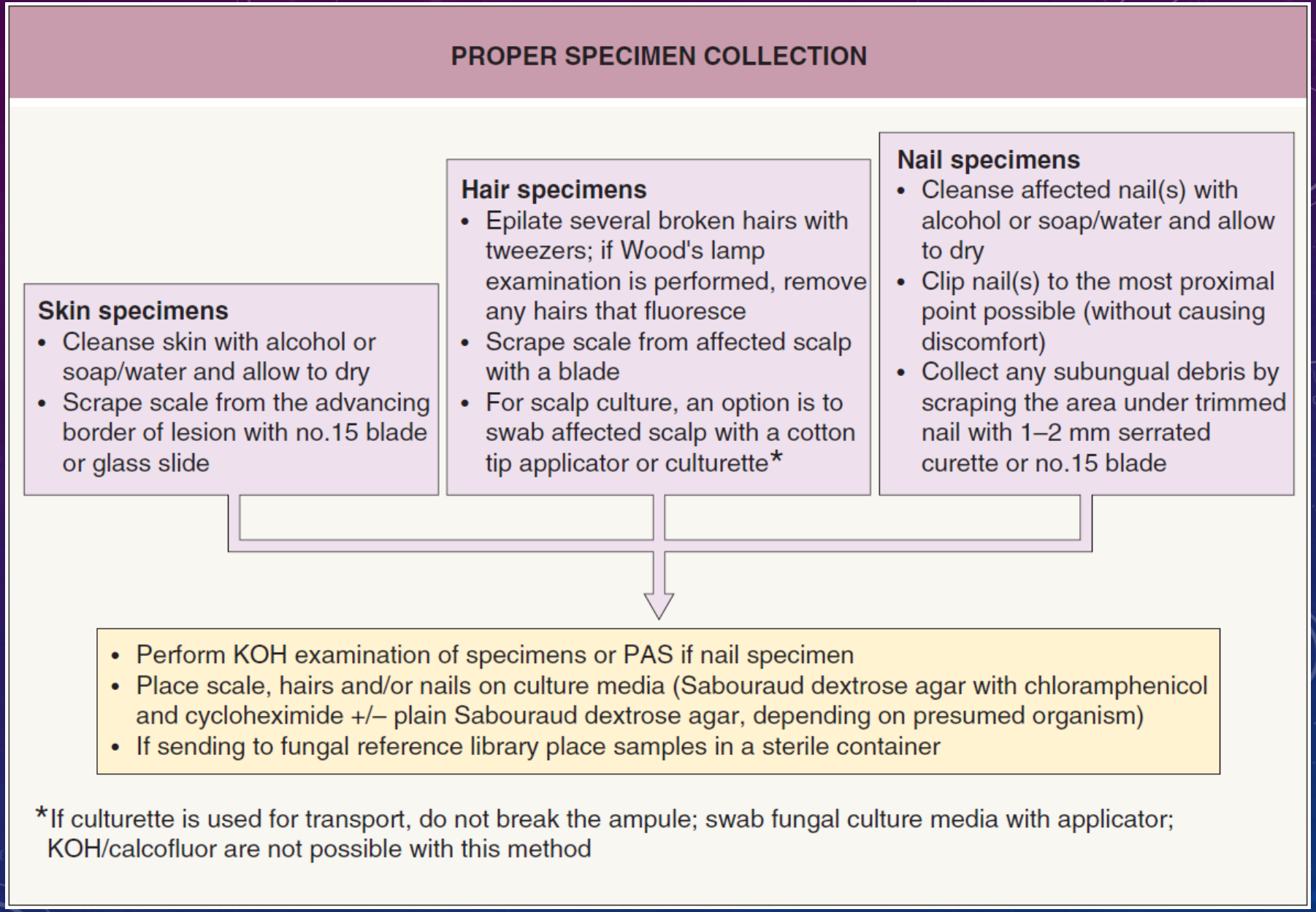

Fig. 77.18 Proper specimen collection. Proper collection of skin, hair, and nails is important. Following these simple guidelines will help the clinician to achieve the most accurate diagnosis.

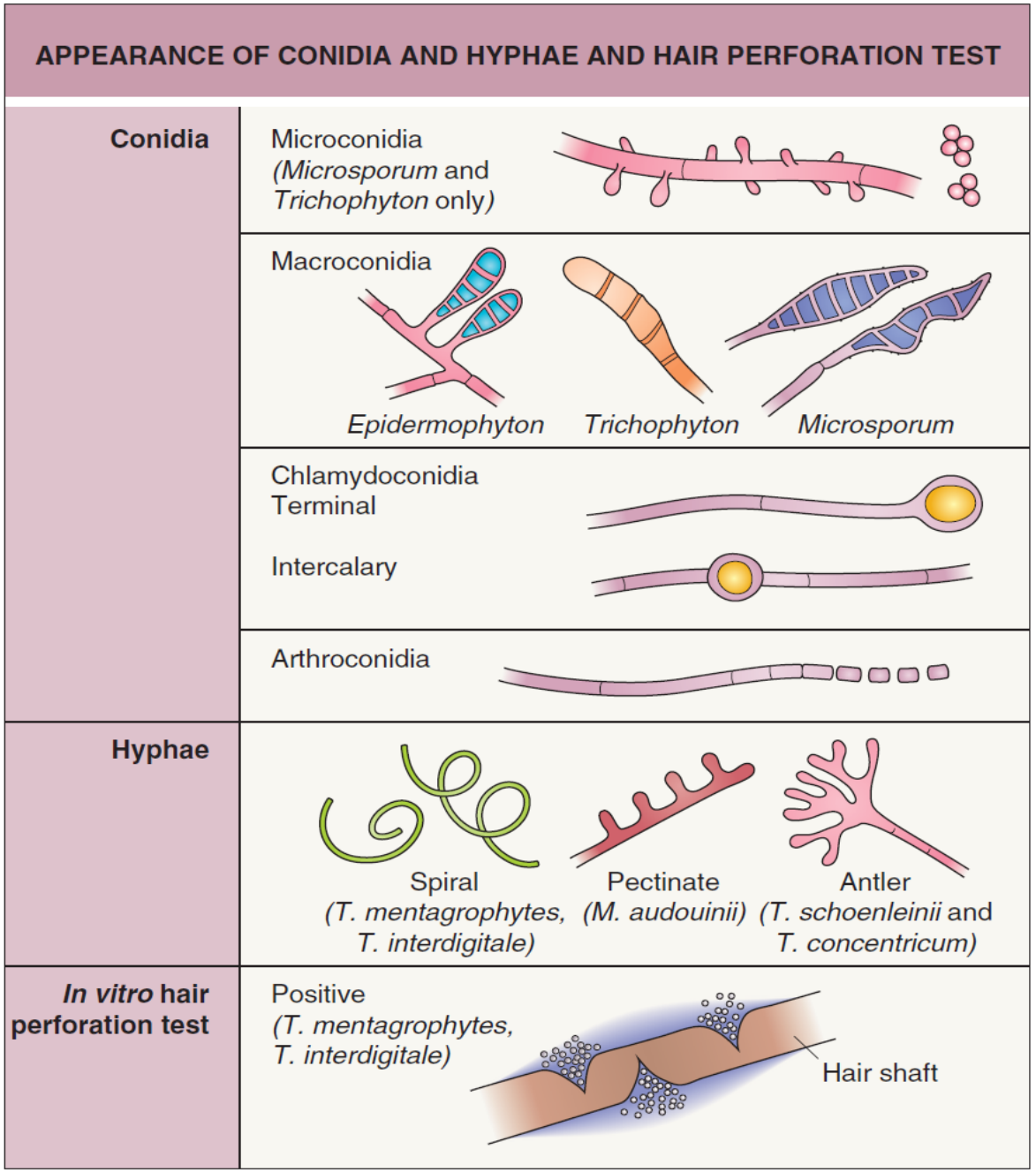

Fig. 77.19 Microscopic appearance of various forms of conidia and hyphae and the *in vitro* hair perforation test.

DIFFERENTIAL DIAGNOSES OF DERMATOPHYTE INFECTIONS				
Tinea corporis	**Tinea cruris**	**Tinea faciei**	**Tinea capitis**	**Tinea pedis**
Dermatitis • Nummular eczema • Atopic • Stasis • Contact • Seborrheic (petaloid) Tinea versicolor Pityriasis rosea Parapsoriasis Erythema annulare centrifugum Annular psoriasis Subacute lupus erythematosus Granuloma annulare Impetigo	Cutaneous candidiasis Intertrigo • Seborrheic dermatitis • Psoriasis Erythrasma Contact dermatitis Lichen simplex chronicus Parapsoriasis/mycosis fungoides Hailey–Hailey disease Langerhans cell histiocytosis	Dermatitis • Seborrheic • Perioral • Contact Rosacea Lupus erythematosus Acne vulgaris Annular psoriasis (children)	Seborrheic dermatitis Alopecia areata Trichotillomania Psoriasis If pustules: • Pyoderma • Folliculitis If scarring: • Lichen planus • Discoid lupus erythematosus • Folliculitis decalvans • Central centrifugal cicatricial alopecia	Dermatitis • Dyshidrotic • Contact Psoriasis • Vulgaris • Pustular Juvenile plantar dermatosis Secondary syphilis If interdigital: • Erythrasma • Bacterial infection, e.g. GNR

Table 77.9 Differential diagnoses of dermatophyte infections. A kerion is sometimes misdiagnosed as an abscess. GNR, Gram-negative rods.

NON-DERMATOPHYTE MOLDS THAT CAN CAUSE ONYCHOMYCOSIS	
Fungus	**Key features**
Fusarium spp.	Superficial white pattern*
Aspergillus spp.	Superficial white pattern*
Acremonium	Superficial white pattern*
Scopulariopsis brevicaulis	Lateral yellow–brown discoloration KOH of nail reveals lemon-shaped conidia and atypical hyphae
Neoscytalidium hyalinum	Distal and lateral nail invasion†
Neoscytalidium dimidiatum	Distal and lateral nail invasion†

*Deeper invasion of the nail plate can also occur.
†May also be associated with paronychia or tinea pedis.

Table 77.12 Non-dermatophyte molds that can cause onychomycosis.

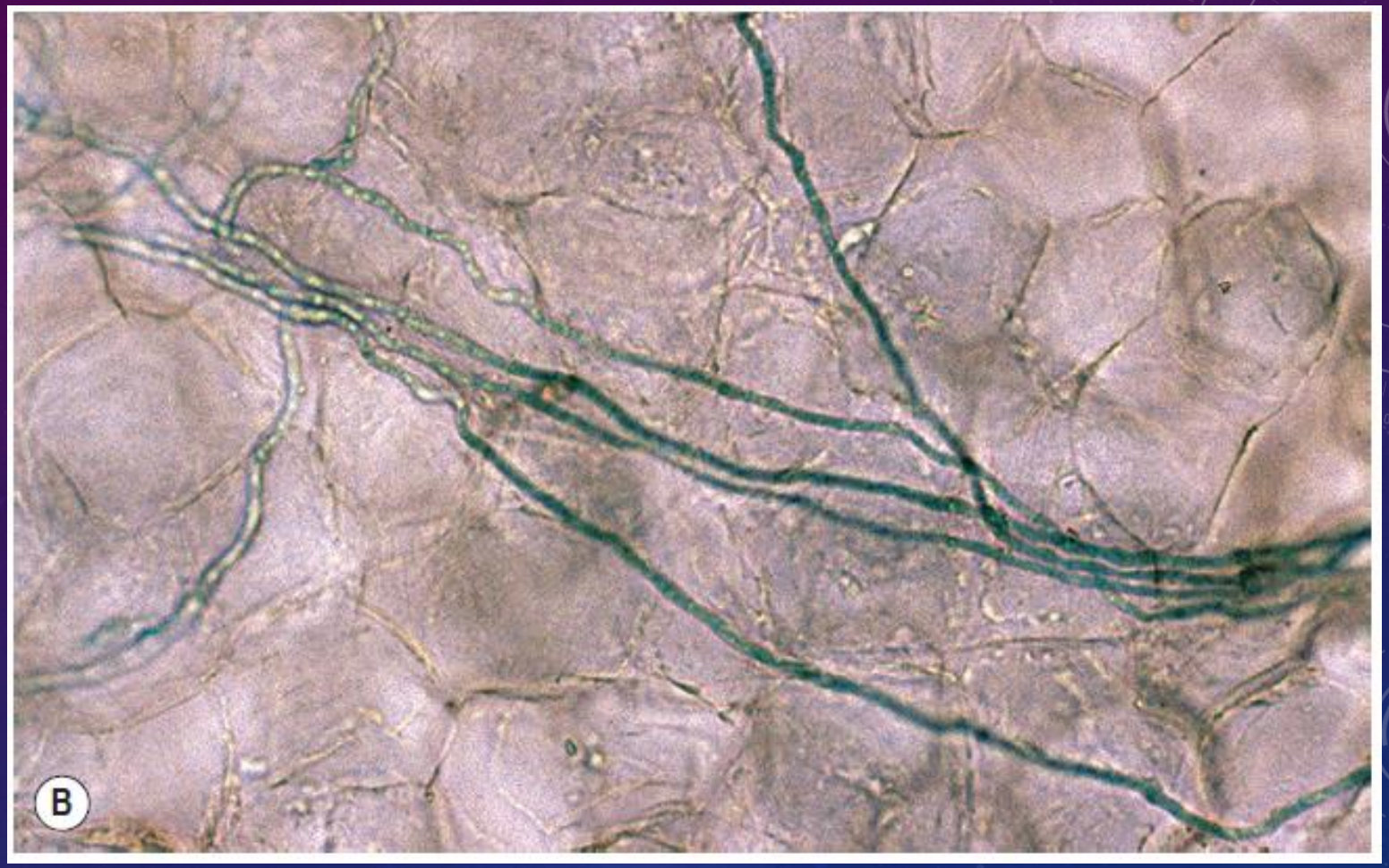

Fig. 77.5 Potassium hydroxide preparations.

- **B.** A dermatophyte, in this case *Trichophyton tonsurans*, demonstrating branching hyphae (chlorazol black stain). Note that the hyphae cross multiple squamous cells.

Treatment

- Topical
  - Localized form of tinea corporis, cruris, and pedis
  - Side effect: irritant or allergic contact dermatitis to vehicle
- Systemic
  - Tinea mannum, tinea capitis, tinea unguium all infection involve extensive area hairy sites and excessive inflammatory reactions
- Combination therapy:
  - topical steroid (Low-potency & typical) anti-inflammatory
  - For reduction of inflammation

- Consideration in tinea unguium
  - Oral antifungal required:
    - except: superficial white onychomycosis
    - Topical: 48 weeks apply of tavaborole and ciclopirox, efinaconazole but cure rate low
    - Systemic: higher mycologic cure rates, clinical cure low
  - Recurrent is common, especially in toenails
  - Preventive measures:
    - breathable footwear, antifungal powders, disinfect old shoe, nail clipping, and avoiding re-exposure

SUGGESTED SYSTEMIC REGIMENS FOR DERMATOPHYTOSES

	Fluconazole	Griseofulvin	Itraconazole*	Terbinafine
Tinea pedis (moccasin type)/ tinea manuum (adults)	150–450 mg/week × 4–6 weeks[27]	750–1000 mg/day (microsize) or 500–750 mg/ day (ultramicrosize) × 4 weeks	200–400 mg/day × 1 week	250 mg/day × 2 weeks
Tinea pedis (moccasin type)/ tinea manuum (children)	6 mg/kg/week × 4–6 weeks	15–20 mg/kg/day (microsize suspension) × 4 weeks	3–5 mg/kg/day (maximum 400 mg) × 1 week	Daily dosing as for tinea capitis (see below) × 2 weeks
Tinea unguium (adults)	Toenail ± fingernail involvement:			
	150–450 mg/week until nails are clear[27]	1–2 g/day (microsize) or 750 mg/day (ultramicrosize) until nails are normal†	200 mg/day × 12 weeks or 200 mg BID × 1 week/month for 3–4 consecutive months	250 mg/day × 12 weeks
	Fingernail involvement only:			
	150–450 mg/week until nails are clear[27]	1–2 g/day (microsize) or 750 mg/day (ultramicrosize) until nails are normal†	200 mg/day × 6 weeks or 200 mg BID × 1 week/month for 2 consecutive months	250 mg/day × 6 weeks
Tinea unguium (children)	6 mg/kg/week × 3–4 months (fingernails) or 5–7 months (toenails), or until nails are clear	20 mg/kg/day (microsize suspension) until nails are normal†	5 mg/kg/day (<20 kg), 100 mg/day (20–40 kg), 200 mg/day (40–50 kg), or 200 mg BID (>50 kg) × 1 week/month for 2 (fingernails) or 3 (toenails) consecutive months	62.5 mg/day (<20 kg), 125 mg/ day (20–40 kg) or 250 mg/day (>40 kg) × 6 weeks (fingernails) or 12 weeks (toenails)
Tinea corporis (extensive, adults)	150–200 mg/week × 2–4 weeks	500–1000 mg/day (microsize) or 375–500 mg/ day (ultramicrosize) × 2–4 weeks	200 mg/day × 1 week	250 mg/day × 1 week
Tinea corporis (extensive, children)	6 mg/kg/week × 2–4 weeks	15–20 mg/kg/day (microsize suspension) × 2–4 weeks	3–5 mg/kg/day (maximum 200 mg) × 1 week	Daily dosing as for tinea capitis (see below) × 1 week
Tinea capitis (adults)‡	6 mg/kg/day × 3–6 weeks	10–15 mg/kg/day (ultramicrosize; usually maximum 750 mg/day) × 6–8 weeks	5 mg/kg/day (maximum 400 mg) × 4–8 weeks	250 mg/day × 3–4 weeks§
Tinea capitis (children)‡	6 mg/kg/day × 3–6 weeks	20–25 mg/kg/day (microsize suspension) × 6–8 weeks	5 mg/kg/day (maximum 500 mg) × 4–8 weeks	Granules: 125 mg (<25 kg), 187.5 mg (25–35 kg) or 250 mg (>35 kg) × 3–4 weeks§

*Not approved in US for use in children.
†No longer commonly used for this indication.
‡Combined with 2.5% selenium sulfide shampoo or ketoconazole 2% shampoo; "id" reaction should not be confused with a medication allergy.
§Not recommended for *Microsporum canis*, unless given at double-dose.

INDICATORS OF MORE SEVERE ONYCHOMYCOSIS WITH A POOR RESPONSE TO TREATMENT	
Nail factors	• Subungual hyperkeratosis >2 mm thick* • Significant lateral involvement • Dermatophytoma† • >50% involvement of nail bed • Slow nail growth rate • Total dystrophic onychomycosis • Matrix involvement
Patient factors	• Immunosuppression • Peripheral arterial disease • Poorly controlled diabetes mellitus

*Measurement of nail plate plus nail bed.
†Streak or patch representing a subungual pocket of densely packed hyphae; removal prior to initiating antifungal therapy can be helpful.

Table 77.14 Indicators of more severe onychomycosis with a poor response to treatment. *Adapted from ref 28.*

Recalcitrant Dermatophytosis

- Mainly in tinea corporis and cruris
- Resistance and Recalcitrant are different
  - resistance is in vitro
  - recalcitrant are both in vitro and other causes of therapeutic failure
- Drugs should reach SC or penetration
- Drugs should persist there or keratin adherence
  - high for KTZ,ITR,TRB & low for FLU ,GRI

Table 1
Antifungals used in dermatophytoses.

Class	Drugs	Mechanism of action
Azoles	**Systemic:** Fluconazole, Ketoconazole, Itraconazole, Voriconazole, Posaconazole, isavuconazole **Topical:**Clotimazole, Miconazole, Econazole, Luliconazole, Lanoconazole, Efinaconazole, Ketoconazole, Sertaconazole, Oxiconazole, Eberconazole, Fenticonazole, Bifonazole	Inhibition of Lanosterol 14α demethylase
Allylamines	**Systemic:** Terbinafine **Topical:** Terbinafine, Butenafine, Naftifine	Inhibition of squalene epoxidase
Heterocyclic benzofuran	Griseofulvin	Inhibition of microtubule aggregation
Polyenes	Nystatin, Natamycin, Amphotericin B (topical)	Disorganization of the cell membrane by formation of pores
Morpholine	Amorolfine (topical)	Inhibition of C-14 reductase and C8 isomerase
Thiocarbamate	Tolnaftate (topical)	Inhibition of squalene epoxidase
Hydroxypyridones	Ciclopirox (topical)	Chelation of trivalent metal cations Inhibition of metal dependent enzymes – catalase, peroxidase Inhibition of enzymes involved in mitochondrial electron transport processes and energy production
Echinocandins	Anidulafungin, Caspofungin, Micafungin	Glucan synthase inhibition
Others	Tavabarole (topical)	Cytoplasmic leucyl tRNA synthetase - inhibition of protein synthesis and termination of cell growth
	ME 111	Succinate dehydrogenase inhibitor

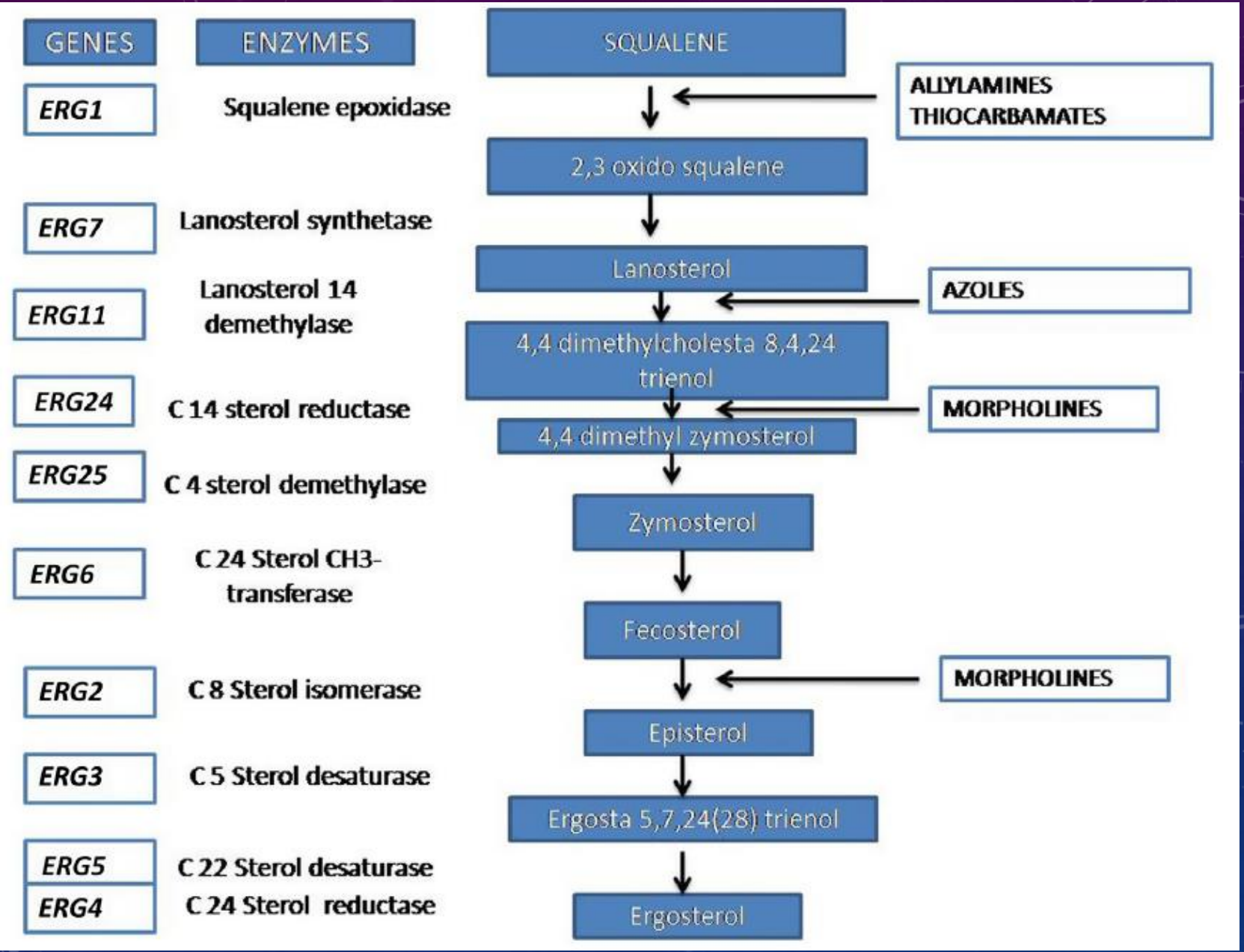

Fig. 1. Steps of ergosterol synthesis in fungal cell membranes, enzymes involved and genes encoding each enzyme. Also mentioned are the sites of action of antifungals used against dermatophytes.

Table 2

Factors responsible for recalcitrance in dermatophytoses (Jones et al., 1990; Sardana and Khurana, 2018).

Factor	Implications/scenarios
Fungal factors	Host adaptability, Virulence factors, Probable variation in drug susceptibility
Host factors	Immunity related • Iatrogenic and disease related immune defects, • Impaired local immunity by topical steroid misuse • Predominance of Th2 immune response Compliance with prolonged treatment
Drug factors	Mechanism of action MFC/MIC ratio Suboptimal absorption, Quality concerns, Levels achieved in skin, keratin adherence, Resistance
Clinical presentation	Onychomycosis (possible role of biofilms) Majocchi's granuloma, Tinea imbricata Involvement of palms/soles

Mechanisms of Ressistance to Azole

1) Drug efflux : by over expression ABC transporter (ATP dependent) they export drug from cell

2) Drug target modification

3) Stress response: of dermatophytes (hsp 70, 90 , …) and stable fungus cell ageist drug

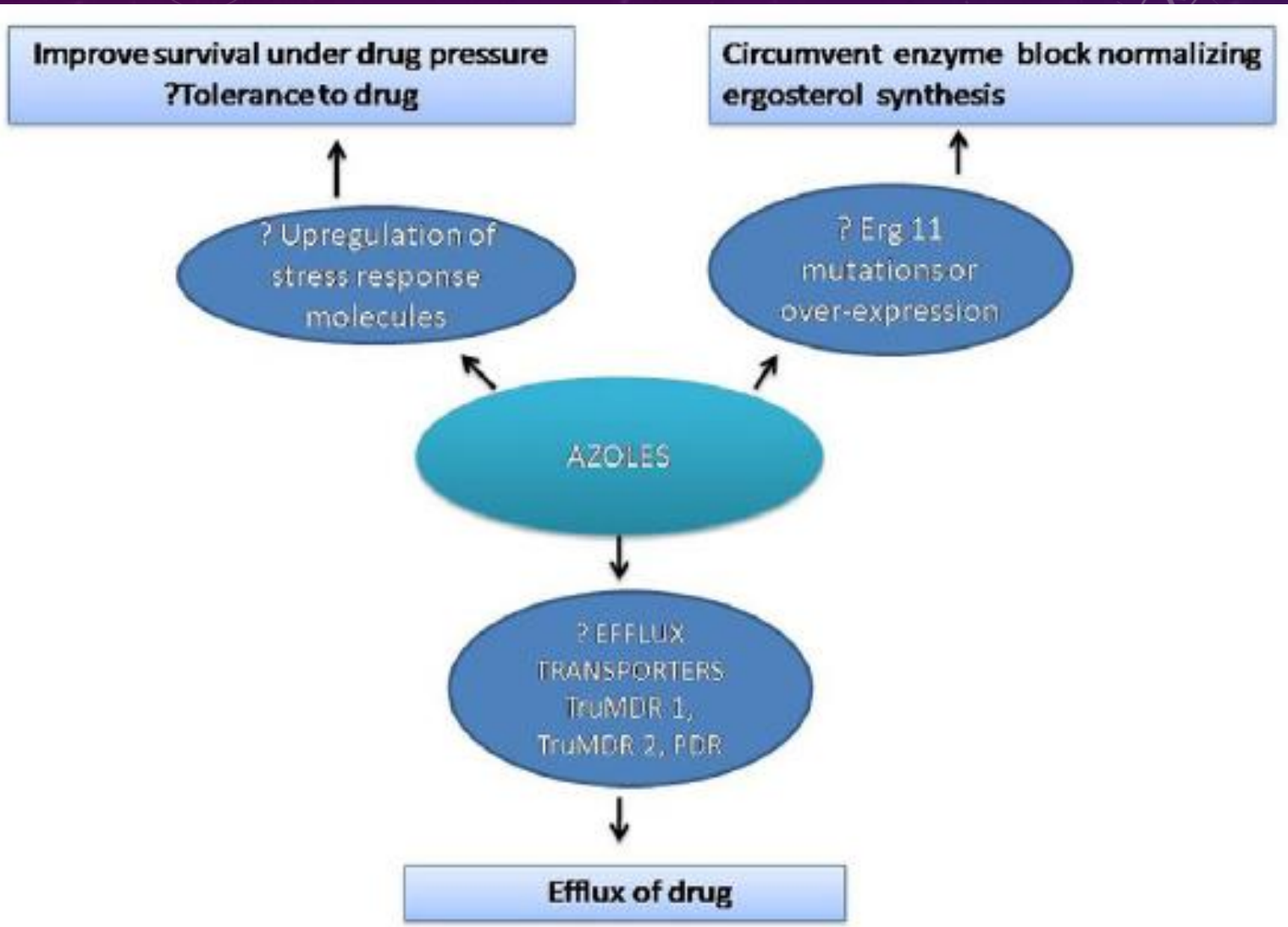

Fig. 2. Possible mechanisms of azole resistance in dermatophytes.

Mechanisms of Resistance to allylamine

1. SQLE gene mutation in dermatophytose affect drug binding site of SQLE
2. Efflux pump
3. Over expression of Sal A gene clearage of naphthalene nucleus of TRB

- No particular mechanism of resistance of GRI
- There is cross resistance between ITR and TRB

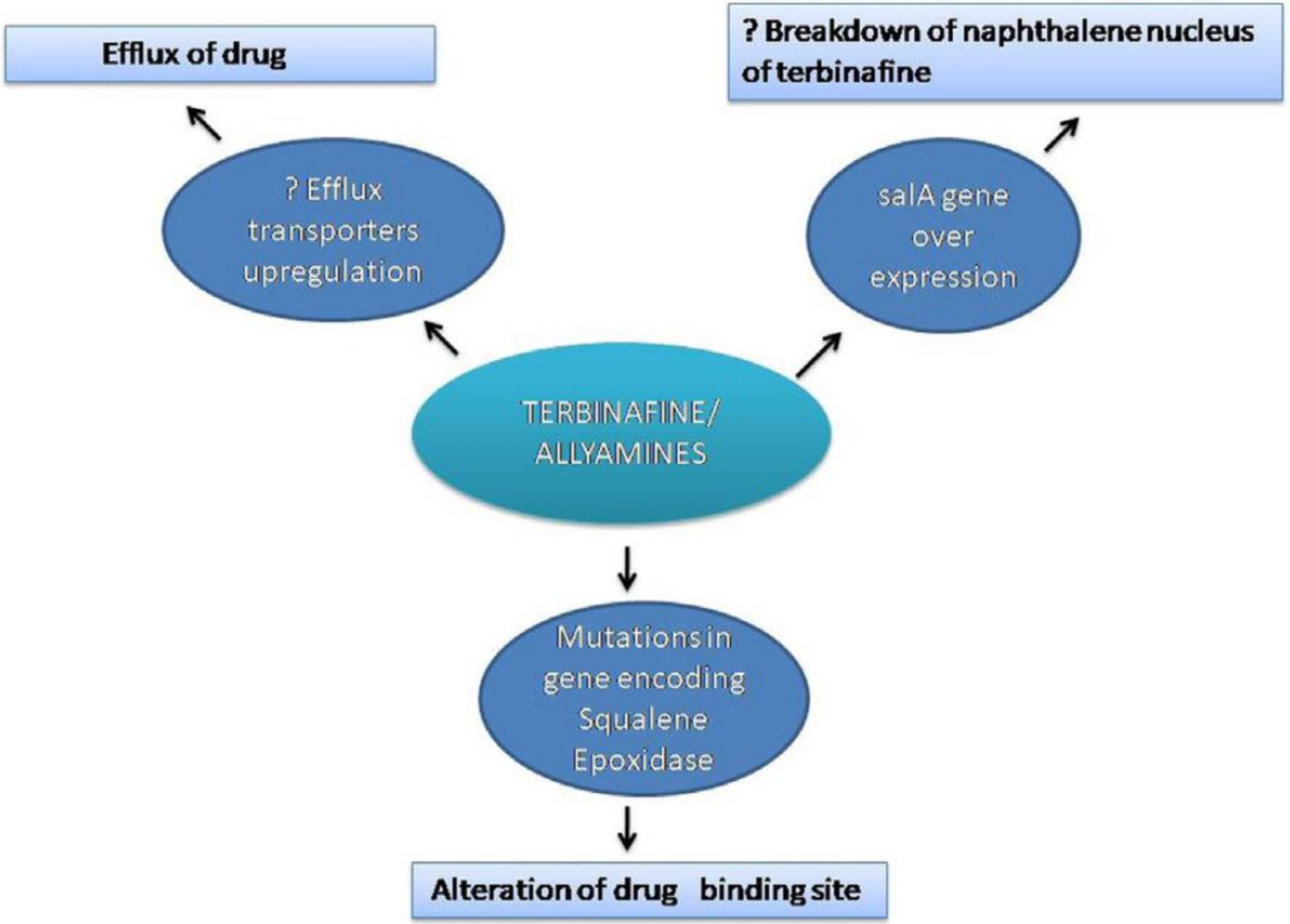

Fig. 3. Mechanisms (proven and proposed) of resistance to terbinafine and other allylamines.

What should we do in Resistance

1) Dose increase
2) Consider Ketoconazol as alternative (hepatotoxicity)
3) Combination of two systemic Anti fungus
4) Combination of different classes of systemic & topical antifungal

What should we do in Resistance …

5) Combination of conventional systemic antifungals with other drugs

- systemic antifungals with systemic cyclosporine or Topical Tacrolimus
  - Decrease resistance
  - Data lacking
- Systemic antifungal with Isotertineon
  - Reduce sebum, interaction
- Antifungal with statin

6) Restrict use of TRB to prevent resistance

- No combination with steroid , no use in onychomycosis


The END
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