NATIONAL PSORIASIS FOUNDATION

Fundamentals of Psoriatic Disease

These informational handouts accompany the Fundamentals of Psoriatic Disease multimedia module that is part of the National Psoriasis Foundation's Psoriatic Disease Curriculum.

This comprehensive, 75-minute learning module is designed to expand basic understanding of psoriasis, psoriatic arthritis (PsA), and comorbidities. We encourage you to view the module and participate in the pre/post assessment to help us determine the impact of this program and continue to improve our educational offerings. You may also directly access each individual lecture in the module by utilizing the links on each handout.

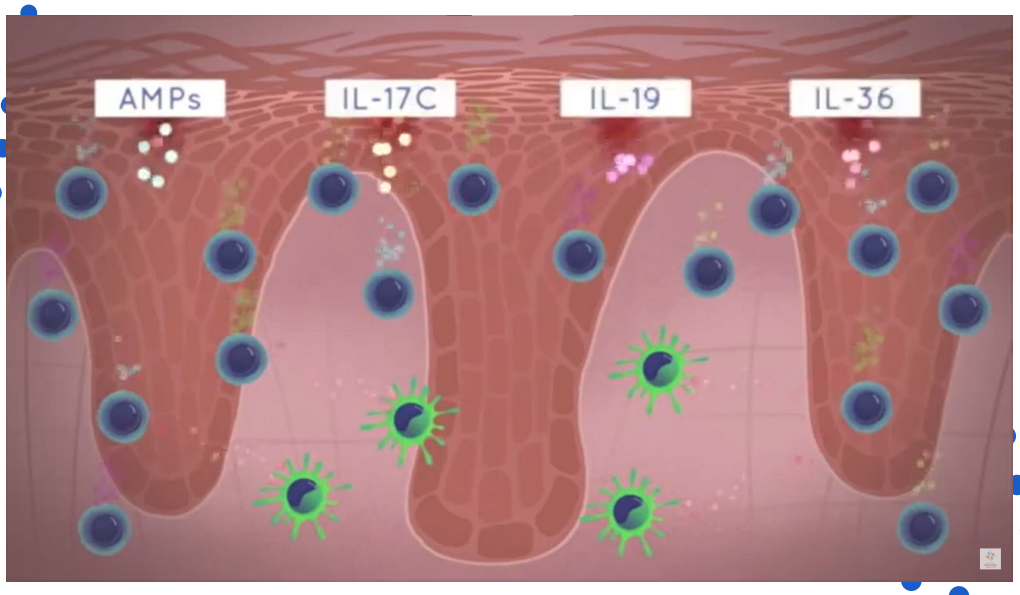
Pre Assessment

Post Assessment

Responses will be kept confidential and only shared in aggregate.

Immunopathogenesis of Psoriasis (1:32)

- The immunopathogenesis of psoriasis is complex – involves interplay between the immune system, genes, and environmental factors.
- Activation of dendritic cells by unknown stimuli is one of the earliest immune events triggering psoriasis plaque development.
- Activated dendritic cells secrete several proinflammatory cytokines such as interferon (IFN) and tumor necrosis factor (TNF), which stimulate other dendritic cells to produce IL-23.
- Increased amounts of TNF and IL-23 activate resident T cells in the skin that begin to expand and produce large amounts of IL-17A and IL-17F, as well as other inflammatory cytokines such as TNF and IL-22. IL-23 sustains the IL-17 producing cells in the skin – which are primarily responsible for clinical features of psoriasis.
- In response to these events, keratinocytes are activated and begin to hyperproliferate, producing more cytokines, including antimicrobial peptides (AMPs), IL-17C, IL-19, and IL-36.
- These keratinocyte derived products result in the recruitment of additional immune cells such as T cells, dendritic cells, and neutrophils which results in a self-amplifying feedforward inflammatory response which is responsible for the psoriatic plaque.
- Psoriasis is associated with systemic inflammation and is the cause of associated comorbidities including psoriatic arthritis, obesity, mental illness, and inflammatory bowel disease (IBD).
- The discovery of the central role of the IL-23/IL-17 signaling pathway in psoriasis has led to the development of highly effective, targeted psoriasis therapies that enable health care providers to reduce the negative effects of psoriasis on the lives of their patients.



The Basics of Psoriasis – Abby Van Voorhees, M.D. (3:46)

- Psoriasis is a chronic immune-mediated disease that affects approximately 2-3% of US population.
- It is a genetic disease that is triggered by environmental factors.
- Caucasians have a higher prevalence than African Americans and African Americans have a higher prevalence than Hispanics.
- Highest incidence in individuals of Scandinavian background.
- Low incidence in Native American & Inuits/Yupik groups.
- 1/3 of patients have a known family history.
- Genetics: There are more than 80 susceptibility genes referred to as the Psors (psoriasis susceptibility loci) 1-15 genes, some of these genes are specific to certain racial/ethnic groups.
- Age of onset: Most common age of onset: 20-30's, second peak of onset: 50-60's.
- Childhood: mean onset is 8.1 years (1% of psoriasis begins in childhood).
- Males and females are affected equally.
- Symptoms of psoriasis that affect the quality of life of the patient:
  - Skin is itchy, scaly, red, burns, has an odor, and bleeds
- Mental and physical burden of disease is higher than most other disease categories.
- Psoriasis has a negative effect on family and social interactions.
- Chronic plaque psoriasis accounts for more than 80% of psoriasis, most commonly appears on the elbows, knees, lower back, area around umbilicus, scalp, and genitalia, and is usually symmetric.
- Auspitz Sign: When scale is removed from the plaques small droplets of blood appear on the erythematous surface.
- Koebner's Phenomenon: Non-specific trauma can cause formation of psoriasis in the area of irritation.

Classic lesions have 3 characteristics

1. Erythematous plaque
2. Distinctive borders
3. Overlying silvery scale

Triggers: variable/broad

- Stress
- Infections (including HIV and strep infections)
- Medications
- Trauma (Koebnerization)

The Basics of Psoriasis – Abby Van Voorhees, M.D. (3:46)

There are 5 types of psoriasis

1. Guttate psoriasis
2. Pustular psoriasis
3. Intertriginous (inverse) psoriasis
4. Plaque psoriasis
5. Erythrodermic psoriasis

80/20 rule:

80% of patients have more limited disease

20% of patients have more severe disease

Gutatte Psoriasis

- Red minute papules with subtle scaling.
- Develops typically in children.
- Often triggered by group A beta-hemolytic streptococcal infection.
- Can resolve completely and not recur after the first episode or can subsequently develop plaque psoriasis.

Pustular Psoriasis -Two variants:

- Localized Pustular Psoriasis: Acute or chronic onset, no systemic symptoms, but can cause severe pain and be associated with disability.
  - Two variants: Palmoplantar disease (Barber) and Acrodermatitis continua of Hallopeau
- Generalized Pustular Psoriasis (Von Zumbusch): Acute onset preceded by systemic symptoms. Can cause cardiovascular and respiratory failure associated with fatality. Pustules present on erythematous skin, which gets so inflamed that blood has to work overtime to perfuse the vital organs as so much blood is being sent out to the skin, trunk extremities, and mucosal surfaces.

Intertriginous (inverse) psoriasis

- Inverse psoriasis affects the body folds such as the intergluteal cleft, axillae, and anywhere skin is touching skin and can be associated with candidiasis.
- Scales are usually not visible on the skin.

Erythrodermic psoriasis

- Skin is diffusely erythematous with associated scaling.
- It can be acute or chronic and is often triggered by infection or medication change.
- It can also be fatal.

Severe disease:

Greater than 10% Body Surface Area (BSA) or involvement of specific body areas including hands, feet, genitals, or face.

Nail psoriasis

- Present on fingernails (50%) and toenails (30%) with symptoms including nail pitting/grooves, nail thickening, splinter hemorrhages, oil spots, onycholysis, discoloration, and crumbling.

Treatments – April Armstrong, M.D., MPH (29:22)

Topical treatments (for patients with limited psoriasis):

- Corticosteroids
- Vitamin D analogs
- Calcineurin inhibitors
- Retinoids
- Tar
- Anthralin

Systemic therapies:

Oral

- Acitretin
- Cyclosporine
- Methotrexate
- Apremilast

Biologics (injectables or infusions)

- TNF inhibitors
- IL-12/23 inhibitors
- IL-17 inhibitors
- IL-23-inhibitors

Treatment overview

- Psoriatic disease is chronic and requires lifelong treatment
- No single treatment works for everyone
- Many treatment options are available for psoriasis and psoriatic arthritis
- Switching treatments is common
- Combination treatment is common

Topical Therapy: Usually first line of treatment for mild disease (BSA 3-5% or less)

- OTC products: salicylic acid, tar, emollients (don't work well alone without other treatments)
- Topical corticosteroids
- Topical calcineurin inhibitors: tacrolimus, pimecrolimus
- Vitamin D analogs: calcipotriene, calcitriol
- Topical retinoids / vitamin A derivatives: tazarotene

Phototherapy

- Effective in 60-80% of patients
- Targeted treatment is used for limited psoriasis (<5% BSA)
- Excimer laser – 308 nm
- Whole-body treatment is used (>5% BSA)
- Narrowband UVB
- Psoralen and UVA
- Requires frequent visits (3 visits/week) to office (NB-UVB can be self-administered at home), so phototherapy may not be practical for all patients.
- Does not treat psoriatic arthritis

Oral Therapies

Methorexate: dihydrofolate reductase inhibitor

- Chronic management for those without access or have contraindications to biologics.
- Long-term side effect profile limits its use: hepatotoxicity, pulmonary and bone marrow toxicity.
- Should not be used in women of child-bearing age (teratogenic).

Cyclosporine: calcineurin inhibitor

- For immediate relief of severe psoriasis.
- Not a long-term option due to side effects (renotoxicity).
- Commonly used as a bridging therapy to biologic.

Acitretin: targeting retinoid receptors such as RXR and RAR in the skin

- Used in palmoplantar psoriasis with modest efficacy.
- Elevations in LFTs and Lipids
- Should not be used in women of child-bearing age (teratogenic).

Apremilast: phosphodiesterase 4 inhibitor

- Used for both psoriasis and PsA with modest efficacy.
- Generally well tolerated except for diarrhea in some patients .

Treatments – April Armstrong, M.D., MPH (29:22)

Biologics :

There are 11 FDA approved biologics. Innovation in biologics transformed the way we treat patients for psoriasis.

- TNF inhibitors: Infliximab, Adalimumab, Etanercept, Certolizumab. All but Infliximab are given subcutaneously and all are approved for psoriasis and PsA.
- IL-12/23 inhibitor: Ustekinumab. Conveniently dosed with a maintenance dose of every 12 weeks.
- IL-17 inhibitors: Secukinumab, Ixekizumab, Brodalumab.
- IL-23 inhibitors: Guselkumab, Tildrakizumab, Risankizumab. They have good safety records and conveniently dosed once every 8-12 weeks.

Currently available biologic agents:

Drug	Dosage frequency	PASI-75 response
Infliximab	5mg/kg week 0, 2, 6 then q8 weeks IV	76-80%
Adalimumab	80mg loading dose, 40mg week 1, then q2 weeks SC	71-80%
Etanercept	50mg twice weekly x 3mo, then 50mg weekly SC	49%
Certolizumab	400 mg q2 weeks, can taper to 200mg q2 weeks at week 6 SC	77-82%
Ustekinumab	< 100kg: 45mg @ week 0, 4 then q12 weeks SC≥100kg: 90mg @ week 0, 4 then q12 weeks SC	66-76%
Secukinumab	300mg weekly x 5 weeks, then 150-300mg q4 SC	67-82%
Ixekizumab	160 mg at week 0; followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12; then 80 mg every 4 weeks SC	87%
Brodalumab	210 mg at weeks 0, 1, and 2, then 210 mg every 2 weeks SC	85-86%
Guselkumab	100 mg at weeks 0 and 4, followed by 100 mg every 8 weeks SC	83%
Tildrakizumab	100 mg at weeks 0 and 4, followed by 100 mg every 12 weeks SC	64-77%
Risankizumab	150 mg at weeks 0 and 4, followed by 150 mg every 12 weeks SC	89%

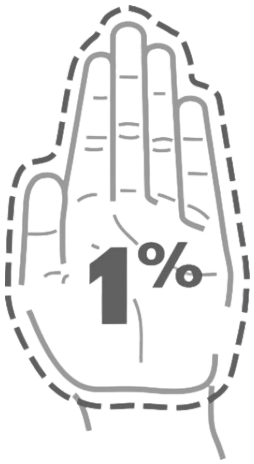
- Despite various and exciting therapies in the psoriasis treatment realm, there is still a way to go between what we have available and what patients can access.
- Most patients are on topicals or no therapy even if they have moderate to severe disease.
- Even many PsA patients are only on topicals or no therapy.
- Patients are often undertreated.

Factors involved in treatment decisions:

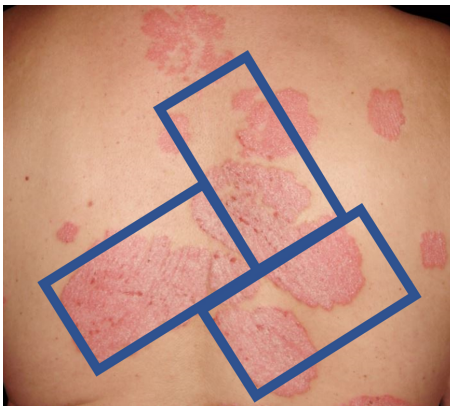
- Effectiveness of the treatment
- Potential side effects and long-term risks
- Comorbid medical conditions, including psoriatic arthritis
- Type of psoriasis
- Disease severity (physical and psychosocial)
- Other health conditions (possible drug interactions)
- Ease of treatment application (patient adherence)
- Insurance coverage/out-of-pocket costs

Body Surface Area and Treatment Adherence – Liz Wallace, M.D. (44:17)

Body Surface Area (BSA) is measured using the patient's hand. The entire patient's hand, including the palm and all five digits, is equal to about 1% BSA.



- BSA estimate is one tool to determine severity:
  - Mild Psoriasis: < 3% BSA
  - Moderate Psoriasis: 3-10% BSA
  - Severe Psoriasis: > 10% BSA
- Use their hand to measure the number of patient hands that fit within the affected area to calculate/estimate BSA (i.e. number of the patient's hands that cover or equal the affected area).
- Add all affected areas together to estimate BSA, only include active areas, not resolved regions, and don't forget to include the scalp or buttocks.
- Psoriasis is a chronic immune-mediated disease necessitating long-term treatment.



- Treatment adherence: More than half of psoriasis patients are dissatisfied with their treatment and up to 40% of patients do not use their medications as intended.
- Treatment satisfaction is closely tied to compliance and patient preferences for treatment.
- Greater psoriatic disease severity is associated with worse quality of life, decreased social functioning, increased prevalence of depression and anxiety, a greater risk for developing psoriatic arthritis, and higher rates of cardiovascular disease.
- Treat to relieve symptoms, decrease risk of comorbidities, and improve QOL.
- Important to not only choose the best treatment (side effect/safety profile/efficacy) but you should choose the best treatment FOR THE PATIENT (a treatment the patient will adhere to).
- Medication adherence: The extent to which patients take their medication as prescribed – filling prescriptions, frequency and timing, using recommended medication.
- There are many factors associated with treatment adherence.
- Topical medication may not be a great option if the patient has multiple body surface areas involved, large BSA involved, fear of side effects, it being time consuming to apply the medication multiple times daily, or cosmetic appearance of the topicals. Emphasize patient education about proper use to prevent side effects.
- Patient satisfaction is generally highly correlated with treatment adherence.
- Adherence generally decreases with increasing disease severity.

Strategies to Improve Medication Adherence:

- Patient-physician relationship: trust and communication
- Educate patients about their disease and set expectations for treatment
- Take time to explore patient treatment preferences
- Involve the patient in treatment decisions
- Make the treatment regimen as simple as possible
- write the instructions for the therapy plan on paper and have the patient take a picture so they can easily reference this information

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Comorbidities of Psoriasis – Wilson Liao, M.D. (56:00)

Psoriasis, while affecting the skin, is a systemic inflammatory condition.

- Comorbidities associated with psoriasis include: psoriatic arthritis, cardiovascular disease, metabolic syndrome, inflammatory bowel disease, liver disease, renal disease, and mood disorders, among others.
- Optimal care: discussing these comorbidities with psoriasis patients and ensuring appropriate screening and referral.

Psoriatic Arthritis

- PsA: chronic, inflammatory disease of the joints, entheses, and spine marked by fatigue, stiffness, pain, and swelling.
- PsA occurs in ~33% of psoriasis patients (range: 6-42%), usually after or concurrently with psoriasis onset (85% of cases).
- Delay in diagnosis as short as 6 months can lead to irreversible joint damage.
- PsA risk factors: obesity, psoriatic nails, inverse psoriasis, scalp psoriasis, severe psoriasis, genetics, family history of PsA.

Cardiovascular Disease

- Cardiovascular disease associations with psoriasis: myocardial infarction, stroke, and cardiovascular mortality.
- Psoriasis is associated with cardiovascular disease independent of traditional cardiovascular risk factors such as BMI, smoking, hypertension, diabetes, dyslipidemia.
- Framingham risk score (10-yr risk of cardiovascular events) is increased by 6% when psoriasis is present.

Metabolic Syndrome

- Metabolic syndrome associations with psoriasis: obesity, hypertension, diabetes, and dyslipidemia.
- The magnitude of association of metabolic syndrome with psoriasis increases with psoriasis severity.
- Genetic studies show that obesity is causal for psoriasis. Weight loss or gastric bypass surgery improves psoriasis.

Inflammatory Bowel Disease

- IBD associations with psoriasis: Crohn's disease and ulcerative colitis (UC).
- Crohn's disease greater association than UC.
- Psoriasis and IBD share 11 genetic loci: JAK2, ZMIZ1, PRDX5, SOCS1, STAT3, FUT2, YDJC, IL23R, IL12B, REL, TYK2.
- Psoriasis is associated with increased risk of other autoimmune diseases such as uveitis, rheumatoid arthritis, alopecia areata, celiac disease, systemic sclerosis, Sjogren's disease, vitiligo, primary biliary cirrhosis.

Liver and Kidney Disease

- Associations with psoriasis: nonalcoholic fatty liver disease and chronic kidney disease.
- A few studies suggest that psoriasis is associated with increased prevalence of nonalcoholic fatty liver disease.
- Moderate to severe psoriasis may be an independent risk factor for chronic kidney disease and end-stage renal disease.

Mood Disorders

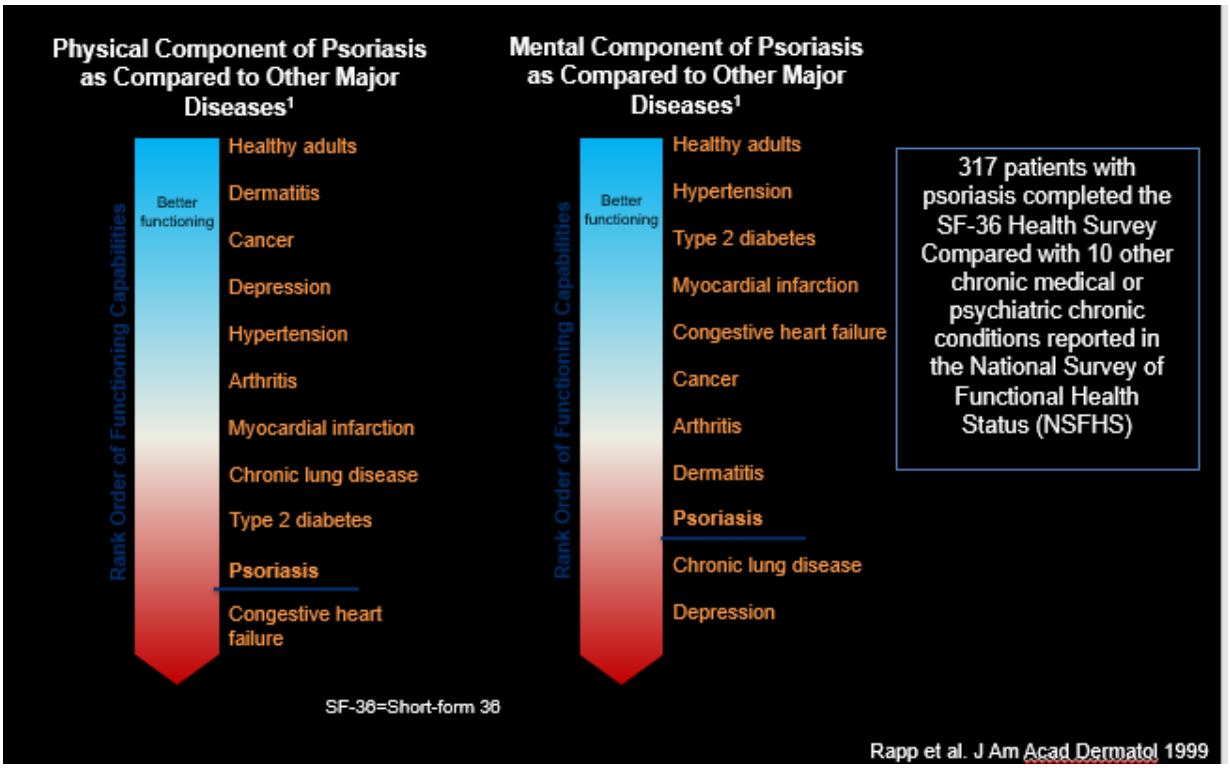
- Associations with psoriasis: depression, anxiety, suicidal ideation.
- Psoriasis is burdensome physically and mentally, leading to an increased prevalence of mood disorders.
- Individuals with psoriasis have decreased sleep quantity and quality, and an increased prevalence of sleep apnea.

Comorbidities of Psoriasis – Wilson Liao, M.D. (56:00)

Comorbidity Screening and Management

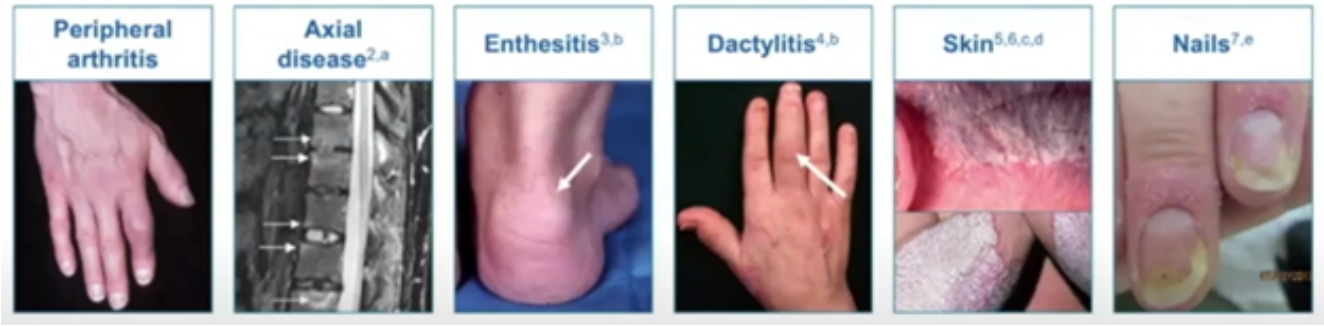
Co-Morbidity	Recommendations for Screening and Management
Psoriatic arthritis	Inform patients of risk; elicit symptoms; consider screening questionnaires; rheumatology referral
Cardiometabolic disease	Inform patients of risk; evaluate for hypertension, diabetes, obesity, hyperlipidemia; refer to primary care if evidence of these; counsel on healthy lifestyle for diet, weight, exercise
Inflammatory bowel disease	Inform patients of risk; elicit bowel symptoms; refer to primary care or gastroenterology for any concerns
Liver and kidney disease	Inform patients of risk; refer to primary care if evidence of these
Mood disorders	Inform patients of risk; elicit symptoms and consider screening questionnaires; refer to appropriate specialist

Impact of psoriasis compared with other chronic diseases



Psoriatic Arthritis – Joseph Merola, M.D., MMSc (1:04:06)

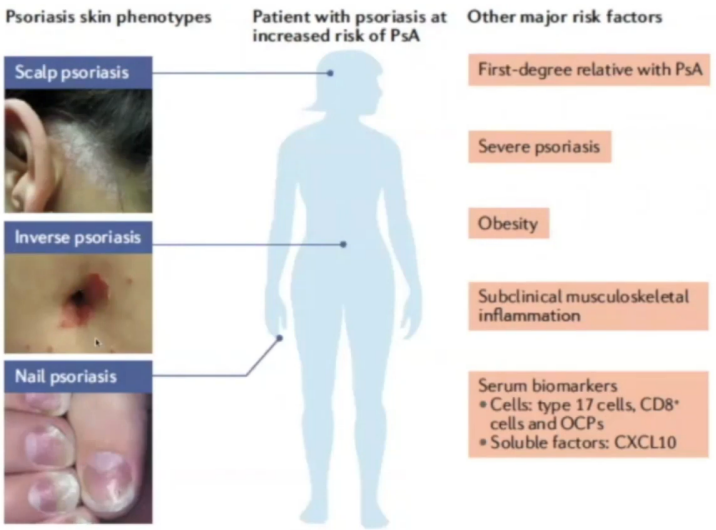
There are 6 domains of disease: peripheral arthritis, axial disease, enthesitis, dactylitis, skin, nails.



- Psoriatic arthritis is underdiagnosed, many patients with psoriasis may have undiagnosed PsA. There is a need to improve screening and diagnosis of PsA.
- A delay in diagnosis is common – leading to worse outcomes for patients, including erosion of bone, deformed joints, and potential functional disability.

Risks for PsA

- Psoriasis phenotypes: scalp psoriasis, inverse psoriasis, and nail psoriasis
- First degree relative with PsA
- Severe psoriasis
- Obesity
- Subclinical musculoskeletal inflammation
- Serum biomarkers present predict the development of PsA



Clinically, PsA presents as:

- Joint pain, stiffness, limited mobility, reduced range of motion
- Can deform the joints in 40-60% of patients with PsA
- Asymmetric oligoarthritis (example: wrist and ankle, or ankle and knee) is most common
- Symmetric polyarthritis (both sides affected equally)
- Distal interphalangeal arthritis (DIP joint)
- Arthritis mutilans – uncommon (about 5%), but quite deforming
- Spinal column involvement (axial involvement, with sacroiliac joint)

- Enthesitis: commonly seen, 30-50% of PsA patients have this manifestation; presents as recurrent tendonitis or plantar fasciitis, involvement of Achilles insertion; often can't see it, but patients have symptoms; elicit through history and physical exam, patients will experience tenderness from pushing on points.
- Dactylitis: inflammation at joint and soft tissue – often called "sausage digit"; can also be seen in other related conditions.
- Differential diagnosis: Osteoarthritis, rheumatoid arthritis, crystal arthropathy, fibromyalgia.

Psoriatic Arthritis – Joseph Merola, M.D., MMSc (1:04:06)

PsA requires a clinical diagnosis – based mostly on history and physical exam

- Testing for PsA
  - Inflammatory markers: ESR, CRP
  - Rheumatoid factor (RF) or anti-CCP antibodies,
  - Imaging considerations:
    - Radiographs: hand/foot x-rays, Sacroiliac-joint films (modified Ferguson view)
    - Additional: MSK U/S with power doppler, MRI
  - Other considerations in preparation for treatment: vaccinations, TB testing, Hep screening, basic labs.
- CASPAR criteria for classification of PsA – these criteria define PsA in patients with PsA .

Key elements of distinguishing inflammatory arthritis vs. non-inflammatory arthritis:

  - Stiffness after a period of inactivity of 30-60 minutes
  - Improvement with activity
  - Redness, warmth, swelling (inflammatory signs)
  - Episode/flare duration
  - Systemic symptoms (fatigue, uveitis)
  - Response to anti-inflammatory agents
  - Family history
- Validated screening tools that can be used – PEST, PASE, ToPAS, PASQ, etc
  - Useful in patients with psoriasis for screening
- Psoriasis skin disease and psoriatic arthritis don't exist in a vacuum, there are many other comorbidities that come with psoriatic disease, and you need to help patients build a team and keep up with PCP and other specialists.

PSA Awareness Tool

if two of these are present, formal screening for PsA should be conducted

Pain in joints

Stiffness (after a period of inactivity of 30-60 minutes)

Sausage digit (dactylitis)

Axial (axial spine/back pain associated with stiffness that improves with activity)