Comorbidities

Peter Foley MBBS, BMedSc, MD, FACD
Associate Professor of Dermatology, The University of Melbourne, Department of Medicine (Dermatology), St Vincent’s Hospital Melbourne
Dermatology Investigation, Biological Therapies and Photobiology Clinics, St Vincent’s Hospital Melbourne
Phototherapy and Biological Clinics, Skin and Cancer Foundation Inc (Victoria)
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- CSL - A, SP
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- 3M/iNova/Valeant - A, I, SP
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- Roche - C, SP, T
- Ascent - C, SP, T
- Clinuvel - A, C, I
- GSK/Stiefel - A, I, SP

- Abbott - A, SP
- BiogenIdec - A, I, SP
- Janssen-Cilag - A, C, SP
- Merck Serono - A, I, SP
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- Amgen - A, I
- Novartis - A, I, SP, T
- Eli Lilly - I
- Celgene - I
- Australian Ultraviolet Services - C
- Aspen - SP
- BMS - I

- A = advisory board
- C = consultant
- I = investigator (clinical trials)
- SP = speaker’s bureaux
- T = travel grants
Psoriasis morbus fortiorium

“Psoriasis: the disease of people in good health”
Comorbidities in Psoriasis

• A distinct number of concomitant disease entities have more frequently been observed than expected
• Such associations referred to as ‘comorbidities’
• May represent effect of shared risk factors
  – Genetic predisposition
  – Environmental exposure
  – Factors related to long course of psoriasis
  – Factors related to treatment of psoriasis
• May represent an artifact because of increased surveillance of patients with psoriasis
Comorbidities in Psoriasis

- Metabolic syndrome
  - Hypertension
  - Diabetes mellitus Type II
  - Dyslipidaemia
- Obesity
- Cardiovascular disease and death
- Psoriatic arthritis
- Inflammatory Bowel Disease
- Anxiety and Depression
- Smoking and Alcohol
- Lymphoma
### Co-morbidities In Psoriasis Patients

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total (n=1000)</th>
<th>Moderate (n=398)</th>
<th>Severe (n=204)</th>
<th>Very Severe (n=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>27%</td>
<td>17%</td>
<td>35%</td>
<td>37%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>23%</td>
<td>20%</td>
<td>23%</td>
<td>28%</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>22%</td>
<td>14%</td>
<td>24%</td>
<td>39%</td>
</tr>
<tr>
<td>Obesity</td>
<td>17%</td>
<td>10%</td>
<td>25%</td>
<td>23%</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>16%</td>
<td>11%</td>
<td>21%</td>
<td>19%</td>
</tr>
<tr>
<td>Depression</td>
<td>16%</td>
<td>12%</td>
<td>16%</td>
<td>22%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11%</td>
<td>6%</td>
<td>14%</td>
<td>16%</td>
</tr>
<tr>
<td>Substance / Alcohol abuse</td>
<td>10%</td>
<td>7%</td>
<td>13%</td>
<td>15%</td>
</tr>
<tr>
<td>All other forms of arthritis</td>
<td>8%</td>
<td>4%</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Skin Cancer</td>
<td>2%</td>
<td>1%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
<td>6%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>None</td>
<td>31%</td>
<td>44%</td>
<td>23%</td>
<td>15%</td>
</tr>
</tbody>
</table>

*EU CHART study report 2004*
<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>328</td>
<td>48.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>178</td>
<td>26.4</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>139</td>
<td>20.6</td>
</tr>
<tr>
<td>Depression</td>
<td>105</td>
<td>15.6</td>
</tr>
<tr>
<td>Diabetes</td>
<td>91</td>
<td>13.5</td>
</tr>
<tr>
<td>Non-melanoma skin cancer</td>
<td>61</td>
<td>9.1</td>
</tr>
<tr>
<td>Liver disease</td>
<td>60</td>
<td>8.9</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>36</td>
<td>5.3</td>
</tr>
<tr>
<td>Other psychiatric illness</td>
<td>30</td>
<td>4.5</td>
</tr>
<tr>
<td>Other cancer</td>
<td>25</td>
<td>3.7</td>
</tr>
<tr>
<td>Melanoma skin cancer</td>
<td>18</td>
<td>2.7</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>18</td>
<td>2.7</td>
</tr>
</tbody>
</table>
Comorbidities of plaque psoriasis

- Increased risk of cardiovascular (CV) disease and CV risk factors\(^1\textsuperscript{-6}\)
  - Including obesity\(^2,3\), diabetes\(^1\textsuperscript{-3}\), metabolic syndrome\(^3,5\), hypertension\(^1\textsuperscript{-3}\), hyperlipidaemia\(^1,2\), and non-alcoholic fatty liver disease\(^5\)
- The development of CV and/or metabolic disease may be linked to:
  - Conventional risk factors for CVD/metabolic syndrome
  - Persistent systemic inflammation associated with chronic psoriasis\(^7,8\)
- Psoriatic arthritis is a common complication, arising in up to one-third of psoriasis patients\(^3\)
  - Clinically unrecognized enthesitis may occur in early PsA\(^9\)
  - Dactylitis is associated with increased radiological damage\(^10\)
- Psoriasis has also been associated with an increased risk of Crohn’s disease, chronic obstructive pulmonary disease, and gastroesophageal reflux disease\(^1,2\)

Psoriasis Severity

• Association with comorbidities

• Higher Psoriasis Disease Severity is Associated with Increased Comorbidities in Europe. Sato R, Piercy J, Kay S, Walker S, Singh A. (Wyeth Research / Adelphi Group Products)
Inflammatory dysfunction is likely to contribute to the development of comorbidities in psoriasis.

- Immune dysregulation and inflammation play an important role in the development and progression of psoriasis\(^1,2\).
- As psoriasis progresses, persistent inflammatory dysfunction may drive the development of comorbid conditions such as cardiovascular disease\(^1,2\).

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The psoriatic march and the development of comorbidities

- Genes
- Environmental triggers
- Psoriasis
- Obesity
- Metabolic syndrome
- Diabetes
- NAFLD
- Hypertension
- Dyslipidaemia
- Smoking
- Cardiovascular diseases
- Psoriatic arthritis

Metabolic Syndrome

- For metabolic syndrome to be diagnosed, at least three of the following apply:
  - Waist circumference $> 102$ cm (men); $88$ cm (women)
  - Serum triglycerides $\geq 1.69$ mmol/L
  - HDL cholesterol $< 1.04$ mmol/L (men); $1.29$ mmol/L (women)
  - Blood pressure $\geq 130/85$ mm Hg
  - Serum glucose $\geq 6.1$ mmol/L

- NIH ATP III (Adult Treatment Panel), www.nhlbi.nih.gov/guidelines/cholesterol
Metabolic Syndrome

• Psoriasis patients:
  – Have ↑ risk of developing metabolic syndrome
  – More severe psoriasis: ↑ risk

• Not known whether link is causative or a result of patient habits eg sedentary life, smoking, alcohol
Psoriasis is associated with an increased risk of the metabolic syndrome

<table>
<thead>
<tr>
<th>Type of rate</th>
<th>OR and 95% CI</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td></td>
<td>2.16</td>
<td>1.16-4.03</td>
</tr>
<tr>
<td>Multivariate†</td>
<td></td>
<td>1.96</td>
<td>1.02-3.77</td>
</tr>
</tbody>
</table>

*Revised NCEP ATP III Definition
†Adjusted for age, sex, race/ethnicity, smoking status, and C-reactive protein (CRP) levels

(US; n = 71 cases, n = 2385 controls)
Hypertension, Diabetes, Dyslipidaemia

- All are more common in pts with psoriasis
  - Obesity, hypertension, heart failure and diabetes were as much as two-fold more prevalent in 2,941 psoriatic inpatients compared to age-matched non-psoriatic patients (Henseler T and Christophers E, Disease concomitance in psoriasis. J Am Acad Dermatol 1995; 32: 982-6).

- **Hypertension**
  - ↑ rate due to obesity or use of cyclosporin
  - Smoking

- **Diabetes Type II**
  - Insulin resistance / metabolic syndrome
  - Associated with obesity

- **Dyslipidaemia**
  - Secondary to medication eg retinoids
  - Associated with obesity
  - Alcohol
Obesity

• Common in psoriasis patients
  – Rates reaching 48%
  – Prevalence ratio of 1.5 in patients with moderate to severe disease
  – Weight loss may improve psoriasis
    • Through reduction of IL-6 and CRP
    • Weight reduction after gastric bypass has resulted in remission of psoriasis
Cardiovascular Disease and Death

- Psoriasis is an independent risk factor for atherosclerosis.
- Severity of psoriasis is independent risk factor for MI regardless of presence of the metabolic syndrome.
- Pts with PASI 10-20 and pts with PASI >20:
  - Similar 10-yr risk of coronary heart disease and stroke
- Compared with general population, 10-yr risk was:
  - 28% greater for coronary heart disease (P<0.001)
  - 11.8% greater for stroke (P=0.02)


- Peripheral vascular disease increased in psoriasis patients.

  *Prodanovich et al (Arch Derm 2009;145(6):700-3)*
Cardiovascular Disease and Death

- Young patients with severe psoriasis have \( \uparrow \) MI / cardiovascular mortality
  - Psoriasis patients treated at least once as an inpatient had a 50% increased risk for cardiovascular mortality compared to the general population
  - Risk was clearly associated with:
    - severity of psoriasis
    - number of hospital admissions
    - admission at a young age

- In UK:
  - Lifespan of patients with severe psoriasis decreased by 5%
  - Patients with onset < 25 yo: Lifespan shortened by 20 years

- Psoriasis most likely predisposes to increased risk of cardiovascular disease by causing increase in \( T_H-1 \) cytokines (TNF-\( \alpha \), IL2, IFN\( \gamma \))
  - Cause upregulation of adhesion molecules and endothelins
  - Cause premature vascular damage and atherogenesis
Psoriasis may confer an independent risk of MI. The RR was greatest in young patients with severe psoriasis.

Severe psoriasis is associated with an increased risk of all-cause mortality.

Hazard ratio (95% confidence interval) for all-cause mortality vs controls

- Severe psoriasis (n=3951)
- Mild psoriasis (n=133,568)

Retrospective, population-based cohort study (UK; n=137,519 cases, n=575,433 controls)

Risk of obesity is significantly increased in patients with psoriasis

Cross sectional studies about risk of obesity in psoriatic patients (odds ratio with 95% confidence interval).

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk of obesity (odds ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herron 2005</td>
<td>2.39</td>
</tr>
<tr>
<td>Naldi 2005</td>
<td>1.9</td>
</tr>
<tr>
<td>Neimann 2006</td>
<td>1.84</td>
</tr>
<tr>
<td>Gisondi 2007</td>
<td>1.19</td>
</tr>
<tr>
<td>Kaye 2008</td>
<td>1.29</td>
</tr>
<tr>
<td>Cohen 2008</td>
<td>1.18</td>
</tr>
<tr>
<td>Naldi 2008</td>
<td>1.7</td>
</tr>
<tr>
<td>Driessen 2008</td>
<td>5.49</td>
</tr>
</tbody>
</table>

Control
- General population (databases)
- Dermatological patients

Populations
- Matching
- Not matching

Type of psoriasis
- Mild and moderate
- Severe

*See slide notes for citations in full.
Obesity is a relevant risk factor for psoriasis and precedes development of psoriasis

- Body mass index is a risk factor independently associated with onset of psoriasis\(^1\)
- Increased adiposity and weight gain are strong risk factors for incident psoriasis in women\(^2\)
- Obesity in early adulthood has also been shown to be a risk factor for psoriatic arthritis\(^3\)

Increased BMI is associated with increased risk of psoriatic arthritis

Psoriasis and obesity: a vicious cycle of systemic inflammation

Skin inflammation – psoriasis
- TNF; IL-1, IL-6, IL-8
- IL-15, IL-18, IL-19, IL-20
- IL-12, IL-23, IFN-γ, IL-17
- S100 proteins
- IL-10 (IL-4, IL-13)

Adipose tissue – obesity
- TNF
- MCP-1, M-CSF
- Leptin, IL-6, IL-5, iNoS
- Adiponectin, PAI-1, renin-angiotensin (angiotensinogen)
- SHBG

Cytokines
Leukocytes
Auto-inflammatory loop

Weight gain may occur in patients receiving anti-TNF-α treatment.

Mean weight change (kg) from baseline to Week 48:

- **Infliximab** (n=50): 1.53 kg, p=0.0001
- **Etanercept** (n=50): 2.18 kg, p=0.007
- **Adalimumab** (n=30): 2.57 kg, p=0.0014

Patients in group showing weight gain:

- Infliximab: 48%
- Etanercept: 44%
- Adalimumab: 40%

Weight gain may occur in patients receiving anti-TNF treatment

In three studies in which patients with plaque psoriasis received anti-TNFs with follow up at 24 weeks:

- Mean body weight increased significantly from baseline in patients receiving etanercept (1.5±2.7 kg) (n=58) or infliximab (2.5±3.3 kg) (n=40) (p=0.004)¹

- A relative increase in bodyweight of 2.6±3.2% was observed in a mixed group of patients receiving either etanercept (n=28) or infliximab (n=12)²
  - Blockade of TNF activity was associated with fat and lean mass gain in psoriasis and psoriatic arthritis patients

- Increased bodyweight was recorded in the majority of patients receiving etanercept (54%) (n=62) or infliximab (53%) (n=36)³

Psoriasis is associated with an increased risk of diabetes

Odds ratios (OR) for diabetes in a psoriasis population vs a control population

<table>
<thead>
<tr>
<th>Type of rate</th>
<th>OR and 95% CI</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude data</td>
<td>1.83</td>
<td>1.71-1.96</td>
<td>&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.33</td>
<td>1.26-1.41</td>
<td>&lt;0.00001</td>
<td></td>
</tr>
<tr>
<td>Age- and gender-adjusted</td>
<td>1.33</td>
<td>1.25-1.40</td>
<td>&lt;0.00001</td>
<td></td>
</tr>
</tbody>
</table>

# Cardiovascular Comorbidities

<table>
<thead>
<tr>
<th></th>
<th>RA</th>
<th>IBD</th>
<th>Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>—</td>
<td>↑</td>
<td>—</td>
</tr>
<tr>
<td>Biomarkers of CV risk</td>
<td>↑sICAM-1 ↑homocysteine ↑CRP ↑IL-6</td>
<td>↑sICAM-1 ↑homocysteine* ↑CRP ↑IL-6</td>
<td>↑sICAM-1 ↑homocysteine ↑IL-6 ↑MCP-1</td>
</tr>
<tr>
<td>Increased mortality</td>
<td>2-3x</td>
<td>1.5x</td>
<td>3-4x</td>
</tr>
<tr>
<td>Reduced life expectancy</td>
<td>10-20 years</td>
<td>unknown</td>
<td>3-20 years</td>
</tr>
</tbody>
</table>

*no association with increased CV risk
Psoriatic Arthritis

- Chronic inflammatory arthritis
  - Causes progressive joint damage, reduced function
  - Uveitis frequently associated

- Prevalence 6-25%
  - Lack of consistency between studies concerning diagnostic criteria for PsA

- HLADR4 +ve: severe destructive form

- Usually develops after onset of psoriasis
  - Typically 10 years later

- Increased mortality in psoriatic arthritis
  - Previously active and severe disease, manifested by:
    - Prior use of medications; and
    - Radiologic changes; and
    - Elevated ESR at presentation (Gladman et al, Arthritis Rheum 1998;41:1103-10).

- TNF-α
  - Plays central role in pathogenesis
  - Triggers osteoclastogenesis and bone resorption
    - By stimulating both receptor activation of NF KappaB and its ligand
    - Expressed in bone marrow osteoclast precursors and stomal cells respectively
Screening tools for psoriatic arthritis

- **Psoriasis Epidemiology Screening Tool (PEST)**\(^1\)
  - 5-item questionnaire
  - Sensitivity 92%; specificity 78%
- **Psoriatic Arthritis Screening and Evaluation Tool (PASE)**\(^2\)
  - 15-item questionnaire
  - Sensitivity 82%; specificity 73%
- **Toronto Psoriatic Arthritis Screen (ToPAS)**\(^3\)
  - 12-item questionnaire
  - Sensitivity 87%; specificity 93%
  - Designed to detect PsA in any population, including non-psoriasis populations
- **Early Arthritis for Psoriatic Patients (EARP)**\(^4\)
  - 10-item questionnaire
  - Sensitivity 85%; specificity 92%

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PEST. Courtesy of Professor P Helliwell.\(^1\)
Depression and Anxiety

• Prevalence of depression 10-62% amongst psoriasis patients
  – Range due to inpatient (high) vs outpatient (low)
  – Higher rates of suicidal ideation in severely affected psoriasis inpatients c/w pts with atopic dermatitis, acne

• PASI not a reliable predictor of depression risk

• Pruritus associated with depression in psoriasis patients ? poor sleep

• Impact that psoriasis has on quality of life is a stronger indicator of psychiatric morbidity than clinical severity

• Patients with PsA and skin psoriasis report significantly worse quality of life; joint pain associated with depression

• Perception of stigmatisation amongst psoriasis sufferers the most important predictor of depression

• Those who developed psoriasis young:
  – Harbour stronger feelings of stigmatisation
  – Lack of support correlated with depression

• Depression is:
  – An independent risk factor for heart disease
  – Associated with excess mortality, particularly from cardiovascular disease

• Anxiety found in up to 43% of psoriasis patients

Hayes & Koo 2010
Inflammatory Bowel Disease (Crohn’s Disease, Ulcerative Colitis)

- Crohn’s disease patients
  - 7x higher risk of developing psoriasis
- Psoriasis patients
  - 3x higher risk of Crohn’s disease
- Ulcerative colitis
  - Statistically significant association with psoriasis but not as high as Crohn’s disease
- Crohn’s disease, ulcerative colitis and psoriasis share the same susceptibility loci (6P21), IL-23 receptor and IL-12B genes
  - IL-23 receptor encodes for a subunit of IL-23, pro-inflammatory cytokine
- Crohn’s disease and psoriasis primarily mediated by Th-1 lymphocyte producing cytokines such as TNF-α and IFNγ
What is non-alcoholic fatty liver disease (NAFLD)?

- Characterised by insulin resistance and strongly associated with type 2 diabetes and obesity\(^1\text{-}^3\)
- Defined by fatty changes in the liver in the absence of a history of excessive alcohol consumption\(^1\)
- The spectrum of the disease ranges from simple steatosis to steatosis with evidence of hepatocellular inflammation (non-alcoholic steatohepatitis, or NASH), advanced fibrosis, and cirrhosis\(^1,^2\)
- NAFLD may be primary (associated with the metabolic syndrome) or secondary (associated with nutrition, drugs, toxins, or metabolic or other diseases)\(^1,^2\)

Psoriasis is associated with non-alcoholic fatty liver disease (NAFLD)

NAFLD is a CV disease risk factor

Excess caloric intake
Sedentary lifestyle
Genetic susceptibility

Deranged adipokine profile

Hyperinsulinaemia
↑ Plasma FFA

↑ Visceral and subcutaneous fat and/or adiposopathy

↑ Adipose tissue IR

↑ Skeletal muscle lipids
↑ Ectopic fat

↑ Skeletal muscle IR
Adipose tissue IR

↑ Ectopic fat in other organs e.g. heart

↑ CV risk
(↑ endothelial dysfunction, ↑ dyslipidaemia, hypercoagulability, ↑ inflammation, ↑ atherosclerosis, CV lipotoxicity)

↑ Hepatic steatosis

↑ Hepatic IR

NASH

IR: insulin resistance

Smoking and Alcohol

• **Smoking**
  - **Positive correlation between smoking and psoriasis**
    - >20 cigarettes per day assoc. with 2.2x ↑ in more severe forms of psoriasis
    - Female smokers: 3.3x ↑ risk of psoriasis
    - Palmoplantar pustulosis has strongest association
  - **Pathophysiology of smoking:**
    - Psoriasis involves a neutrophil - predominantly inflammatory infiltrate
    - Smoking thought to alter the morphology and function of neutrophils
    - Also causes damage via oxidation
      - Anti-oxidant levels are low in psoriasis patients, making them more susceptible to oxidative damage

• **Alcohol**
  - Psoriasis patients have higher prevalence of excess alcohol intake
  - Disease severity positively correlated with alcohol intake
  - Excess alcohol intake shown to precipitate psoriasis
  - Excess alcohol consumption a known association with anxiety and depression
Traditional systemic treatments for psoriasis may impact CV risk factors

- **Methotrexate**\(^1-3\)
  - Few studies are available in the psoriasis population and data are not conclusive
  - One study suggested no significant impact on risk of MI, with a trend towards reduced risk in younger patients\(^1\)
  - Another study indicated that moderate doses may reduce the risk of vascular disease versus non-treated psoriasis patients\(^2\)
  - May induce hyperhomocysteinaemia, a risk factor for thrombosis\(^3\)
  - May favour steatohepatitis\(^4\)

- **Ciclosporin**\(^3\)
  - May increase blood pressure (induce or worsen hypertension)
  - May alter glucose tolerance
  - May promote hyperlipidaemia

- **Retinoids**\(^3\)
  - May promote hyperlipidaemia

Therapeutic Potential for Biologics in Managing Comorbidities

• **Metabolic Syndrome**
  - Insulin resistance
    • Biologics inhibit pro-inflammatory cytokines, potentially improving insulin sensitivity
    • Isolated cases of psoriasis and rheumatoid arthritis pts with diabetes developing unpredictable hypo- or hyperglycaemia after commencing anti-TNF-α treatment
  - Body Mass Index and weight
    • Reports of anti-TNF-α medications associated with significant weight gain and increases in BMI
      
    • Weight gain may aggravate preexisting metabolic syndrome
    • Biologics with a fixed-dose regimen may have a compromised efficacy in heavier individuals
      
    • Fully human monoclonal anti-p40 antibody not associated with weight gain

• **Blood lipids**
  - Biologics' effects on blood lipids: mixed and unclear results

• **Cardiovascular Disease**
  - Biologics inhibit pro-inflammatory cytokines
    • Potentially decreasing cardiovascular risk and mortality
  - TNF-α antagonist contraindicated in pts with moderate-severe forms of congestive heart failure
Therapeutic Potential for Biologics in Managing Comorbidities

• Psoriatic Arthritis
  – Clinical trials have shown that TNF-α antagonists:
    • Markedly inhibit inflammation
    • Reduce structural joint damage
      – Radiographic evidence of inhibition of progressive joint disease

• Inflammatory Bowel Disease
  – Crohn’s disease and ulcerative colitis
    • Anti-TNF-α antibodies have proven beneficial effect
    • Etanercept: Lack of efficacy
      – Report of development of Crohn’s disease in treated pts
Biologic treatments for psoriasis: impact on CV risk factors

- Data gathered from rheumatoid arthritis populations receiving anti-TNFs indicate potential for:
  - Reduced insulin resistance
  - Control of inflammation (CRP, IL-6)
  - Increased HDL-cholesterol
  - Decreased risk of arteriosclerotic plaque formation

- In a retrospective study of patients with psoriasis or psoriatic arthritis (n=8845), those treated with TNF inhibitors (n=1673) showed:
  - Significant reduction in MI risk vs topical agents
  - Significantly lower MI incident rate vs topical agents

Management of Comorbidities

- Look closely for comorbidities
  - e.g. signs of insulin resistance
- Be aware of the risk profile
  - e.g. early onset, severe psoriasis increase risk

- For all psoriasis patients:
  - Take complete history
    - DLQI, Smoking, Alcohol
  - Physical examination
    - incl. blood pressure
  - Laboratory screening
    - incl. fasting glucose and lipids
  - CXR, ? ECG
  - Regular monitoring of risk factors
    - Disease associated
    - Medication associated
Management of Comorbidities

• Encourage lifestyle changes (diet, exercise, stop smoking)
  • High body mass index is associated with a reduced short-term clinical response to all systemic treatments
    
    \[\text{(Naldi et al. Dermatology 2008; 217:365-73)}\]

  • Weight loss improves the response of obese patients with moderate-to-severe chronic plaque psoriasis to low-dose ciclosporin therapy
    

• Early referral, eg:
  – Metabolic syndrome: refer to endocrinologist / cardiologist
  – Diabetes: refer to diabetic educator / endocrinologist
  – Anxiety / Depression: Psychologist / psychiatrist
  – Liaise closely with GPs eg hypertension control, lipid-lowering meds
Psoriasis: Beyond the Skin

• Need to recognise psoriasis as a chronic inflammatory disorder

• *Choices for therapy should take into account adverse effects of drugs on co-morbidities and dangerous drug interactions*

• Therapy of psoriasis is influenced by and may affect other organ systems and co-morbid diseases;
  – High index of suspicion of side effects associated with systemic treatments

• Therapy of psoriasis may benefit from treating associated metabolic disorders
Psoriasis: Beyond the Skin

- Inflammation associated with moderate-to-severe psoriasis confers a higher cardiovascular morbidity and mortality risk; therefore long-term disease control with systemic therapy may reduce cardiovascular morbidity and mortality in psoriasis patients.

- Patients with psoriasis need a global approach, taking into account their cardiovascular risk profile.

- Assessment of psoriasis severity should take a broader view than just a PASI assessment; address comorbidities such as:
  - Cardiovascular risk factors
  - Psoriatic arthritis
  - Psoriasis symptoms (pruritus, cutaneous pain, burning, bleeding, desquamation)
  - Quality of life

- Broader assessment may indicate earlier treatment than when using PASI alone to assess psoriasis severity.
QUESTIONS?