MSS

Microbiology

LEC no. 4

Writer: Sara Khalaf

Corrector: Omar Smadi

Doctor: Malik Sallam

Cutaneous infections that manifest in papules, plaques, and patches

Malik Sallam, M.D., Ph.D.
School of Medicine
The University of Jordan

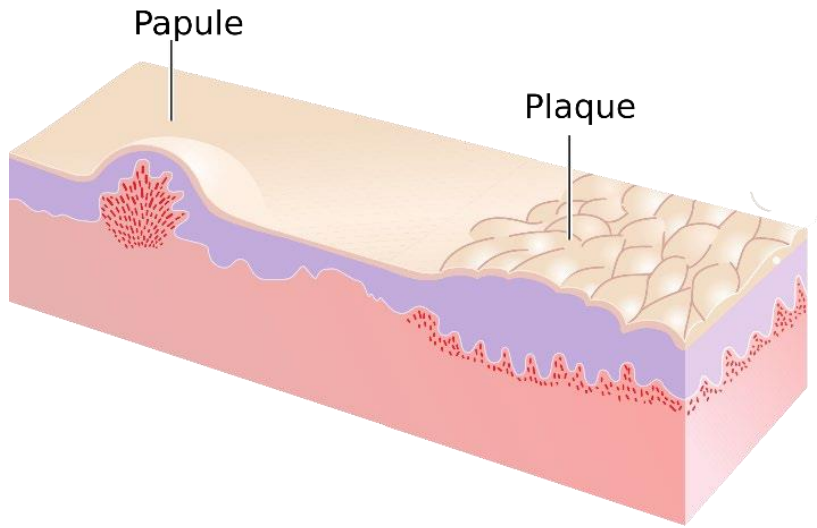
The most important things that you should know about diseases in this lecture:
-How it appears on skin (papules, patches, nodules).
-Type of the causing agent (virus, bacteria, fungus) to determine the treatment.
-Severity of these lesions (benign, disappears by itself, needs treatment, indicates cancer, indicates underlying immune suppression).

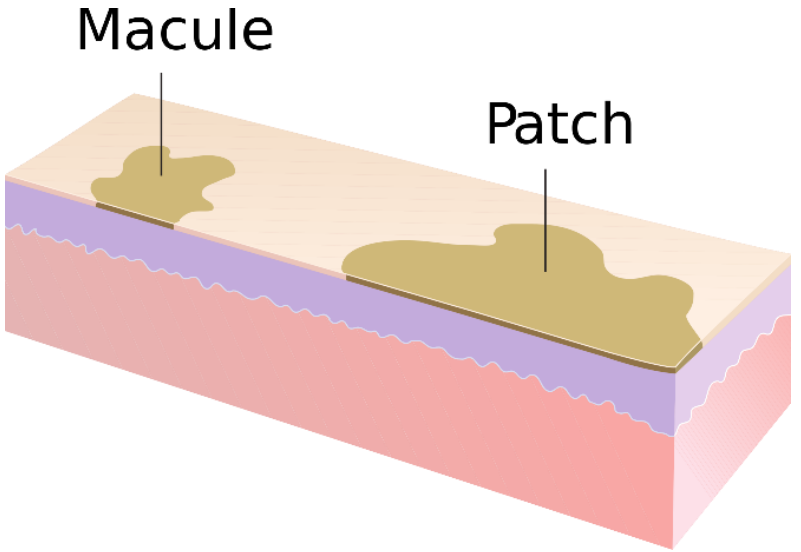
Outline

- Pityriasis versicolor — Fungi, patches
- Cutaneous candidiasis
- Dermatophytoses — Fungi, patches /nodules
- Erythrasma
- Cellulitis — bacteria
- Erysipelas — bacteria
- Subcutaneous necrotizing infections — Bacteria , deep
- Tinea nigra — fungi
- Lyme disease
- Kaposi sarcoma — nodules
- MCC — Large nodules
- Molluscum contagiosum
- Condyloma lata
- Common warts
- Blastomycosis
- Piedra — Fungi, small stones on hair

Overview

- Papules are raised palpable lesions that are usually less than 1 cm in diameter.
- Plaques (nodules) are **raised** palpable lesions larger than 1 cm in diameter and are frequently formed by a confluence of many papules.
- Patches are **flat**, non-palpable lesions larger than 1 cm in diameter.

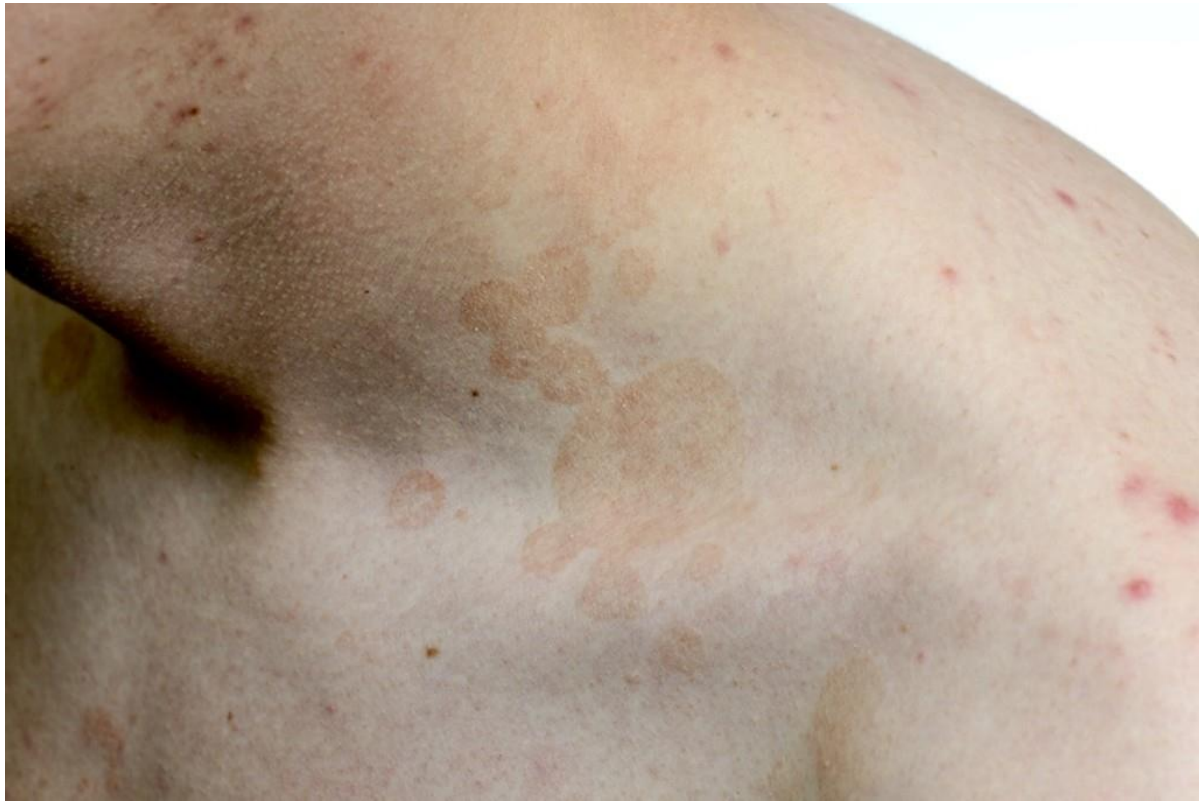




Hypo-/hyper-pigmented patches: Pityriasis versicolor

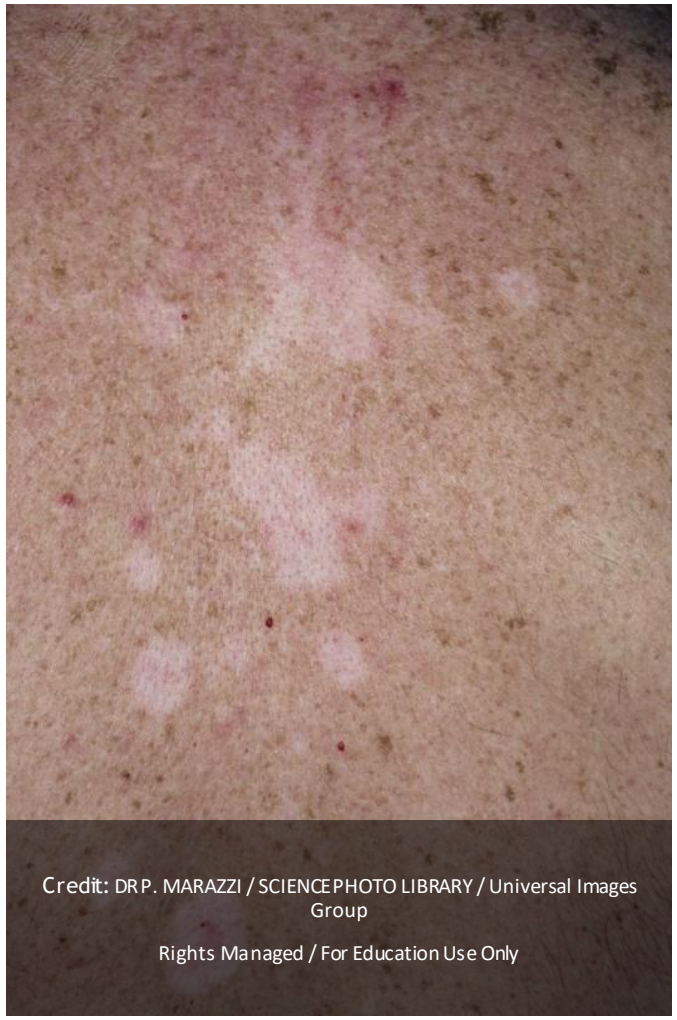
- **Pityriasis versicolor** (tinea versicolor) is a common cutaneous fungal infection of the keratinized epithelial cells in the stratum corneum.
- It is caused by ***Malassezia furfur***, a dimorphic lipophilic fungus, which is a commensal present on the skin of most humans.
- Superficial hyper- or hypopigmented macules or **patches** appear mostly on the chest or back.

Or Trunk or extremities or neck.



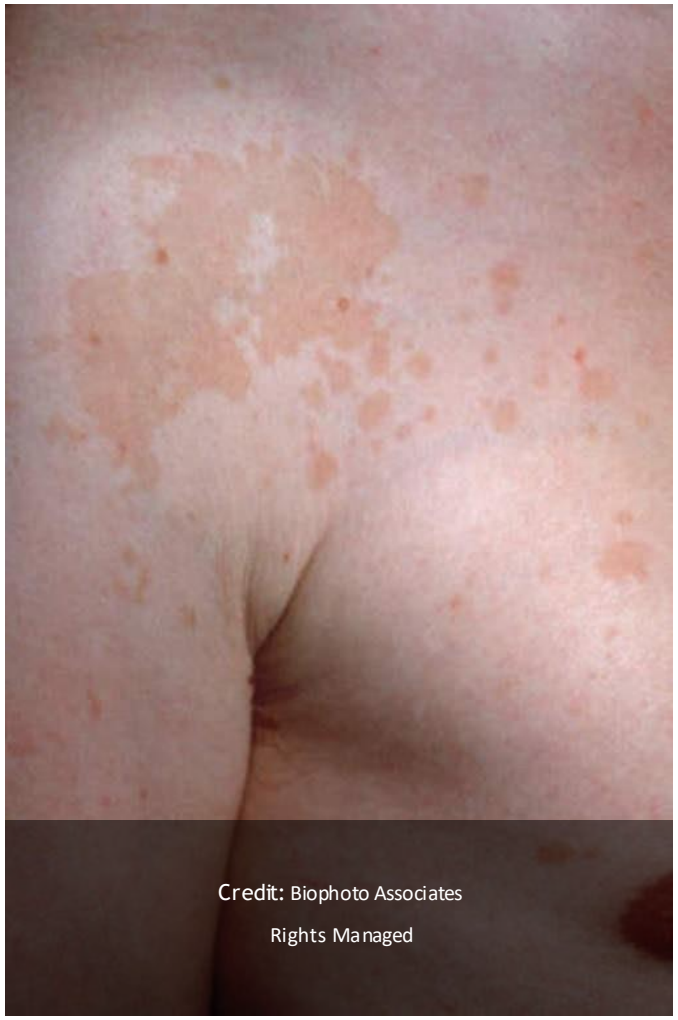
Credit: Science Photo Library
Rights Managed

Pityriasis versicolor



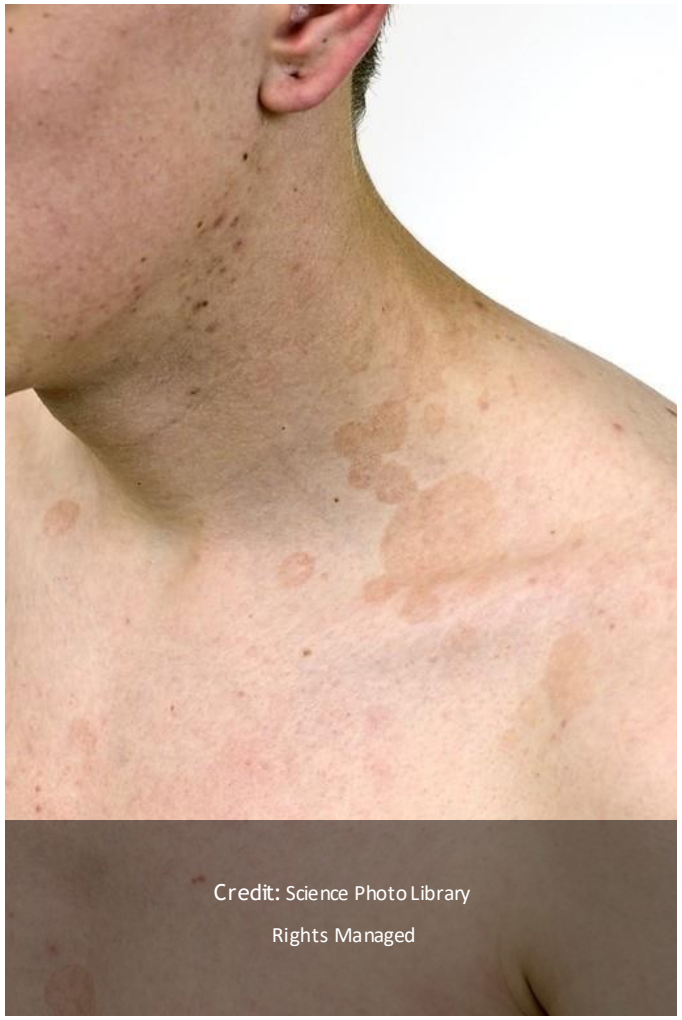
Credit: DR P. MARAZZI / SCIENCE PHOTO LIBRARY / Universal Images Group

Rights Managed / For Education Use Only



Credit: Biophoto Associates

Rights Managed



Credit: Science Photo Library

Rights Managed

Pityriasis versicolor - Epidemiology

Remember these examples on normal skin microbiome: Bacteria (*staph. Epidermidis*), fungi (*M.Furfur*).

- *M. furfur* is normal flora on the skin in 90-100% of adults.
- The prevalence of pityriasis versicolor is 2-8% and it is common in young adults.
- Higher predisposition to pityriasis versicolor is seen in warm moist climates and among pregnant women or those with immunodeficiency states (e.g., HIV infection, diabetes).
- Fungal growth on skin is facilitated by higher temperatures and humidity.

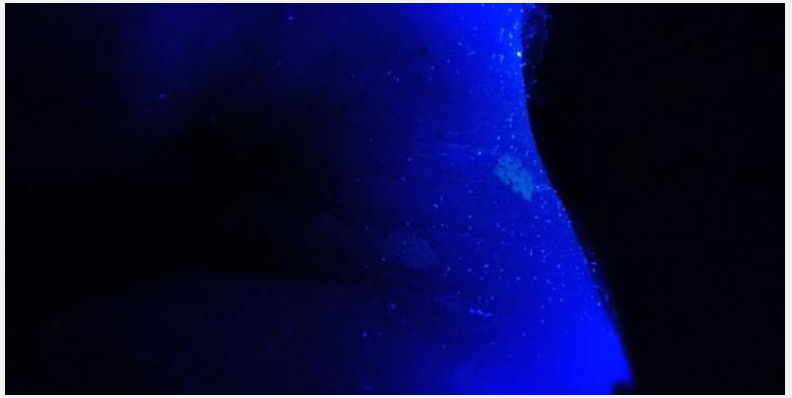
Pityriasis versicolor - Pathogenesis

- *M. furfur* infection remains in the stratum corneum.
- Environmental and host factors can lead to the conversion of the saprophytic yeast to the parasitic mycelial morphologic form.
- *M. furfur* produces dicarboxylic acids, which inhibit tyrosinase, an enzyme involved in melanocyte pigment formation causing hypopigmentation.
- In hyperpigmented macules, *M. furfur* induces an enlargement of melanosomes, which are produced by melanocytes at the basal layer of the epidermis.

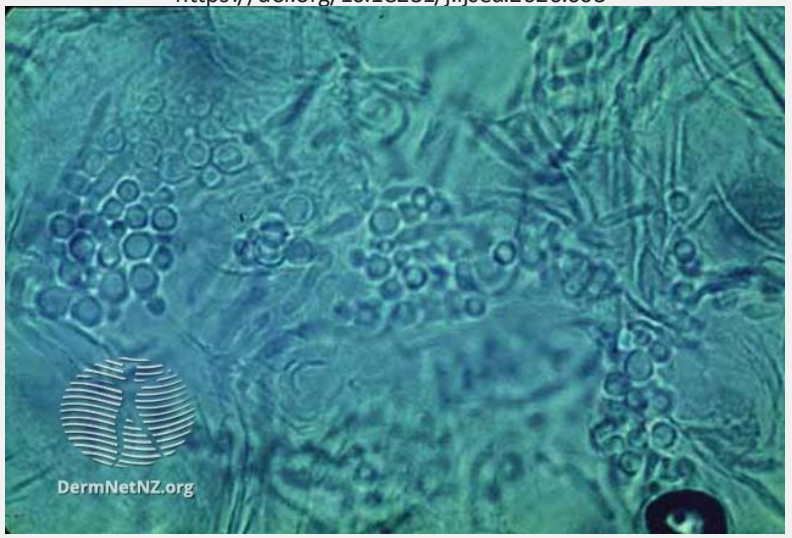
In summary, it inhibits an enzyme that works on melanin formation.

Pityriasis versicolor – Diagnosis

- Diagnosis of pityriasis versicolor is based on the clinical examination of the lesions.
- A Wood lamp (produces a peak wavelength of 365nm) can be used to demonstrate white, pale yellow to orange fluorescence due to pityrialactone by *M. furfur*.
- Skin scrapings clarified with 10% KOH and stained with methylene blue may show round budding yeast cells and short fat hyphae described as "**spaghetti and meatballs**".



Credit: Arumugakani V et al.
https://doi.org/10.18231/j.ijced.2020.063



Credit: DermNet.
https://dermnetnz.org/topics/pityriasis-versicolor

Pityriasis versicolor – Treatment

- Topical agents used to treat pityriasis versicolor include selenium sulfide, sodium sulfacetamide, and ciclopiroxolamine.
- Systemic treatment with ketoconazole, fluconazole, or itraconazole are also effective.
- There is a high recurrence rate.

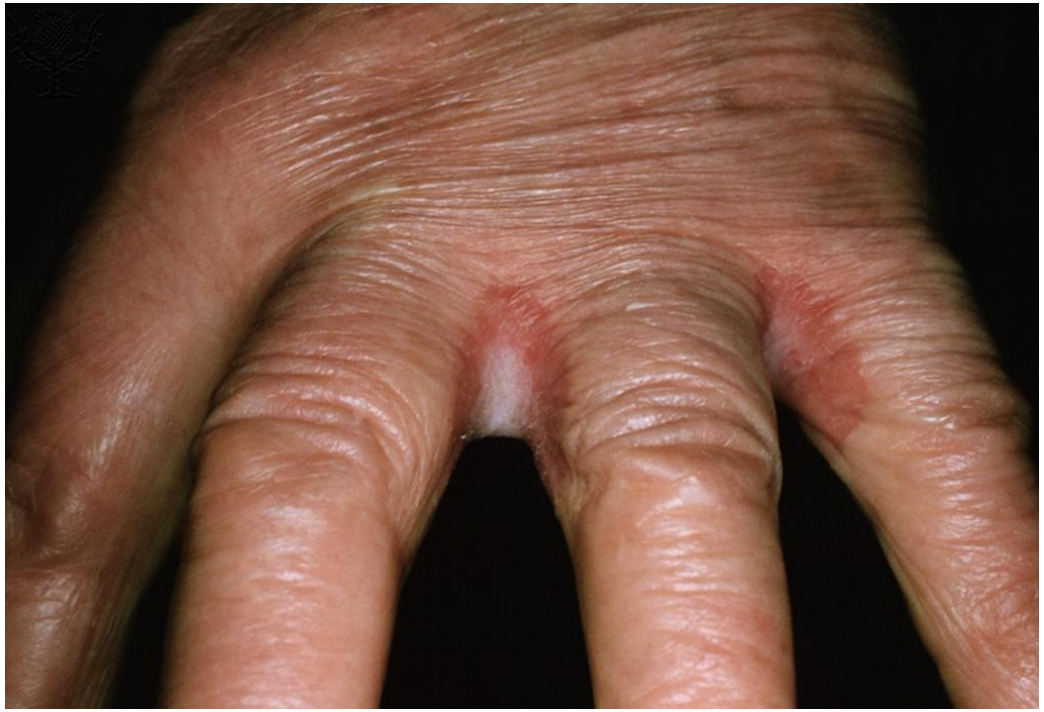
We use antifungals as a treatment for cosmetic reasons only since it can disappear without using anything.

Pityriasis versicolor (tinea versicolor):
-Fungal infection.
-Hyper- or hypopigmented patches (>1 cm in diameter).
-Caused by *Malassezia furfur* (normal skin microbiome).
-Benign and can be treated by antifungals.
-Common condition.
-Wood lamp is used in diagnosis to demonstrate white, yellow to orange fluorescence.
-Can be diagnosed by scrapings of the lesion showing "spaghetti and meatballs" due to the presence of yeast and hyphae.

Erythematous patches/plaques: Cutaneous Candidiasis

Yeast or pseudohyphae.

- *Candida* spp. is a fungal commensal of the skin and can overgrow, causing infections of the skin and mucous membranes.
- Infections of the skin are common in immunocompetent persons and even more common among immunocompromised patients.
- The most common cause of cutaneous candidiasis is *C. albicans*. Others are *glabrata, parapsilosis, tropicalis, krusei*.



Credit: Science Photo Library
Rights Managed

Cutaneous Candidiasis - Clinical Manifestations

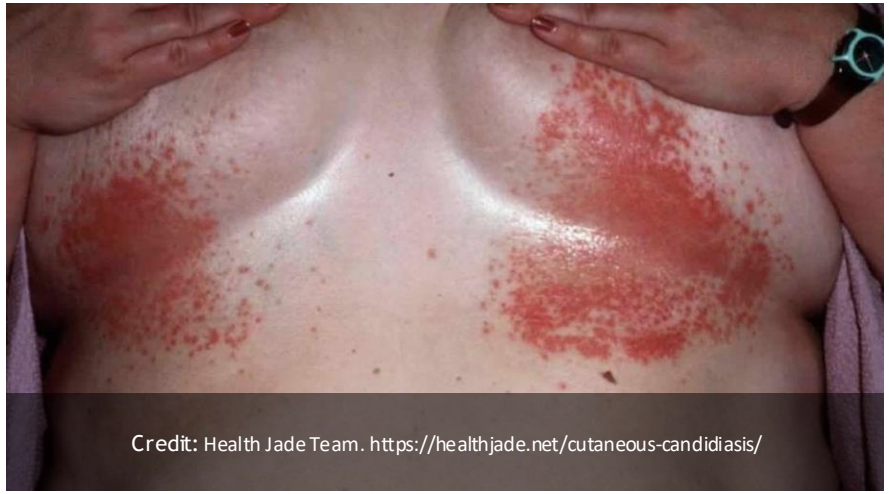
Sometimes these patches transform to nodules.

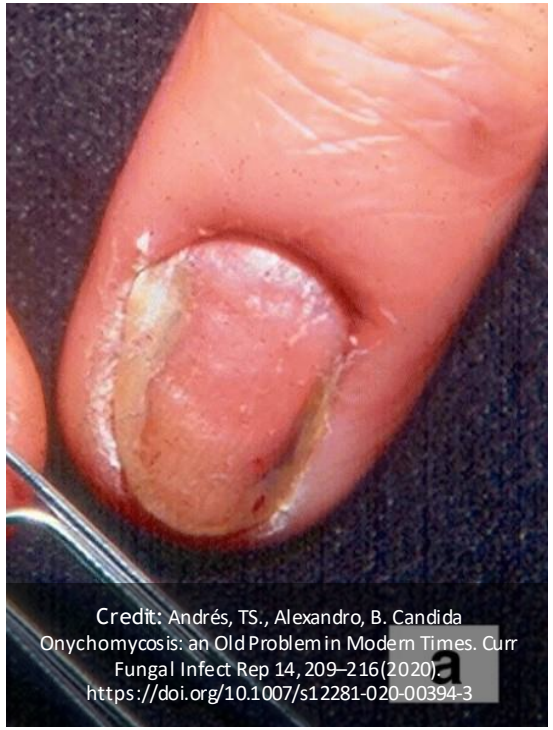
- Red patches/plaques are usually found in the groin, axillae, vagina, mouth, angle of the mouth, glans penis, and inframammary and obesity folds.
- Common conditions are **diaper rash**, **oral thrush**, and **perlèche**. Nails can be affected as well (*Candida* **onychomycosis**). Thrush is an infection of the mucous membranes, which become red and covered with a creamy-white, loosely adherent pseudomembrane.
- Perlèche fissures occur at **angles of the mouth**.

In moist humid hot or worm conditions.

Cutaneous Candidiasis - Clinical Manifestations


Credit: DR P. MARAZZI / SCIENCE PHOTO LIBRARY / Universal Images Group
Rights Managed / For Education Use Only


Credit: Health Jade Team. https://healthjade.net/cutaneous-candidiasis/


Credit: Andrés, TS., Alexandro, B. Candida Onychomycosis: an Old Problem in Modern Times. Curr Fungal Infect Rep 14, 209–216(2020). https://doi.org/10.1007/s12281-020-00394-3


Credit: Perri Dermatology. https://perridermatology.com/dr-perris-blog/candida-perleche/

Cutaneous Candidiasis - Epidemiology G Pathogenesis

- Immunocompromised patients, diapered infants, and patients who are pregnant, obese, or immobile are at increased risk of developing cutaneous candidiasis.
- *C. albicans* is normal flora of the skin in up to 50% of the general population.
- Predisposing factors can allow overgrowth of this organism, resulting in clinical manifestations.
- Cutaneous candidiasis infection is usually limited to the stratum corneum.

Or patients on steroids.

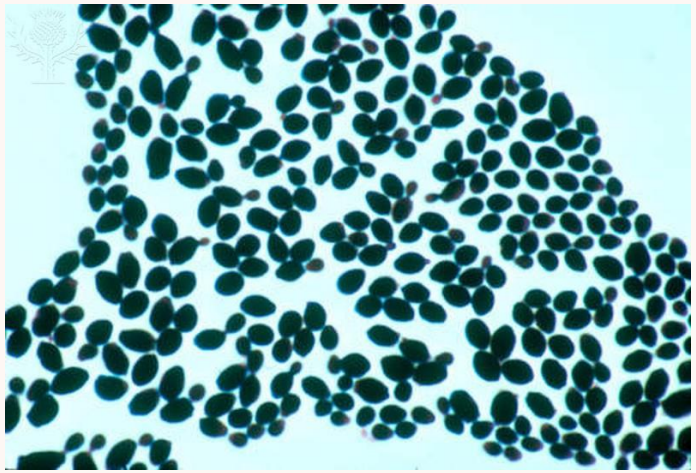
Cutaneous Candidiasis - Diagnosis

10% KOH melts all epithelial cells making fungal elements easily visible.

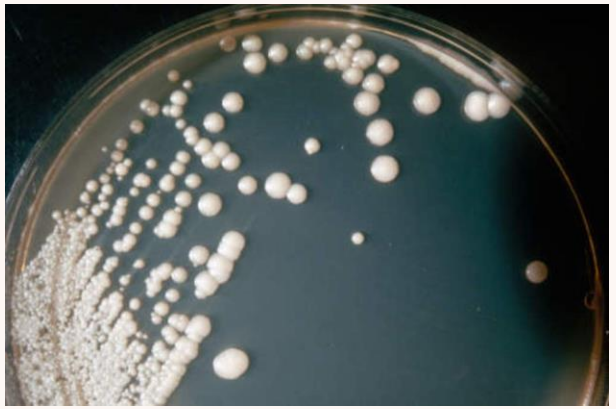
- Wet mounts in 10% KOH show budding yeast and pseudohyphae.
- Only *C. albicans* and *C. dubliniensis* produce germ tubes in medium containing serum.
- *Candida* can be cultured on Sabouraud agar.
- Species identification can be done using chromogenic agar.
- Lesions do NOT fluoresce when exposed to a Wood lamp.

Sabouraud agar is a selective media (it contains gentamicin).

Species identification is important because there is different antifungal susceptibility profile among different species. Don't forget to watch lab lecture!



Credit: Michael Abbey / Photo Researchers / Universal Images Group Rights Managed / For Education Use Only



Credit: Science Source; Rights Managed

Cutaneous Candidiasis - Treatment and Prevention

- Topical treatment with antifungal creams containing nystatin or miconazole may be helpful.
- If topical treatment fails, treatment with systemic ketoconazole may eliminate the disease.
- It is important to prevent skin abrasions and to keep the area dry.

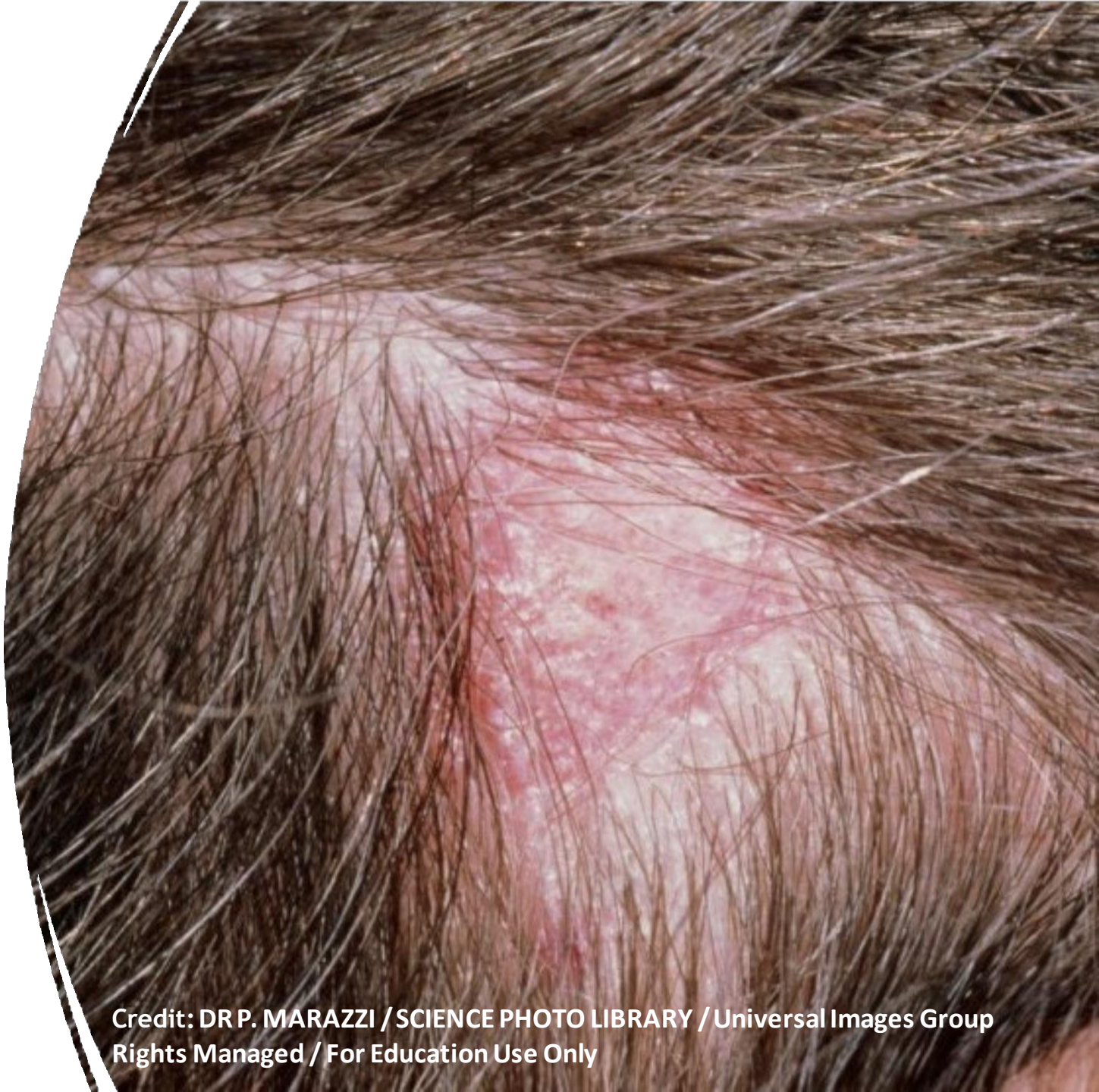
Cutaneous candidiasis:
-Fungal infections that manifest in erythematous patches/plaque.
-Common especially in immunocompromised patients, diabetics in children.
-Most common species is *candida albicans.*
-Manifestations are Diaper rash, oral thrush, Perlèche fissures (occur at angles of the mouth), nail infection (onychomycosis).
-Cutaneous candidiasis can be also found on skin folds or obesity folds or submammary folds.
-The source of the infection is from normal skin microbiome.
-Diagnosis by culture or microscopy (we'll find yeast or germ tube formation).
-Using Wood lamp on lesions caused by candida will not produce fluorescence.
-For treatment antifungals are used (topical or systemic).

Erythematous plaques: Tinea (Dermatophytoses)

- Dermatophytoses are superficial fungal skin infections that can occur on every part of the body. This includes tinea capitis (head), tinea corporis (body), tinea cruris (groin), tinea pedis (foot), tinea manus (hand), tinea barbae (beard), and tinea unguium, or onychomycosis (nail).
- *Microsporum*, *Trichophyton*, and *Epidermophyton* (collectively called the dermatophytes) are the most common causes of dermatophytoses.
- Tinea lesions start as pruritic erythematous macules that become with scaling or vesicles.
- If the infection involves the scalp, hair loss is common (alopecia).

Tinea capitis

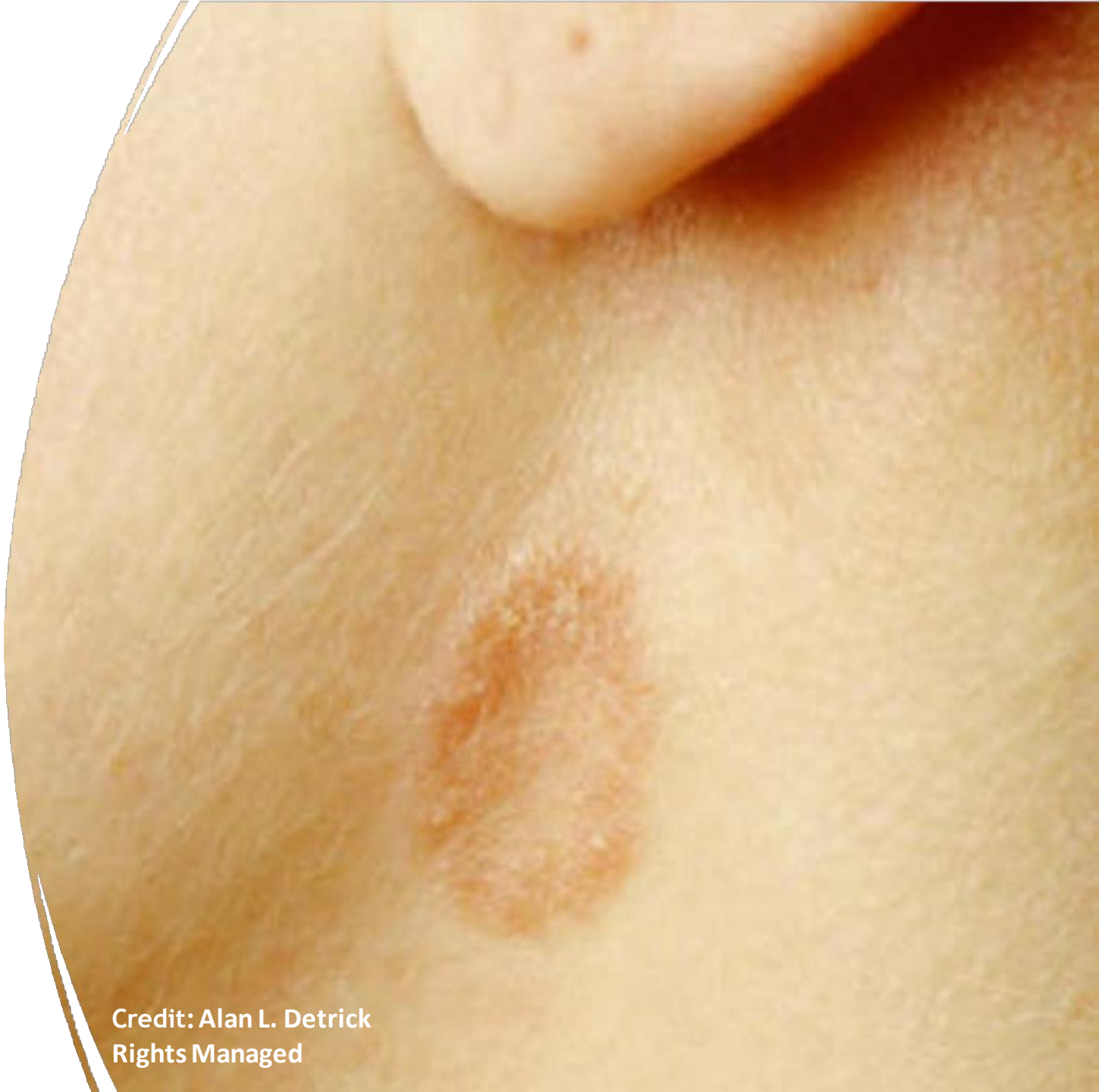
- Fungal infection of the scalp.
- Infections of the hair frequently result in broken hair and alopecia.



Credit: DR P. MARAZZI / SCIENCE PHOTO LIBRARY / Universal Images Group
Rights Managed / For Education Use Only

Tinea corporis

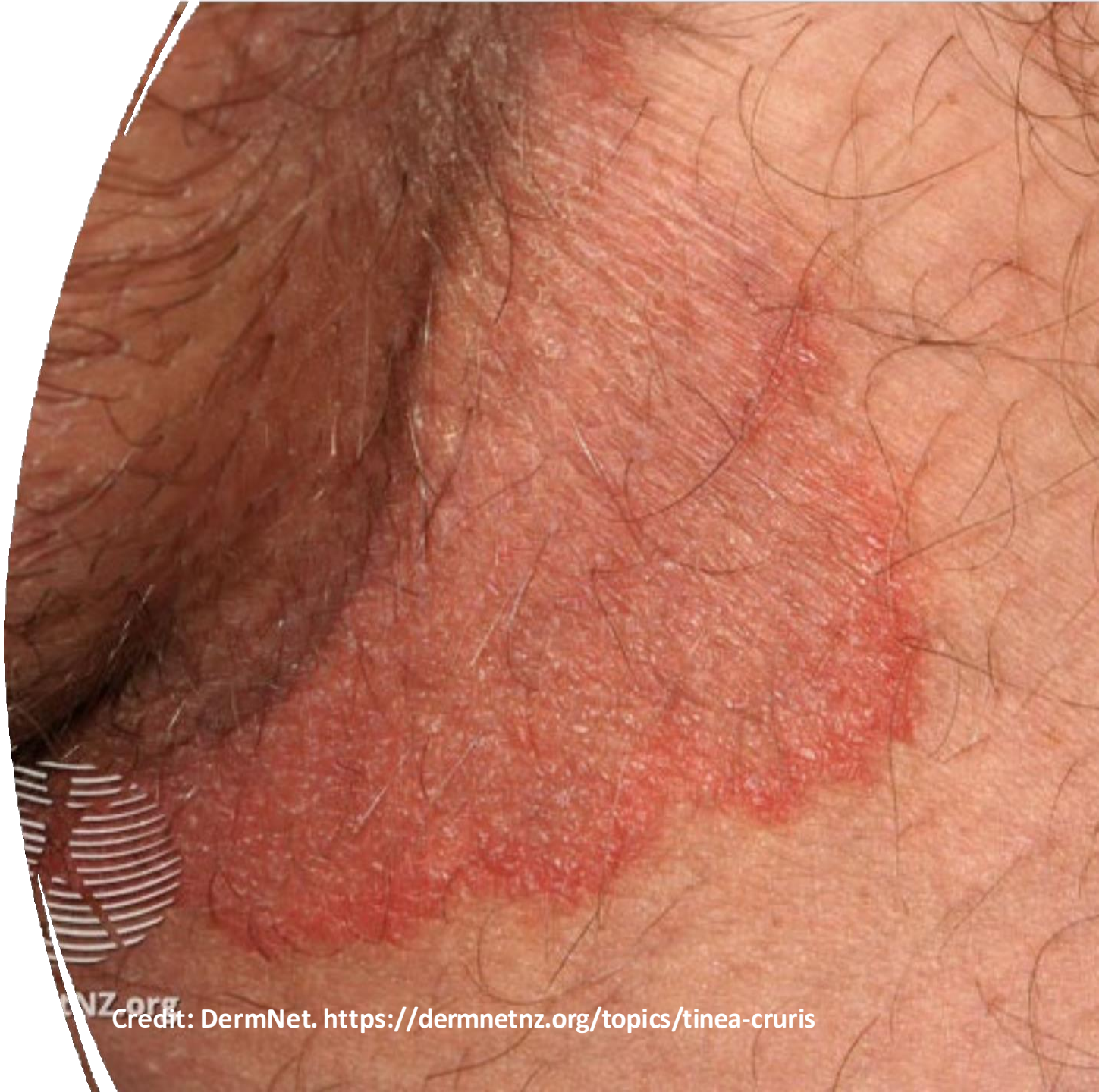
Erythematous plaques with central clearing and elevated borders on the trunk.



Tinea cruris

Plaques present on the groin and perineum.

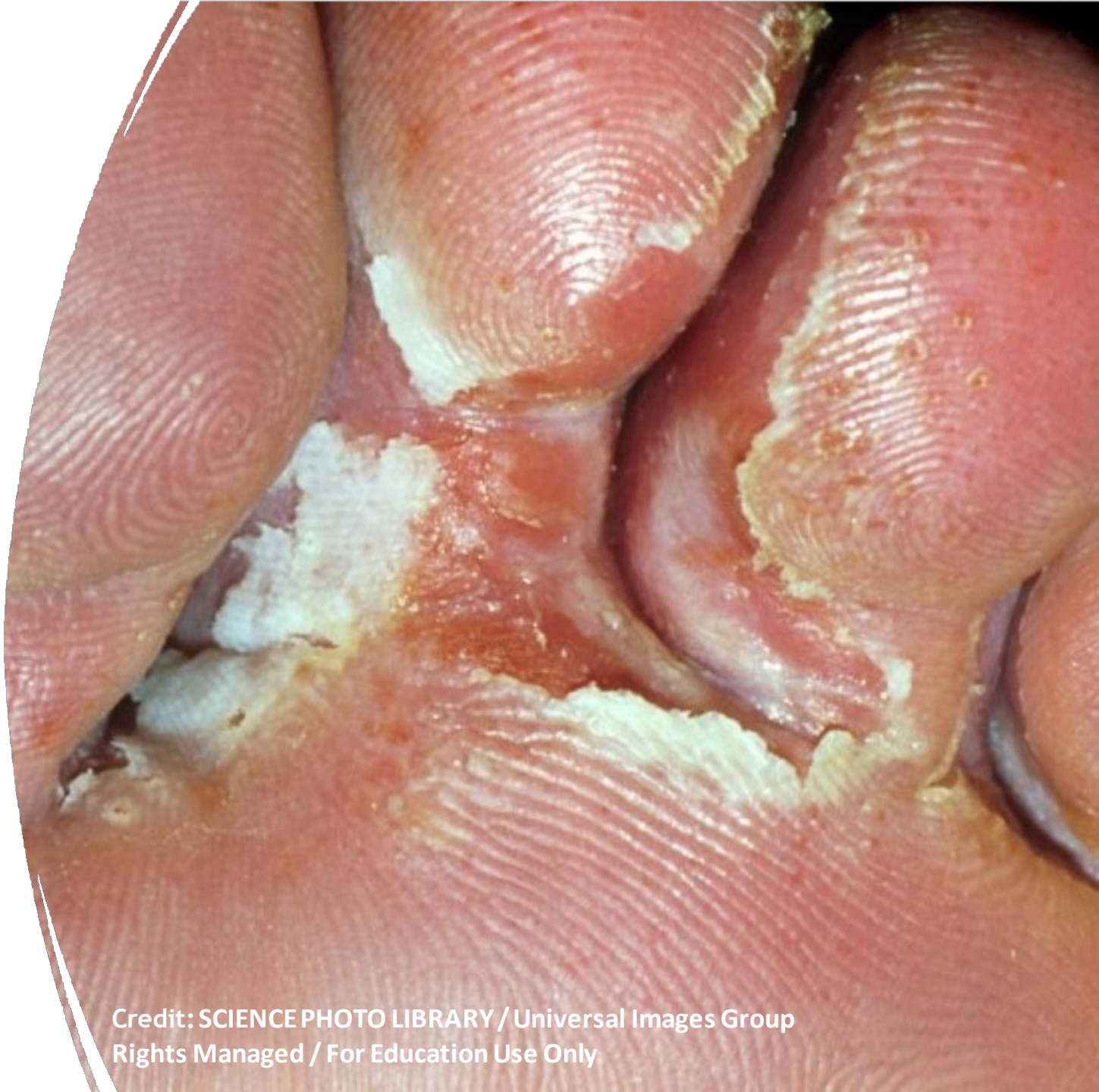
Common in truck drivers. It is classified as patch but if it is slightly elevated then it's a plaque.



Tinea pedis

Athelete's foot

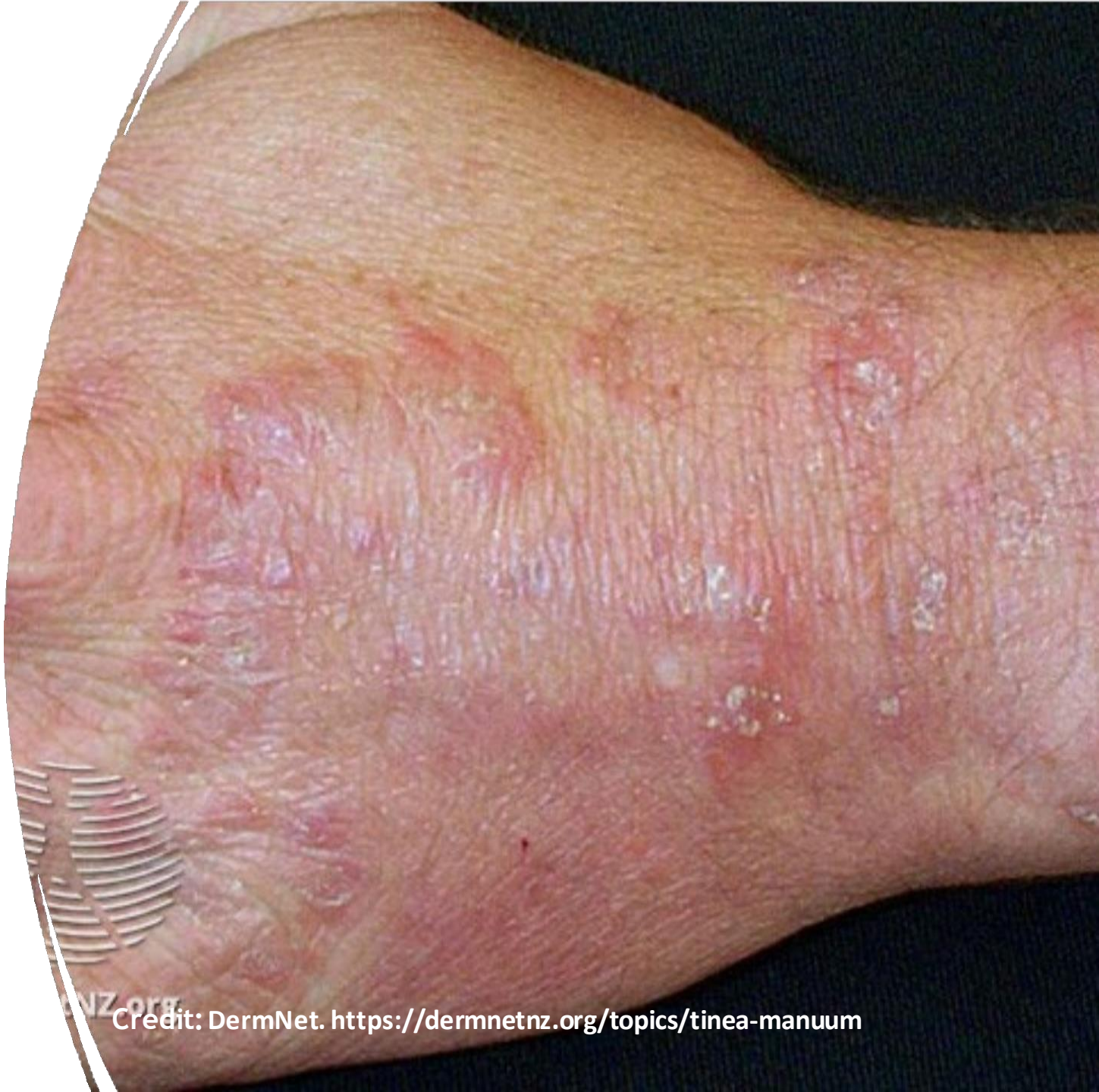
- The most common of all dermatophytoses.
- Results in fissured toe webs, inflamed soles, or thick friable toenails.



Credit: SCIENCE PHOTO LIBRARY / Universal Images Group
Rights Managed / For Education Use Only

Tinea manuum

Inflamed scaly hands.

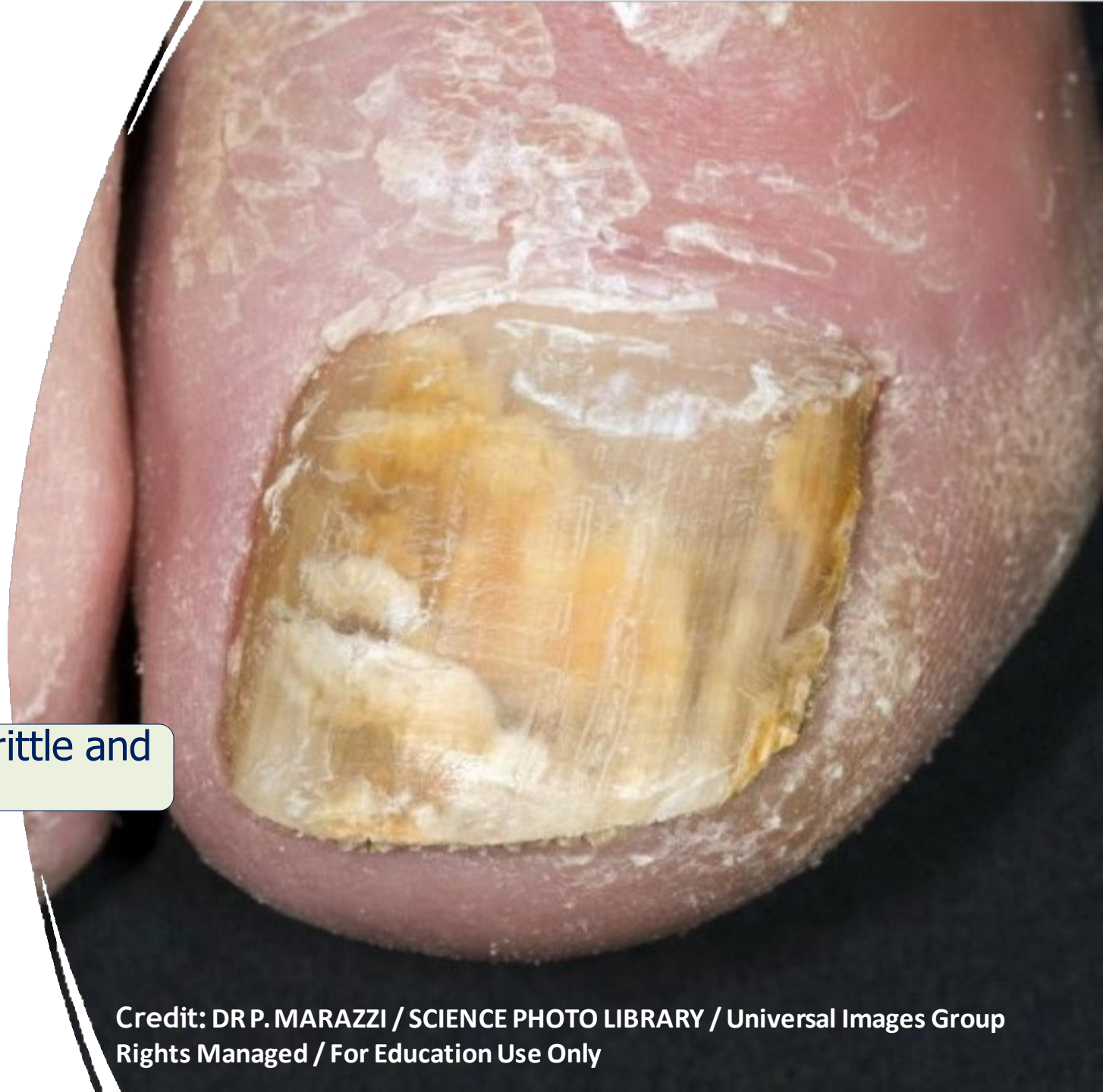


Tinea unguium (onychomycosis)

Or yellowish discoloration.

- Brown discoloration at the edge of the nails.
- Nails become soft, thick, and irregular and separate from the nail bed.
- Tinea unguium usually results from untreated tinea pedis or tinea manuum.

Nails become brittle and easily broken.



Credit: DR P. MARAZZI / SCIENCE PHOTO LIBRARY / Universal Images Group
Rights Managed / For Education Use Only

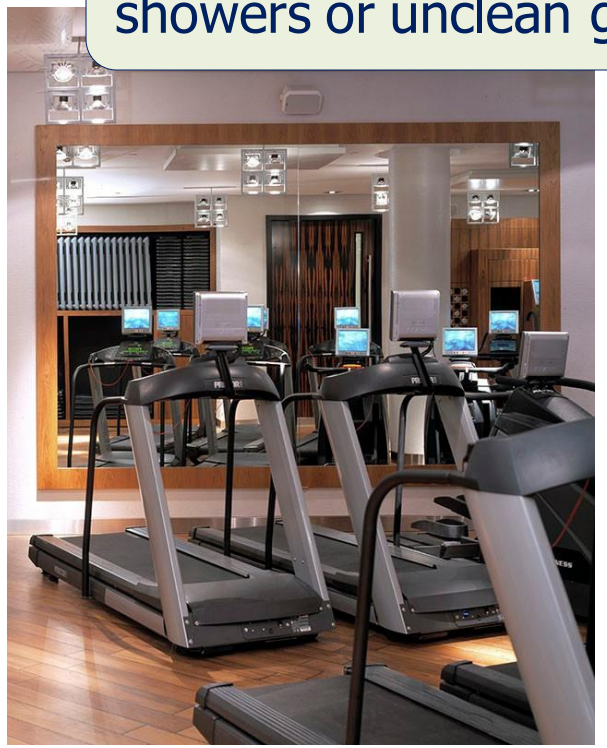
Tinea (Dermatophytoses) - Epidemiology

- Dermatophytoses affect about 20–25% of the global population.
- **The most common dermatophyte infection is tinea pedis.**
- Tinea capitis is common in children.
- Tinea capitis, tinea pedis, and tinea cruris are more common in men than in women.
- Tinea unguium on the fingernails is more common in women; however, the same infection on the toenails is more common in men.

Tinea (Dermatophytoses) - Epidemiology

- Conditions predisposing to dermatophytoses include moist environments and impaired cell-mediated immunity.
- Dermatophytes are transmitted from human to human (**anthropophilic** such as *T. tonsurans*, *E. floccosum*), from animals (**zoophilic** such as *M. canis*), or from soil (**geophilic** such as *M. gypseum*).
- Infections from zoophilic and geophilic dermatophytes are more severe than anthropophilic dermatophytoses.

It can be transmitted in common showers or unclean gym facilities.



Credit: Chris Gascoigne / View Pictures/ Universal Images Group Rights Managed / For Education Use Only; Dorling Kindersley / Universal Images Group
Rights Managed / For Education Use Only

Tinea (Dermatophytoses) – Pathogenesis

- Colonization starts at the stratum corneum with restriction of deeper invasion by the growth requirement for keratin.
- After 2–3 weeks, the advancing border of the infection becomes inflamed (ringworm lesions) due to delayed-type hypersensitivity reaction.
- Invasion of hair follicles results in inflamed nodules, deep-seated pustules, and abscesses.

Tinea (Dermatophytoses) – Pathogenesis

You only need to know that there will be a reaction from the body triggered by the presence of dermatophytes which gives part of the manifestations of the disease.

- Based on the cell-mediated immune status of the patient, there are two outcomes:

(1) Normal cell-mediated immunity leads to an acute or inflammatory infection (which may heal spontaneously), or it will respond well to treatment.

(2) Weak cell-mediated immunity results in chronic or non-inflammatory infection with dryness, erythema, scaling, pruritus, and fissures. It relapses frequently and responds poorly to therapy.

Tinea (Dermatophytoses) - Diagnosis

Microscopic examination is used to identify the organism.

- Diagnosis of dermatophytoses is based on clinical appearance.
- Most lesions do **NOT** fluoresce when examined with a Wood lamp.
- A scraping of the lesions followed by 10% KOH treatment is helpful.
- Scrapings from the lesions are cultured on Sabouraud agar.
- Cultures are incubated at room temperature, with **growth observed within 7-14 days**.

Or clipping the nail in case of onychomycosis then it's cultured.

Credit: JOHN DURHAM / SCIENCE PHOTO LIBRARY. / Universal Images Group
ights Managed / For Education Use Only

Incubation takes more time than in bacterial culture since fungal growth is slower.

Tinea (Dermatophytoses) – Treatment and Prevention

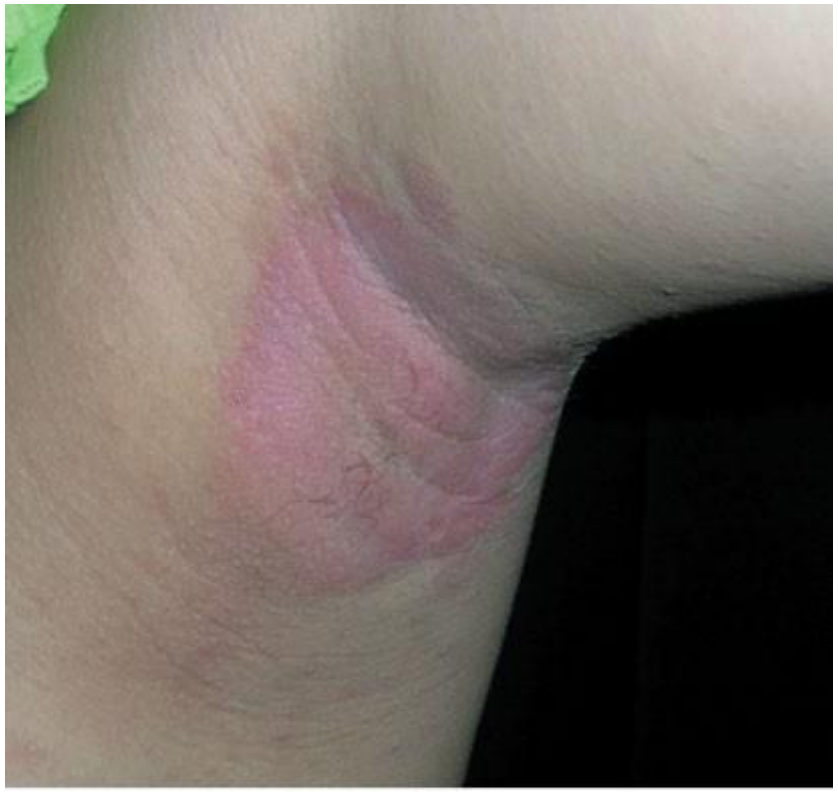
- Antifungal agents such as terbinafine, clotrimazole, itraconazole, or fluconazole are helpful.
- Avoid environments where there is chronic moisture, areas with many spores (e.g., shower-room floors), and avoid wearing tight clothing.

Tinea (Dermatophytes):
-Erythematous plaques that can occur on every part of the body.
-Caused by the three fungal genera: *Microsporum*, *Trichophyton*, *Epidermophyton* (.collectively called Detrmatophytes).
-Tinea lesions start as pruritic erythematous macules that become with scaling or vesicles then they develop to erythematous plaques.
-Large lesions named depending on the area:
  -Tinea capitis (scalp), common in children, can result in hair loss (alopecia).
  -Tinea corporis (body), remember that plaques indicates a large elevated/ raised lesions.
  -Tinea cruris (inguinal area), common in truck drivers, patch or slightly elevated plaques.
  -Tinea pedis (athletes' foot), **the most common**.
  -Tinea manuum (hands)
  - Tinea unguium/ onychomycosis (nails), usually results from untreated tinea pedis tinea manuum. It involves yellowish discoloration and makes toenails brittle/weak.
-Dermatophytes are transmitted either from human to human (anthropophilic) in common showers/unclean gym facilities or from animal to human (zoophilic) or from soil (geophilic).
-Tinea is localized in stratum corneum (epidermis).
-Diagnosed by taking scraping from the lesions or clipping in the case of onychomycosis then it is cultured in sabouraud dextrose agar (fungal growth is slower than bacteria's so, the result takes days). Microscopy is used to identify the organism.
-Treated by antifungal agents.

Erythematous plaques: Erythrasma

- **Erythrasma** is **a bacterial infection of the skin folds under the arms, in the groin and between the toes** that is similar in appearance to tinea cruris and diaper rash.
- Differences in the fluorescence of the lesions following examination with a Wood lamp help in determining if the infection is erythrasma (**coral-red fluorescence**), tinea or diaper rash (no fluorescence).

(Cutaneous candidiasis)



RP, Smith MA, Mayeaux EJ, Chumley HS: *The Color Atlas*
ne, Second Edition: www.accessmedicine.com
McGraw-Hill Companies, Inc. All rights reserved.

Credit: Courtesy of Richard P. Usatine, MD., https://basicmedicalkey.com/erythrasma/

Erythematous plaques: Erythrasma

- Erythrasma is caused by a bacterium that is part of the normal flora called *Corynebacterium minutissimum*.
- The lesions of erythrasma are brown to red-brown well-defined patches/plaques, which may have fine scales.
- Lesions are usually observed on the inner thighs, crural region, scrotum, and toe webs. The axillae, sub-mammary area, peri-umbilical region, and inter-gluteal fold can be affected but are less commonly reported.

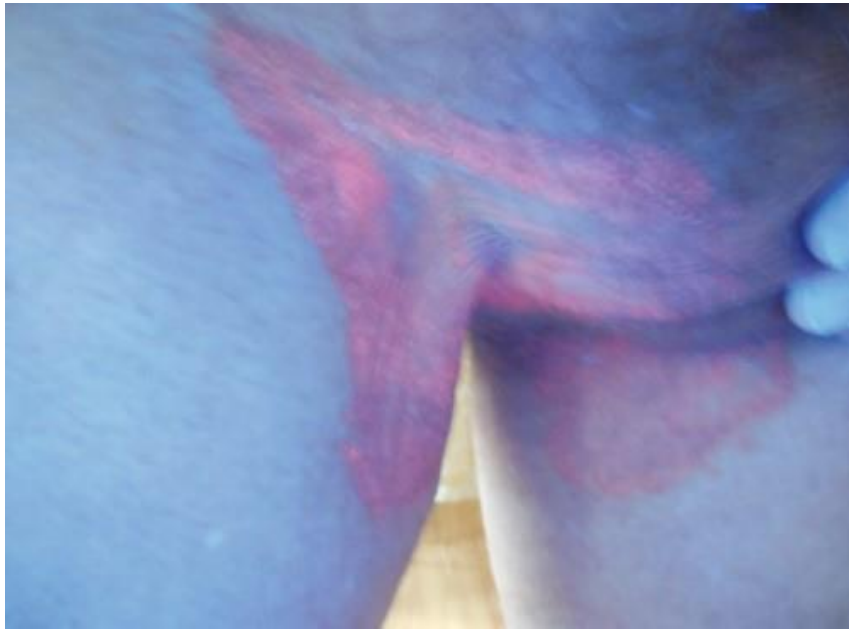
Erythrasma – Epidemiology/Pathogenesis

- Predisposing factors include excessive sweating, obesity, diabetes mellitus, and other immunocompromised states.
- In patients with erythrasma, the bacteria invade the upper third of the stratum corneum and multiply in hot humid environments.
- The stratum corneum thickens, and the organisms can be seen in the intercellular spaces as well as within cells. *C. minutissimum* can dissolve keratin.

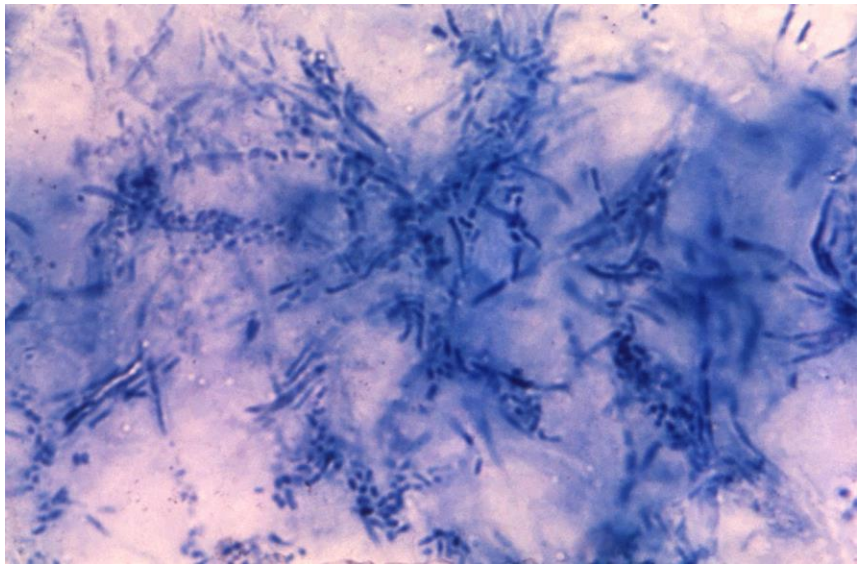
Erythrasma - Diagnosis

Wood lamp is used to differentiate it from tinea cruris.

- The **coral-red** fluorescence seen when lesions are examined by Wood lamp is secondary to the production of porphyrin by bacteria.
- Skin scraping reveals **gram-positive rods**.
- The skin scrapings also can be cultured to identify the organism.



Credit: Tanya & Philip.
https://escholarship.org/uc/item/9zh116s1



Credit: CDC public health image library.
https://phil.cdc.gov/Details.aspx?pid=21834

Erythrasma - Treatment and Prevention

- Erythrasma can be treated with topical antibiotic such as fusidic acid cream and clindamycin solution.
- Extensive infections can be treated with oral erythromycin or tetracycline.
- To prevent recurrences, patients should be encouraged to improve hygiene and keep the area dry.

Erythrasma:
-Erythematous plaque (large, slightly elevated).
-Caused by a bacterium called *Corynebacterium minutissimum.*
-Axilla, inguinal area (might be mistaken for tinea cruris), inner thighs, crural region, sub-mammary area (might be mistaken for cutaneous candidiasis)
-Predisposing factors include excessive sweating, obesity, diabetes and other immunocompromised states.
-To differentiate it from tinea cruris we use Wood lamp, in tinea cruris no fluorescence is produced but in erythrasma coral-red fluorescence is seen.
-Skin scraping reveals gram-positive rods.
-Treated by antibacterial agents/antibiotics such as fusidic acid or clindamycin.

Erythematous plaques: Cellulitis

Some of the causative agents: S. Pyogenes, S. aureus, beta hemolytic streptococci, gram-negative bacteria (E. Coli, klebsiella, enterobacter, serratia, P. aeruginosa).

- Cellulitis is an acute infection of the dermis and subcutaneous tissues caused by different bacteria.
- *S. pyogenes* and *S. aureus* are common causes of cellulitis commonly seen in association with wounds or in burn patients. *Streptococci* groups B, C, D, and G are less common causes of cellulitis. *S. pneumoniae* can cause cellulitis in certain groups (DM, SLE, drug users, patients with hematologic disorders).
- Gram-negative bacilli (e.g., *E. coli*, *P. aeruginosa*) cause cellulitis resulting in foot ulcers in DM patients. *P. aeruginosa* cellulitis and osteomyelitis often occur following trauma to the foot. *P. aeruginosa* cellulitis is also common in burn patients.
- *Pasteurella multocida* cellulitis is associated with **dog or cat bites**.

Cellulitis - Clinical Manifestations

Large erythematous plaques.

(this feature is used to differentiate between cellulitis and erysipelas)

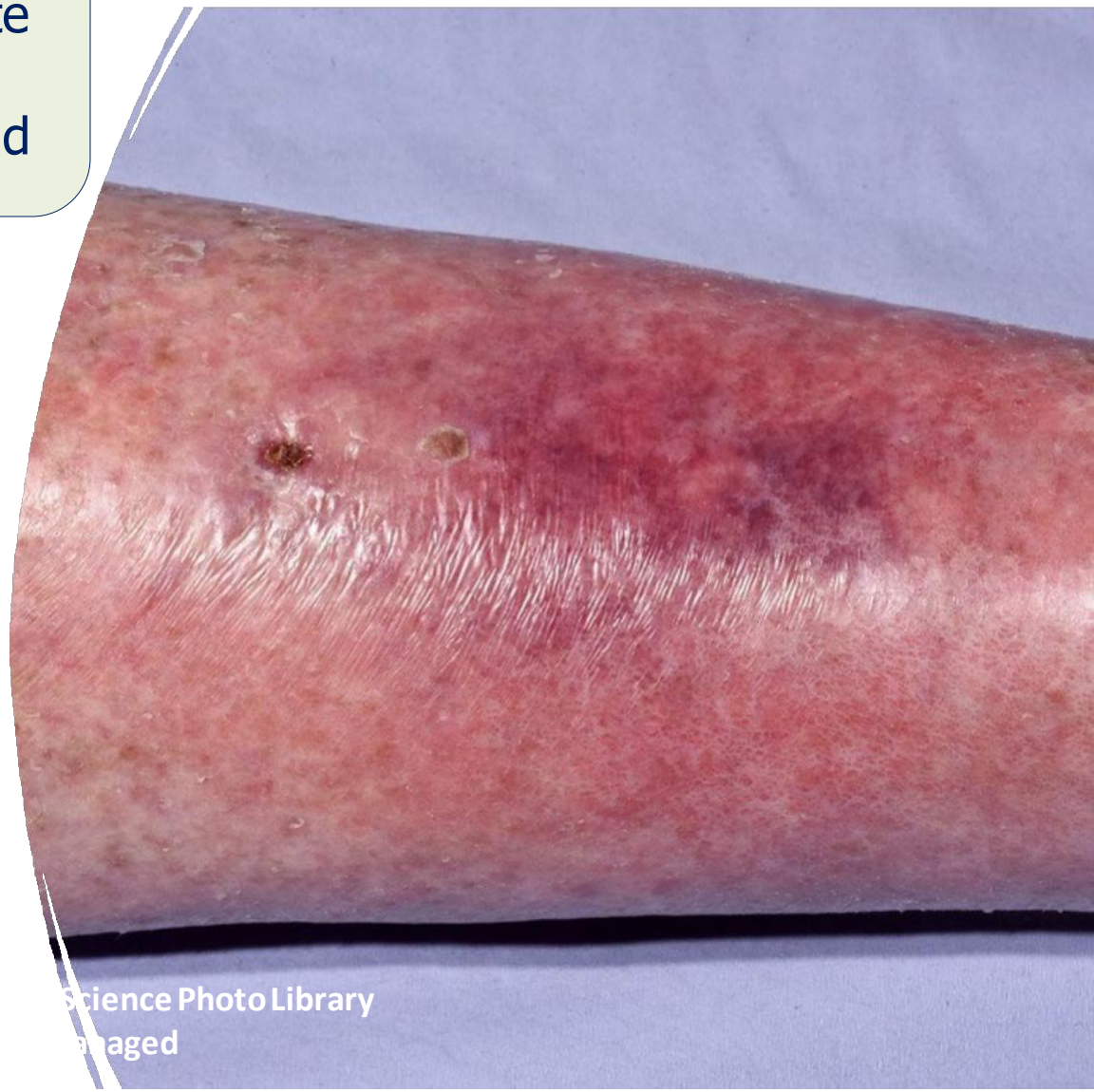
- Acute inflammation is seen within the subcutaneous tissues. **The borders of the lesions are usually indistinct.**

Causing ulcers.

- Vesicles and bullae may develop and rupture, occasionally with necrosis of the involved skin. Associated red streaking is characteristic of ascending lymphangitis.

Systemic symptoms:

- Manifestations include regional lymphadenopathy, fever, malaise, preceding the cutaneous findings by a few hours.

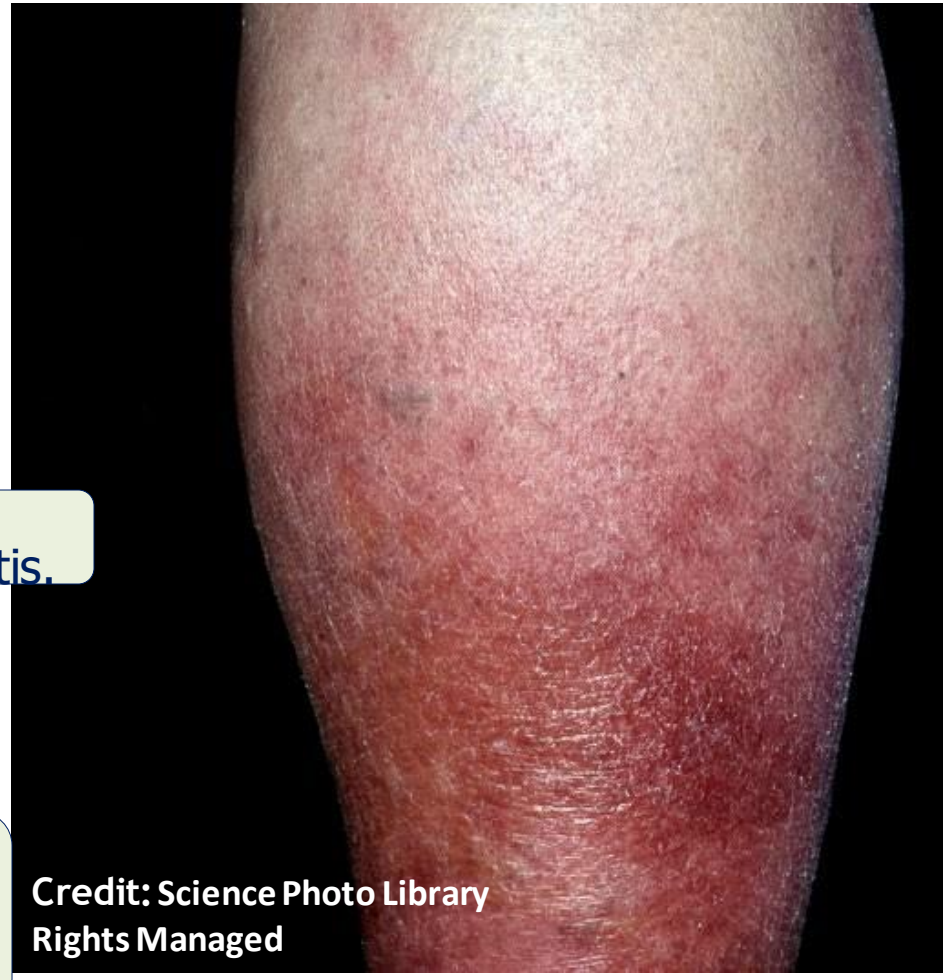


Cellulitis - Epidemiology

- Cellulitis is most common in the lower extremities.
- Conditions that predispose patients to increased risk of developing serious or rapidly spreading cellulitis include DM, immunodeficiency (e.g., chronic steroid use), varicella.
- Skin trauma, ulceration, and edematous tissue, usually precedes cellulitis.
- Cellulitis following infection with gram-negative rods is more common in immunocompromised hosts.

As a result of itching in patients with chickenpox a secondary bacterial infection occurs including cellulitis.

These conditions facilitate bacterial penetration causing cellulitis.



Credit: Science Photo Library
Rights Managed

Cellulitis - Pathogenesis

- A diffuse infection occurs due to various virulence factors released by the bacteria such as streptokinase, DNase, and hyaluronidase.
- Cellulitis extends deeper into skin than does erysipelas and may result in osteomyelitis.
- Cellulitis results in serious systemic illness by uncontrolled spread to contiguous tissues, to the lymphatics, or to the bloodstream.

Cellulitis - Diagnosis, Treatment, and Prevention

Diagnosis involves knowing the etiologic agent.

Clinically, it is important to differentiate between cellulitis and deep venous thrombosis.

- Diagnosis of cellulitis is based on clinical findings.
- Culture and AST can be useful. Results of blood cultures are often positive.

AST: Antimicrobial susceptibility testing.

- Serologic tests, especially a rising anti-DNase B titer, confirm a streptococcal cause.
- Oral or parenteral antibiotics are frequently used to treat patients with mild cellulitis.

Systemic antibiotics should be used.

- Patients with severe cellulitis must be admitted to the hospital and treated with IV antibiotics. Empiric antimicrobial agent coverage for *S. pyogenes* and *S. aureus* should be given.

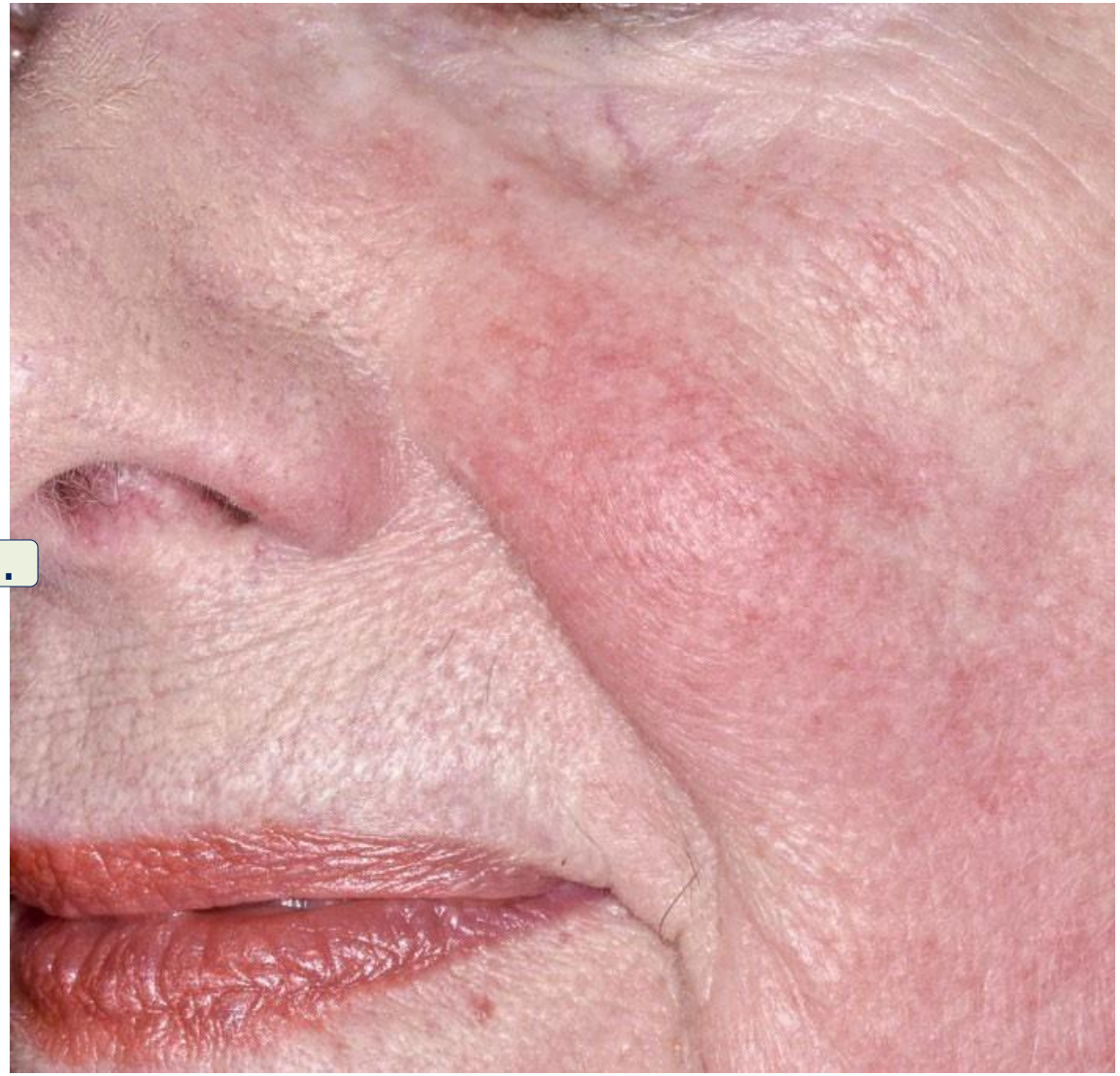
Cellulitis:
-Large erythematous plaques at different parts of the body (lower extremities, foot...)
-Acute infection of the dermis and subcutaneous tissue.
-S. Pyogenes, S. aureus, beta hemolytic streptococci, gram-negative bacteria (E. Coli, klebsiella, enterobacter, serratia, P. aeruginosa).
-Pasteurella multocida cellulitis is associated with dog or cat bites.
-The borders of the lesions are usually indistinct (this feature is used to differentiate between cellulitis and erysipelas)
-Vesicles and bullae may develop and rupture causing ulcers.
-Causes systemic symptoms: Fever, malaise (preceding the cutaneous finding).
-Conditions that predispose patients to develop cellulitis: diabetes or immunodeficiency, varicella (secondary infection is a complication of the chickenpox because of itching).
-Skin trauma, ulcers usually precedes cellulitis (facilitates penetration of bacteria to deeper tissues).
-The pathogenesis is related to the virulence factors of bacterial agents.
-Diagnosis involves knowing the etiologic agent (clinically, it's important to differentiate between cellulitis and deep venous thrombosis).
-Systemic antibiotics are used to treat cellulitis (culture and AST can be useful).

Erythematous plaques: Erysipelas

- Erysipelas is a superficial bacterial infection that extends into the cutaneous lymphatics.

Or group C, group F, group G beta hemolytic streptococci.

- Most cases are due to streptococci, with *S. pyogenes* present in about two thirds of cases, and group G streptococci in a third of cases.
- The lesions are raised and **well demarcated**.



Credit: Science Photo Library
Rights Managed

Erysipelas - Epidemiology/Pathogenesis

- The highest incidence of erysipelas occurs in patients aged 60 to 80 years.
- Erysipelas lesions are most seen on the legs (in about 85% of cases), and the next most common location is the face.
- Erysipelas is more commonly seen in patients who are immunocompromised and those with lymphedema.
- The bacteria are initially inoculated into an area of skin trauma. The source of the bacteria is usually from the host nasopharynx.

The causative agents are usually colonizers of the skin.

Erysipelas - Diagnosis, Treatment, and Prevention

- Blood, wound, and nasopharyngeal samples should be obtained and cultured. AST is used for diagnosis of erysipelas.
- Elevation and rest of the affected limb are recommended to reduce local swelling and inflammation.
- Treatment includes oral or intramuscular injection of antibiotics such as penicillin, erythromycin, or azithromycin.
- Following treatment, the lesion usually desquamates but can resolve with pigmentary changes that may resolve over time.

Erysipelas:
-Erythematous plaques.
-Lesions are raised and well demarcated.
-Causative agents are usually beta hemolytic streptococci (colonizers of the skin) *S. Pyogenes* and sometimes by group C, F and G beta hemolytic streptococci.
-Highest incidence in elderly.
-Lesions are usually on the face or legs.
-Samples are obtained and cultured or tested for AST.
-Treatment is by using systemic antibiotics such as penecillin G.

Erythematous plaques: Subcutaneous necrotizing infections

- Subcutaneous necrotizing infections cause extensive destruction of the subcutaneous tissues and fascia, and some also cause extensive necrosis of the muscles. Can affect bones causing osteomyelitis.
- Diseases include necrotizing fasciitis, non-clostridial anaerobic cellulitis, clostridial myonecrosis (gas gangrene), Fournier gangrene. Necrotizing infection in scrotal region.
- The etiologic agents include: ***S. pyogenes*** (the most common cause of necrotizing fasciitis), ***S. aureus***, anaerobes, ***Enterobacteriaceae***, ***Clostridium perfringens*** (the common cause of gas gangrene), among other ***Clostridium spp***.

Subcutaneous necrotizing infections - Clinical Manifestations

- Subcutaneous edema and necrosis are seen.
- With progression, violaceous discoloration and bullae, crepitus, palpable gas in tissues, and dermal gangrene may develop.
- When male genitalia are involved, the disease is called **Fournier gangrene**.

Subcutaneous necrotizing infections - Epidemiology

- The mortality rate with treatment is 20–30%.
- The most common site of involvement is an extremity and may occur from infected cutaneous ulcers or infectious complications of previous injury.
- The second most common site of involvement is the perineum, which is usually a complication of prior surgery.
- DM predisposes patients to subcutaneous necrotizing disease.

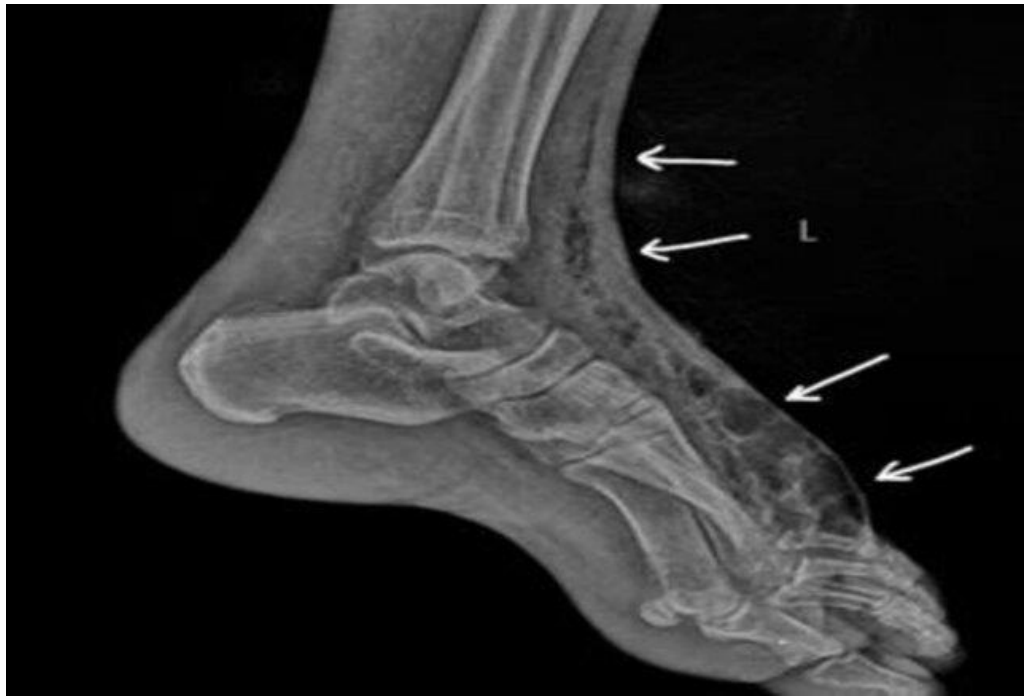
Subcutaneous necrotizing infections - Pathogenesis

- Infection extends into the subcutaneous tissue following trauma.
- Occlusion of small subcutaneous vessels, arterioles and venules leads to tissue ischemia and dermal gangrene.
- Ischemia, edema, and inflammation in the subcutaneous tissue decrease O_2 and permit growth of obligate anaerobes while promoting anaerobic metabolism by facultative organisms.
- Anaerobic metabolism often produces hydrogen and nitrogen, relatively insoluble gases that may accumulate in subcutaneous tissues and cause **crepitus**.

Hearing a sound when touching the tissue (palpation) or can be seen in radiography.

Subcutaneous necrotizing infections - Diagnosis

- **The disease is an emergency.** Differentiation of cellulitis from clostridial gas gangrene is critical to proper management.
- X-rays of the affected area often show soft tissue gas.
- Rapid progression of tissue damage requires surgical exploration.
- Pus aspirated into a syringe percutaneously or during surgery provides the most suitable material for Gram stain and aerobic and anaerobic cultures.



Credit: Bakhshi et al: http://dx.doi.org/10.18203/2349-2902.isj20203816

Subcutaneous necrotizing infections - Treatment and Prevention

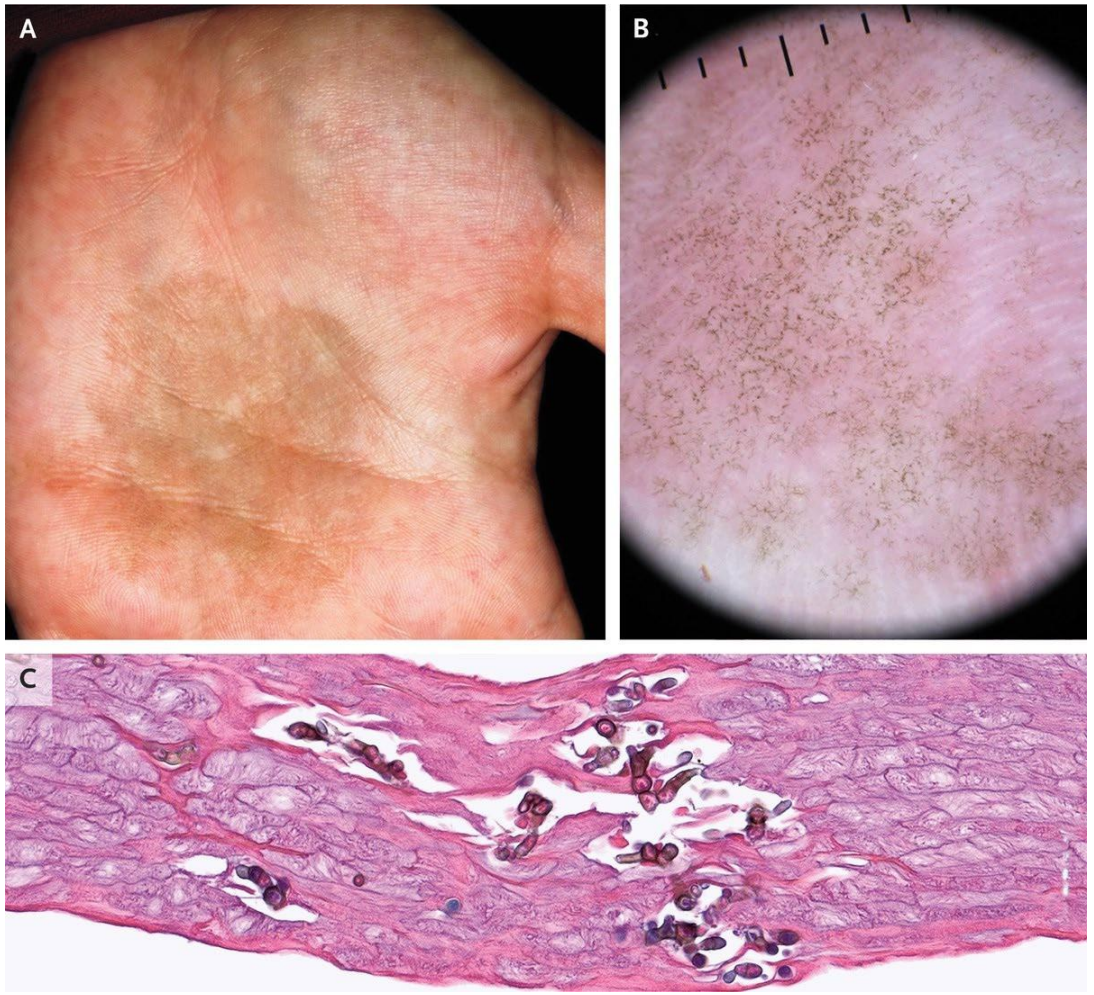
- Gentamicin combined with clindamycin, or cefoxitin or imipenem alone is appropriate treatment of subcutaneous necrotizing infections pending results of cultures.
- Therapy involves incision and extensive debridement.
- Hyperbaric oxygen therapy is also used.
- Prevention involves proper care of wounds and trauma sites.

Extensive surgical treatment to remove dead tissue is needed along with antibiotics.

Subcutaneous necrotizing infections:
-Starts as erythematous plaques then it involves deeper layers causing necrotizing infections, includes intensive destruction of the subcutaneous tissue and fascia.
-Extensive necrosis involves the muscles and bones causing osteomyelitis.
-Diseases include necrotizing fasciits, clostridial myonecrosis (gas gangrene), Fournier gangrene (necrotizing infection in scrotum).
-Etiologic agents like S. pyogenes (flesh eating bacteria) which is the most common cause, S. aureus, anaerobs, clostridium perfringens (cause of gas gangrene), Enterobacteriaceae.
-Antibiotics are used for treatment but most importantly there should be extensive surgical treatment to remove necrotic/dead tissue.
-Hyperbaric oxygen therapy is also used.
-High mortality rate.
Occlusion of small subcutaneous vessels, arterioles and venules leads to tissue ischemia and dermal gangrene.
-Anaerobic metabolism often produces hydrogen and nitrogen (insoluble gases) that accumulate and cause crepitus.
-It is a medical emergency since it causes death rapidly.
-X-rays of the affected tissue often show tissue gases.
-Prevention involves proper care of wounds and trauma.

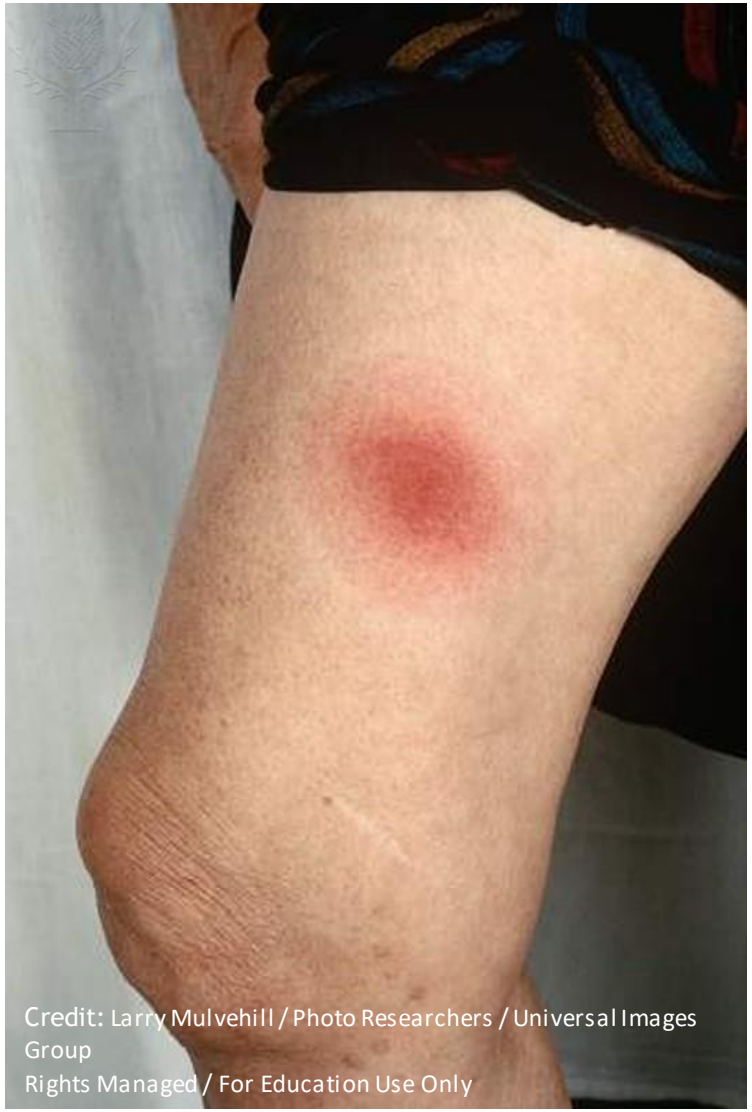
Patches: Tinea nigra

- Tinea nigra is a superficial infection of the stratum corneum caused by the dematiaceous fungus ***Hortaea werneckii***.
- The lesions are dark patches often on the palm.
- Microscopic examination of skin scrapings shows branched, septate hyphae and budding yeast cells with melanized cell walls.
- Tinea nigra will respond to treatment with keratolytic solutions, salicylic



Nodules: Lyme disease

- **Lyme disease is the most common tick-borne illness in the US**.
- Lyme disease is caused by the spirochete *Borrelia burgdorferi*.
- Within 3–30 days after a patient experiences a tick bite, a red macule will appear at the site.
- **The macule expands radially as a nodele with central clearing and swelling (erythema migrans)**.
- Other manifestations are variable and include a flu-like syndrome consisting of malaise, fatigue, chills, fever, headache, stiff neck, myalgias, and arthralgias.



Lyme disease: Epidemiology

- The highest incidence in summer and early fall.
- The incidence is highest in children 5–10 years.
- Deer, mice, sheep, and dogs serve as reservoirs for *B. burgdorferi*.
- *B. burgdorferi* is transmitted from animal reservoirs to humans via a bite from tick (*Ixodes* spp.)

Credit: David M. Phillips / Photo Researchers / Universal Images Group
Rights Managed / For Education Use Only

Lyme disease: Pathogenesis

- Although any body part can be infected, *B. burgdorferi* shows a distinct tropism for the **skin**, CNS, heart, joints, and eyes.
- Once in the skin, the bacteria produce the characteristic skin lesion (**erythema migrans**).
- Hematogenous dissemination can occur within days to weeks following the initial infection.

Lyme disease: Diagnosis

- Presumptive diagnosis of Lyme disease is based on the typical erythema migrans rash and associated neurologic, cardiac, or rheumatic abnormalities.
- Definitive diagnosis requires a serologic test for the presence of antibodies to *B. burgdorferi*.
- An ELISA that detects *B. burgdorferi* IgM and IgG antibodies is done to confirm the diagnosis.

Lyme disease: Treatment and Prevention

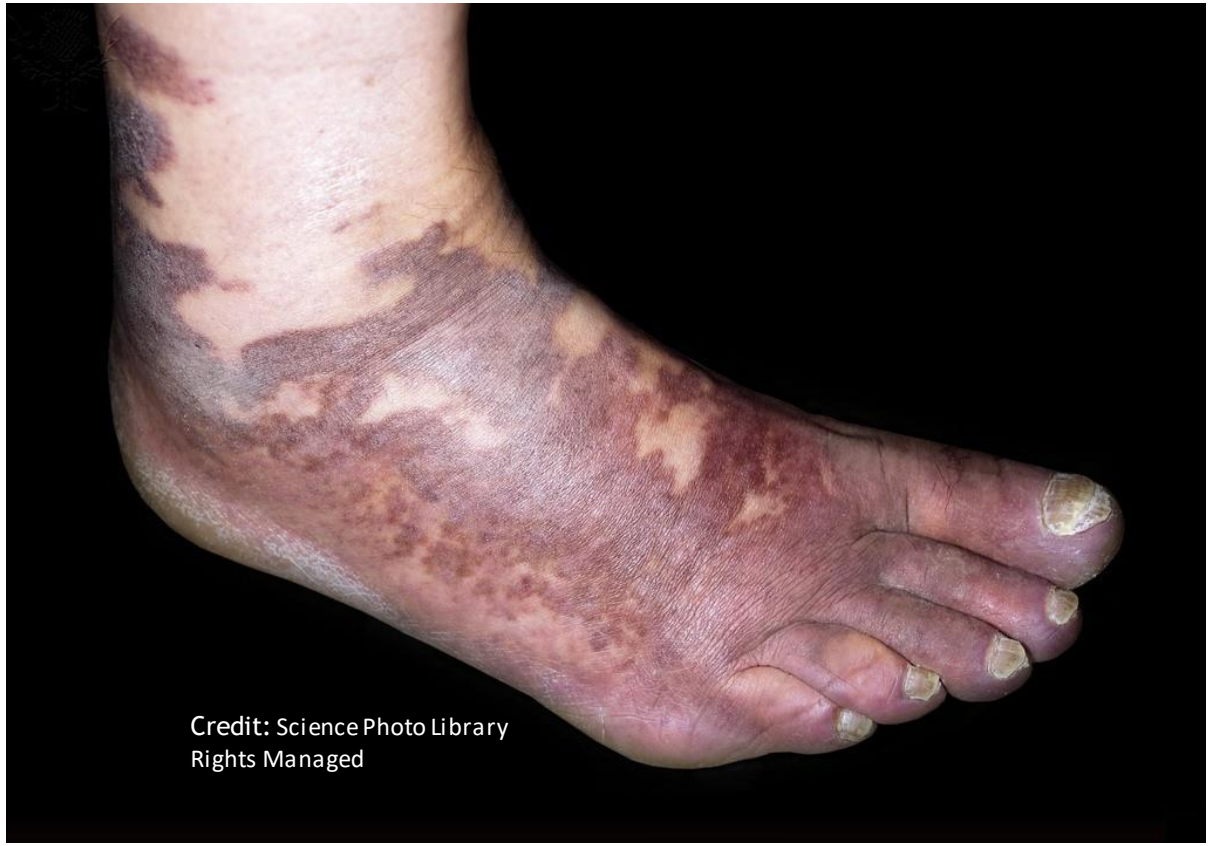
- Doxycycline, amoxicillin, or cefuroxime can be given to a patient bitten by a tick from an area that is endemic for Lyme disease.
- To prevent tick bites, avoid tick habitats, wear appropriate clothing (long-sleeved garments and long pants) when outdoors, and use insect repellants.
- Because it can take several hours for the bacteria to infect a person, prompt removal of attached ticks can prevent infections.

Lyme disease:
-Multi-organ disease and in some cases, there are skin lesions (nodules). Caused by the spirochete bacteria *Borrelia burgdorferi*.
-It is transmitted by tick bites.
-It causes myalgias and arthralgias.
-The skin condition is called erythema migrans (a macule or specifically a nodule that extends radially with central clearing and swelling).
-Treatment: Antimicrobials like doxycycline.

Nodules: Kaposi Sarcoma

-It is a cancer caused by a virus, pink or purple plaques or nodules on skin and mucosa but mainly on the forehead, arms and legs.
-It is AIDS defining condition (if we see kaposi sarcoma we should suspect AIDS)

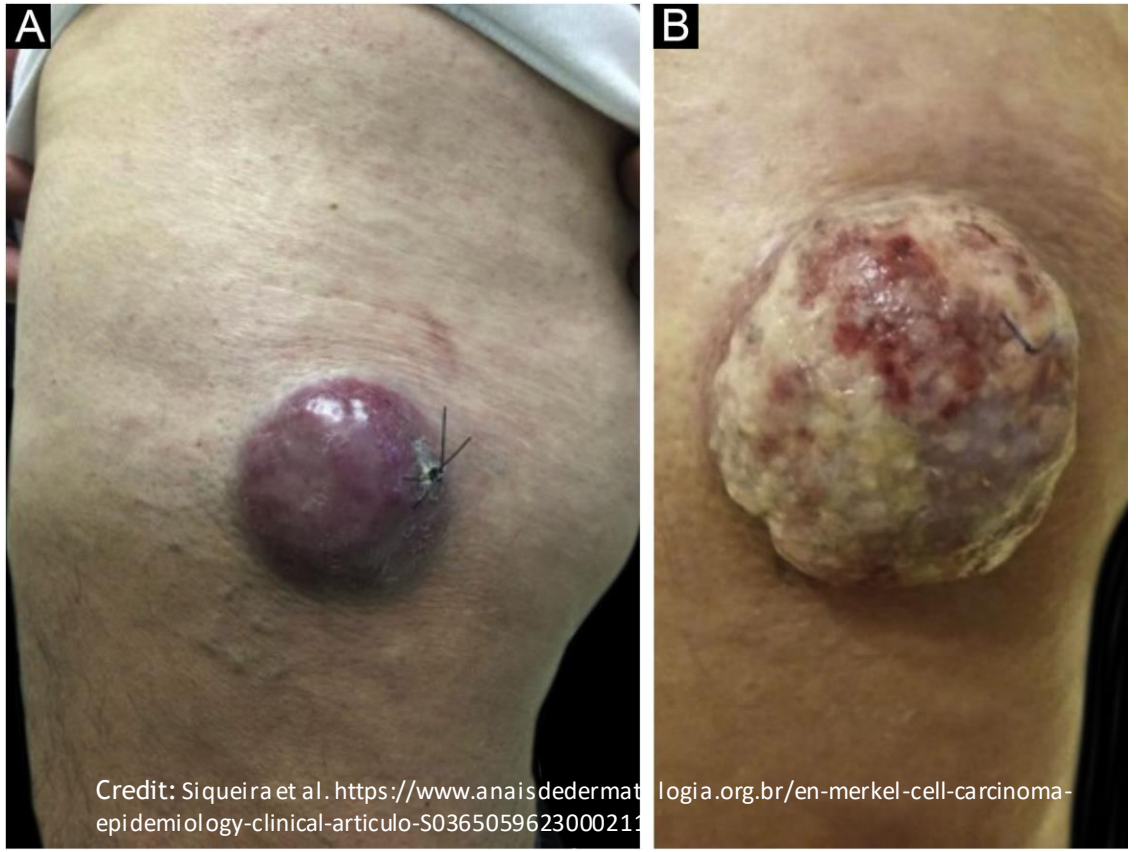
- Kaposi sarcoma due to HHV-8 (Kaposi sarcoma herpesvirus) occurs in patients with immunosuppression (e.g., AIDS).
- Kaposi sarcoma is a vascular lesion presenting as a violaceous **pink to purple plaque/nodule** on the skin or mucocutaneous surfaces.
- Patients with HIV-related Kaposi sarcoma respond well to HAART.



Nodules: Merkel cell carcinoma

- Merkel cell carcinoma (MCC) is a rare, very aggressive skin cancer with a high mortality rate and a high tendency of metastatic spread. Caused by Merkel cell polyomavirus.
- The global incidence of MCC ranges from 0.1 to 1.6 cases per 100,000 people per year.
- MCC is manifested by a rapidly growing, painless, **erythematous/violaceous nodule or plaque**.
- The acronym AEIOU captures these features: A = asymptomatic, E = expanding rapidly, I = immune suppression, O = older than 50 years of age and U=UV-exposed site.

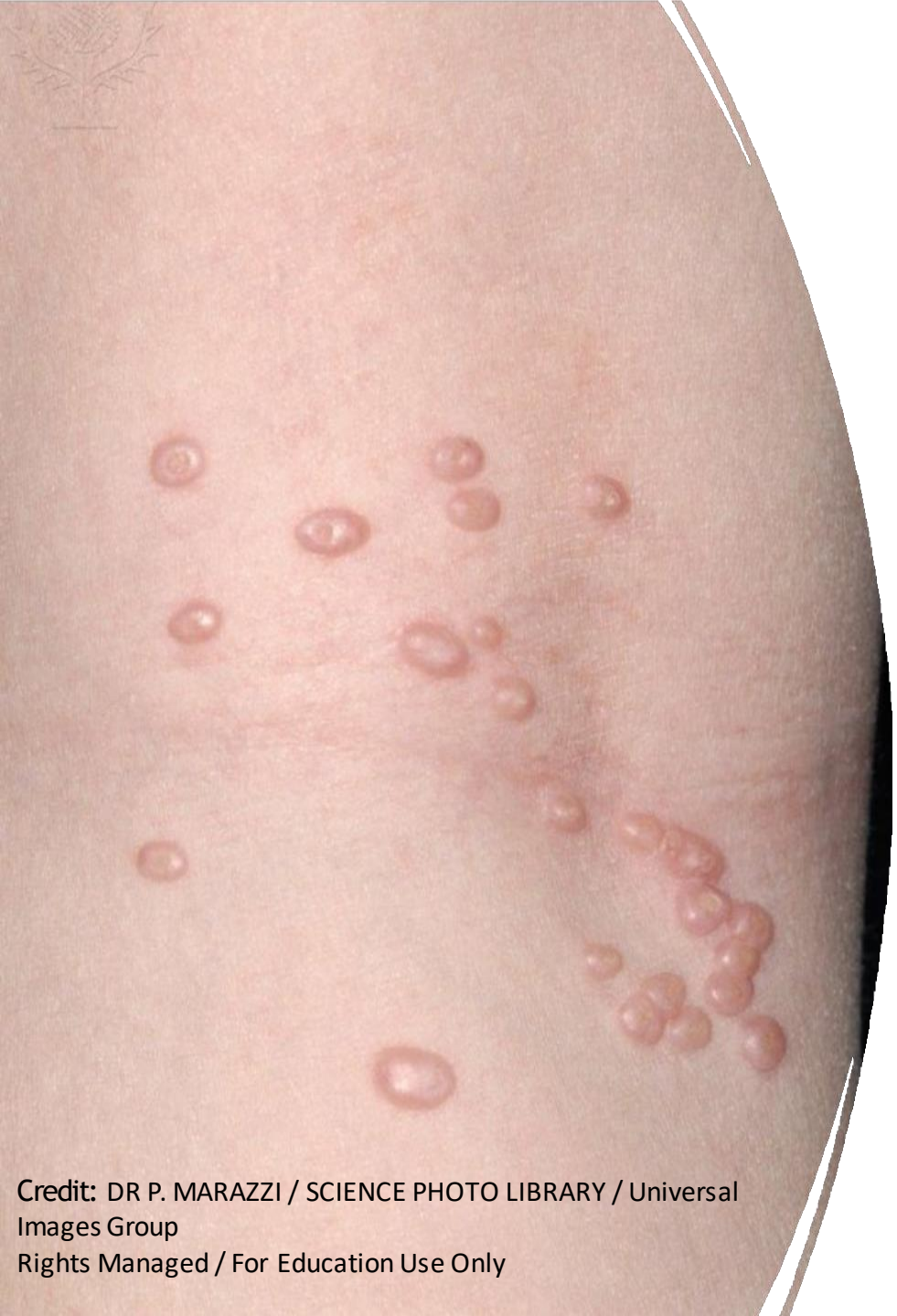
Usually in individuals with fair skin.



Credit: Siqueira et al. https://www.anaisdedermatologia.org.br/en-merkel-cell-carcinoma-epidemiology-clinical-articulo-S0365059623000211

Smooth papules: Molluscum contagiosum

- Molluscum contagiosum is a viral infection that produces papules with a central depression (**umbilicated lesions**).
- Molluscum contagiosum virus (MCV) is a large DNA poxvirus.
- The lesions are flesh-colored, dome-shaped papules 2–10 mm in diameter. The center of the lesion is depressed (umbilicated).
- Lesions can appear anywhere on the body, including the mucous membranes.
- Lesions are widespread and persistent in AIDS patients.
- The disease is self-limiting in patients with a normally functioning immune system; however, lesions can remain for years.



Credit: DR P. MARAZZI / SCIENCE PHOTO LIBRARY / Universal Images Group
Rights Managed / For Education Use Only

Smooth papules: Molluscum contagiosum

- Most infections occur in children and result from direct skin-to-skin contact or by contact with contaminated fomites (on bath towels, sponges, and gymnasium equipment).
- Molluscum contagiosum is usually a sexually transmitted infection in healthy adults. Few lesions are present and are usually limited to the genitalia, lower abdomen, or buttocks.

Molluscum contagiosum – Diagnosis, Treatment, and Prevention

- Diagnosis is based on the **distinctive central umbilication of the dome-shaped lesions**. PCR can also be used.
- Without treatment, molluscum contagiosum lesions will heal within several months or years.
- To prevent autoinoculation or transmission to close contacts, therapy may be beneficial and includes topical (e.g., podophyllin, trichloroacetic acid, cryotherapy with liquid nitrogen).
- In immunocompromised patients, improvement of lesions can be observed following treatment with intravenous and topical ritonavir, cidofovir, zidovudine, or intralesional interferon alpha.
- To prevent spread, contact with infected persons should be avoided

Treatment: Removed surgically by excision or freeze by liquid nitrogen or using antiviral agents.

Molluscum contagiosum:
-Papules with central depression (umbilicated lesions) which helps in clinical diagnosis.
-Caused by Molluscum Contagiosum virus (MCV) which is a poxvirus.
-Benign condition.
-Treatment: Removed surgically by excision or freeze by liquid nitrogen or using antiviral agents but if not treated it will resolve spontaneously within months.

Smooth papules: Condyloma lata

- Condyloma lata are peri-mucosal skin papules in secondary syphilis.
- The lesions are pink or gray papules that occur at the mucocutaneous junctions and in moist or intertriginous areas of the skin.
- The lesions are infectious.
- Lesions of condyloma lata appear 6–8 weeks after the appearance of the primary chancre.
- The disease is usually acquired by unprotected sexual contact with an infected individual.

Smooth papules: Condyloma lata

- Lesions are similar to and frequently misdiagnosed as condyloma acuminata.
- Condyloma lata are smoother and softer than the rough and hard condyloma acuminatum lesions.
- Condyloma lata are treated with benzathine penicillin.
- Intimate contact with infected persons and with the lesions should be avoided.

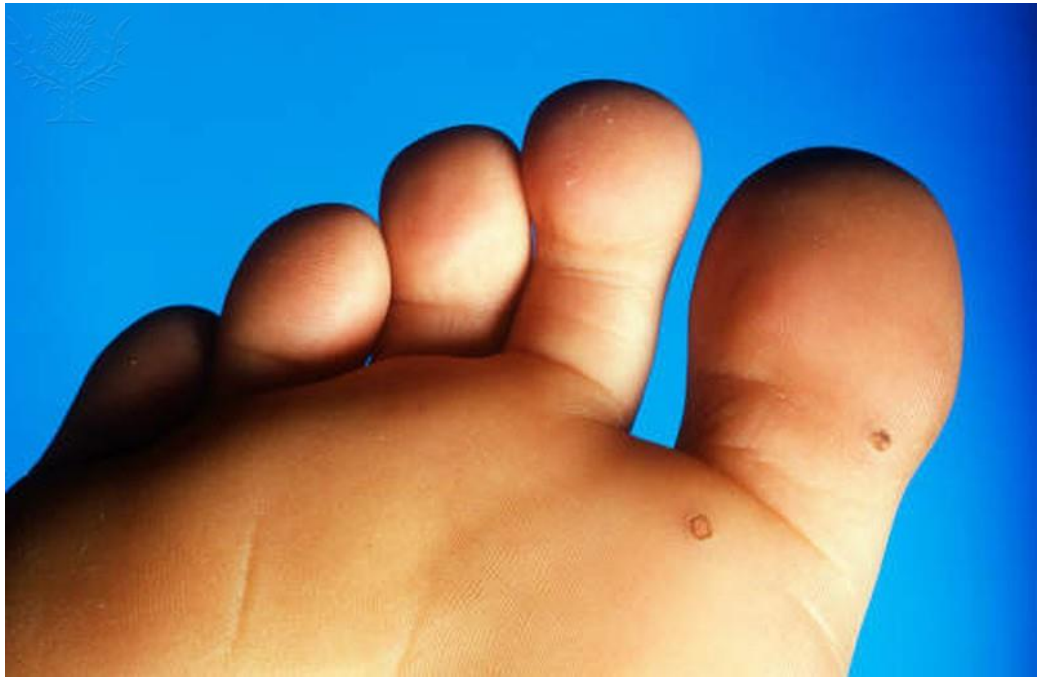
Condyloma lata:
-Skin papules (raised lesions) in secondary syphilis (we see in secondary syphilis macules and papules).
-Penicillin G is used for treatment.

Verrucous lesions: Warts

- Common infection by HPV. Lesions can occur anywhere in the skin and on mucous membranes. Over 100 different types of HPV have been identified as agents of human infection.
- **Common warts (verruca vulgaris)** are hyperkeratotic papules with a rough irregular surface and range from less than 1 mm to larger than 1 cm. They can occur on any part of the body.
- Lesions are usually caused by HPV-2 and HPV-4 (most common), followed by types 1, 3, 27, 29, and 57.

Warts: Clinical Manifestations

- Flat (plane) warts, are flat or slightly elevated flesh-colored papules that may be smooth or slightly hyperkeratotic and range in size from 1–5 mm.
- Lesions may appear in a linear distribution because of trauma (**Koebner phenomenon**).
- Flat warts can occur anywhere; however, the face, hands, and shins are the most affected areas.
- HPV types 3, 10, and 28 usually cause these lesions.



Credit: Erich Schrempp / Photo Researchers / Universal Images Group
Rights Managed / For Education Use Only

Warts: Clinical Manifestations

- Deep palmo-plantar warts occur on the soles of the feet (plantar surface) and are commonly found on weight-bearing areas (e.g., metatarsal head and heel).
- Lesions are usually caused by HPV type 1 (most common), followed by types 2, 3, 4, 27, 29, and 57.
- Anogenital warts (condyloma acuminata) are papules or nodules of the genitalia, perineum, crural folds, penile shaft, anus, and rectum.
- About 30 different HPV types are known to cause genital warts with types 6 and 11 being the most common.

Warts: Epidemiology

- Warts are common worldwide and are estimated to affect about 10% of the population.
- About 10% of the general population is infected by genital HPV at some point during their lifetime.
- The HPV viruses can resist desiccation, freezing, and prolonged storage outside host cells (non-enveloped virus).
- Most cases of HPV are transmitted by direct or indirect contact.
- **Anogenital warts are the most common sexually transmitted infection worldwide.**

Warts: Pathogenesis

- The HPV virus infects the basal epidermal cells. As the cells differentiate and move to the surface, the virus becomes active and induces epidermal proliferation. Many warts resolve spontaneously within a few years. Cell-mediated immunity plays a significant role in wart regression.
- Many anogenital warts are benign. Some anogenital infections that are caused by HPV and are more likely to be malignant usually do not produce the wart-like lesion.
- HPV types 16, 18, 31, and 33 (16 and 18 are the most common) are commonly associated with anogenital malignancy.

Warts: Diagnosis, Treatment, and Prevention

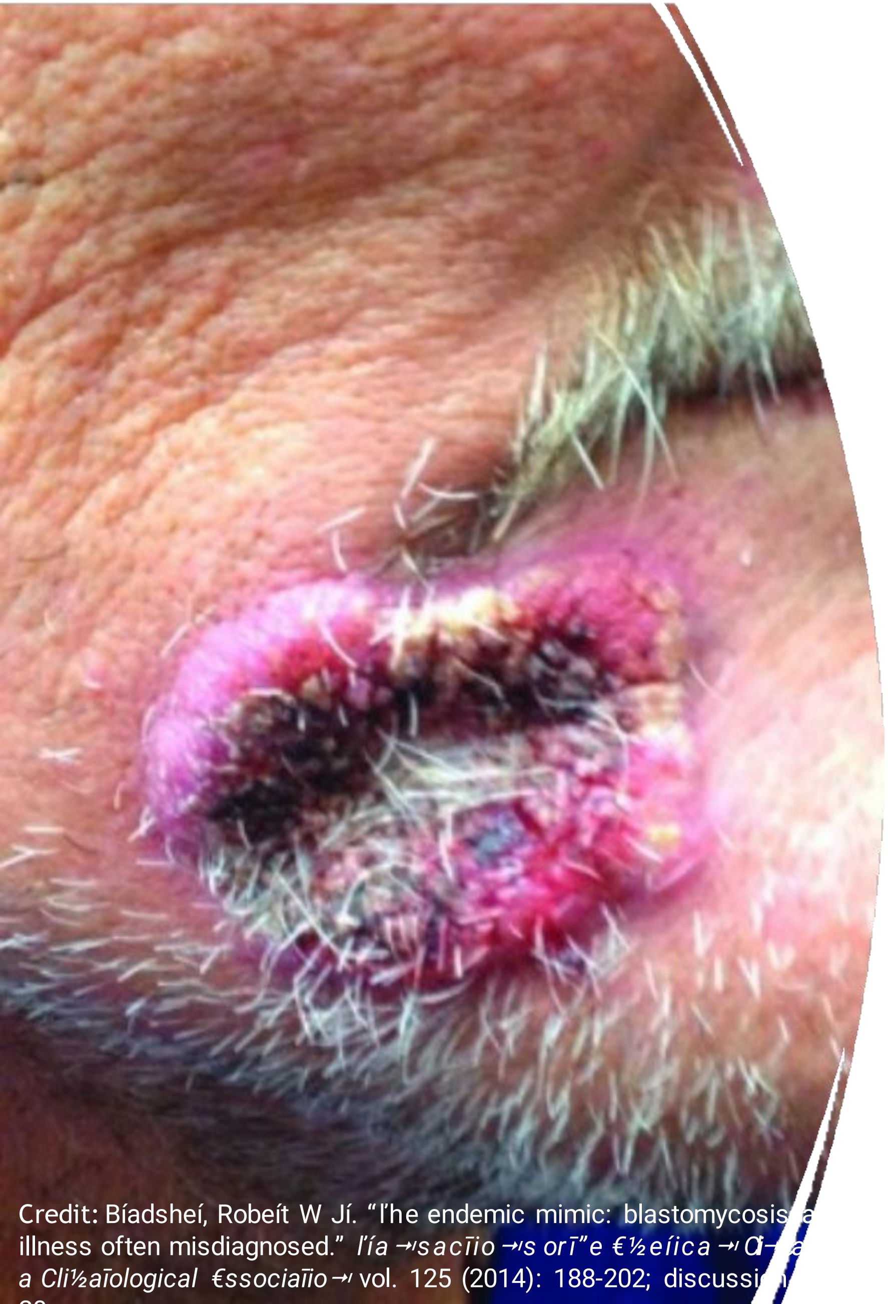
- The diagnosis of warts is based on clinical findings. PCR can be used to detect viral DNA.
- Treatment of warts can be difficult with recurrences. Treatment include application of topical agents such as salicylic acid and podophyllin and treatments with cryosurgery, lasers, and surgical excision. Most common warts usually disappear within 2 years without treatment. Contact with lesions should be avoided.
- Three HPV vaccines: nona-valent HPV vaccine (Gardasil 9), quadrivalent (Gardasil), and bivalent (Cervarix) have been licensed. The nona-valent vaccine protects against nine types (6, 11, 16, 18, 31, 33, 45, 52, and 58).
- HPV vaccine is recommended for routine vaccination at age 11 or 12 years.

To know what to study from vaccines read the next page.

Common warts (verruca vulgaris):
-Verrucous lesions.
-Outgrowth of the keratinized area of the skin.
-Caused by the benign types of HPV thus, they will never transform to cancer, there is no vaccine for them since HPV vaccines protects only from high-risk types such as 16 and 18 and low risk types that cause genital warts (condyloma acuminatum) HPV 6 and 11.
-Treated by surgical excision or freezing using liquid nitrogen.

Verrucous lesions: Blastomycosis

- *Blastomyces dermatitidis* is a dimorphic fungus. Organisms grown at 37°C are in the yeast phase. At room temperature, the organism becomes a mold.
- An infection of the lungs precedes the appearance of the skin lesions in patients diagnosed with blastomycosis, with skin lesions occurring in about 25% of patients.
- A fully developed lesion appears as an **elevated purplish red verrucous patch**.



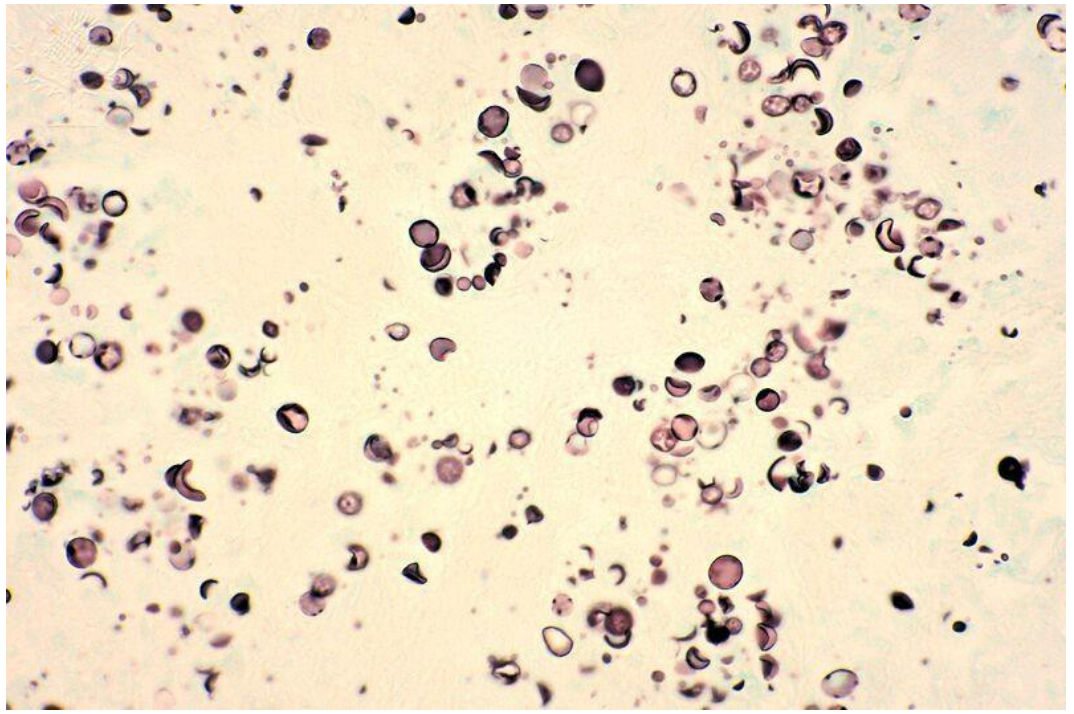
Credit: Bíadsheí, Robeít W Jí. "l'he endemic mimic: blastomycosis a illness often misdiagnosed." *l'ía→sacīio→s orī"e €½eíica→ Ci→a a Cli½aīological €ssociaīio→* vol. 125 (2014): 188-202; discussi

Blastomycosis: Pathogenesis

- *B. dermatitidis* are inhaled and infect the lungs. The conidia become yeast in the lung and are phagocytized by macrophages. The macrophages carry the organisms to other parts of the body (e.g., **skin**, bones, genitourinary tract, and other reticuloendothelial organs).
- At least 50% of primary infections are asymptomatic. Cell-mediated immunity plays a significant role in eliminating blastomycosis infection. Patients with cell-mediated immune deficiencies are particularly susceptible to this infection and can be difficult to treat.

Blastomycosis: Diagnosis, Treatment, and Prevention

- Culture provides definitive diagnosis. Identification is aided by microscopy of sputum, pus, or urine specimens showing characteristic thick-walled unencapsulated yeasts (8–15 µm) with **broad-based buds**.
- Amphotericin B is used to treat blastomycosis.
- Prevention by avoiding certain recreational activities that would increase their risk of exposure.



Credit: Science Photo Library \ UIG
Rights Managed / For Educational Use Only

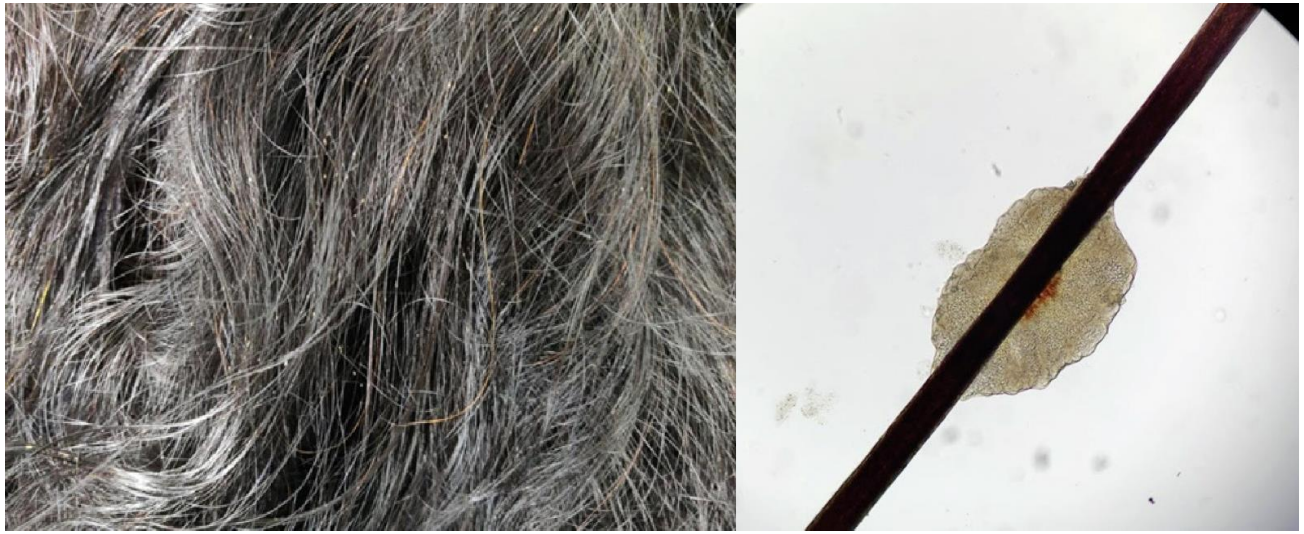
Blastomycosis:
-Verrucous lesions.
-Caused by *blastomyces dermatitidis* which is a dimorphic fungus.
-This fungus sometimes affect the skin causing elevated purplish red verrucous patches or nodules.
-Diagnosis: If take a sample under body temperature (37 degrees) we'll find a yeast with broad-based buds, but if we cultivate the sample and see it under the microscope in cold conditions (25 degrees) we'll see a hyphae/mold.
-Treatment: Systemic antifungals like amphotericin B.

Hair nodules: Piedra

- Black piedra is a nodular infection of the hair shaft caused by *Piedraia hortae*.
- White piedra, due to infection with *Trichosporon* species, presents as larger, softer, yellowish nodules on the hairs.
- Axillary, pubic, beard, and scalp hair may be infected. Treatment for both types consists of removal of the infected hair and application of a topical antifungal agent. Piedra is endemic in tropical countries.
- Shaving the infected hair is curative.

Piedra:
-Nodules that looks like small stones on the hair shaft, caused by a fungi called piedra.
-It looks white (white piedra) or black (black piedra).
-Treated by removing the affected hair.

Hair nodules: Piedra



Gaurav V, Grover C, Das S, Rai G. White Piedra: An Uncommon Superficial Fungal Infection of Hair. Skin Appendage Disord. 2022 Jan;8(1):34-37. doi: 10.1159/000517807.

Khatu SS, Poojary SA, Nagpur NG. Nodules on the hair: a rare case of mixed piedra. Int J Trichology. 2013 Oct;5(4):220-3. doi: 10.4103/0974-7753.130421.

Thanks for listening!