MODERN DISEASE REVIEW


Psoriasis is a disease of the keratinization. In keratinization the live, nucleated basal cells of the epidermis are gradually changed to dead, enucleated horny cells. It forms the outermost layer of the epidermis known as stratum corneum. At the advent of keratinization progresses, the cellular constituents become fibrous and the cells become flattened as and when they move outwards.

Keratohyaline granules comprise a nebulous substantial rich in histidine. This protein is known as filaggrin because it causes clump of keratin subunits into arrays of filaments. The precursor of filaggrin, profilaggrin, gathers in keratohyaline granules. During the final stages of epidermal maturation, profilaggrin is transformed to filaggrin and the phosphate is detached. Defects in numerous steps in the course of keratinization may clue to cutaneous ailments, most of these genetically spread.

(IADVL Textbook of Dermatology. Page.799)

History

The biblical word ‘lepra’ was applied to several cutaneous sicknesses counting psoriasis, vitiligo, and alopecia areata. The Roman sage Aurelius Cornelius Celsus has ascribed with the first clinical description of Psoriasis. Galen used the word psoriasis and Robert Willan (1808) precisely illustrated it as a distinguishable entity. In 1841, Hebra definitively differentiated the clinical features of psoriasis from leprosy.


EPIDEMIOLOGICAL ASPECTS

Prevalence

Genetic and environmental factors greatly influence the clinical development of psoriasis. Further, patients with minimal clinical manifestations often do not seek medical attention. Most studies occurrences are based on data from clinical checkups, discussions, census studies and mail forms. Assessments of the incidence of psoriasis in different parts of the world vary from 0.1 to 3%.
Age of onset

Psoriasis is most common in the second to fourth decades of life however it can appear just afterward to birth or in old age. Indian studies have testified the highest incidence in the second decade or in the reproductive age group. A North Indian study found that the mean age of onset was higher for males than females (37 vs. 29 years).

Familial occurrence

A high familial occurrence of psoriasis (7%-36%) suggests that genetic factors play a role in its causative factors. In Kaur et al’s study, the mean age of onset disease in patient with family history was 23 years as compared to 28 years in others.

Sex ratio

Psoriasis happens with nearly equal incidence in males and females. However, a higher prevalence in males has been prominent in maximum Indian studies.

DEFINITION:

1. Psoriasis is a non-infectious, inflammatory disease of the skin, characterized by well-defined erythematous plaques with large, adherent, silvery scales.

2. Psoriasis is a common, chronic and non-infectious skin disease characterized by well-defined, slightly raised, dry erythematous macules with scales and typical extensor distribution.

3. Psoriasis is a genetically determined disease of the skin consisting of well defined, pink or dull red lesions surrounded by a chronic relapsing nature and variable clinical features.
ETIOPATHOGENESIS:

Genetic factors

Various studies supports the conclusion that genetic predisposition has a major role in the pathogenesis of psoriasis. Genetic predisposition does not mean that all will have a history of genetic influence; other factors such as injury of infection may act together with genetic predisposition to start the disease process.

Supporting evidence for genetic predisposition includes:

- There is a higher frequency of psoriasis in relatives of persons with psoriasis, ‘familial tendency’ to grow the disease; but, in some people with psoriasis there is no such history.
- There is greater incidence of psoriasis in offspring when one or both parents have psoriasis.
- In studies of twins, psoriasis is more possible to seem in both identical twins than in both non identical twins, a conclusion that also confirms that more than one gene must be innate to establish genetic susceptibility for psoriasis.

THE EPIDERMAL CELL CYCLE IN PSORIASIS:

The epidermis is chiefly comprises of three cell sections: a non-viable compartment comprising of the horny layer, a feasible distinguished cell section encompassing of the stratum Malpighi and the stratum granulosum, and the germinative cell section. Normally about 10% of the germinative cells go through mitosis. The intermission between the division of a basal cell and the next one of the daughter cell is called the cell cycle time. The cell cycle have four stages. (1) Mitotic phase, (2) G1 interphase, (3) synthetic phase and (4) G2 interphase.

After mitosis, the cell move in the G1 phase where biochemical preparation for the succeeding phase follows. During the synthetic the DNA couples, during the G2 phase a cell synthesizes RNA and proteins and prepares for the next mitosis. Still the exact duration of the cell cycle in psoriasis is not clear. Maximum values are established on incidental calculations with innate defects. The transit time of cells from the basal cell sheet to the uppermost row of squamous cells exhibited a shortening from 13 days in normal epidermis to only 2 days in psoriatic epidermis.

ARACHINIC ACID METABOLISM AND PSORIASIS:

Psoriasis occurs at the sites of trauma. This may be instigation of the arachidonic acid cascade with succeeding release of numerous mediators corresponding leukotrienes, prostaglandins and 12-hydroxyeicosatetraenoic acid. Psoriasis epidermis comprises raised levels of 12-hydroxyeicosatetraenoic acid and arachidonic acid. It seems that psoriatic skin has an endogenous inhibitor of cyclo-oxygen are causing diversion of arachidonic acid to the lipoxygenase pathway.

Drugs like salicylates, indomethacin, oxyphenobutazone, phenylbutazone and ibuprofen have been informed to aggravate psoriasis.


POLYAMINES AND PSORIASIS:

Polyamines are low molecular weight organic amines such as spermidine. They play a key role in the regulation of cellular multiplication and are amplified in the involved and uninvolved skin of psoriasis. Treatments with PUVA, retinoid and topical corticosteroids decrease the level of polyamines in psoriasis. Henceforth it is conceivable that these polyamines has a role in the course of psoriasis.


THE IMMUNOLOGIC BASIS OF PSORIASIS:

It is controversial if some Immunologic mechanisms play a role in the etiopathogenesis of psoriasis. Maximum treatments like corticosteroids, PUVA methotrexate and retinoids are helpful in the management of psoriasis. They have intense immunosuppressive effects. A significant mediator system, supposed to be involved in the pathology of psoriasis, is stratum corneum antigen antibody reaction. In a psoriasis-prone person, vasodilatation takes place following trauma or infection, and is accompanied by an invasion of neutrophils into the epidermis. Proteolytic enzymes
released by neutrophils expose the stratum corneum antigen. Stratum corneum antibodies escape into the epidermis and fix the freshly exposed antigen. It is observed that stratum corneum antibodies are frequently found in the horny layer of psoriatic lesions. Generally IgG deposits are found, though additional immunoglobulins and complement components are also seen. The antigen-antibody interactions generate the complement cascade and advances inflammatory reactions. It is still unknown how the immunological events cause the unusual multiplying and variation of epidermal cells characteristic of psoriasis.

Another opinion by the immunologists is the basal cell layer of the epidermis. In normal being the basal cell nuclear material is not predictable by the immunological system. A genetic copy of suppressor T cells stops such recognition. It is hypothesized that a genetic fault or a virus leads to malfunctioning of such a clone of suppressor cells, leading to the recognition of basal cell nuclear material as antigen. Consequently antibodies are formed in contradiction of this antigen that leading to an immunological reaction that results in the epidermal cell multiplication typical of psoriasis.

**TRIGGERING FACTORS:**

Psoriasis is a chronic ailment marked by periods of remissions and exacerbations. Remissions may continue for a month to several years.

Local factors:

Psoriasis lesions tend to develop at sites of injury to the skin. The Koebner phenomenon refers to the initiation of lesions by cutaneous trauma. Dr. Koebner described a patient with psoriasis in the 19th Century who developed new lesions where his horse wounded him. Only epidermal trauma does not induce the lesions; involvement of papillary layer is must. The trauma may be physical, chemical, or of any other nature. This phenomenon may be elicited at sites of operation wounds, vaccination and other skin lesions. This disease may occur as a Koebner phenomenon at the sites of bites (insects, animals), burns, drug reactions, skin tests etc.

Skin Trauma such as:

- Acupuncture
- Bites
- Bruises
- Burns
- Chemical irritation
- Cuts and scrapes
- Pressure against the skin
- Shaving
- Tattoos
- Vaccinations


**SEASONAL VARIATION:**

The majority patients (89% in one study) experience worsening of their skin lesions throughout winter. In humid condition is usually beneficial. Sunlight may worsen psoriasis in some but improves it in many.

(Farber EM, NallMI. The natural history of psoriasis in 5,600 patients. Dermatological 1974;148:1-18.)

**PREGNANCY:**

Psoriasis may remit during the time of pregnancy. Rarely, generalized pustular psoriasis may be precipitated during pregnancy most likely due to increased levels of progesterone at the latter half of pregnancy.

(Sharma T, Sepha GC. Psoriasis- clinical study..Indian J. Dermatol Venereol 1964; 30:191-197.)

**EMOTIONAL STRESS:**

Psoriasis is quite ‘sensitive’ than many other skin diseases. Lots of hectic events of daily life may aggravate psoriasis. The diseases itself can cause a reactive depression in the patient, which could promote the deterioration of psoriasis.

Stress might provoke alterations in the psoriatic lesion by increasing the neuropeptide content with a concomitant decline in activity of neuropeptide degrading enzymes particularly mast cell chymase.

**DRUGS THAT EXACERBATE PSORIASIS:**

Numerous drugs can aggravate psoriasis. Beta adrenoreceptor blocking drugs like propranolol, metoprolol etc. induce a papulosquamous eruption that resembles psoriasis.

Contrary to popular belief and some early unreliable reports, nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, meclofenate, phenylbutazone and ibuprofen, which are commonly used in orthopedics and surgery, have not been reported to either precipitate or exacerbate psoriasis.

Prompt withdrawal of corticosteroid with psoriasis patient may result in precipitation of generalized pustular psoriasis or exfoliative dermatitis. Seldom, topical corticosteroids cause such exacerbations.

Chloroquine also exacerbates psoriasis, often leading to exfoliative dermatitis, but the exact mechanism of such exacerbation is not fully understood.

**CLINICAL FEATURE:**

Psoriasis is characterized by well distinct, erythromatous, dry, flaking papules and plaques of various sizes ranging from a pinhead to palm-size. Hardly, lilaceous or bluish hue lesions are seen on the legs or trunk.

The lesions are plentiful, dry and silvery white or micaceous. Whiteness is because of air trapped in between the layers of scales.

When the scales are scraped off, the basement membrane of the skin is exposed and is seen because of dilated capillaries. On further scarping, there is visibility of multiple bleeding points. This is known as Auspitz sign. The erythema of the lesions results from dilatation of the papillary capillaries.

Each and every lesion starts as a papule and outspreads periphery to form nummular plaques, many such nummular lesions unite to form large plaques.
CLASSIFICATION:
Psoriasis can be clinically classified as follows:

2. Chronic plaque psoriasis.
3. Exfoliative psoriasis.
4. Pustular psoriasis.
5. Psoriasis unguis.
6. Arthropathic psoriasis.

**Guttate psoriasis:** Frequently common in children and adolescents and may be the first sign of psoriasis. The lesions often appear quickly and lesions are droplet shaped and small.

**Chronic plaque psoriasis:**
This is the commonest type of psoriasis. It is manifested with coin sized to large palm-sized well-defined erythematous plaques. The lesions are steady and remain unaffected for a longer period. Extensor surfaces of the body, elbows, lumbosacral area and back are usually involved.

**Exfoliative psoriasis:**
It is characterized by widespread erythema and scaling usually triggered by sudden withdrawal of systematic corticosteroids or by over usage with tar or diathranol.

**Pustular psoriasis:**
When Psoriasis is accompanied with tiny, superficial, sterile pustules, then called as pustular psoriasis. It is triggered by over treatment with topical tar or potent steroids or corticosteroids.

**Psoriasis unguis:**
When Psoriasis affects nail then it is known as Psoriasis unguis. The common changes are pitting of the nail plate, split-up of the nail bed and crumbing of nail plate. If the whole nail matrix is involved in the psoriasis process, the nail plate becomes opaque, discolored and irregular and may be thickened.
Psoriatic arthritis:
Psoriatic arthritis an inflammatory condition of the joints associated with psoriasis. Usually with a negative rheumatoid factors. Arthritis occur about 5-10% of patients with psoriasis. Like cutaneous psoriasis, it is a genetically determine disorder. Environmental influences like strain may precipitate arthritis.
(Moll JHM, Wright V. Psoriatic arthritis. Semin Arth Rheumat 1973;3:55-78.)

REGIONAL VARIATIONS:
- Scalp
- Face
- Eyes
- Body flexures
- Scrotum
- Lumbosacral area
- Napkin area
- Palms and soles
- Joints.

TREATMENT:
The progress and prognosis in particular patients are impulsive. A drug that completely cures psoriasis is yet to be discovered. Numerous topical and systemic treatments may give suggestive relief to the patient and may delay remission.
Four types of treatment are available-
  a) Topical agent: (Emolients) corticosterone, vitamins D agonist (calcipotrene), weak tar or Diathranol preparation.
  b) PUVA means psoralen+ UVA or ultraviolet B therapies.
  c) Systemic agent: Immunosuppressive – Ciclosporin, Retinoids – Tazarotene
  d) Intensive treatment with topical agent and UV-rays under medical observation.
Treatment of psoriasis depends on the type, site and spreads of the disease.
All patients are instructed to avoid unnecessary drying and irritation of the skin and to sustain adequate cutaneous hydration.
Localized plaque type psoriasis can be managed with

1. Mid potency topical glucocorticoid.
   Side effect: Long term use often accompany with loss of efficacy or atrophy of the skin.
2. Topical vitamine-D analog calcipotriene.
3. Topical retinoids.
   They have largely replaced coaltar, anthrailine, salisyalic acid.

In wide spread disease-
Oral glucocorticoid should not be used for treatment of Psoriasis due to the potential for developing life threatening pustular psoriasis when the treatment is withdrawn.

1. Ultra-violet B (UV-B): Rarely alone or in combination with coat tar and anthraline can be administered.
2. Ultra-violet A (UV-A): Spectrum with either oral or topical psoralen (PUVA) is also extremely effective but long-term use leads to-
   a) Squamous cell carcinoma.
   b) Melanoma of skin
   Side effect: Liver toxicity, Bone marrow depression.
4. Synthetic Retionid: Acitertin
   Side Effect: Potent teratogenic and should not be used in female patient of child bearing age.
5. As it is a T-cell mediated disorder.
   a) Cyclosporin- Is highly effective in selected group of patient with severe disease.
   b) Etanercept- A tumour necrosis factor α- (TNF- α) inhibitor is now approved for the psoriatic arthritis and psoriasis.
   c) Other agent in clinical trial target TNF- α and other pro inflammatory cytokines, T-cell activation and lymphocytes trafficking to suppress inflammation in psoriasis.