Papulosquamous diseases

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Learning Objectives:

- **Define the *papulosquamous disease***
- **Highlight on the pathogenesis of papulosquamous diseases**
- **Discuss the clinical features of papulosquamous diseases**
- **Highlight on the papulosquamous diseases treatment**

Papulosquamous disease

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

Papulosquamous Diseases:

- **PSORIASIS**
- **Pityriasis rosea**
- **Lichen planus**
- **Seborrheic dermatitis**
- **Pityriasis rubra pilaris**
- **Secondary syphilis**
- **Miscellaneous mycosis fungoides, discoid lupus erythematosus, ichthyoses**

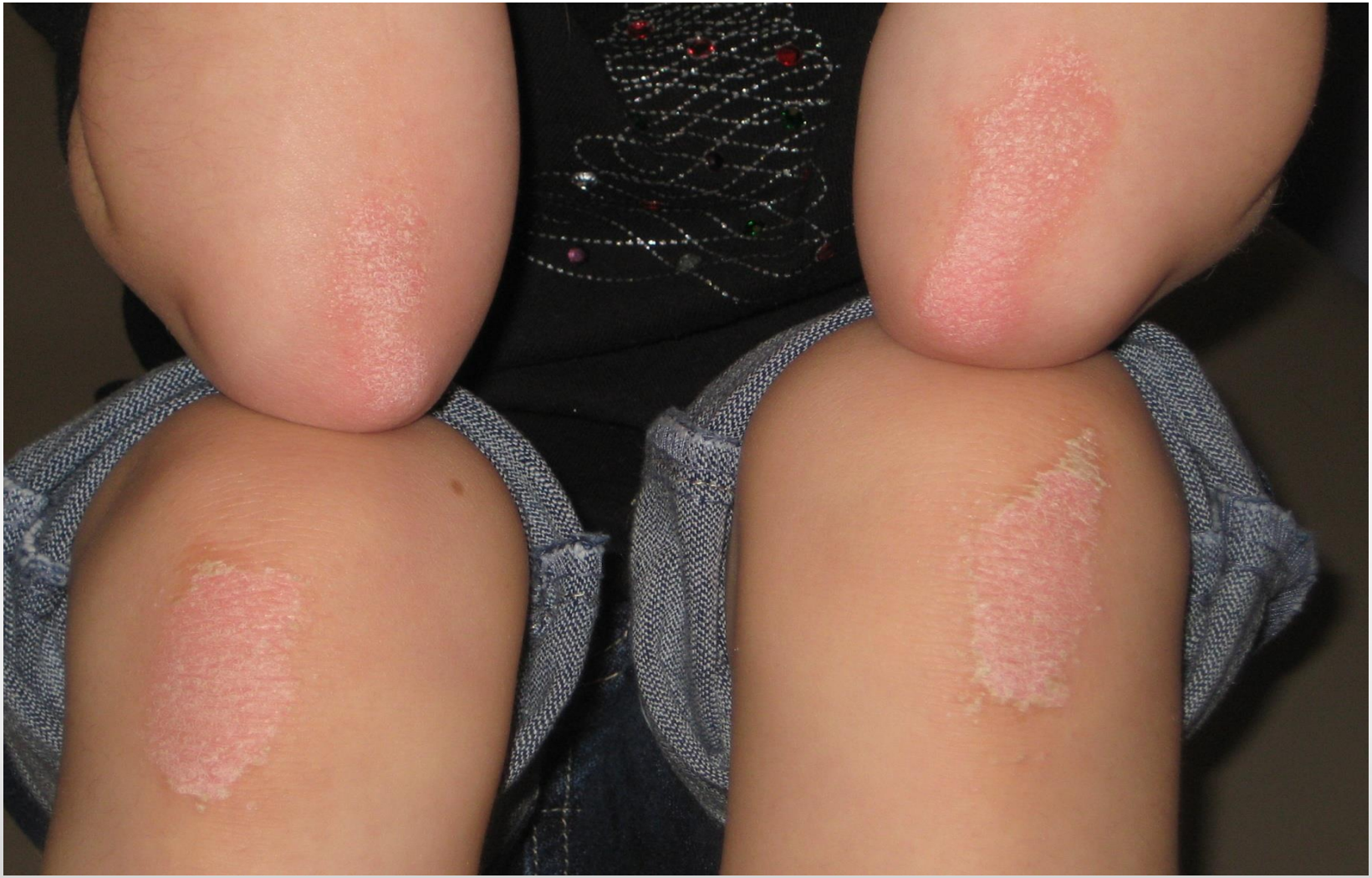
Psoriasis

Psoriasis

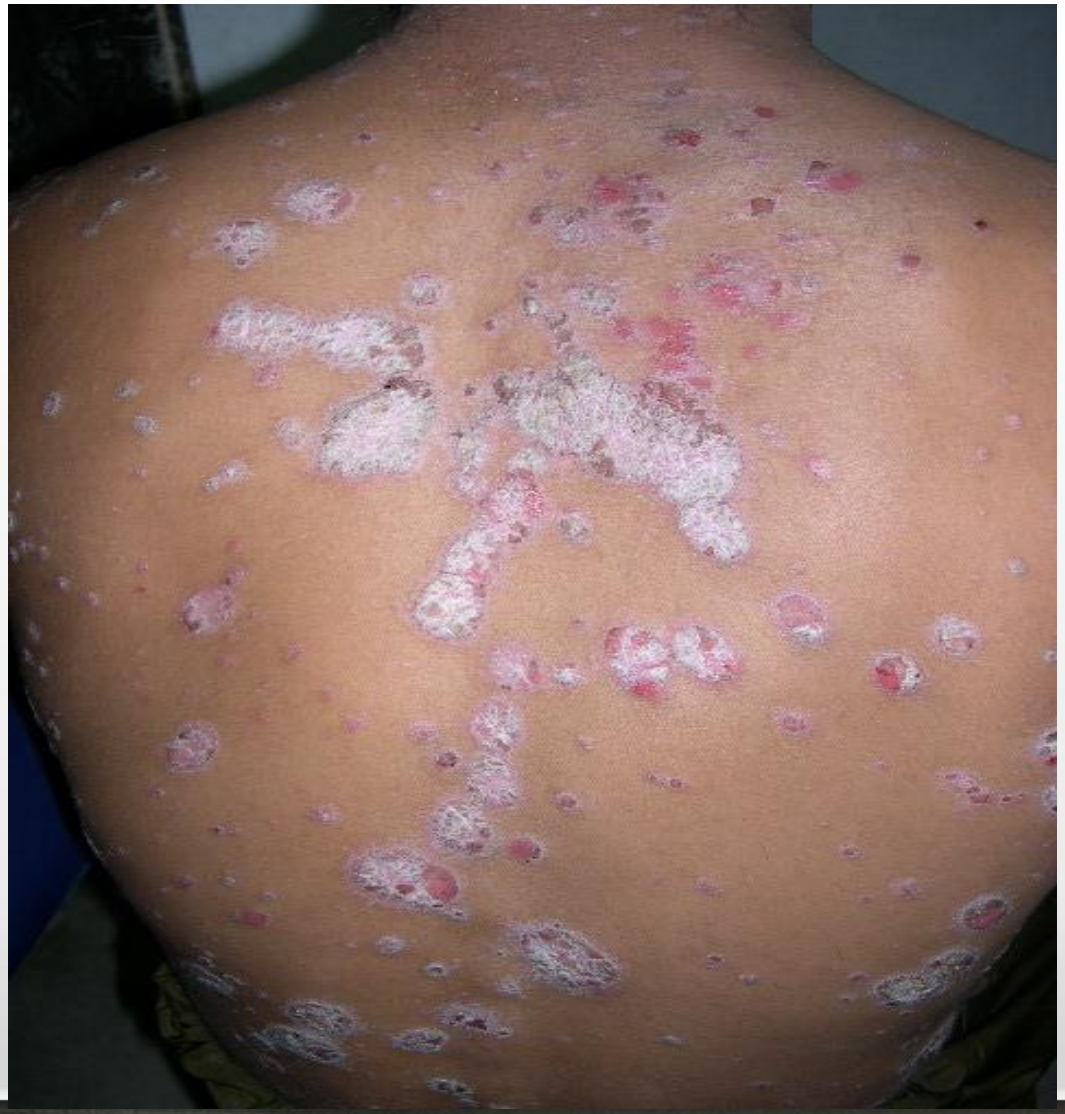
Definition:

- Psoriasis is a common, chronic ,non-infectious , inflammatory skin disease.
- which affects the skin and joints(is connected with the metabolic syndrome) .
- causes rapid skin cell reproduction resulting in red, dry patches of thickened skin

Psoriasis



Psoriasis



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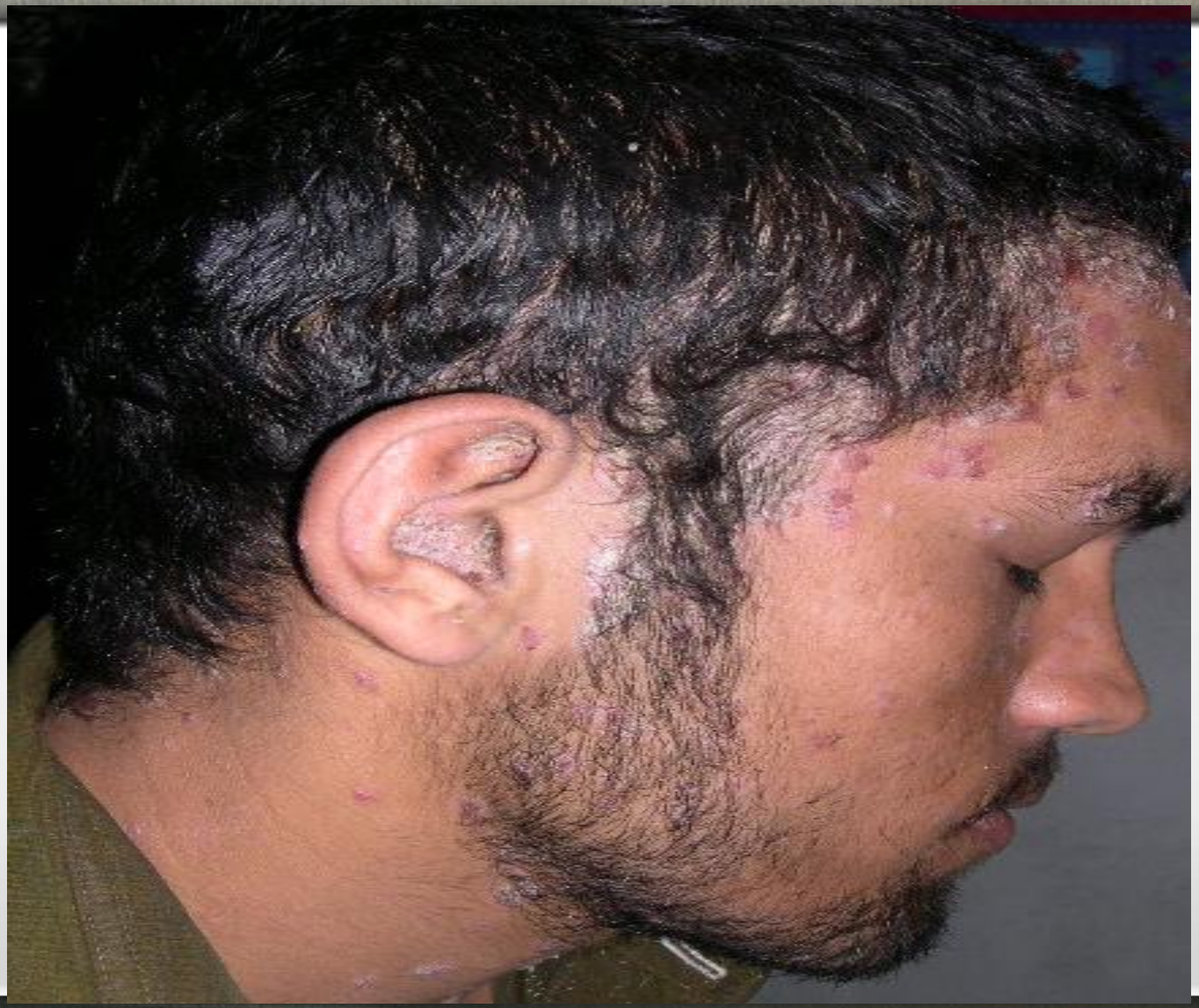
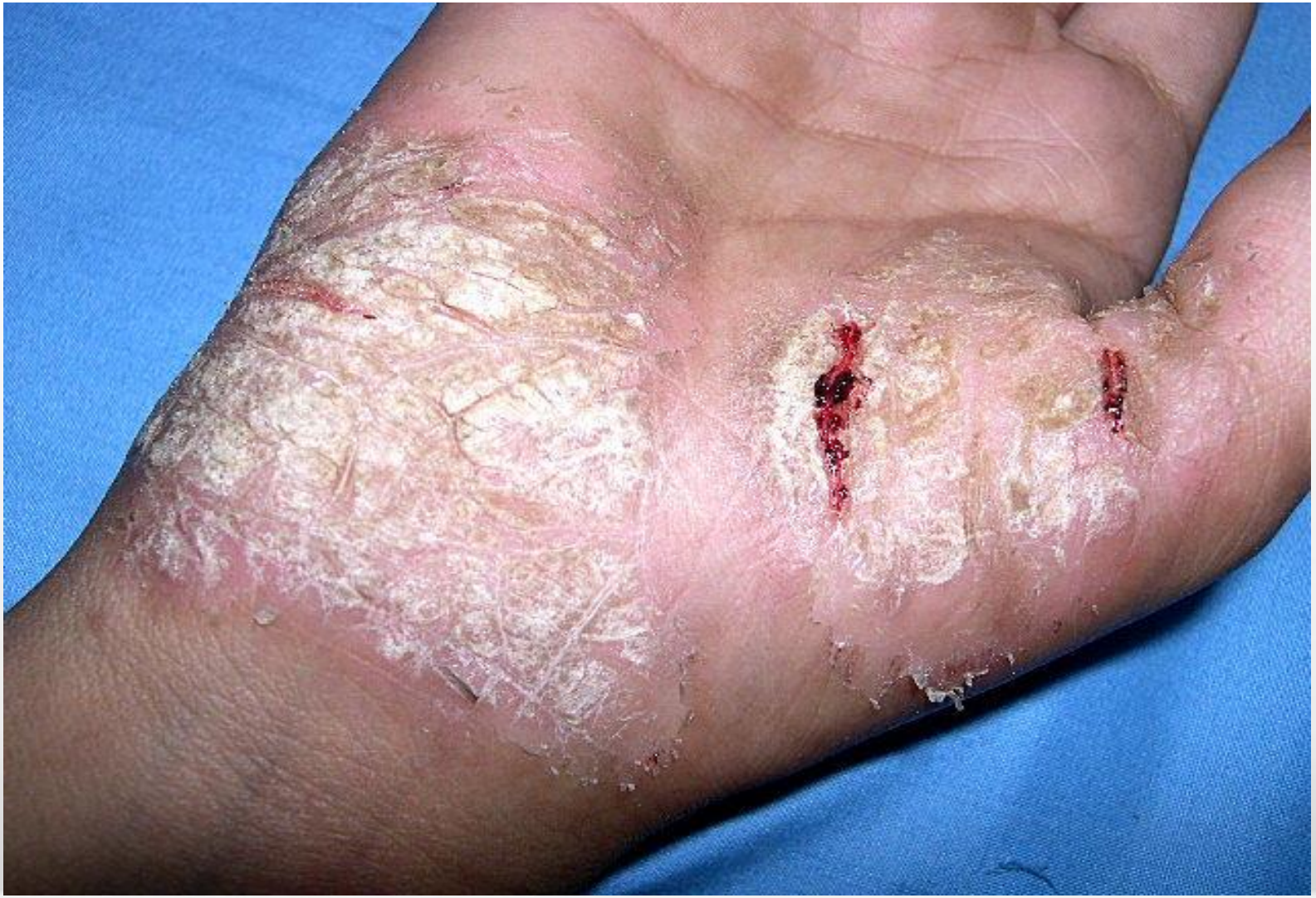
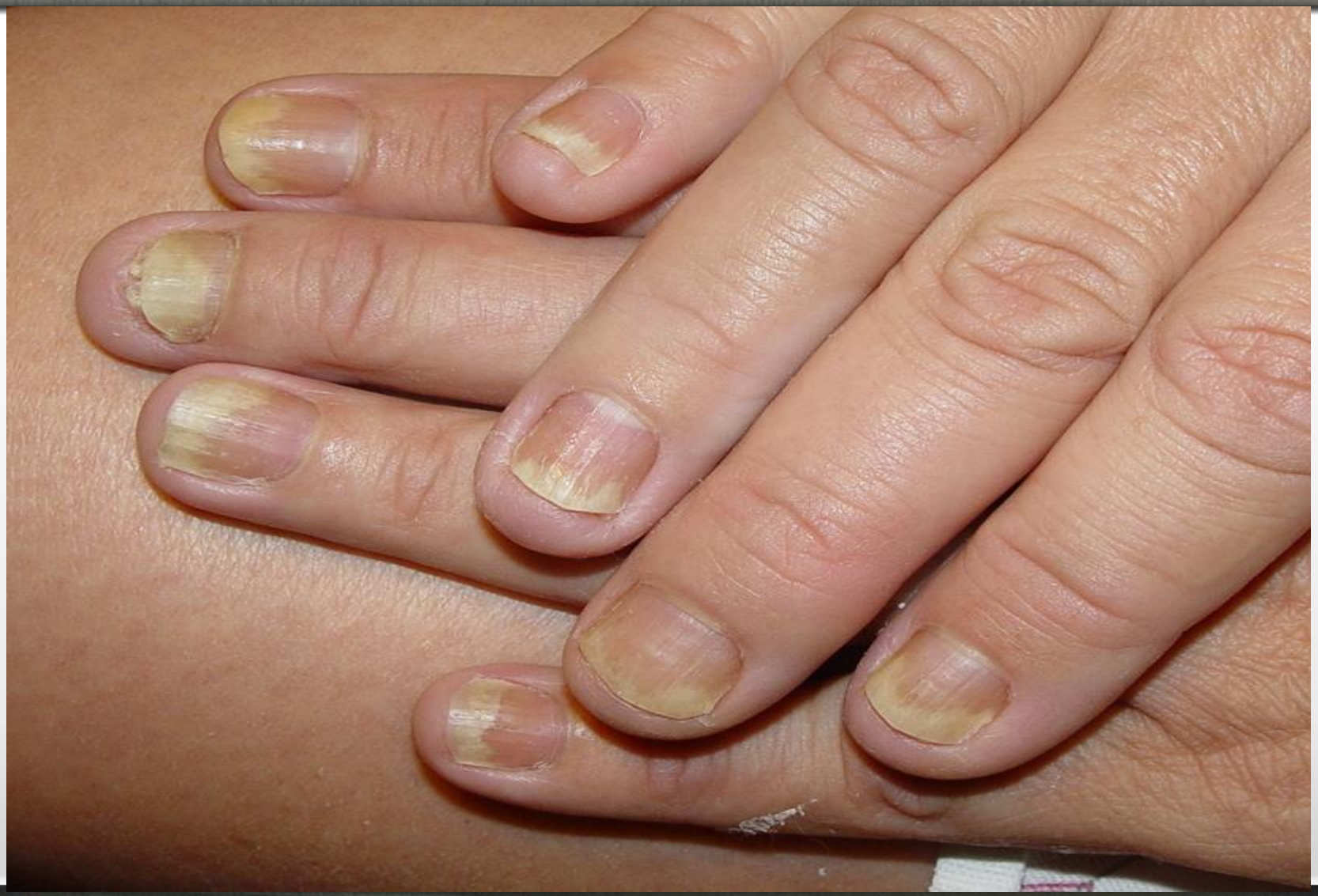


Psoriasis



Psoriasis



Psoriasis

Incidence and aetiology:-

- 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

Psoriasis

Pathogenesis:-

- Exact cause is unknown

-Multi-factorial causes:-

Psoriasis

Pathogenesis

1-Genetic factor:-

-There are two types:-

-type I psoriasis was more likely to be familial, have a severe clinical course and is associated with HLA-Cw6, −B13 and −B57

b-Late onset, or type II psoriasis, generally occurs in those between the ages 50 to 60 and is correlated with HLA-Cw2 and −B27

Psoriasis

Pathogenesis

-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 10 loci have been identified (psors-1 to 10)

Psoriasis

Pathogenesis

2-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 to 60 days in normal skin

Psoriasis

Pathogenesis

3-Inflammtory factors:-

-Increase level of TNF

-TNF receptors are upregulated

-Increase level of interferon gamma

-Increase level of interleukin 2 , 12 ,23 and 17

Psoriasis

Pathogenesis

4-Immunological factors:-

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

- T cells

- Auspits sign

Psoriasis

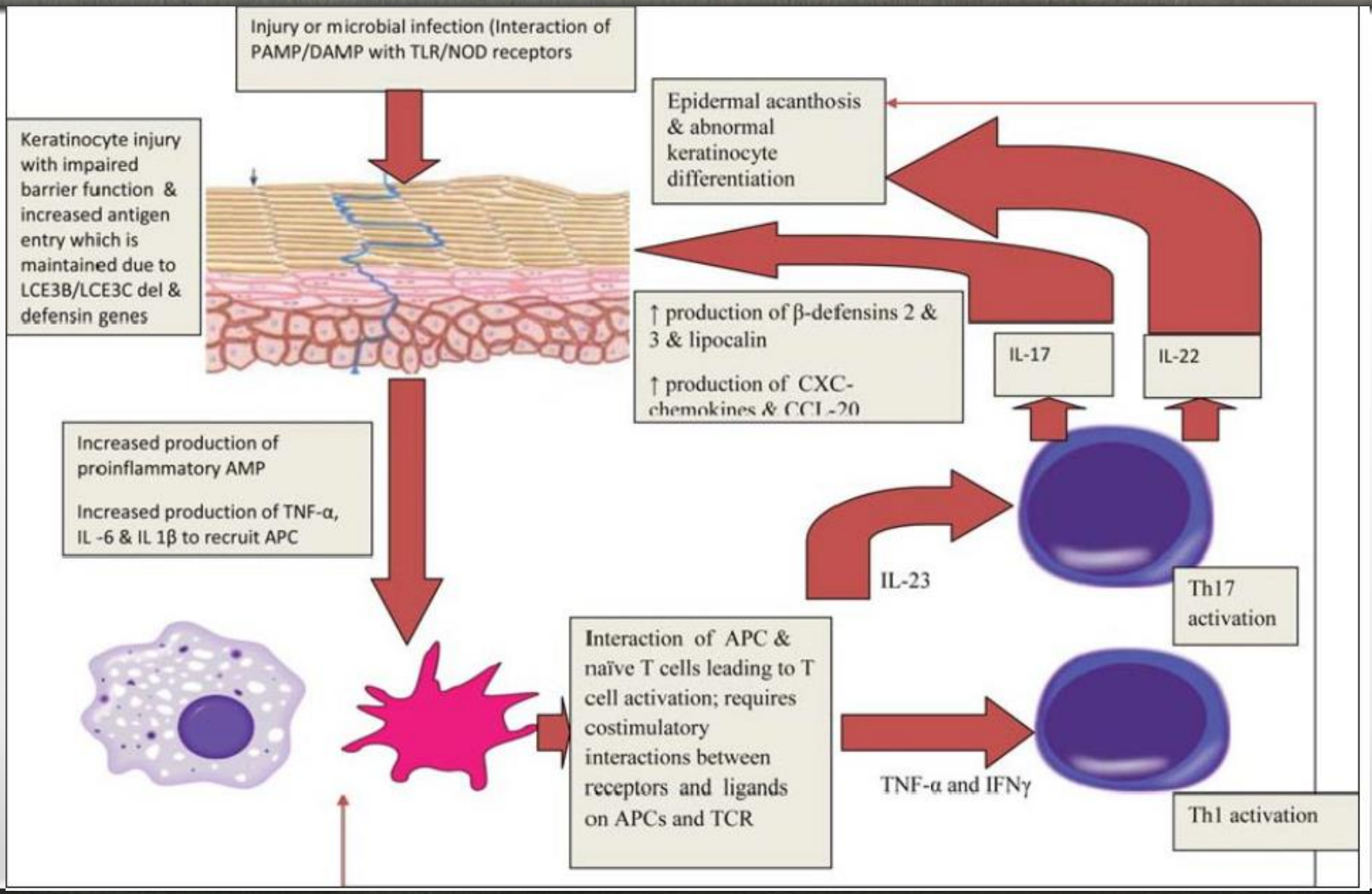
Pathogenesis

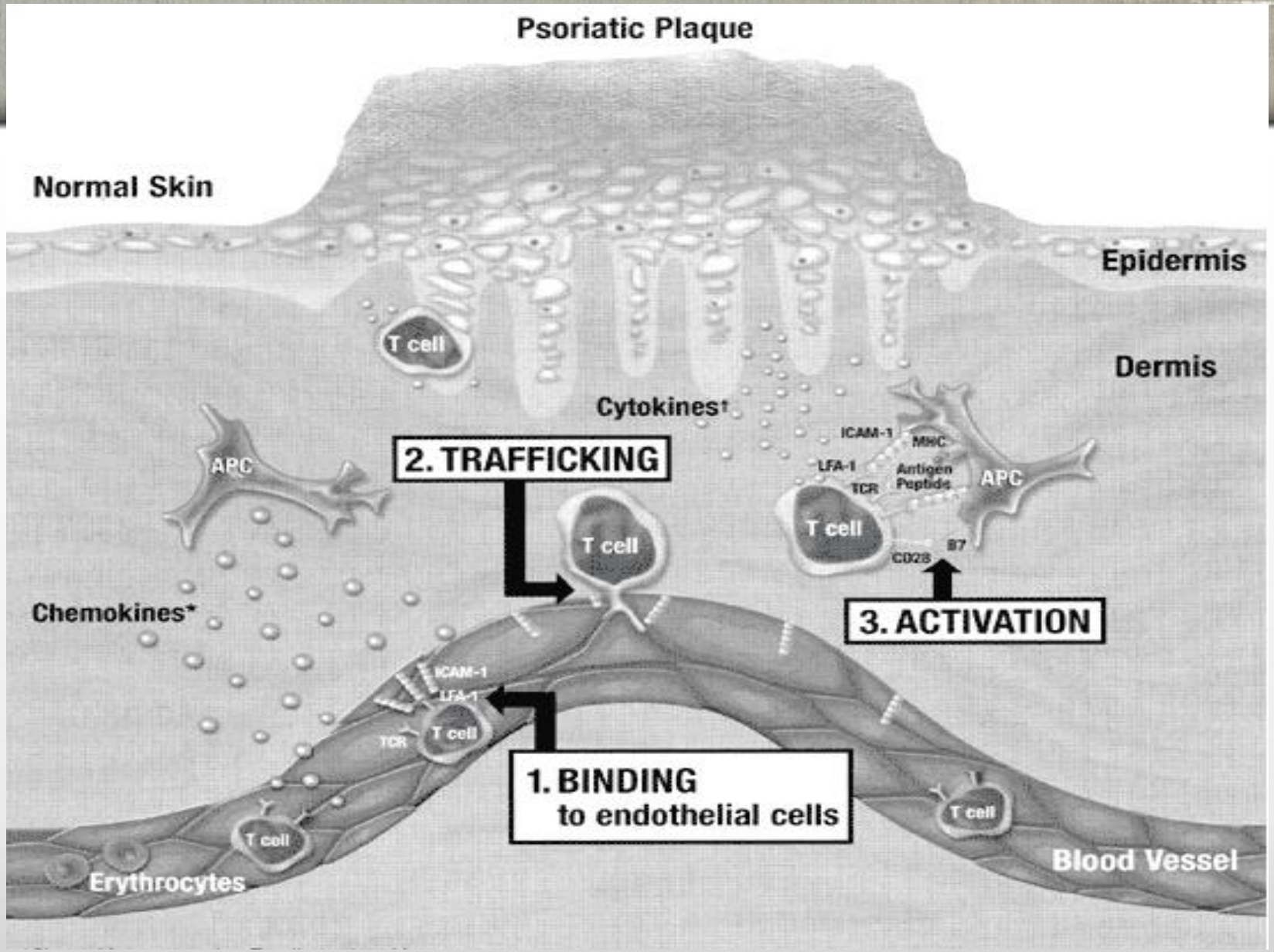
5-Environmental factors:-

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

Psoriasis

Pathogenesis




Psoriatic Plaque
Normal Skin
Epidermis
Dermis
T cell
Cytokines†
APC
2. TRAFFICKING
ICAM-1
MHC
LFA-1
Antigen Peptide
TCR
APC
T cell
CD28
B7
3. ACTIVATION
Chemokines*
T cell
ICAM-1
LFA-1
TCR
T cell
1. BINDING
to endothelial cells
T cell
T cell
Erythrocytes
Blood Vessel

Psoriasis

Histology:

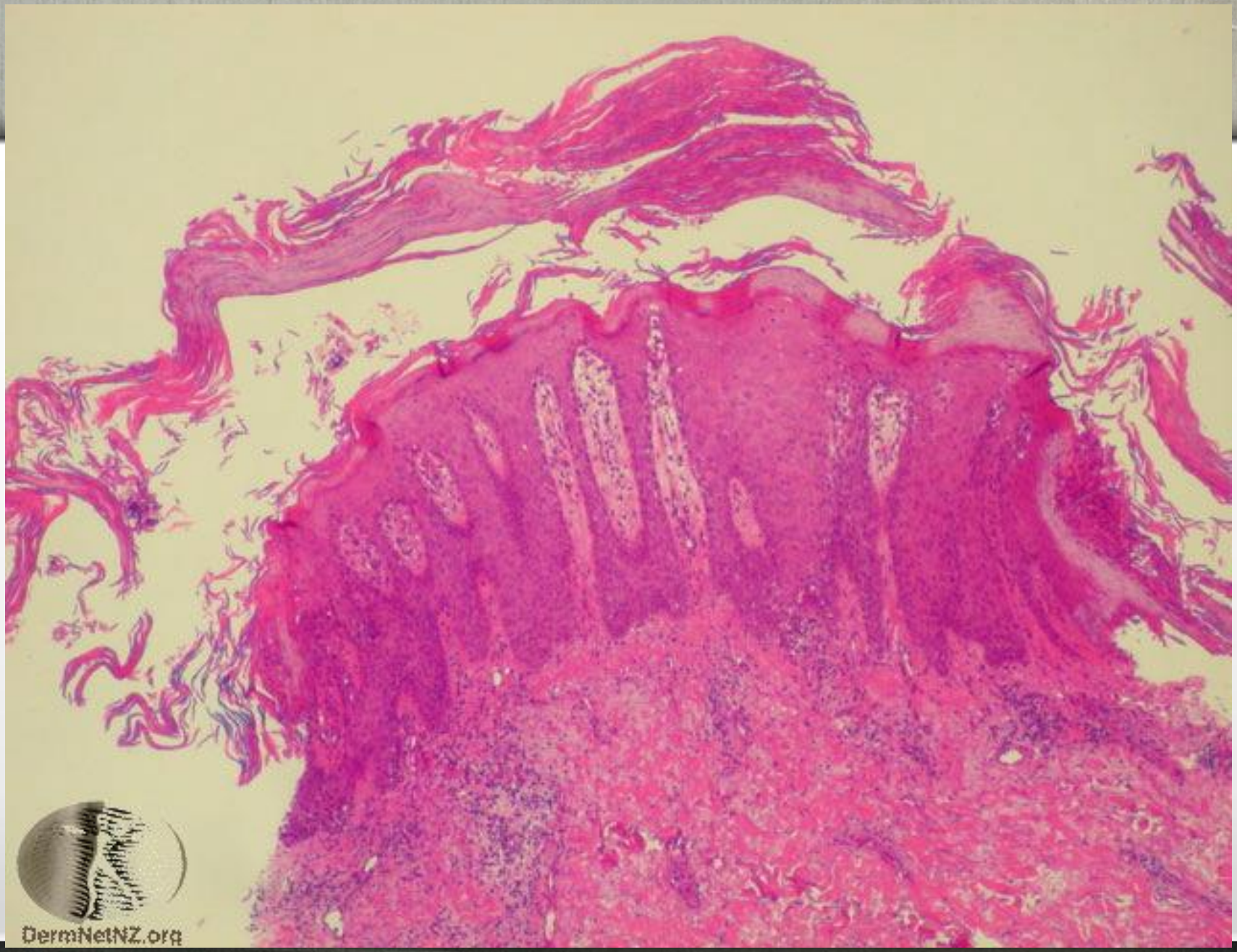
-parakeratosis(nuclei retained in the horny layer)

-irregular thickening of the epidermis over 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



Psoriasis

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

Types

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

Psoriasis

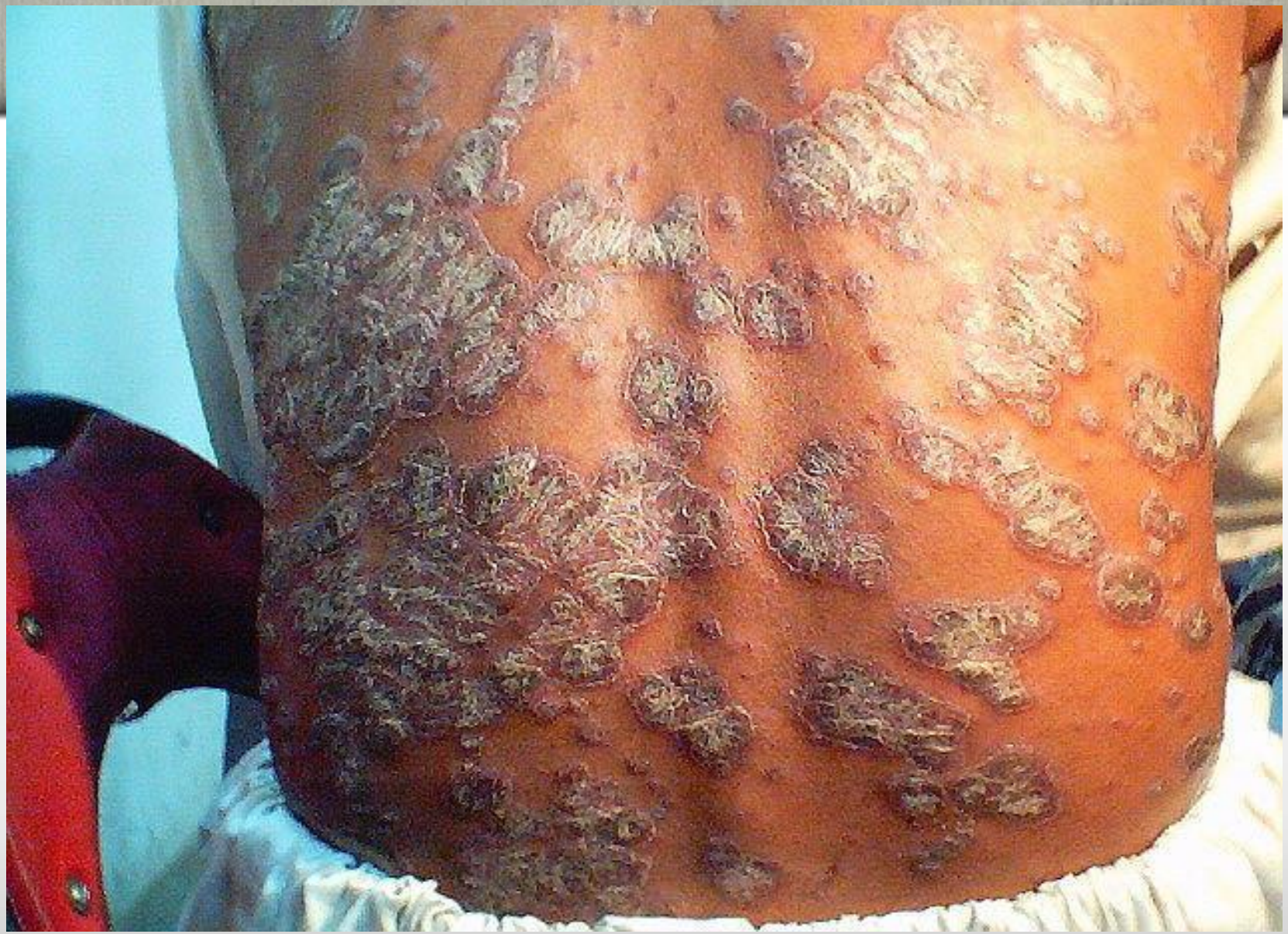
Types

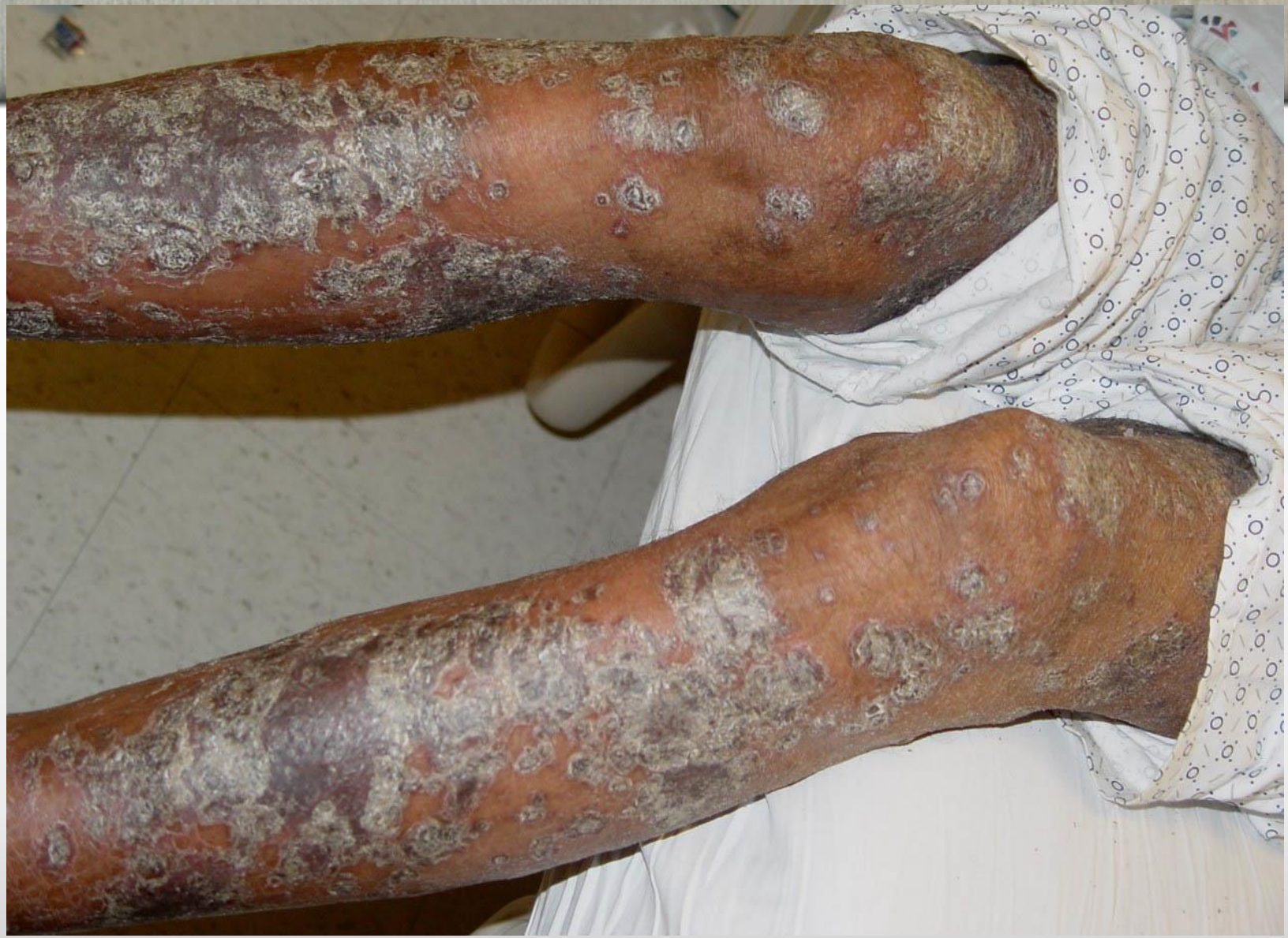
1-plaque psoriasis(psoriasis vulgaris) :-

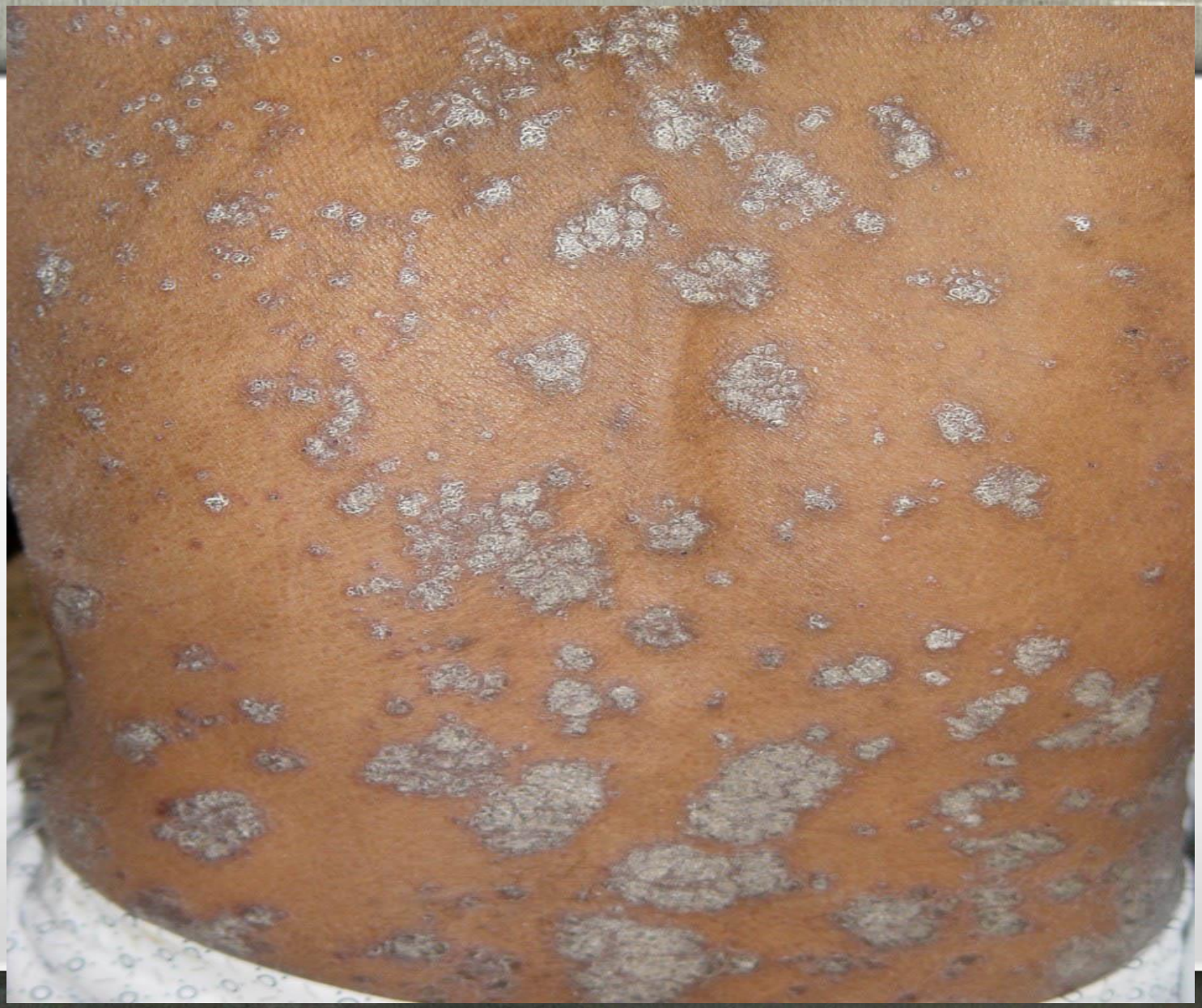
- the most common

- characterized by round-to-oval red plaques and 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





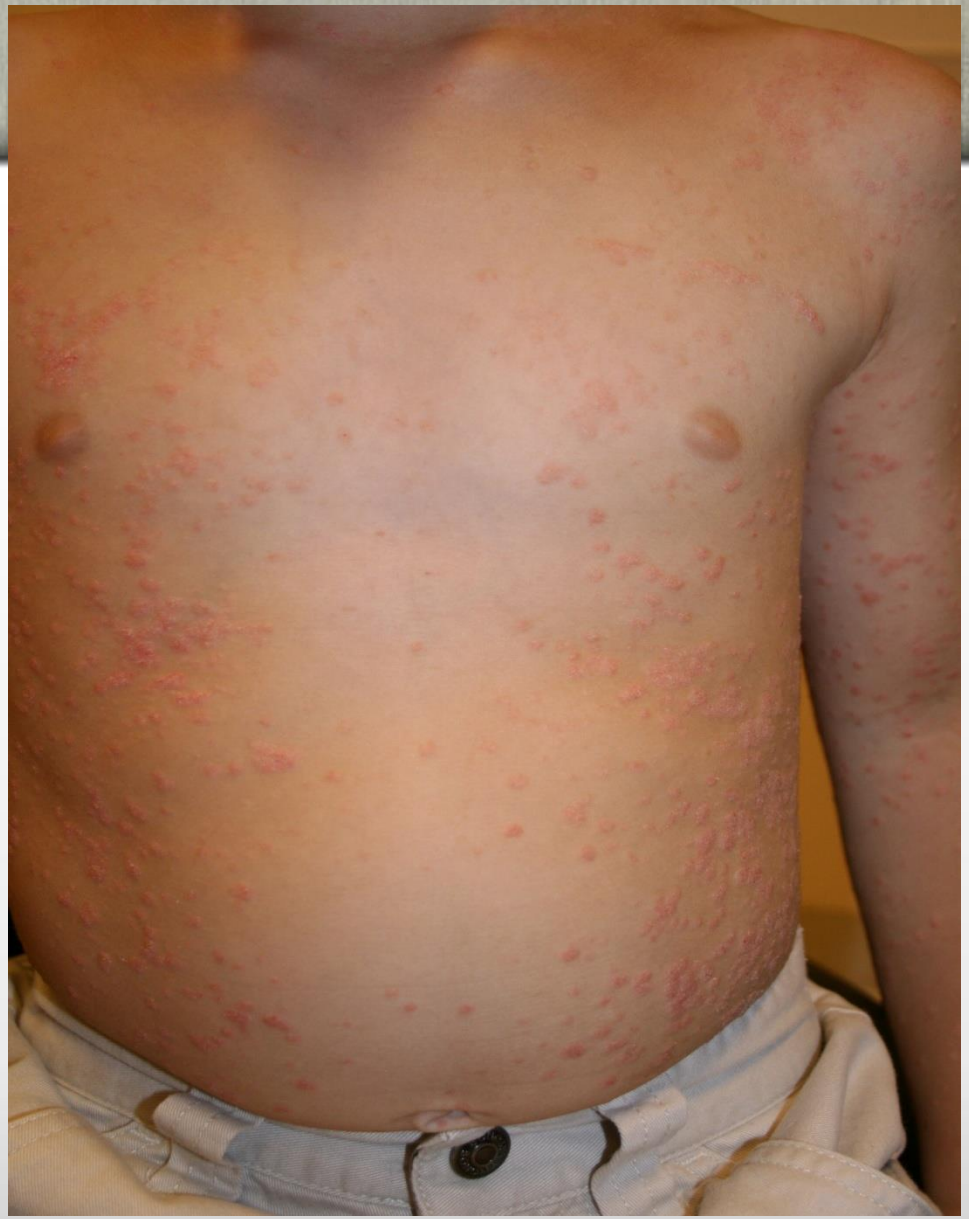


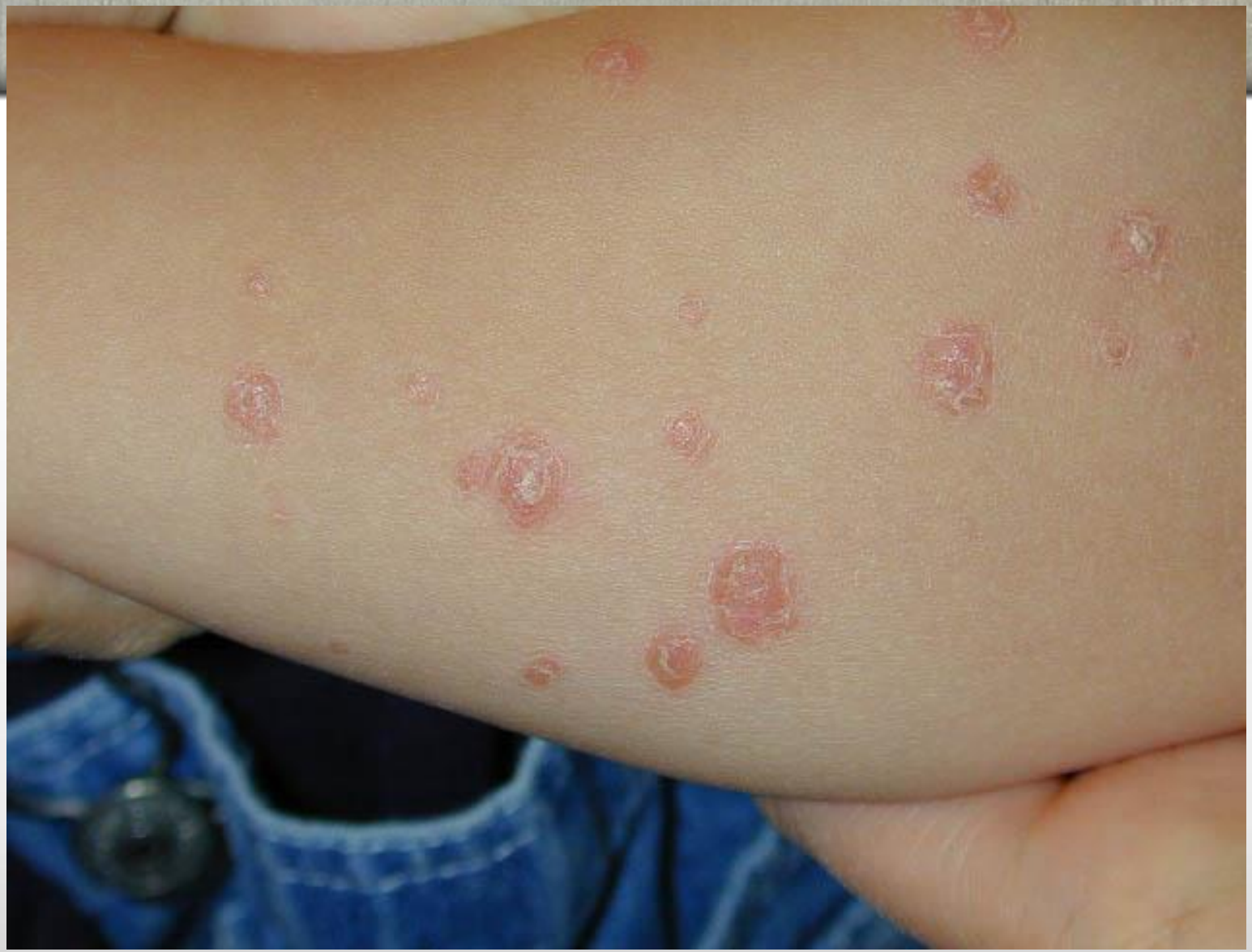
Psoriasis

Types

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



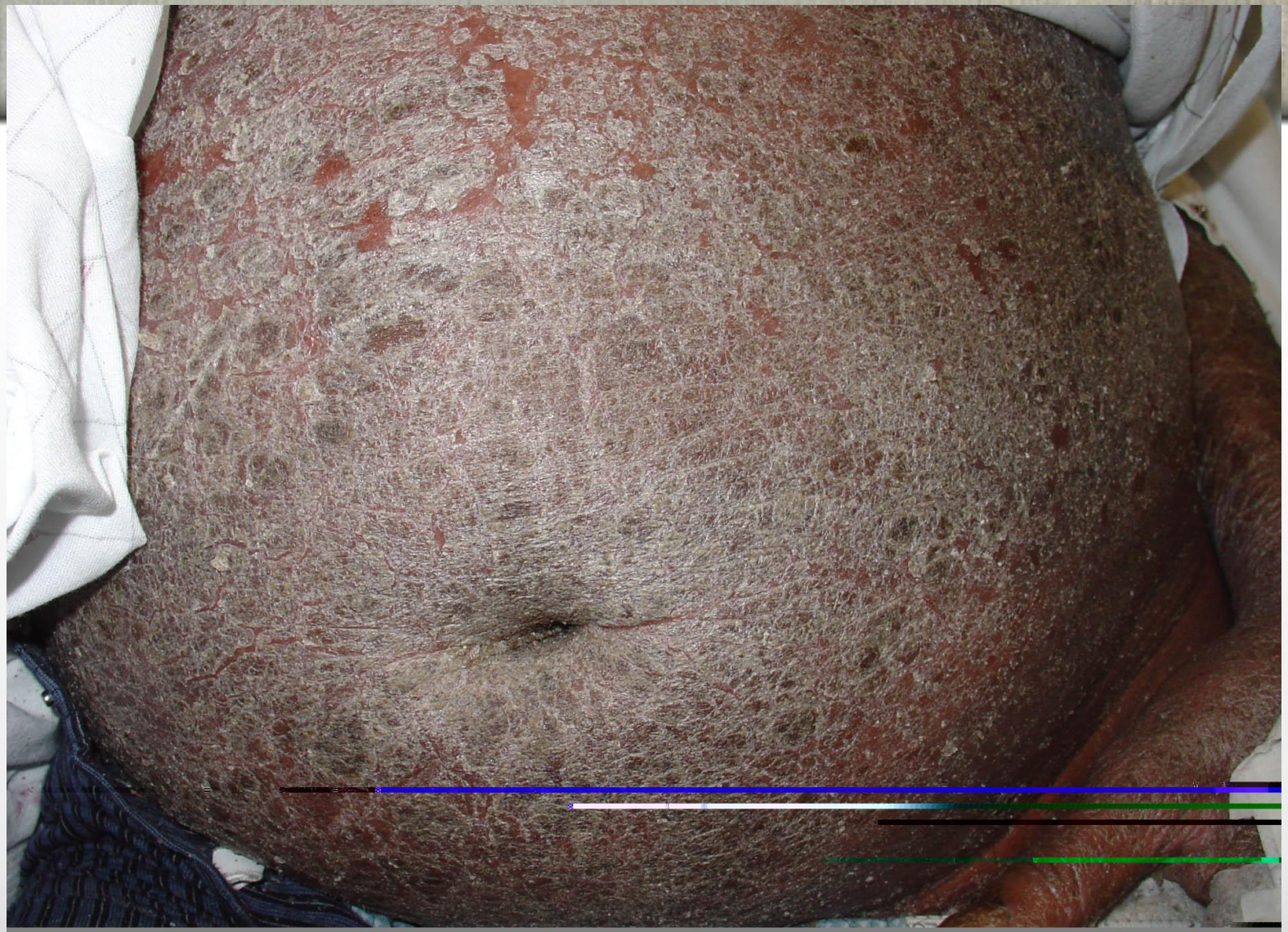


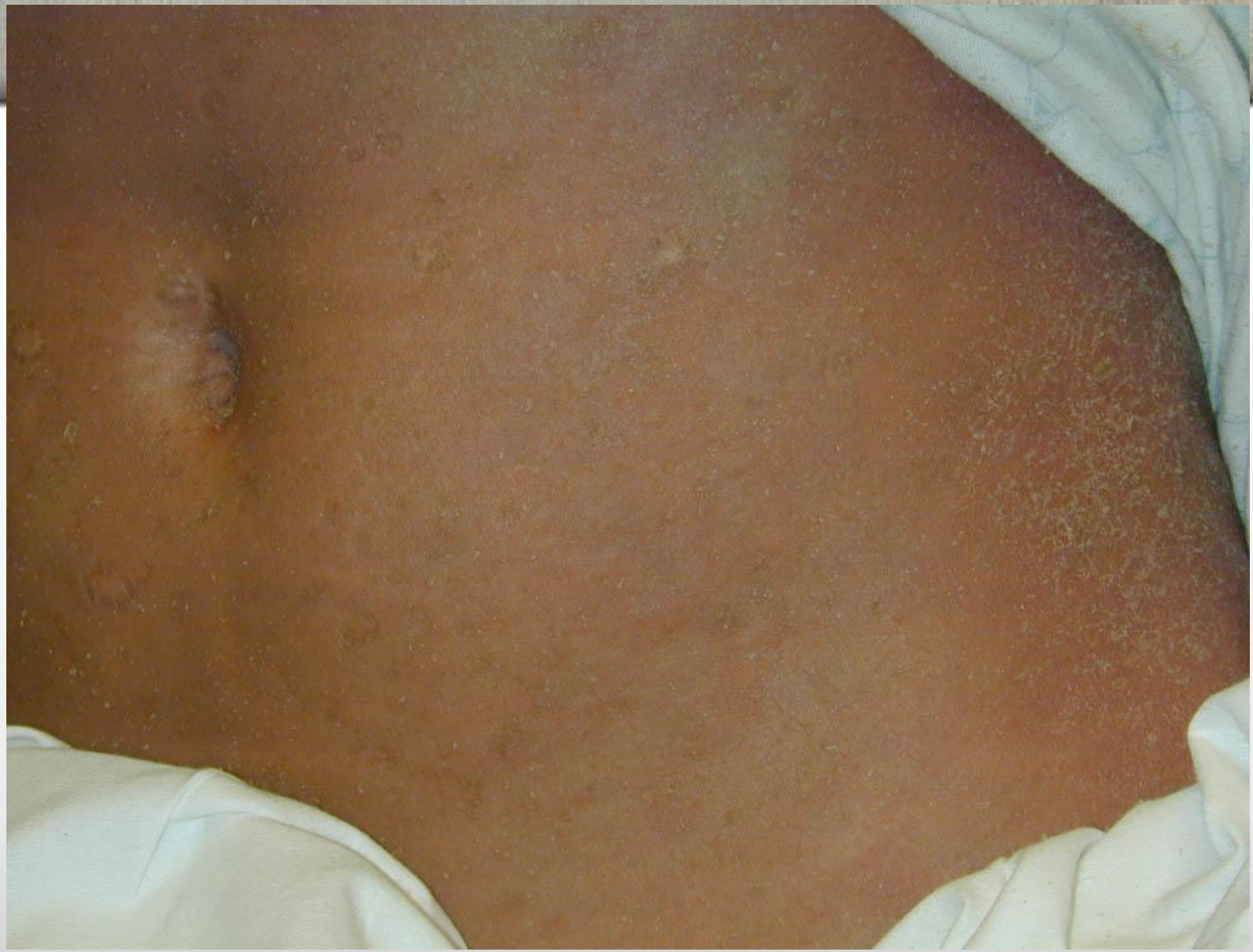
Psoriasis

Types

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





Psoriasis

Types

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

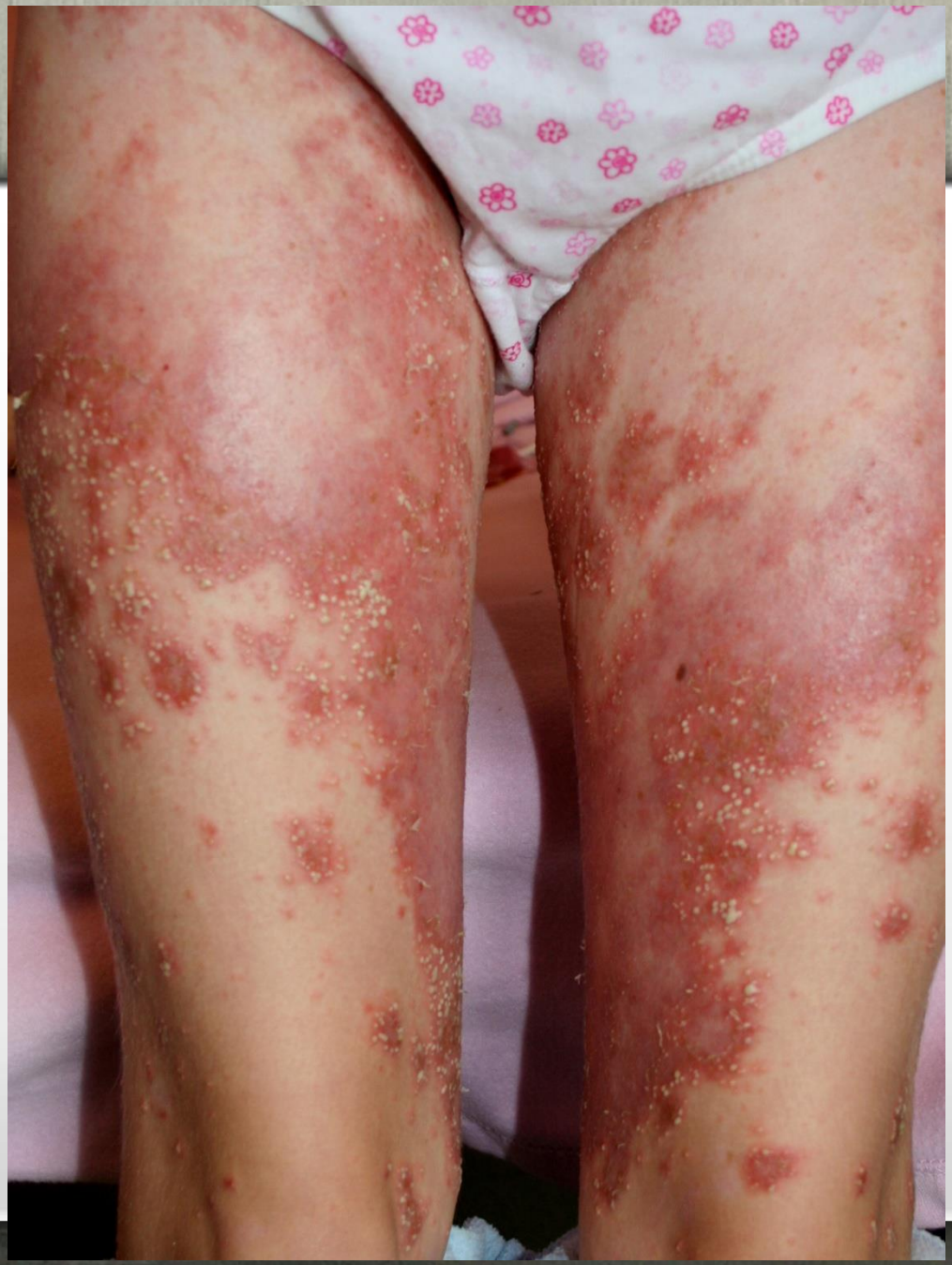
2-Localized form (palms and soles)

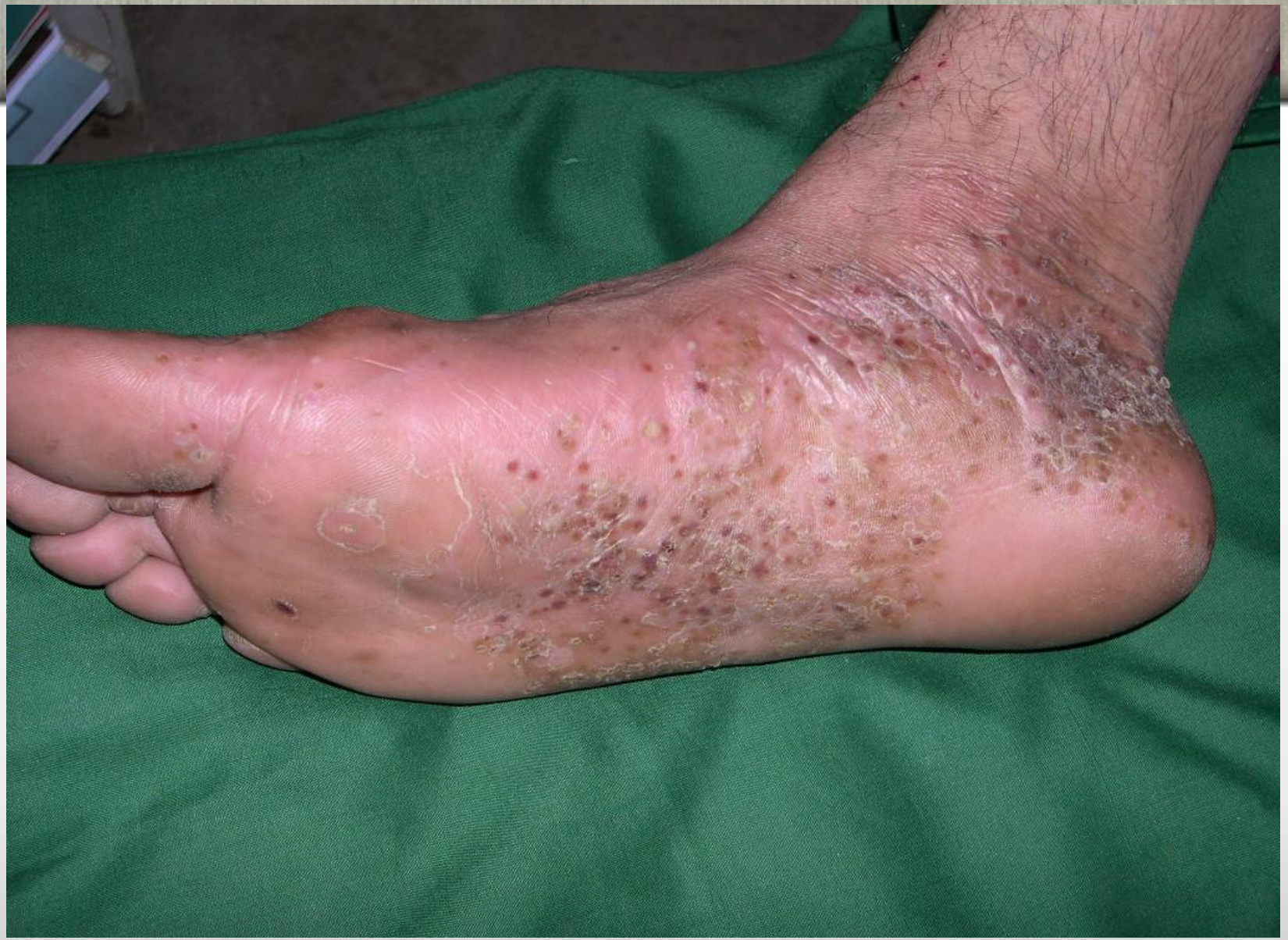
Psoriasis

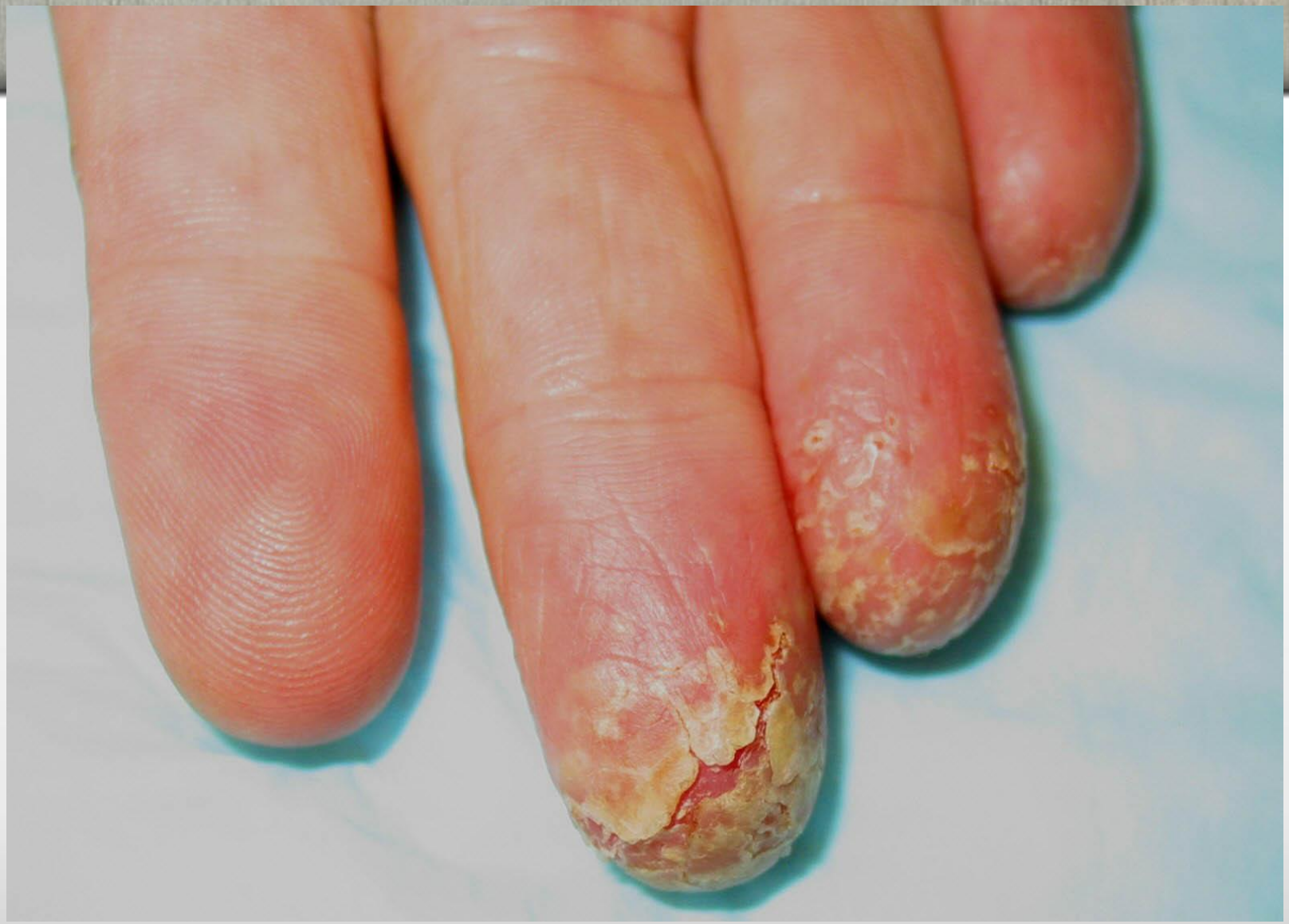
Types

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





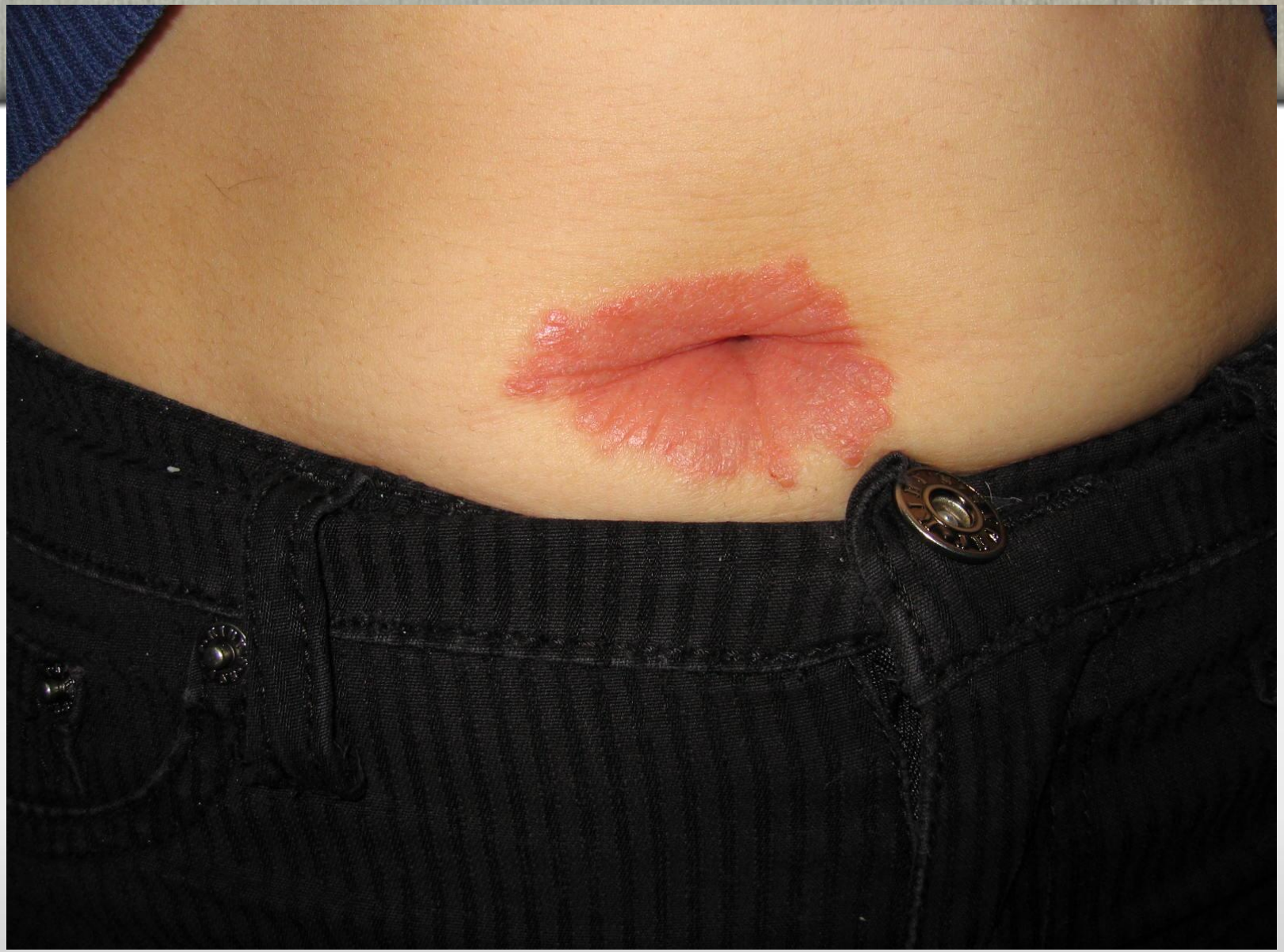


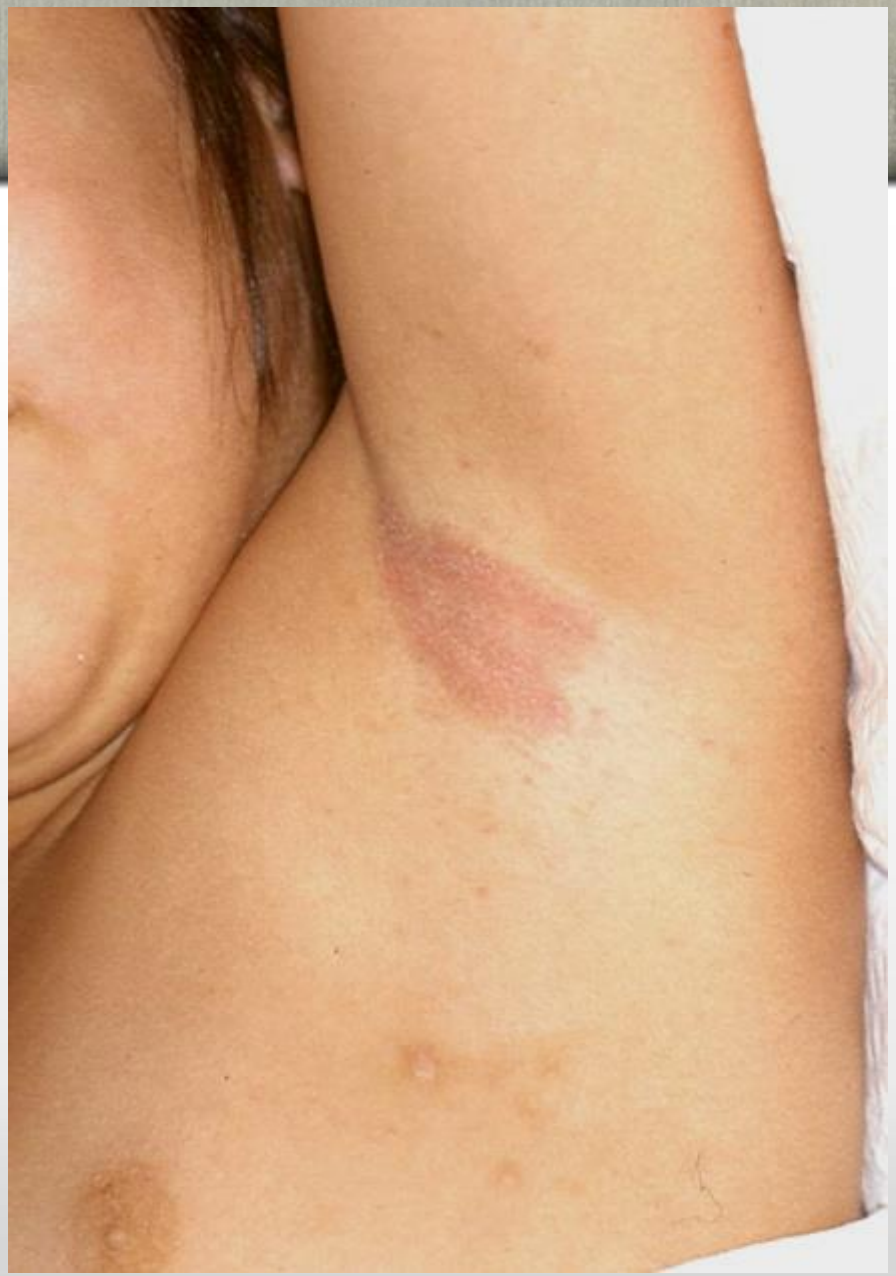
Psoriasis

Types

5-Psoriasis inversus(sebopsoriasis):-

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





Psoriasis

Types

6-Psoriatic Arthritis:-

- 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

Psoriasis

Types

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
- Oil drop or salmon patch/nail bed Pitting
- Subungual hyperkeratosis
- Onycholysis
- Beau lines

Psoriasis

Types

Differential diagnosis:-

1. Bowes Disease
2. Cutaneous T-Cell Lymphoma
3. Drug Eruptions
4. Erythema Annulare Centrifugum
5. Extramammary Paget Disease
6. Lichen Planus
7. Lichen Simplex Chronicus
8. Lupus Erythematosus, Discoid
9. Lupus Erythematosus, Subacute Cutaneous
10. Nummular Dermatitis
11. Parapsoriasis
12. Pityriasis Rosea
13. Pityriasis Rubra Pilaris
14. Seborrheic Dermatitis
15. Syphilis

Psoriasis

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

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)

secukinumab

1-Janus kinase inhibitor

-cytokines function by binding to and activating type I and type II cytokine receptors

-These receptors in turn rely on the Janus kinase (JAK) family of enzymes for signal transduction

-drugs that inhibit the activity of these Janus kinases block cytokine signalling.

-**Tofacitinib AND** ruxolitinib

2-Phosphodiesterase 4 (PDE4) is a key enzyme in the regulation of immune responses of inflammatory diseases through degradation of the second messenger, cyclic adenosine 3',5'-monophosphate (cAMP). Apremilast, a selective PDE4 inhibitor

Lichen Planus

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.

Lichen Planus

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

Lichen Planus

Pathophysiology:-

- The cause of LP is unknown
- LP may be a cell-mediated immune response
- 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

Lichen Planus

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
- 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

Lichen Planus

Clinical features

- 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

Lichen Planus

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

Lichen Planus

Variations in LP

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;-

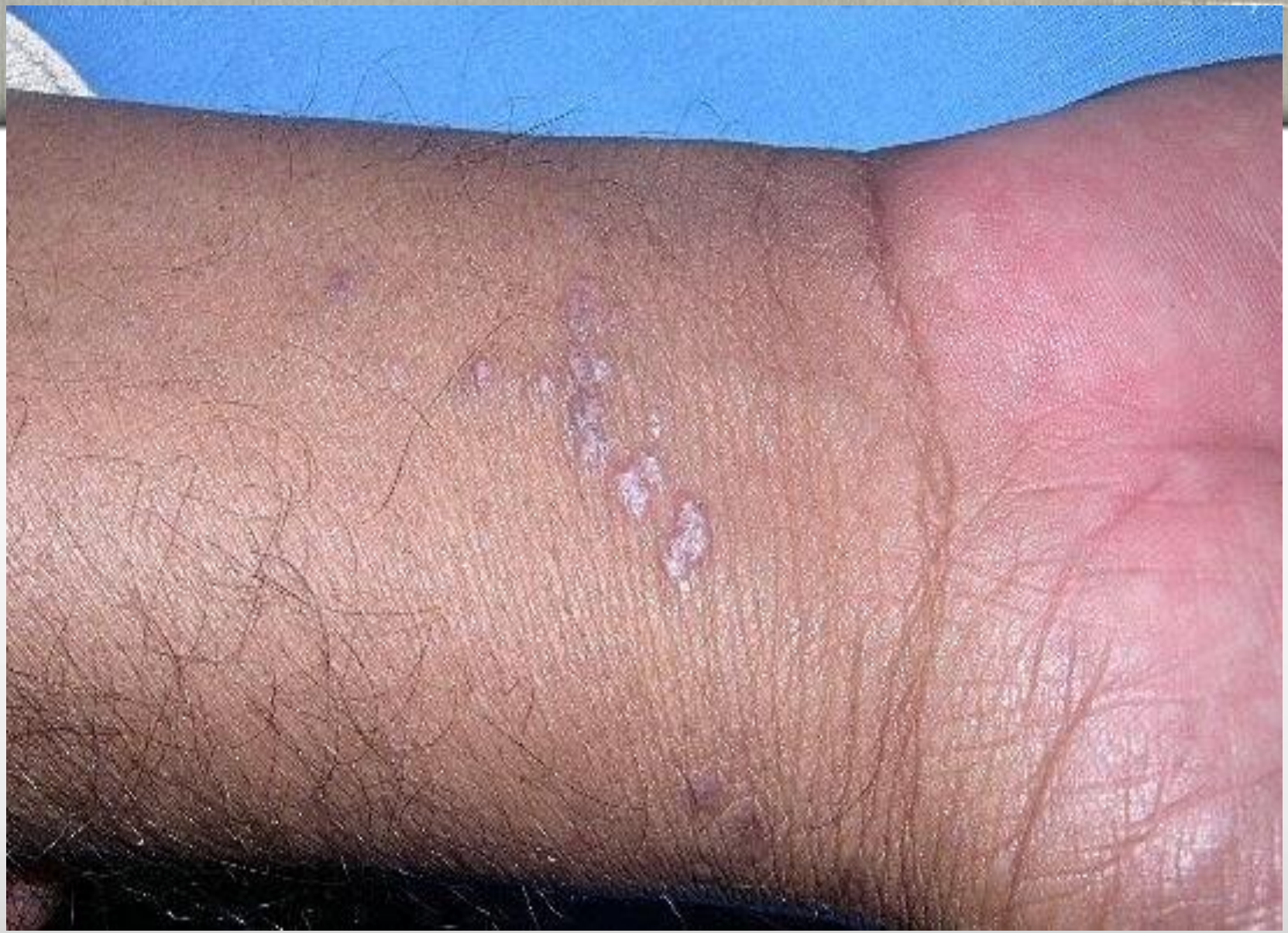
-common in persons with darker-pigmented skin

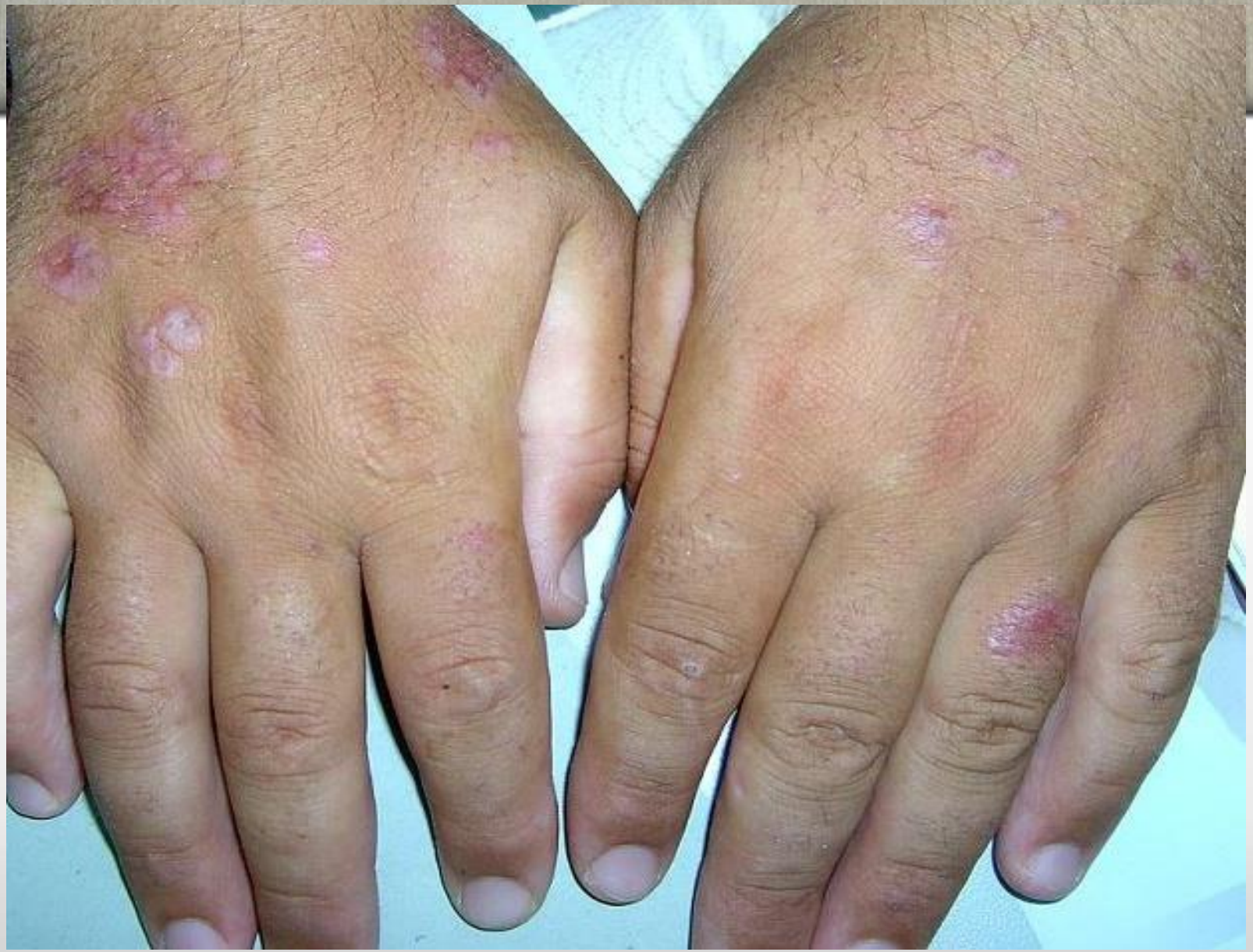
-usually appears on face and neck

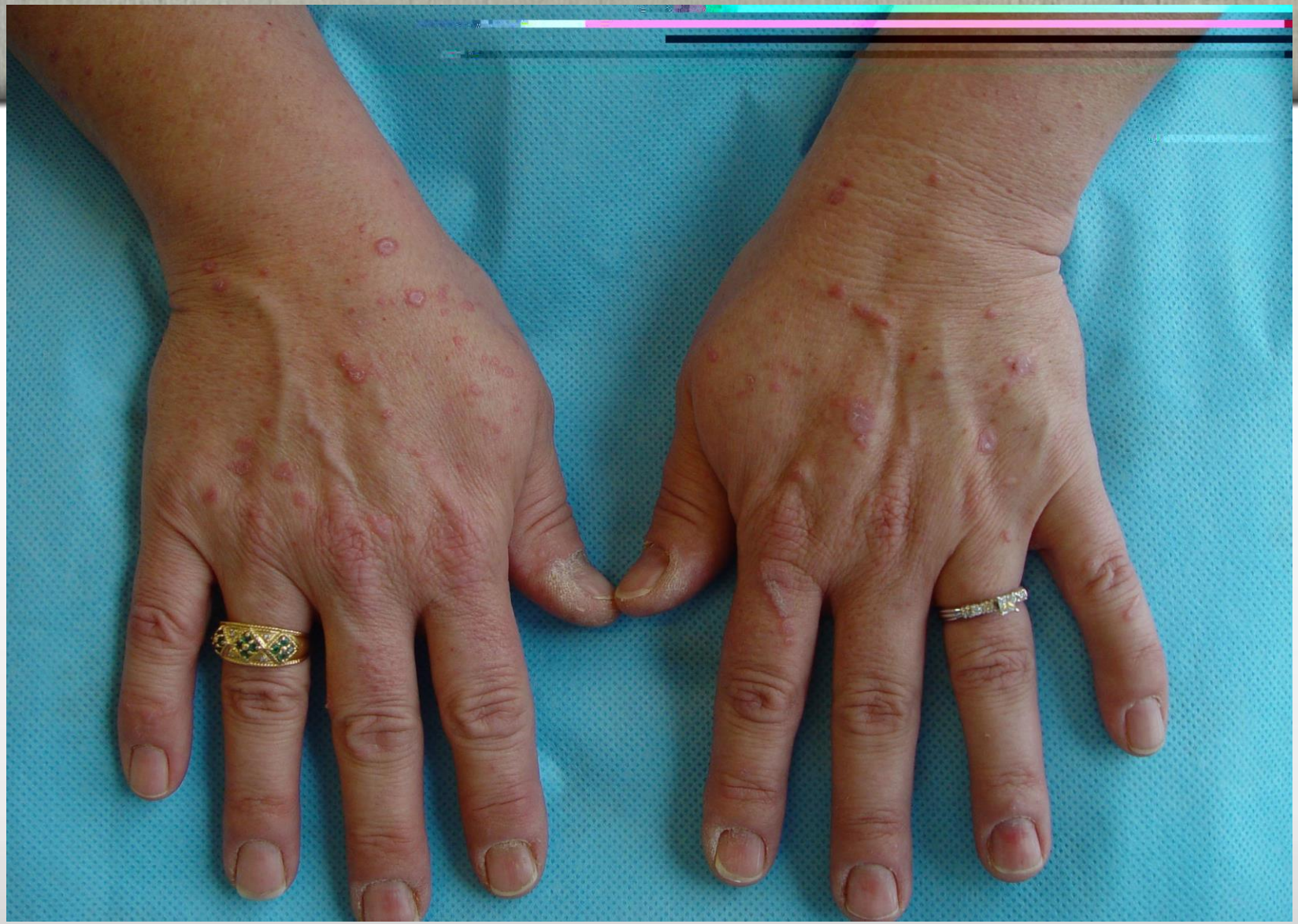
Lichen Planus

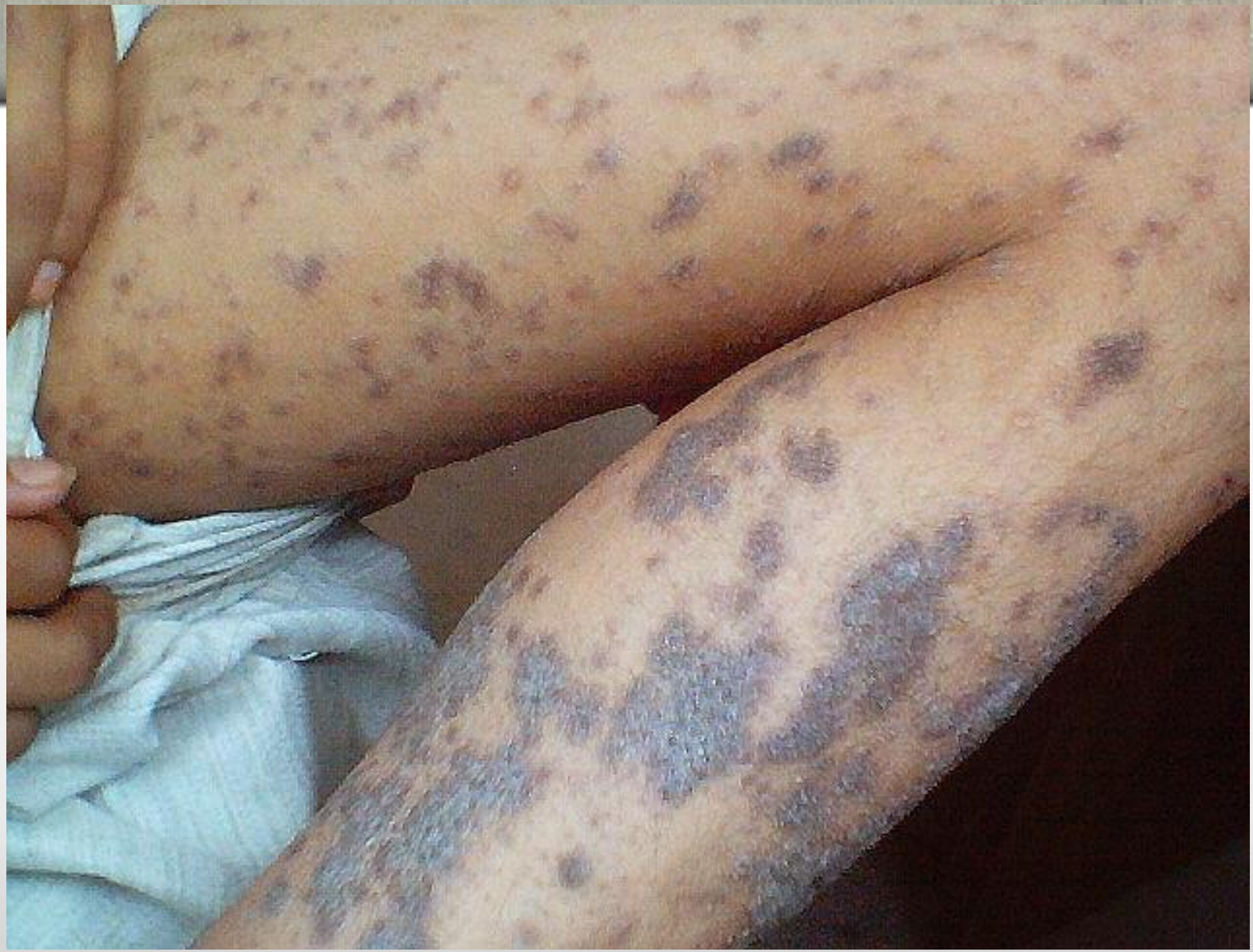
LP and nail:-

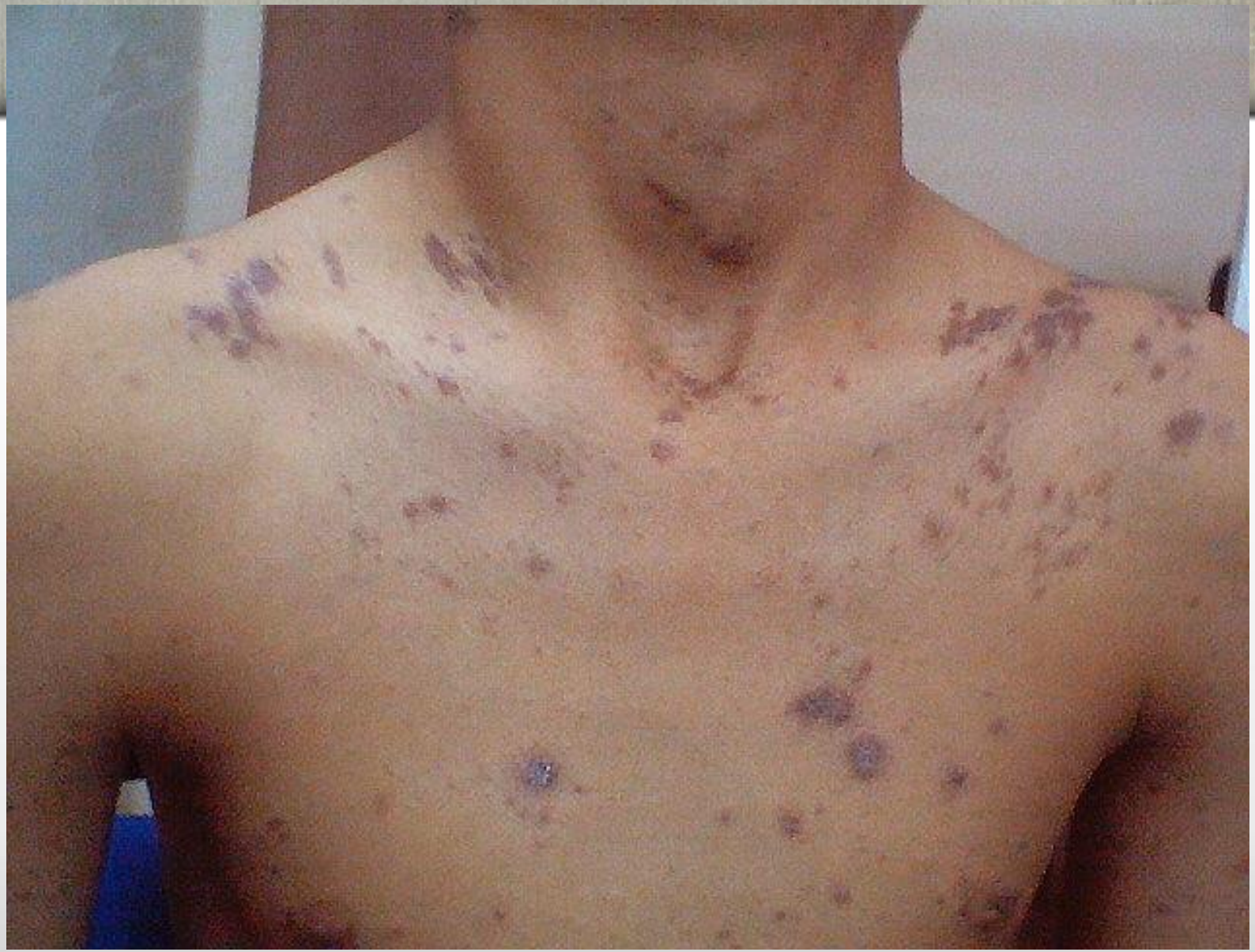
- In 10% of patients
- nail plate thinning causes longitudinal grooving and ridging
- subungual hyperkeratosis, onycholysis
- Rarely, the matrix can be permanently destroyed with prominent pterygium formation
- twenty-nail dystrophy

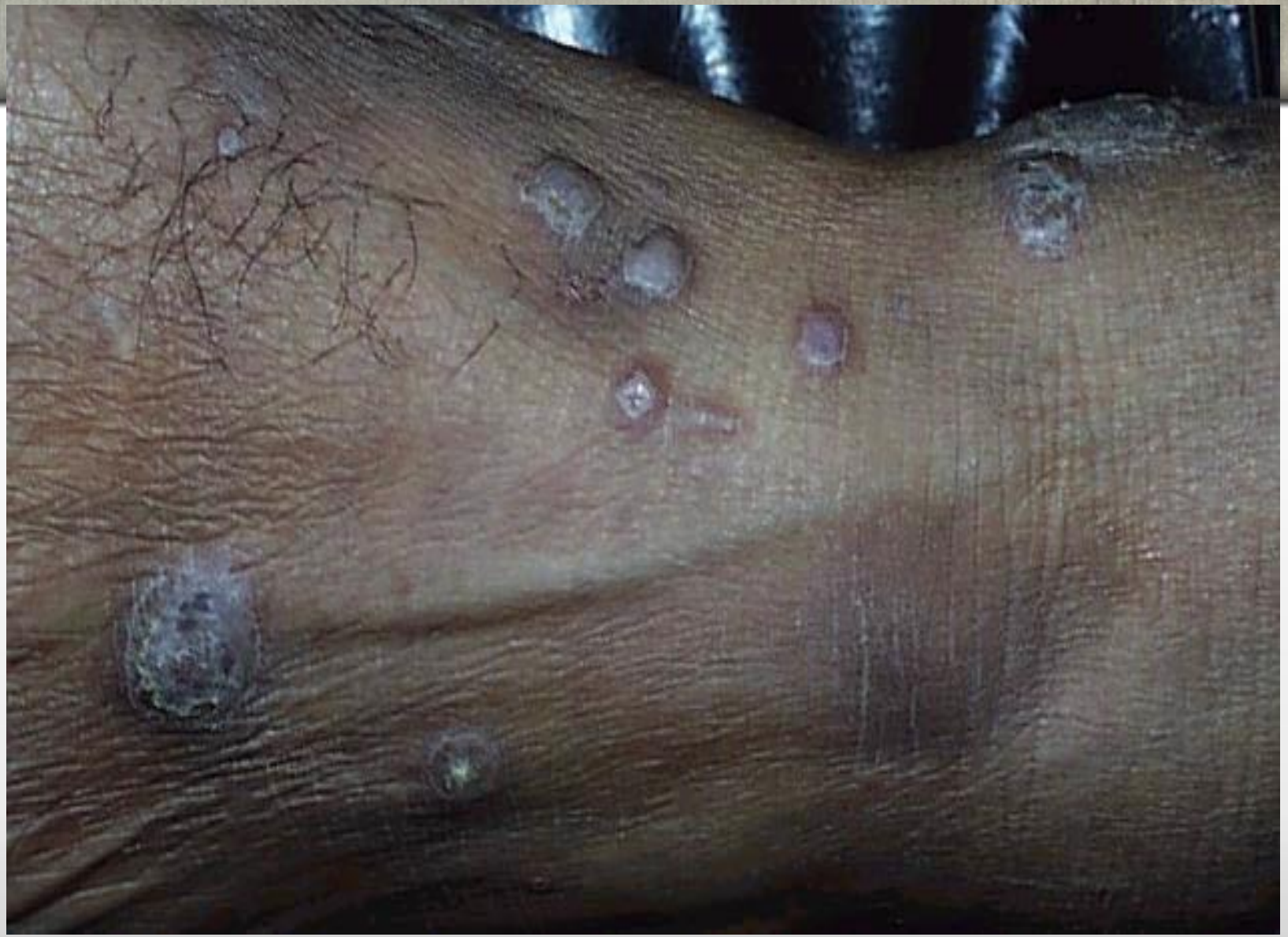


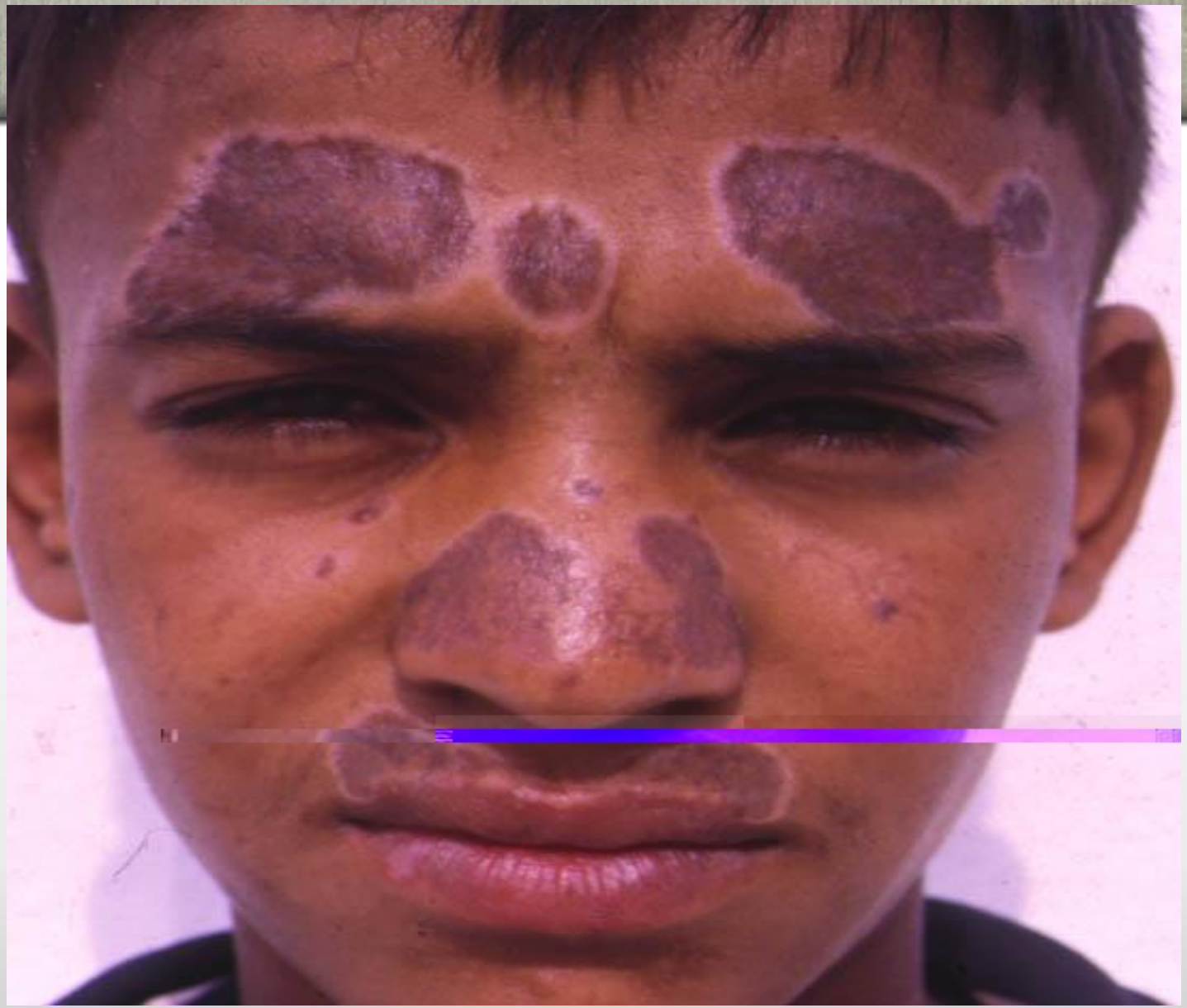


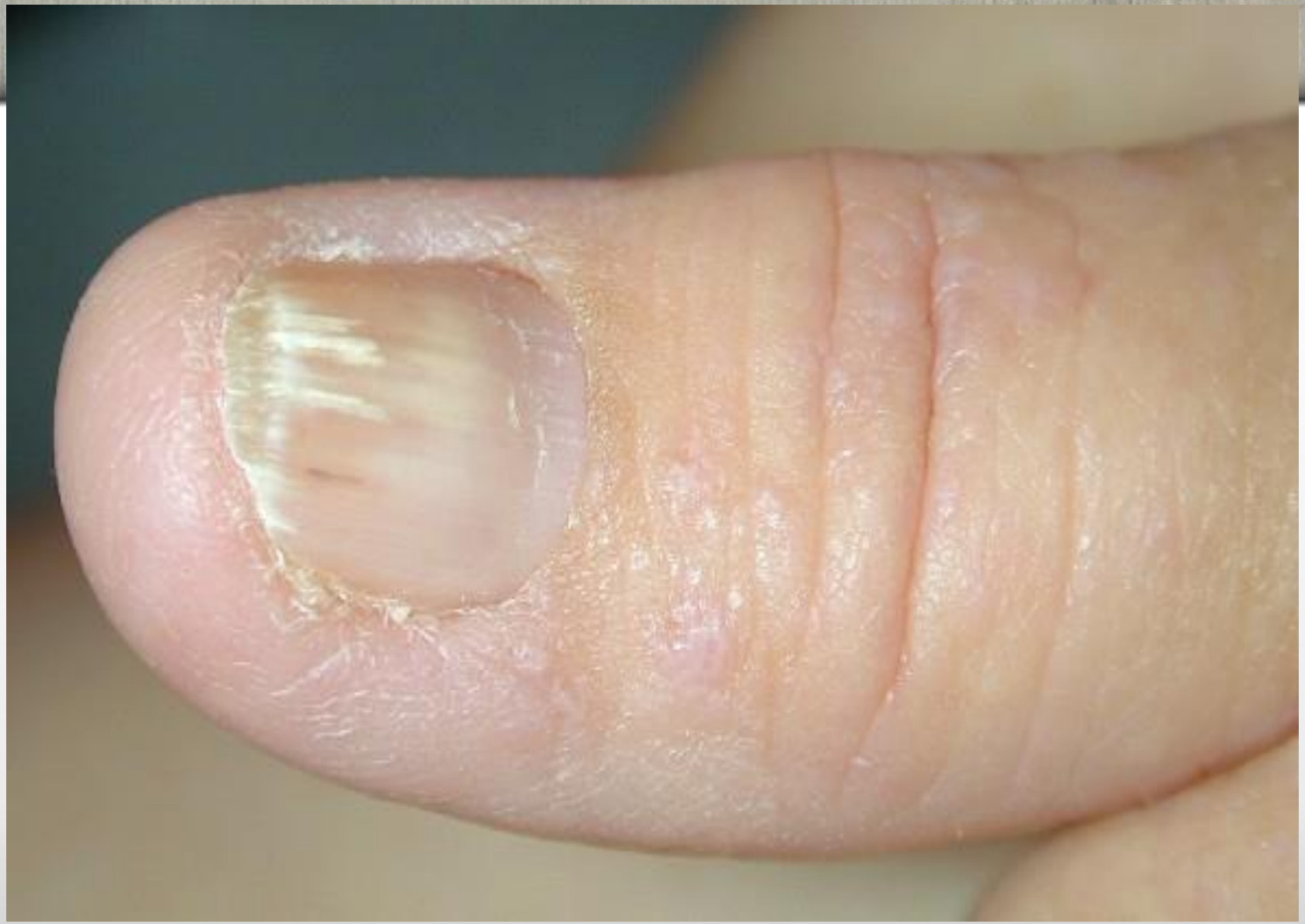


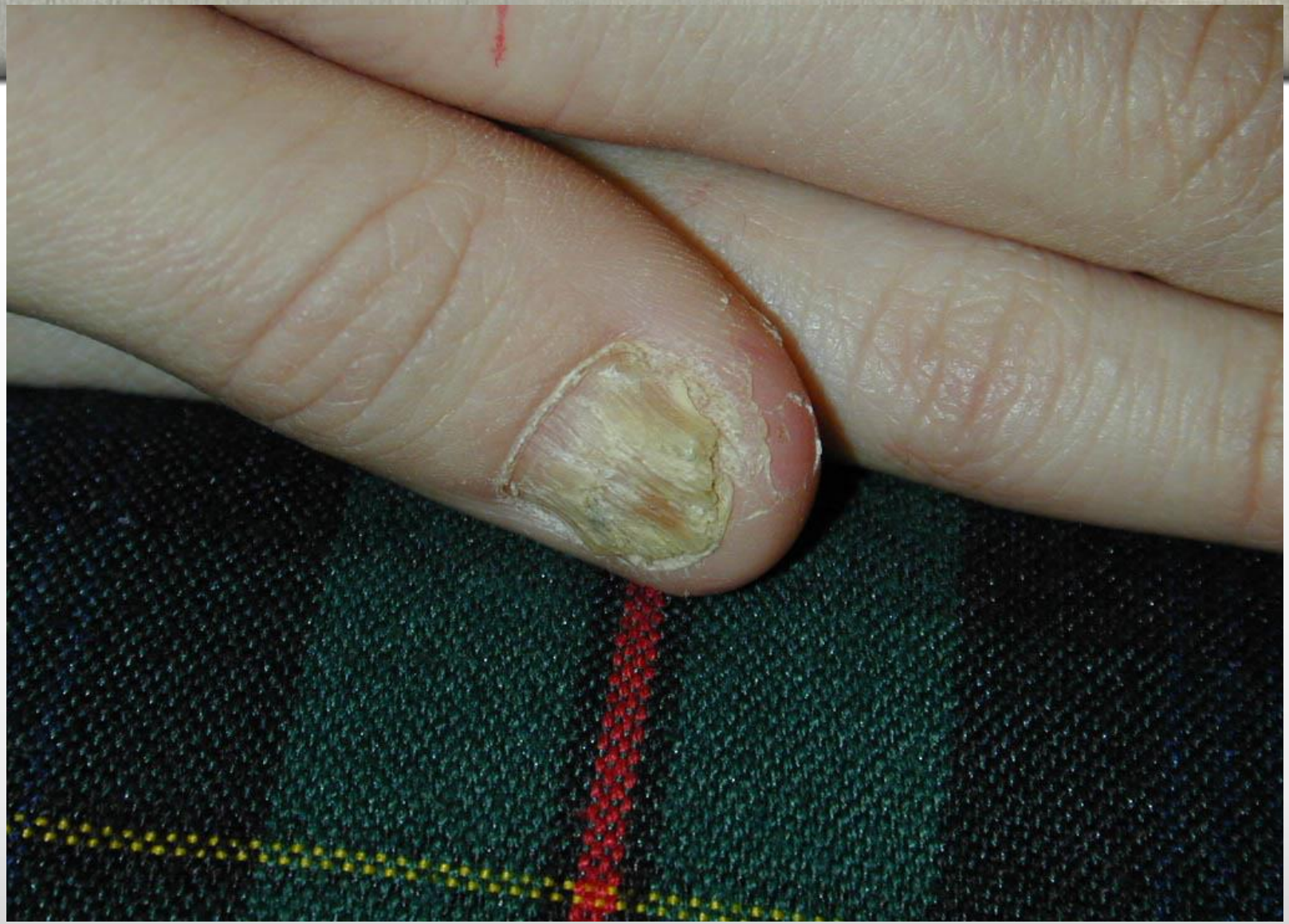


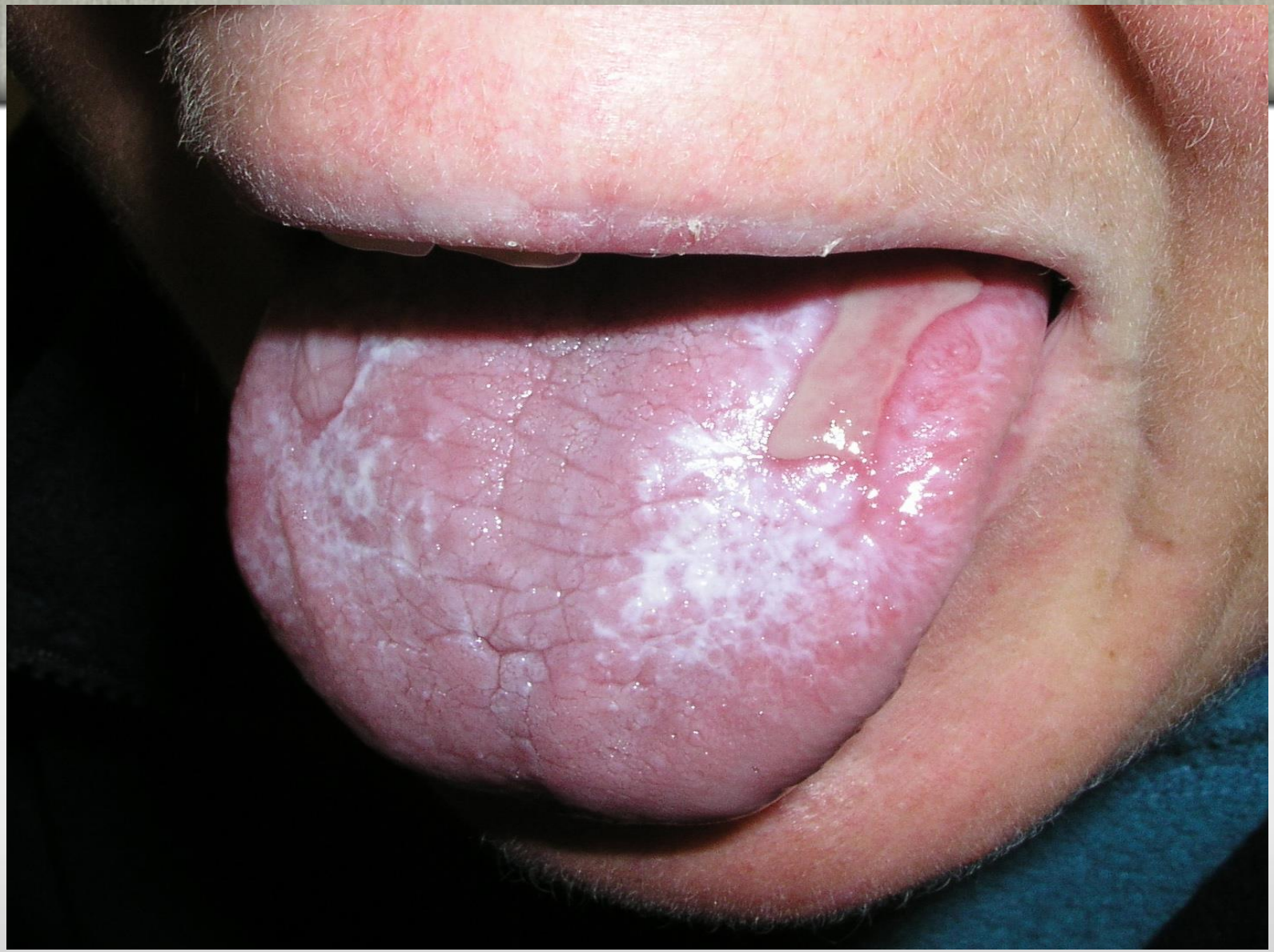


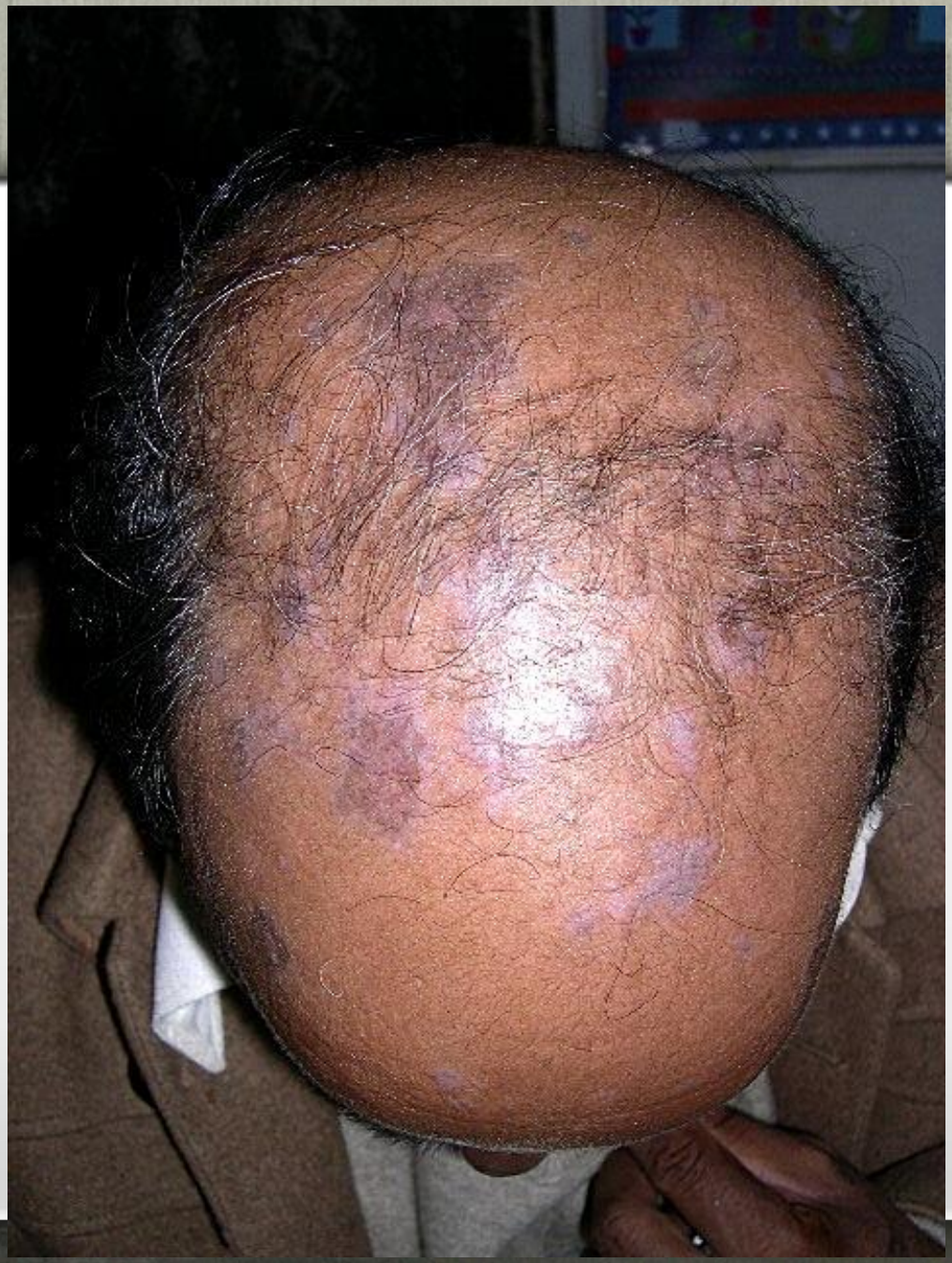












Lichen Planus

DIFFERENTIALS:-

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

Lichen Planus

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

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 dermatologi outpatient visits

-PR is more common in women than in men

Pityriasis Rosea

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.

Pityriasis Rosea

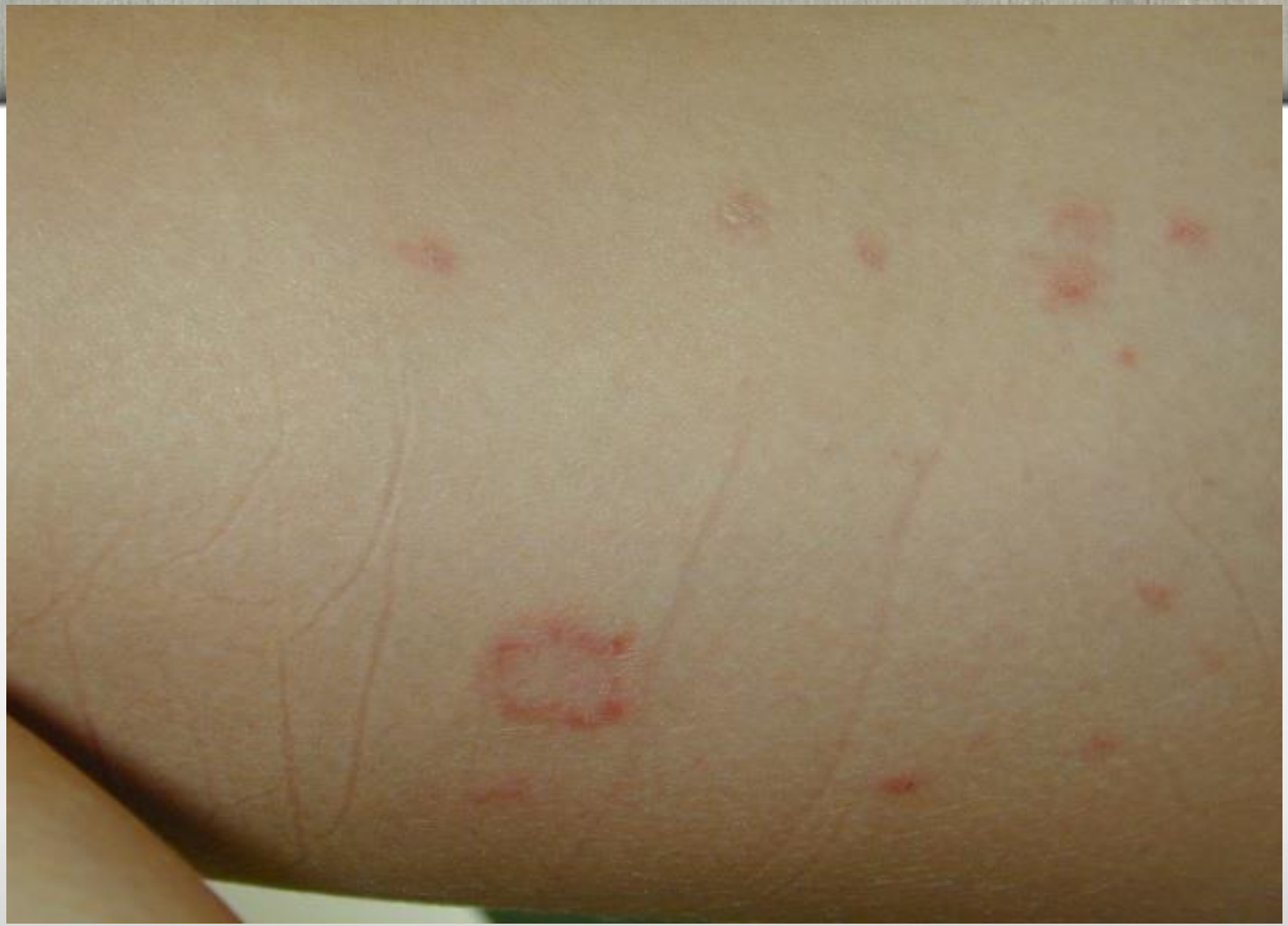
CLINICAL FEATURES:-

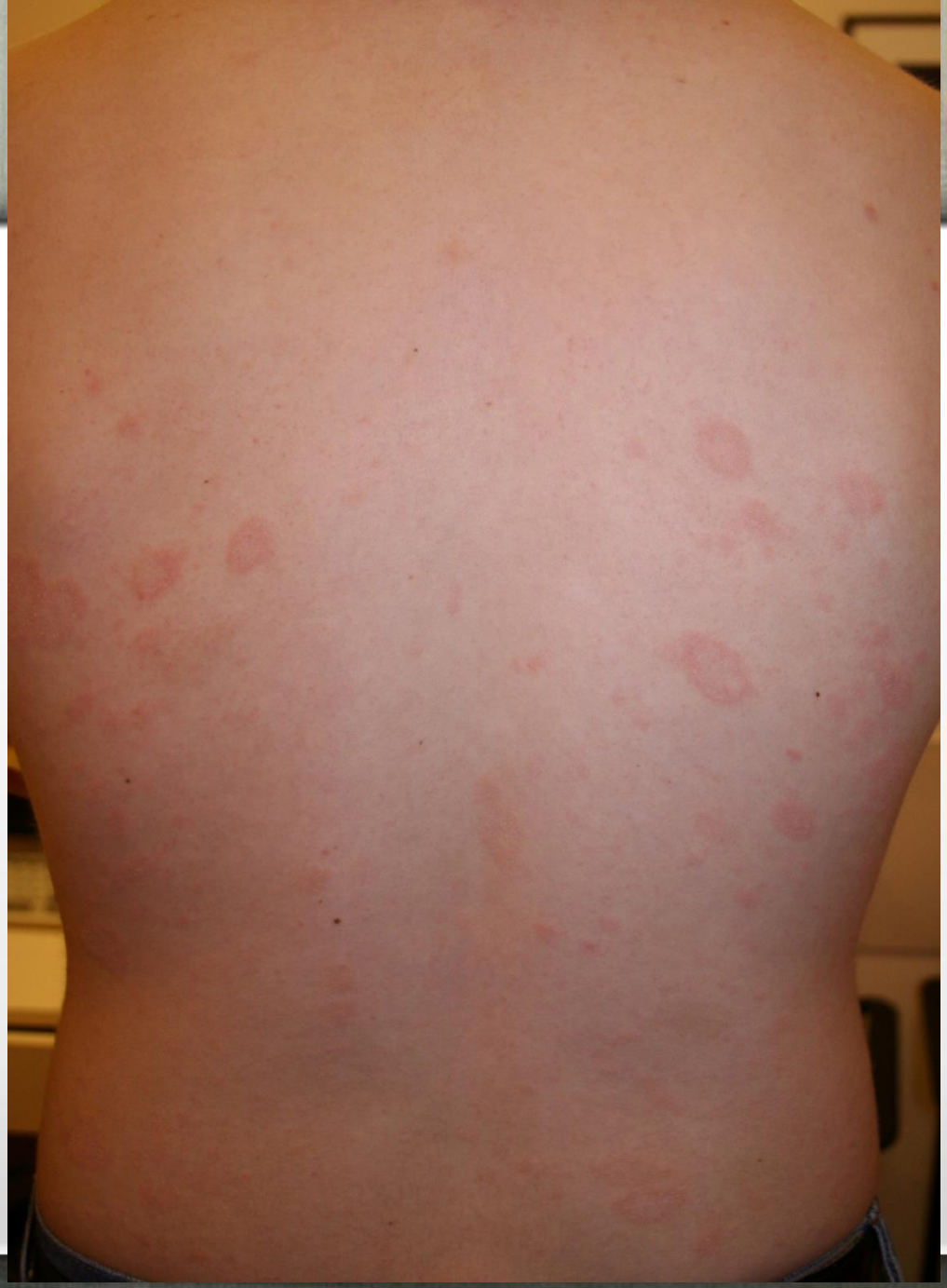
- Begins with a solitary macule that heralds the eruption(herald spot/patch)
- Usually a salmon-colored macule
- 0ver a few days it become a patch with a collarette of fine scale just inside the well-demarcated border
- Within the next 1-2 weeks, a generalized exanthem usually appears
- Bilateral and 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

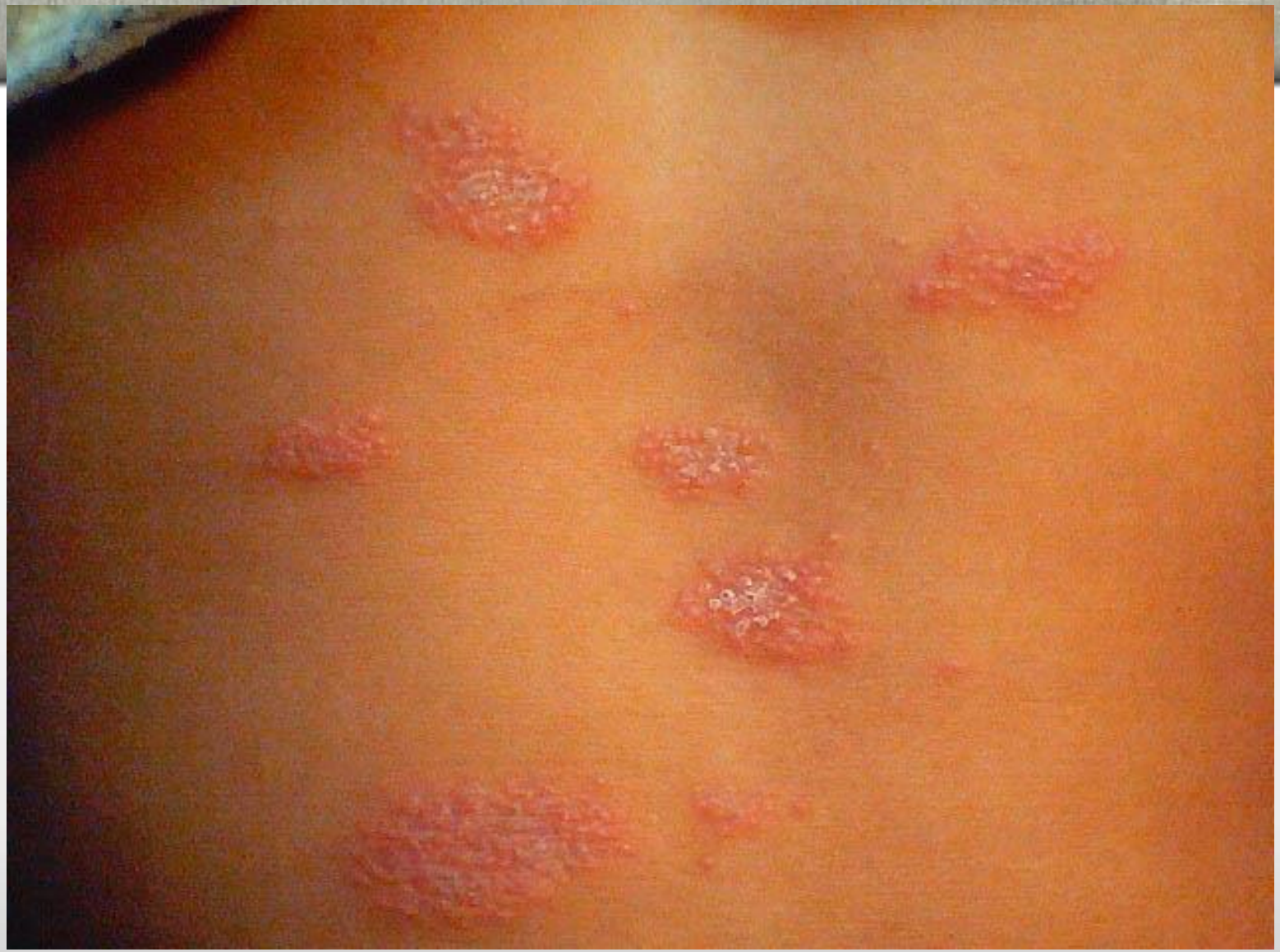
Pityriasis Rosea

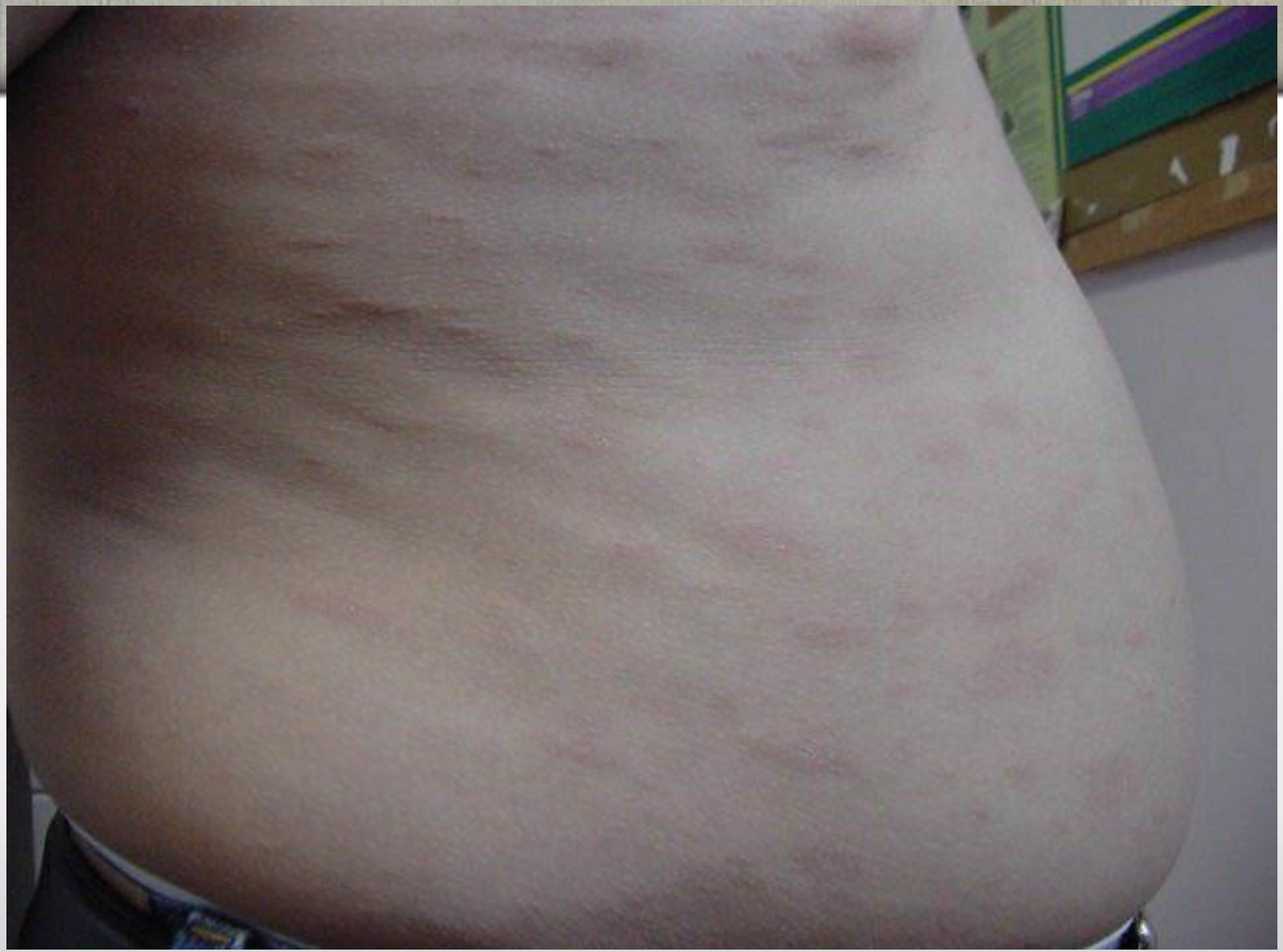
Atypical form of PR:-

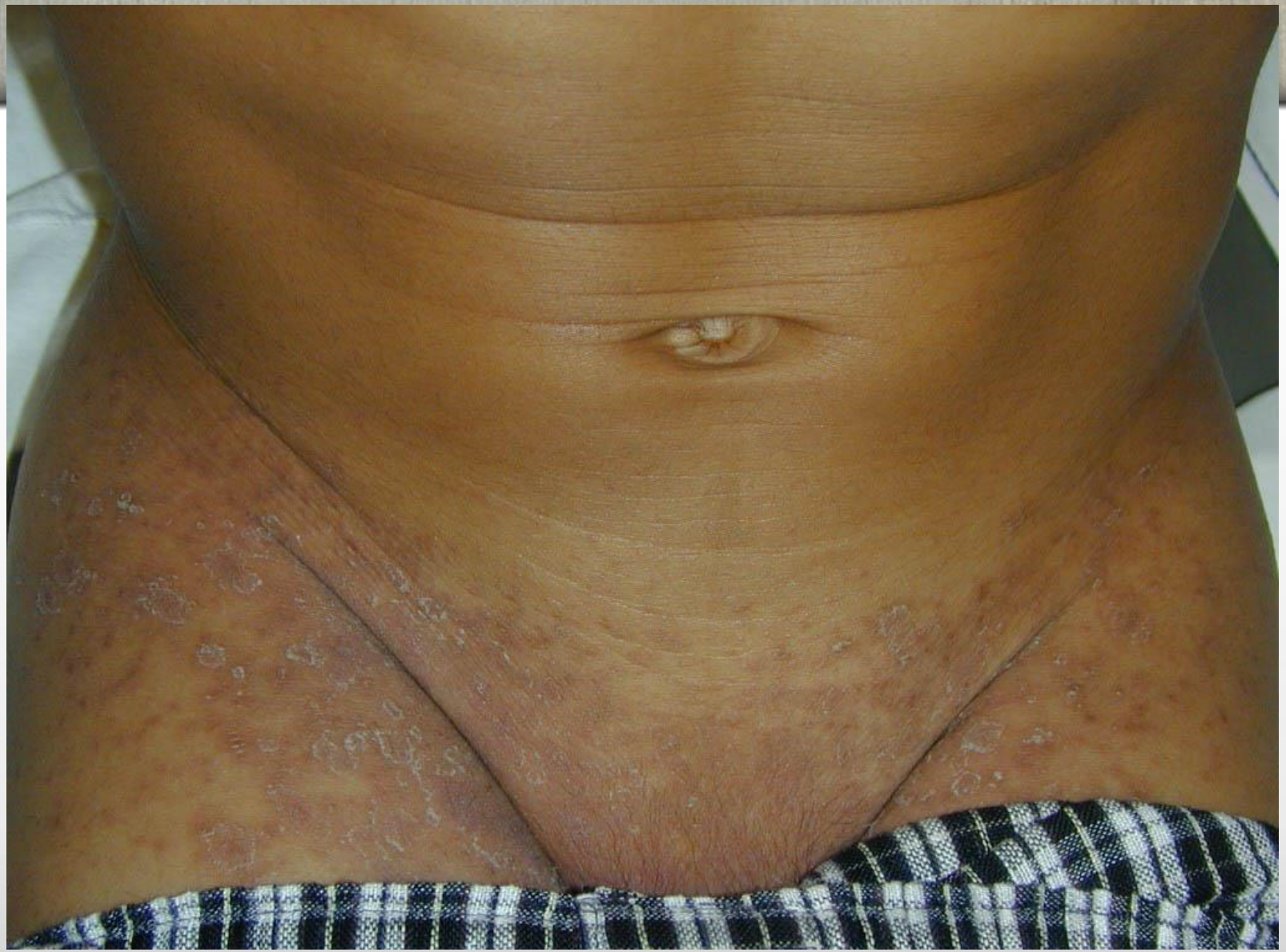
- Occurs in 20% of patients
- Inverse PR
- Unilateral variant
- Papular PR
- Erythema multiforme–like
- Purpuric PR











Pityriasis Rosea

DIFFERENTIALS:-

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

Pityriasis Rosea

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