Case Studies in Psoriasis

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Sponsored by Abbott

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Psoriasis
What is psoriasis?

- A skin disease affecting ~3% of population
  - Exaggerated proliferation of keratinocytes
- Activated immune system
  - Mediated by TNFα, IL23
- An inherited disease most common in Caucasians
  - Polygenic
  - M=F; onset 20-39M, 40-59F
- Many different diseases
  - At least 10 different clinical types
  - Early onset vs late onset
What is psoriasis?

- A systemic disease
  - Arthritis, metabolic syndrome: cardiovascular disease, hypertension, dyslipidaemia, type 2 diabetes, renal disease
- A lifestyle disease
  - Aggravated by obesity, alcohol, smoking, stress

- Especially if:
  - Large plaques
  - Early onset
  - Severe
Clinical characteristics of psoriasis

- Raised, well-defined erythematous plaques with irregular borders and silvery scales
- Predilection for scalp, elbows, knees and trunk
- Very high negative impact of quality of life
- Requires long-term treatment
- Associated with decreased life span
Psoriasis
Molecular genetics: complicated\textsuperscript{1}!

- Genetic variations studied by PCR & microarrays:
  - Single nucleotide polymorphisms (SNPs)
  - Copy number variants (CNVs)
  - Copy-neutral loss of heterozygosity (LOH)

- Psoriasis-susceptibility loci PSORS 1-9
  - Some loci also code for metabolic syndrome, cardiovascular disease, type 2 diabetes, familial hyperlipidaemia

- Gene expression data analysis
  - Psoriasis is chronic interferon- and T-cell-mediated immune disease of the skin where imbalance in epidermal cellular structure, growth and differentiation arises from molecular antiviral stress signals initiating inappropriate immune responses

\textsuperscript{1}Al Robaee A A, Molecular genetics of Psoriasis. Int J Health Sci (Qassim) 2010;4:103-127
Psoriasis is a systemic disease
Immunopathogenesis: complicated¹!

- Activated by environmental factors
  - Mechanical trauma, infections, medications, emotional stress
  - Release of IL1, TNFα, heat shock proteins
- Stimulates innate immunity
  - Dendritic cells in epidermis & dermis, keratinocytes
  - Release chemokines, cytokines, growth factors
- DC processes antigen (?what) triggering adaptive immunity
  - Th1 cells produce INF-γ, TNF-α & IL-2
  - Th17 cells produce IL-17, TNF-α, IL-6 & IL-22
  - Tc1 cells produce TNF-α, INF-γ, perforins & granzyme B

Immunopathogenesis: complicated\(^1\)!

- Activated T-cells migrate to the epidermis & dermis
  - Produce numerous cytokines, chemokines, antimicrobial peptides
- Activated dendritic cells
  - Produce more cytokines: IL12, IL23 amplifying Th1 and Th17 response
  - IL20, IL22 stimulates keratinocytes to proliferate
  - IL17 stimulates keratinocytes to produce antimicrobial peptides
  - TNF-\(\gamma\) stimulates keratinocytes to produce IL-8, IP-10, IL-1, TNF-\(\alpha\) and growth factors favouring angiogenesis
  - Nitric oxide (iNOS) causes vasodilatation
- Involves toll-like receptors
- Etc.

Figure 1: Main proteins produced by dendritic cells (DCi) and myeloid dendritic cells of the inflammatory type (DCi), auxiliary T lymphocytes type 1 (Th1), auxiliary T lymphocytes type 17 (Th17) and keratinocytes (K) in psoriasis. FC: growth factors; iNOS: synthetase inducer of production of nitric oxide.
Why do we have to know about this?

- Partly the same pathway as pathogenesis of atherosclerosis
  - Patients with psoriasis have higher incidence of cardiovascular diseases and metabolic syndrome
- Biologic medications have immunological targets
  - Anti T-cell (not so effective: e.g. alefacept)
  - Anti TNF-α (adalimumab, etanercept, infliximab, golimumab)
  - Anti IL12/23 (ustekinumab, briakinumab [in Phase III trials])

Compared to conventional treatments, they are more effective, safer and more convenient. They also may reduce mortality from comorbidities.
Psoriasis: phenotypic classification

- Localised
  - Plaque psoriasis
    - Limbs
    - Trunk
  - Facial psoriasis
  - Flexural psoriasis
  - Scalp psoriasis
  - Palmoplantar psoriasis

- Widespread
  - Guttate psoriasis
  - Generalised pustular
  - Erythrodermic psoriasis

- Consider also:
  - Stable/unstable
  - Small/large plaque
  - Onset <40 yrs / >40 yrs
  - ±Nail involvement
  - Follicular

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First, assess the patient

- Type, extent, severity and distribution of psoriasis
- Age, sex, occupation, domicile of patient
- Comorbidities, medications, adverse reactions
- Skin type, photosensitivity
Case 1 – localised plaque psoriasis

- 48 year-old female
- Psoriasis for 4 years
- Confined to elbows, knees and buttocks
- Complains of mild itch and significant embarrassment
Case 1 – topical options

- Topicals are suitable for every patient
- The only treatment required by those with mild psoriasis
- But not very effective and sometimes difficult to apply

- Emollients
- Keratolytics
- Topical steroids
- Vitamin-D derivatives
- Coal tar
- Dithranol
Emollients

Reduce:
- Itch
- Stinging
- Dryness

Choose:
- Lotion
- Cream
- Ointment
Keratolytics

- Urea 10% cream
- Salicylic acid
- Lactic acid

In:
- Cetomacrogol cream
- Paraffin
Potent topical steroid ointments

- Suitable for trunk, limbs
- Unsuitable for flexures
- Ineffective on palms/soles

- Courses of 2-4 weeks

Then:
- Weekend pulses
Vitamin D derivatives

- Calcipotriol Daivonex®
- Ointment > Cream > Solution
- Max. 100 g/week
- May irritate and peel
- Erythema tends to persist
Coal tar

- Messy & smelly
- Especially for scalp (leave-ons & shampoos)
- Wash off after an hour or more
- Refined coal tar less messy but less effective than crude coal tar (LPC 2-20%)
Dithranol

- Stains & burns
- Short-contact
- Suitable for large plaques only
Case 2 – Facial psoriasis

- 8 year-old boy
- Psoriasis for 6 months
- Facial psoriasis concerns parents
Case 2 – tx topical steroid

- Clobetasone butyrate suitable for face, flexures
- Ineffective elsewhere

- Courses of 2-4 weeks

Then:
- Weekend pulses
Option for thin skin: calcineurin inhibitor

- Pimecrolimus cream
  Elidel®
- For face & flexural psoriasis
- Children & adults
- Twice daily, longterm
- May burn at first

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Case 3 – flexural psoriasis

- 60 year-old moderately obese woman
- Chronic intertrigo: under breasts, abdominal folds, natal cleft, umbilicus
- Embarrassing & painful during mammogram
Case 3 – topical tx for moist skin folds

- Calcipotriol cream bd
- If itchy, use qd hydrocortisone cream
- Use potent topical steroids sparingly e.g. for 2 weeks prior to mammogram
Case 4 – scalp psoriasis

- 25 year-old woman
- Complained of itch, scale and patchy hair loss
- Shampooing daily without improvement
Case 4 – shampoo options

- One-month trial of ketoconazole shampoo
- If ineffective, recommend tar shampoo
- May add conditioner of choice
Case 4 – to lift adherent scale

- Soften scale with salicylic acid and tar prior to shampooing - try Coco Scalp cream
Case 4 – to teach red patches

- Add topical steroid solution or lotion two or three times weekly
- If plaques thin, add calcipotriol solution bd
- Do not let solution drip onto facial skin
Antifungals

- *Malassezia* yeasts provoke sebopsoriasis
- Scalp, face, chest, groin
- Ketoconazole & ciclopirox shampoo & cream
- Trial of oral itraconazole for severe scalp psoriasis

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Case 5 – acute guttate psoriasis

- 17 year-old presents with numerous small plaques
- 2 weeks prior to onset, acute streptococcal tonsillitis treated with penicillin
Cace 5 – topical tx for psoriasis

- Small plaques: emollients
- Itching: hydrocortisone cream
Case 5 - referred for phototherapy

- Moderate to severe thin plaque psoriasis on trunk and limbs
- Patient must live nearby & has transport
Contraindications for phototherapy

- Skin type 1
- Photosensitivity
- Skin cancer: melanoma
- Inaccessibility
Phototherapy for thin plaque psoriasis

- Sunlight
- UVB
  - Broadband
  - Narrowband - 311nm
  - Targeted
- PUVA
  - Whole body (outmoded)
  - Localised
Phototherapy regime

- 3 times weekly, 6-12 weeks
- Protect genitals & face
- Aim for pink skin (not red)
- Increase dose progressively
Complications of phototherapy

- Burns
- Photosensitive rashes
- Photoaging
- Skin cancer
Case 6 – keratoderma of palms & soles

- New onset plaques on both palms
- Longstanding scaly feet
- Fissuring – painful to walk
- Unsightly nail dystrophy
- Resistant to topical therapy
Case 6 – topical tx for keratoderma

- Keratolytic emollients to descale e.g., salicylic acid ointment
- Use ultrapotent topical steroid bd for 4 weeks then 2 or 3 times per week, if necessary under occlusion
- Coal tar ointment is messy - may help soles
Case 6 – localised phototherapy

- Hands & feet can be treated by bathwater PUVA soaks
- Three times weekly for ≥3 months
Case 7 – palmoplantar pustulosis

- 58 year-old smoker
- Itchy, painful, unsightly

Palmoplantar pustulosis is no longer considered Psoriasis
Case 7 – options for pustulosis

- Crude coal tar effective but no longer available
- Limited benefit from:
  - Emollients
  - Refined coal tar ointment
  - Ultrapotent topical steroid
- Doxycycline 100mg x 3 mth
- Refer for phototherapy + acitretin
Case 6 & 7 – acitretin: Neotigason®

- Special authority application
- 10 - 50 mg daily
- Emollients

Contraindication:
- Pregnancy
- Childbearing potential
- Untreated hyperlipidaemia
Monitoring acitretin

- CBC, LFT, lipids
  - Monthly x 3
  - 3-monthly
- Review patient regularly for efficacy and to manage mucocutaneous side effects
Adverse reactions to acitretin

- Teratogen
- Mucocutaneous dryness
- Retinoid dermatitis
- *Staph. aureus* infection
  - Cheilitis
  - Paronychia
- Tiredness
- Hypertrygliceridaemia
- Hepatitis (rare)

It can make your hair curl!
Case 8 – chronic plaque psoriasis

- 45 year-old woman with longstanding plaque psoriasis
- Nail dystrophy
- Painful swollen finger joints
- Heavy smoker
- Recently flare
Case 8 – assessment of psoriasis

- BSA 15%
- PASI score 20
- DLQI score 20
Assessment: PASI score (0-70)

Psoriasis Area Severity Index (PASI) Calculator (1.6.6)

The Psoriasis Area Severity Index (PASI) is an index used to express the severity of psoriasis. It combines the severity (erythema, induration and desquamation) and percentage of affected area.

This free online application helps physicians and patients in the computation of the PASI. If you find this application useful, you can help with the costs of hosting with a small contribution.

Complete the section if your patient has severe chronic plaque psoriasis of the whole body.

PASI calculation and body diagram

- Head
  - Erythema
  - Induration
  - Desquamation

- Arms
  - Erythema
  - Induration
  - Desquamation

- Trunk
  - Erythema
  - Induration
  - Desquamation

- Legs
  - Erythema
  - Induration
  - Desquamation

Area

Erythema
Induration
Desquamation (scaling)

Area

Erythema
Induration
Desquamation (scaling)

PASI =

If PASI > 10, psoriasis is severe.
If BSA > 10, psoriasis is severe.

http://pasi.corti.li

http://www.dermnetnz.org/scaly/pasi.html
Assessment: DLQI (score 0-30)

The scoring of each answer is as follows:

- Very much: scored 3
- A lot: scored 2
- A little: scored 1
- Not at all: scored 0
- Not relevant: scored 0
- Question unanswered: scored 0
- Question 7: "prevented work or studying": scored 3

The DLQI can also be analysed under six headings or dimensions as follows:

- Symptoms and feelings: Questions 1 and 2. Score maximum 6
- Daily activities: Questions 3 and 4. Score maximum 6
- Leisure: Questions 5 and 6. Score maximum 6
- Work and School: Question 7. Score maximum 3
- Personal relationships: Questions 8 and 9. Score maximum 6
- Treatment: Question 10. Score maximum 3

If DLQI >10, psoriasis has significant impact.
Case 8 – nail dystrophy

- Pitting, onycholysis, ridging, subungual hyperkeratosis, nail thickening or splitting
- May resemble onychomycosis – if in doubt, obtain clippings for mycology
- Treatment-resistant
- Associated with psoriatic arthritis affecting digits
Case 8 – psoriatic arthritis?

- PsA affects ~30% who have psoriasis
  - 70% skin first
  - 15% joints first
  - 15% skin with joints
  - Often nails / distal fingers
- Presents with:
  - PIP, DIP synovitis
  - Dactylitis (sausage finger)
  - Enthesitis (heel, plantar)
  - Oligoarthritis large joints
  - Spinal involvement
Psoriatic arthritis assessment

- Screening questionnaire
  - E.g. PASE
  - 7 Q symptoms, 8 Q function
  - PASE >47 = high risk
- Refer if:
  - Morning stiffness >2 hr
  - Nail disease
  - Pain a.m. > p.m.
  - Swelling / dactylitis
  - Enthesitis

Psoriatic Arthritis Screening and Evaluation (PASE) Questionnaire

Please circle or mark ONLY ONE of the five choices on the following 15 questions. The answers to these questions will help us better understand your symptoms. This should take about 5 to 6 minutes to complete. Thank you for your time.

Symptom Score (Max 15)

- Add scores for questions 1-7 and write next to A.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I feel tired for most of the day</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. My joints hurt</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. My back hurts</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. My joints become swollen</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. My joints feel 'hot'</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Occasionally, an entire finger or toe becomes swollen, making it look like a 'sausage'</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. I have noticed that the pain in my joints moves from one joint to another, e.g. my wrist will hurt for a few days then my knee will hurt and so on</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

- Add scores for questions 8-15 and write next to B.

<table>
<thead>
<tr>
<th>Function</th>
<th>Strongly disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>8. I feel that my joint problems have affected my ability to work</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>9. My joint problems have affected my ability to care for myself, e.g. getting dressed or brushing my teeth</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>10. I have had trouble wearing rings on my fingers or my watch</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>11. I have had trouble getting in or out of a car</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>12. I am unable to be as active as I used to be</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>13. I feel stiff for more than 2 hours after waking up in the morning</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>14. The morning is the worst time of day for me</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>15. It takes me a few minutes to get moving to the best of my ability, any time of the day</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

- Add scores in boxes A and B and write next to C.

| Total PASE Score (Max 30) | Add scores in boxes A and B and write next to C. |

| Symptom Score (Max 15) | Function Score (Max 40) | Total PASE Score (Max 30) |

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Case 8 – consider exacerbating factors?

- Infection – bacterial, viral
- Injuries including sunburn
- Psychological stress
- Smoking
- Metabolic syndrome
- Drugs:
  - lithium, interferon, antimalarials, beta blockers etc
Case 8 – co-morbidities?

- Abdominal obesity
- Type 2 diabetes
- Low HDL cholesterol
- High triglycerides
- High blood pressure
- Coronary heart disease

- Metabolic syndrome leads to psoriasis that is:
  - Extensive
  - Resistant to treatment
  - Release of TNFα
  - Abdominal fat releases growth factors
  - Phototherapy burns, ineffective
Benefits of weight loss

- Lowered blood pressure
- Reduced total cholesterol and improved LDL/HDL cholesterol ratio
- Lowered triglyceride levels
- Improved insulin sensitivity
- Reduced extent & severity of psoriasis
Case 8 - topical tx for trunk & limbs

- Large plaques: calcipotriol ointment twice daily
- Potent or ultrapotent topical steroid ointment (e.g., Dermol®, Elocon®) as weekend pulses
- Extensive psoriasis unlikely to clear with topical therapy
- Poorly motivated to treat extensive areas long term
Risks from ultrapotent steroids

- Cushing’s if applied to large areas for long periods
- Localised skin atrophy
- Monitor prescriptions
- Use intermittently
  - 2 days per week
- Examine the patient
Treat arthritis before it’s mutilating

- NSAID symptoms only
- MTX
- Sulfasalazine
- Lefluimide
- TNF\(\alpha\) inhibitor
  - Etanercept
  - Adalimumab
  - Infliximab
  - Golimumab
Case 8 – oral treatment options

- Metformin for metabolic syndrome & for psoriasis
- Methotrexate: helps PsA
- Acitretin
- Ciclosporin
Case 8 – methotrexate

- 15 mg once weekly
- Folic acid 2 days/week
- Slowly effective over 3 months

Pretreatment checks:
- No liver disease
- Minimal EtOH
- Using contraceptives (M + F)
- Not on other folate antagonists e.g. trimethoprim
Monitoring methotrexate

- CBC, LFT, Renal
  - Weekly x 4
  - Monthly x 3
  - 3-monthly
- P3NP collagen
  - Baseline + 6-monthly
- Transient elastography
  - Baseline + 3-yearly
- Liver biopsy
  - If abnormal
Adverse reactions to methotrexate

- GI disturbance
- Mouth ulceration
- Hepatitis
- Hepatic fibrosis & cirrhosis
Case 9 – severe resistant psoriasis

- A 56 year old farmer with psoriasis since his 20s.
- Non-smoker, moderate alcohol.
- Psoriatic arthritis hands & feet.
- Past melanoma – unsuitable for phototherapy
- Acitretin, ciclosporin unhelpful
Case 9 – other options

• Ciclosporin
• Hydroxyurea
• Azathioprine
• 6-mercaptopurine
• Mycophenolate
• Biologic agents
Case 9 – ciclosporin: Neoral®

- 2.5 - 5 mg/kg/day until clear
- Drug interactions ++
- Motivated patients:
  - Severe psoriasis
  - Failed to clear with other meds
  - Adverse effects from other meds
- Works quickly for most patients
Contraindications to ciclosporin

- Renal dysfunction
- Uncontrolled hypertension
- Skin cancers
- Non-compliant patient
Monitoring ciclosporin

- Creatinine
  - 2-weekly x 8 weeks
  - Monthly
- BP
  - 2-weekly x 8 weeks
  - Monthly
  - Treat if increased (or dose reduction)
- LFT, uric acid, lipids
  - 3-monthly
Adverse effects from ciclosporin

- Hypertension
- Renal dysfunction
- Skin cancer
- GI disturbance
- Paraesthesias, tremors
- Hirsutism
- Dependence
Other options – hydroxyurea

- 500 - 1000 mg daily
- Monitor CBC
  - Macrocytosis
  - Leucopaenia
- Slow to be effective
- Can induce leg ulcers and skin cancers
Azathioprine and 5-mercaptopurine

- Rarely used for psoriasis as not very effective
- Pretreatment assessment thiopurine methyltransferase
- 50 to 150 mg daily
- Monitor CBC, LFT every 2 weeks for 8 weeks then monthly
- Complications
  - Pancytopaenia
  - Hepatitis
  - Risk of skin cancer, lymphoma
Mycophenolate: Cellcept®

- Now on Special Authority to dermatologists for treatment-resistant skin disease including psoriasis
- Contraindications:
  - Pregnancy
- 1 to 1.5 g twice daily
- Complications:
  - Anaemia
  - GI tract symptoms
  - Infections
Case 9 – assessment

- Failed ciclosporin
- PASI 20 on methotrexate
- DLQI 15
- Grade 2-3 hepatic steatosis, psoriatic arthritis, meniere’s, hypertension
- Negative tests for TB, hepatitis viral serology
- Considered for biologic treatment
Case 9 - adalimumab: Humira®

- Special Authority application if PASI $\geq 15$ on treatment and failed phototherapy, mtx, acitretin, ciclosporin
- TNFα blocker
- Workup includes:
  - TB: CXR, Mantoux, quantiferon Gold
  - Hepatitis B, C, HIV
Case 9 at 3 months

- Adalimumab 80mg sc stat, 40mg after one week then 40mg every 2 weeks
- PASI 3, DLQI 0
Case 10 – Longstanding severe psoriasis with exanthematic flares

- A 58 year-old early childhood teacher.
- Non-smoker, moderate alcohol.
- Obesity, type 2 diabetes, hypertension, depression.
- Failed treatment included: acitretin, methotrexate, ciclosporin, UVB
Case 10 – work up for adalimumumab

- 95kg
- PASI = 16
- DLQI = 10
- PASE = 57
- Negative tests for TB, hepatitis viral serology

- Treated with adalulimab
  - PASI = 3 at 3 months
Case 10 – tx with adalimumab

- PASI = 3 at 3 months
- DLQI = 0
- PASE = 57
Case 10 – relapse

- On adalimumab for 6 months
- PASI = 10
- PASE = 57
- Unhappy patient!
Case 10 – tx with etanercept

- Etanercept 50mg twice weekly for 3 months, expecting to reduce to once weekly in July 2011
- At 2 months, verbal report is that psoriasis is nearly clear
- Adverse effects: bronchitis and superficial skin infection
Etanercept: Enbrel®

- Special Authority application if PASI $\geq 15$ on treatment and failed phototherapy, mtx, acitretin, ciclosporin
- TNFα blocker
- Workup includes:
  - TB: CXR, Mantoux, quantiferon Gold
  - Hepatitis B, C, HIV
Biologic agents for severe psoriasis

TNF blockers:
- Infliximab IV infusion
- Adalimumab SC every 2 wks
- Etanercept SC every week

Anti-IL 12/23:
- Ustekinumab every 3 months (unfunded)
Advantages of biologic agents

• Very effective
  • PASI 75 in 60% at 3-6 months
• Well tolerated
• Very happy patients!
Disadvantages of biologic agents

- Expensive
- Increase infection
  - Treat aggressively
  - Monitor for TB
- May increase risk of lymphoma (rare)
- Relapse may occur
- They can cause skin rashes including psoriasis!
For further information:

DermNet NZ: the dermatology resource

- About us: DermNet NZ
- News & notices: NZ Dermatological Society
- NZOSI Members log in here
- NZ Dermatology Trainees log in here
- Dermatology nurses
- Patients with skin problems, their relatives & friends
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- Other dermatology resources
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- Install DermNet NZ search plugin for Firefox or IE
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