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# *papulosquamous disease:-*

-The term *squamous* refers to scaling that represents thick stratum corneum and thus implies an abnormal keratinization process

-lesions are characterized by sharply demarcated, red to violaceous papules and plaques that result from thickening of the epidermis or underlying dermal inflammation.

# Papulosquamous Diseases:-

-PSORIASIS

-Pityriasis rosea

-Lichen planus

-Seborrheic dermatitis

-Pityriasis rubra pilaris

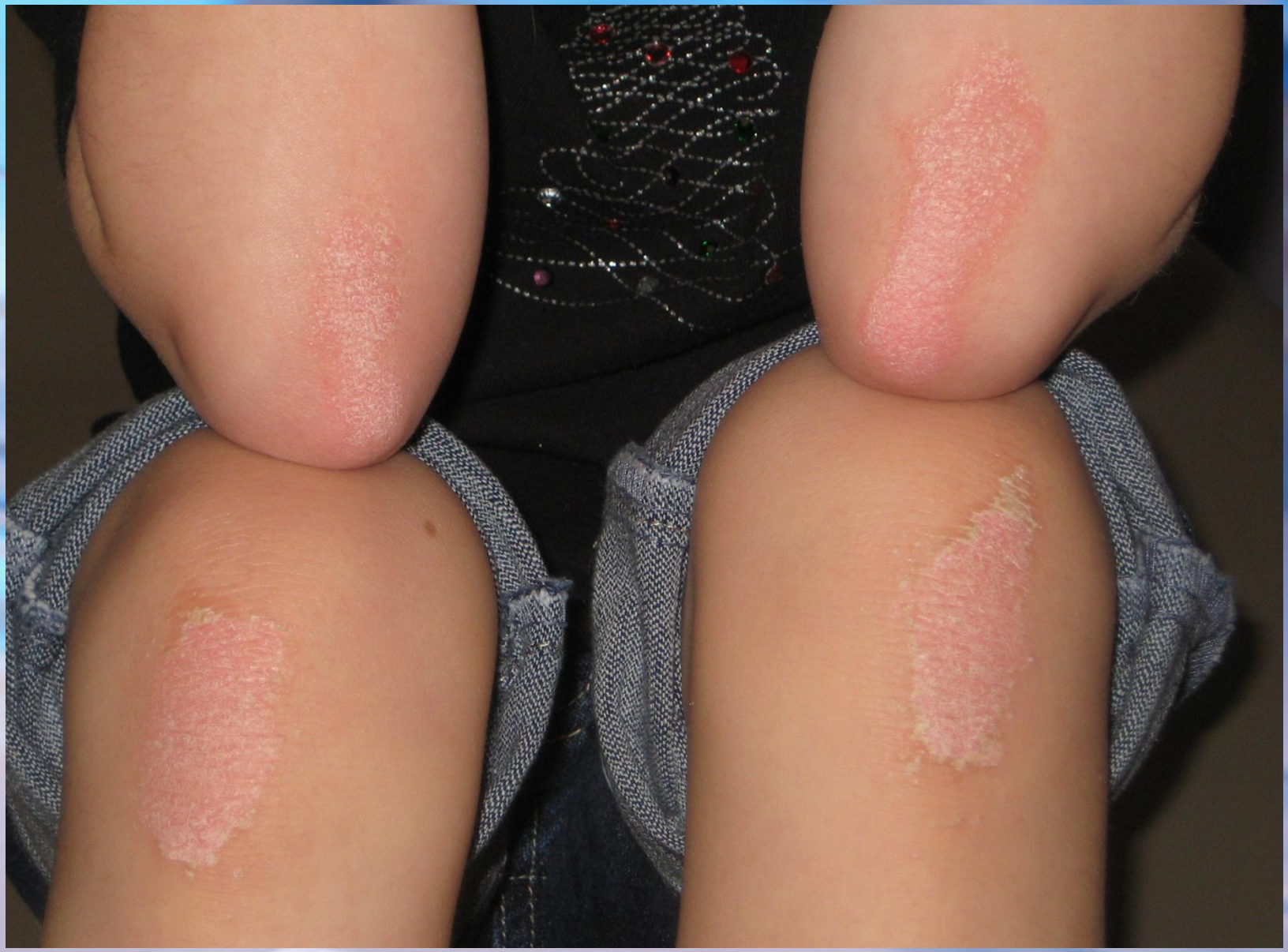
-Secondary syphilis

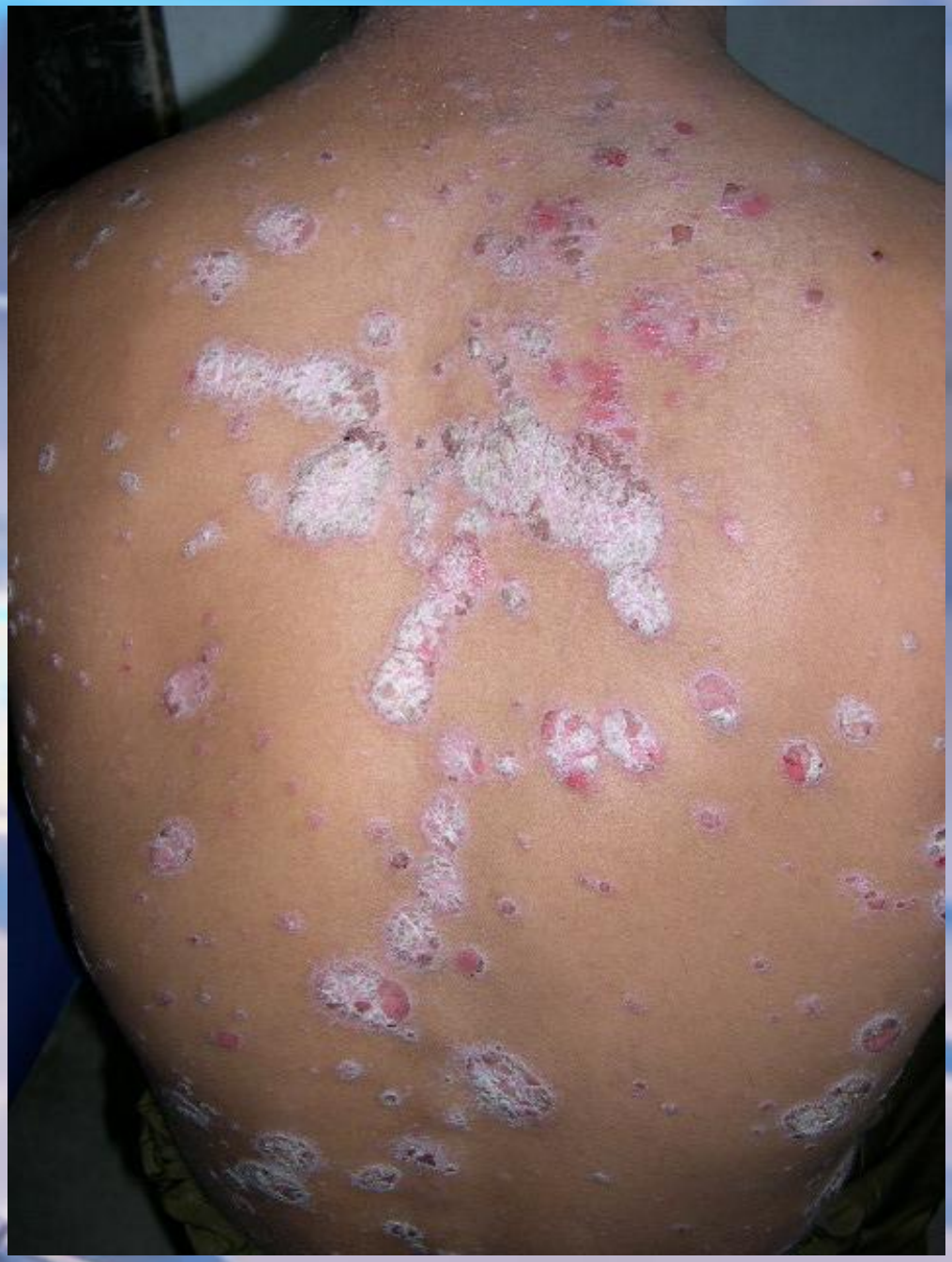
-Miscellaneous mycosis fungoides,
discoid lupus erythematosus, ichthyoses

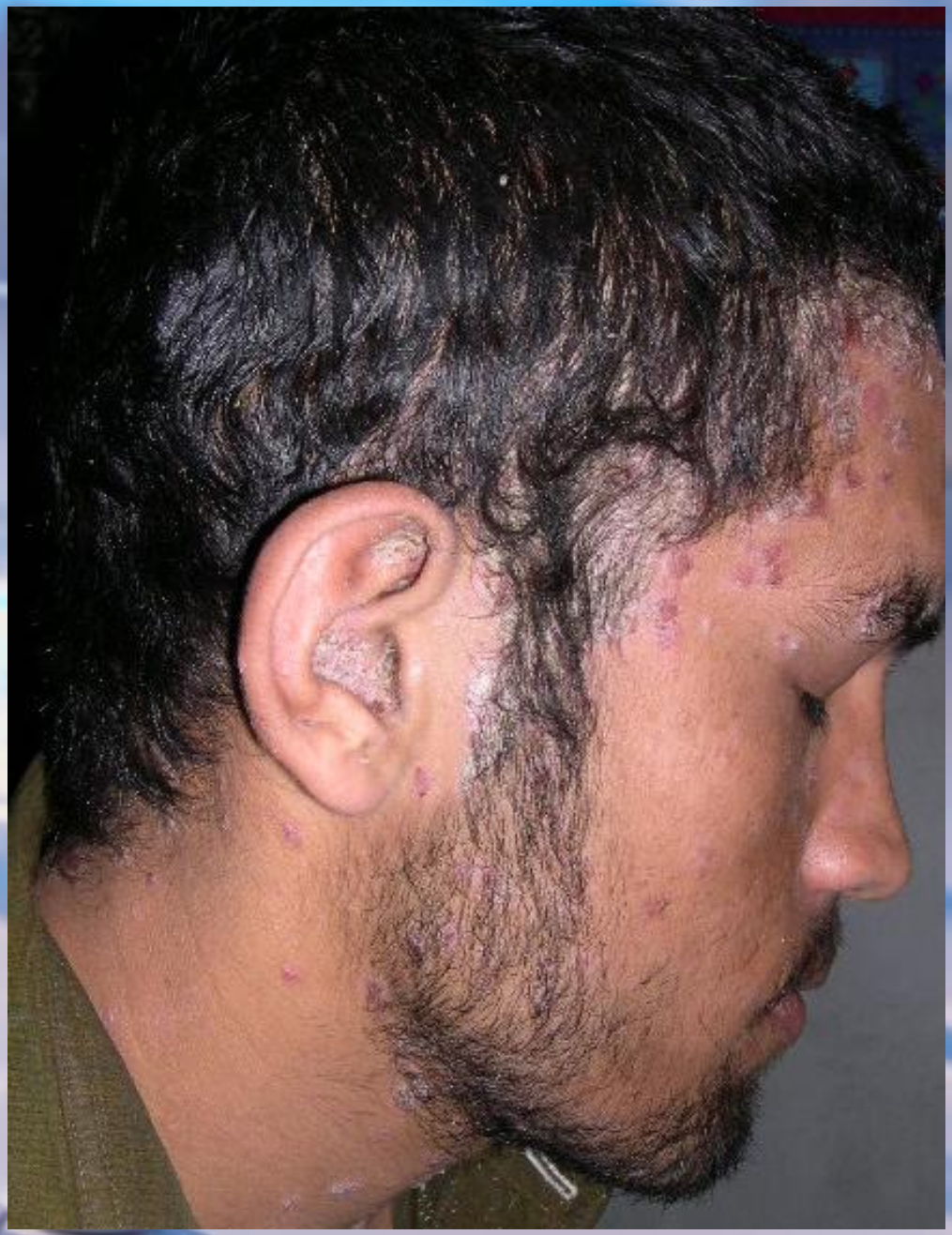
# Psoriasis

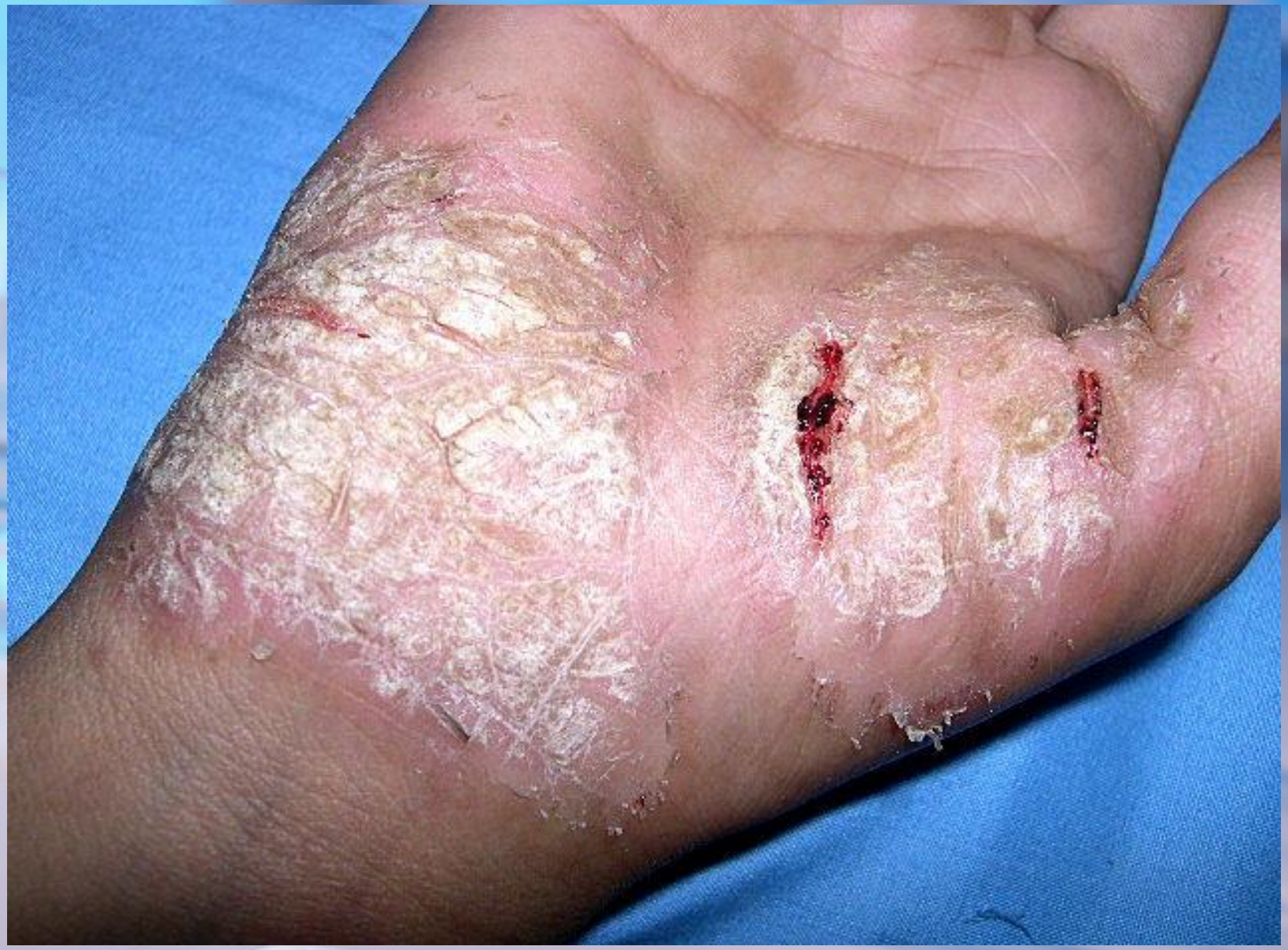
## Definition

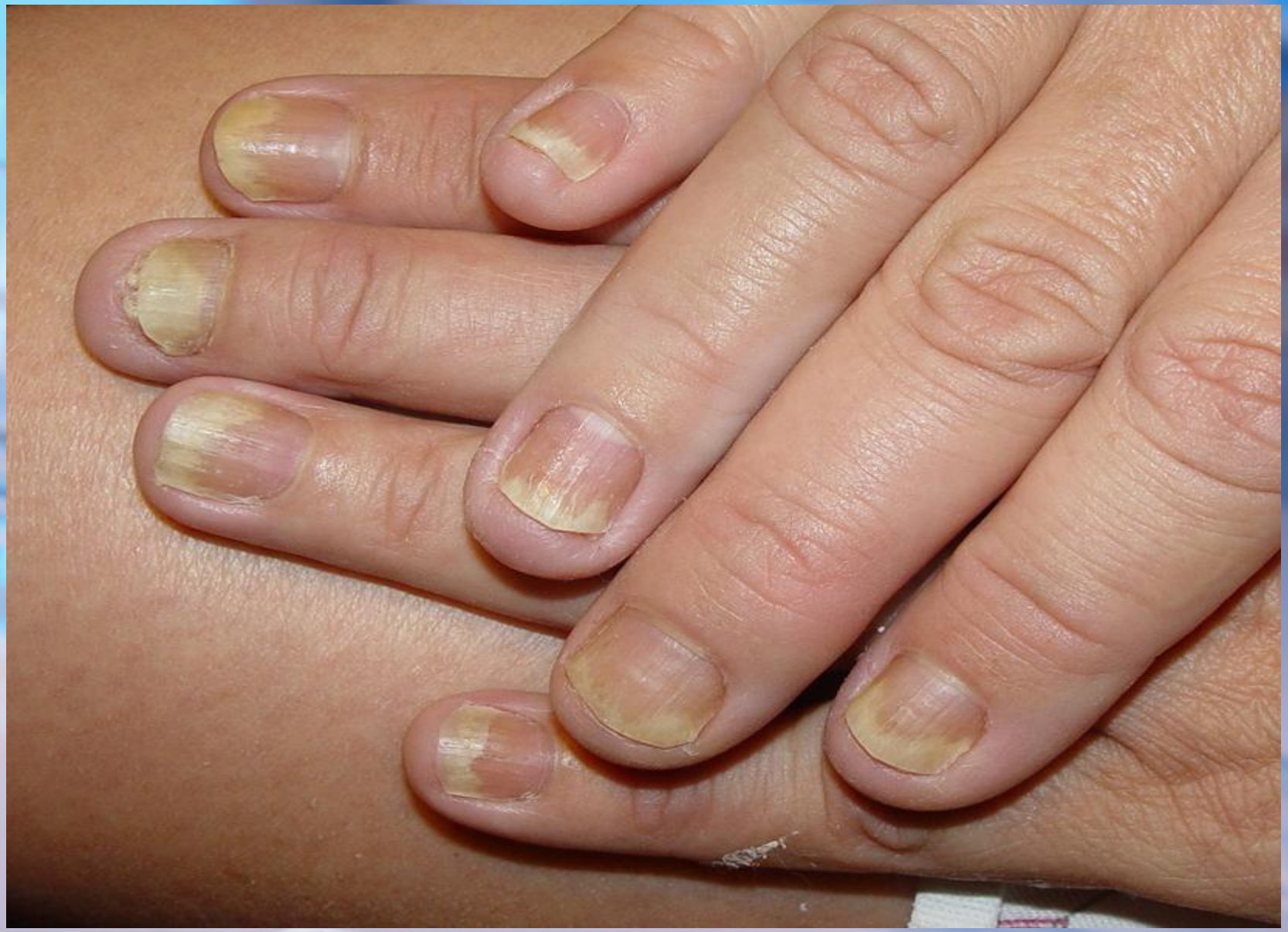
**-Psoriasis is a common, chronic ,non-infectious , inflammtory skin disease.**
-characterized by well-defined salmon-pink plaques bearing large adherent silvery scales-
**- which affects the skin and joints .**
**-causes rapid skin cell reproduction resulting in red, dry patches of thickened skin**











# Incidence and aetiology:-

- The cause of PS still unknown
- 1-3%(under-estimate)
- F=M
- Any age (two peak of onset)
- Race:-any race; however,

  epidemiologic studies have shown a higher prevalence in western European and Scandinavian populations.

# Pathogenesis:-

- Exact cause is unknown
- Multi-factorial causes:-

# 1-Genetic factor:-

-ps is a multi factorial disease with a complex genetic trait

-there are two inheritance mode:-

a-one has onset in younger age with family history of ps

b-the other has onset in late adulthood without family history of ps

-a child with one affected parent……16%
-both parents……50%
-non-psoriatic parents with affected child……10%
-monozygotic twins……70-
dizygotic twins……20%
-at least 9 loci have been identified(psors-1 to 9)

# Epidermal cell kinetics

-the growth fraction of basal cells is increased to almost 100% compared with 30% in normal skin

-the epidermal turnover time is shortened to less than 10 days compared with 30 10 60 days in normal skin

## 2-Inflammtory factors:-

- Increase level of TNF
- TNF receptors are upregulated
- Increase level of interferon gamma
- Increase level of interleukin 2 and 12

# 3-Immunological factors:-

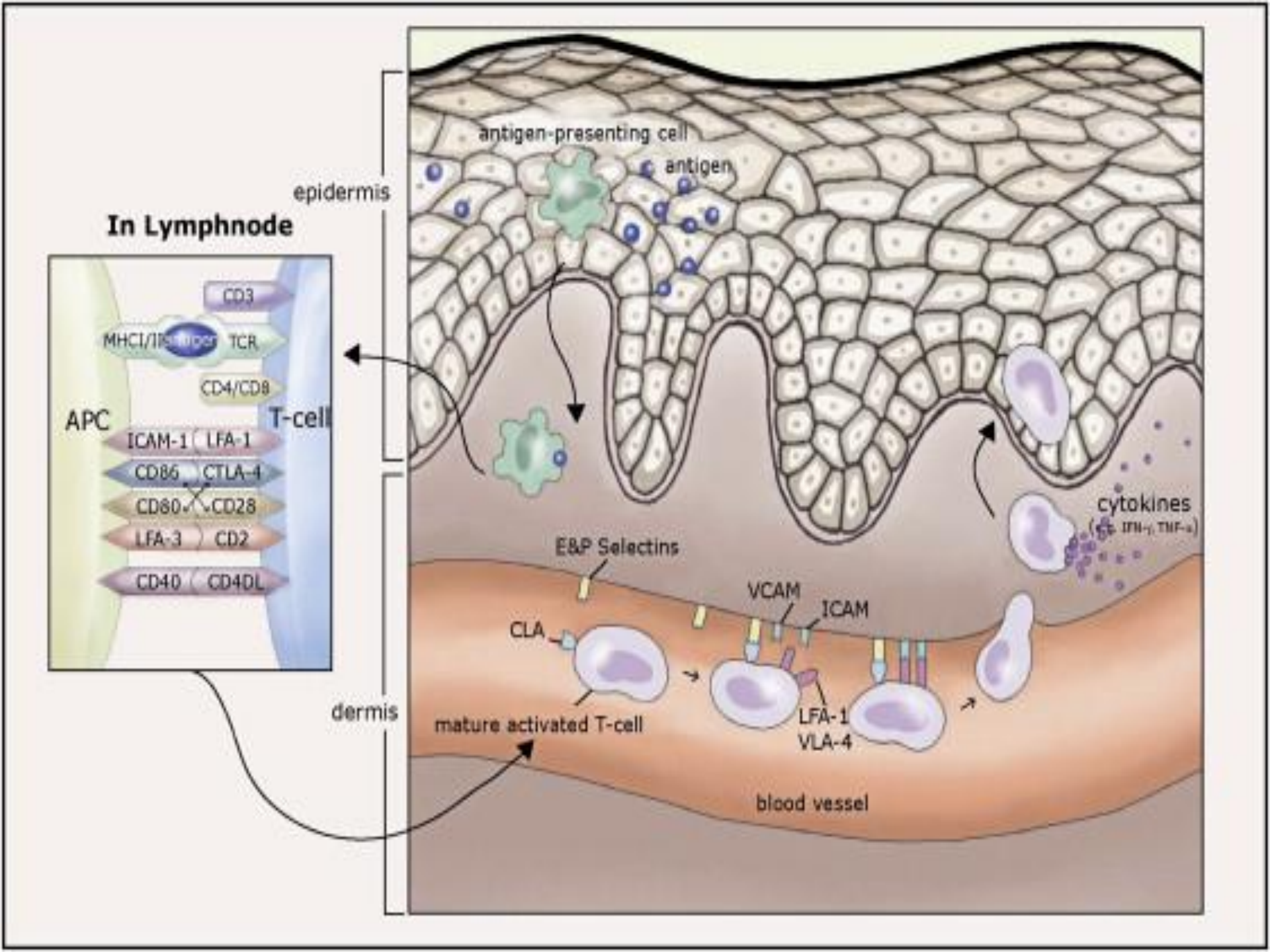
- Psoriasis is fundamentally an inflammatory skin condition with reactive abnormal epidermal differentiation and hyperproliferation

- The inflammatory mechanisms are immune based and most likely initiated and maintained primarily by T cells in the dermis

- Antigen-presenting cells in the skin, such as Langerhans cells
- Tcells
- Auspits sign

# 4-Environmental factors:-

- Infection (streptococcal infection)
- Physical agents (eg,stress, alcoholism, smoking)
- Koebner phenomenon
- Drugs (lithium,anti- malarials ,nsaid,beta-blockers)


epidermis
dermis
antigen-presenting cell
antigen
In Lymphnode
APC
T-cell
CD3
MHCI/II
TCR
CD4/CD8
ICAM-1
LFA-1
CD86
CTLA-4
CD80
CD28
LFA-3
CD2
CD40
CD40L
E&P Selectins
VCAM
ICAM
CLA
mature activated T-cell
LFA-1
VLA-4
cytokines
blood vessel

# Histology

-parakeratosis(nuclei retained in the horny layer)
-irregular thickening of the epidermis oever the rete ridges but thinning over dermal papillae
-epidermal polymorphonuclear leucocyte infiltrates (munro abscesses)
-dilated capillary loops in the dermal papillae
-T-lymph infiltrate in the upper dermis

# There are many types of psoriasis:-

1- **Plaque :-** Most common form of the disease

2- **Guttate :-** Appears as small red spots on the skin

3- **Inverse :-** Occurs in armpits, groin and skin folds

4- **Pustular :-** sterile small pustules, surrounded by red skin

5- **Erythrodermic :-** Intense redness over large areas

6- **Psoriatic arthritis :-**

# Psoriasis can occur on any part of the body:-

- Scalp psoriasis
- Genital psoriasis
- Around eyes, ears, mouth and nose
- On the hands and feet
- Psoriasis of the nails

# 1-plaque psoriasis(psoriasis vulgaris) :-

- the most common
- characterized by round-to-oval red plaques distributed over extensor body surfaces and the scalp
- up to 10-20% of patients with plaque psoriasis may evolve into more severe disease, such as pustular or erythrodermic psoriasis

# cardinal features of plaque psoriasis:-

1- **Plaques: Psoriasis manifests as elevated lesions that vary in size from one to several centimeters**

- **The number of lesions may range from few to many at any given time**

- **The plaques are irregular to oval and are most often located on the scalp, trunk, and limbs, with a predilection for extensor surfaces such as the elbows and knees**

- **Fissuring within plaques can occur when lesions are present over joint lines or on the palms and sols**

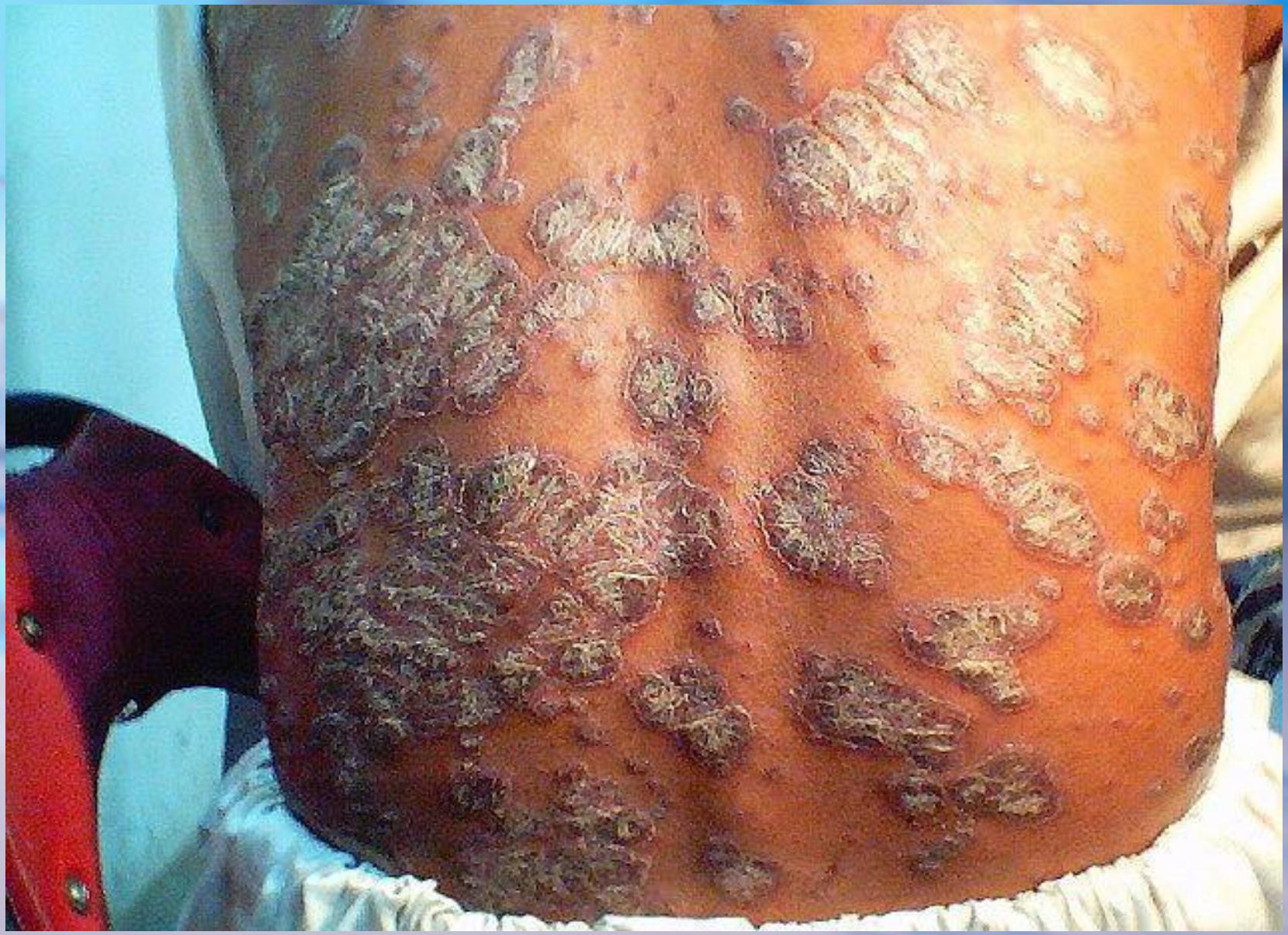
- **Well-circumscribed margins: Psoriatic plaques are well defined and have sharply demarcated boundaries**

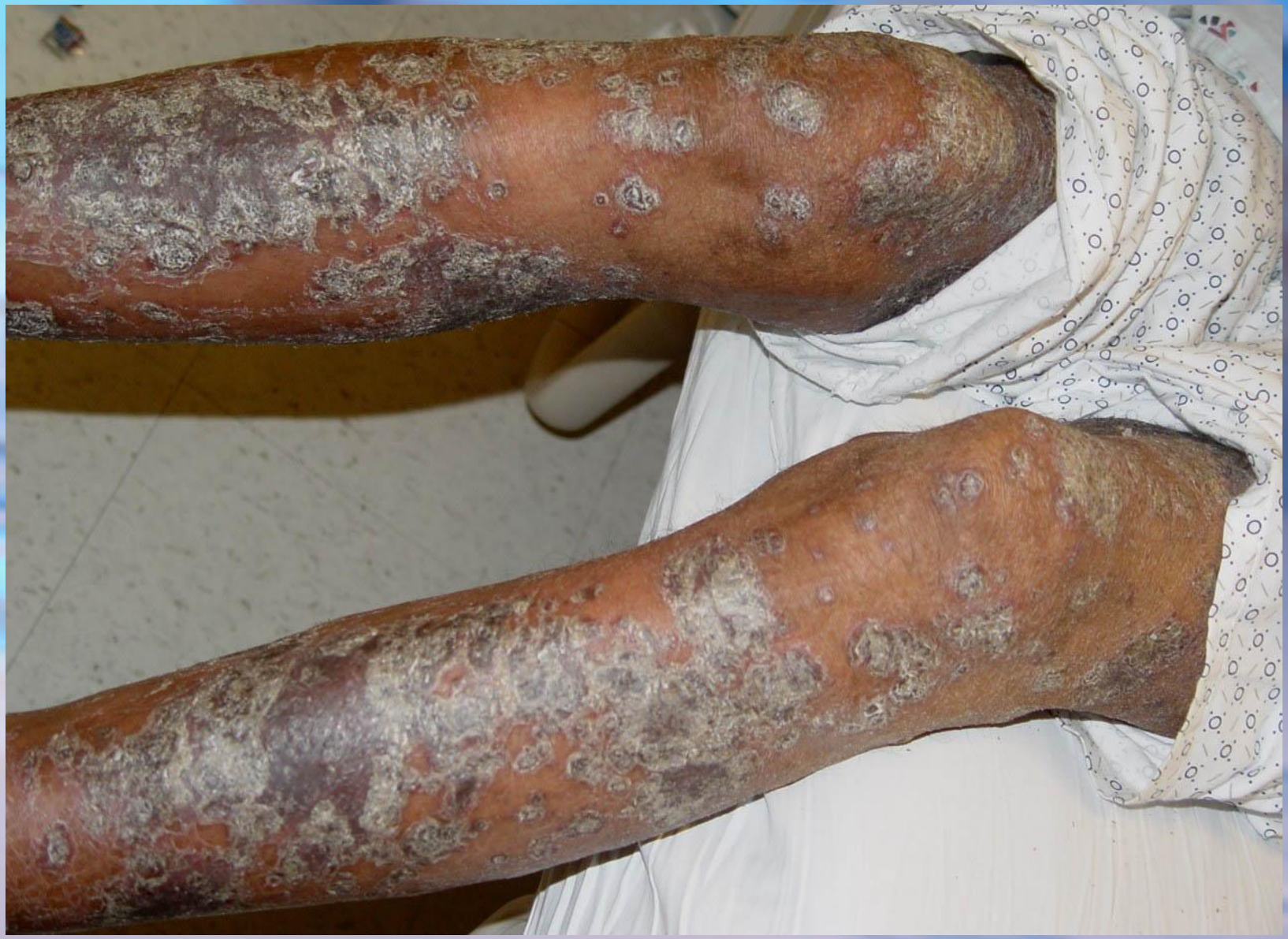
-Psoriatic plaques occasionally appear to be immediately encircled by a paler peripheral zone referred to as the halo or ring of Woronof

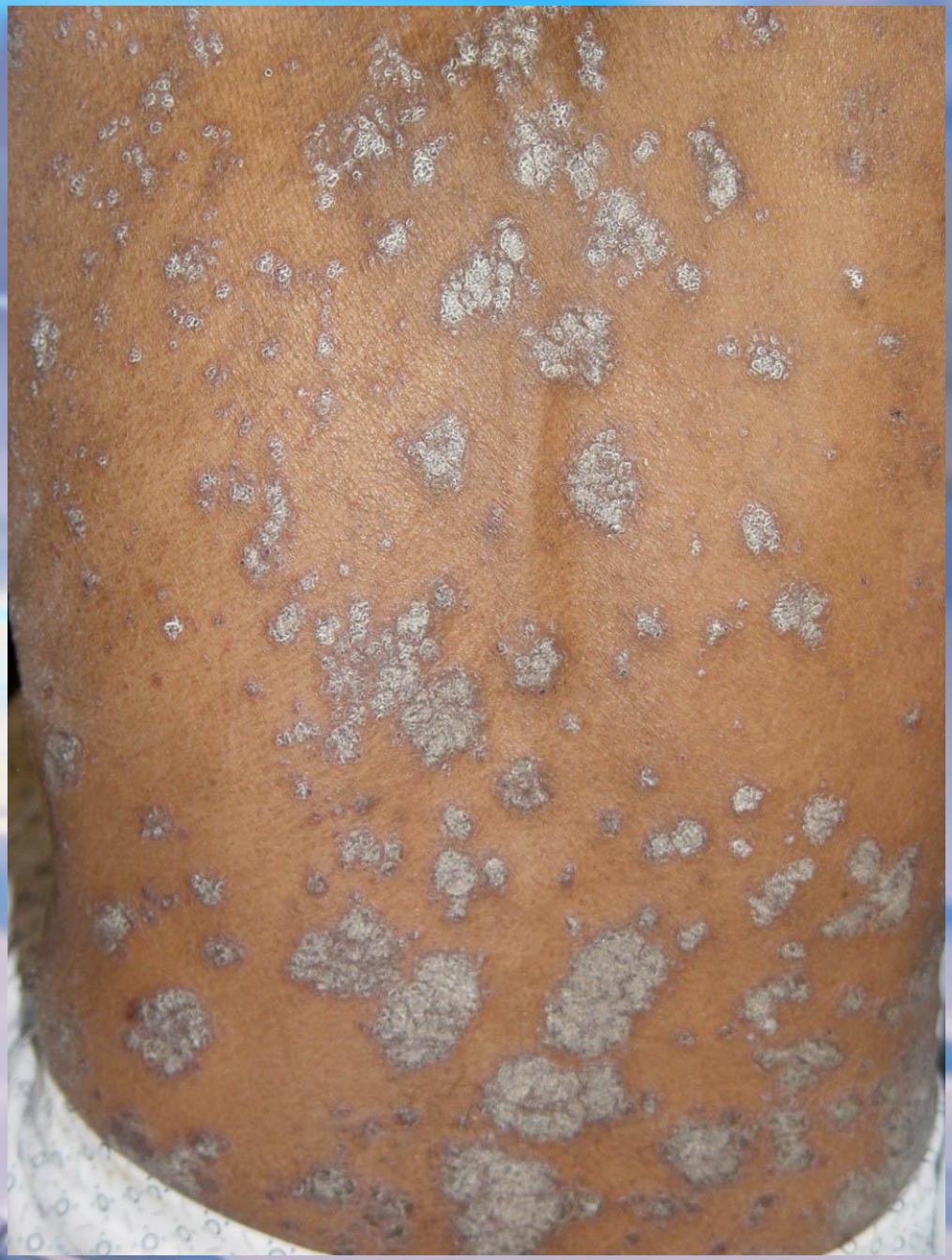
2- Red color: The color of psoriatic lesions is a very distinctive rich, full, red color

3- Scale: Psoriatic plaques typically have a dry, thin, silvery-white or micaceous scale;. Removing the scale reveals a smooth, red, glossy membrane with tiny punctate bleeding points. These points represent bleeding from enlarged dermal capillaries after removal of the overlying suprapapillary epithelium. This phenomenon is known as the Auspitz sign

4- Symmetry: Psoriatic plaques tend to be symmetrically distributed over the body.

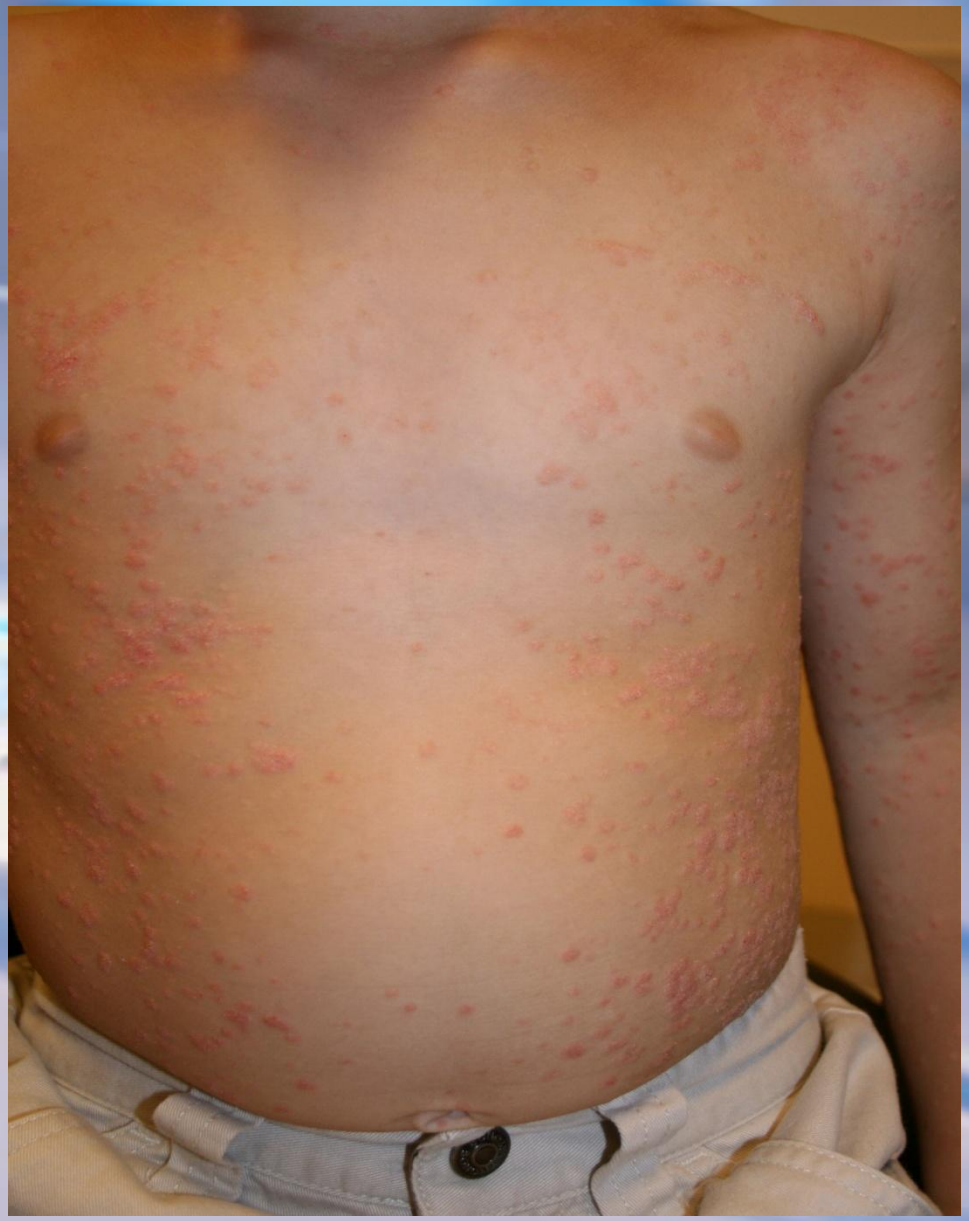


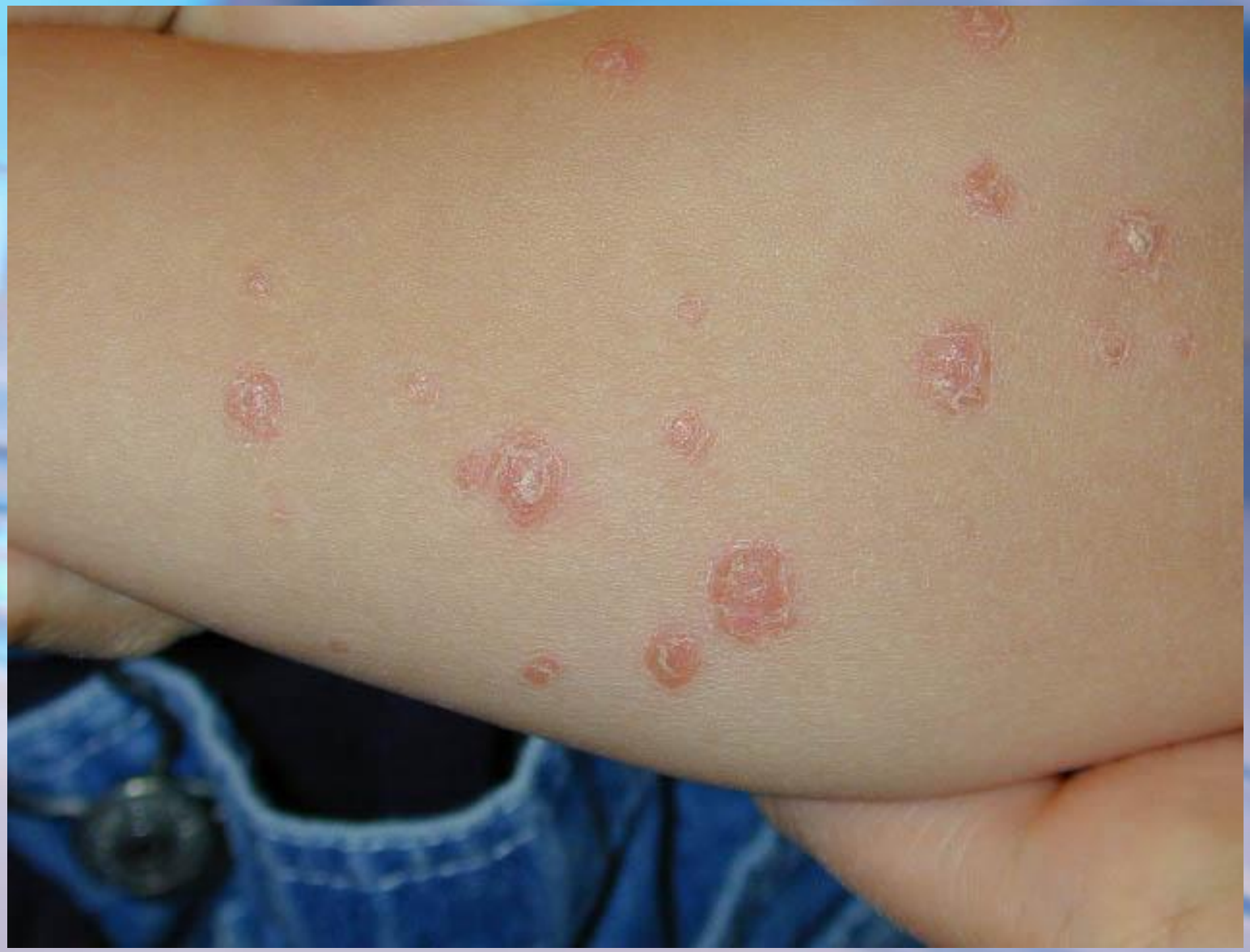




# 2-Psoriasis, Guttate:-

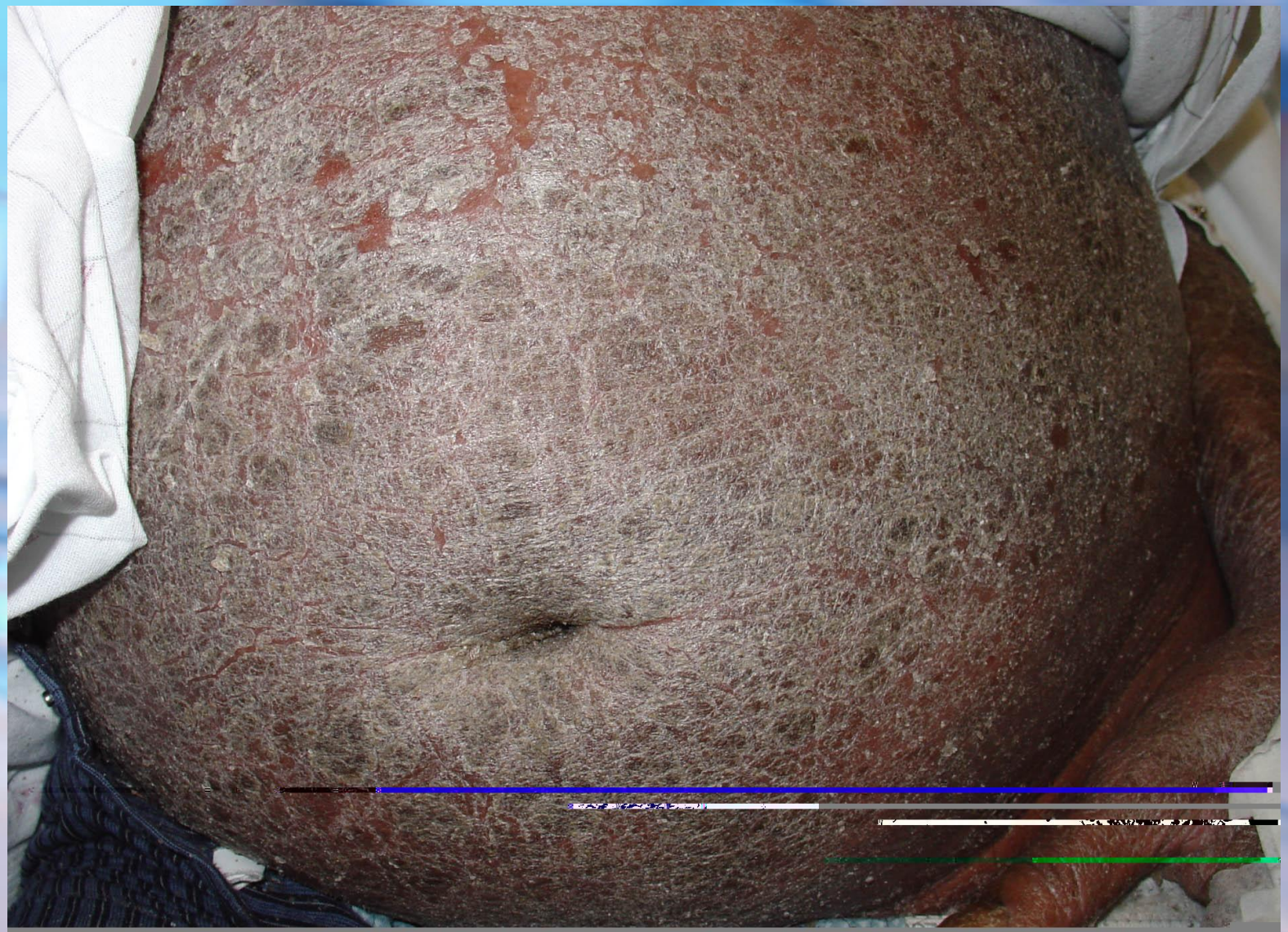
- Small, droplike, 1-10 mm in diameter, salmon- pink papules, usually with a fine scale
- Younger than 30 years
- Upper respiratory infection secondary to group A beta-hemolytic streptococci
- On the trunk and the proximal extremities
- Resolution within few months

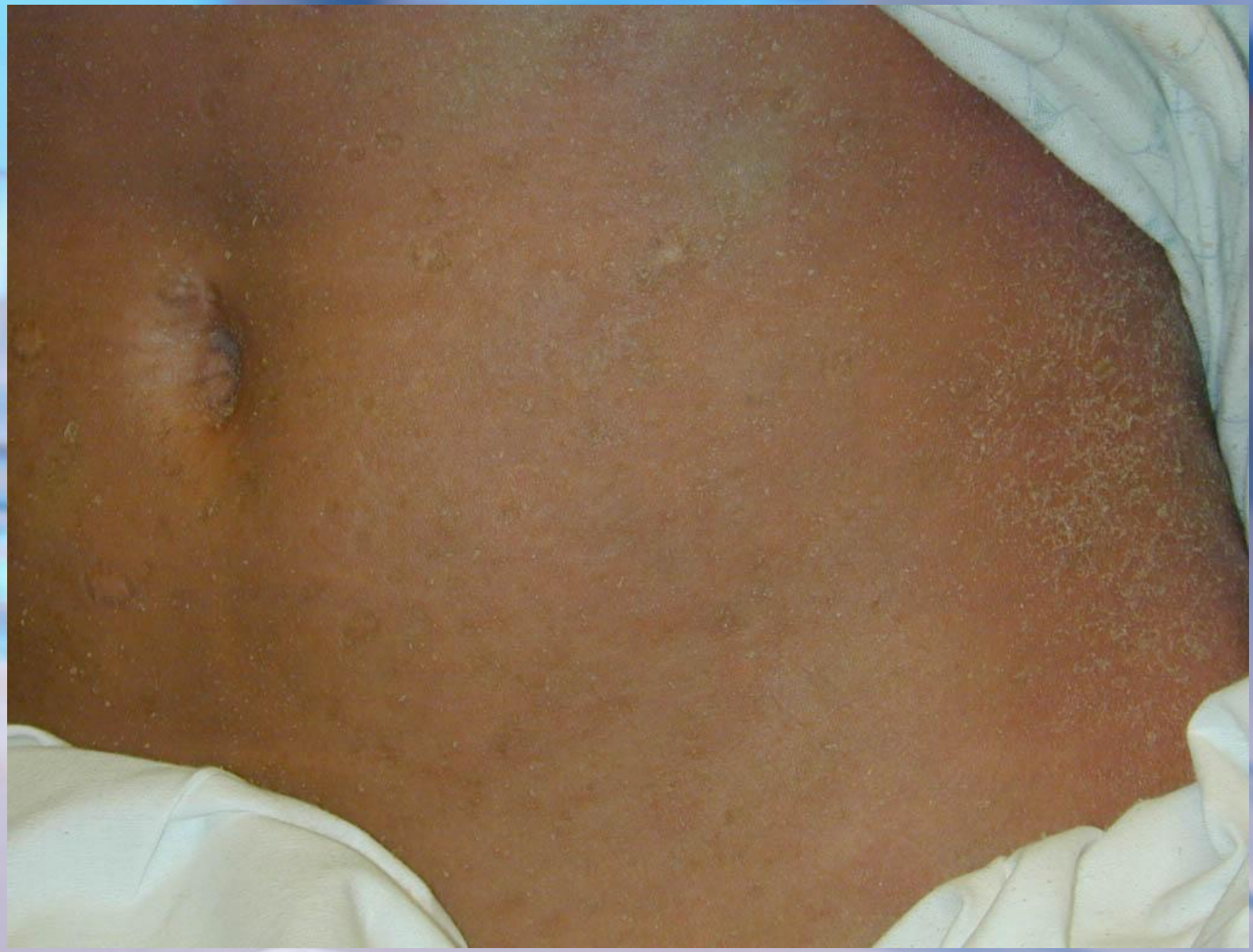




# 3-ERYTHRODERMIC PSORIASIS:-

- Scaly erythematous lesions, involving 90% or more of the cutaneous surface
- hair may shed; nails may become ridged and thickened
- Few typical psoriatic plaques
- Unwell,fever,leucocytosis
- excessive of body heat and hypothermia
- increase cut blood flow
- Increase per-cut loss of water,protein and iron
- Increase per-cut permeability





# 4-Psoriasis, Pustular:-

- uncommon form of psoriasis
- pustules on an erythematous background
- psoriasis vulgaris may be present before, during, or after
- pustular psoriasis may be classified into several types

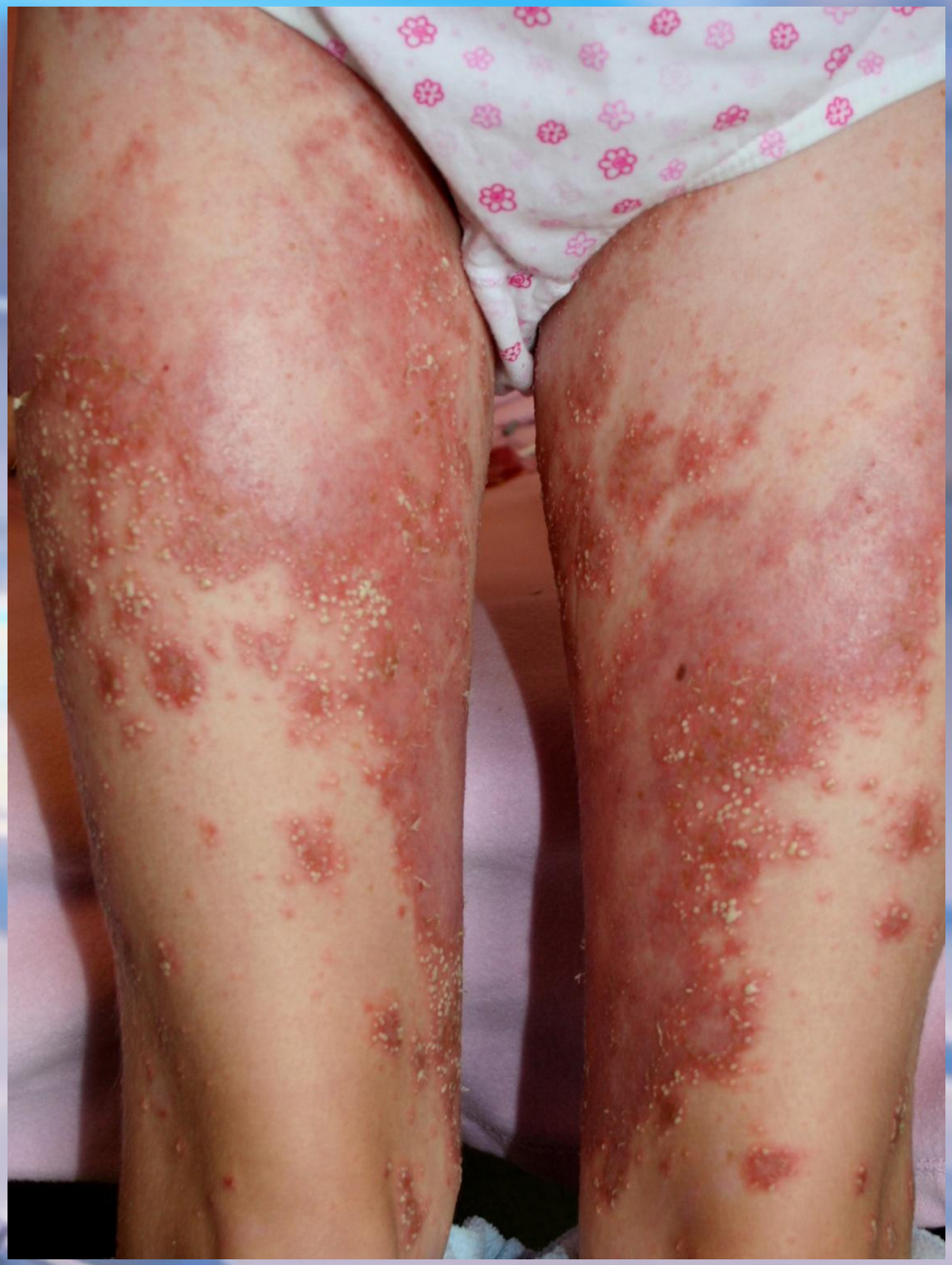
## 1-generalized type(von Zumbusch variant):

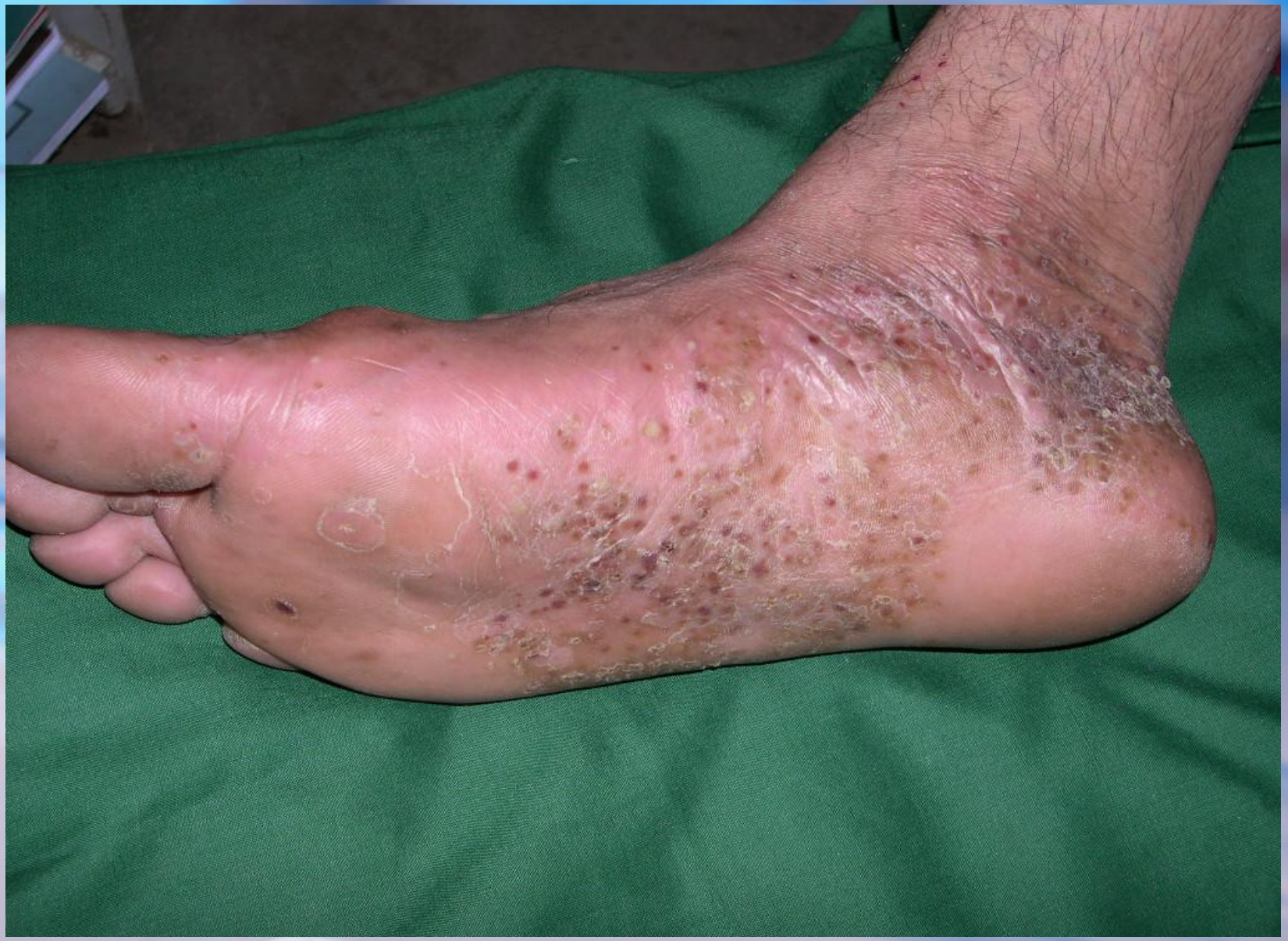
- generalized erythema studded with interfolecular pustules
- fever, tachypneic, tachycardic
- absolute lymphopenia with polymorph nuclear leukocytosis up to 40,000/µL

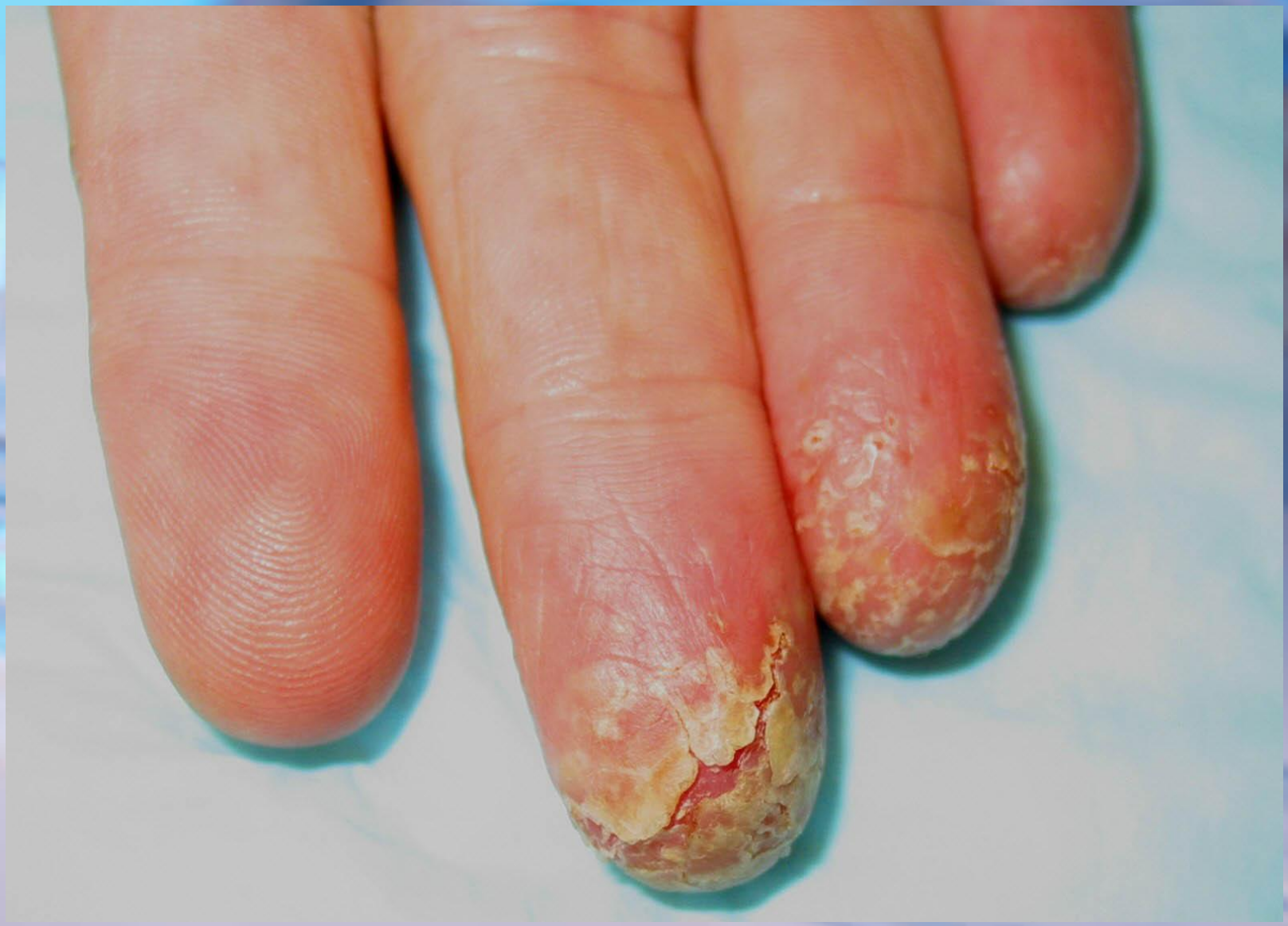
## 2-Localized form (palms and soles)

# Causes of pustular ps:-

1- Withdrawal of systemic steroids
2- Drugs, including salicylates,, lithium, phenylbutazone,, hydroxychloroquine,, interferon
3- Strong, irritating topicals, including tar, anthralin, steroids under occlusion, and zinc pyrithione in shampoo
4- Infections
5- Sunlight or phototherapy
6- Cholestatic jaundice
7- Hypocalcemia
8- Idiopathic in many patients

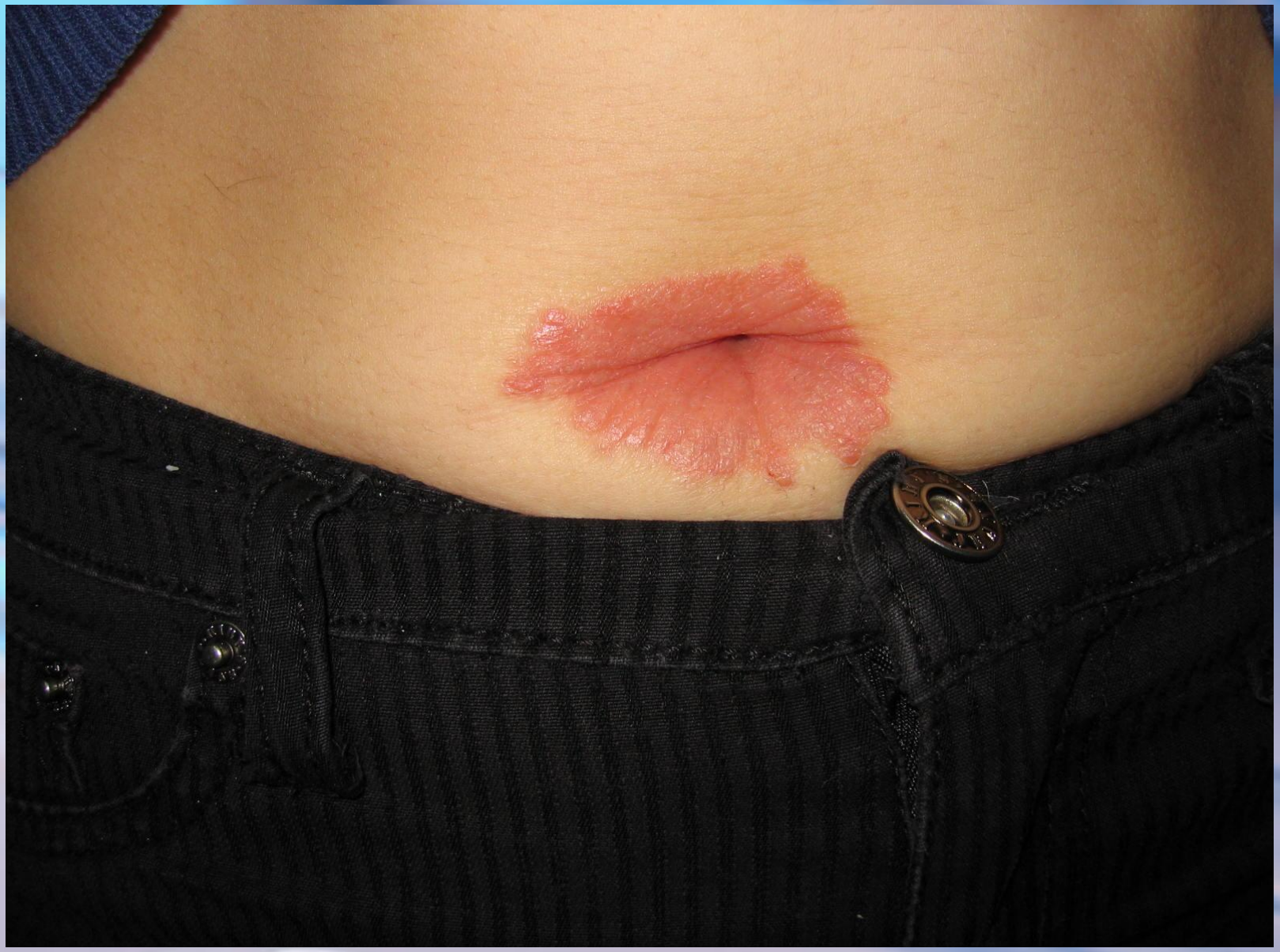


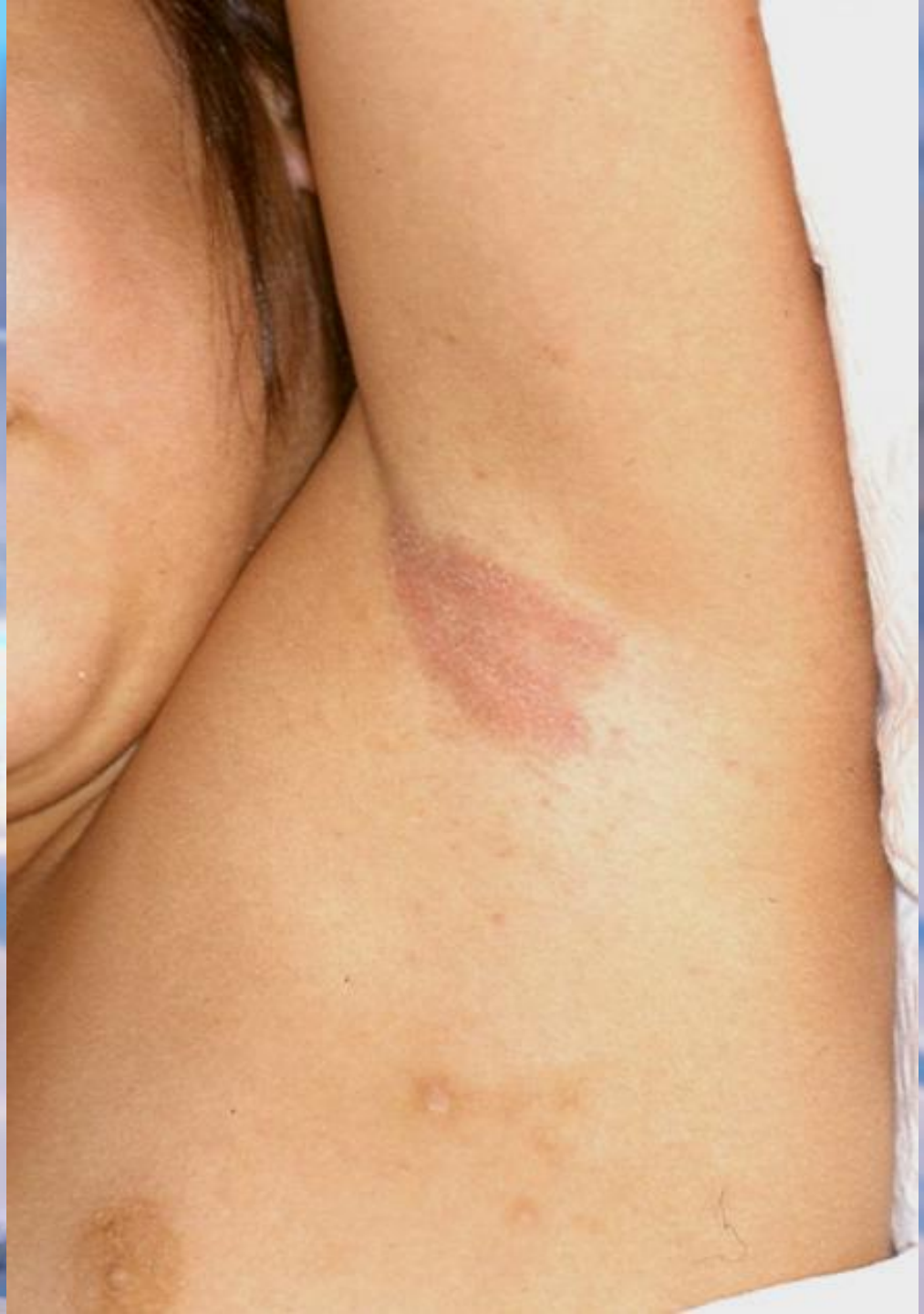




# 5-Psoriasis inversus(sebopsoriasis):-

- Over body folds
- The erythema and scales are very similar to that seen in seborrhoeic dermatitis





# 6-Psoriatic Arthritis:-

- Psoriatic arthritis is a chronic inflammatory arthritis that is commonly associated with psoriasis
- 5%of patients with psoriasis develop psoriatic arthritis
- most commonly a seronegative oligoarthritis
- Asymmetric oligoarthritis occurs in as many as 70% of patients with psoriatic arthritis
- DIP joint involvement occurs in approximately 5-10 of patients with psoriatic arthritis
- Arthritis mutilans is a rare form of psoriatic arthritis occurring in 5% of patients with psoriatic arthritis
- Spondylitis occurs in about 5% of patients with psoriatic arthritis and is often asymptomatic

# 7-Psoriatic nail:-

- Psoriatic nail disease occurs in 10-55% of all patients with psoriasis
- Less than 5% of psoriatic nail disease cases occur in patients without other cutaneous findings
- Nail changes are seen in 53-86% of patients with psoriatic arthritis
- Oil drop or salmon patch/nail bed
- Pitting
- Subungual hyperkeratosis
- Onycholysis
- Beau lines

# Differential diagnosis:-

- Bowes Disease
- Cutaneous T-Cell Lymphoma-
- Drug Eruptions-
- Erythema Annulare Centrifugum-
- Extramammary Paget Disease-
- Lichen Planus-
- Lichen Simplex Chronicus-
- Lupus Erythematosus, Discoid-
- Lupus Erythematosus, Subacute Cutaneous
- Nummular Dermatitis
- Parapsoriasis-
- Pityriasis Rosea-
- Pityriasis Rubra Pilaris-
- Seborrheic Dermatitis-
- Syphilis-
- Tine Corporis-

# Lab Studies:-

-Skin biopsy

-others

# Treatment of psoriasis

- What influences therapy choice?
  - Clinical type and severity of psoriasis (eg, mild vs moderate-to-severe), assessed by Psoriasis Area and Severity Index (PASI)
  - Response to previous treatment
  - Therapeutic options
  - Patient preference
- The "1-2-3" step approach is no longer generally accepted for disease more than mild in severity
  - Level 1: Topical agents—do not work
  - Level 2: "Phototherapy"—difficult; not always available
  - Level 3: Systemic therapy
- Risk in relation to benefit must be evaluated

Camisa C. *Cleve Clin J Med*. 2000;67:105-119.

# Topical Agents

- Initial therapeutic choice for mild-to-moderate psoriasis
  - Emollients
  - Keratolytics (salicylic acid, lactic acid, urea)
  - Coal tar
  - Anthralin
  - Vitamin $D_3$ analogues (calcipotriene)
  - Corticosteroids
  - Retinoids (tazarotene, acitretin)
- Compliance can be difficult due to amount of time required to apply topicals 2 to 4 times/day

Camisa C. *Cleve Clin J Med*. 2000;67:105-119.

# Phototherapy

- Used to treat moderate-to-severe psoriasis
- Phototherapy causes death of T cells in the skin
  - Natural sunlight
  - Ultraviolet (UV) B light
  - UVB light + coal tar (Goeckerman treatment)
    - Best therapeutic index for moderate-to-severe disease
  - UVB light + anthralin + coal tar (Ingram regimen)
  - Usually 3 treatments/week for 2 to 3 months is needed
  - Accessibility to a light box facility and compliance necessary

Camisa C. *Cleve Clin J Med*. 2000;67:105-119.

# Uva Light with psoralen (PUVA)

- Psoralen is a drug that causes a toxic reaction to skin lymphocytes when it is activated by UVA light
- Psoralen can be given systemically or topically
- Effective treatment—longest remissions of any treatment available
- Adverse effects
  - Nausea, burning, pruritus
  - Risk of cancer with cumulative use—both squamous cell carcinoma and melanoma
    - >160 cumulative treatments

Greaves MW, et al. *N Engl J Med*. 1995;332:581-588.

# Methotrexate

- Folic acid metabolite
  - Blocks deoxyribonucleic acid synthesis, inhibits cell proliferation
- Dose
  - Start at about 15 mg/week; maximum 30 mg/week
  - Can also be given intramuscularly
- Adverse effects
  - Headache, nausea, bone marrow suppression
  - Cumulative dose predictive of liver toxicity
    - Prospectively identify risk factors for liver disease
    - Guidelines recommend liver biopsy after 1.5 g
    - Teratogenic in men and women

Greaves MW, et al. *N Engl J Med*. 1995;332:581-588.

# Acitretin: Orel Retinoid

- Frequently used in combination with topical agents, systemic therapies, and UV light
- Less effective as monotherapy for plaque psoriasis
- Plaque psoriasis dose
  - Start at 10 to 25 mg/day
- Adverse effects (fewest dose-related adverse effects)
  - Peeling/dry skin, alopecia, muscle pain
  - Lipid abnormalities
- Teratogenic: avoid pregnancy

Greaves MW, et al. *N Engl J Med* 1995;332:581-588.

# Cyclosporine

- Reserved for severe, recalcitrant disease
- Inhibits the proliferation of activated T cells
- Dose: 4 mg/kg/day, not to exceed 5 mg/kg/day
  - Tapering slowly may improve remission
- Use not recommended for >1 year
  - Renal toxicity
- Patients relapse 2 to 4 months after discontinuing
- Adverse effects
  - Immunosuppression: infections, possible malignancy
  - Hirsutism, gingival hyperplasia, muscle pain, infection
  - Serious: hypertension, renal failure

Lebwohl M, et al. *J Am Acad Dermatol*. 1999;39:464-475.

# Biologic Therapies Currently Approved for the treatment of psoriasis

- Alefacept
- Efalizumab
- Etanercept

# Alefacept (Amevive) :-

-Is the first biologic agent approved by the FDA for the treatment of psoriasis

-It works by blocking T cell activation and proliferation by binding to CD2 receptors on T cells

-This stops the T cells from releasing cytokines, which is the primary cause of the inflammation

-7.5 mg by intravenous injection or 15 mg by intramuscular injection once weekly for 12 weeks

-S/E:-dizziness, cough, nausea, itching, muscle aches, chills, injection site pain and injection site redness and swelling

-Infections

# Efalizumab (Raptiv)

- Recombinant humanized IgG1-kappa isotype monoclonal antibody
- Anti-CD11a antibody
- Down-regulates (decreases) surface expression of CD11a by 75-85% at psoriasis doses
- Initial dose: 0.7 mg/kg SC. Subsequent doses: 1 mg/kg/wk SC

- S/E: -headache, chills, fever, nausea, vomiting
  -thrombocytopenia
  -may increase infection risk

# Etanercept (enbril):-

-This molecule serves as an exogenous TNF receptor and prevents excess TNF from binding to cell-bound receptors

-50mg SC given twice weekly for 3 mo, then 50 mg SC qwk

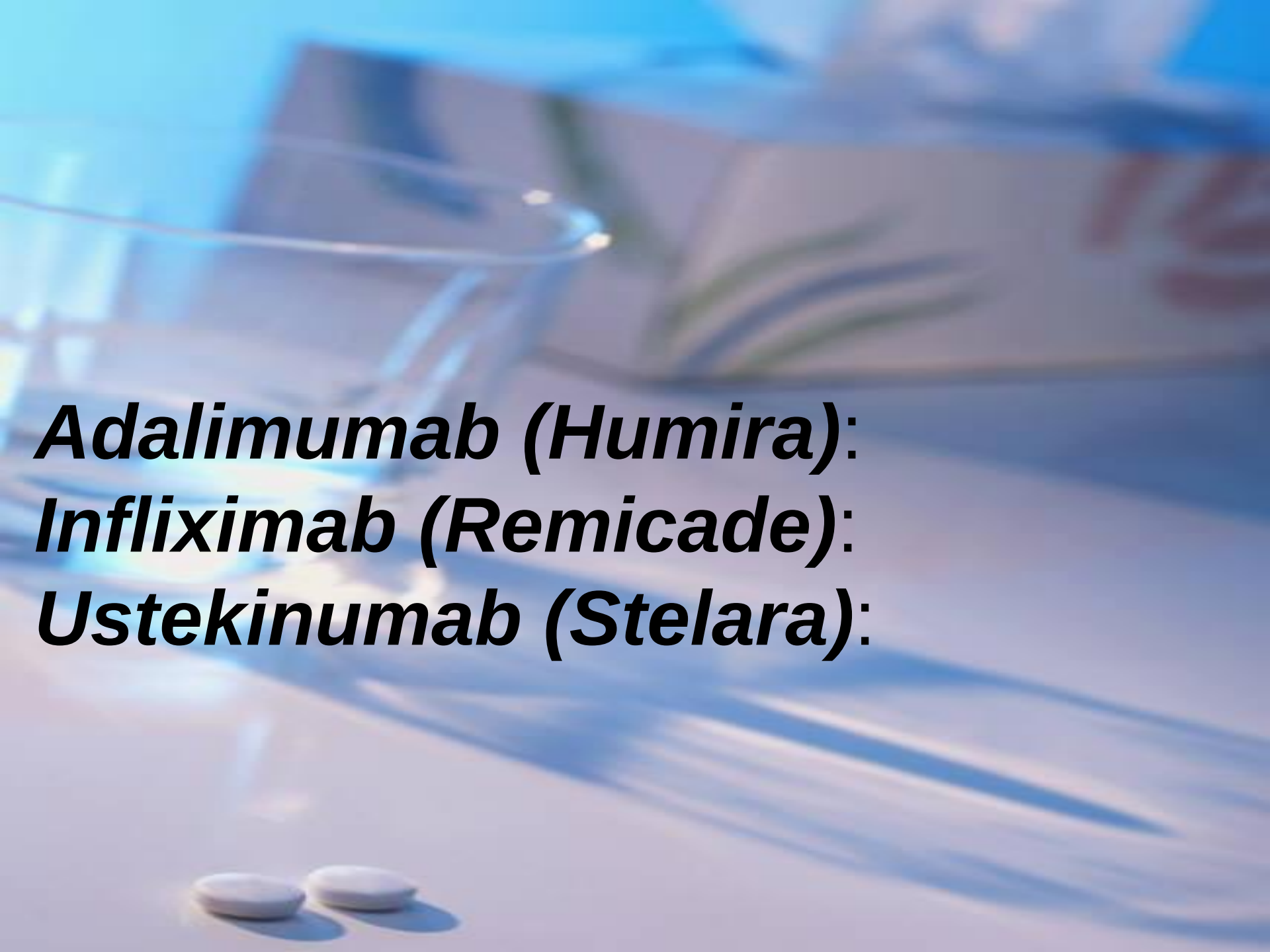
-Contraindications:-

-sepsis, active infection, concurrent live vaccination

-S/E:-

-injection site reactions (most commom)

-upper respiratory tract infections


*Adalimumab (Humira)*:
*Infliximab (Remicade)*:
*Ustekinumab (Stelara)*:

# Lichen Planus:-

- **Background:**
- **Lichen planus (LP) is a pruritic, papular eruption characterized by its violaceous color; polygonal shape; and, sometimes, fine scale**
- **It is most commonly found on the flexor surfaces of the upper extremities, on the genitalia, and on the mucous membranes.**

# Epidemiology:-

-Approximately 1% of all new patients seen at health care clinics

-Rare in children

-F=M

-No racial predispositions have been noted

-LP can occur at any age but two thirds of patients are aged 30-60 years

# Pathophysiology:-

- The cause of LP is unknown
- LP may be a cell-mediated immune response of unknown origin
- LP may be found with other diseases of altered immunity like ulcerative colitis, alopecia areata, vitiligo, dermatomyositis
- An association is noted between LP and hepatitis C virus infection ,chronic active hepatitis, and primary biliary cirrhosis
- Familial cases
- Drug may induce lichenoid reaction like thiazide,antimalarials,propranolol

# Clinical features:-

- Most cases are insidious
- The initial lesion is usually located on the flexor surface of the limbs
- After a week or more, a generalized eruption develops with maximal spreading within 2-16 weeks-
- Pruritus is common but varies in severity
- Oral lesions may be asymptomatic or have a burning sensation
- In more than 50% of patients with cutaneous disease, the lesions resolve within 6 months, and 85% of cases subside within 18 months

- The papules are violaceous, shiny, and polygonal; varying in size from 1 mm to greater than 1 cm in diameter
- They can be discrete or arranged in groups of lines or Circles
- Characteristic fine, white lines, called Wickham stria, are often found on the papules
- Oral lesions are classified as reticular, plaquelike, atrophic, papular, erosive, and bullous
- Ulcerated oral lesions may have a higher incidence of malignant transformation
- Genital involvement is common in men with cutaneous disease
- Vulvar involvement can range from reticulate papules to severe erosions

# Variations in LP:-

## 1-Hypertrophic LP:-

-These extremely pruritic lesions are most often found on the extensor surfaces of the lower extremities, especially around the ankles

## 2-Atrophic LP:-

-is characterized by a few lesions, which are often the resolution of annular or hypertrophic lesions

## 3-Erosive LP

## 4-Follicular LP:-

-keratotic papules that may coalesce into plaques

-A scarring alopecia may result

## 5-Annular LP:-

-Annular lesions with an atrophic center can be found on the buccal mucosa and the male genitalia

## 6-Vesicular and bullous LP:-

-develop on the lower limbs or in the mouth from preexisting LP lesions

## 7-Actinic LP:-

-Africa, the Middle East, and India

-mildly pruritic eruption

-characterized by nummular patches with a hypopigmented zone surrounding a hyperpigmented center

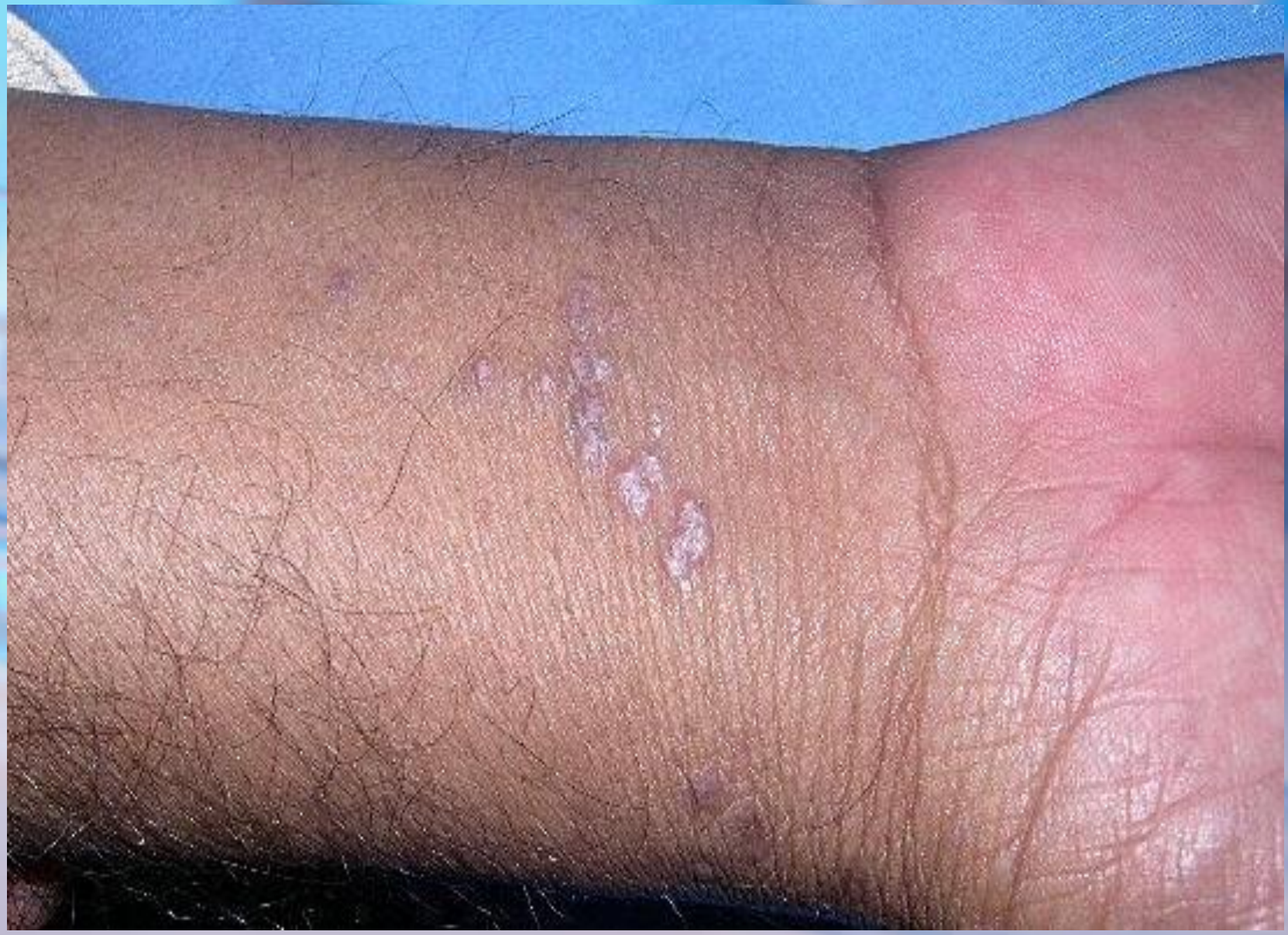
## 8-LP pigmentosus;-

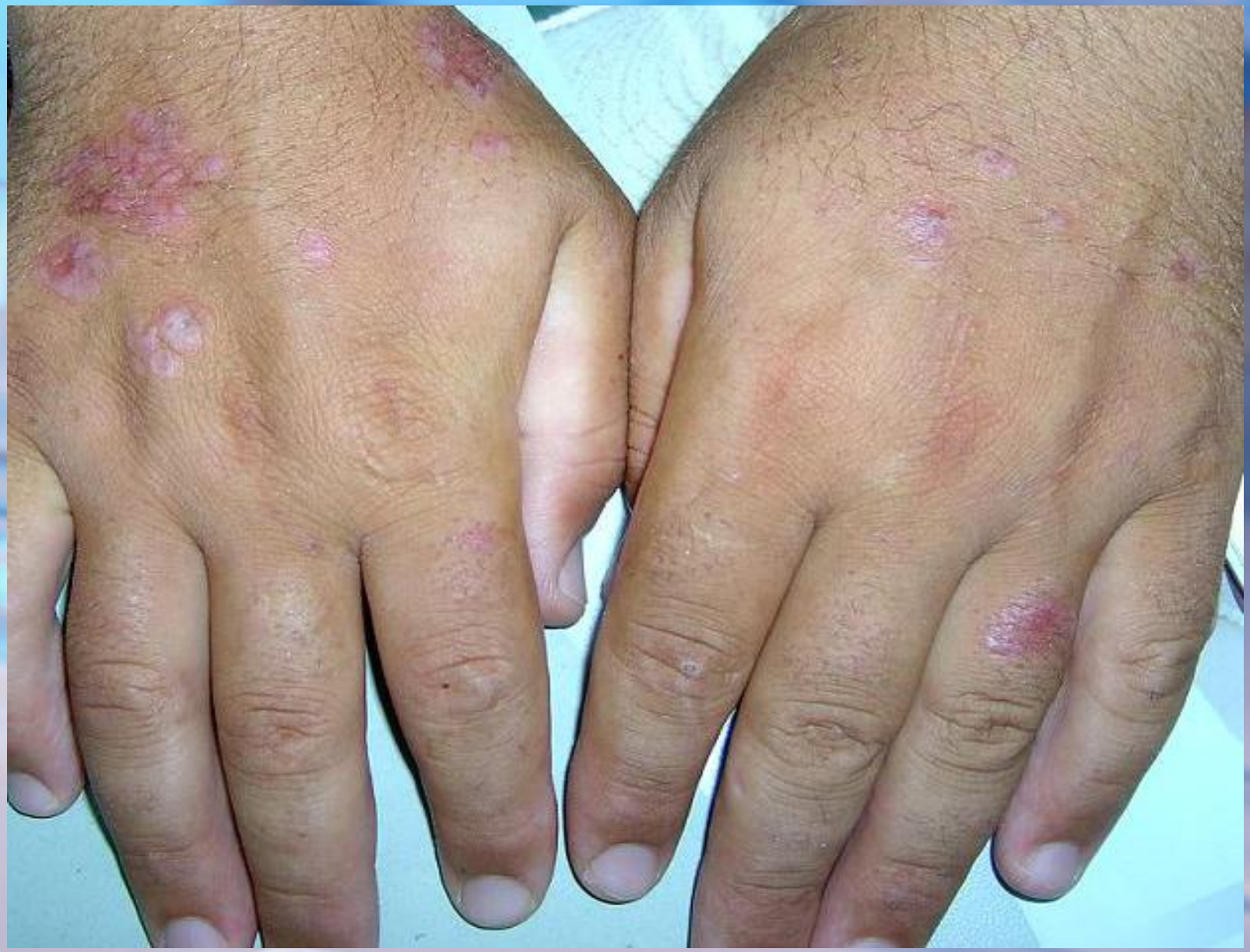
-common in persons with darker-pigmented skin

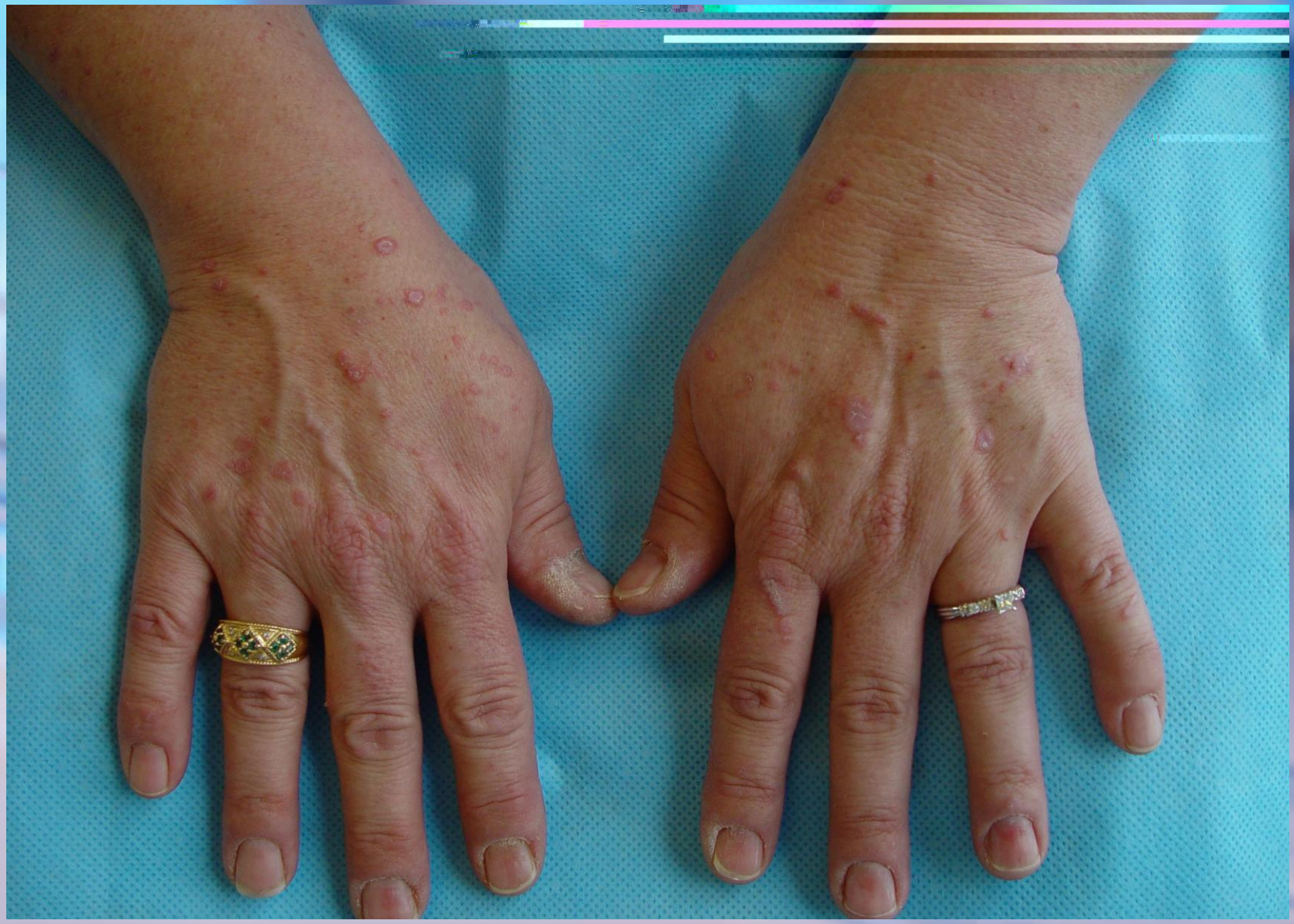
-usually appears on face and neck

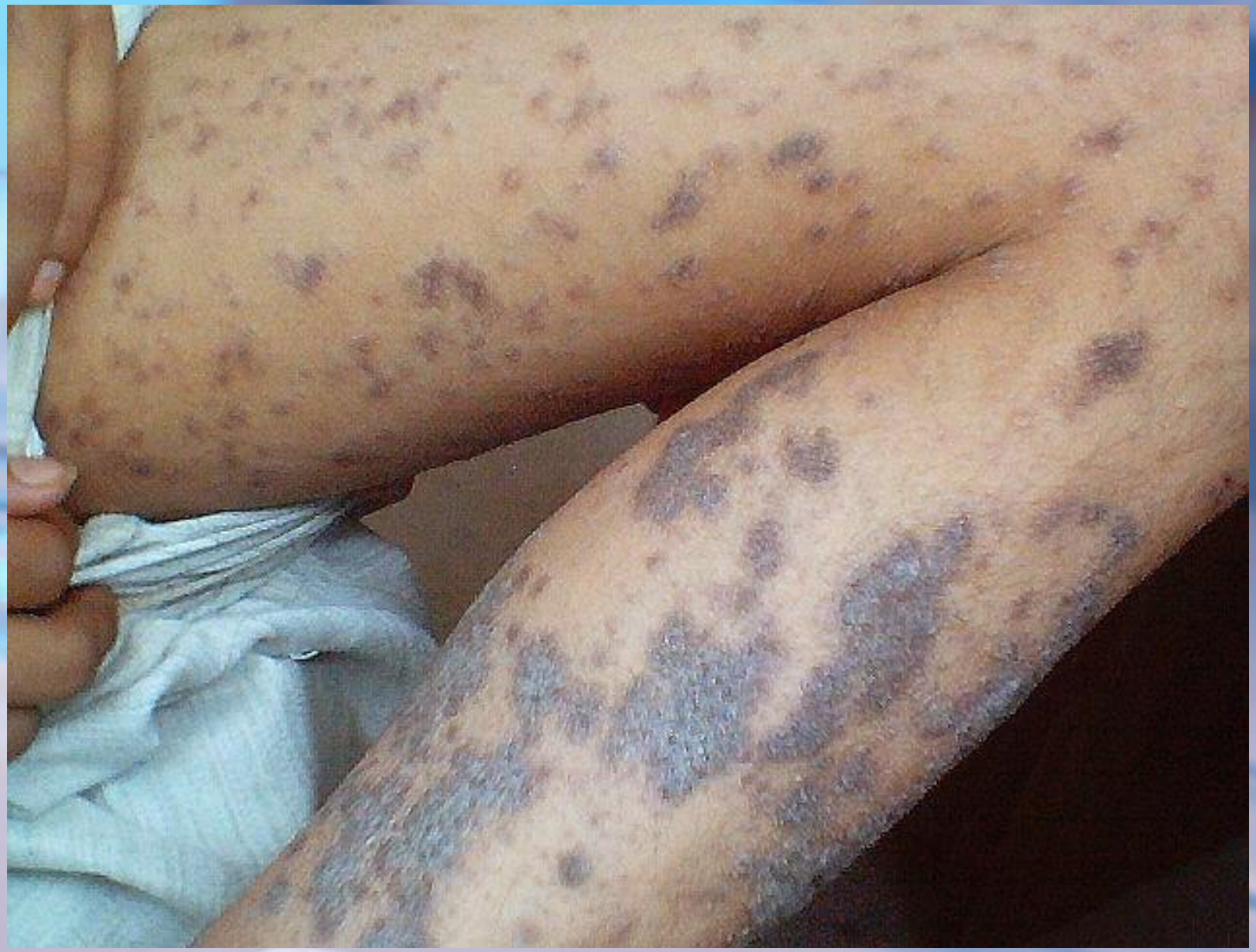
# LP and nail:-

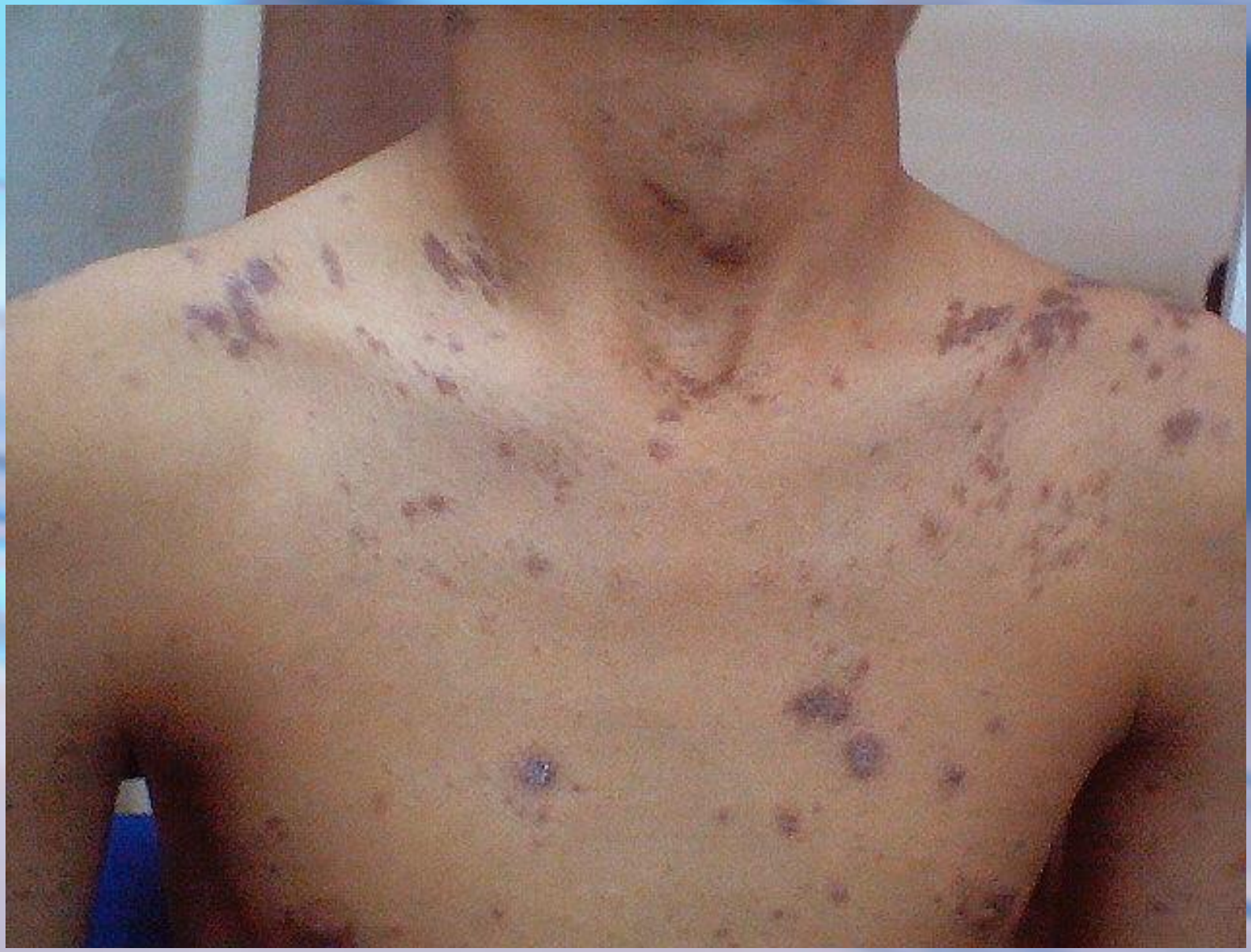
- In 10% of patients
- nail plate thinning causes longitudinal grooving and ridging
- subungual hyperkeratosis, onycholysis
- Rarely, the matrix can be permanently destroyed with prominent pterygium formation
- twenty-nail dystrophy

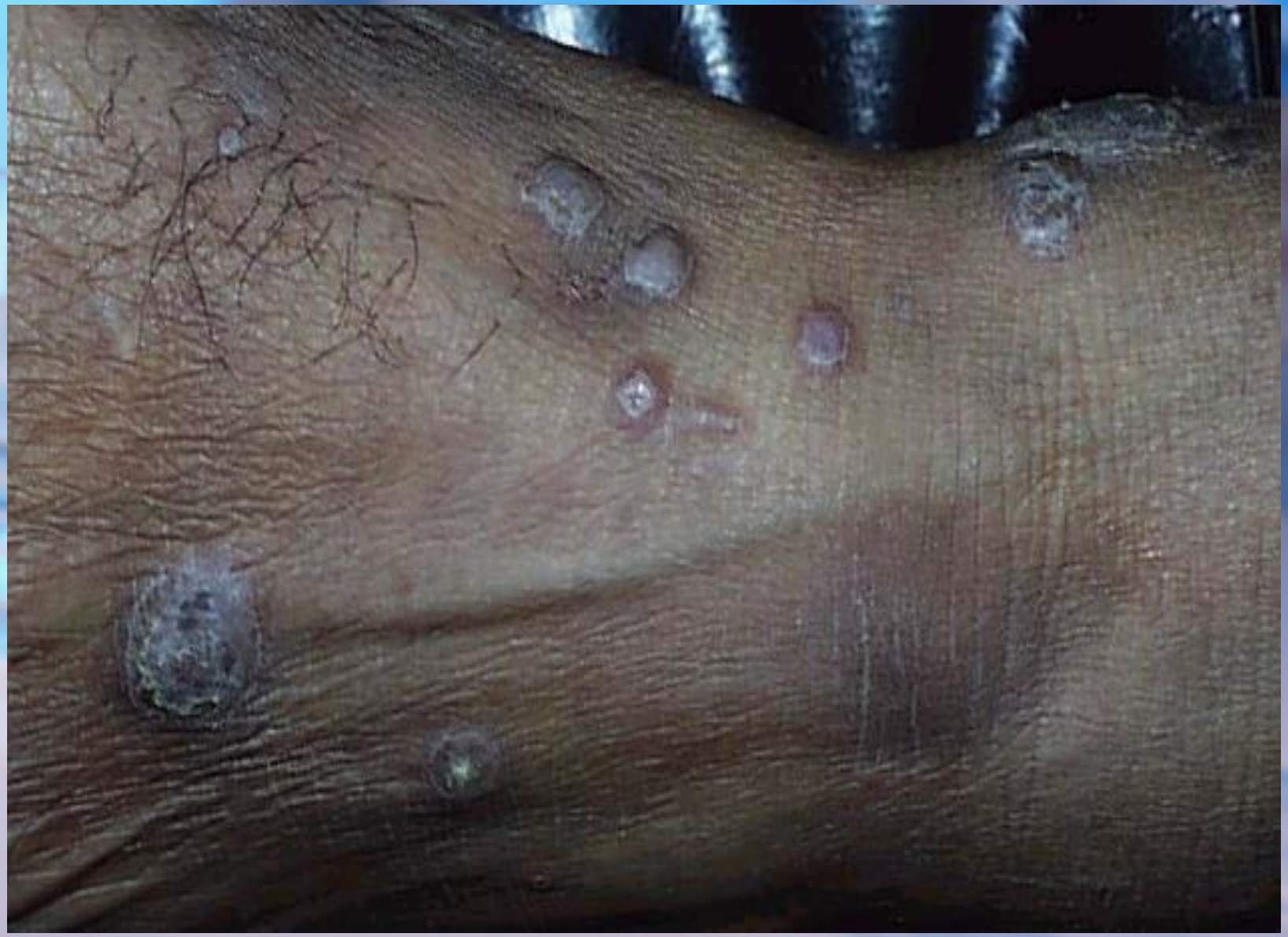


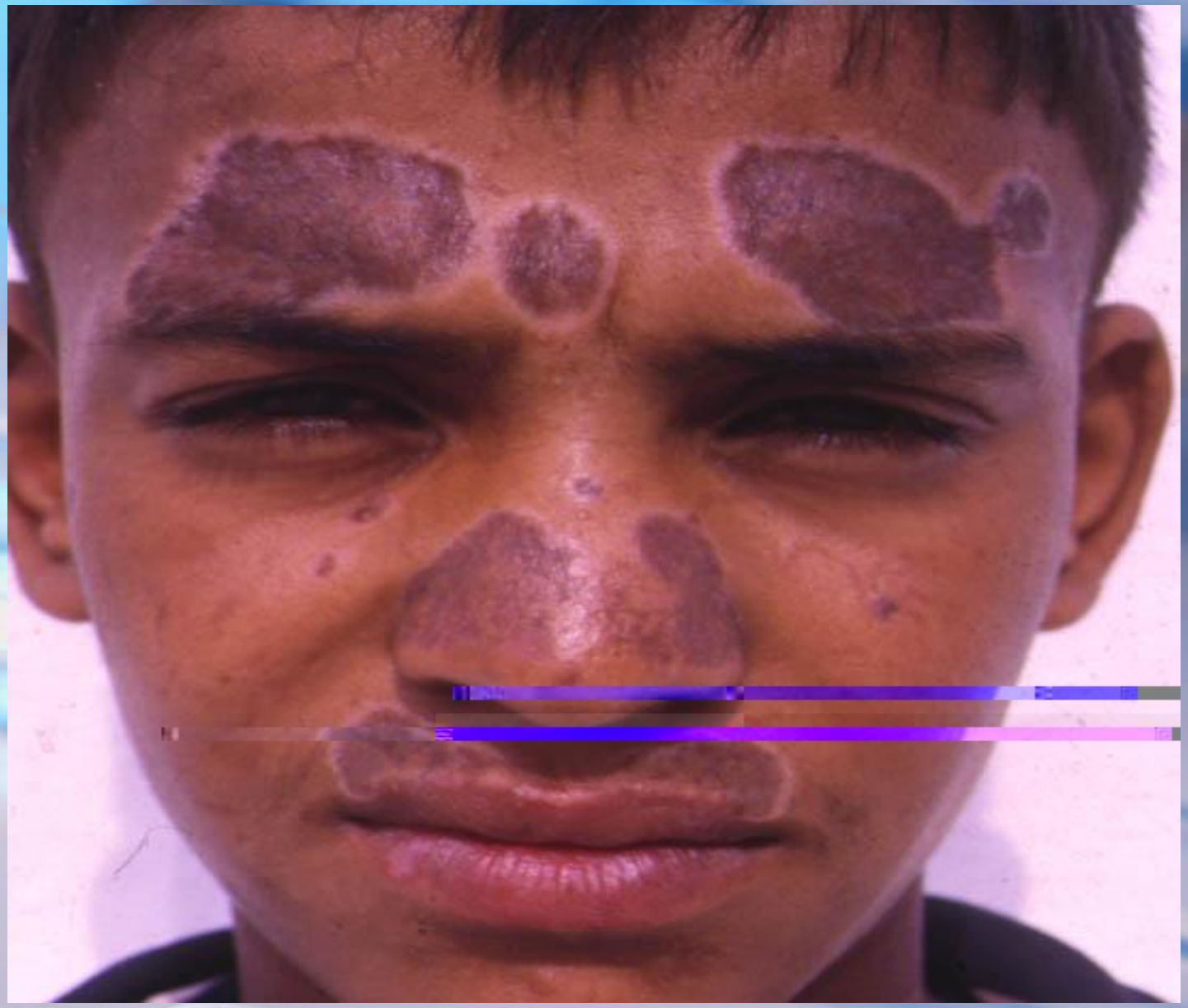


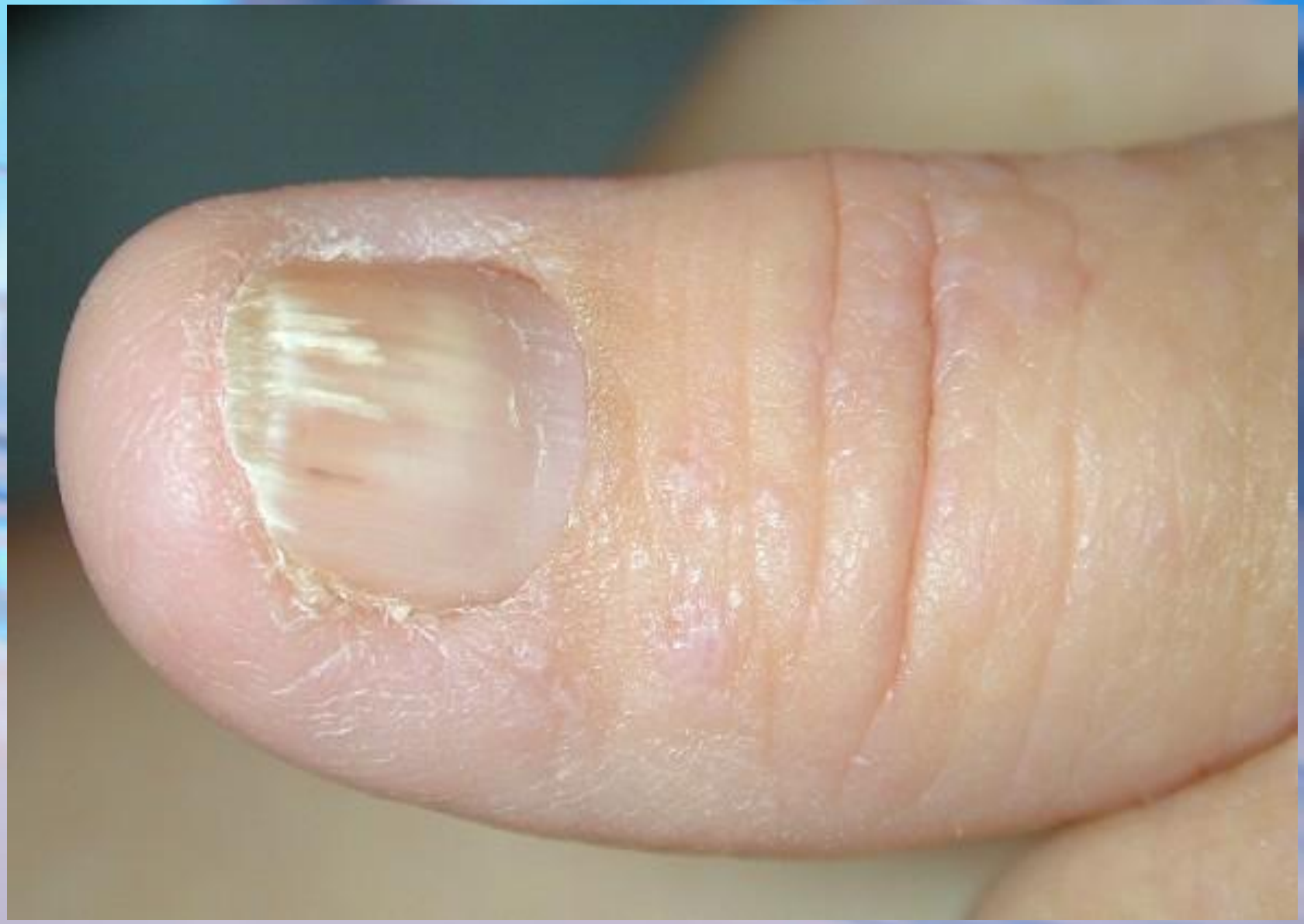


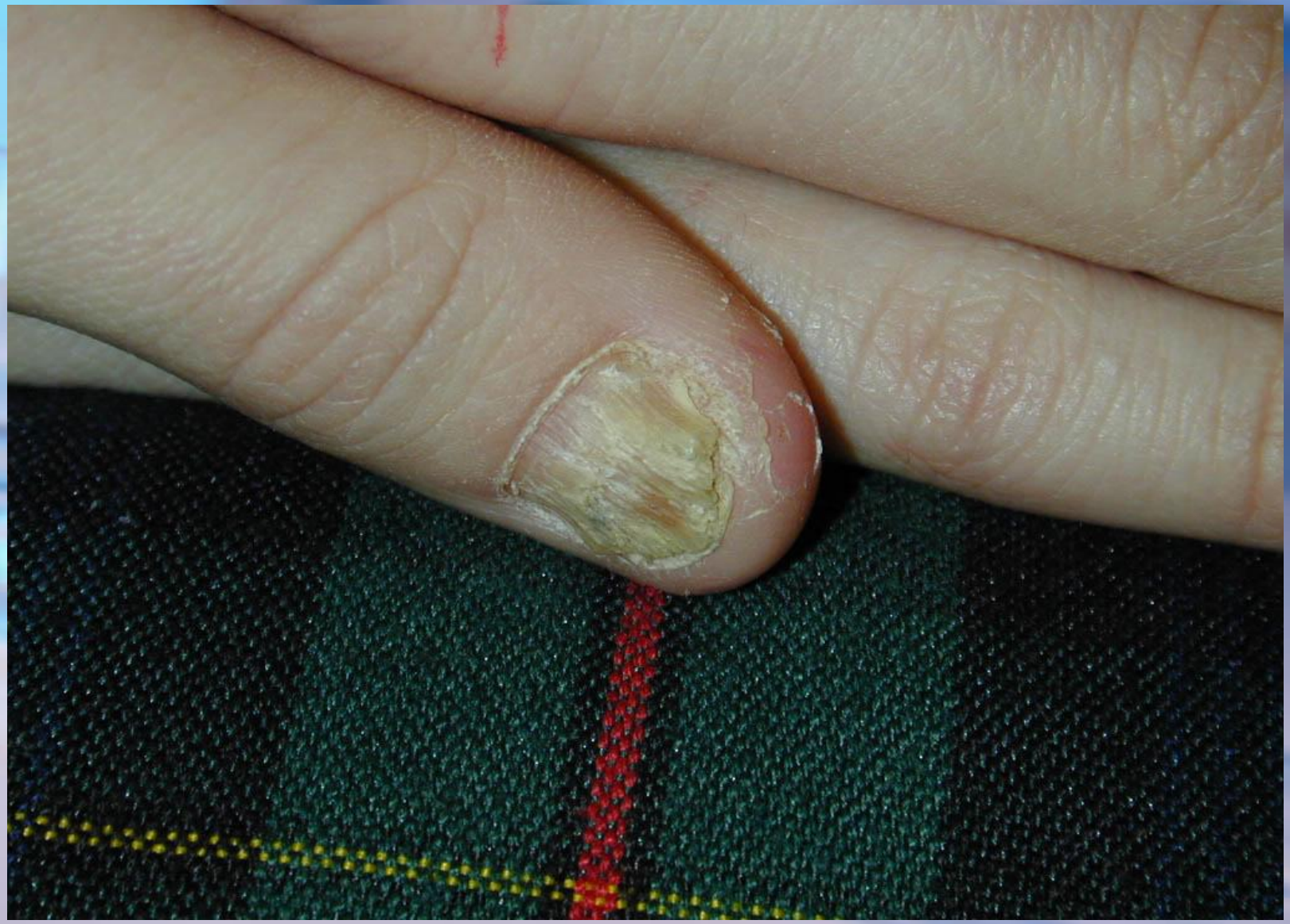


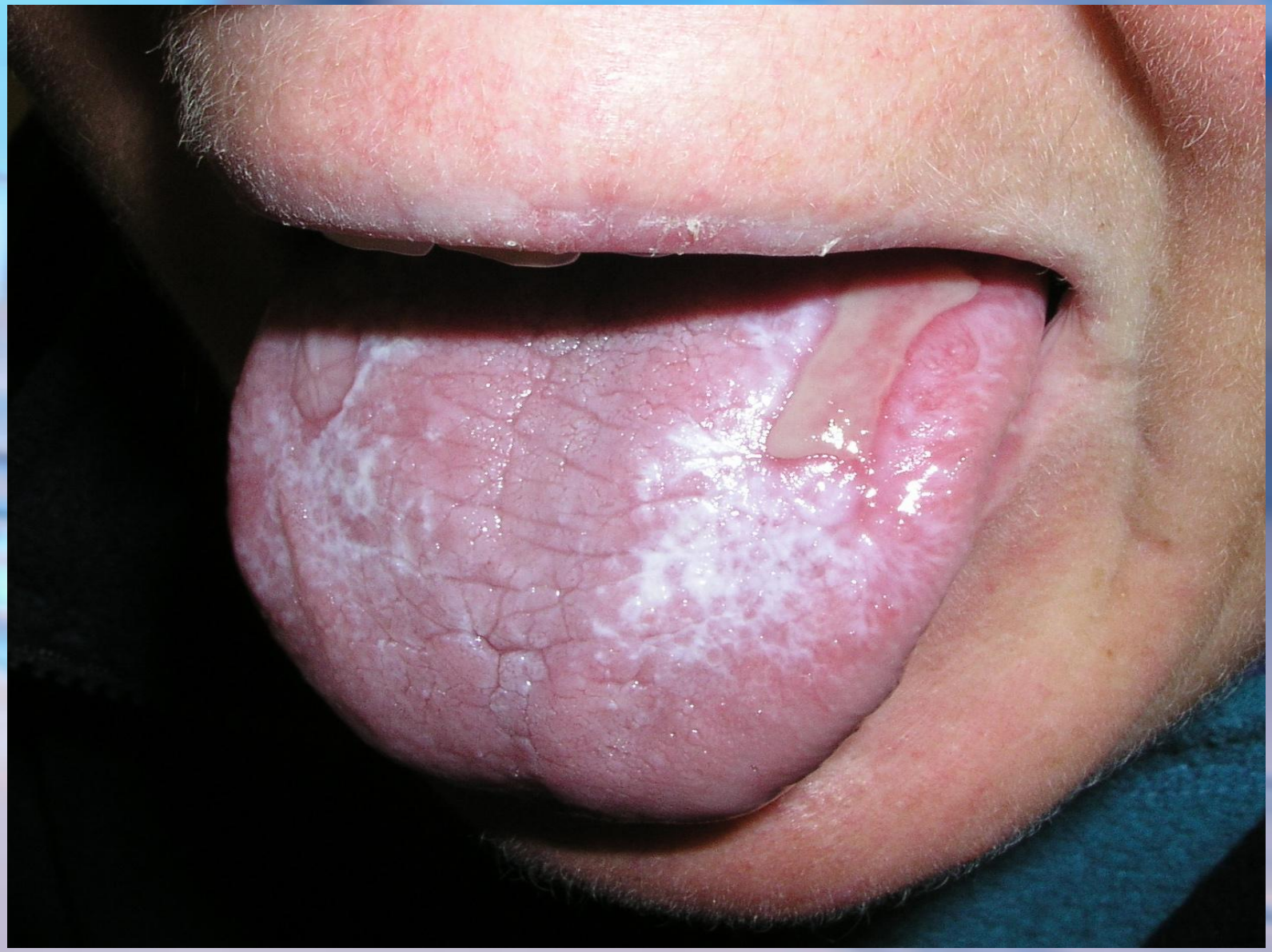


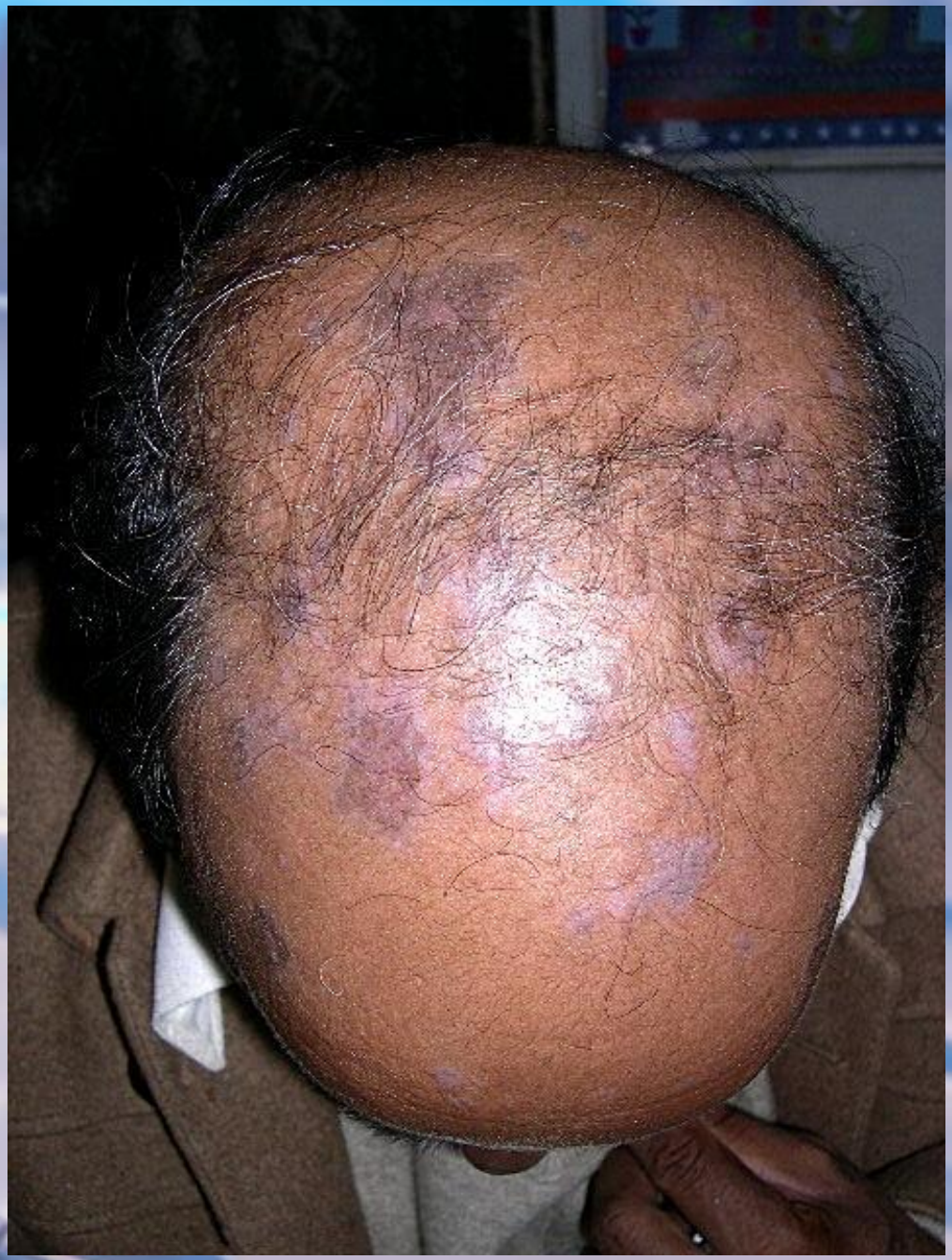












# DIFFERENTIALS:-

- Graft Versus Host Disease
- Lichen Nitidus
- Lichen Simplex Chronicus
- Pityriasis Rosea
- Psoriasis, Guttate
- Psoriasis, Plaque
- Syphilis
- Tine Corporis

# TREATMENT

- self-limited disease that usually resolves within 8-12 months
- Anti-histamine
- topical steroids, particularly class I or II ointments
- systemic steroids for symptom control and possibly more rapid resolution
- Oral acitretin
- Photo-therapy
- Others

# Pityriasis Rosea

## Definition:-

-Acute mild inflammtory exanthem.

-Characterized by the development of erythematous scaly macules on the trunk.

## Epidemiology:-

-In children and young adult

-Increased incidence in spring and autum

-PR has been estimated to account for 2% of dermatologic outpatient visits

-PR is more common in women than in men

# Pathophysiology:-

-PR considered to be a viral exanthem

-Immunologic data suggest a viral etiology

- Families and close contacts

-A single outbreak tends to elicit lifelong immunity

-Human herpesvirus (HHV)–7and HHV-6

-PR-like drug eruptions may be difficult to distinguish from non–drug-induced cases

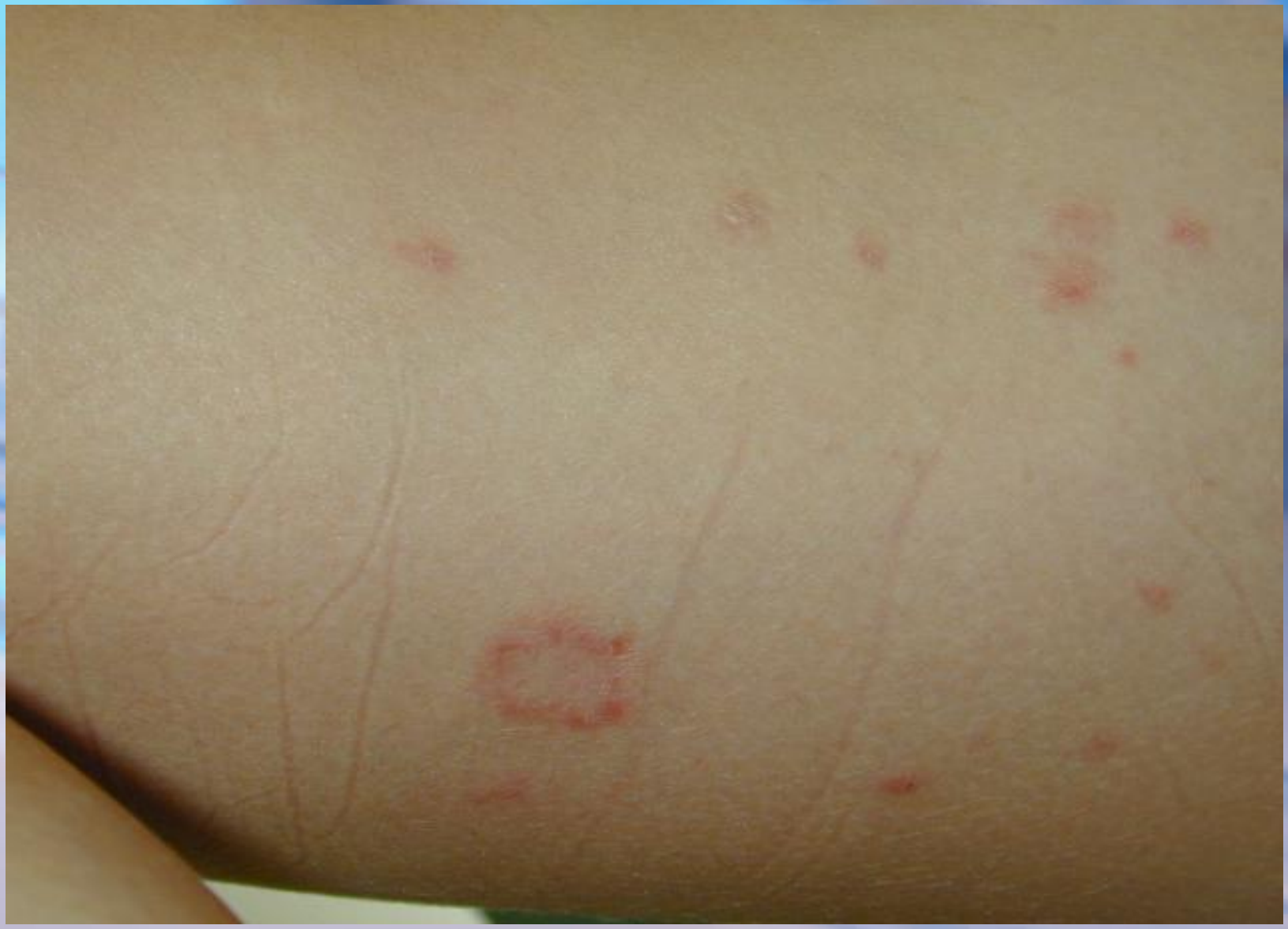
-Captopril, metronidazole, isotretinoin, penicillamine, bismuth, gold, barbiturates, and omeprazole.

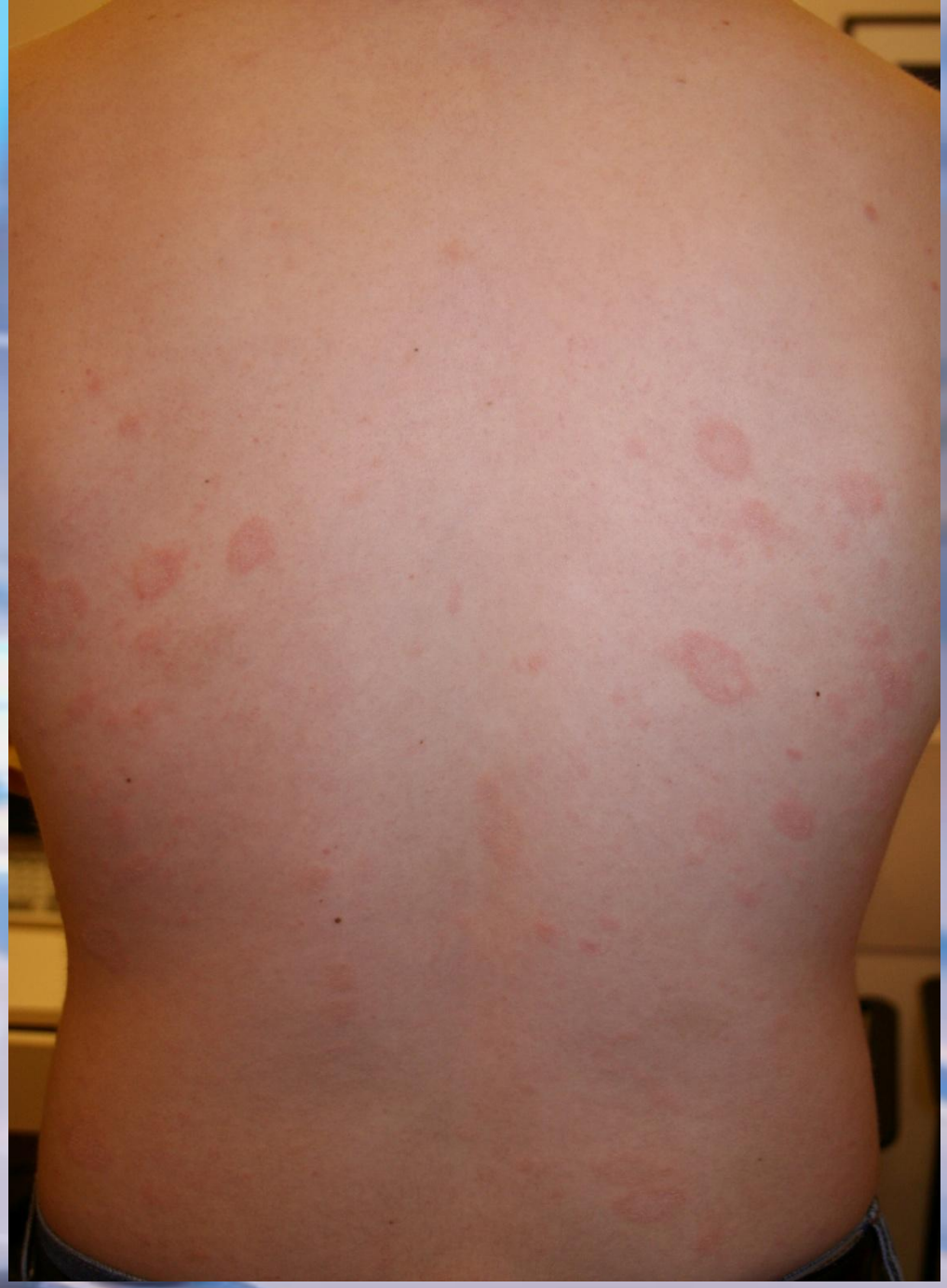
# CLINICAL FEATURES:-

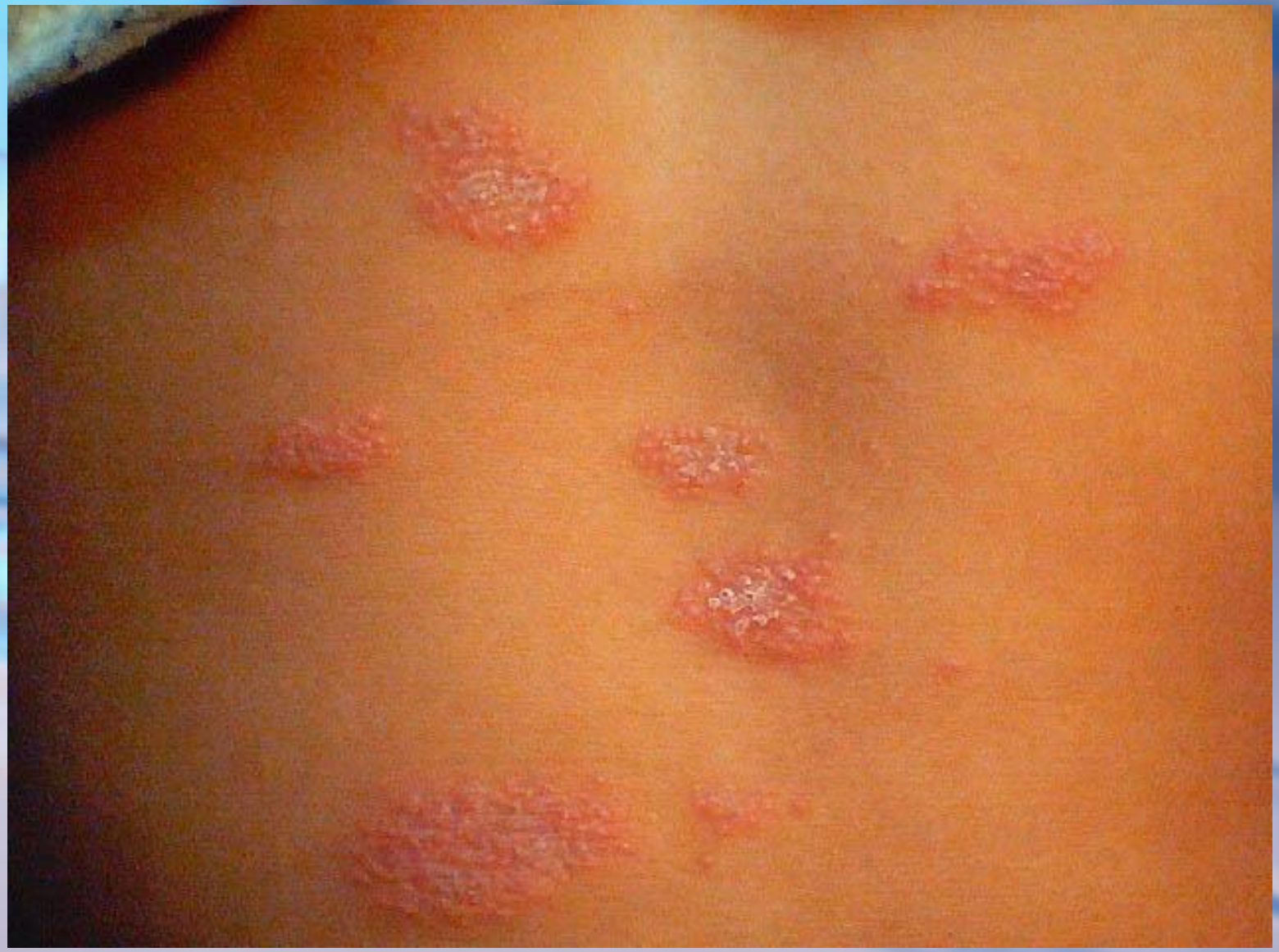
- Begins with a solitary macule that heralds the eruption(herald spot/patch )
- Usually a salmon-colored macule
- 0ver a few days it become a patch with a collarette of fine scale just inside the well-demarcated border
- Within the next 1-2 weeks, a generalized exanthem usually appears
- Bilateral and symmetric macules with a collarette scale oriented with their long axes along cleavage lines
- Tends to resolve over the next 6 weeks
- Pruritus is common, usually of mild-to-moderate severity
- Over trunk and proximal limbs

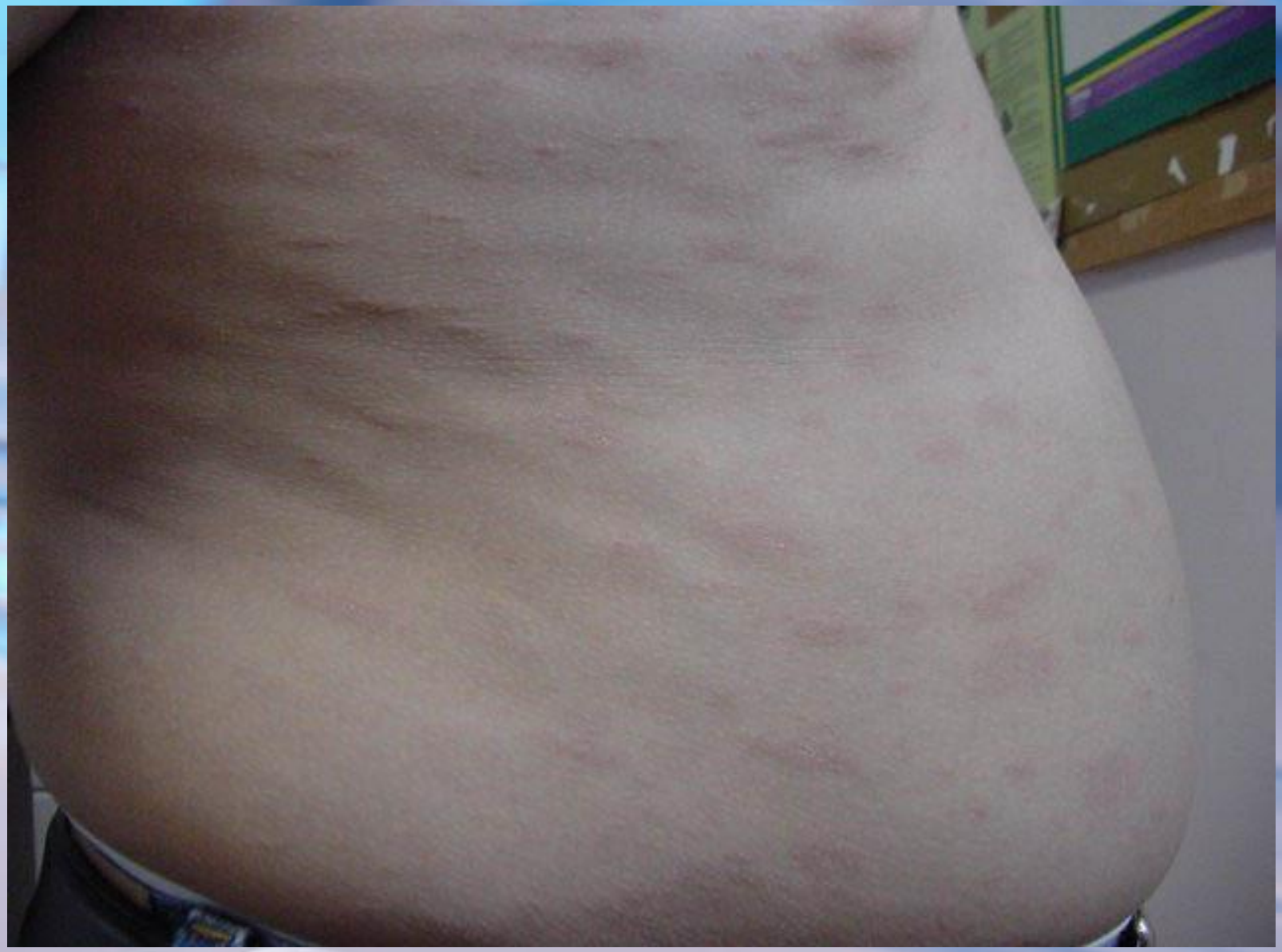
# Atypical form of PR:-

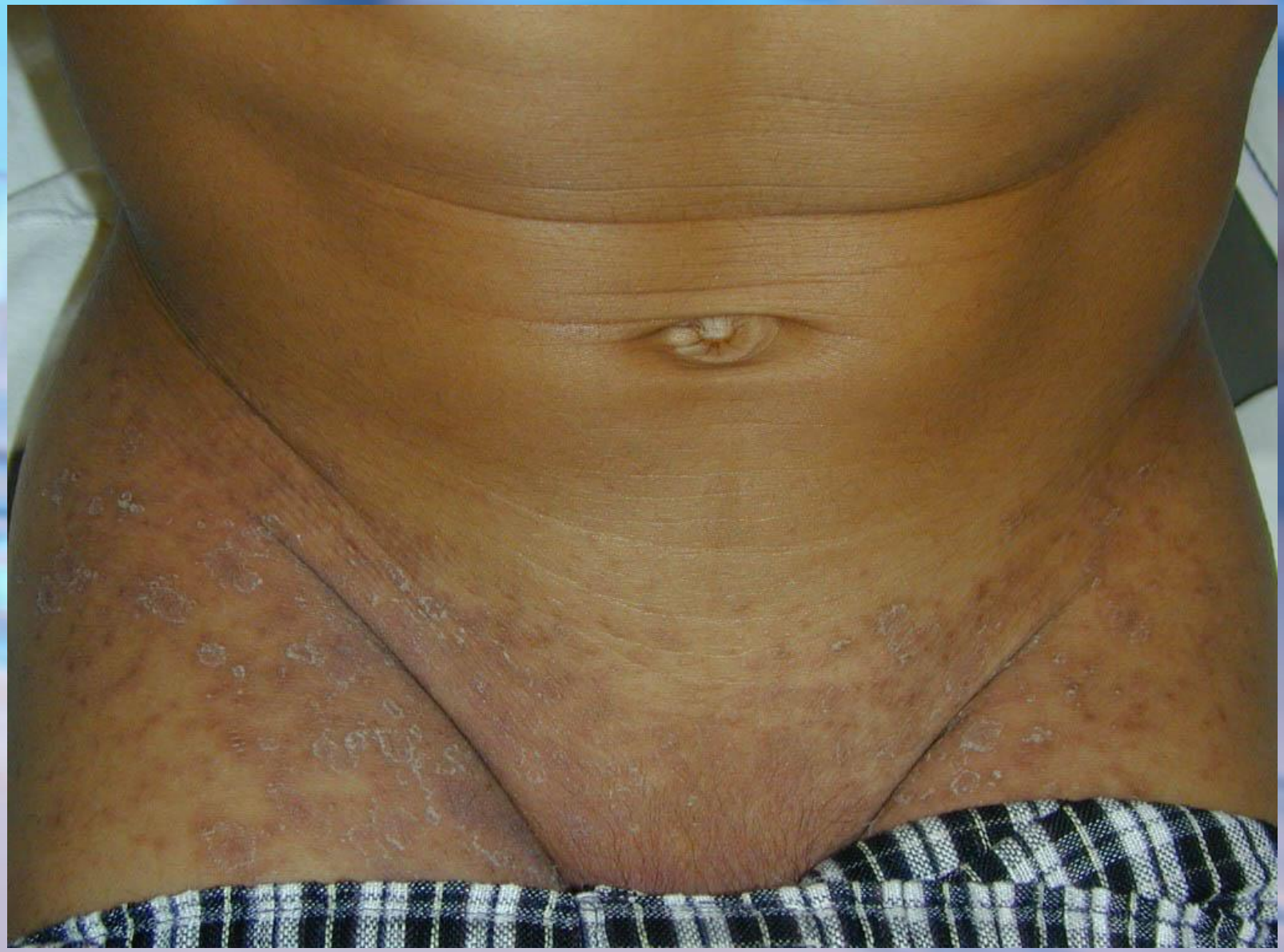
- Occurs in 20% of patients
- Inverse PR
- Unilateral variant
- Papular PR
- Erythema multiforme–like
- Purpuric PR











# DIFFERENTIALS:-

- Lichen Planus
- Nummular Dermatitis
- Pityriasis Lichenoides
- Psoriasis, Guttate
- Seborrheic Dermatitis
- Syphilis
- Tine Corporis

# TREATMENT

- Reassurance that the rash will resolve
- Relief of pruritus
- Topical menthol-phenol lotion
- Oral antihistamines
- Topical steroids
- Systemic steroids
- Ultraviolet B (UV-B) light therapy