Psoriasis: An Inflammatory Overactive Autoimmune System Disease

- Localized and systemic inflammation
  - Increased antigen presentation
  - Defects in T regulatory cells
  - Upregulation of Th1 and Th17 cells, antigen-presenting cells, and cytokines
  - Associated with increased CRP values and other markers of inflammation

- Epidermal hyperproliferation
  - Clinically evident as scaling, cracking
  - Associated with elevated uric acid and oxidative stress

- Angiogenesis
  - Clinically appreciated as Auspitz’s sign
  - Associated with increased circulating vascular endothelial growth factor

CRP = C-reactive protein; Th = T helper.
Top photo courtesy of Dr Joel Gelfand, Department of Dermatology, University of Pennsylvania.
Bottom photo courtesy of Dr Rose Elenitsas, Department of Dermatology, University of Pennsylvania.
A Majority of Patients With Moderate to Severe Psoriasis Are Undertreated

- **NPF Survey, 2003-2011 (n = 5604)**

<table>
<thead>
<tr>
<th>Psoriasis</th>
<th>Not Receiving Guideline-Recommended Treatment</th>
<th>Untreated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>30%</td>
<td>36%</td>
</tr>
<tr>
<td>Severe</td>
<td>22%</td>
<td>30%</td>
</tr>
</tbody>
</table>

- **NPF Survey, 2007 (n = 1657)**

  BSA = body surface area; NPF = National Psoriasis Foundation.

Physical and Mental Rankings of Psoriasis and Other Diseases

From Best Functioning (1) to Worst Functioning (11)

- Congestive heart failure
- Psoriasis
- Type 2 diabetes
- Chronic lung disease
- Myocardial infarction
- Arthritis
- Hypertension
- Depression
- Cancer
- Dermatitis
- Healthy

Patients With Psoriasis Are at Increased Risk for Cardiometabolic Disorders

Prevalence of Diseases in Patients With Psoriasis¹

<table>
<thead>
<tr>
<th>Disease</th>
<th>Psoriasis (n = 581)</th>
<th>Control (n = 1044)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>DM</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

Disease Proportion in Patients With Psoriasis²

<table>
<thead>
<tr>
<th>Disease</th>
<th>Psoriasis (n = 16,850)</th>
<th>Control (n = 48,677)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30</td>
<td>25</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>DM</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Obesity</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

CHD = coronary heart disease; DM = diabetes mellitus.

Psoriasis Is Associated With Increased Risks for Mortality, Cardiovascular Disease, Myocardial Infarction, Stroke, and Diabetes

- 50% increased risk of mortality\(^a,1\)
  - Die 3.5-4.4 years younger
- Increased risk for cardiovascular disease\(^3\)
  - 58% increased risk for major adverse cardiac events\(^a,4\)
  - 57% increased risk for cardiovascular death\(^a,5\)
- Increased risk for myocardial infarction\(^2\)
  - Risk increases with disease severity
- 43% increased risk for stroke\(^a,6\)
- 62% increased risk for diabetes\(^a,7\)

\(^a\)Severe psoriasis.

BSA = body surface area.
Conventional Systemic Therapies

- Acitretin
  - Often used in conjunction with UV light
  - PASI 75 highly variable
  - Generally takes 3-6 months for response
  - Efficacy is dose-dependent
- Cyclosporine
  - Recommended to treat severe psoriasis after failure of ≥1 other systemic therapy
  - PASI 75 achieved in 50%-70% of patients after 8-16 weeks
  - Use limited to 1 year
- Methotrexate
  - Most commonly prescribed systemic therapy
  - PASI 75 achieved in 36%-60% of patients after 16 weeks
  - Recommended for treatment of patients with moderate or severe psoriatic arthritis

PASI = Psoriasis Area and Severity Index.

Considerations When Prescribing Acitretin, Cyclosporine, and Methotrexate

- **Acitretin**
  - Significant risk of increased cholesterol levels, particularly triglycerides

- **Cyclosporine**
  - Potential for increased cyclosporine levels with alcohol
  - Potential for exacerbation of gout
  - Patients who have high blood pressure are not good candidates for cyclosporine

- **Methotrexate**
  - Increased risk of hepatotoxicity with alcohol
  - Females of childbearing potential or patients who have liver disease are not good candidates for methotrexate
New Consensus Guidelines: Key Points

- Biologic agents do not carry the risk of end-organ toxicities
  - Can be considered for first-line use in some cases
- Conventional systemic drugs are effective but have significant toxicities

PUVA = psoralen plus UV light A.

Bone Proliferation: An Important Feature of Psoriatic Arthritis

- Periosteal reaction along proximal phalanx of long finger (arrows)
- Marginal erosions at heads of middle and proximal phalanges (arrowheads)
- Periosteal reaction initially is exuberant and fluffy; later, it matures into solid new bone, causing a widened appearance to the shafts
Enthesitis: The Hallmark of Psoriatic Arthritis

- Entheses are the regions at which a tendon, ligament, or joint capsule attaches to bone

- Overexpression of tumor necrosis factor—α, conceivably induced by microtrauma, a subclinical infection, or both, leads to osteitis and entheseseal inflammation

- Inflammation at the entheses is called enthesitis

## FDA-Approved Biologic Agents for Treatment of Patients With Psoriatic Arthritis: TNF-α Blockers

<table>
<thead>
<tr>
<th>Biologic</th>
<th>Structure</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>Human monoclonal antibody</td>
<td>80 mg SC, followed by 40 mg SC every other week</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>Novel Fc-free, PEGylated, anti-TNF-α monoclonal antibody</td>
<td>400 mg SC (given as 2 injections of 200 mg each) initially and at week 2 and 4, followed by 200 mg every other week</td>
</tr>
<tr>
<td>Etanercept</td>
<td>Human IgG1 Fc region fused to TNF type 2 receptor</td>
<td>50 mg SC twice weekly for 12 weeks, then 50 mg SC each week</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Chimeric monoclonal antibody</td>
<td>5 mg/kg IV at weeks 0, 2, 6, then every 8 weeks</td>
</tr>
<tr>
<td>Golimumab</td>
<td>Recombinant, human IgG1 monoclonal antibody</td>
<td>50 mg IM once every 4 weeks alone or in combination with methotrexate</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>Human IgG1 monoclonal antibody specific to p40 protein subunit of IL-12 and -23 cytokines</td>
<td>45 mg SC initially and 4 weeks later, followed by 45 mg every 12 weeks</td>
</tr>
</tbody>
</table>

FDA = Food and Drug Administration; Ig = immunoglobulin; IL = interleukin; IM = intramuscularly; IV = intravenously; SC = subcutaneously; TNF = tumor necrosis factor.

National Psoriasis Foundation: Treatment Recommendations for Pregnancy

- First line
  - Topical therapies including emollients
  - Low- to moderate-potency topical steroids as needed in second and third trimesters

- Second line
  - Narrowband ultraviolet B phototherapy or broadband ultraviolet B when narrowband ultraviolet B is not available
  - Tumor necrosis factor–α inhibitors may used with caution throughout pregnancy
  - Cyclosporine and systemic steroids may be used with caution in second and third trimesters

### Pregnancy Categories of Systemic Psoriasis Treatments

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA Pregnancy Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nonbiologics</strong></td>
<td></td>
</tr>
<tr>
<td>Acitretin</td>
<td>X</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>C</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>X</td>
</tr>
<tr>
<td><strong>Biologics</strong></td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>B</td>
</tr>
<tr>
<td>Etanercept</td>
<td>B</td>
</tr>
<tr>
<td>Infliximab</td>
<td>B</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>B</td>
</tr>
</tbody>
</table>

*FDA = Food and Drug Administration.*
# Pregnancy and Psoriasis: The Risks

<table>
<thead>
<tr>
<th>Pregnancy Complication</th>
<th>Women With Psoriasis (n = 358)</th>
<th>Women Without Psoriasis (n = 131,424)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous abortion</td>
<td>28.1%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>21.7%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Severe pre-eclampsia or eclampsia</td>
<td>14.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Placenta previa with/without hemorrhage</td>
<td>18.6%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>13.6%</td>
<td>3.0%</td>
</tr>
</tbody>
</table>

Biologic Therapy: Monitoring Recommendations

- Tumor necrosis factor–α blockers: adalimumab, etanercept, infliximab
  - Complete blood cell count + platelets: baseline and every 2-6 months
  - Chem screen + liver function test: baseline and every 3-4 months
  - Tuberculosis skin test: baseline and annually thereafter
  - Vaccinations

- Ustekinumab
  - Tuberculosis skin test: baseline
  - Vaccinations

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\[a\] No standardized recommendations are available at this time.
Biologic Therapy: Vaccination Recommendations

- Tumor necrosis factor–α blockers: adalimumab, etanercept, infliximab
  - Baseline, standard,\(^{a}\) annual trivalent inactivated influenza vaccine, no live vaccines

- Ustekinumab\(^{b}\)
  - Baseline, standard, no live vaccines
    - Non-live vaccines may not elicit adequate response
    - Caution when live vaccines are given to household member because of risk of shedding

\(^{a}\)When practical; \(^{b}\)No standardized recommendations are available at this time.
Impact of Psoriasis on Quality of Life

- Physical
  - 72% suffer from itching, 70% from physical irritation, 59% from pain
- Psychosocial
  - Social stigmatization
  - >70% are angry, frustrated, embarrassed, and/or helpless
  - 39% increased risk of depression, 31% increased risk of anxiety, and 44% increased risk of suicidality
- Everyday activity
  - 80% said psoriasis was a “moderate” or “large” problem in everyday life
  - 30% reported that psoriasis interferes with sexual activities
- Occupational
  - 25% with psoriasis and 50% with psoriatic arthritis reported the disease negatively affects job
  - 31% of patients missed >10 days due to psoriasis per month

Medications That Block Tumor Necrosis Factor–α Reduce Depressive Symptoms

<table>
<thead>
<tr>
<th>Etanercept¹</th>
<th>Ustekinumab²</th>
<th>Adalimumab³</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 618</td>
<td>N = 1230</td>
<td>N = 96</td>
</tr>
<tr>
<td>• 55% reduction in depressive symptoms measured by BDI ($P &lt; .0001$)</td>
<td>• 29.3% improvement in HADS-Depression ($P &lt; .001$)</td>
<td>• 6-point reduction in ZDS score ($P &lt; .001$)</td>
</tr>
<tr>
<td>• 43% improvement in HAM-D ($P = .0048$)</td>
<td>• 13.9% improvement in HADS-Anxiety ($P &lt; .001$)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 76.2% improvement in DLQI ($P &lt; .001$)</td>
<td></td>
</tr>
</tbody>
</table>

BDI = Beck Depression Inventory; DLQI = Dermatology Life Quality Index; HADS = Hospital Anxiety and Depression Scale; HAM-D = Hamilton Rating Scale for Depression; ZDS = Zung Self-Rating Depression Scale.

Patient’s Perspective: Self-Reported Causes for Nonadherence

Reasons You Are Not Using a Prescription Medication (n = 422)

- Concerns about risks and side effects: 34%
- Cost: 28%
- Nothing works: 16%
- Don’t need it: 14%
- Other: 4%
- Too much hassle: 4%

Effective Patient-Provider Relationship to Improve Treatment Adherence

- Take time to ask questions
  - Discuss treatment outcomes and adverse events of previous medications
- Educate patients about psoriasis, importance of adherence, how treatment will help
  - Connect patients to accurate outside resources
  - Address adverse events
- Involve patients in treatment plan
  - Become a partner in setting patient treatment goals
  - Follow monitoring guidelines; reward and reinforce adherence behavior
- Give clear written instructions
- Schedule return visits