

## etiology:

Psoriasis is a common inflammatory skin disorder which can be present at any age. The following medical conditions may be higher in psoriatic patients than in the general population:

① Psoriatic patients also have increased incidence of diabetes, obesity, and atherogenic lipid profile (and of course ①cardiovascular risk, ②metabolic syndrome, and ③ Obesity ④ hypertension), inflammatory bowel disease, multiple sclerosis and Lymphoma.

② Psychiatric/psychological such as ①depression (up to 60%) and may be severe enough that patients contemplate suicide), ②anxiety, ③sexual dysfunction and ④poor self-esteem الاعتزاز بالنفس. The emotional and psychological impact of psoriasis may not be reflected by the severity of the psoriatic skin condition

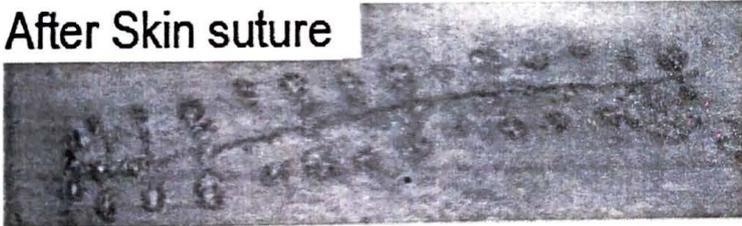
### A. Environmental factors:

#### 1. Trauma

All types of trauma have been associated with the development of plaque psoriasis (e.g., physical, chemical, electrical, surgical, infective, and inflammatory injury). Even excessive scratching can aggravate or precipitate localized psoriasis. The development of psoriatic plaques at a site of injury is known as the Koebner reaction.

Koebner phenomenon in psoriasis, also known as isomorphic response, 38-76% of patients recognize that new lesions appear at sites of injury 7-14 days following local trauma or injury to the skin (it has to be to the epidermis and upper part of dermis (papillary dermis))

#### After Skin suture



#### After tattoo



#### 2. Sunlight

Most patients report a decrease in illness severity during the summer months. However, a small minority of patients find that their symptoms are aggravated by strong sunlight.

#### 3. Infection

Pharyngeal streptococcal infections have been shown to produce a clinically distinctive disease flare known as guttate psoriasis.

#### 4. HIV infection

An increase in psoriasis activity has been observed in patients who are infected, or become infected, with HIV.

#### 5. Drugs

A number of medications have been shown to cause an exacerbation of psoriasis ① Lithium ② withdrawal from systemic corticosteroids, ③ Beta-blockers, ④ anti-malarial, and ⑤ non-steroidal anti-inflammatory drugs (NSAIDs) have also been implicated.

#### 6. Psychogenic/emotional factors

Many patients report an increase in psoriasis severity with psychological stress

#### 7. Smoking and Alcohol consumption

#### 8. Endocrinal factors

Psoriasis severity has been noted to fluctuate with hormonal changes. Disease incidence peaks at puberty and during menopause. During pregnancy, symptoms are more likely to improve than worsen, if any changes occur at all. In contrast, the disease is more likely to flare in the postpartum period, again if any changes occur at all.

### B. Genetic factors

Psoriasis is more common in monozygotic twins compared with dizygotic twins.

About 30 percent of individuals with psoriasis have a family history of the disease in a first- or second degree relative.

Lifetime risk of developing psoriasis if no parent, one parent, or both parents have psoriasis was found to be 0.04, 0.28, and 0.65, respectively.

① HLA-B13, -B17, and HLA -Cw6 are all associated with plaque psoriasis.

② Psoriasis susceptibility 1 (*PSOR1*) on chromosome 6, which is associated with up to 50% of cases. Eight other psoriasis susceptibility loci (*PSOR2-9*) have been discovered, as well as the transcription factor *RUNX1* (Runt-related transcription factor 1).

*PSOR8* gene on chromosome 16 (which links to both psoriasis and Crohn's disease), *PSORS2*, *PSORS3*, and *PSORS4* on chromosome 17, 4, and 1 respectively are which links to both psoriasis and metabolic syndrome, type 2 diabetes, familial hyperlipidemia, and cardiovascular disease.

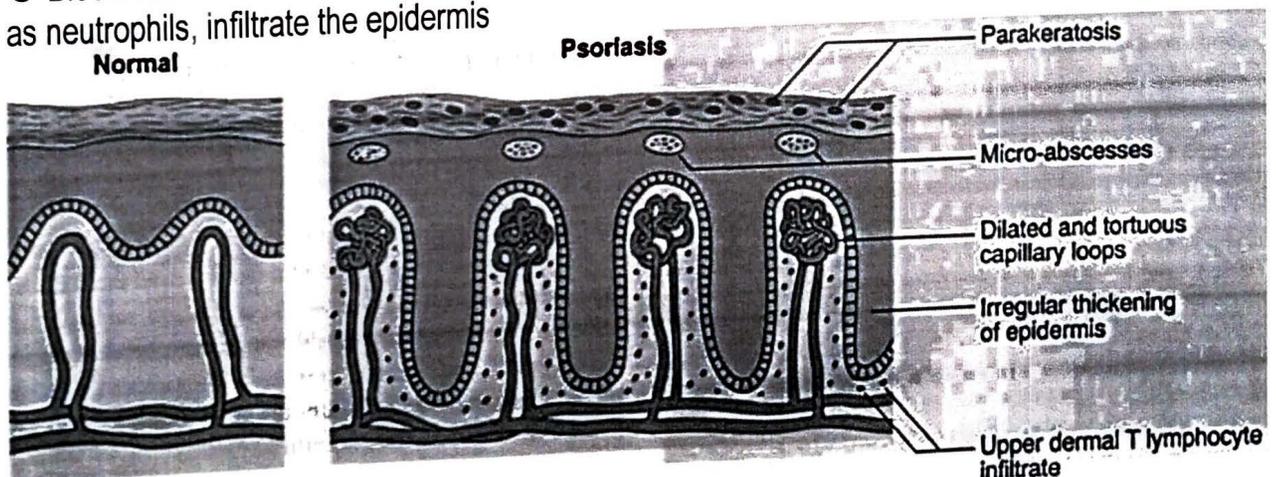
### Pathophysiology:

Keratinocyte proliferation is central to the clinical presentation of psoriasis.

Keratinocytes are skin cells producing keratin which act as a skin barrier.

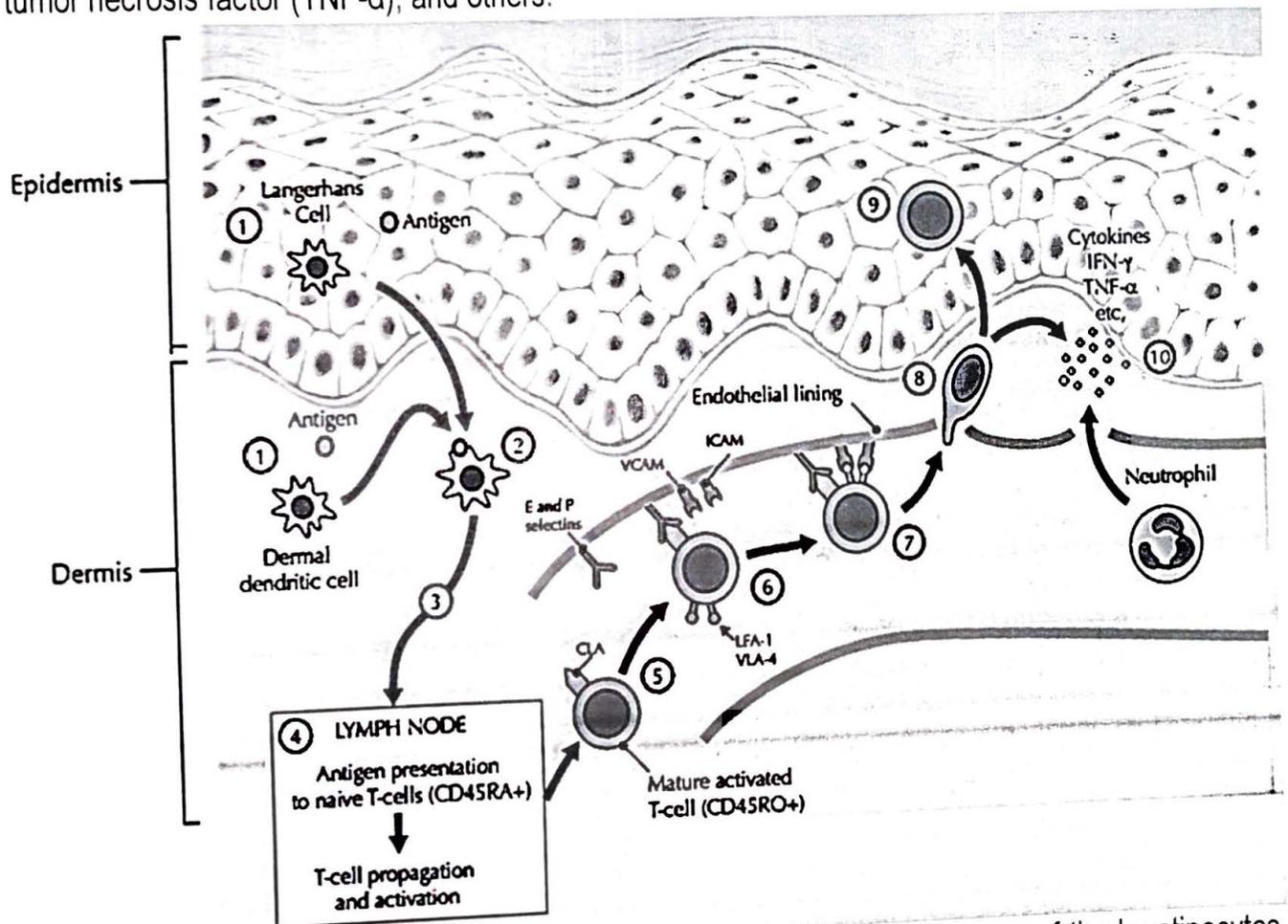
In psoriatic skin:

- ① the epidermal cell cycle is accelerated. TNF- $\alpha$  that lead to keratinocyte proliferation.
  - a. Cell division in the basal layer occurs every 1.5 days (normally once every two weeks)
  - b. Migration of keratinocytes to the stratum corneum occurs within just four days or so (Normally 30-40 days).
- ② Since the cells move to the surface so rapidly,
  - a. they do not differentiate and mature properly.
  - b. The stratum corneum is not fully keratinized, and epidermal cells build up abnormally and become thick scaly skin lesions.
  - c. The epidermis in psoriatic lesions is three to five times thicker than normal.
- ③ Blood vessels in the papillary layer of the dermis dilate in psoriasis, and inflammatory cells, such as neutrophils, infiltrate the epidermis



Initial generation of an immune response in skin:

- (1) Dendritic cells appear to be involved in the pathogenesis of psoriasis. One type of dendritic cell involved is the Langerhans cells and dermal dendritic cells capture antigen.
- (2) While antigen is processed and presented on the surface of the APC, maturation occurs with the expression of costimulatory molecules.
- (3) The APC migrate via the afferent lymphatics to the skin-draining lymph node.
- (4) In the lymph node, they present the processed antigen to naïve T-cells (CD45RA+) causing T-cell maturation, activation and proliferation.
- (5) Mature activated T-cells (CD45RO+) express CLA antigen (cutaneous lymphocyte-associated antigen).
- (6) CLA antigen is able to bind to E- and P-selectins expressed by endothelial cells in the dermis.
- (7) This interaction stimulates T-cells to express LFA-1 and VLA-4 (lymphocyte function-associated antigen-1 and Very Late Antigen-4) and endothelial cells to produce intercellular and vascular adhesion molecules (ICAM and VCAM).
- (8) The interaction of these molecules allows the activated T-cells to migrate through the post-capillary venules into the dermis.
- (9) The activated T-cells can then migrate to areas of antigen expression in the dermis or epidermis.
- (10) Activated T cells begin releasing cytokines including interleukin-2 (IL-2), interferon- $\gamma$ , (IFN- $\gamma$ ), tumor necrosis factor (TNF- $\alpha$ ), and others.



TNF- $\alpha$  and IFN- $\gamma$  are continually produced result in a regenerative phenotype of the keratinocytes, manifested as

- ① Epidermal hyper-proliferation with elongation of the rete ridges,
  - ② Loss of the granular layer and
  - ③ Retained nuclei in the stratum corneum (parakeratosis).
- TNF- $\alpha$  induces keratinocytes to produce IL-8 that is chemotactic for neutrophils

TNF- $\alpha$  may have a role in disease severity;

- ① TNF- $\alpha$  up-regulates endothelial and keratinocyte expression of ICAM-1 (Intercellular Adhesion Molecule 1,
- ② Activates T cells,
- ③ Enhances T-cell infiltration,
- ④ Augments keratinocyte proliferation.

Biochemical studies have recognized specific changes in the expression of many cellular markers in psoriasis.

A. The markers of epidermal proliferation which are usually increased in psoriasis:

- ① The keratins (K6, K10, K16, and K17),
- ② Epidermal growth factor (EGF) receptor,
- ③ Ornithine decarboxylase.

B. The markers which are usually decreased in psoriasis:

- ① Filaggrin, which is essential for the development of the stratum corneum
- ② Differentiation-related keratins K1, K2

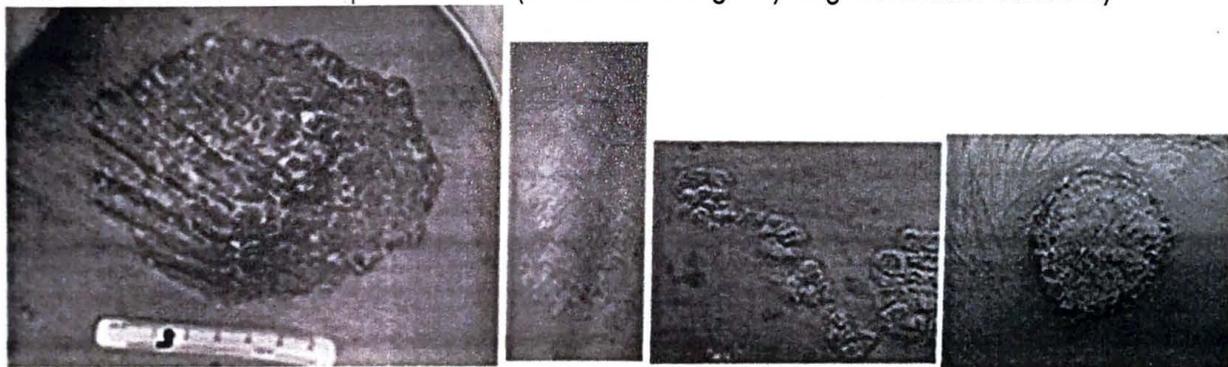
C. Differentiation is associated with its own biochemical markers, including

- ① Keratinocyte transglutaminase,
- ② Migration inhibitory factor-related protein,
- ③ Skin-derived anti-leuko-proteinase,
- ④ Involucrin
- ⑤ Small protein rich protein

Keratinocytes contain a variety of immune-modulating cytokines, such as interleukin-1 (IL-1), IL-6, IL-8, and tumor necrosis factor (TNF) the last two increased in psoriasis

### **Clinical Presentation of Psoriasis**

Clinical Presentation of Plaque Psoriasis (or Psoriasis vulgaris) vulgaris: means common)



## **Plaque-type psoriasis**

### General

- About 80% of people with psoriasis have this type
- Patients have small discrete to generalized confluent lesions over the entire body.

### Symptoms

- Patients may complain of severe itching (25%).

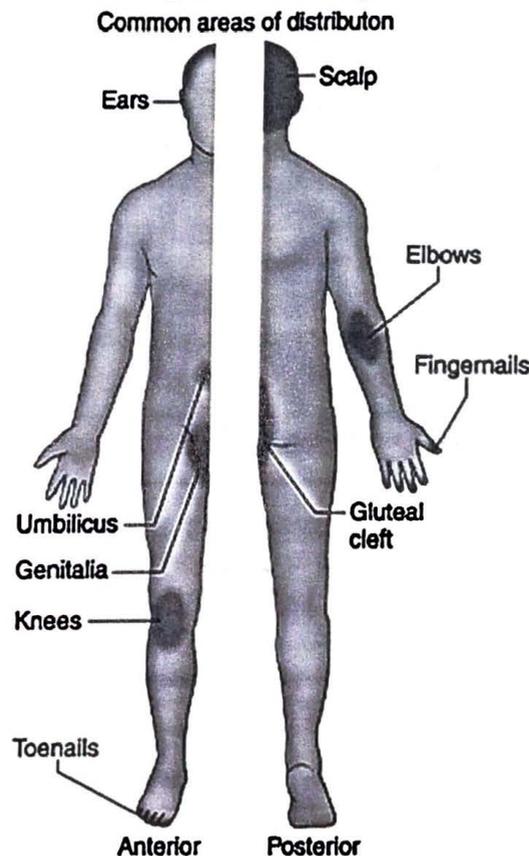
### Signs

- Lesions are raised and are red to violet in color (commonly known as plaques).
- Lesions have sharply demarcated borders except where confluent.
- Lesions are loosely covered with silvery-white scales, which if lifted off, show small pinpoint of bleeding (Auspitz sign).

# Auspitz sign



- Plaques appear most commonly on the elbows, knees, scalp, umbilicus, and lumbar areas, and often extend to involve the trunk, arms, legs, face, ears, palms, soles, and nails.



- Nail involvement

## ①Pitting:

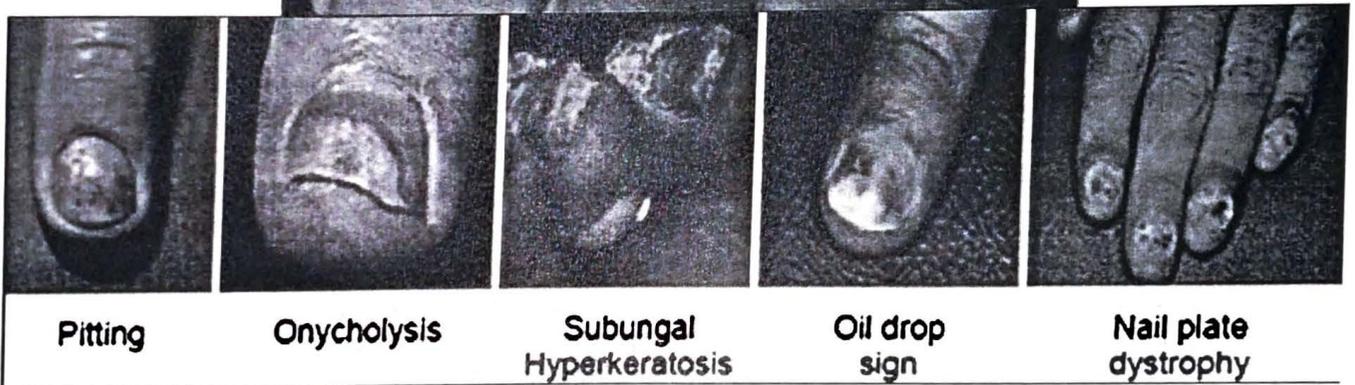
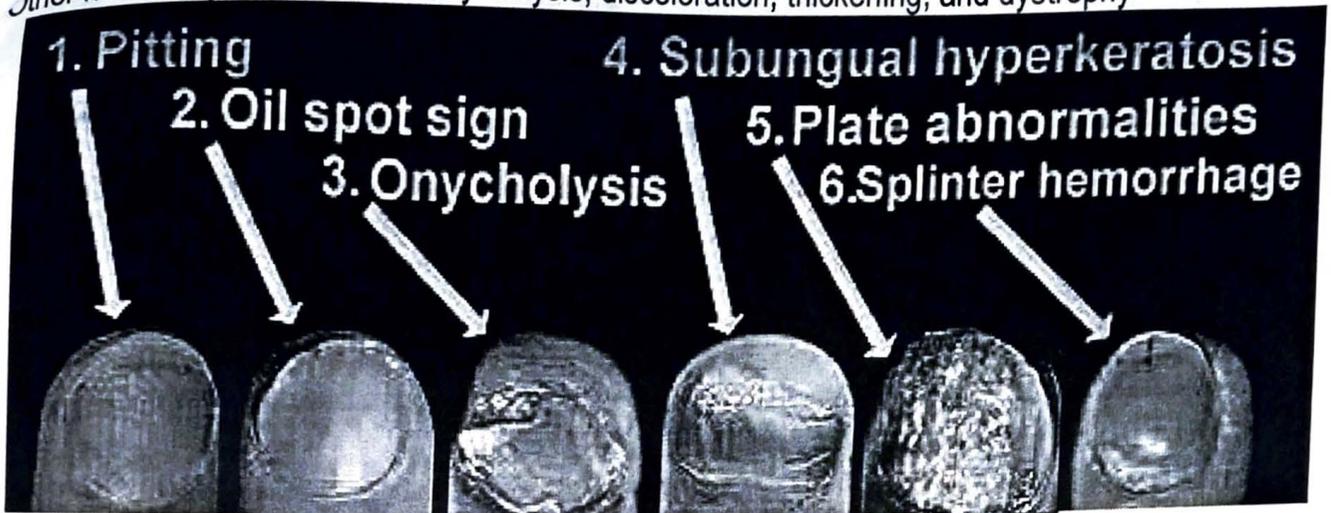
This is the most frequent nail abnormality with psoriasis. The nail has tiny, punched-out depressions that grow out with the nail.

Oil Spots: is a term used to describe yellow-brown discolorations underneath the fingernail. Skin debris and fluid often collects in the spaces caused by nail separation. This results in brownish-yellow spots, hence the fitting name.

Nail Separation: Psoriasis can cause the nail bed to pull away from the nail itself. The nail plate may turn yellow

Nail Deformity: Psoriasis can affect the nail matrix, the area of the finger where the fingernail is made. This can cause the nail to crumble and break easily.

Other nail changes can include onycholysis, discoloration, thickening, and dystrophy



### Clinical Presentation of Other Types of Psoriasis

#### 1. Inverse psoriasis.

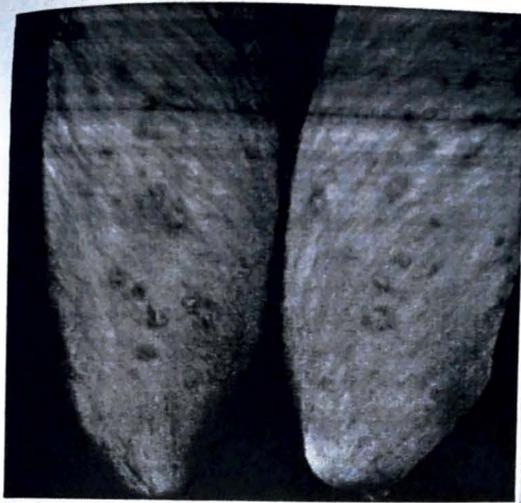
Inverse psoriasis consists of bright red, smooth (not scaly) patches found in the folds of the skin. The most common areas are under the breasts, in the armpits, near the genitals, under the buttocks, or in abdominal folds. These irritated and inflamed areas are aggravated by the sweat and skin rubbing together in the folds. Yeast overgrowth, common in skin folds, may trigger the skin lesions of psoriasis.

#### 2. Guttate psoriasis. (Guttate meaning drop)

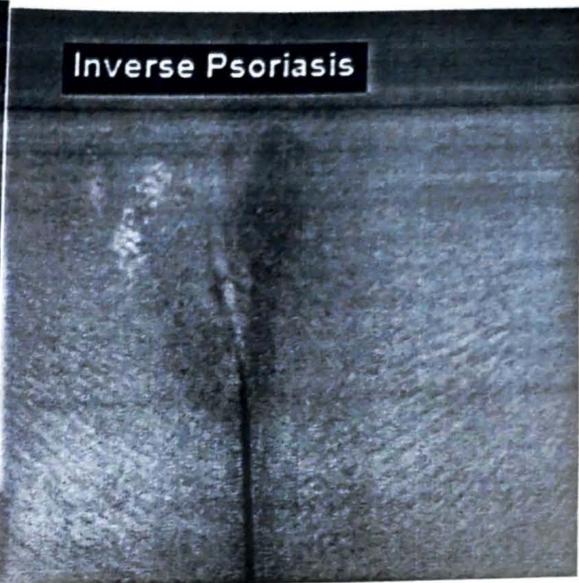
Acute guttate psoriasis occurs in children, adolescents, and young adults approximately two weeks after an acute beta-hemolytic streptococcal infection, such as tonsillitis or pharyngitis, or a viral infection.

Acute guttate manifests as a fine scale on the drop-like lesion that is much finer than the scales in plaque psoriasis, a sudden eruption of small, disseminated erythematous-squamous papules.

Acute guttate psoriasis is usually self-limited, resolving within 3-4 months.



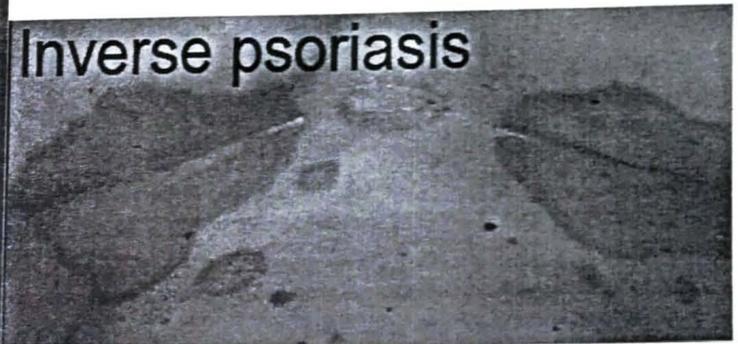
Guttate psoriasis. Widespread small, drop-like, red scaly papules that may coalesce into plaques.



Inverse Psoriasis



Guttate psoriasis



Inverse psoriasis

3. Pustular psoriasis:

Pustular Psoriasis *may* be localized or generalized and may be an acute emergency requiring systemic therapy.

Pustular psoriasis is an uncommon form of psoriasis. People with pustular psoriasis have clearly defined, raised bumps on the skin that are filled with pus (pustules).

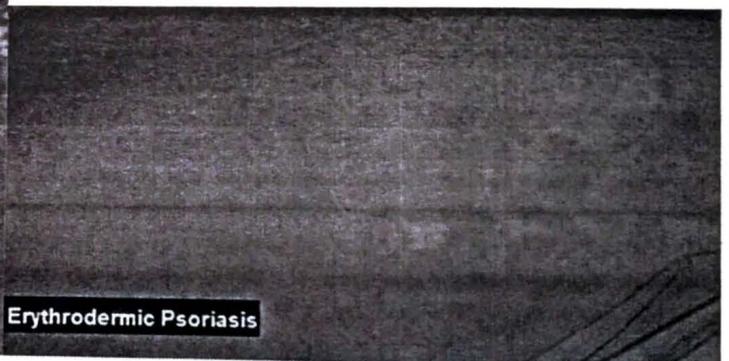
5. Erythrodermic psoriasis:

Erythrodermic Psoriasis is generalized (A very large area of the body, if not most of the body), that presents with erythema (body can appear to be covered in bright red rash), the rash usually itches or burns, desquamation, edema.

Erythrodermic psoriasis, also life threatening, involves the entire body surface and can result in hypothermia, hypoalbuminemia, anemia, infection, and high-output cardiac failure

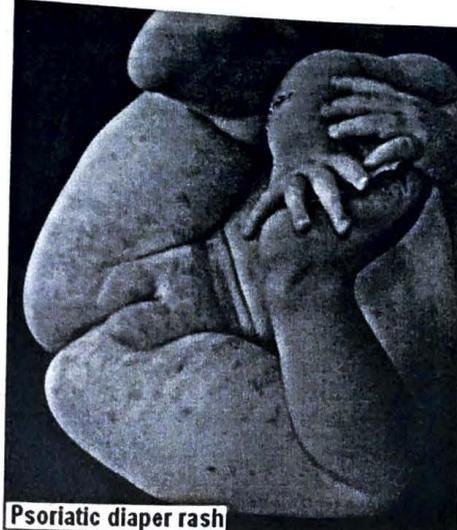


Pustular Psoriasis



Erythrodermic Psoriasis

Psoriatic diaper rash is the most common type of psoriasis in children under 2 years old. This usually affects inguinal folds and greater than 90% of psoriatic diaper rash cases may have involvement outside the diaper area.

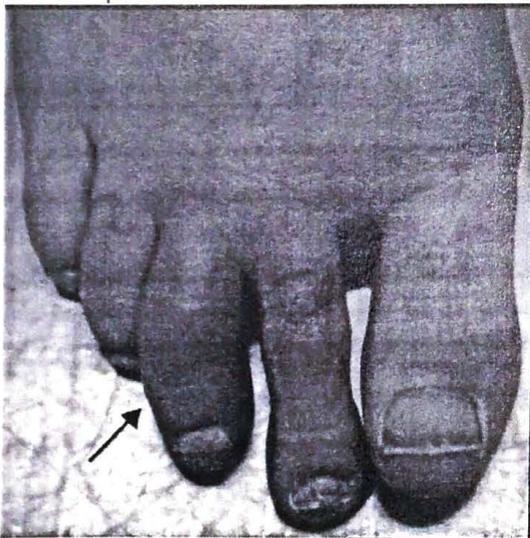


Psoriatic diaper rash

### Psoriatic Arthritis

Ten% to 30% of patients with psoriasis may also have psoriatic arthritis. In 10% to 15% of psoriatic patients with arthritis, joint symptoms actually appear prior to skin involvement.

Psoriatic arthritis is a specific condition in which a person has both psoriasis and arthritis. Psoriatic arthritis is an autoimmune disease, meaning that the immune system is misdirected to cause inflammation of one's own tissues. Rarely, a person can have psoriatic arthritis without having skin psoriasis. Moreover, the arthritis can precede the psoriasis by months or years, or present after years of psoriasis



Psoriatic Arthritis