Pediatric Psoriasis:
What’s New, What’s True?

Kelly M. Cordoro, M.D.
Associate Professor of Dermatology and Pediatrics
University of California, San Francisco

Kelly.cordoro@ucsf.edu
Consultant for Pfizer, Celgene and Valeant.
What's New, What's True?

The Strep Story

Monogenic Variants

Comorbidities and Screening
Environmental Factors

Genetic Susceptibility

Adaptive and Innate Immune Responses

Psoriasis: complex inflammatory disease

Identifiable triggers common in kids, especially infections.

HLA-Cw6 dominant susceptible allele.

~50% of heritability, early onset pso.

Guttate psoriasis, severity, chronicity.

39 genetic loci map to immune pathogenesis pathways (TNF, IL-12, IL-23R, IL-17).

Lu Y et al. 2013
Strep as a trigger *may* impart favorable prognosis.

**Ko et al. J Dermatol 2010:**
- Preceding strep pharyngitis predicted guttate morphology and eventual resolution

**Mercy et al. Pediatr Dermatol 2013:**
- Preceding strep pharyngitis predicted guttate morphology but not severity
- Initial guttate morphology *in absence of strep* predicted progression to severe pso
Strep may impart a favorable prognosis, look for and treat it.

Consider more aggressive management in strep negative cases given risk of progression to severe disease.

Especially FHx +
Strep and Psoriasis

...for patients with recurrent guttate psoriasis or chronic plaque psoriasis,

there is to date no good evidence that antibiotics or tonsillectomy are beneficial.

Not all strep is in the tonsils.
Pediatric Psoriasis Comorbidity Update

- 1/3 of patients develop psoriasis before age 20
  - Many before age 2

- Does the comorbidity clock start ticking in childhood?
Pediatric Psoriasis

- High risk behavior
- Quality of Life
- Mood Disorders
- Arthritis
- Lymphoma?
- Obesity
- CVD?
- Metabolic Syndrome
- Autoimmune Diseases/IBD
Quality of Life

Mood Disorders
anxiety/depression

Obesity

Best Evidence

Paller et al. NEJM 2008
Boccardi et al. BJD 2009
Augustin BJD 2010
Koebnick et al. J Pediatr 2011
Paller et al. JAMA Derm 2013
Cordoro et al. In Prog 2017

De Jager et al. BJD 2010
Bilgic et al. Ped Derm 2010
Kimball et al. JAAD 2012
Remrod et al. BJD 2013
Tollefson MM. PCNA 2014
Kim et al. Ped Derm 2015
In absence of obesity, less evidence for association with other components of metabolic syndrome.
Metabolic Syndrome
At risk for CVD?
Obesity
Metabolic Syndrome
Hypertension
Dyslipidemia
Insulin Resistance/DM
Psoriasis confers an independent risk for atherosclerosis, MI, stroke and early CV-related mortality.

Persistent systemic inflammation is proposed to contribute to this association.

Psoriatic March

Concept proposed to explain how severe psoriasis drives CV morbidity/mortality.

Boehncke et al. Exp Dermatol 2011
Boehncke & Schön Lancet May 2015
OBESITY
Systemic Inflammation
Atherosclerosis
Endothelial Dysfunction
Insulin Resistance
Systemic Inflammation

Thrombotic Event
MI / Stroke

Boehncke et al. Exp Dermatol 2011
Boehncke & Schön Lancet May 2015
If the *psoriatic march* is real, we may be able to prevent the progression by modifying psoriasis severity and obesity.

Finally!


1st systemic therapy approved to treat pediatric psoriasis.

• Other biologic approvals are on the horizon
  – Ustekinumab submitted to FDA
  – IL-17 inhibitors and PDE4 (apremilast) in pediatric trials currently
Psychiatric and Emotional Comorbidities

- Anxiety
- Depression
- Bipolar disorder
- Eating disorders
- Social isolation
- Risky behavior (drugs, alcohol)
- Poor QOL
- Caregiver QOL

Situational and intrinsic.

Bilgic et al Pedi Derm 2010
Kim et al Pedi Derm 2010
Kimball et al JAAD 2012
Todberg T et al BJD 2016
Tollefson et al JAAD 2017
Reciprocal exacerbating factors.

Each represents an insult to self-esteem and overall well-being.
What to do in general?

Remain vigilant at each visit.

Identify those at greatest risk.

Overweight and obese; severe disease; low mood, risky behaviors.

Refer to relevant experts for help.

*Obesity/nutrition experts*

*Psychologists, therapists, psychiatrists*
A multidisciplinary initiative to create a guidance document for practitioners based on the best available evidence.

- Overweight, Obesity
- Hypertension
- Dyslipidemia
- Type 2 Diabetes
- NAFLD
- Inflammatory Bowel Disease
- Psoriatic Arthritis
- Depression and Anxiety
- Substance Abuse
- Quality of Life

Drs. E Osier, A Wang, L Eichenfield- UCSD
CSI: Screening for Psoriasis Patients Aged 2-21

Annual

• Blood pressure
• BMI (body mass index)
• Arthritis screen
  – Joint pain / swelling / inflammation
  – Joint stiffness after rest or sleep
  – Limp
• Mood disorders screen
  – Anxiety, depression, substance abuse

Additional screening for DM, dyslipidemia and fatty liver based on weight, other risk factors.

Key: Screening guidelines do not exceed AAP or EU age-based screening recs.

Osier et al. JAMA Derm 2017.
What to do specifically?

Involve primary care MD.
Psoriasis comorbidity screening recs do not depart from AAP or EU age-based recs.
Clinical Variants of Pustular Psoriasis

- GPP without Plaque
- GPP with Plaque
- Palmoplantar Pustular
- Acroderm Continua Hallopeau
- Neonatal Onset GPP
Genetic Advances have Reclassified a Subset of GPP as Monogenic Autoinflammatory Disorders

- IL36RN AR Mutations
- DITRA
- IL1RN AR Mutations
- DIRA
Monogenic Autoinflammatory Disorders Due to Mutations in Genes within the IL-1 Superfamily

AR Mutations in IL36RN lead to unopposed pro-inflammatory signaling by IL36 α β and γ.

AR Mutations in IL1RN lead to unopposed pro-inflammatory signaling by IL-1 α and β.

Pustular Psoriasis

GPP without Plaque

Neonatal Onset GPP
Sugiura et al. JAAD 2014.

DITRA: Def of IL-36 R Antagonist.
IL36 in epithelial (skin, GI) tissues.


DIRA: Def of IL-1 R Antagonist.
IL1α active in epithelia, bone, CNS.

Infant or adult onset GPP; often in absence of psoriasis vulgaris.

DIRA: Def of IL-1 R Antagonist.
IL1α active in epithelia, bone, CNS.

Perinatal onset GPP, multifocal aseptic osteomyelitis, periostitis.

Sugiura et al. JAAD 2014.
DITRA: Def of IL36 R Antagonist.
Inherited and sporadic cases reported.

Range of phenotypes is evolving. Definitive Rx not yet identified.

Sugiura et al. JAAD Vol 71;5, 2014.
Response to Anakinra (2 months only).
Decreased expression of IL-17^{+}CD4^{+} and CD8^{+} T cells compared to adult psoriasis

Increased expression of IL-22^{+}CD4^{+} and CD8^{+} T cells compared to adult psoriasis
Key Messages: Prognosis and Comorbidities

Recent data suggest course/severity impacted by +/- strep, age of psoriasis onset and family hx of psoriasis.

Obesity and psychosocial impairment are dominant comorbidities. In absence of signs/sx, evidence does not support lab screening beyond standardized age-based pediatric guidelines.

Identify at-risk patients, optimize physical and mental health to halt progression/prevent downstream effects.
Key Messages: Monogenic Variants of GPP

Genetic advances allowed reclassification of a subset of GPP as monogenic AI diseases. Specific Rx by genotype (DIRA).

Molecular techniques can clarify affected tissue immune phenotypes and individualize therapy choices.

Utilize a collaborative approach on your patient’s behalf. You may help your patient and learn something.
Thank you!
kelly.cordoro@ucsf.edu