

**Introduction****Immune cell within skin**

- Epidermis: Langerhans cells are the only dendritic cells (DC)
- Dermis: at least 2 subsets of DCs (distinguished based on expression of langerin)
  - Also contains mast cells & memory T cells

**Hapten and immune response**

- 1) Hapten activated dendritic cells in epidermis/dermis
- 2) Haptens induce cytokine production in skin
- 3) Dendritic cells migrate as antigen presenting cells
- 4) B cell (memory) IgE and/or T cell activation

**Haptens:** penetrate into dermis & available to the immune cells

- Pre-hapten: molecule that undergoes chemical reaction environmentally (oxidation) prior to interacting with body
  - Haptens: elicit immune response directly
    - Small molecules that covalently binds proteins
    - Forms adduct = single rxn product containing all atoms of all components
    - Can be soluble or receptor proteins
    - Can bind to MCH I and II directly
    - Becomes immunogenic
  - Pro-haptens: metabolized into haptens
- T-cell receptor binding: activating T cells
- Pharmacological interaction with immune receptors theory
  - Non-covalent interaction - REVERSIBLE

**Psoriasis**

- Autoimmune mediated: skin is "non-self"
  - Dendritic cells & T-cells migrate from dermis → epidermis
  - Cytokine release
    - Inflammatory response
    - Keratinocytes proliferate

**Factors**

- Common onset young adults
- Genetic: inherited susceptibility
- Even gender split

**Complications**

- 7x ↑ risk for MI
- Depression
- Psoriatic arthritis

**Precipitating factors**

- Skin injury
- Discontinuation of systemic corticosteroids
- Cold weather
- Streptococcal throat infections
- Emotional stress
- Alcohol
- Smoking
- HIV
- Medications: B-blockers, ACE inhibitors, lithium, antimalarial

**Classification****Pustular**

- Raised, NONINFECTIOUS pustules
- Surrounding skin is red, tender, inflamed
- Localized or generalized

**Non-pustular**

- Most common (80-90%)
- Papules → plaques
  - Well defined
  - Raised
  - Red
  - Scales = silver/white

**Diagnostics**

- Auspitz sign: punctate bleeding spots where scale is scratched off
- Candle sign: skin under edges of scales look greasy/shiny
- Sign of last Hautchen: lesion is dry to final layer

**Lesion locations:** scalp, elbows, legs, knees, nails, lower back, palm/soles, buttocks

**Pathology**

- Keratinocyte proliferation
- HYPERKERATOSIS: thickening of epidermis
- Dilated blood vessels (immune response)
- Elongation of rete pegs (epithelial extensions into connective tissue under skin)

**Psoriasis Area and Severity Index: PASI score**

- Intensity of redness, thickness and scaling is assessed as none (0) → very severe (4)

**Types of psoriasis****Plaque psoriasis: MOST COMMON**

- Raised, red patches covered with a silvery white buildup of dead skin cells
- Plaques on scalp, knees, elbows and lower back
- ITCHY AND PAINFUL
- May crack and bleed (risk of infection)

**Guttate psoriasis: 2<sup>nd</sup> most common**

- Dot-like lesions
- Onset in childhood
- Adult forms often triggered by strep infection

**Inverse psoriasis: red lesions in body folds (knee, arm, groin)**

- Can become smooth & shiny
- Comorbid with another type of psoriasis

**Erythrodermic psoriasis: rare but severe generalized form**

- Widespread, fiery redness over most of body
- Severe itching and pain → makes skin come off in sheets
- Appears on people who have unstable plaque psoriasis

**Pustular psoriasis: non-infectious**

- White pustules (blisters of non-infectious pus) surrounded by red skin
- The pus consists of dead WBCs and is not contagious
- Occurs most often on hands or feet

**Retinoic acids for psoriasis****Systemic (orally): for pustular forms = ACITRETIN**

- Synthetic non-selective vitamin A derivative
- Converted to etretinate (more toxic parent drug) in vivo
  - Conversion promoted by ethanol = ALCOHOL STRICTLY AVOIDED during treatment and for 2 months after discontinuing therapy

**Topically: less severe forms**

- Retinoic acid
- Tazarotene

**Calcipotriene: synthetic Vit D3 derivative for treatment of psoriatic plaques****MOA: increase differentiation & inhibit proliferation of keratinocytes**

- Vitamin D receptor VDR form heterodimers with the RXR receptor that bind DNA to regulate transcription of target genes

**Adverse effects:** burning, itching, mild irritation, dryness and erythema of treated area, HYPERCALCEMIA

**Alefacept: treatment of mod-severe chronic plaque psoriasis****MOA: anti-CD2 antibody (protein near T cell receptor)**

- Blocks CD4 (T-helper cell) activation
- Reduces CD2 +ve T lymphocytes & circulating total CD4 (helper) & CD8 (cytotoxic) T lymphocyte counts

**Adverse effects:** CD4 lymphocyte counts can drop; increased risk of cancer

**Pimecrolimus****Immunosuppressant**

- Impairs development of both mature helper T cells & killer T cells in thymus
- Inhibits T cell activation by blocking the transcription of cytokine genes, including those of IL-2 and IL-4

**Uses:** topically as ointment

- Mild psoriasis
- Atopic & allergic contact dermatitis

**Mechanism:** calcineurin inhibitor

- Binds to tacrolimus binding protein (FKBP)
  - Complex binds to calcineurin & blocks its phosphatase activity
- Prevents activation of NFAT (Nuclear Factor of Activated T cells) which prevents transcription of interleukin IL-2

**Adverse effects:** application site reactions (pruritis, burning or worsening of atopic dermatitis)

**Coal Tar:** antipruritic properties due to phenolic groups in tar

**Adverse effects**

- Irritant folliculitis (reversible)
- Phototoxicity (avoid sun exposure)
- Allergic contact dermatitis