

DISCLOSURE

- RESEARCH FUNDING PAID TO MEDICAL SCHOOL:
 - AMGEN PROMIUS SYMBIO
 - GSK - MAYNE - LEO
- ADVISORY BOARD/LECTURES:
 - AMGEN
 - ORTHO
 - MAYNE
 - LEO

OVERVIEW

- What are the unique risks for the pediatric patient with psoriasis?
- How familiar are pediatricians with pediatric psoriasis and its management?
- What are the currently available medications for the pediatric patient with psoriasis?
- Why are there so few medications for pediatric patients with psoriasis?

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AAD PEDIATRIC PSORIASIS GUIDELINES

Joint American Academy of Dermatology—National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients



Alan Menter, MD (Co-Chair), ^a Kelly M. Cordoro, MD, ^b Dawn M. R. Davis, MD, ^c
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JAAD January 2020

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PEDIATRIC PSORIASIS

• EACH YEAR, ABOUT 20,000 CHILDREN < 10 YEARS OF AGE ARE DIAGNOSED WITH PSORIASIS

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PEDIATRIC PSORIASIS

- A CHRONIC, MULTISYSTEM INFLAMMATORY DISEASE THAT AFFECTS 1% OF CHILDREN
- MOST COMMON TIME OF ONSET: ADOLESCENCE
- ONE THIRD OF CASES OF PSORIASIS START IN CHILDHOOD
- MULTIPLE COMORBIDITIES: **PSORIATIC ARTHRITIS** HAS LARGEST EVIDENCE BASE

AAD GUIDELINES: Journal American Academy of Dermatology 2020





PEDIATRIC PSORIASIS

- Prevalence : 0.7%
- · More pruritic in children than in adults
- Majority of children have plaque psoriasis
- Family incidence of psoriasis may be as high as 89%



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PEDIATRIC PSORIASIS





OVERVIEW

- OBESITY = QUICKLY INCREASING IN PEDI POPULATION
- MAY EXPLAIN INCREASING INCIDENCE AND PREVALANCE OF CHILDHOOD PSORIASIS



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COMORBIDITIES IN PEDI PSORIASIS

- PSORIATIC ARTHRITIS
- OBESITY
- HYPERLIPIDEMA
- DIABETES MELLITUS
- RHEUMATOID ARTHRITIS
- INFLAMMATORY BOWEL DISEASE

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> JAMA Dermatol. 2017 Jul 1;153(7):698-704. doi: 10.1001/jamadermatol.2017.0499.

Pediatric Psoriasis Comorbidity Screening Guidelines

Emily Osier ¹, Audrey S Wang ², Megha M Tollefson ³, Kelly M Cordoro ⁴, Stephen R Daniels ⁵, Andrew Eichenfield ⁶, Joel M Gelfand ⁷, Alice B Gottlieb ⁸, Alexa B Kimball ⁹, Mark Lebwohl ¹⁰, Nehal N Mehta ¹¹, Amy S Paller ¹², Jeffrey B Schwimmer ¹³, Dennis M Styne ¹⁴, Abby S Van Voorhees ¹, Wynnis L Tom ¹⁵, Lawrence F Eichenfield ¹⁵

Affiliations + expand

PMID: 28514463 PMCID: PMC5748031 DOI: 10.1001/jamadermatol.2017.0499

Free PMC article

PSORIATIC ARTHRITIS: SCREEN FOR UVEITIS



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PSORIATIC ARTHRITIS IN PEDI PTS

- PSORIATIC ARTHRITIS IN ALL PTS: 5 TO 40%
- ONSET OF SKIN DISEASE TYPICALLY PRECEDES ONSET OF JOINT DISEASE BY 10 YEARS
- PEAK ONSET BETWEEN AGES 9 AND 12 YEARS
- UP TO 20 % OF ALL CHILDHOOD ARTHRITIS IS PSORIATIC ARTHRITIS





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PREVALENCE OF THE METABOLIC SYNDROME IN CHILDREN WITH PSORIAISIS

GOLMINZ AM PEDIATR DERM VOL 30 (6); 700-705, 2013

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PSORIASIS

INDEPENDENT RISK FACTOR FOR THE DEVELOPMENT OF:

- ATHEROSCLEROSIS
- CARDIOVASCULAR DISEASE

CARDIOVASCULAR RISK ASSESSMENT IS CURRENTLY ADVISED FOR ADULT PTS WITH MODERATE TO SEVERE PSORIASIS

AUTHORS SUGGEST: HEALTHY LIFESTYLE FOR KIDS

JENSEN P

ACTA DERM VENEREOL 2014; 94: 76-78

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PSYCHOLOGICAL IMPACT OF PSORIASIS ON PEDIATRIC PATIENTS

CANNOT BE IGNORED

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Actas Dermosifiliogr. 2018 Oct;109(8):667-669. doi: 10.1016/j.ad.2018.09.001.

The Importance of Measuring the Psychological Impact of Psoriasis and How We Treat Pediatric Patients With Psoriasis.

[Article in English, Spanish] Pérez Ferriols A¹.

Author information

1 Sección Fototerapia. Servicio de Dermatología. Hospital General Universitario de Valencia, Valencia, España. Electronic address: perez_ampferr@gva.es.

Acta Dermosifiliogr Oct 2018; 109 (8): 667-669

(

> Pediatr Dermatol. 2019 May;36(3):290-297. doi: 10.1111/pde.13772. Epub 2019 Feb 21.

A Retrospective Cohort Study to Evaluate the Development of Comorbidities, Including Psychiatric Comorbidities, Among a Pediatric Psoriasis Population

Amy S Paller ¹, Jennifer Schenfeld ², Neil A Accortt ³, Gregory Kricorian ³

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> JAMA Dermatol. 2019 Nov 27;156(1):72-78. doi: 10.1001/jamadermatol.2019.3717. Online ahead of print.

Association Between Quality of Life and Improvement in Psoriasis Severity and Extent in Pediatric Patients

Finola M Bruins ¹, Inge M G J Bronckers ¹, Hans M M Groenewoud ², Peter C M van de Kerkhof ¹, Elke M G J de Jong ¹, Marieke M B Seyger ¹

Affiliations + expand

PMID: 31774449 PMCID: PMC6902114 DOI: 10.1001/jamadermatol.2019.3717

Conclusions and relevance: This cohort study in a real-world setting found that the greatest improvements in QOL were associated with PASI 90 or greater, a decrease in BSA involvement of 90% or greater, and systemic treatments. These findings suggest that reaching PASI 90 or greater and decreasing BSA involvement by at least 90% may be clinically meaningful treatment goals that will help pediatric patients with psoriasis reach optimal QOL.

TREATMENT STRATEGIES: PEDIATRIC PSORIASIS

TOPICALS
ORAL MEDICATIONS
PHOTOTHERAPY
BIOLOGICS

WILL DISCUSS OFF LABEL USE: PUBLISHED

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JAAD Jan 2020

PEDIATRIC PSORIASIS THERAPY

- Only 6 FDA medications approved for pediatric patients
- · Biologics:

Etanercept: ≥ 6 yearsUstekinumab : ≥12 years

- Ixekizumab: ≥ 6 years

- · Topicals:
 - Calcipotriene Foam 0.005%: ≥ 4 years scalp and body
 - Calcipotriene 0.005% and betamethasone 0.064% **foam**:

≥12 years: mild to severe plaque psoriasis

- Calcipotriene 0.005% and betamethasone 0.064%

suspension:

scalp and body: ≥ 12 years

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FUTURE PEDIATRIC PSORIASIS THERAPY

BIOLOGICS:

Secukinub: IL 23 inhibitor: 6 to 17 years of age

Brodalumab: anti IL 17: 6 to 17 years of age

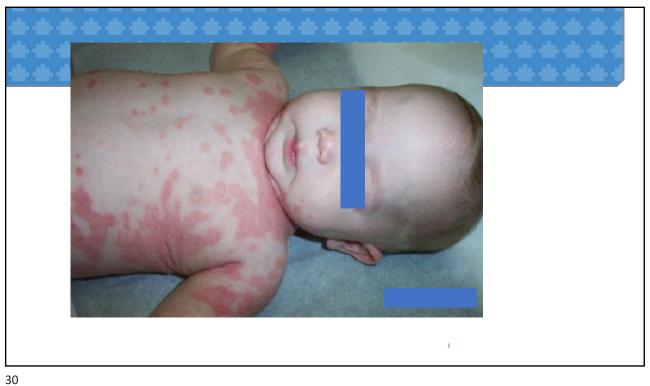
Tildrakizumab: IL 23 inhibitor: 12 to 17 years of age

TOPICALS:

Halobetasol 0.01%/ tazarotene 0.045% lotion Roflumilast: PDE 4 inhibitor: 2 to adulthood - used systemically in COPD in adults

PEDIATRIC PTS WITH PSORIASIS

• INFANTS







THERAPIES

- EDUCATION
- COAL TAR
- TOPICAL STEROIDS
- MOISTURIZERS

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YOUNG CHILDREN

- CONSIDER STREP THROAT
- TAR
- TOPICAL STEROIDS
- TOPICAL CALCINEURIN INHIBITORS (INVERSE PSORIASIS)
- PHOTOTHERAPY

Pharmacotherapeutic management of psoriasis in adolescents and children

S. D'Adamio, D. Silvaggio, A. Massaro, P. Lombardo, L. Bianchi, M. Talamonti & M. Galluzzo

To cite this article: S. D'Adamio, D. Silvaggio, A. Massaro, P. Lombardo, L. Bianchi, M. Talamonti & M. Galluzzo (2019) Pharmacotherapeutic management of psoriasis in adolescents and children, Expert Opinion on Pharmacotherapy, 20:14, 1777-1785, DOI: 10.1080/14656566.2019.1636032

To link to this article: https://doi.org/10.1080/14656566.2019.1636032

Expert Opinion Pharmacother 2019 Oct(14):1777-1785

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OLDER CHILDREN WITH PSORIASIS

- TOPICAL STEROIDS / OTHER TOPICALS
- PHOTOTHERAPY / LASER
- METHOTREXATE
- CYCLOSPORIN
- RETINOIDS: TOPICAL / ORAL
- BIOLOGICS

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> Br J Dermatol. 2020 Jun 8. doi: 10.1111/bjd.19301. Online ahead of print.

Treatment Persistence in Paediatric and Adolescent Psoriasis Patients Followed Into Young Adulthood: From Topical to Systemic Treatment - A Prospective, Longitudinal, Observational Cohort Study of 448 Patients

F M Bruins 1 , I M G J Bronckers 1 , R Cai 2 , H M M Groenewoud 3 , M Krol 2 , E M G J de Jong 1 , M M B Seyger 1

Affiliations + expand

PMID: 32510578 DOI: 10.1111/bjd.19301

Results: Of 448 patients, 62.3% stayed on solely topical treatment until data-lock; 14.3% switched from topical to phototherapy, but not to systemic treatment; and 23.4% switched to systemic treatment. Median time from psoriasis onset until i) solely topical discontinuation was 7.3 years and ii) switch to systemics was 10.8 years. Higher Psoriasis Area and Severity Index and a (Children's) Dermatology Life Quality Index >5 were independently associated with switching to systemic treatment.

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VITAMIN D ANALOGUES

- OFTEN USED IN CONJUNCTION WITH TOPICAL STEROIDS
- AAD GUIDELINES
- USE OF UP TO 45 G/ WEEK/ M2
 - NO EFFECT ON SERUM CALCIUM LEVELS
- LOCALIZED IRRITATION OF SKIN

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PEDIATRIC PSORIASIS THERAPY

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- · Topicals:
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 - Calcipotriene 0.005% and betamethasone 0.064% **foam**:

≥12 years: mild to severe plaque psoriasis

- Calcipotriene 0.005% and betamethasone 0.064%

suspension: scalp and body: ≥ 12 years

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METHOTREXATE

- USED FOR PSORIASIS SINCE THE 1950'S
- USED SAFELY IN AGES 2 TO 16 FOR ERYTHRODERMIC, PLAQUE, PUSTULAR PSORIASIS AND PSORIATIC ARTHRITIS
- DOSE RANGE: 0.2 TO 0.7 MG/KG/ WEEK
- I STILL GIVE A TEST DOSE AND CHECK CBC IN ONE WEEK

METHOTREXATE

Table XXXVII. Recommendations for pediatric psoriasis and methotrexate therapy

| Recommendation No. | Recommendation | Strength of recommendation |
|-----------------------|---|-------------------------------|
| 18.1 | Methotrexate is recommended as an effective systemic therapy for moderate to severe plaque psoriasis and other psoriasis subtypes in children. | В |
| 18.2 | Methotrexate is recommended as an effective systemic therapy for pustular psoriasis in children. | В |
| 18.3 | Methotrexate weight-based dosing is recommended in younger children, ranging from 0.2 to 0.7 mg/kg/wk (maximum, 25 mg/kg/wk). | В |
| 18.4 | Folic acid supplementation daily or 6 times weekly during treatment with methotrexate is recommended. | В |
| 18.5 | Routine clinical and laboratory monitoring is recommended before and during treatment with methotrexate. | В |

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AAD GUIDELINES FOR **PEDIATRIC** PSORIASIS:SYSTEMIC

Table XXXVI. Suggested monitoring for nonbiologic systemic medications for pediatric psoriasis*

| Medication [†] | Baseline | Follow-up | Miscellaneous | References |
|---|--|--|--|-------------|
| Methotrexate Dose range: 0.2-0.7 mg/kg/wk | CBC with diff, platelets Renal function [†] Liver function | CBC with diff, platelets (5-7 days after initiating therapy) Repal function Repal function | Liver enzymes rise after dose; check labs 4-6 days after the last dose Liver biopsy often avoided/not | 101,133,134 |
| Maximum: 25 mg/wk (see text for details) | If at risk: hepatitis A, B, C, HIV PPD or other TB tests for latent TB screening [†] | LFTs (monthly for the first 3 months, then every 3 to 6 months) Annual TB test if at risk [†] | indicated in pediatric patients but should be individualized to clinical context Avoid in children with liver risk factors Chest radiograph for symptoms | |
| Acitretin | CBC | Liver function and fasting lipids after | Bone imaging based on symptoms | 101,133,134 |
| Dose range: 0.1-1 mg/kg/d (see text for details) | Fasting lipids Liver function Pregnancy test (if | 1 month of treatment and with dose increases, then every 1-3 months | and duration of treatment (see text) | |
| | appropriate) | Monthly pregnancy test (if appropriate) | | |
| Cyclosporine Dose range: 2-5 mg/kg/d (see text for details) | Blood pressure CBC Renal function | Blood pressure once a week for the first month and at follow-up visits as needed. | Whole-blood cyclosporine trough level if inadequate clinical response or concomitant use of potentially | 101,133,134 |
| | Liver function Fasting lipids Serum magnesium and potassium uric acid HIV if at risk | CBC, serum creatinine, BUN, uric acid, potassium, lipids, and magnesium every 2 weeks for the first month and then at least monthly thereafter | interacting drugs | |

BUN, Blood urea nitrogen; CBC, complete blood count; diff, differential; LFT, liver function test; PPD, protein derivative test; TB, tuberculosis.

"Some monitoring suggestions are not evidence-based recommendations and are expert consensus. These recommendations may vary based on patient age and specific protocols. Practicing physicians should individualize monitoring protocols according to the clinical context. For all pediatric patients receiving long-term systemic therapy, §

"Dosing is based on actual weight.

"At the discretion of the physician based on the clinical situation/individual risk factors.

JAMA Dermatol. 2020 Feb 5. doi: 10.1001/jamadermatol.2019.4835. [Epub ahead of print]

A Comparison of Psoriasis Severity in Pediatric Patients Treated With Methotrexate vs Biologic Agents.

Bronckers IMGJ¹, Paller AS^{2,3}, West DP^{2,3}, Lara-Corrales I⁴, Tollefson MM⁵, Tom WL^{6,7}, Hogeling M^{8,9}, Belazarian L¹⁰, Zachariae C¹¹, Mahé E¹², Siegfried E^{13,14}, Blume-Peytavi U¹⁵, Szalai Z¹⁶, Vleugels RA¹⁷, Holland K^{18,19}, Murphy R²⁰, Puig L²¹, Cordoro KM^{22,23}, Lambert J²⁴, Alexopoulos A²⁵, Mrowietz U²⁶, Kievit W²⁷, Seyger MMB¹; Psoriasis Investigator Group, the Pediatric Dermatology Research Alliance, and the European Working Group on Pediatric Psoriasis

CONCLUSION: BIOLOGIC RESPONSE BETTER THAN METHOTREXATE

Jama Dermatol 2020 FEB

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CYCLOSPORIN

- OFF LABEL IN PEDI PSORIASIS
- FDA APPROVAL FOR PEDI TRANSPLANT 6 MONTHS
- EFFECTIVE AND TOLERATED FOR PSORIASIS TX IN KIDS AS YOUNG AS 11 MOS
- IN DOSES FROM 1.5 MG TO 5 MG/KG/DAY FOR 6 WEEKS TO 2 YEARS
- OFTEN USED IN COMBINATION WITH TOPICALS

CYCLOSPORIN

- ACTS RAPIDLY
- CLINICAL IMPROVEMENT AS EARLY AS 2 WEEKS; MAY REQUIRE 4 TO 8 WEEKS FOR FULL RESPONSE
- AS KIDS HAVE HIGHER BSA TO WEIGHT RATIOS AND AGE DEPENDENT DIFFERENCES IN IN PHARAMACOKINETICS, MAY REQUIRE HIGHER DOSES THAN ADULTS
- MAY NEED 5 MG /KG/DAY

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AAD GUIDELINES FOR **PEDIATRIC PSORIASIS:SYSTEMIC**

| Medication [†] | Baseline | Follow-up | Miscellaneous | References |
|--|---|--|--|-------------|
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| | latent TB screening [†] | | Avoid in children with liver risk factors Chest radiograph for symptoms | |
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| | appropriate) | Monthly pregnancy test (if appropriate) | | |
| Cyclosporine Dose range: 2-5 mg/kg/d (see text for details) | Blood pressure CBC Renal function Liver function | Blood pressure once a week for the first month and at follow-up visits as needed. CBC, serum creatinine, BUN, uric acid. | Whole-blood cyclosporine trough level if inadequate clinical response or concomitant use of potentially interacting drugs | 101,133,134 |
| | Fasting lipids Serum magnesium and potassium uric acid HIV if at risk | potassium, lipids, and magnesium every 2 weeks for the first month and then at least monthly thereafter | interacting drugs | |

BUN, Blood urea nitrogen; CBC, complete blood count; diff, differential; LFT, liver function test; PPD, protein derivative test; TB, tuberculosis.

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Dosing is based on actual weight.

At the discretion of the physician based on the clinical situation/individual risk factors.

CYCLOSPORIN

VACCINATIONS:

- MAY BE LESS EFFECTIVE DURING THERAPY
- LIVE ATTENUATED VACCINES TO BE AVOIDED

METABOLISM BY P450 SYSTEM:

ADVISE REGARDING FOOD AND DRUG INTERACTIONS

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REVIEW

Management of pediatric plaque psoriasis using biologics

Perla Lansang, MD, ^{a,b,c} James N. Bergman, MD, ^d Loretta Fiorillo, MD, ^e Marissa Joseph, MD, ^{b,c} Irene Lara-Corrales, MSc, MD, ^e Danielle Marcoux, MD, ^f Catherine McCuaig, MD, ^f Elena Pope, MSc, MD, ^c Vimal H. Prajapati, MD, ^g Sue Z. J. Li, PhD, ^h and Ian Landells, MD ^f Toronto, Ontario; Vancouver, British Columbia; Edmonton and Calgary, Alberta; Montreal, Quebec; and St Jobn's, Newfoundland, Canada

Background: Psoriasis is a chronic inflammatory disease with clinical manifestations of the skin that affect adults and children. In adults, biologics have revolutionized the treatment of moderate to severe plaque psoriasis where clear or almost clear is a tangible goal. Research on biologics has recently been extended to children. The introduction of these new therapeutic options has outpaced the limited guidelines in this population.

Objective: To provide a review of current data on biologics, with a proposal for a clinically relevant treatment algorithm on the management of moderate to severe plaque psoriasis in the pediatric population.

Metbods: A Canadian panel with expertise in psoriasis, pediatric dermatology, and experience with consensus recommendation processes was selected to review the current landscape of pediatric psoriasis and clinical data on biologies plus identify special considerations for baseline workup and monitoring. Recommendations were reviewed and edited by each expert in an iterative process.

Conclusion: A treatment algorithm for moderate to severe plaque psoriasis in pediatric patients is presented, incorporating approved biologics. Guidance on baseline screening and ongoing monitoring is

JAAD 2019 May

Triggers of Pediatric Psoriasis

Triggers:

Group A β hemolytic Streptococcal infection (M protein)
Beta blockers Lithium Biologics Systemic steroids on cessation of therapy

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ORIGINAL ARTICLE: GASTROENTEROLOGY



Infliximab-Induced Psoriasis and Psoriasiform Skin Lesions in Pediatric Crohn Disease and a Potential Association With IL-23 Receptor Polymorphisms

*Mary E. Sherlock [†]Thomas Walters, [‡]Merit M. Tabbers, [†]Karen Frost, [†]Mary Zachos, [†]Aleixo Muise, [§]Elena Pope, and [†]Anne M. Griffiths

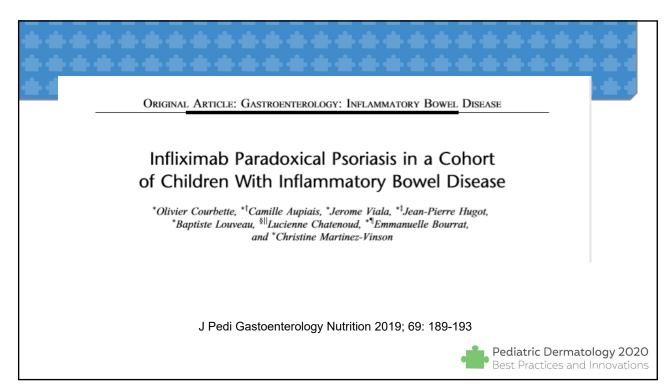


FIGURE 1. Scaly erythematous plaque at base of toe (patient no. 10).

FIGURE 1. Scaly erythematous plaque at base of toe (patient no. 10). among patients developing psoriasis following IPX therapy in comparison with patients with CD treated with IFX, but who did not develop psoriasis. Of note, despite similar allele frequencies, only 1 of these 3 polymorphisms (no 1489/8629, was able to clearly distinguish subjects with CD from subjects with UC. The effects demonstrated were independent in an additive fashion, with the simultaneous homozogous carriage of both rs 10489/628 and 107/89/29 having the highest risk of IFX-induced psoriasis (odds ratio 17.5, P=0.02, 95% CI 1.6–196.3). Interestingly, neither of the variants previously recognized to have an independent association with psoriasis do novo (rs/2018/41) and rs 11209026; demonstrated any association with EV-induced psoriasis More important, we were unable to demonstrate an association between SNP rs11209026 (RS3810), the II-238 SNP that has the strongest independent association with both CD and psoriasis susceptibility, and the development of IFX-induced psoriasis; all (25/35) subjects were homozogous for the common (G) allele of rs 11209026. Numerically, more patients with UC than CD carried the protective "A" allele for this SNP (696 vs 1.5%, NS). Results of II-23R SNP analyses are summarized in Table 3.



FIGURE 2. Erythematous lesion behind ear, with surface scaling and exudates (patient no. 5).



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Nail Involvement as a Predictor of Disease Severity in **Paediatric Psoriasis**: Follow-up Data from the Dutch ChildCAPTURE Registry.

Bronckers IMGJ, Bruins FM, van Geel MJ, Groenewoud HMM, Kievit W, van de Kerkhof PCM, Pasch MC, de Jong EMGJ, Seyger MMB.

Acta Derm Venereol. 2019 Feb 1;99(2):152-157. doi: 10.2340/00015555-3036.

PMID: 30206638 Free article. Clinical Trial.

Acta Derm Venereol 2019 Feb 1; 99(2): 152-157

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- Calcipotriene 0.005% and betamethasone 0.064%

suspension: scalp and body: ≥ 12 years



Mimickers of Pediatric Psoriasis

Mimickers:

Sodium valproate-induced psoriasiform drug eruption

Sanitizing hand and diaper wipes containing:

- -Methylchorothiazolinone
- periorificial or perineal psoriasisform distribution

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CONCLUSION

- MANY CHILDREN DO SUFFER WITH PSORIASIS
- FEW CURRENT FDA APPROVED MEDICATIONS
- FEWER STUDIES IN CHILDREN THAN ADULTS
- RECENT LITERATURE TO GUIDE THERAPY

