Psoriasis
Pharmacology IV (PHL 425)

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WHAT IS PSORIASIS?

• “Psora” means “itch”
• A common, life-long, genetic, autoimmune, inflammatory disease of skin and joints.
• Chronic, non-contagious disease characterised by silvery white scales which are attached, more or less firmly to a reddish vascular base (erythematous and elevated scaly plaques)
• Course of disease often unpredictable
EPIDEMIOLOGY

- Estimated incidence: ~ 60 per 100,000 per year.
- 2% of the world wide population.
- Two-thirds of affected individuals were suffering from mild psoriasis, while one-third had more severe involvement.
- Psoriasis can appear at any age.
- Two peaks in age of onset have been reported: one at 20–30 years of age and a second peak at 50–60 years. [Mean age: ~ 23–37 years]
- Prevalence equal in males and females but age of onset is earlier in women than in men.
MOST FREQUENTLY EXPERIENCED SYMPTOMS OF PSORIASIS

- Scaling: 94%
- Itching: 79%
- Skin redness: 71%
- Tightness of skin: 31%
- Bleeding: 29%
- Burning sensation: 21%
- Fatigue: 19%
- Other: 5%

Percentage of respondents (n = 17,425)
COMMON TRIGGER FACTORS

Can be divided into **Local (External) and Systemic Factors:**

- **Skin trauma** / Direct skin injury
- **Infections** (e.g. streptococcal, viral)
- **Hormonal factors** (e.g. pregnancy, menopause)
- **Sunburn**
- **Psychological stress**
- **Alcohol, Smoking, Obesity**
- **Drugs** (e.g. lithium, β-blockers, Antimalarials)
- **Cold Weather**
- **Metabolic factors** (e.g. calcium deficiency)
- **Discontinuation of systemic corticosteroids**
- **HIV infection**
COMMON TRIGGER FACTORS

Skin Trauma:
- Physical, chemical, electrical, surgical, infective and inflammatory injury or
- Even excessive scratching can aggravate or precipitate localized psoriasis

Infections:
- Pharyngeal streptococcal (most common) infections have been shown to produce guttate psoriasis.

Hormonal changes
- Psoriasis severity has been noted to fluctuate with hormonal changes. Disease incidence peaks at puberty and during menopause.

Sunlight:
- Most patients consider sunlight to be beneficial for their psoriasis and report a decrease in severity during the summer months or periods of increased sun exposure;
- However, a small minority find that their symptoms are aggravated by strong sunlight

Psychogenic stress:
- A well-established systemic triggering factor in psoriasis.
- It has been associated with initial presentations of the disease as well as flares of pre-existing psoriasis
Alcohol consumption:
• Alcohol consumption has been associated with psoriasis.

Smoking:
• An increased risk of chronic plaque psoriasis exists in smokers.

Obesity:
• Some studies have suggested that obesity appeared to be a consequence of psoriasis, whereas other studies have suggested that weight gain often proceeds the development of psoriasis.

Drugs:
• Several drugs have been incriminated as inducers of psoriasis. Rapid taper of systemic corticosteroids can induce pustular psoriasis as well as flares of plaque psoriasis.

LIMBS
• L: Lithium
• I: Interferon
• M: anti-Malarials
• B: Beta blockers
• S: Steroids/NSAIDs

Cold Weather:
• Sudden exposure to cold weather (at high altitudes and in cold weather climates) can trigger psoriasis.
PSORIASIS IS A T-CELL MEDIATED, AUTOIMMUNE DISEASE

• Current hypothesis:
  – Unknown skin antigens stimulate immune response
    • Antigen-specific memory T-cells are primary mediators
  – Leads to impaired differentiation and hyperproliferation of keratinocytes
Silver scaling of skin fails to release adequate lipids which leads to flaking and scaling.

Epidermal hyperplasia & improper cell maturation

Superficial blood vessels dilated & vascular engorgement

Large production of various cytokines (IFN, ILs)

Dysregulated inflammatory process

Epidermis infiltration & keratinocytes proliferation

Hyperactive T-cells

Stress, genetic, autoimmune reactions, and medications cause
COMMON SITES AFFECTED BY PSORIASIS

• Can affect any part of the body – typically scalp, elbow, palm, knees, nails, and sacrum

• Extent of disease varies
TYPES OF PSORIASIS

1. Chronic plaque (~90%)
2. Guttate
3. Flexural
4. Erythrodermic
5. Pustular
   - Localized and generalized
6. Local forms
   - Palmoplantar
   - Scalp
   - Nail (psoriatic onychodystrophy)
1. CHRONIC PLACQUE PSORIASIS

- Most common type – affects ~90%
- Features pink, well-defined plaques with silvery scale
- Lesions may be single or numerous
- Plaques may involve large areas of skin
- Classically affects elbows, knees, buttocks, emblicus and scalp.
- Plaques may persist for months to years at the same locations.
2. GUTTATE PSORIASIS

– Numerous and small lesions (0.5-1.5 cm): ~ 1 cm diameter **papules**
– Pink with less scale than plaque psoriasis
– Commonly found on **trunk and proximal limbs**
– More commonly seen in **children and adolescents** (individuals < 30 years)
– Often preceded by an upper respiratory tract streptococcal infection
3. FLEXURAL PSORIASIS

- Lesions in skin folds particularly axillae and sub-mammary regions
- Often **minimal or absent scaling**
- Common sites of flexural psoriasis are:
  - Axillae
  - Umbilicus
  - Penis
  - Vulva
  - Natal (intergluteal) cleft (groove between buttocks)
  - Around the anus
  - Retroauricular (behind the auricle of ear)
4. ERYTHRODERMIC PSORIASIS

- Relatively uncommon
- The most prominent feature is generalized erythema with superficial scaling on entire skin surface
- May evolve slowly from chronic plaque psoriasis.
- Patients may become febrile, hypo/hyperthermic and dehydrated.
- Patients lose excessive heat because of generalized vasodilatation, and this may cause hypothermia.
- Complications include cardiac failure, infections, malabsorption and anemia.
Two forms:

• **Localized form: More common**
  – Presents as deep-seated lesions with multiple small pustules on palms and soles

• **Generalized form: Uncommon**
  – Associated with fever and widespread pustules across inflamed body surface
6. LOCAL FORM

PALMOPLANTAR PSORIASIS

SCALP PSORIASIS

ORAL

NAIL PSORIASIS
Psoriasis coverage & severity

1% = Surface area of the palm.

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<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
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<td>Less than 3%</td>
<td>3%-10%</td>
<td>More than 10%</td>
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– ~20% have associated arthritis
– More prevalent among patients with relatively severe psoriasis.
– Severe psoriasis is associated with up to 7X risk for developing myocardial infarction, especially at a younger age and increased mortality (~5 year shorter life span)
TREATMENT OPTIONS

• Stepwise approach is advised

• Treatments include:
  – General measures and topical therapy
  – Phototherapy
  – Systemic and biological therapies

• Combination therapies and rotational therapy may reduce toxicity and improve outcomes
TREATING PSORIASIS:

GENERAL MEASURES

• Reduce/eliminate potential trigger factors:
  – Stress
  – Smoking
  – Alcohol
  – Trauma
  – Drugs
  – Infections
TOPICAL THERAPIES:

Approximately 70% of patients with mild-to-moderate psoriasis can be managed with topical therapies alone.

**Emollients**

- Include aqueous cream, white soft paraffin and wool fats
- Regular use can:
  - reduce scale
  - enhance penetration of concomitant topical therapy
  - hydrate dry and cracked skin
- Soap should be avoided
TOPICAL THERAPIES:

Keratolytics
- OTC Drugs: E.g. Salicylic acid, Urea
- Help **dissolve keratin to soften** and lift psoriasis scales
- May **enhance penetration of other agents**

Salicylic Acid
- Promotes **removing of dead skin cells and reduces scaling**
- Sometimes combined with other medications, such as topical corticosteroids or coal tar, to increase its effectiveness.
- **Medicated shampoos and scalp solutions** to treat scalp psoriasis
TOPICAL THERAPIES:

Coal tar

- **Reduces Inflammation** but may cause **local skin irritation**.
- **Use is limited** because of distinctive smell and ability to stain clothing and skin

Dithranol

- **Anti-proliferative**, particularly effective in **thick plaque psoriasis**
- Initiate therapy at very low concentrations – **can burn skin**
- **Not suitable for face, flexures or genitals**
- Stains clothes permanently and skin temporarily
TOPICAL THERAPIES:

Retinoids [E.g. Tazarotene]

- Like other vitamin A derivatives, it normalizes DNA activity in skin cells and may **decrease inflammation**
- **Applied once daily in evening** for treatment of **chronic plaque psoriasis**
- Most common **side effect** is local skin irritation, increase sensitivity to sunlight
- Although the risk of **birth defects** is far lower for topical retinoids than for oral retinoids, tazarotene **isn't recommended in pregnant or breast-feeding**
TOPICAL THERAPIES:

Calcipotriol (Synthetic vitamin D analogue)

- For **chronic plaque-type psoriasis**
- Slow down the growth of skin cells
- Reverses abnormal keratinocytes changes by:
  - Inducing differentiation
  - Suppressing proliferation of keratinocytes
- Response may require 4–6 weeks
- **Adverse effects** include erythema and irritation
TOPICAL THERAPIES:

Corticosteroids

- Possess anti-inflammatory, anti-proliferative and immuno-modulatory properties
- Reduce superficial inflammation within plaques
- **Potency choice** depends on disease severity, location and patient preference
- **Adverse effects** associated with long-term use include:
  - Skin atrophy
  - Hypopigmentation
  - Rapid **relapse** or rebound on stopping therapy
  - Precipitation of **pustular psoriasis**
Calcipotriol / Betamethasone dipropionate ointment

- For **plaque-type psoriasis**
- Steroids and the combination of a steroid and vitamin D is the **most effective treatment** with the **least risk of side effects**
- Application of steroid or the **combination product responded** better to treatment than participants who used vitamin D alone
- **Side effects** of these treatments were **irritation, itching** and **skin pain** at the site of application
PHOTOTHERAPY

• For psoriasis resistant to topical therapy and covering > 10% of body surface area
• Brief, daily exposure of sunlight may improve psoriasis, but intense sun exposure can worsen symptoms
• Immunomodulatory and anti-inflammatory effects
• Three main types of phototherapy:
  – Broadband UVB
  – Narrowband UVB
  – PUVA (Psoralen administration before UVA exposure): 2–3 times/week
• Used to treat single patches, and widespread psoriasis
• Side effects: nausea, headache, redness, itching and dry skin
• Using a moisturizer may decrease these side effects.
SYSTEMIC THERAPIES

- Reserved for patients with widespread or severe psoriasis
- Potentially serious adverse effects and drug interactions
- Many require PBS authority prescription from dermatologist

Methotrexate

- Most commonly used systemic treatment for psoriasis
- Most common choice for acute pustular psoriasis
- Slows epidermal cell proliferation (decreasing the production of skin cells) and acts as immunosuppressant.
- It may also slow the progression of psoriatic arthritis
- Closely monitor kidney, liver and bone-marrow function
- Perform PASI score before starting treatment
SYSTEMIC THERAPIES:

CYCLOSPORIN

- A fat soluble peptide antibiotic
- **Immunosuppressive agent** so increases risk of infection & cancer
- For patients with **severe psoriasis that are refractory to other treatments**
- Closely monitor **blood elements, renal and liver function**
- **Disadvantages:** Nephrotoxicity
BIOLOGICAL AGENTS

• **Proteins** derived from living organisms
• For moderate-to-severe chronic plaque psoriasis who are candidates for phototherapy or systemic therapy
• Most administered **subcutaneously**
• Target key parts of immune system that drive psoriasis
• Biological agents include:
  – **Tumour necrosis factor-alpha (TNF-α) inhibitors**
    • Etanercept, Adalimumab, Infliximab
  
  – **Interleukin (IL-12 and IL-32) inhibitor**
    • Ustekinumab: (human anti-IL-12/IL-23 mAb)