Papulosquamous Diseases

DR.MOHAMMED ALSHAHWAN
Consultant & Associate professor

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

***Epidemiology**:*

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

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 .

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)

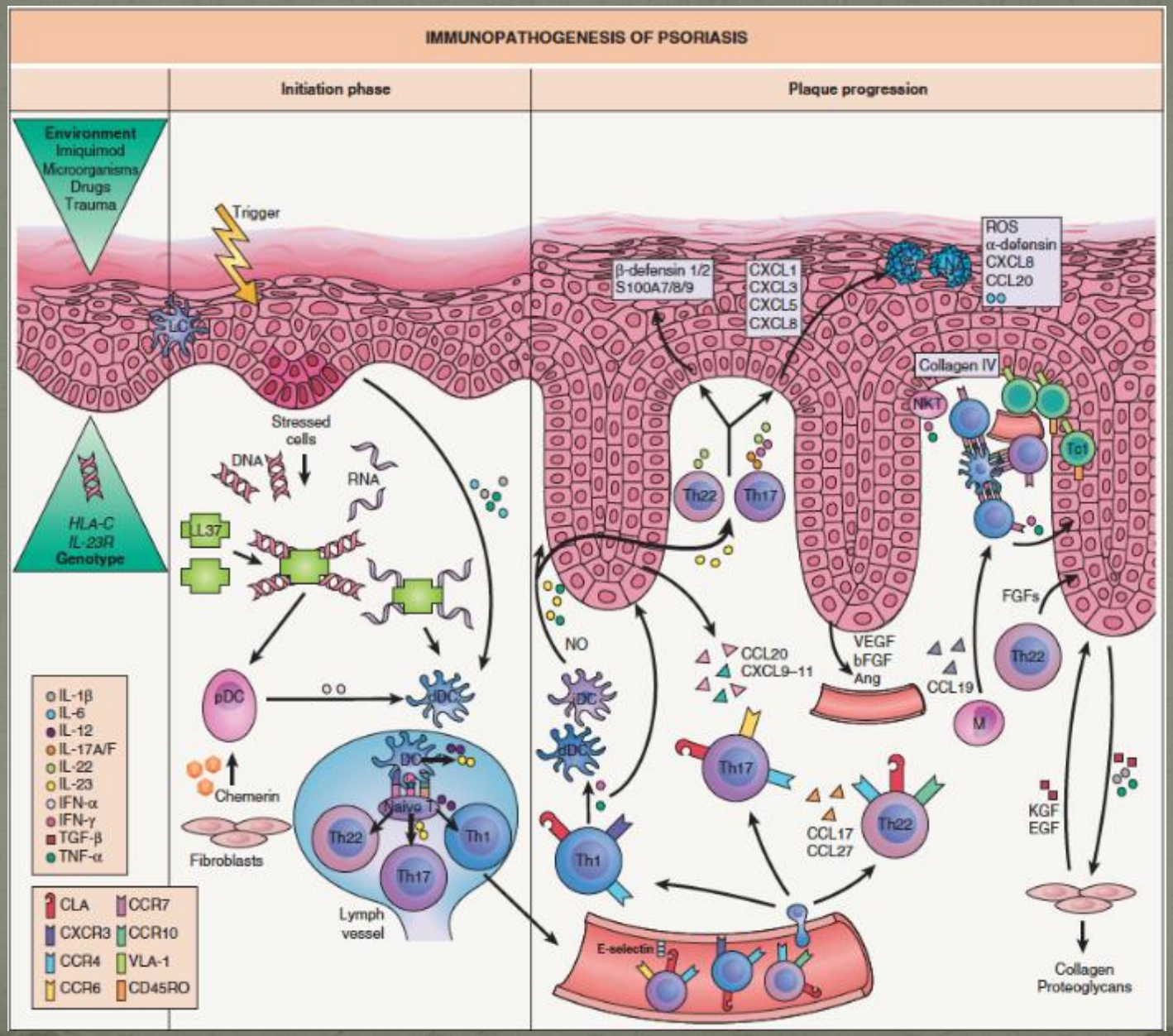
Late-onset disease, no family history and a lack of expression of HLA-Cw6

(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 OF PSORIASIS
Initiation phase
Plaque progression
Environment
Imiquimod
Microorganisms
Drugs
Trauma
Trigger
LC
HLA-C
IL-23R
Genotype
Stressed cells
DNA
RNA
LL37
pDC
mDC
Chemerin
Fibroblasts
DC
Naive T
Th22
Th17
Th1
Lymph vessel
IL-1β
IL-6
IL-12
IL-17A/F
IL-22
IL-23
IFN-α
IFN-γ
TGF-β
TNF-α
CLA
CXCR3
CCR4
CCR6
CCR7
CCR10
VLA-1
CD45RO
β-defensin 1/2
S100A7/8/9
CXCL1
CXCL3
CXCL5
CXCL8
ROS
α-defensin
CXCL8
CCL20
Collagen IV
NKT
Tc1
NO
CCL20
CXCL9–11
VEGF
bFGF
Ang
CCL19
M
FGFs
KGF
EGF
CCL17
CCL27
E-selectin
Collagen
Proteoglycans

Triggers

Trauma

Stress

Infections: e.g. Streptococcal infections, especially pharyngitis

Drugs: e.g. lithium, IFNs, β-blockers, and antimalarial

Hypocalcemia has been reported to be a triggering factor for generalized pustular psoriasis.

chronic plaque psoriasis

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

Guttate psoriasis (more common in children and adolescents and preceded by an upper respiratory tract infection)

Flexural psoriasis

sebopsoraisis : indeterminate stage

Pustular psoriasis

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.

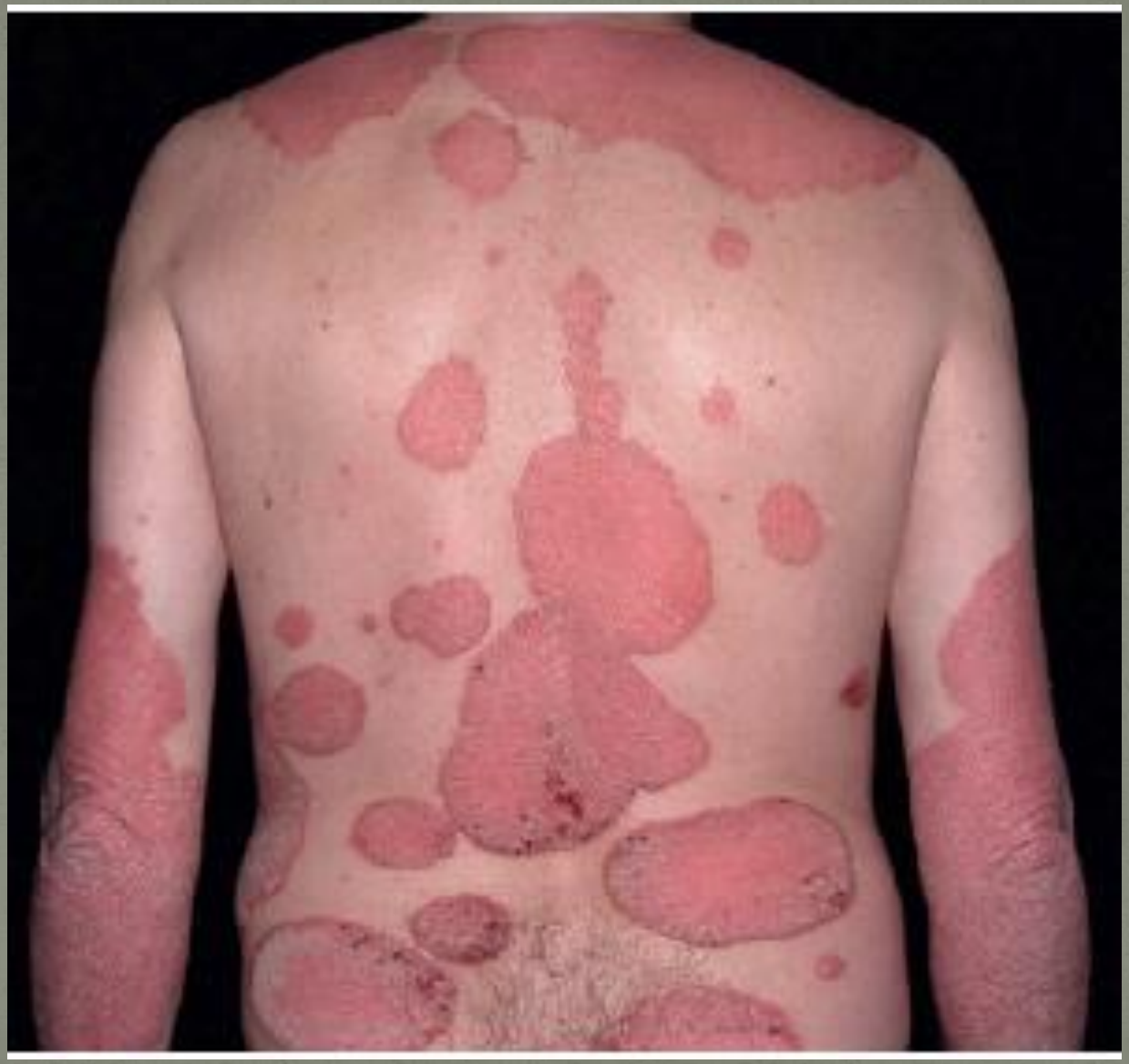
Palmopalnter pustulosis

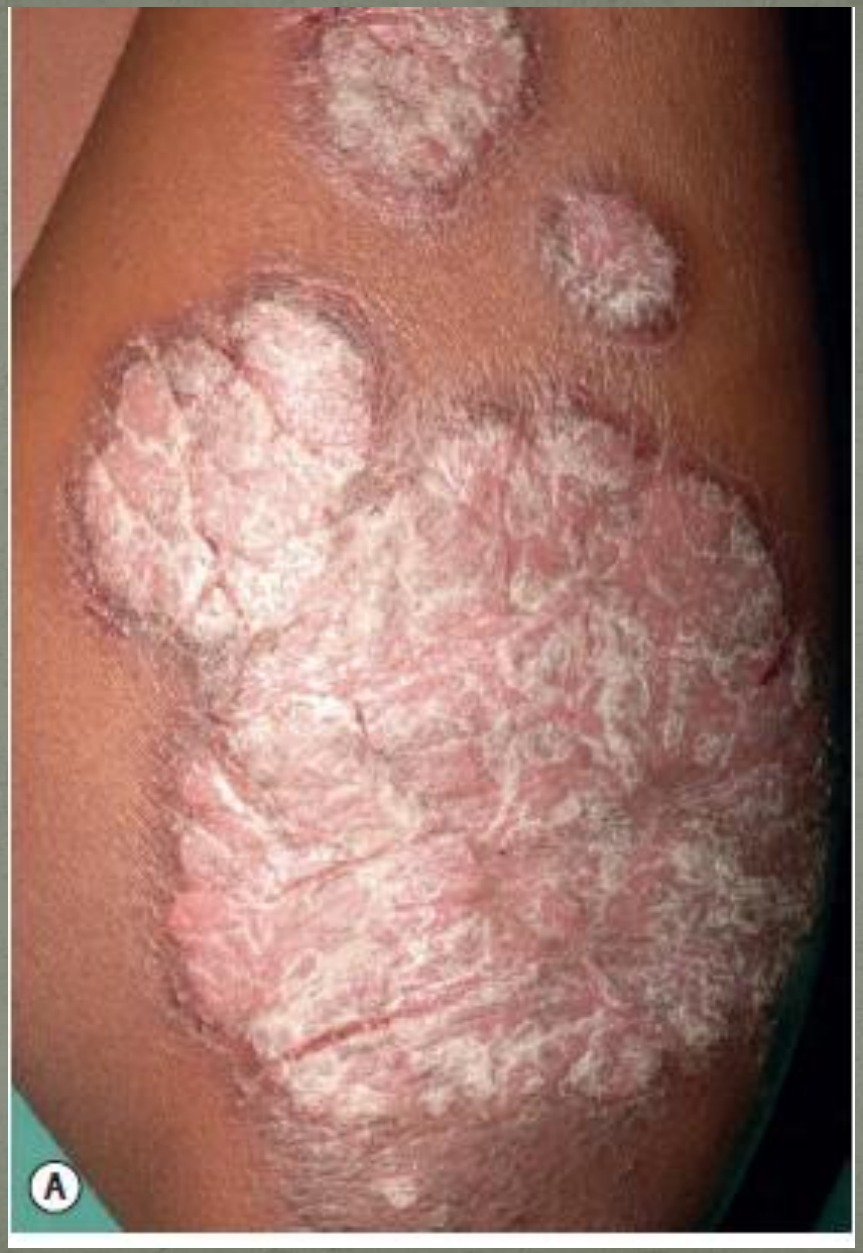
Associated with SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis)

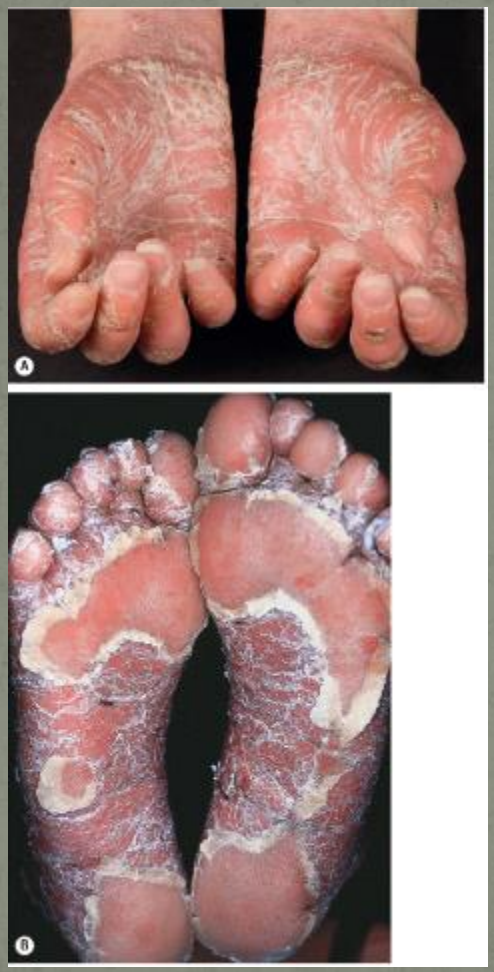
Acrodermatitis continua of Hallopeau

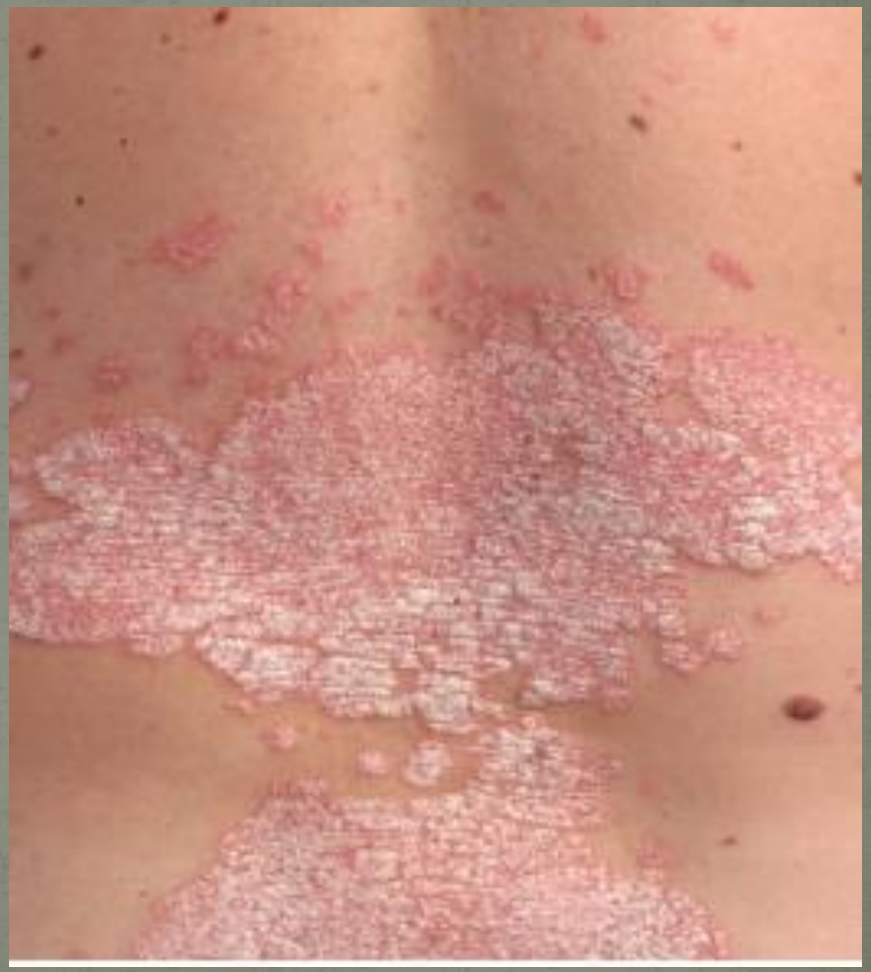
pustules over the distal portions of the fingers followed by scaling and crust formation. Pustules may also form subungual which might cause shedding of nail plates.

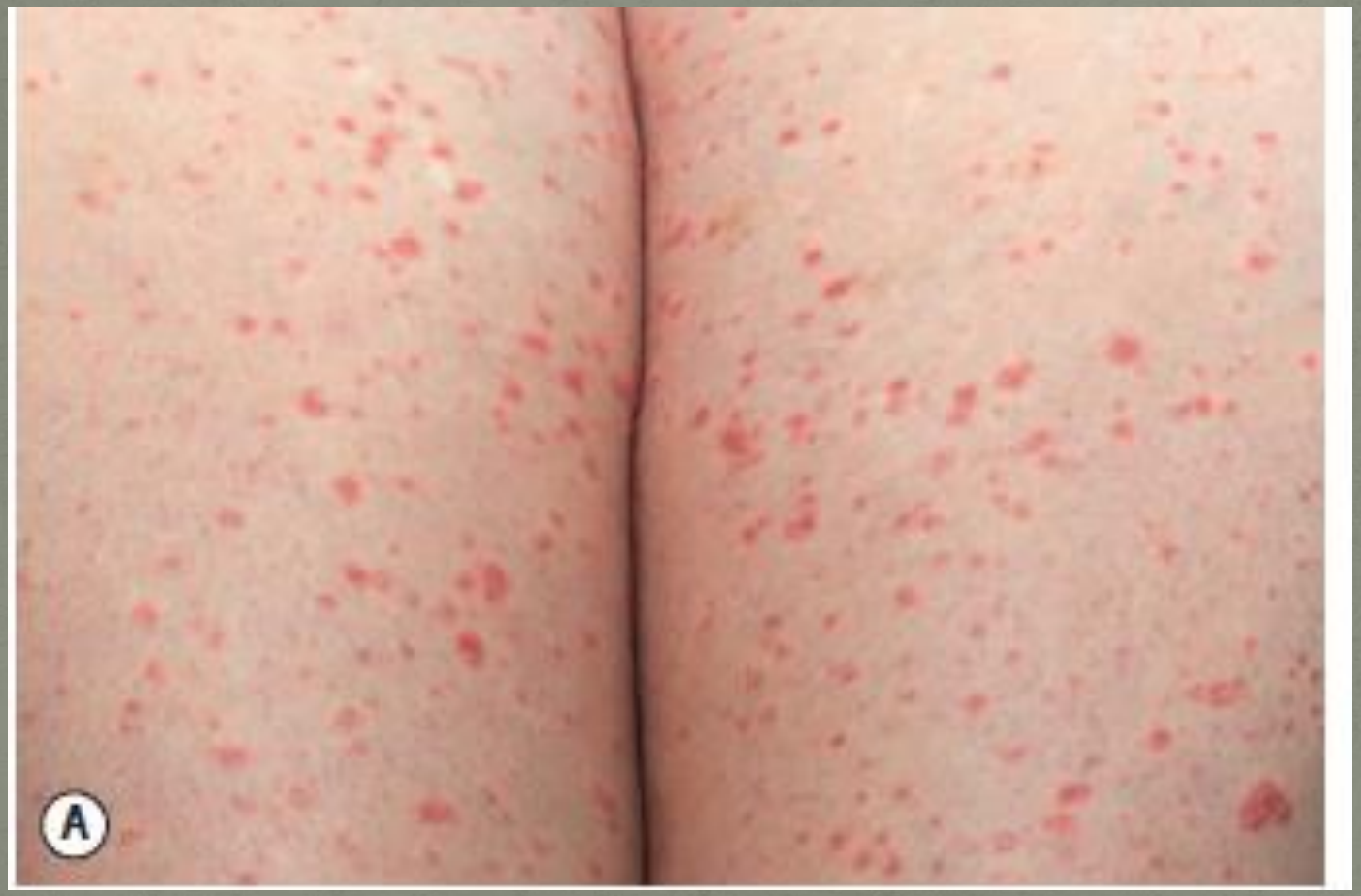
Erythrodermic Psoriasis

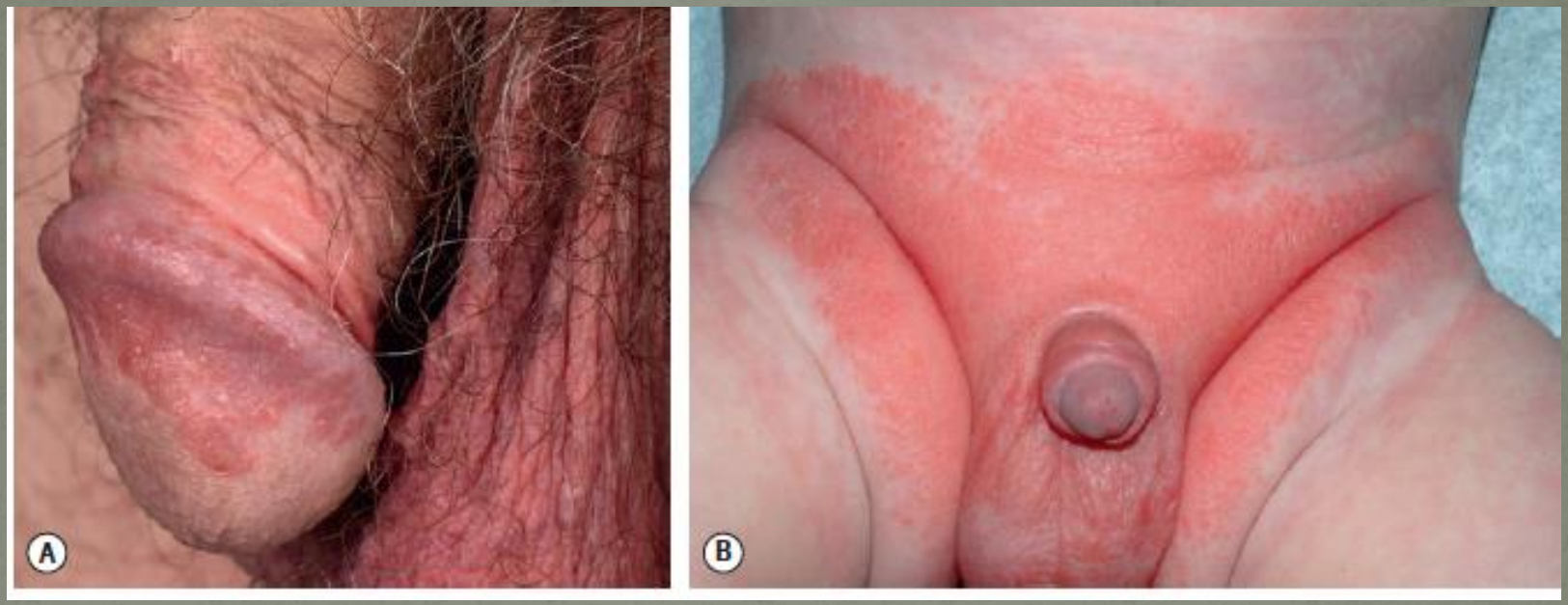


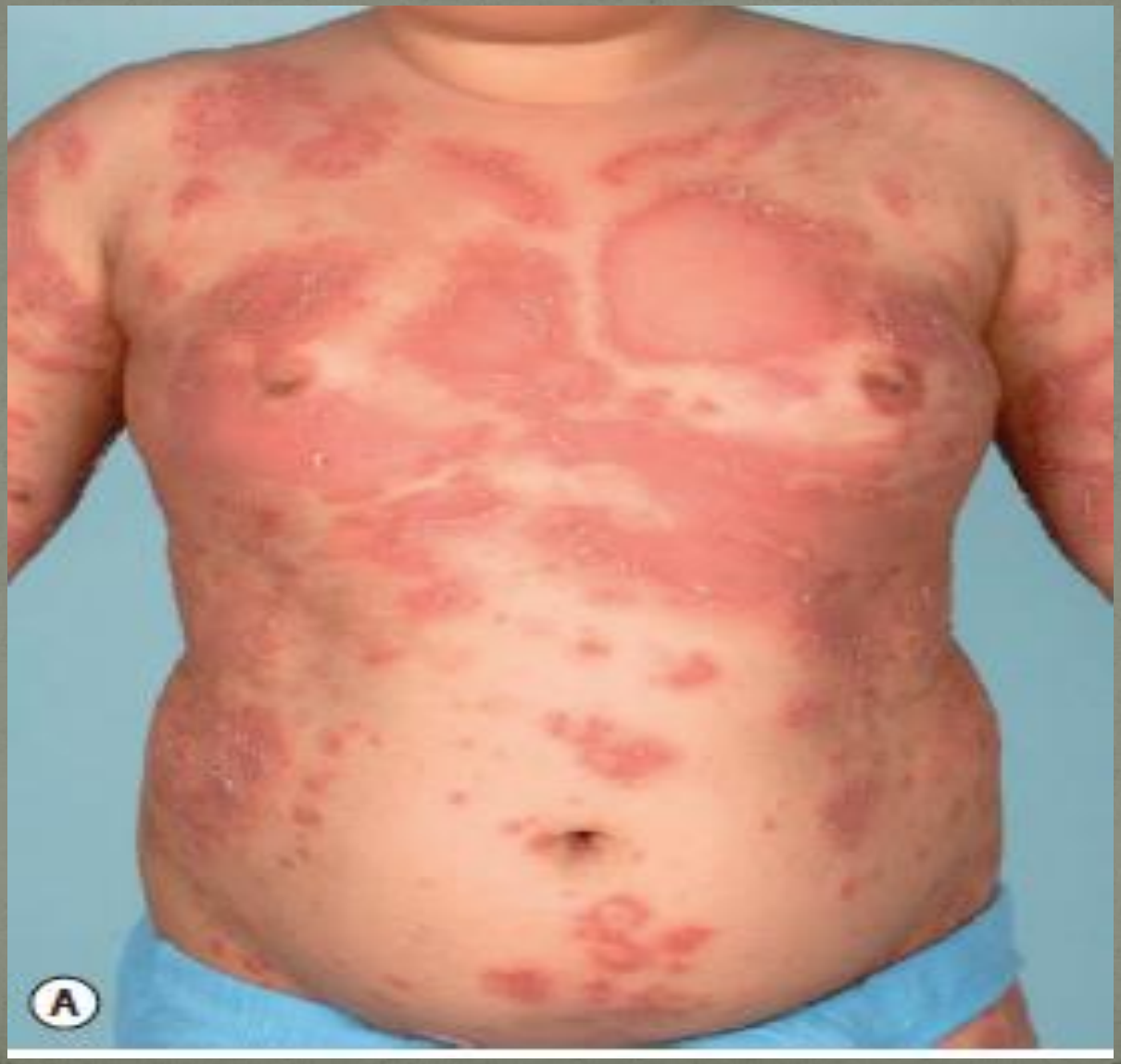

A

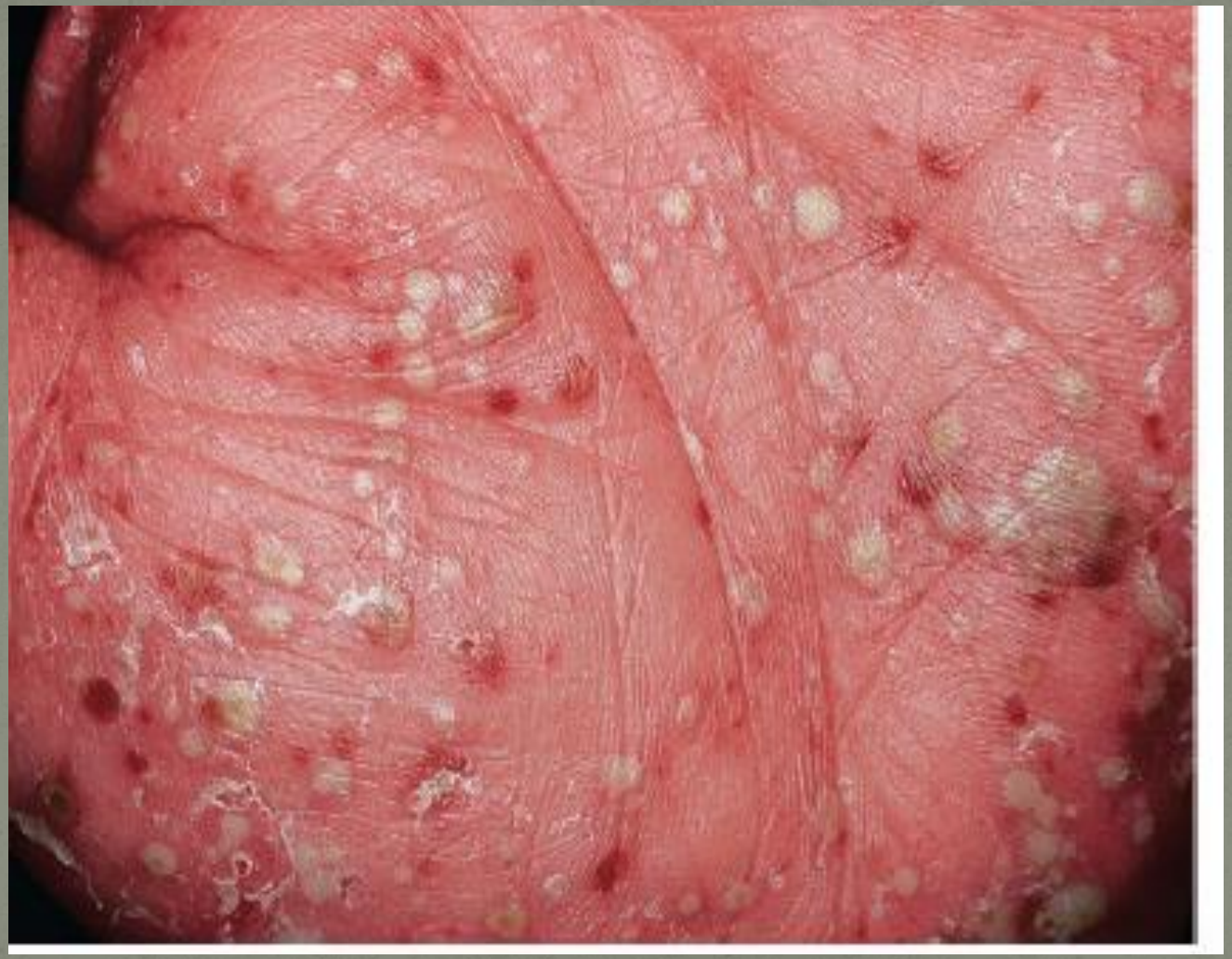

A
B

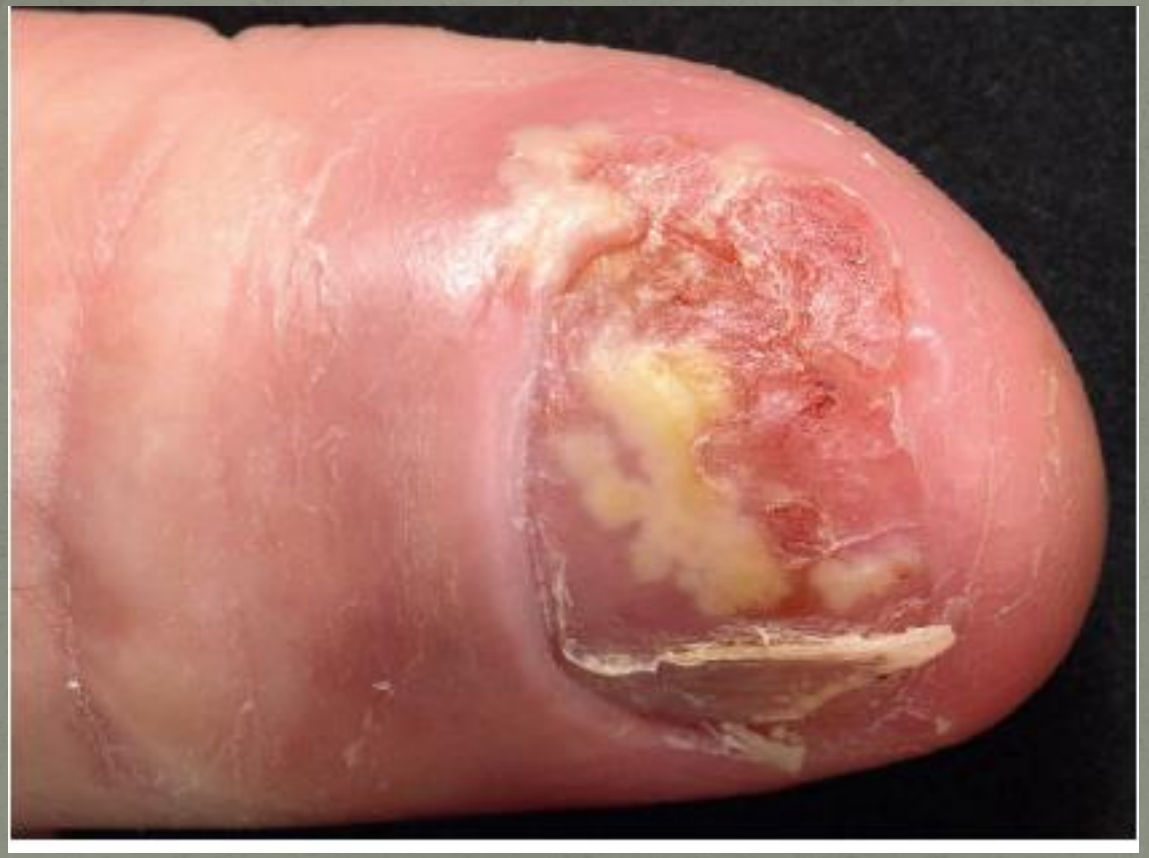



A


A
B


A





Nail :

Involved in 80% of patients

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

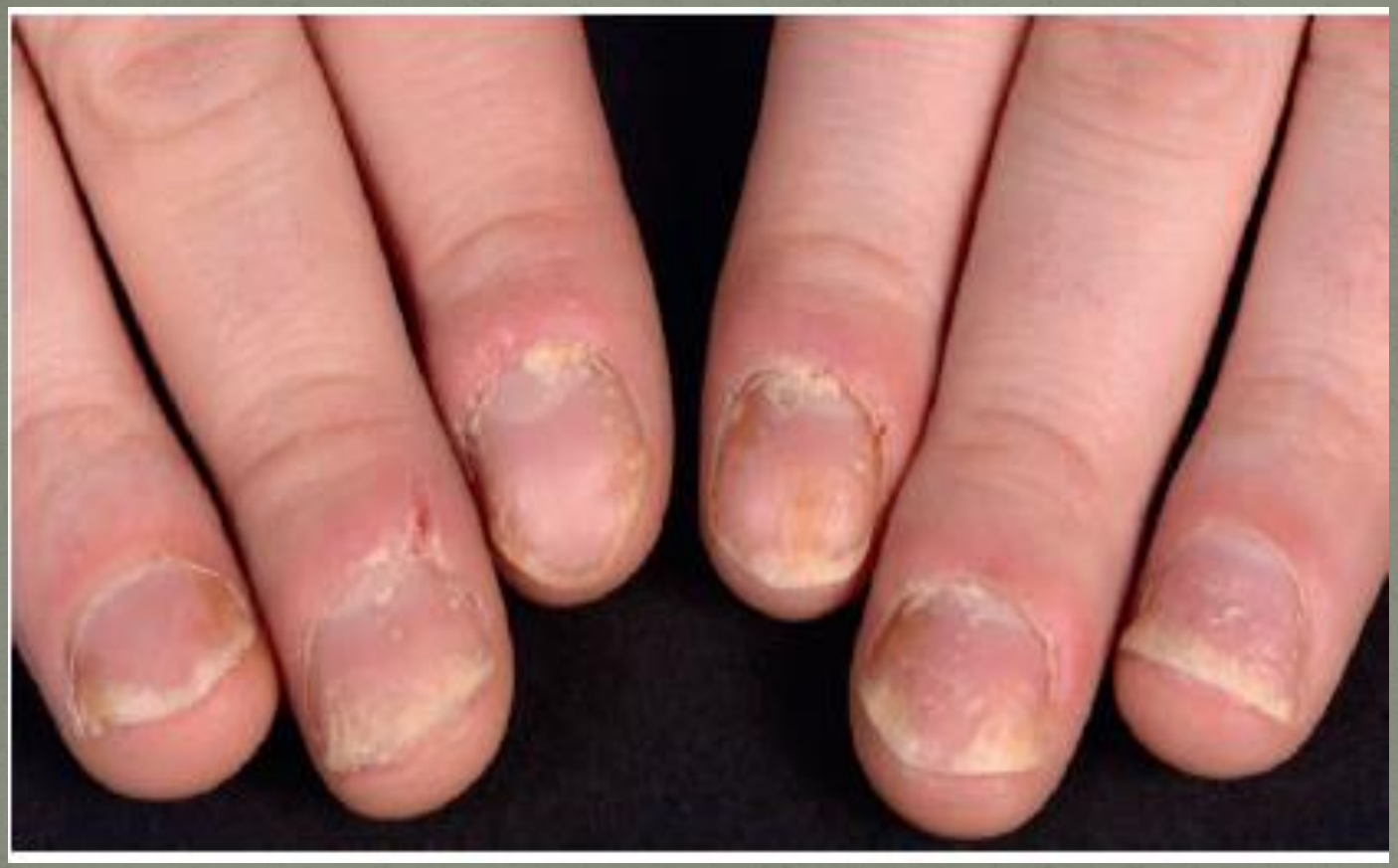
Pitting (parakeratosis of the nail matrix)

Oil-spot (leukocytes beneath the nail plate)

Onycholysis with subungual hyperkeratosis (parakeratosis of the distal nail bed)

Oral mucosa:

Migratory annular erythematous lesions with hydrated white scale over the tongue (geographic tongue) observed mainly in pustular psoriasis patients.



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*

Least common presentations:

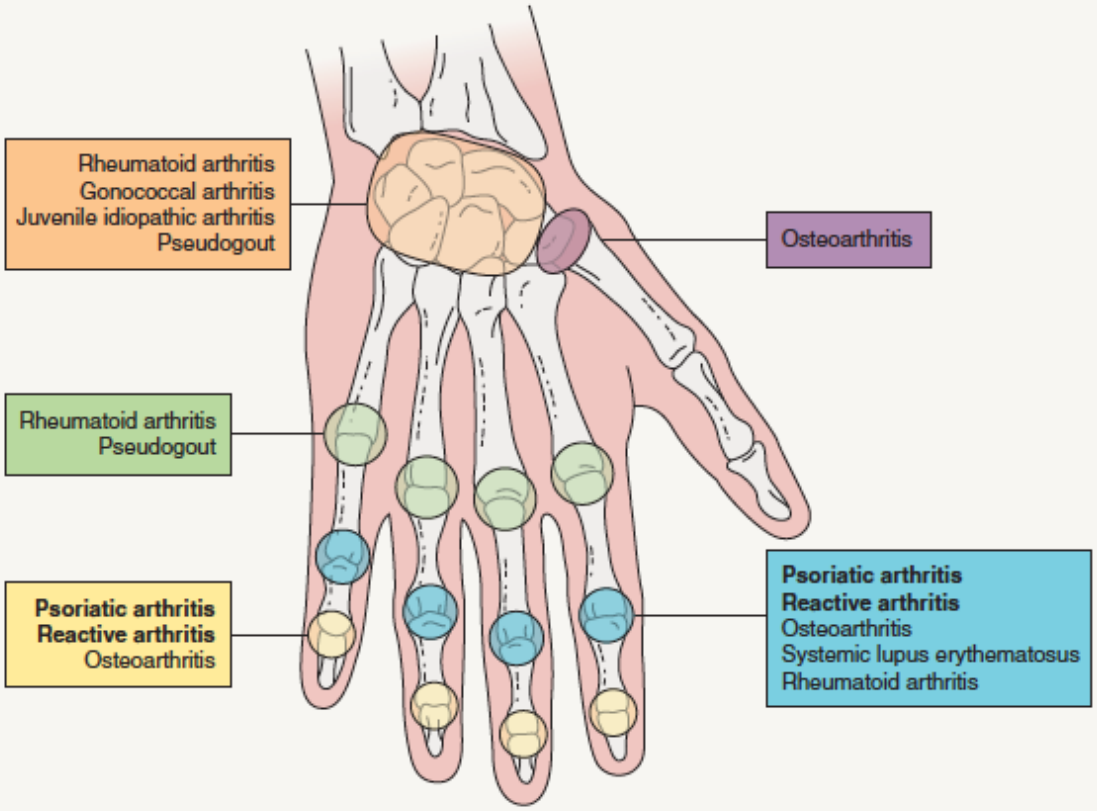
Rheumatoid arthritis-like

(Symmetric polyarthritis that involves small and medium-sized joints)

Arthritis Mutilans

Spondylitis and Sacroiliitis

SITES OF INVOLVEMENT IN PSORIATIC ARTHRITIS AND REACTIVE ARTHRITIS



Associations:

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

Pathology:

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)

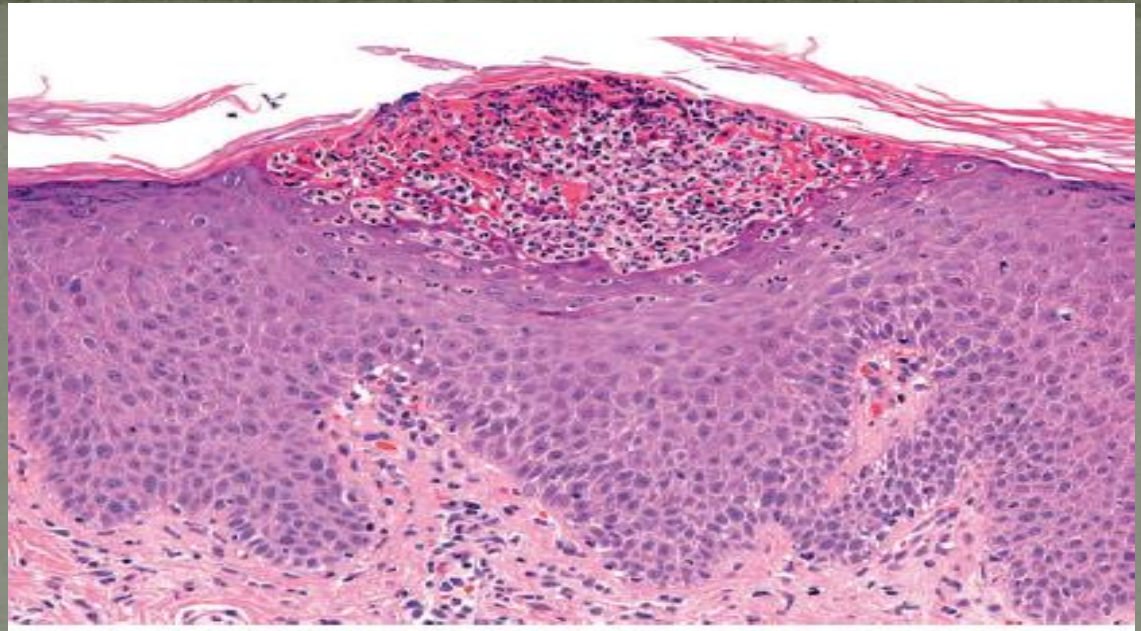
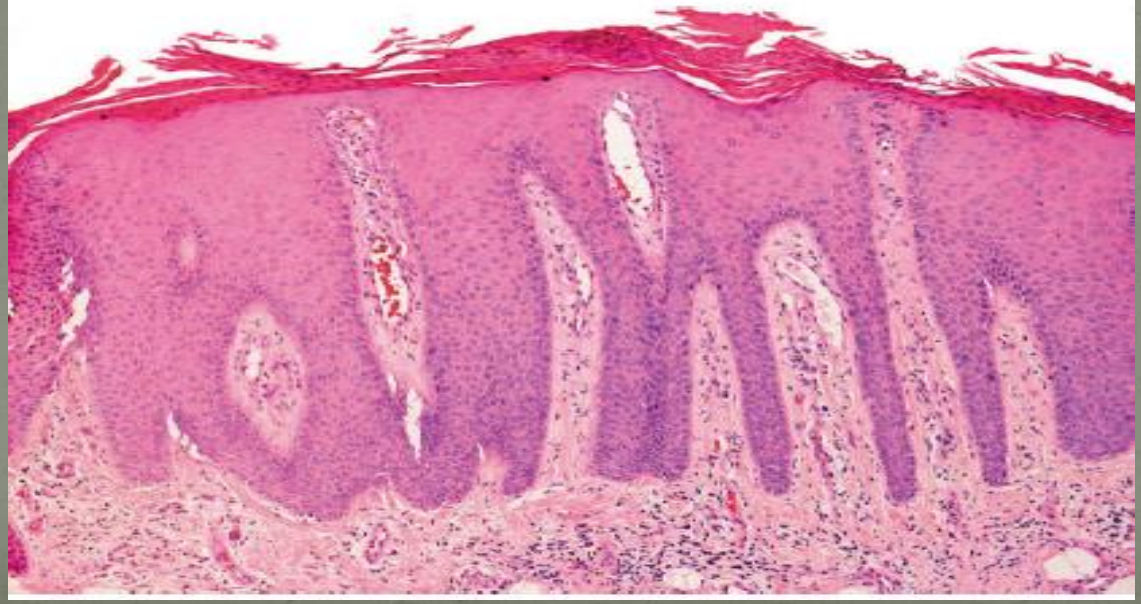


Fig. 8.19 Spongiform pustule of Kogoj. A collection of neutrophils is seen within the upper stratum spinosum. *Courtesy, Lorenzo Cerroni, MD.*



Treatment:

Focal disease

Topical corticosteroids

VitD3 analogues(calcipotriene)

Coal tar

Anthralin

Tazarotene

10% salicylic acid

Widespread disease:

Chronic plaque type

MTX

NBUVB/PUVA

Anti-TNF

Anti-IL 12/23

Anti-IL 17A

cyclosporine

Retinoids (acitretin)

Pustular type

Retinoids

Cyclosporine

MTX

NBUVB/PUVA

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*

Cutaneous LP affects less than 1% of population
Oral LP (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 LP have mucosal involvment sp. Oral
25% of Oral LP have cutaneous LP
Some expert consider them separate disease

Causes

Idiopathic complex polygenetic condition

Genetic predisposition

**Six single nucleotide polymorphisms (SNPs) were found to be associated the HLA-DQB1*05:01 haplotype associated with LP*

**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

Pathogens *(Viral hepatitis-HCV)*

~ geographic variation

~ IFN therapy initiate or worsen LP

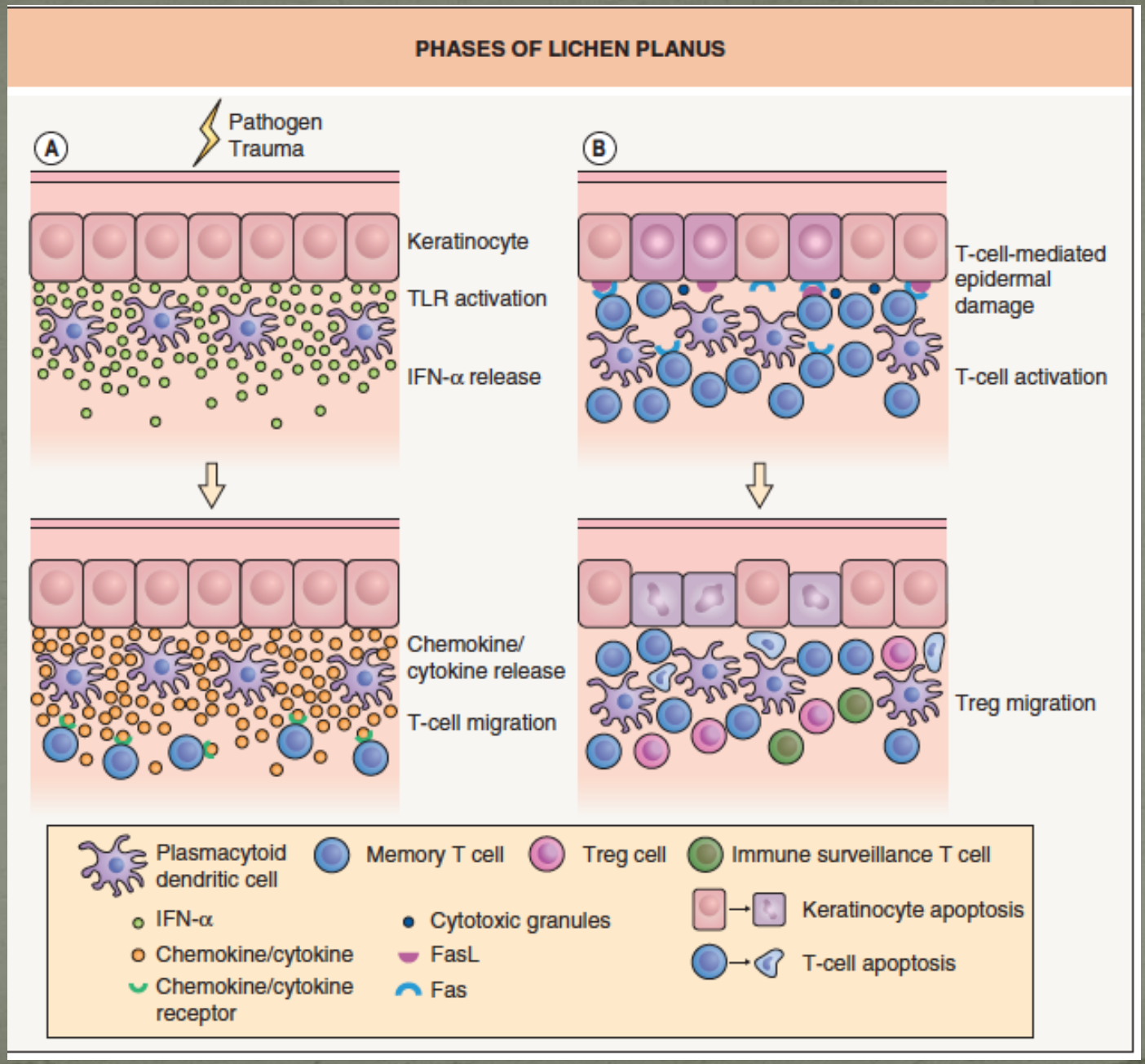
~ Liver disease e.g. sclerosing cholangitis

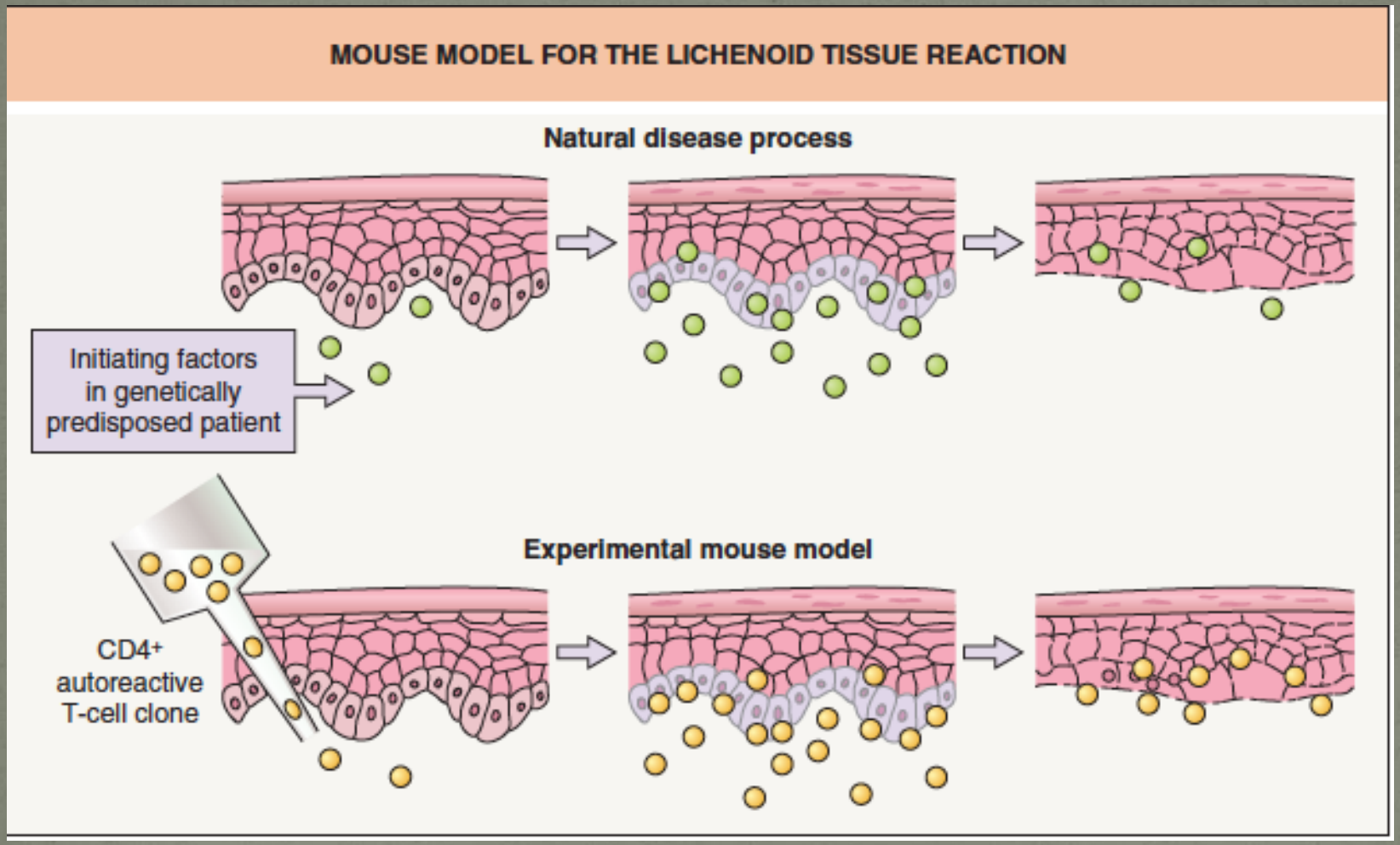
chronic liver disease

Vaccination

Medication *(Lichenoid drug eruption)*

Contact sensitizer *e.g. mercury amalgam, color film developers, methacrylic acid esters, dimethylfumarate in sofas and radiotherapy*


PHASES OF LICHEN PLANUS
A
Pathogen
Trauma
Keratinocyte
TLR activation
IFN-α release
B
T-cell-mediated
epidermal
damage
T-cell activation
Chemokine/
cytokine release
T-cell migration
Treg migration
Plasmacytoid
dendritic cell
Memory T cell
Treg cell
Immune surveillance T cell
IFN-α
Chemokine/cytokine
Chemokine/cytokine
receptor
Cytotoxic granules
FasL
Fas
Keratinocyte apoptosis
T-cell apoptosis


MOUSE MODEL FOR THE LICHENOID TISSUE REACTION
Natural disease process
Initiating factors in genetically predisposed patient
Experimental mouse model
CD4+ autoreactive T-cell clone

Clinical presentation

Itchy (rubbing) pruritic polygonal purple flat-toped papule & plaques with Wickham's striae over flexural surface of extremities ,wrist, legs, lower abdomen and genitalia.

Variants:

**Hypertrophic-leg*

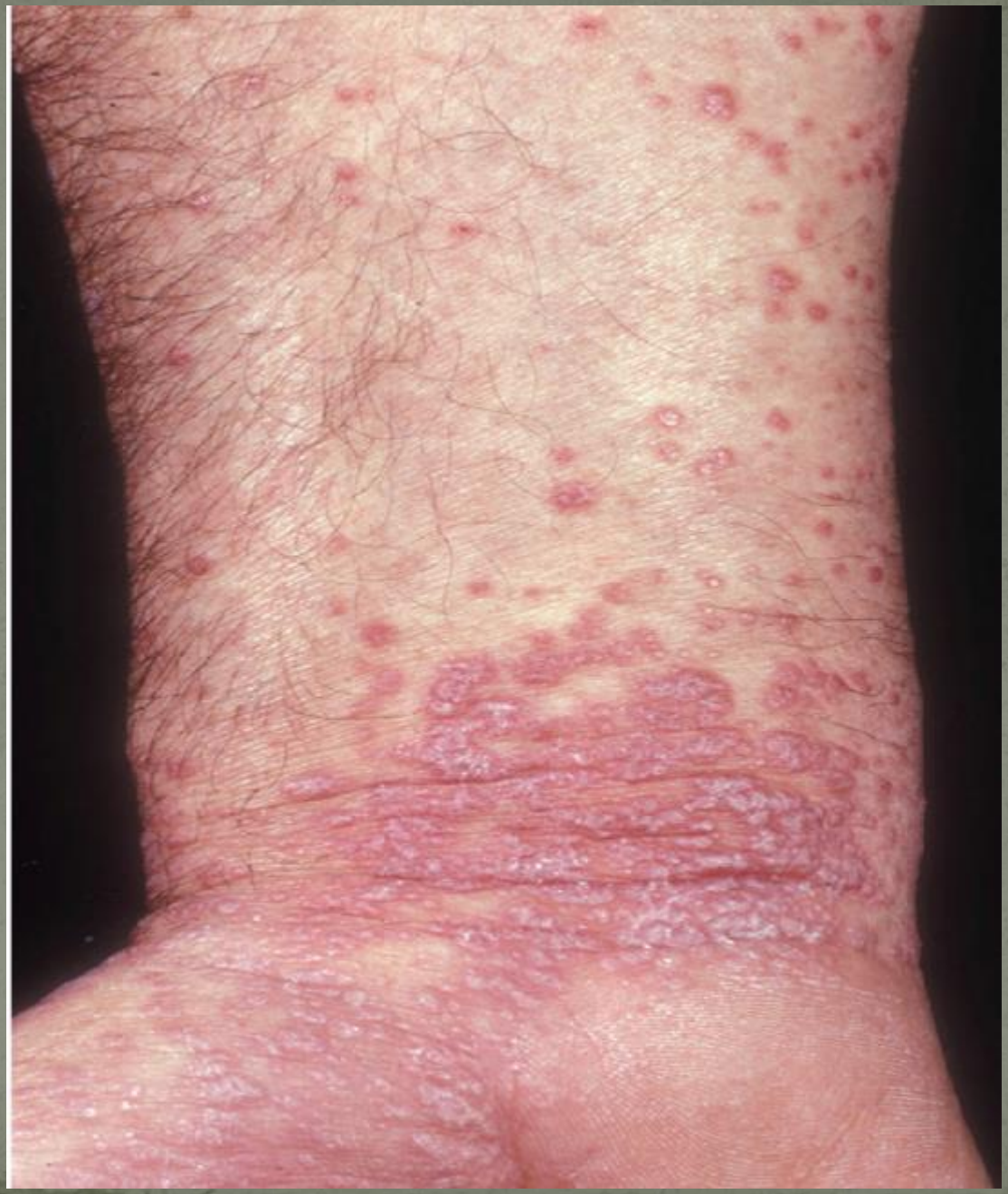
**Atrophic*

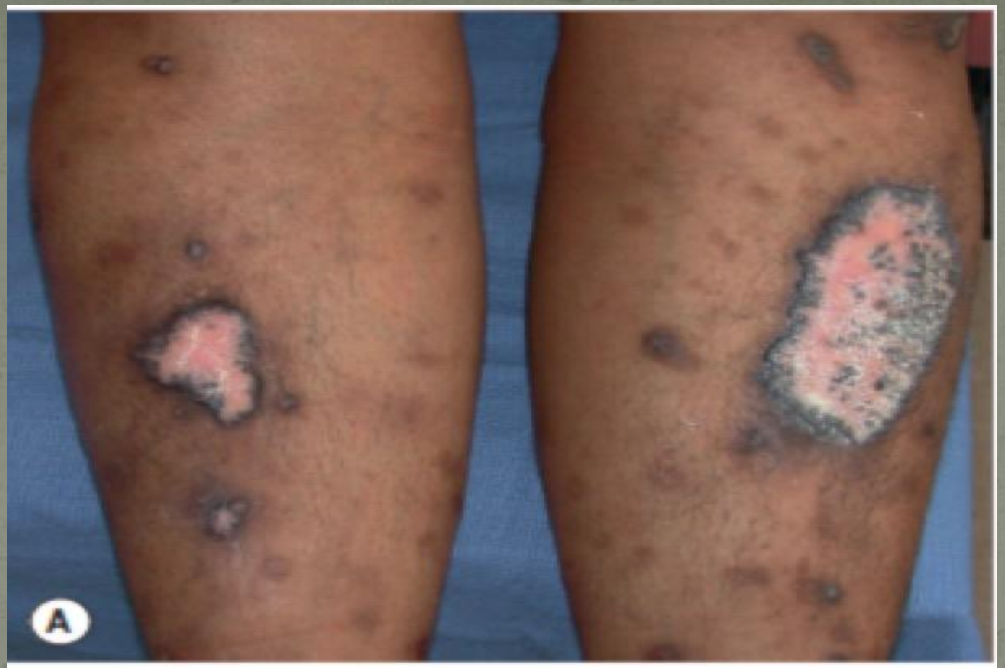
** Ulcerative-palm/soles*

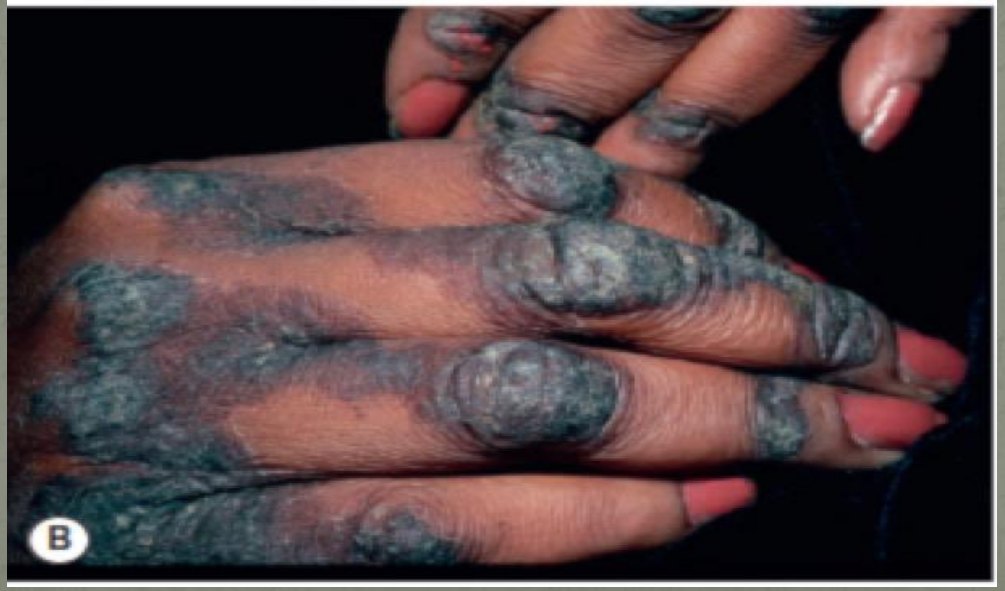
**Bullous*

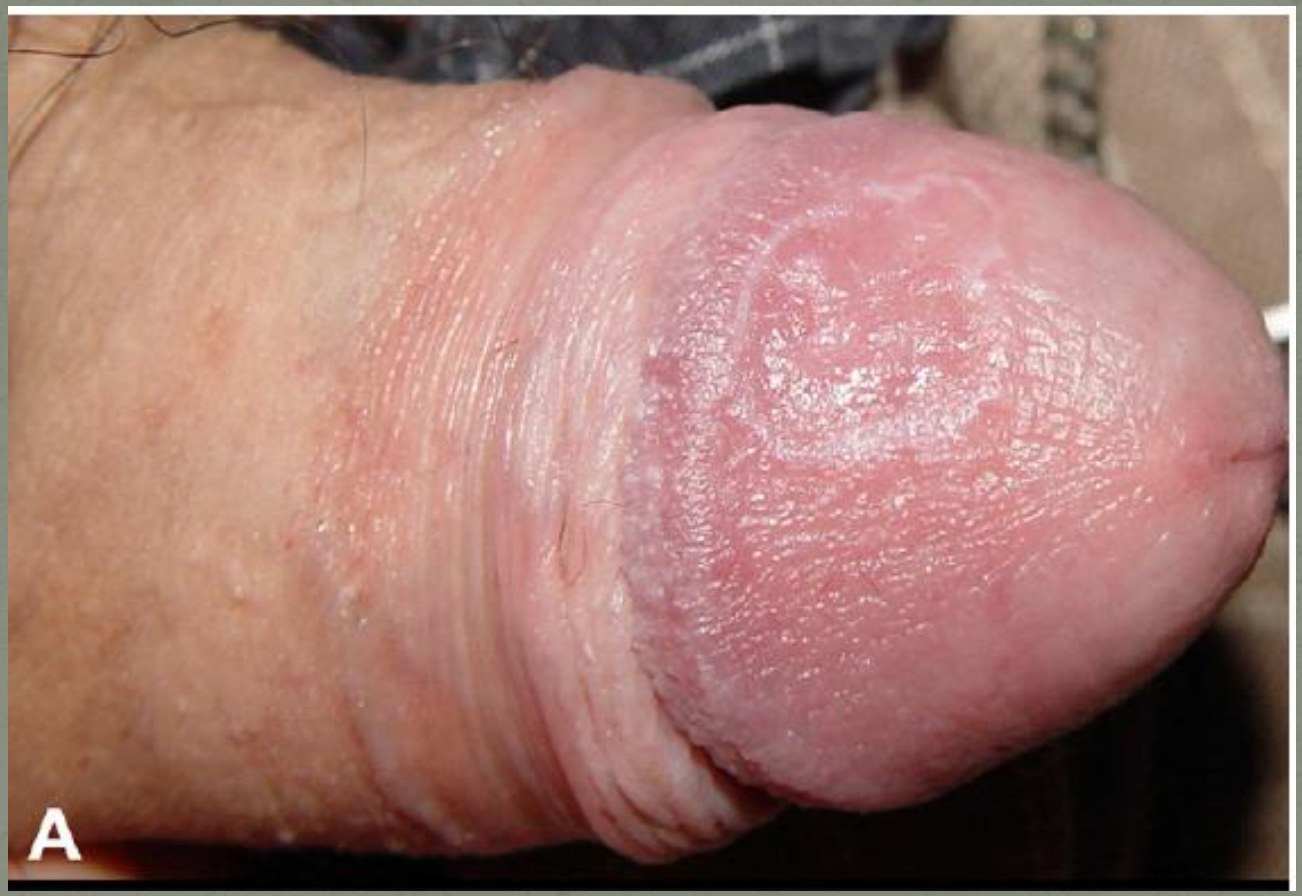
** Annular-penis*

** Linear*




A

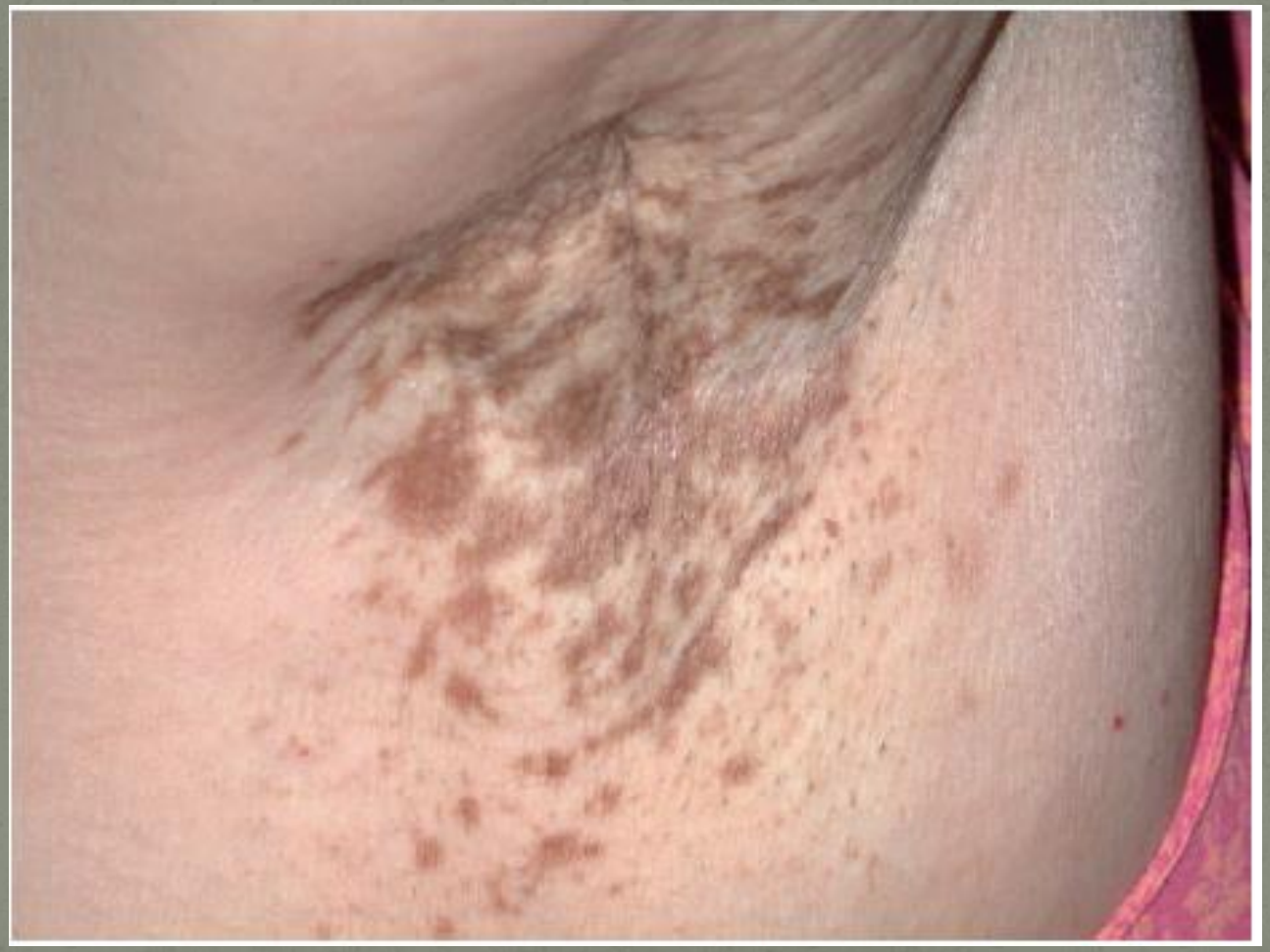

B


A

LP 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

LP Actinicus *(sun exposed area)*



Mucosal LP

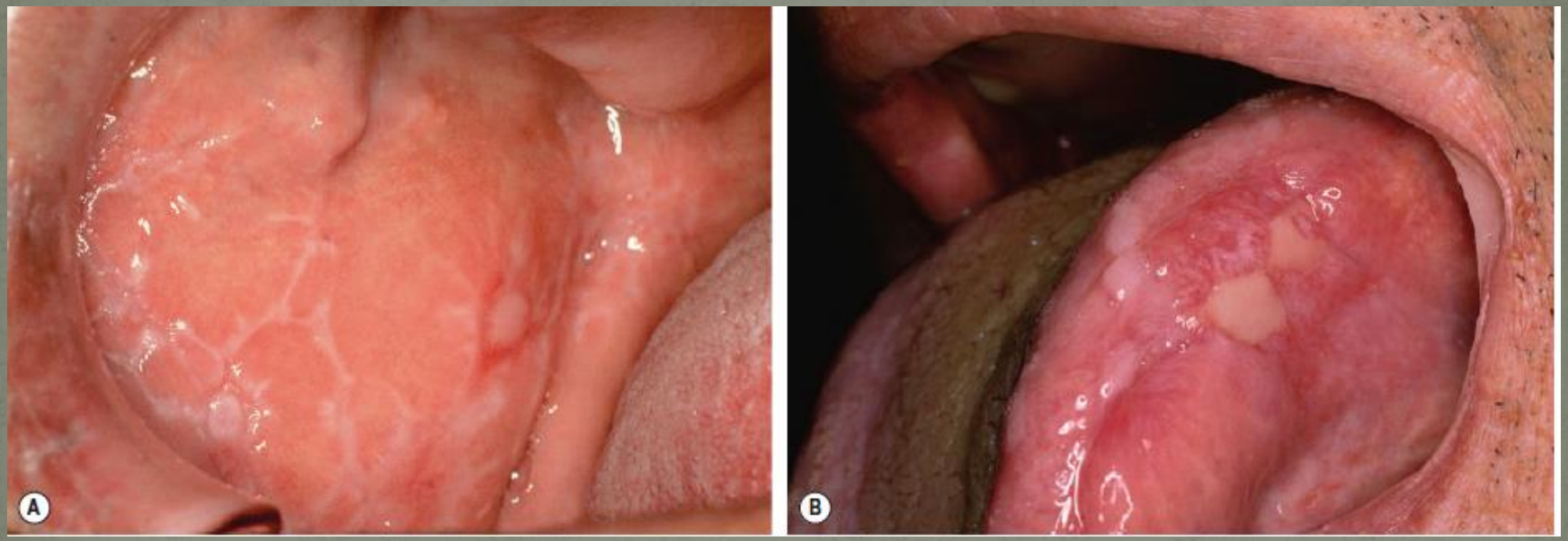
The most common site of involvment is the oral mucosa which usually present as well-defined reticulated violaceous plaques over buccal mucosa ,lips and gingiva- ***Reticulated***

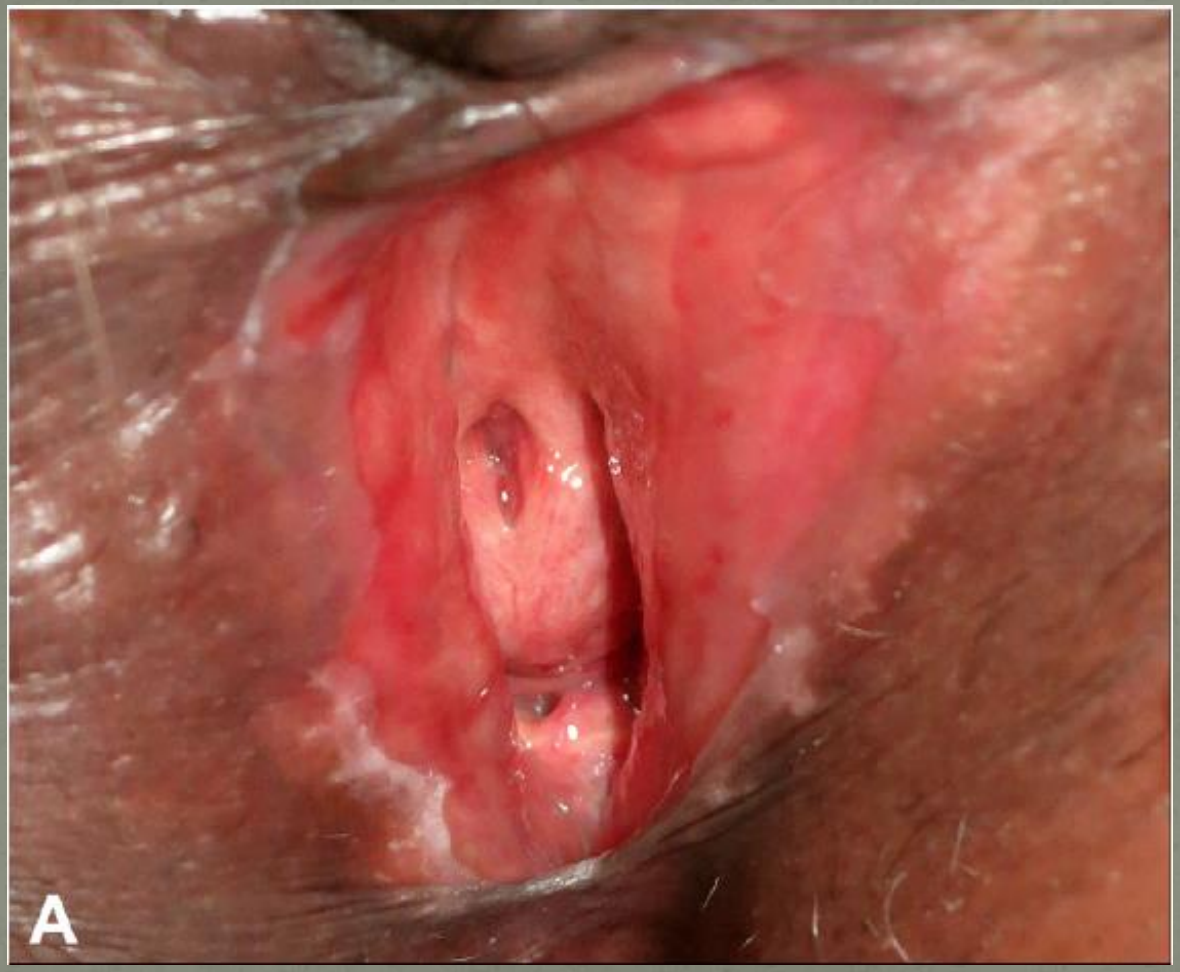
Erosive *(less than 1% risk of SCC)*

Atrophic

Hypertrophic

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


A
B


A

Nail LP

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

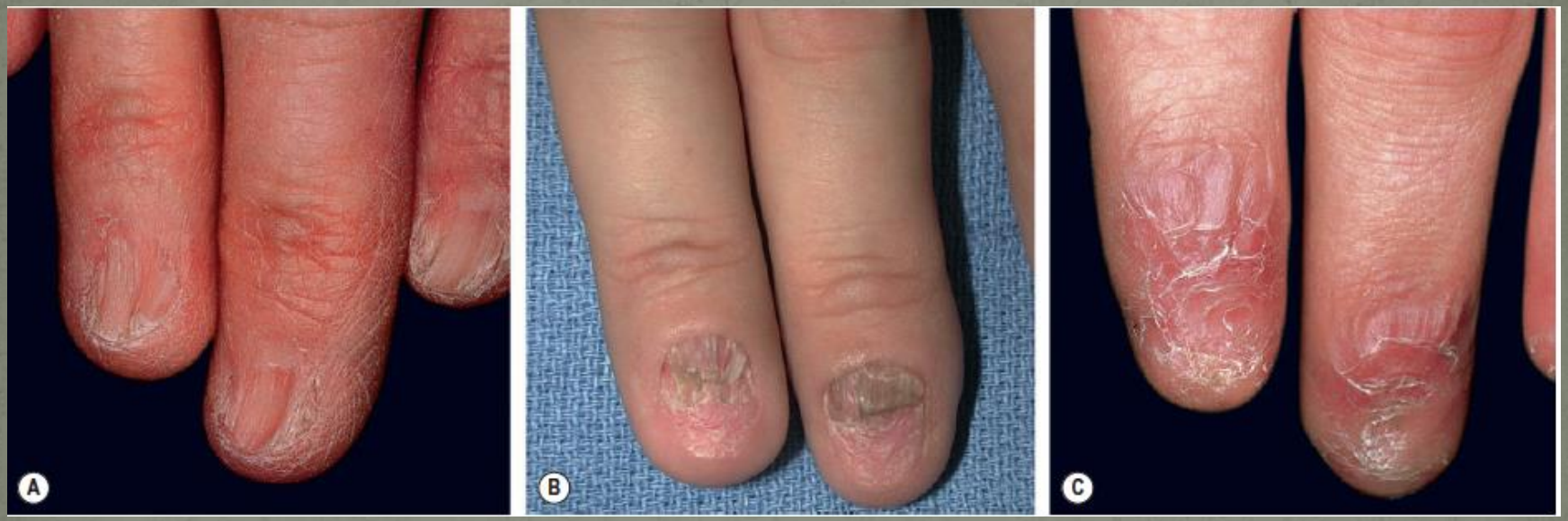
Dorsal Pteryigum

Lateral thinning

Longitudinal ridging

Distal splitting

20 Nail Dystrophy


A
B
C

Lichen planopilaris-LPP

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

Graham-Little–Piccardi–Lassueur syndrome *is triad of :*

(1) non-scarring alopecia of pubic and axillary hairs and disseminated spinous or acuminated follicular papules

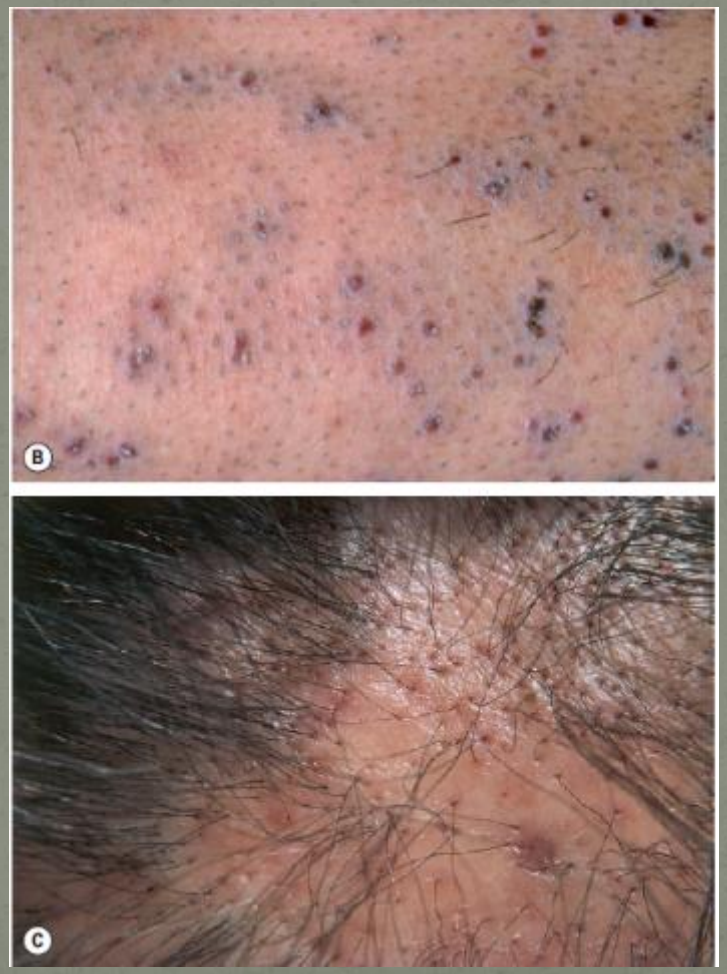
(2) Typical cutaneous or mucosal LP

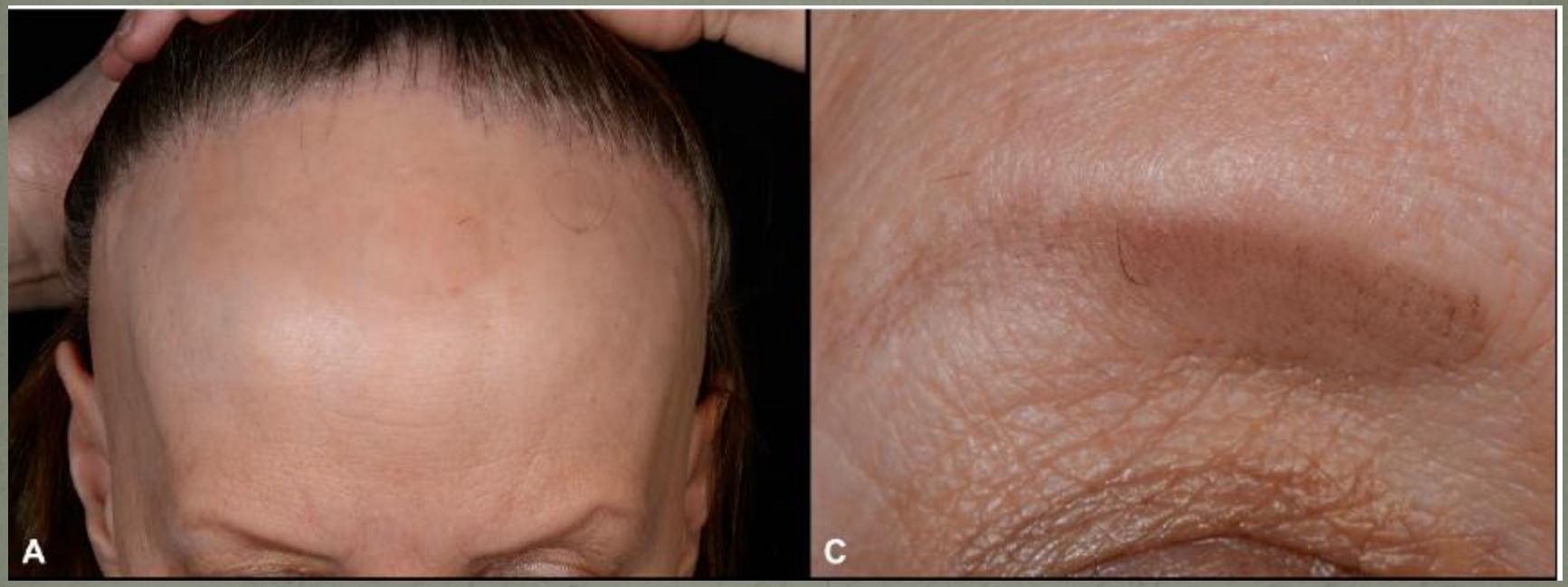
(3) Scarring alopecia of the scalp

Frontal fibrosing alopecia

It usually affect postmenopausal female

It presents as frontal hair-line scarring alopecia with eyebrows thinning


B
C


A
C

Lichnoid drug eruption

It is a drug eruption that resemble LP 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

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

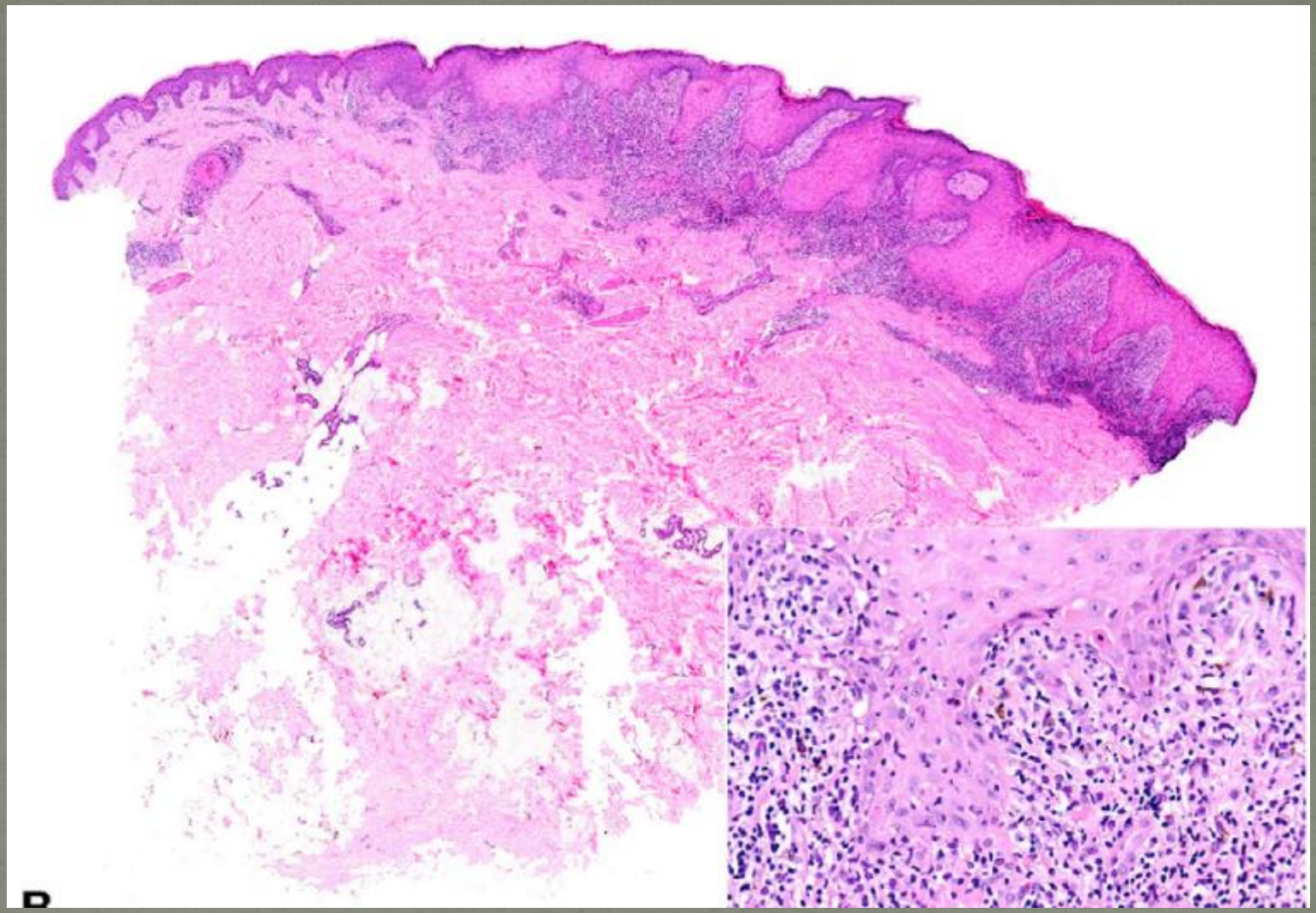
Classic LP pathology & IF

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

***IF** Shaggy band of fibrinogen along the DEJ and colloid bodies staining with immunoglobulins at the papillary dermis*

Lichenoid drug eruption

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


B

LP 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.

Treatment

Focal

Topical corticosteroids

Intralesional corticosteroids ***-LPP***

Generalized

Phototherapy

NBUVB/PUVA

Systemic therapy

Systemic Corticosteroids

Systemic Retinoids e.g. Acitretin

Antimalaria- Hydroxychloroquine- LPP

Immunosuppressive therapy- MTX

Cyclosporine

PITYRIASIS ROSEA

PR is a common acute self-limiting exanthematous eruption that usually affect adolescent (10-30 years)

It doesn't have any gender/race predilection

The etiology of PR is unknown but most expert believe that the reactivation of HHV6/7 play a significant rule in the pathogenesis of the disease

Although, PR can be seen all year around, it is more frequent in winter, fall and spring.

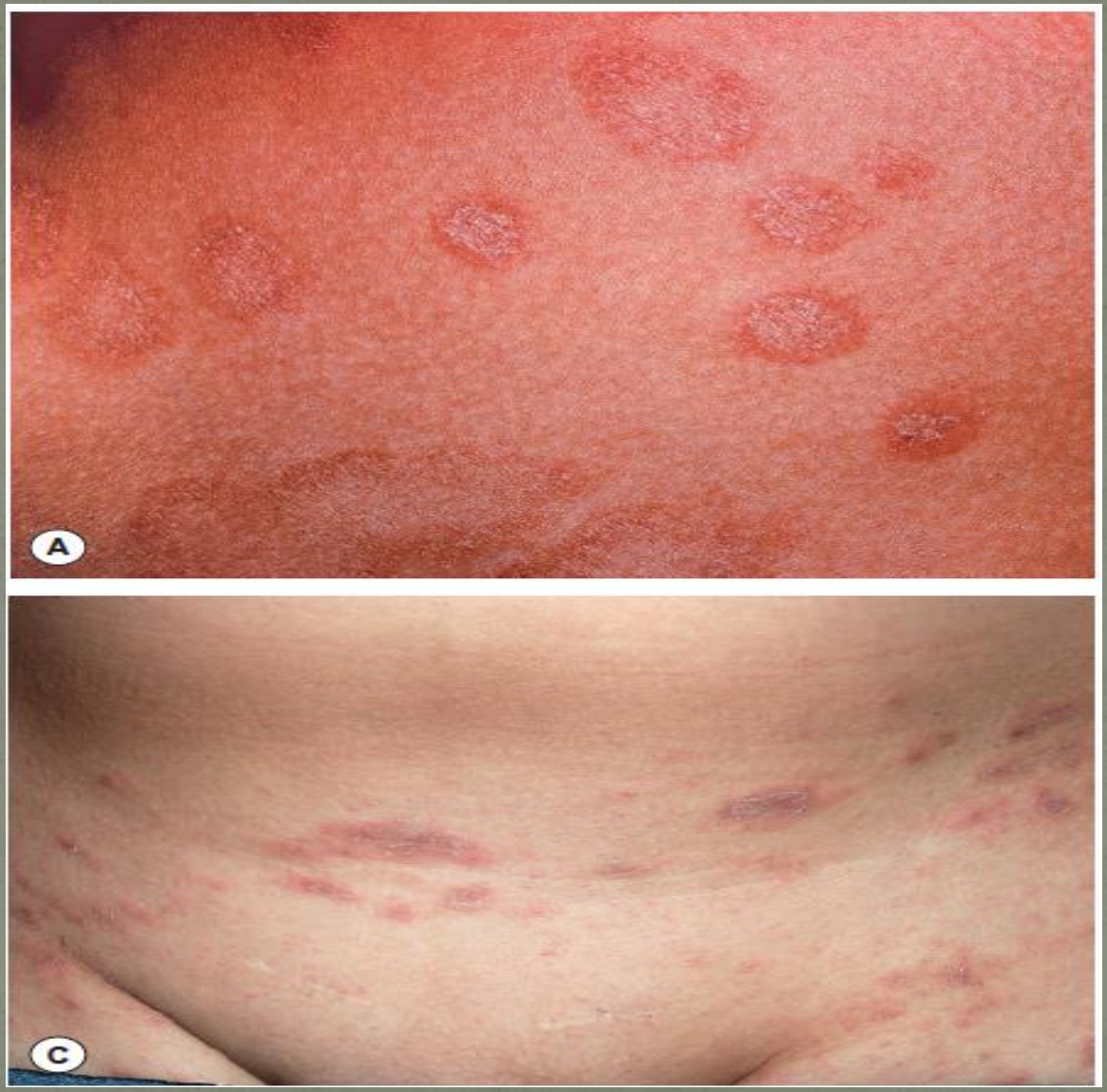
Typical PR

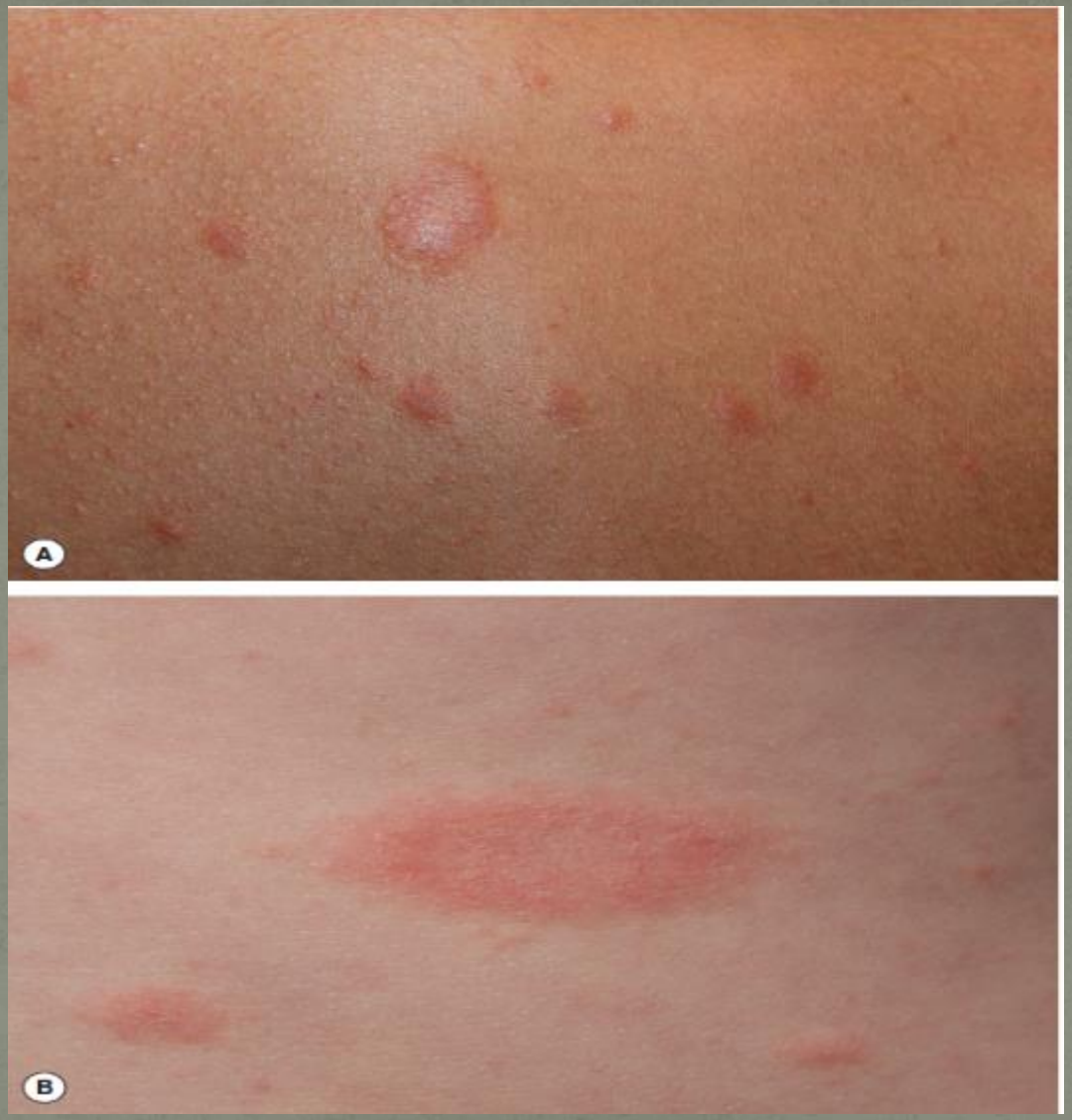
*Single well-defined oval (~4cm) pink-erythematous patch with collarette scale over the trunk/proximal limbs (**Herald patch 50%**) followed after average of 2 weeks with similar daughter lesions on the trunk /proximal limbs(~ charismas tree) with whole illness ranging between 6-12 weeks*

75% complain of pruritus

75% complain of Viral prodrome

10% oral lesions : erosion/ulcer (most common), purpura and erythematous patch


A
C


A
B

Atypical PR

Herald patch

No

multiple

Morphology

papular~ common in dark skin people and children

vesicular

Some PR have purpura or Targetoid lesion

Distribution

PR Inversa~ affect axilla, groin and distal extremities

Course and duration

Persistent PR~ duration longer that 12 weeks and usually up to 6 months with aggressive course and presentation.

Relapsing PR~ 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)

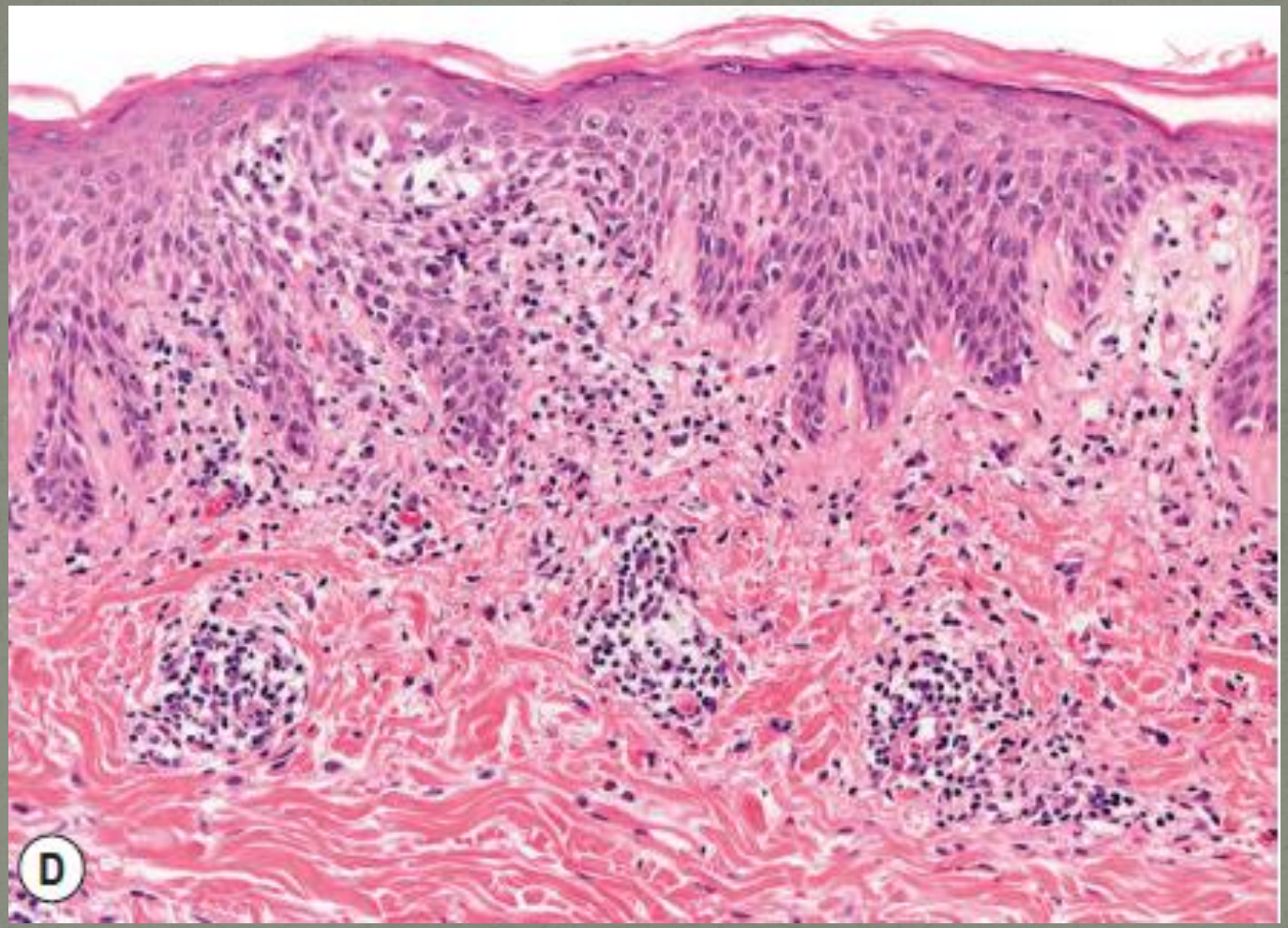
PR & Pregnancy

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


D

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 *e.g. 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