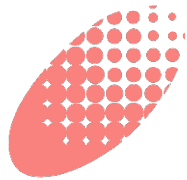


Predicting the **Response** to Phototherapy for Psoriasis Patients

Is it possible ?



NATIONAL
SKIN
CENTRE

Dr Eugene Tan
Consultant Dermatologist
National Skin Centre



Adding years of healthy life

1

**Overview of
Psoriasis**

2

**Phototherapy
for Psoriasis**

3

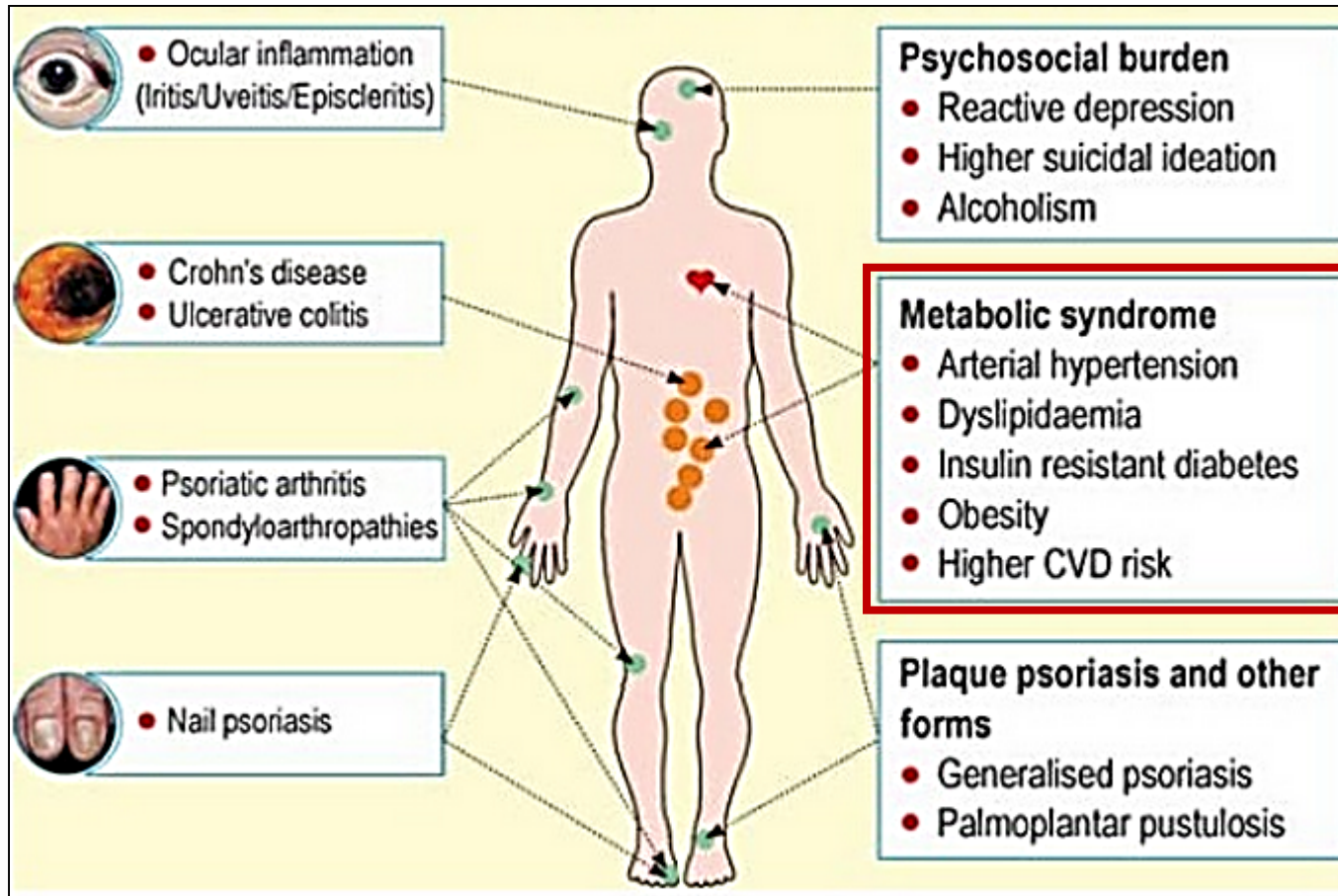
**Predicting
Response to
Phototherapy**

What is **Psoriasis** ?



- Chronic inflammatory skin disorder, with abnormal rapid proliferation of keratinocytes
- Well-defined **red scaly plaques**
- Common sites – scalp, ears, knees, elbows, umbilicus
- Frequently affects **nails & joints**

Co-morbidities in Psoriasis



Prevalence of Psoriasis

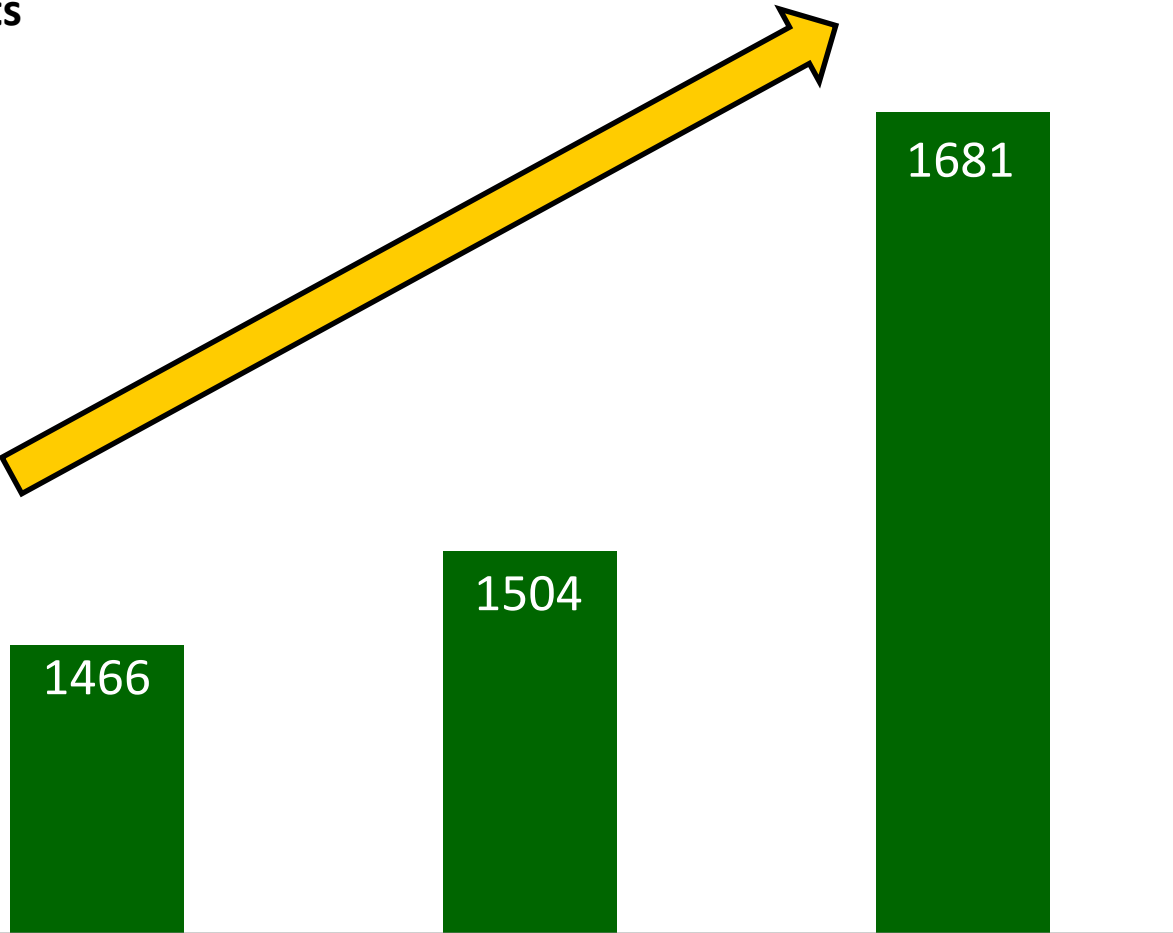


1-2%
of population

New Cases of Psoriasis in NSC

Number of patients

1700
1650
1600
1550
1500
1450
1400
1350



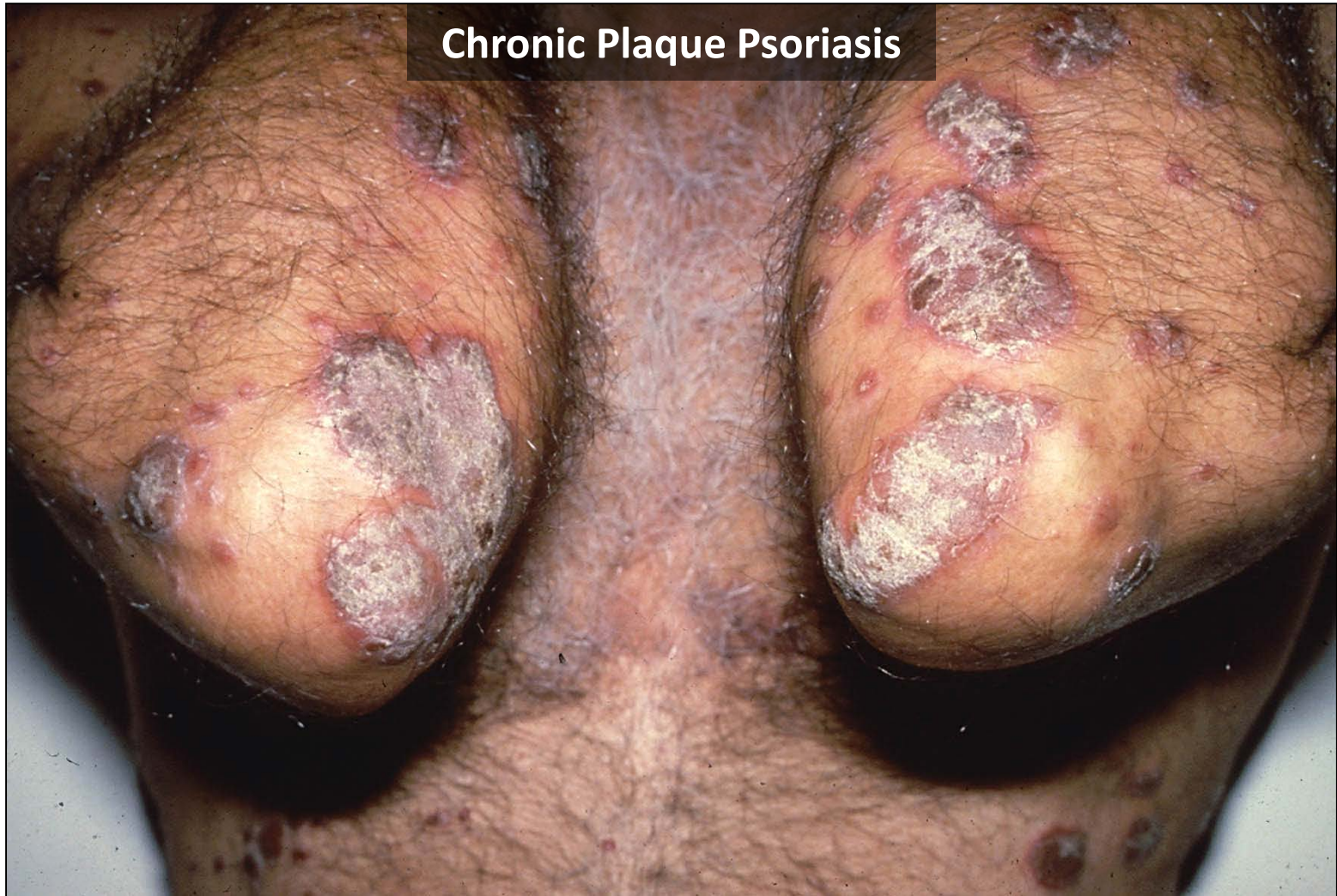
2012

2013

2014

Year

Most Common Type of Psoriasis



Other **Variants** of Psoriasis



Guttate Psoriasis

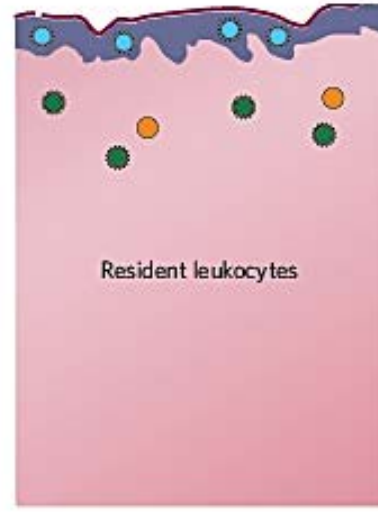
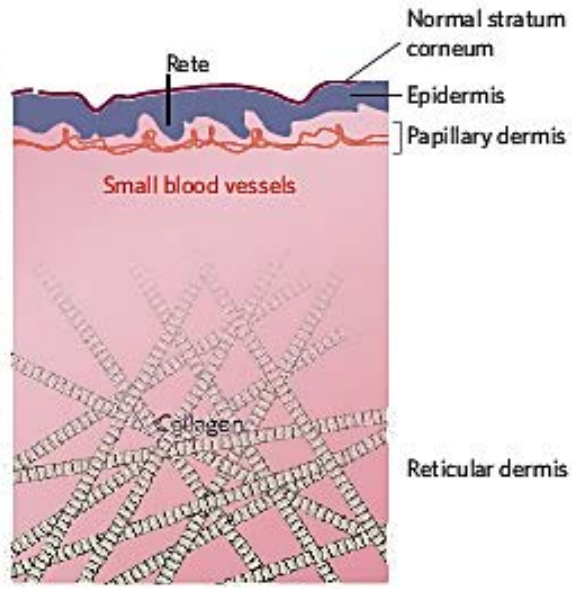
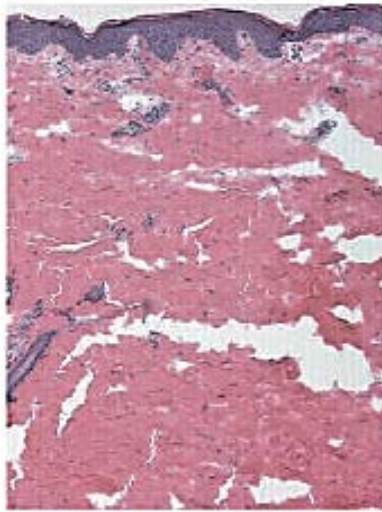


Inverse Psoriasis



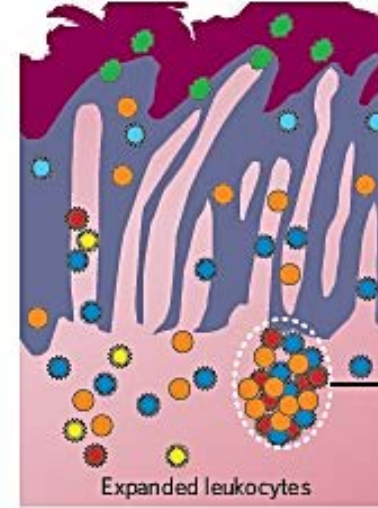
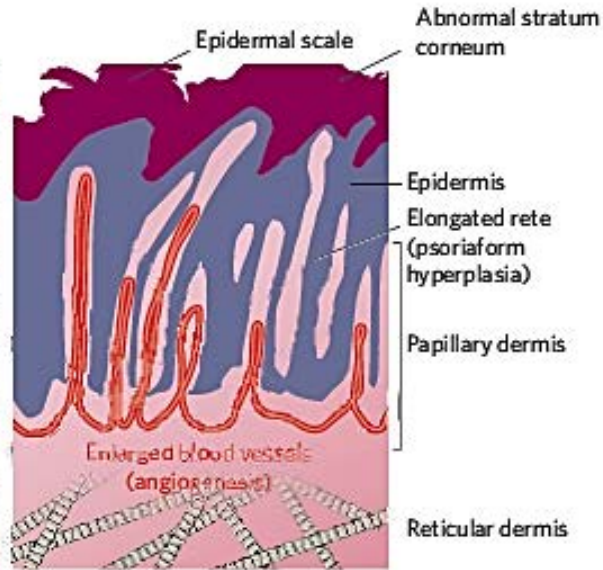
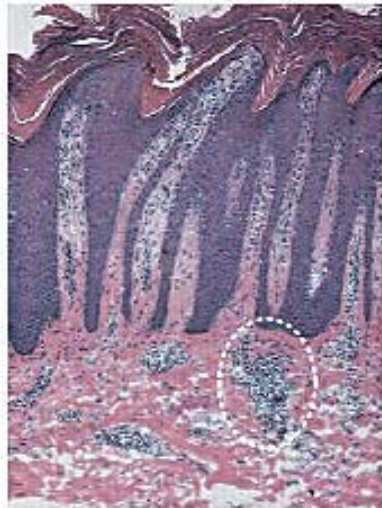
Pustular Psoriasis

Adjacent skin (normal appearance)



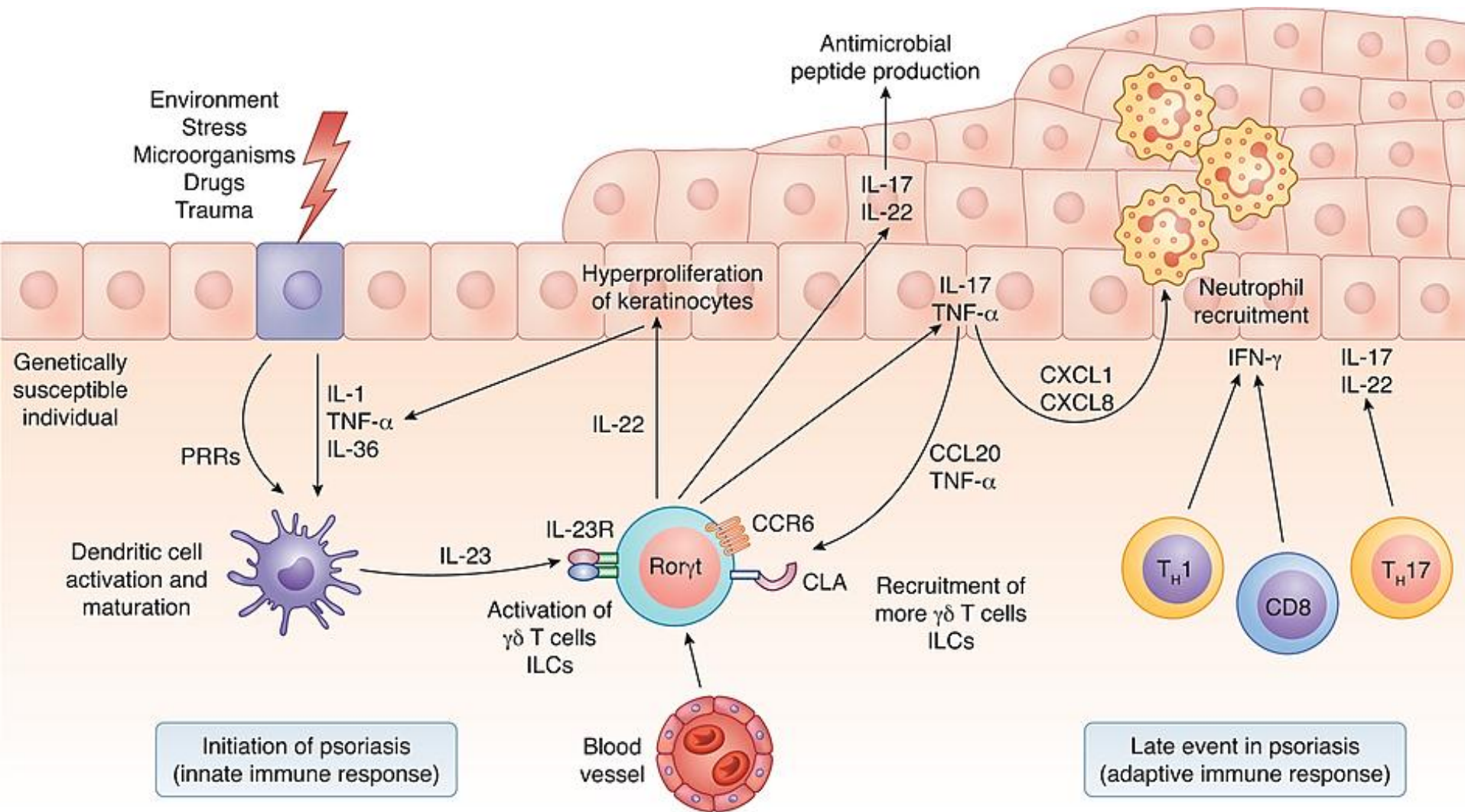
Normal Skin

Psoriatic plaque



Psoriasis

- Langerhans cell
- Immature CD11c⁺ DC
- Inflammatory DC (TIP-DC)
- Mature DC (DC-LAMP⁺ or CD83⁺)
- Plasmacytoid DC
- Skin-homing T cell
- Neutrophil



Treatment of Psoriasis

1. Topical therapy

- topical steroids, vitamin D analogues, coal tar, calcineurin inhibitors

2. Phototherapy

- NBUVB, PUVA

3. Systemic therapy

- methotrexate, ciclosporin, acitretin

4. Biologic therapy

- infliximab, etanercept, adalimumab, ustekinumab, secukinumab

1

Overview of
Psoriasis

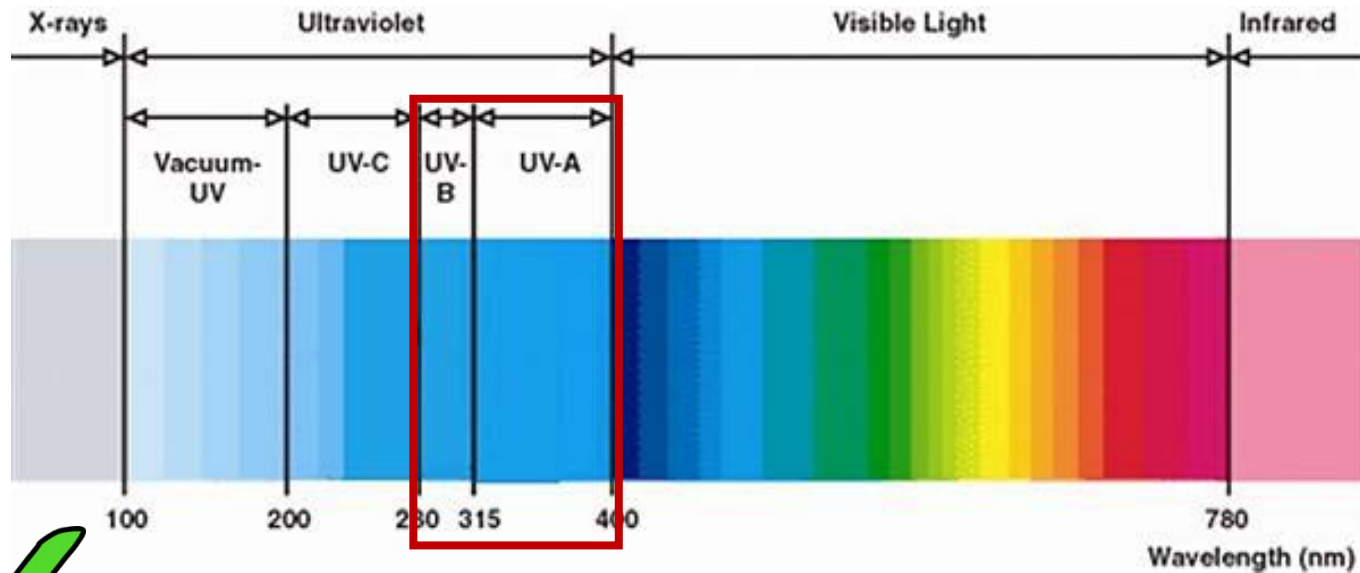
2

Phototherapy
for Psoriasis

3

Predicting
Response to
Phototherapy

Phototherapy for Psoriasis



NBUVB
(Narrowband UVB)

311 (± 2) nm

PUVA
(Psoralen with UVA)

Slightly greater efficacy but
higher risk of skin cancer

How **NBUVB** Clears Psoriasis

- ↓ **Langerhans cells** in epidermis, impairs antigen presentation & migration to lymph nodes
- Induces **apoptosis** of infiltrating **T-cells**
- Photo-isomerization of trans- to **cis-urocanic acid**
- Converts **Th1** → **Th2** immune response
(↓ IFN- γ , IL-2, IL-12 ; ↑ IL-4, IL-10)
- Suppresses the **IL-23/IL-17** axis

NBUVB for Psoriasis



- 2 to 3 times per week
- Starting dose determined by:
 1. Minimal Erythema Dose testing
 2. Skin Phototype
- Dose gradually increased
- **Two-thirds** show significant **improvement** ($\geq 75\%$ clearance)
- Long term \uparrow risk of skin cancer

1

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Predicting
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Can we **Predict Response** to NBUVB?

A



B



Very limited evidence in the literature to guide us

Clinical and genetic predictors of response to narrowband ultraviolet B for the treatment of chronic plaque psoriasis

C. Ryan,* L. Renfro,† P. Collins,* B. Kirby* and S. Rogers*

2010

- Prospective study in Ireland; N = 119
- Predictors of **faster response** to reach clearance: (p<0.05)

1. Lower baseline psoriasis severity
2. Female gender
3. Lower body weight
4. Higher number of previous courses of NBUVB
5. **Taq1 VDR polymorphism** predicted remission duration (homozygous C allele → shorter remission)

Toll-like receptor 9 promoter polymorphism as a predictive factor of narrow-band UVB phototherapy response in patients with psoriasis

Jorge Romani¹, Marc Julià², Francisco Lozano³, Carlos Muñoz-Santos⁴, Antonio Guilabert⁴, José M Carrascosa⁵, Mercedes Rigla⁶ & Jesús Luelmo¹

2014

- Prospective study in Spain; N = 39
- TLRs activate innate immune system → psoriasis
- Analysed role of functional SNPs of TLR2, 5, 4, 9

TLR9-1486 T/C SNP variants:

- **TC & CC** genotypes showed **better response** to NBUVB phototherapy, than TT genotype



Serum IL-22 correlates with psoriatic severity and serum IL-6 correlates with susceptibility to phototherapy

Lo YH, Torii K, Saito C, Furuhashi T, Maeda A, Morita A.

2010

- Japanese study; 32 psoriasis pts + 5 healthy controls
- Blood obtained before & after phototherapy

1. **IL-22 & IL-17** significantly higher in psoriasis pts.
Only **IL-22** correlated well with psoriasis severity.
2. **IL-6** correlated well with % improvement in disease severity after phototherapy
→ **High baseline serum IL-6** levels may confer higher susceptibility to phototherapy

Itch and scratching as predictors of time to clearance of psoriasis with narrow-band ultraviolet B therapy

A.W.M. Evers,*† M.M. Kleinpenning,† T. Smits,† J. Boezeman,† P.C.M. van de Kerkhof,† F.W. Kraaimaat* and M.J.P. Gerritsen†

2009

- Prospective study in Netherlands; N = 109

- 1. Higher levels of itch & scratching** increase the number of phototherapy sessions needed to achieve clearance.
- 2. Baseline psoriasis severity & skin phototype** **NOT** correlated with response to phototherapy.

Importance of Predicting Response to NBUVB Phototherapy

- NBUVB is **commonly used** to treat psoriasis
- **One-third** of patients do **NOT** respond to NBUVB
 - Wastage of time, money
 - Potential risk of skin cancers
 - Disease progression & complications
 - Inefficient utilisation of healthcare resources

Research **Opportunity**

To determine **predictors of response to phototherapy** in psoriasis patients

- **Clinical factors**
- **Genetic factors**
- **Biomarkers** (tissue / blood)

eugenetan@nsc.com.sg