Derma Team 436

Papulosquamous Diseases

Objectives :

NOT GIVEN

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Before you start.. CHECK THE EDITING FILE

Sources:doctor's slides and notes

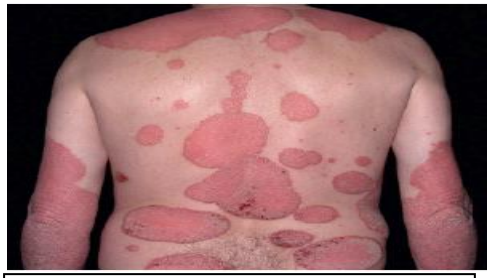
[Color index: Important| gold|doctor notes|Extra]

Papulosquamous Diseases:

- The term squamous refers to scaling that represents thick stratum implies an abnormal keratinization process.
- Papulosquamous diseases are group of disorders characterized by scaly papules and plaques:
  1- Psoriasis.
  2- Lichen planus.
  3- Pityriasis rosea.

1) Psoriasis:

Psoriasis is an immune-mediated polygenic skin disorder. Various environmental triggering factors, e.g. trauma , stress, infections and medications, may elicit disease in genetically predisposed individuals



- Chronic plaque type
- Well demarcated erythematous scaly plaques

Epidemiology:

- 2% of population (0.7% of Asian/African) (more common in Caucasians)
- 0.7% juvenile psoriasis
- Only 25% have severe psoriasis
- Bimodal disease (20-30s/50-60s) (has two age peaks)
- Two third of patients have family history of psoriasis(significant family history)
- Child risk : one parent 14% two parent 40%

Genetic predisposition:

- Nine psoriasis susceptibility regions (PSORS1–9) in different chromosomal locations.
- PSORS1 (on chromosome 6p), account for up to 50% of psoriasis risk.
- PSORS1 contains genes such as HLA-Cw6.(from every two patients, one has this gene)

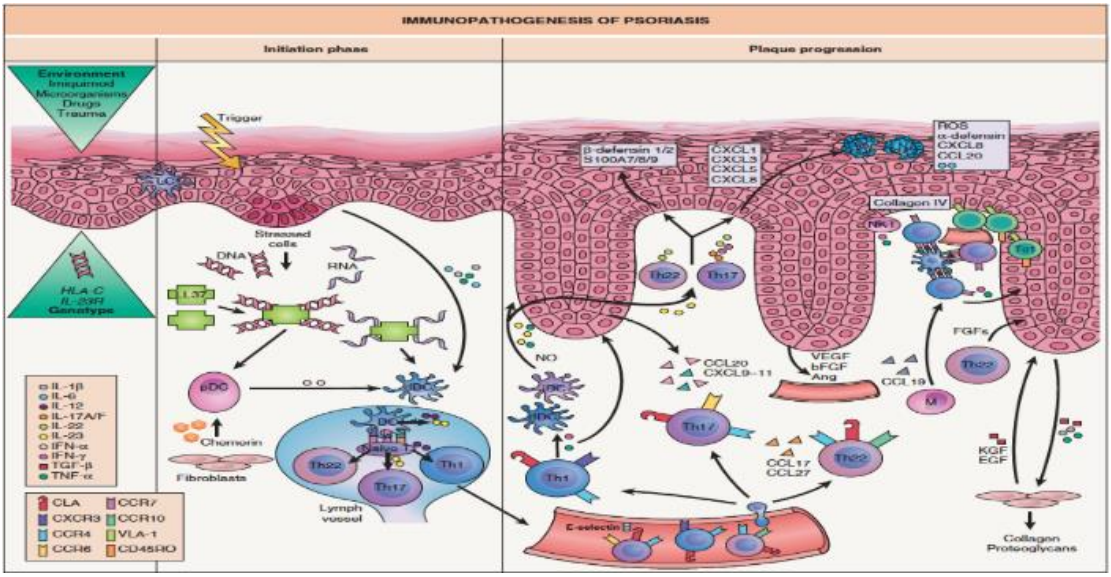
HLA-Cw6 is strongly linked to the age of onset of psoriasis.

- 90% of the patients with early-onset psoriasis
- 50% of the patients with late-onset psoriasis
- Early-onset psoriasis, positive family history and expression of HLA-Cw6 (type I psoriasis)
- Late-onset disease, no family history and a lack of expression of HLA-Cw6 (type II psoriasis)

PSORIASIS SUSCEPTIBILITY GENES					
Class	**Gene(s)**	**Pathway**	**Protein function**	**OR**	**Disease overlap**
Skin specific	*LCE3B/3C/3D*	Skin barrier formation	KC structural protein	1.26	
	KLF4	Skin barrier formation IL-17 signaling	Transcription factor	1.12	
	ETS1	Unknown	Transcription factor	1.12	
Innate immunity	*IL-28RA*	IFN signaling	IL-29 receptor subunit	1.21	
	IFIH1	IFN signaling	Innate antiviral receptor	1.27	
	RNF114	IFN signaling	E3 ubiquitin ligase	1.16	
	ELMO1	IFN signaling	Involved in TLR-mediated IFN-α signaling	1.11	
	DDX58	IFN signaling	Innate antiviral receptor	1.11	
	NOS2	Inflammation	Induced nitric oxide synthase	1.22	
	REL	NF-κB signaling	NF-κB subunit	1.17	RA
	TNIP1	NF-κB signaling	Inhibitor of TNF-induced NF-κB activation	1.59	
	TNFAIP3	NF-κB signaling	Inhibitor of TNF-induced NF-κB activation	1.23	
	NFKBIA	NF-κB signaling	Inhibitor of NF-κB activation	1.16	
	FBXL19	NF-κB signaling	Putative inhibitor of NF-κB activation	1.16	
	CARD14	NF-κB signaling	Activator of NF-κB pathway	1.11	
	*CARMI1**	NF-κB signaling	Transcriptional coactivator of NF-κB	1.17	
	*UBE2L3**	NF-κB signaling	Ubiquitin-conjugating enzyme	1.13	Cel, RA, Cro
At the interface between innate and adaptive immunity	*TRAF3IP3*	IL-23/IL-17 axis NF-κB signaling	Adaptor molecule mediating IL-17-induced NF-κB activation	1.52	
	IL-12B	IL-23/IL-17 axis	Shared subunit of IL-12/IL-23	1.58	
	IL-23A	IL-23/IL-17 axis	Unique subunit of IL-23	1.39	
	TYK2	IL-23/IL-17 axis IFN signaling	Tyrosine kinase associated with cytokines receptors	1.88	
	HLA-C	Antigen presentation	MHC class 1 antigen	4.32	
	ERAP1	Antigen presentation	Enzyme processing MHC class 1 ligands	1.2	AS
Adaptive immunity	*IL-23R*	IL-23/IL-17 axis	Unique subunit of IL-23 receptor complex	1.52	AS, UC, Cro
	*STAT3**	IL-23/IL-17 axis	Transcription factor	1.15	
	*IRF4**	IL-17 signaling	Transcription factor	1.12	
	RUNX3	T-bet pathway	Transcription factor	1.13	AS, Cel
	IL-4/IL-13	IL-4/IL-13 signaling	IL-4 and IL-13 cytokines	1.18	
	*TNFRSF9**	T-cell differentiation	Adaptor molecule	1.13	
	TAGAP	T-cell activation	Rho GTPase-activating protein	1.12	RA
	ZMIZ1	TGF-β signaling	Protein inhibitor of activated STAT (PIAS) family of proteins	1.1	MS
	SOCS1	Type II IFN signaling	Suppressor of cytokine signaling	1.13	
Other	*PRDX5*	Intracellular redox signaling	Antioxidant enzyme	1.09	
	B3GNT2	Carbohydrate metabolism	Enzyme	1.12	AS
	*MBD2**	Unknown	Transcriptional repressor	1.12	
	ZC3H12C	Unknown	Zinc finger protein with putative RNase function	1.14	

*Most notable gene mapped by the identified SNP.

immunopathogenesis:



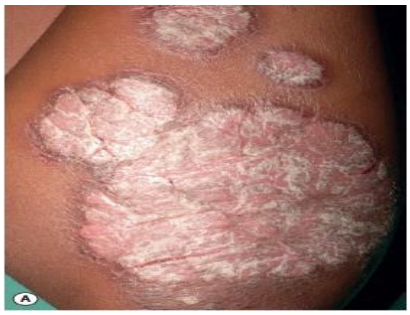
In psoriasis Th1 is dominant with some cytotoxic cells

IL-2 & 12

Triggers:

- Trauma
- Stress
- Infections: e.g. Streptococcal group A infections, especially pharyngitis(most common infection to cause psoriasis)
- Drugs: e.g. lithium, IFNs, β-blockers, and antimalarial (these four drugs are very important(they cause psoriasis), IFNs and antimalarial drugs cause lichen planus)
- Hypocalcemia has been reported to be a triggering factor for generalized pustular psoriasis.(could happen in pregnancy)

1- chronic plaque psoriasis: MOST COMMON 80-90% of all psoriasis



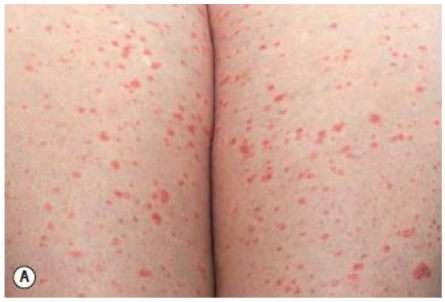
If scratched causes candle sign
if pealed causes auspitz sign

Symmetric sharply defined erythematous plaques with thick silvery scale over the scalp, elbows, knees and lumbosacral area which is associated sometimes with hyperketatosis of the hands and feet

Has these signs:

1- Auspitz sign: when removing a scale pinpoint bleeding occurs which represents the dilated capillaries
2- Woronoff sign: hypopigmented rim due to topical steroids use
3- Candle sign

Types of chronic plaque psoriasis:



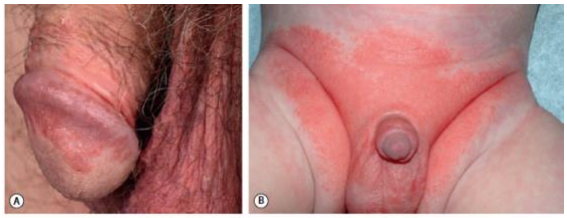
Guttate psoriasis

A- Guttate psoriasis:

more common in children and adolescents and preceded by an upper respiratory tract infection (especially GAS nasopharyngitis, it can be treated with antibiotics(penicillin) and it might treat it)

B- Flexural psoriasis:

affects Axillae, groin and genital areas and presents as well demarcated erythematous plaque without scales.

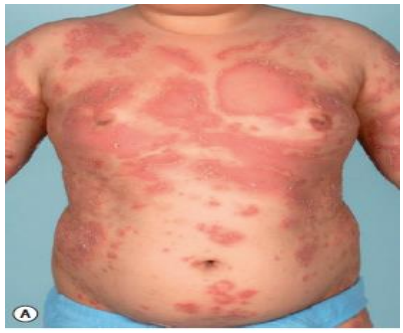


Flexural psoriasis. notice there isn't any scaling

C- sebopsoraisis:

indeterminate stage (too advanced for us)

2- Pustular psoriasis :(all are the same but named according to site of involvement)



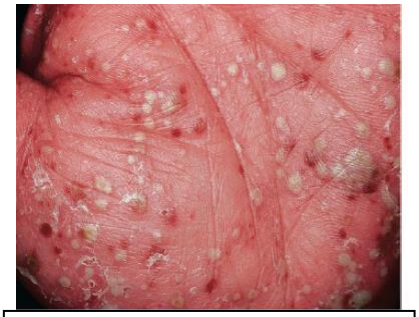
Pustular psoriasis. sheets of erythema with pustules

A- Generalized pustular psoriasis (von Zumbusch pattern):

ill patient with constitutional symptoms present with generalized abrupt painful eruption with erythema and pustulation starting over the intertriginous areas and trunk. (sometimes the pustules look brown here)

B- Palmopalnter pustulosis:

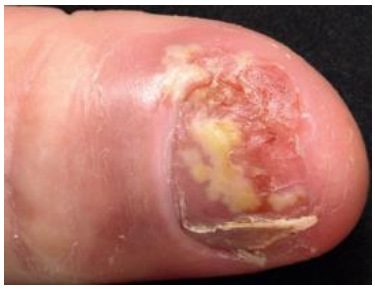
Associated with SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis)



Palmoplantar pustulosis. some pustules are brown

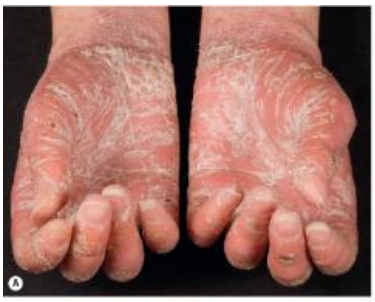
C- Acrodermatitis continua of Hallopeau:

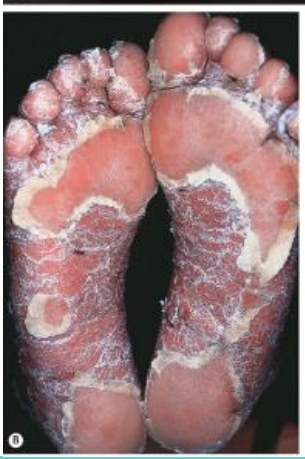
pustules over the distal portions of the fingers followed by scaling and crust formation. Pustules may also form subungual which might cause shedding of nail plates.

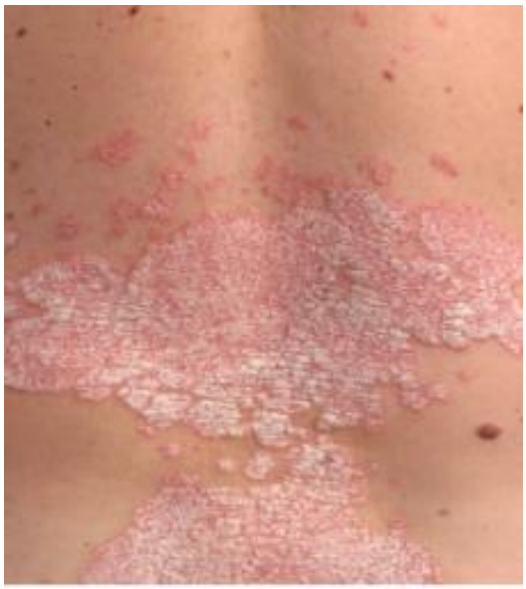


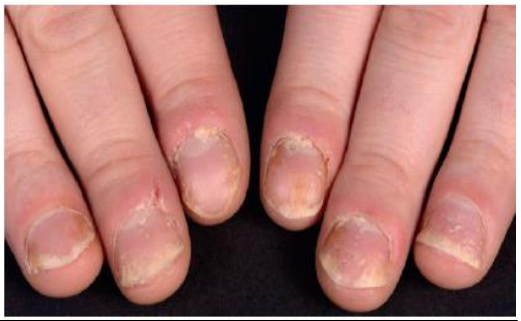
Acrodermatitis

3- Erythrodermic Psoriasis EMERGANCY









Clinical Features:

A- **Nail** : click for helpful material

- Involved in 80% of patients

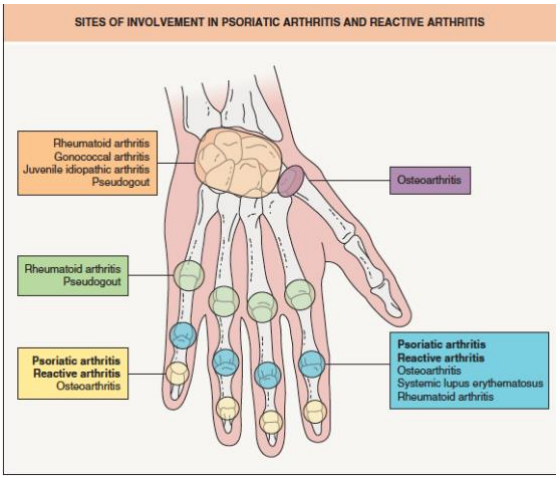
Patients with nail involvement appear to have an increased incidence of psoriatic arthritis.

1- Pitting (parakeratosis of the nail matrix)
2- Oil-spot (leukocytes beneath the nail plate)
3- Onycholysis with subungual hyperkeratosis (parakeratosis of the distal nail bed)
4- Thickening

- Pitting
- Oil-spot
- Onycholysis
- subungual hyperkeratosis and thickening of the nail in general

B- Oral mucosa:

Migratory annular erythematous lesions with hydrated white scale over the tongue (geographic tongue) observed mainly in pustular psoriasis patients. psoriasis rarely affects mucosa, and most common presentation in mucosa is geographic tongue



C- Psoriatic Arthritis:

- 25% of patients

Asymmetric mono-oligoarthritis (most common type) Inflammation of the DIP and PIP joints of the hands and feet Involvement of both the DIP and PIP joints of a single digit can result in "sausage" digit asymmetrical oligo-arthritis over the distal small joints(most common prenstation)

Least common presentations:

1. Rheumatoid arthritis-like (Symmetric polyarthritis that involves small and medium-sized joints)
2. Arthritis Mutilans (severe deformity in joints could cause shortening of digits)
3. Spondylitis and Sacroiliit

D- Associations:

- Hyperlipidemia and metabolic syndrome
- Atherosclerosis
- Non-alcoholic steatohepatitis
- Depression
- Substance addiction
- Parkinsonism

Fig. 8.19 Spongiform pustule of Kogoj. A collection of neutrophils is seen within the upper stratum spinosum. Courtesy Lorenzo Cerroni, MD.

Pathology:

- Superficial peri vascular infiltrate(lymphocytes)
- Dilated vessels
- Even elongation

Classically, Superficial perivascular lymphocytic infiltrate with even elongation of rete ridges ,dilated capillaries in papillary dermis which associated with spongiosis, acanthosis and parakeratosis .
In late lesions, accumulation of neutrophils within a spongiotic pustule "spongiform pustule of Kogoj" or sub-corneal accumulation of neutrophil "microabscess of Munro" (exaggerated in pustular psoriasis)

Treatment:

1- **Focal disease:** topical corticosteroid and calcipotriene are better than other drugs and even better when together

- Topical corticosteroids
- VitD3 analogues(calcipotriene)
- Coal tar
- Anthralin
- Tazarotene
- 10% salicylic acid

2- **Widespread disease:** systemic steroids are contraindicated for treating psoriasis because of conversion(turns chronic plaque type into pustular). can be used in pustular psoriasis of pregnancy for safety(biologic therapy is safer)

Chronic plaque type	Pustular type
Methotrexate first line	Retinoids(Acitretin) first line
NBUVB/PUVA	Cyclosporine
Anti-TNF	Methotrexate
Anti-IL 12/23	NBUVB/PUVA
Anti-IL 17A	
Cyclosporine	
Retinoids (Acitretin)	

2) Lichen planus:

Lichen Planus is an immune-mediated polygenic skin disorder. Various environmental triggering factors, e.g. Stress, infections and medications may elicit the disease in genetically predisposed individuals.

Epidemiology:

- Cutaneous Lichen planus affects less than 1% of population.
- Oral Lichen planus (1-5%).
- It usually affect adult (30-60 years) but it can rarely affect children.
- It doesn't have any gender/race predilection.
- Familial cases are underestimated (some about 10%)
- 75% of cutaneous Lichen planus have mucosal involvment sp. Oral
- 25% of Oral Lichen planus have cutaneous Lichen planus.Some expert consider them separate disease

Causes and Genetic predisposition:

- Idiopathic complex polygenetic condition

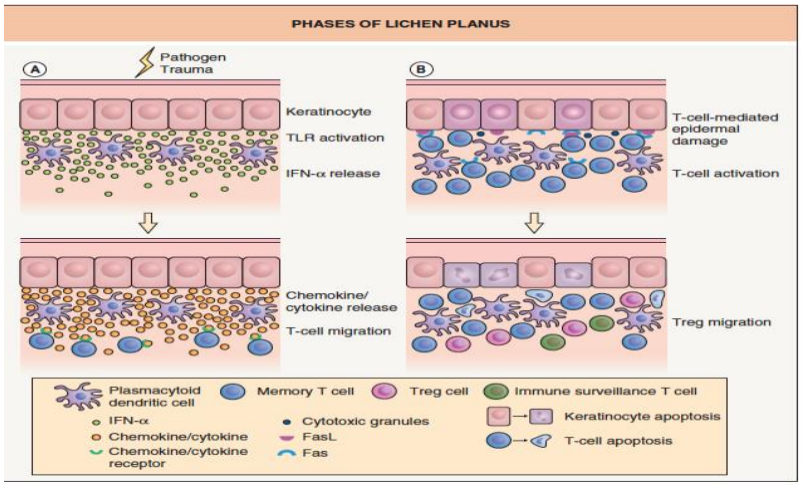
*Six single nucleotide polymorphisms (SNPs) were found to be associated the HLA-DQB1*05:01 haplotype associated with Lichen planus.
*HLA-A5 ,HLA-A3,147,148, HLA-B7,143 HLA-DR1,149,150 HLA-DR10 in Arab population
HLA-DRB1*01:01 in Sardinian &Mexican population

Antigenic Triggers: (it's associated with liver disease)

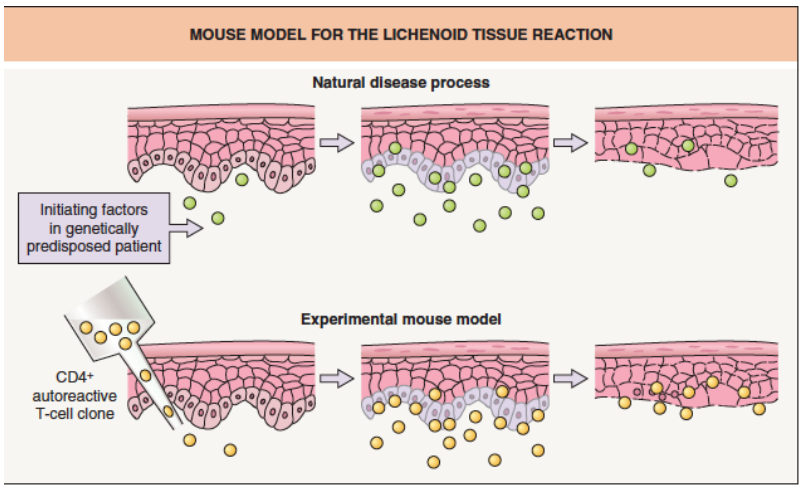
- **Pathogens** (Viral hepatitis-HCV)
- geographic variation
- IFN therapy initiate or worsen LP
- Liver disease e.g. sclerosing cholangitis chronic liver disease
- **Vaccination**
- **Medication** (Lichenoid drug eruption)(antimalarials and IFNs)

- **Contact sensitizer** e.g. mercury amalgam(changing it to ceramic will improve the disease), color film developers, methacrylic acid esters, dimethylfumarate in sofas and radiotherapy.

immunopathogenesis:



Cytotoxic cells predominate here with Th cells



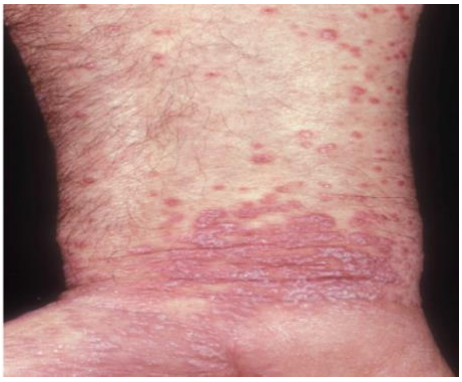
Clinical presentation:

Itchy (rubbing)not scratching pruritic polygonal purple flat-toped papule & plaques with Wickham's striae is pathognomic over flexural surface of extremities ,wrist, legs, lower abdomen and genitalia. pruritic well defined flat topped violaceous plaques and papules

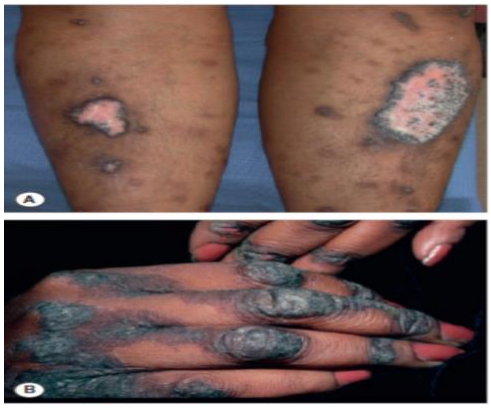
Variants:

By Morphology	By Configuration
Hypertrophic-leg thickening and scaling	Annular-penis few lesion and doesn't become lichen planus and involve other areas
Atrophic	Linear
Ulcerative-palm/soles ulceration	
Bullous	

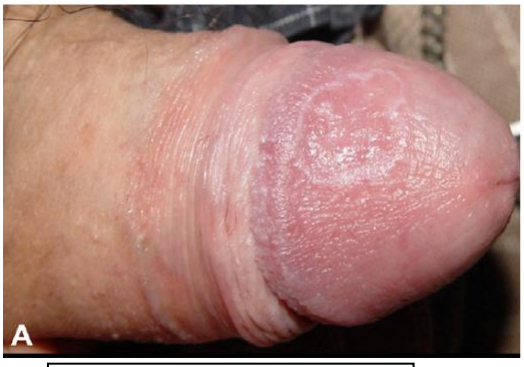
- Important types are hypertrophic, ulcerative, annular and pigmentosus
- Lichenoid morphology means flat topped



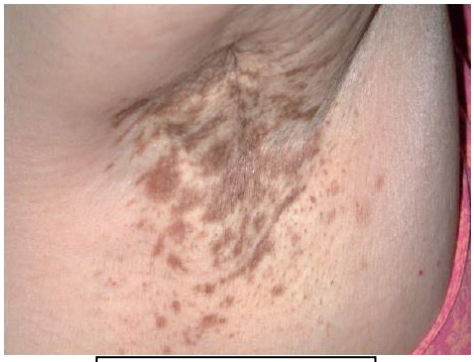
Pruritic flat topped violaceous plaques and papules in the wrist



Lichen planus pigmentosus(generalized) and actinicus(sun exposed areas)
Well defined slate gray patches sometimes with violaceous rim or hypopigmented halo, but it's not in the picture



Annular Lichen planus of penis (never progress)



Pigmentosus (no rim neither halo)

Lichen planus Pigmentosus:

It is more common in dark skin people and it presents as well-defined brown to slate-gray patchs with/without violaceous indurated border or hypopigmented halo over axilla/groin & proximal limbs

Lichen planus Actinicus:

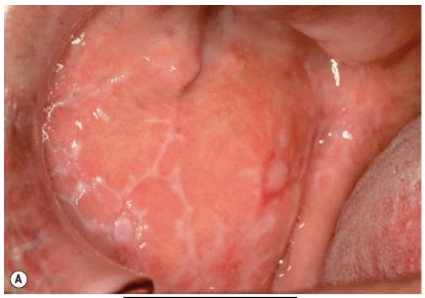
(sun exposed area) same disease and presentation as Lichen planus Pigmentosus but named according to site of involvement.

Mucosal Lichen planus:

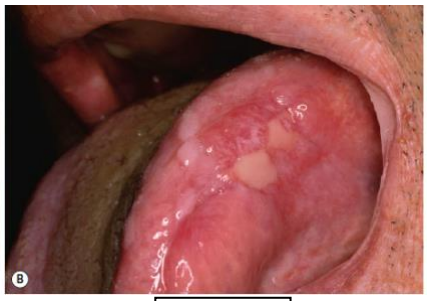
The most common site of involvment is the oral mucosa which usually present as well-defined reticulated violaceous plaques over buccal mucosa, lips and gingiva.

- **Reticulated**
- **Erosive** (less than 1% risk of SCC)
- **Atrophic**
- **Hypertrophic**

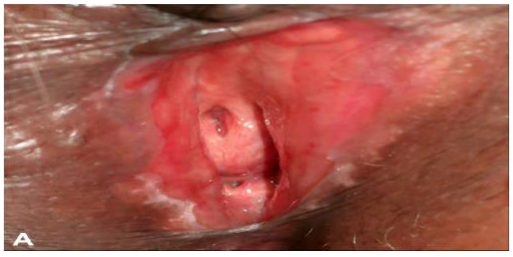
It can affect other mucosal surfaces e.g. vulvar, vaginal and penile- Vulvovaginogingival syndrome sever erosive



reticulated



erosive

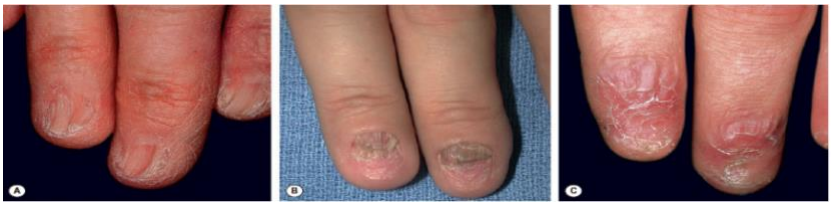


Erosive vulvovaginitis

Nail Lichen planus:

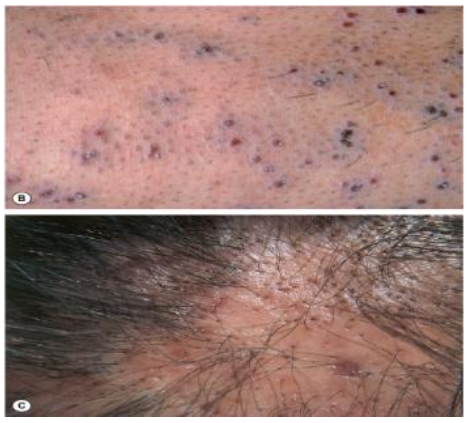
Nail involvment usually occur in 20% and it is more common in children

- Dorsal Pteryigum
- Lateral thinning
- Longitudinal ridging
- Distal splitting
- thinning of the nail
- 20 Nail Dystrophy when all 20 nails are destroyed. Can be caused by other diseases



Lichen planopilaris-LPP(scarring):

It usually present as multiple, keratotic plugs surrounded by a narrow violaceous rim are observed primarily on the scalp, although other hair bearing areas can also be affected. The inflammatory process usually result in scarring alopecia when it doesn't cause scarring it's called lichen spinulosus



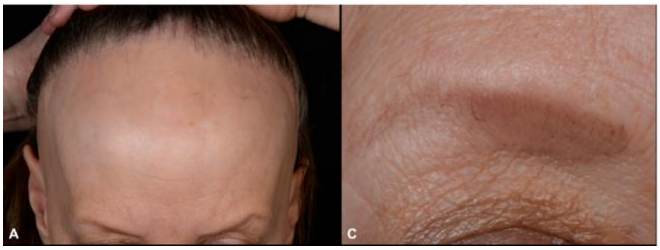
Lichen planopilaris
(Later causes scarring)

Graham-Little–Piccardi–Lassueur syndrome:

Is a Triad of:
(1) non-scarring alopecia of pubic and axillary hairs and disseminated spinous or acuminated follicular papules
(2) Typical cutaneous or mucosal LP
(3) Scarring alopecia of the scalp

Frontal fibrosing alopecia:

- It usually affect postmenopausal female
- It presents as frontal hair-line scarring alopecia with eyebrows thinning



Lichnoid drug eruption:

It is a drug eruption that resemble Lichen planus with the following clinical differences

- Morphology: more psoriasiform/eczematous
- Distribution: start as photo-distributed then generalized
- Usually no mucosal involvment and Wickham's striae

It can appear anytime between weeks and years after exposure (commonly diuretics cause it)

FEATURES FOR DISTINGUISHING LICHENOID DRUG ERUPTION FROM LICHEN PLANUS

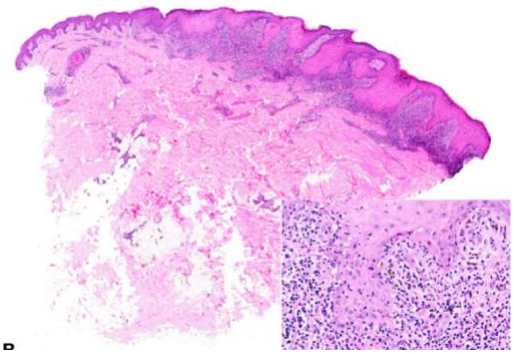
Feature	Lichenoid drug eruption	Idiopathic lichen planus
Mean age	65 years	50 years
Location	More generalized (including the trunk) and symmetric; often spares the "classic" sites of LP	Wrists, flexor forearms, presacral area, lower legs, genitalia
Morphology	More eczematous, psoriasiform or pityriasis rosea-like	Shiny, flat-topped, polygonal, violaceous papules
Wickham striae	Uncommon	Present
Hyperpigmentation	Very common, sometimes persistent	Common
Photodistribution	Frequent*	Unusual
Mucous membranes	Usually spared	Often involved
Histology	Varying degree of eosinophilic and/or plasma cell infiltrates	Eosinophils and plasma cells uncommon
	Deep perivascular infiltrate may be present (<50% of cases)	Dense band-like infiltrate of lymphocytes in the papillary dermis
	Focal parakeratosis and focal interruption of the granular layer	Parakeratosis uncommon
	Cytoid bodies in cornified, granular and upper spinous layers	Cytoid bodies in lower spinous layer

*Especially with medications such as hydrochlorothiazide.

Pathology:

1- Classic Lichen planus pathology:

- Superficial lymphocytic infiltrate with vacuolar interface reaction at the DEJ with dyskeratotic keratinocyte (Civatte bodies) & colloid bodies which is associated with "wedge-shaped" hypergranulosis (Wickham's striae) and "saw-tooth" rete ridges.



2- Lichenoid drug eruption:

The infiltrate is more deep with eosinophils/plasma cell with the presence of parakeratosis.

Lichen planus course:

It follow a relatively short course with relapse/remit nature that self-limit usually within 1-2 years except for oral and follicular LP which tend to be more chronic.
Leave very bad pigmentation

Treatment:

- **Focal**
- Topical corticosteroids
- Intralesional corticosteroids -LPP

- **Generalized**
  - Phototherapy
    - NBUVB/PUVA
  - Systemic therapy
    - Systemic Corticosteroids
    - Systemic Retinoids e.g. Acitretin
    - Antimalaria- Hydroxychloroquine- LPP can treat it and cause
    - Immunosuppressive therapy- MTX
    - Cyclosporine

3) PITYRIASIS ROSEA:

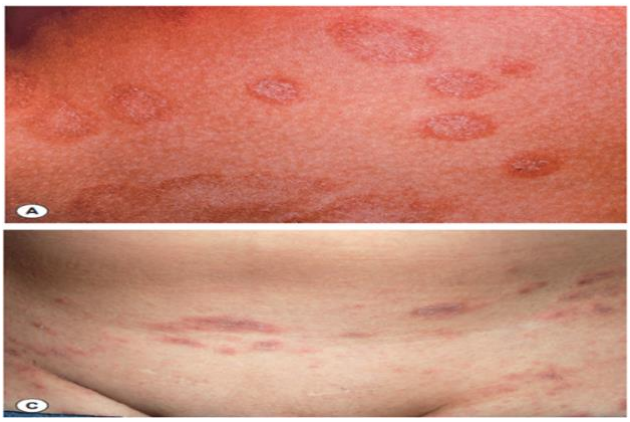
Epidemiology:

PITYRIASIS ROSEA is a common acute self-limiting exanthematous eruption that usually affect adolescent (10-30 years).
It doesn't have any gender/race predilection. once a life usually

Etiology:

- The etiology of PITYRIASIS ROSEA is unknown but most expert believe that the reactivation of HHV6/7 play a significant rule in the pathogenesis of the disease.
- Although, PITYRIASIS ROSEA can be seen all year around, it is more frequent in winter, fall and spring.

Typical PITYRIASIS ROSEA: only 50% are typical

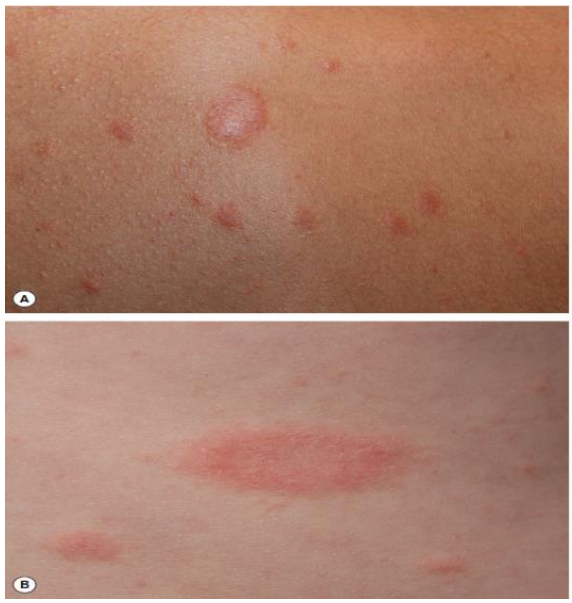


Oval pinkish collarette scales(pointing inwards)

Single well-defined oval (4cm) pink-erythematous patch with collarette scale over the trunk/proximal limbs (Herald patch 50%) when it's large it called PITYRIASIS ROSEA gigantea followed after average of 2 weeks with similar daughter lesions on the trunk /proximal limbs(charismas tree) with whole illness ranging between 6-12 weeks

- 75% complain of pruritus
- 75% complain of Viral prodrome
- 10% oral lesions : erosion/ulcer (most common), purpura and erythematous patch

Atypical PITYRIASIS ROSEA:



- Herald patch

  No

  Multiple
- Morphology

  papular common in dark skin people and children

  vesicular

  Some PITYRIASIS ROSEA have purpura or Targetoid lesion
- Distribution

  PITYRIASIS ROSEA Inversa affect axilla, groin and distal extremities

Course and duration:

- Persistent PITYRIASIS ROSEA duration longer that 12 weeks and usually up to 6 months with aggressive course and presentation.

- Relapsing PITYRIASIS ROSEA more than estimated (5%) but carry a mild and shorter course with few attacks over 3-5 years duration

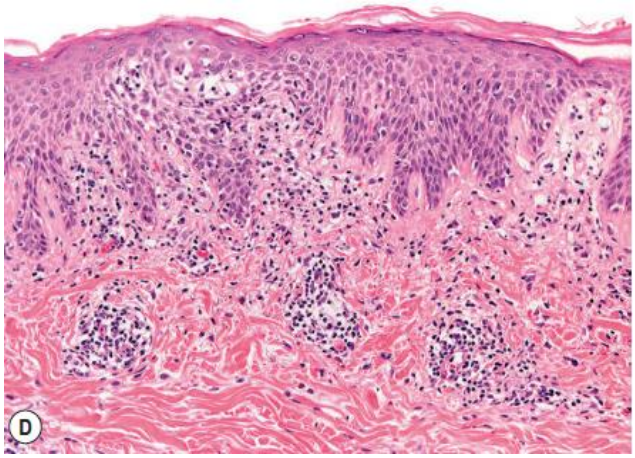
(usually due to the time the immune system take to gain full control over HHV6/7)

PR & Pregnancy: not important

Since pregnancy is a state of altered immune response, a risk of viral reactivations and intrauterine transmission of HHV-6/7 exists.
On the whole, the total abortion rate among women with pregnancy PR is the same as that of the general population but noteworthy, when PR develops within the 15th

gestational week, the abortion rate is higher probably because the risk of intrauterine transmission of HHV-6 (or less commonly HHV-7) is increased.

Histopathology of PR:



focal parakeratosis, spongiosis and acanthosis of the epidermis with superficial perivascular lymphohistocytic infiltrate accompanied by some extravasated RBC

PR-like eruption:

An eruption that resemble PR with the following differences:

- **lacking herald patch and viral prodrome**
- **Papular** morphology
- **Acrofacial** distribution
- **Histology** : Superficial perivascular lymphocytic infiltrate with eosinophil and vacuolar interface reaction and necrotic keratinocytes within the epidermis
- HHV6/7 serology negative

Medications:

Barbiturates, methopromazine, captopril, clonidine, gold, metronidazole, D – penicillamine, isotretinoin, levamisole, Pyribenzamine, NSAID, omeprazole, terbinafine, ergotamine tartrate, tyrosine kinase inhibitors & Adalimumab

Vaccinations:

diphtheria, smallpox, pneumococcal, hepatitis B virus, BCG and HPV

Treatment of PR:

Symptomatic with topical corticosteroids and antihistamine

- Antiviral treatment (Acycolvir 800mg 5 times for 10 days) indicated in the following settings :

- Persistent PR
- Relapsing PR
- Severe PR at the first trimester of pregnancy

تم بحمد الله وفضله.

كلمات الشكر لا تفي حق من شارك في إنجاح هذا العمل ...

أعضاء فريق الجلدية:

خالد العكرش	خالد شراحيلي	سعد الرشود
صقر التميمي	عبدالرحمن المالكي	عبدالكريم المهيدلي
محمد المهوس	محمد خوجه	باسل العنزي
مؤيد احمد	معاذ الغصون	مهند محمد الزهراني
	يزيد المطيري	

كتب الله اجرهم جميعًا..

قائد الفريق: عبدالله الناصر