



Psoriasi in età pediatrica

Prof. Annalisa Patrizi

Psoriasi pediatrica

Due fattori vanno considerati:

- Età pediatrica/ infanzia/adolescenza

- Varietà di psoriasi

Infanzia/adolescenza

- L'**infanzia** è un periodo della vita di un individuo compreso tra la nascita e la pubertà.
- Il **periodo dell'infanzia** è quello da **zero a dieci anni**. Solitamente viene fatta anche una distinzione tra vari periodi dell'infanzia:
- Prima infanzia: dalla nascita ai due anni;
- Seconda infanzia: dai tre ai cinque anni;
- Terza infanzia: dai sei ai dieci anni.

L'adolescenza è l'età di transizione tra l'infanzia e l'età adulta. Comprende il periodo dagli 11-12 ai 18-19 anni nella femmina, e dai 12-14 ai 20-21 nel maschio.

Adolescenza

- L'adolescenza si può suddividere in età prepuberale, pubertà, e giovinezza, che porta fino alla maturità psicofisica, che si raggiunge attorno ai 20 anni.
- Descrizioni più precise distinguono tra preadolescenza ed adolescenza. Alla prima assegnano gli anni dai 10/11 ai 14/15 e alla seconda gli anni dai 14/15 ai 18/20.

Psoriasi: definizione

• Malattia infiammatoria cronica o cronicorecidivante, non contagiosa, di natura probabilmente autoimmune, solitamente caratterizzata da chiazze eritematose con squame argentee localizzate in sedi più o meno tipiche.







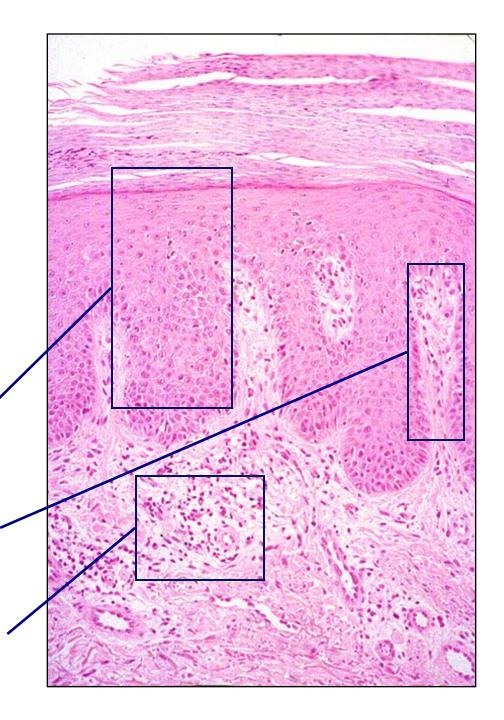
Psoriasi



Eccessiva proliferazione e alterata differenziazione dei cheratinociti

Angiogenesi (vasodilatazione, aumentata permeabilità)

Infiammazione (neutrofili, cellule dendritiche, monociti, linfociti T, cellule NK)



Medscape

- Psoriasis is a common condition that affects about 3.5% of the population.
- In greater than 33% of patients, the initial presentation of psoriasis occurs within the first two decades of life.
- It is estimated that 10% of patients develop psoriasis before the age of 10.
- In a review of 1.262 cases of psoriasis, initial disease onset occurring before the age of 2 years was found in more than 1/4 of pediatric cases.

Open Access Research

BMJ Open Epidemiology of psoriasis and palmoplantar pustulosis: a nationwide study using the Japanese national claims database

Kiyoshi Kubota,^{1,2} Yukari Kamijima,^{1,2} Tsugumichi Sato,^{1,3} Nobuhiro Ooba,^{1,4}
Daisuke Koide,⁵ Hajime Iizuka,⁶ Hidemi Nakagawa⁷

_{Kubota K, et al. BMJ Open 2015;5:e006450.}

Age (years)	Psoriasis* N			PPP N		
	0–9	3376	3177	6553	396	382
10-19	4430	5046	9476	689	923	1612
20-29	9800	9904	19 704	1821	3673	5494
30-39	27 915	22 251	50 166	5049	9388	14 437
40-49	34 637	21 588	56 225	7256	13 237	20 493
50-59	44 963	28 146	73 109	10 318	23 157	33 475
60–69	59 510	33 907	93 417	12 384	23 021	35 405
70-79	48 072	30 930	79 002	7070	11 559	18 629
80-	21 070	20 957	42 027	2265	3636	5901
Total	253 773	175 906	429 679	47 248	88 976	136 224

^{*}Patients with both psoriasis and PPP diagnosis codes are classified as having psoriasis.

JNDB, Japanese national database of health insurance claims; PPP, palmoplantar pustulosis.

Age and say distribution of nationts with psoriasis and PPP in the INDR

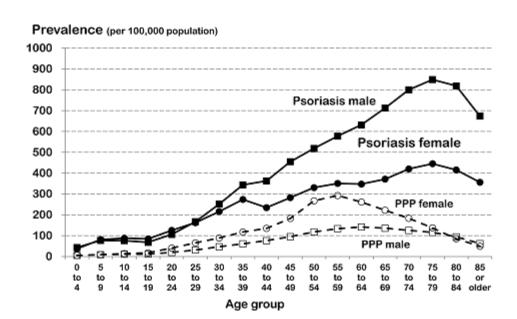
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Figure 1 Prevalence of psoriasis and palmoplantar pustulosis (PPP) in the Japanese population. The prevalence of psoriasis and PPP in Japan was estimated by dividing the number of patients with a psoriasis or PPP diagnosis code by the size of the population according to the census of October 2010.



Psoriasi pediatrica

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- La familiarità è frequente
- La psoriasi pediatrica è per lo più lieve, talora minima.
- Prevale in adolescenza (psoriasi moderata/severa).
- L'età mediana di insorgenza è tra 7 e 10 anni di vita.
- L'età media di esordio attorno ai 10 anni.

INCIDENCE OF PSORIASIS IN CHILDREN: A POPULATION-BASED STUDY

Megha M. Tollefson, MD¹, Cynthia S. Crowson, MS², Marian T. McEvoy, MD¹, and Hilal Maradit Kremers, MD MSc²

Background—Although psoriasis is considered to have a "dual peak" in age of onset, currently no studies exist regarding the incidence of psoriasis in children.

Objective—The objective of this study is to determine the incidence of psoriasis in childhood.

Methods—A population-based incidence cohort of children aged <18 years first diagnosed with psoriasis between January 1, 1970 and December 31,1999 was assembled. The complete medical record of each child was reviewed and psoriasis diagnosis was validated by a confirmatory diagnosis in the medical record by a dermatologist or medical record review by a dermatologist. Age- and sex-specific incidence rates were calculated and were age- and sex-adjusted to 2000 U.S. white population.

Results—The overall age and sex adjusted annual incidence of pediatric psoriasis was 40.8 per 100,000 (95% confidence interval ¹: 36.6, 45.1). When psoriasis diagnosis was restricted to dermatologist confirmed subjects in the medical record, the incidence was 33.2 per 100,000 (95% CI: 29.3, 37.0). Incidence of psoriasis in children increased significantly over time from 29.6 per 100,000 in 1970 to 1974 to 62.7 per 100,000 in 1995-1999 (p<0.001). Chronic plaque psoriasis was the most common type (73.7%), and the most commonly involved sites were the extremities (59.9%) and the scalp (46.8%).

Limitations—The population studied was a mostly Caucasian population in the upper Midwest.

Conclusion—The incidence of pediatric psoriasis increases with increasing age. There is no apparent "dual-peak" in incidence. The incidence of pediatric psoriasis increased in recent years in both boys and girls.

J Am Acad Dermatol. 2010 June; 62(6):

Long-term safety and efficacy of etanercept in children and adolescents with plaque psoriasis

Amy S. Paller, MD,^a Elaine C. Siegfried, MD,^b David M. Pariser, MD,^c Kara Creamer Rice, MS,^d Mona Trivedi, MD,^d Jan Iles, MD,^d David H. Collier, MD,^d Greg Kricorian, MD,^d and Richard G. Langley, MD^e

The overall annual incidence of psoriasis in children and adolescents in the United States (from birth to 18 years of age) was estimated to be 41 cases per 100,000 person-years during the period from 1970 through 1999, and the annual incidence increased during that time. Approximately one third of adult patients with psoriasis report the development of psoriasis symptoms before adulthood. 2,3

Psoriasis in Children and Adolescents: Diagnosis, Management and Comorbidities

I. M. G. J. Bronckers¹ · A. S. Paller² · M. J. van Geel¹ · P. C. M. van de Kerkhof¹ · M. M. B. Seyger¹

L'incidenza della psoriasi pediatrica si è più che duplicata dal 1970 al 2000. Un aumento dei fattori scatenanti? Diversi stili di vita?

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2 Epidemiology

Prevalence rates vary slightly, depending on age, gender, geographical location, definition of prevalence, study design and case definition. Clinical presentation and psoriasis severity may also contribute to variation in prevalence and incidence numbers [3]. Although pediatric psoriasis is not uncommon, limited epidemiology data are available to date. It is estimated that approximately 30-50 % of adults with psoriasis developed psoriasis before 20 years of age [5, 13, 14]. Gelfand et al. found that the prevalence of psoriasis in childhood in the UK was about 0.55 % in children aged 0-9 years and 1.37 % in children aged 10-19 years [4]. This study also demonstrated that the prevalence increased more rapidly in females compared with males younger than 20 years. This finding is probably not due to females paying closer attention to their skin, but suggests an interaction between sex and the development of the psoriasis phenotype in young patients [4]. Comparable prevalence results have been reported within the German (age 0-9, 0.18 %; age 10-19, 0.83 %) [1] and Dutch populations (age 0-10, 0.4 %; age 11-19, 1.0 %) [13]. In contrast to Europe, pediatric psoriasis was almost absent in an epidemiological study on childhood dermatoses performed in Asia [15, 16].

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CLINICAL REPORT

Clinical Characterisation at Onset of Childhood Psoriasis – A Cross Sectional Study in Sweden

Josefin LYSELL1, Mesfin TESSMA2, Pernilla NIKAMO1, Carl-Fredrik WAHLGREN1 and Mona STÅHLE1

Previous studies have reported earlier age of onset in girls (33). This was not the case in our material where gender did not influence age of onset.

Psoriasis in Children and Adolescents: Diagnosis, Management and Comorbidities

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Most studies report no gender bias in pediatric psoriasis. Tollefson et al. described a female to male gender ratio of 1.10 [6]. These findings were similar to other epidemiological studies from Australia, the USA, India and China [5, 21–24]. However, a recent multicenter, cross-sectional study performed in 181 children with plaque psoriasis in the USA reported a female to male gender ratio of 1.48 [25]. This female predominance was also demonstrated by others [26, 27]. The mean age of onset varied from 8 to 11 years [6, 28-30]. Interestingly, Augustin et al. demonstrated an almost linear increase in prevalence rates between 0 and 18 years rather than a "peak of onset" [1].

Psoriasis in Children and Adolescents: Diagnosis, Management and Comorbidities

I. M. G. J. Bronckers¹ · A. S. Paller² · M. J. van Geel¹ · P. C. M. van de Kerkhof¹ · M. M. B. Seyger¹

About 30 % of individuals with psoriasis (children and adults) have an affected first-degree family member [17].

The prevalence of psoriasis patients with an affected family member is observed to be greater in early-onset psoriasis (defined as psoriasis onset before the age of 16) than in adult-onset psoriasis (defined as psoriasis onset after the age of 16) [5, 29, 31, 32]. Chiam et al. compared a Dutch and Singaporean group of children with psoriasis and reported that more Dutch children than Singaporean children had a first- or second-degree family member with psoriasis (73.3 vs. 13.6 %) [26]. In an Australian population, 71 % of children with psoriasis had a first-degree relative with psoriasis. A positive family history of psoriasis was reported in 51.4 % of pediatric psoriasis patients in a multicenter, cross-sectional trial in the USA, with affected members being first-degree relatives in 59.8 % of those cases [25]. These differences point to the role of genetic background within each population of patients with juvenile psoriasis [23, 28]. Pediatr Drugs (2015) 17:373-384



Pediatric psoriasis: an update

REVIEW

Nanette B Silverberg

Pediatric and Adolescent Dermatology, St. Luke's-Roosevelt Hospital Center, New York, NY, USA

> **Abstract:** Pediatric psoriasis consists broadly of 3 age groups of psoriatic patients: infantile psoriasis, a self-limited disease of infancy, psoriasis with early onset, and pediatric psoriasis with psoriatic arthritis. About one-quarter of psoriasis cases begin before the age of 18 years. A variety of clinical psoriasis types are seen in childhood, including plaque-type, guttate, erythrodermic, napkin, and nail-based disease. Like all forms of auto-immunity, susceptibility is likely genetic, but environmental triggers are required to initiate disease activity. The most common trigger of childhood is an upper respiratory tract infection. Once disease has occurred, treatment is determined based on severity and presence of joint involvement. Topical therapies, including corticosteroids and calcipotriene, are the therapies of choice in the initial care of pediatric patients. Ultraviolet light, acitretin and cyclosporine can clear skin symptoms, while methotrexate and etanercept can clear both cutaneous and joint disease. Concern for psychological development is required when choosing psoriatic therapies. This article reviews current concepts in pediatric psoriasis and a rational approach to therapeutics.

Psoriasi pediatrica

- L'incidenza nella popolazione pediatrica è in aumento
- Non sembra esservi predilezione di sesso per la psoriasi a placche detta anche volgare che è la forma più frequente anche in età adulta.
- In passato sembrava che il sesso femminile presentasse un'età di esordio della psoriasi inferiore rispetto al sesso maschile.
- La familiarità è frequente
- La psoriasi pediatrica è per lo più lieve, talora minima.
- Le forme più gravi di psoriasi prevalgono in adolescenza (psoriasi moderata/severa).
- L'età mediana di insorgenza è tra 7 e 10 anni di vita.
- L'età media di esordio attorno ai 10 anni.

Psoriasis in Children: A Review

Matteo Megna[#] & Maddalena Napolitano[#], Anna Balato, Massimiliano Scalvenzi, Teresa Cirillo, Lucia Gallo, Fabio Ayala, and Nicola Balato*



Fig. (1). Common clinical manifestations of psoriasis in children.

P. unghie

Segni caratteristici

- Depressioni cupoliformi
- Chiazze color salmone
- Onicolisi
- Ipercheratosi subungueale

P. volgare: clinica

- L'eruzione cutanea è in genere simmetrica
- Le sedi cutanee più frequentemente colpite sono le regioni più soggette a sfregamento (gomiti, ginocchia e zona pretibiale,cuoio capelluto)

Psoriasi infantile peculiarità

- Squame meno spesse ed evoluzione più rapida rispetto all'adulto
- Passaggio a forme cliniche diverse negli anni
- Interessamento ungueale talora isolato

le squame possono essere più sottili e meno adese e parzialmente coprire un eritema moderato o lieve

 esclusiva dell'età pediatrica

 colpisce tipicamente un solo dito

- entità separata?
- varietà clinica di psoriasi ungueale?
- manifestazione clinica di dermatite atopica o da contatto?

I patch tests sono utili per escludere la diagnosi di dermatite da contatto

Terapia: topici emollienti

Spesso, negli anni, si assiste ad una guarigione spontanea

Pediatr Dermatol. 1999 Nov-Dec;16(6):439-43.

Psoriasiform acral dermatitis: a peculiar clinical presentation of psoriasis in children.

Patrizi A1, Bardazzi F, Neri I, Fanti PA.

Author information

Abstract

Recently an unusual chronic dermatosis, considered a new clinical entity and closely resembling psoriasis, has been described in the literature under the term psoriasiform acral dermatitis (PAD). It is characterized by cutaneous involvement of the digits without nail dystrophy. We describe three young patients, ages 6 to 8 years, in whom this condition was associated with psoriasis. Two children were affected by psoriasis vulgaris, while the third had a palmoplantar psoriasis. All laboratory investigations performed were within normal limits. Skin biopsy specimens taken from the fingers of two patients revealed the pathologic features of subacute spongiotic dermatitis. Histologic examination of a biopsy specimen taken from an erythematous squamous patch confirmed the clinical diagnosis of psoriasis in two patients. The dermatitis showed a fluctuating course in all three patients, with only a moderate to strong improvement with therapy with calcipotriol ointment (50 microg/g). During follow-up, two patients experienced marked spontaneous, persistent improvement, while the disease slightly worsened in the third. The children had features similar to those described in PAD, but were also suffering from psoriasis. Whether PAD is a distinctive entity or just a clinical manifestation of psoriasis in children is still an open question. We strongly believe this latter hypothesis, although further studies are needed to confirm it.

Psoriasiform acral dermatitis

- Lesioni tipiche in altre sedi
- Alterazioni ungueali
- Modesta risposta al calcipotriolo e allo steroide topico
- Istologia spongiforme (?)

Psoriasi Clinica (segni)

 Nei bambini le lesioni sono spesso molto modeste tali da non evocare il sospetto diagnostico

 Nei lattanti le lesioni sono spesso in sede gluteo perineale, ove la macerazione indotta dalle urine e dal pannolino elimina completamente la desquamazione lasciando solo una cute arrossata

Psoriasi Clinica (sintomi)

- Classicamente la malattia non dovrebbe essere pruriginosa ma taluni pazienti lamentano prurito, mentre altri sensazione di bruciore e pochi dolore.
- Talvolta il paziente si lamenta di sintomi vaghi che nel bambino sono apprezzabili con una maggiore irritabilità.
- Le forme più severe quali la psoriasi eritrodermica e pustolosa possono essere febbrili.

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Psoriasi: artrite psoriasica

- Definizione. Artrite sieronegativa, spesso acrale, che appare in associazione con la psoriasi ed ha un aspetto radiologico relativamente tipico.
- I bambini ne sono affetti raramente.
- L' artrite psoriasica può precedere o seguire la psoriasi; nel 10% circa dei casi i due problemi appaiono contemporaneamente.

Psoriasis in Children and Adolescents: Diagnosis, Management and Comorbidities

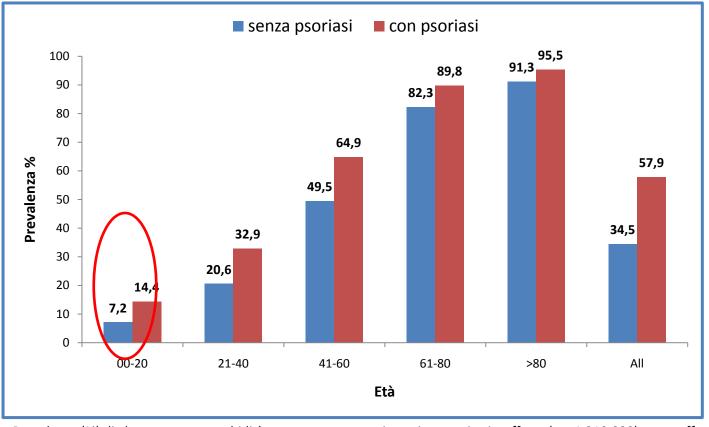
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- Nei bambini la psoriasi differisce talora come distribuzione e morfologia delle lesioni rispetto agli adulti.
- Non vi sono a tutt'oggi linee guida internazionali per la terapia della psoriasi pediatrica
- La psoriasi pediatrica impatta fortemente sulla qualità di vita dei pazienti e delle famiglie
- E' associata ad altre patologie come iperlipidemia, obesità, ipertensione, diabete.



Aumento del rischio

Comorbilità associate alla psoriasi pediatrica



Prevalenza (%) di almeno una comorbidità tra persone con assicurazione sanitaria affette (n = 1,310,090) e non affette (n = 33,981) da psoriasi suddivise per intervalli di età.

I pazienti con psoriasi presentano un rischio aumentato di comorbidità significative, incluse altre malattie infiammatorie¹

In uno studio epidemiologico condotto in Germania, nella popolazione più giovane (< 20 anni) è stato riscontrato un rischio di presenza di comorbidità doppio nei pazienti con psoriasi rispetto a persone senza psoriasi²



Comorbidità in pazienti giovani con psoriasi

	% senza psoriasi	% con psoriasi	Prevalence rate nei bambini [95% CI] ¹
Ipertensione arteriosa	0.83	1.65	1.89 [1.47–2.67]
Diabete	0.43	0.86	2.01 [1.32-3.04]
Iperlipidemia	0.99	2.12	2.15 [1.65–2.80]
Obesità	4.90	8.40	1.70 [1.49–1.93]
Malattia cardiaca ischemica	0.49	0.75	1.52 [0.97–2.38]
Malattia di Crohn	0.14	0.51	3.69 [2.15–6.35]
Artrite reumatoide	4.90	8.40	5.21 [1.40–19.44]
Tutte le comorbidità (almeno una)	7.20	14.40	2.00 [1.82–2.20]

Prevalenza delle comorbidità (%) in individui (range 0–20 anni) con psoriasi (n = 2549) e senza psoriasi (n = 331 758)



Considerazioni sui trattamenti della psoriasi pediatrica

- Pochisssime terapie sono state studiate e approvate specificatamente nei bambini e i dati pubblicati sono limitati^{1–3}
- L'aderenza al trattamento è fondamentale per il raggiungimento di un risultato clinicamente rilevante¹
- E' opportuno tenere in considerazione come obiettivo nel lungo termine l'impatto della terapia sulle comorbidità e sulla qualità di vita
- I trattamenti non sono scevri da potenziali effetti collaterali; il rapporto rischio- beneficio deve essere attentamente valutato^{1,2}
- 5 Impatto psicosociale della malattia^{1,4}
- Assenza di linee guida specifiche per il trattamento della Psoriasi nel bambino⁵

Scelta del trattamento nella psoriasi pediatrica



Nei bambini con psoriasi generalmente viene utilizzato un approccio terapeutico a step progressivi¹

- 1. Topici
- 2. Foterapia
- 3. Sistemici



La maggior parte dei bambini si presenta con psoriasi lieve che può essere gestita con successo tramite terapie topiche²



Terapie sistemiche nei bambini sono indicate in caso di malattia moderata-severa resistente ad altri trattamenti²



Pediatric considerations: topical corticosteroids

1

Widely prescribed and often a first-choice treatment in pediatric psoriasis^{1,2}

2

Some corticosteroid preparations are approved for use in pediatric psoriasis (minimum age of approval depends on the specific agent)^{3,4}

3

Effective in the treatment of pediatric plaque psoriasis⁵

4

Different topical corticosteroid potencies are available; prolonged or extensive use of very potent agents should be avoided in children^{1,6}

- → Children may be more vulnerable to corticosteroid-induced hypothalamic-pituitary-adrenal (HPA) axis suppression than adults due to their higher surface area to body mass ratio^{4,7}
- → Only least potent corticosteroids should be used in the diaper area³



Pediatric considerations: topical Vitamin D analogs

1

Calcipotriol (calcipotriene) and calcitriol are not specifically approved for use in pediatric psoriasis, although they are widely prescribed^{1,2}

2

Calcipotriol is an effective and reasonably well tolerated therapeutic option in mild-to-moderate pediatric psoriasis (<30% of body surface)³

3

Calcitriol also appears to be an effective treatment for pediatric psoriasis, with only mild side effects⁴

4

Pediatric studies suggest no serious side effects or influence on calcium and bone metabolism when Vitamin D analogs are correctly used without exceeding recommended age-dependent maximum dose³



Pediatric considerations: phototherapy*

1

Narrow band ultraviolet B (NB-UVB) therapy is effective in the treatment of pediatric plaque and guttate psoriasis, with comparatively mild side effects over studied treatment durations¹

2

Due to potential side effects (burns, skin aging, risk of skin cancer), and because the treatment process may cause anxiety in younger children, NB-UVB should not be used in toddlers and infants¹

3

UVB phototherapy may be considered for older children and adolescents with moderate/severe widespread disease in which topical treatments have failed^{2,3}

→ Should be used with care, particularly in patients with fair skin1

4

PUVA (psoralen plus UVA exposure) is not generally used in children, but may be considered in adolescents in some circumstances; a topical psoralen is preferred to avoid side effects^{1,2}

*or Heliotherapy: natural sun light (e.g. Dead Sea)

Cary S. Crall^a, Jillian F. Rork, MD^b, Sophia Delano, MD^a, Jennifer T. Huang, MD^{a,*}

Abstract Phototherapy can be a safe and effective treatment for various skin diseases in children. Special considerations governing the use of this treatment modality in pediatric populations include patient, family, and facility-based factors that are oriented around heightened concerns with regard to safety and tolerability of treatment. Although phototherapy has been found to be effective in a wide range of dermatologic conditions affecting pediatric populations, including psoriasis, atopic dermatitis, pityriasis lichenoides, cutaneous T-cell lymphoma, and vitiligo, there is need for additional research on other conditions in which phototherapy has shown promise.

Cary S. Crall^a, Jillian F. Rork, MD^b, Sophia Delano, MD^a, Jennifer T. Huang, MD^a,*

Common pediatric indications for phototherapy

Psoriasis

Modalities Supporting	NBUVB , broadband UVB (BBUVB), PUVA Multiple large retrospective reviews
Supporting evidence	Withitiple large retrospective reviews
Indications	Potential first-line treatment for patients with diffuse involvement, especially those with guttate psoriasis or thin plaque disease

In all, 92% of children treated with NBUVB had greater than 75% improvement with full clearance achieved in 51%. ¹² This response rate was similar to that of prior retrospective cohort studies

Cary S. Crall^a, Jillian F. Rork, MD^b, Sophia Delano, MD^a, Jennifer T. Huang, MD^{a,*}

Study	Modality	N	Mean age (years)	Mean no. of treatments	Mean cumulative dose (mJ/cm ²)	Mean max dose/ treatment (mJ/cm ²)	Response
Pavlosky (2011) ¹²	NBUVB	88	12 (8-16)		46,500		92% with > 75% improvement
Tan (2010) ¹⁹	NBUVB	38	11.3 (8.5- 15.5)	27.8 (4-76)	20,370 (161.5-89,091) with median of 13,113	1388 (15-2996) with median of 490	90% with > 75% improvement
Zamberk (2010) ²⁰	NBUVB	20	13 (5-17)	Median 28 (10-59)	Median 40,841 (5992-144,037)	3000 (873-3000)	52% with > 90% improvement in PASI
Kortuem $(2010)^{21}$	Goeckerman treatment	65	11.6 (0.25-18)	20 (8-37)	NR	NR	85% with > 80% clearance
Ersoy-Evans (2008) ²²	NBUVB	28	12 ± 2.5	25.8 ± 10.6	20,000 (3000-85,000)	1000 (300-6000)	92.9% with > 75% improvement
Jain $(2008)^{23}$	NBUVB + mineral oil	18	(5-14)	20.56 ± 3.06	2956 ± 1070	297 ± 100	100% with clearance of disease
` '	NBUVB alone	18	(5-14)	23.78 ± 3.14	$4,088 \pm 1236$	395 ± 115	
Jury (2006) ¹¹	NBUVB	35	Median 12 (4-16)	Median 17.5 (9-35)	NR	NR	63% with clearance or minimal residual disease
Pasic (2003) ²⁴	UVA + NBUVB	20	9.5 (6-14)	19 (10-39)	6610 (2400-24,500)	340 (30-500)	45% excellent response 40% good-moderate response

Cary S. Crall^a, Jillian F. Rork, MD^b, Sophia Delano, MD^a, Jennifer T. Huang, MD^{a,*}

Phototherapy regimens that include adjuvant therapy with other topical and systemic agents have been studied with variable results. Topical agents had efficacy in patients receiving phototherapy include serous-based emollients (ie, mineral oil), topical corticosteroids, vitamin D analogs (must be applied after phototherapy), coal tar, or topical retinoids^{23,25–27}; however, topical salicylic acid may decrease the efficacy of phototherapy.²⁶ Systemic retinoids have been reported to increase efficacy of UV therapy, whereas methotrexate should be used with caution because of the increased risk of photosensitivity. 26,28

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Phototherapy has also been found to be more effective in treating guttate psoriasis and thin plaque disease.³⁰ It may also be considered a first-line treatment in patients with diffuse or debilitating lesions.

In conclusion, NBUVB, BBUVB, and PUVA are effective treatments for pediatric psoriasis. Although many factors may influence a clinician's choice among these treatment modalities, we recommend NBUVB as the preferred regimen because of its relatively positive safety profile, efficacy, and ease of administration.



Pediatric considerations: retinoids (vitamin A derivatives)

1

Systemic retinoids are not approved for use in pediatric psoriasis due to a lack of clinical studies in this setting^{1,2}

2

Etretinate is an effective treatment for pediatric pustular and erythrodermic psoriasis, but side effects are frequently seen³

3

Acitretine (natural metabolite of etretinate) can be used in severe, particularly pustular, psoriasis in adolescents, but has not been sufficiently investigated to draw conclusions on its use²⁻⁵

4

Retinoids are highly teratogenic^{4,5}

→ Should be used with caution in girls of childbearing age in conjunction with oral contraception and counselling to avoid pregnancy during and for 3 years after treatment

5

Premature epiphyseal closure and impaired bone growth is a concern with retinoids in children⁵

→ Lowest effective dose should be used to minimize this risk⁶

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Background: Acitretin is licensed for and is most commonly used to treat psoriasis. Little information exists about its efficacy and safety in childhood and adolescent psoriasis.

Methods: Retrospective analysis of a group of children and adolescents (<17 years of age) with moderate to severe plaque psoriasis treated with acitretin between 2010 and 2014 at Italian dermatology clinics. Patients were identified through databases or registries.

Results: The study population consisted of 18 patients with a median age of 9.5 years at the start of therapy. The median maintenance dosage per day was 0.41 mg/kg. Eight patients (44.4%) achieved complete clearance or good improvement of their psoriasis, defined as improvement from baseline of 75% or more on the Psoriasis Area and Severity Index at week 16. Three had three or more courses of treatment with short disease-free intervals. In three patients, acitretin treatment was ongoing at the time of data collection. The mean total duration of treatment in responders was 22.7 months. One patient discontinued treatment because of arthralgia. The remaining nine patients (50%) discontinued treatment because it was ineffective. Mucocutaneous adverse effects occurred in all patients, but did not affect therapy maintenance.

Conclusions: In this retrospective case series, acitretin was a moderately effective, well-tolerated treatment in children with moderate to severe plaque psoriasis. Given the small number of patients, statements about long-term safety are not possible.

TABLE 1. Overview of Clinical Characteristics, Treatment Course and Outcome of 18 Children and Adolescents with Plaque Psoriasis Treated with Acitretin

Characteristic	Value
Male, <i>n</i> (%)	12 (66.6)
Female, n (%)	6 (33.3)
Age at start of acitretin, years, range (median)	2–14 (9.5)
Daily dose at start of acitretin, mg/kg	0.2 - 0.5
Daily maintenance dose, mg/kg, median ± SD	0.41 ± 0.14
Responders, n (%)	8 (44.4)
Total treatment duration in responders, months, mean \pm SD	22.7 ± 12.0

The median baseline PASI score \pm standard deviation (SD) was 17.4 ± 7.8 . All patients had undergone topical treatment before. Two (11.1%) had been treated with nbUVB and five with cyclosporine; one had also been treated with psoralen UVA. Thus, in 13 patients (72.2%), acitretin had been administered as first-line systemic treatment.

TABLE 2. Comparison of Responders and Nonresponders

Characteristic	Responders, $(n = 8)$	Nonresponders, $(n = 10)$
Male, n	5	6
Female, n	3	4
Age at start of acitretin, years, mean \pm SD	9.6 ± 3.3	9.2 ± 4.1
Previous systemic treatments, <i>n</i>	3	2
Baseline Psoriasis Area and Severity Index score, mean ± SD	17.5 ± 8.5	17.3 ± 7.6
Maintenance acitretin dose, mg/kg/day, mean ± SD	0.44 ± 0.13	0.38 ± 0.14

British Association

of Dermatologist guidelines do not recommend acitretin in children (21). De Yager et al (6) and Van Geel et al (7) concluded that the efficacy and safety of retinoids is mainly documented in pustular and erythrodermic pediatric psoriasis, whereas studies in childhood plaque psoriasis are lacking. As a result, therapeutic algorithms (6,7) propose methotrexate as the systemic therapy of choice of childhood psoriasis, suggesting acitretin be considered only in pustular and erythrodermic psoriasis. Acitretin was administered in 11.2% of children attending a tertiary referral psoriasis clinic (23).

CONCLUSIONS

Acitretin may be moderately effective in children with moderate to severe plaque psoriasis. Given the small number of patients, statements about long-term safety are not possible. Because of the need for prolonged, usually lifelong, treatment also in children with psoriasis, health systems should support the design of disease or patient registries. Extensive databases may be useful for recording prospective data on efficacy, safety profiles, and suitable dosages of available therapies for childhood psoriasis.



Pediatric considerations: methotrexate

Methotrexate is not approved for use in pediatric psoriasis¹

2

Use in children is generally reserved for severe psoriasis unresponsive to other treatments²

→ It is an effective treatment option for moderate-to-severe pediatric psoriasis, with most evidence available for plaque psoriasis³

3

Long-term data on safety and efficacy in pediatric psoriasis lacking, but is available from its use in juvenile idiopathic arthritis³

4

Short-term side effects in children are usually mild and can be treated, but careful monitoring of patients is needed due to possible severe side effects (hematotoxicty, hepatotoxicity)^{3,4,5}

5

Dose should be tapered to lowest effective once stability or adequate clearance is achieved⁴

Treatment of Moderate to Severe Pediatric Psoriasis: A Retrospective Case Series

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Background: Psoriasis has an estimated prevalence of 0.5% to 2.0% in children. There is a paucity of data regarding the management and safety of treatments currently available for children with moderate to severe psoriasis. The aim of this study was to evaluate the treatment response and safety of systemic therapies used to manage moderate to severe pediatric psoriasis in a single referral center. Despite a small sample size, it was hypothesized that multiple therapeutics used for adult psoriasis would have a similar side-effect profile and positive disease response when used in a pediatric population.

Methods: A retrospective case series evaluated 51 children with moderate to severe psoriasis treated with systemic therapies for adverse event occurrence and for disease response using a 5-point Physician Global Assessment scale. Results: Fifty-one patients, some of whom used multiple treatment options, produced 80 treatment data points. Adverse events were reported in 29 of these 80 treatments, with most being minor, subjective side effects. Overall, the most commonly reported side effect was fatigue, which was reported in 7.5% of treatments. Because of the small sample size, the data collected are limited and may not represent a comprehensive safety profile, nor do they allow comparison of efficacy between therapies. This case series found that biologic and immunomodulating therapies provide well-tolerated treatments with positive

Conclusion: Although sample size and study design limit the data from this study, the study provides some guidance where little exists and helps to support the use of these treatments in this setting.

disease response for moderate to severe pediatric psoriasis.

Treatment of Moderate to Severe Pediatric Psoriasis: A Retrospective Case Series

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Monotherapy—Nonbiologic Systemic Therapies

Methotrexate Monotherapy Fourteen patients (ages 7–18 yrs) used methotrexate for 4 to 100 weeks (11.1 patient-years). Dosing ranged from 3.8 to 21.4 mg weekly (mean 12.8 mg, median 13.9 mg). All patients were concomitantly prescribed folic acid 1 mg daily. Methotrexate was administered orally (n = 13) or subcutaneously (n = 1).

From a baseline of 2.4, the PGA fell to 1.4 at 5 to 7 months and 1.5 at 1 year. Three patients failed to respond to methotrexate. Two patients, one who failed etanercept monotherapy and another who failed adalimumab monotherapy, had a PGA reduction when switched to methotrexate. One patient who switched from adalimumab plus methotrexate to methotrexate monotherapy had a PGA reduction. No CVD, malignancies, bone marrow toxicity, or hospitalizations occurred.

 TABLE 2. Characteristics of Participants According to Receipt of Monotherapy or Combination Therapy

	Moderate-to-severe pediatric psoriasis treatments									
	Number of patients	Patient- years		Age at initiation of therapy, yrs	Baseline PGA	PGA at 5–7 mos	Mean PGA change at 5–7 mos	PGA at 1 yr	Mean PGA change at 1 yr	Adverse events (n, % of subjects)
Etanercept	23	24.6	Mean Median Range	13.7 14.0 8.0–18.0	3.0 3.0 0.0–4.0	1.5 1.0 0.0–4.0	1.5 2.0	2.1 2.3 0.0–3.7	0.9 0.7	Injection site pain (4, 17.4%), injection site reaction (2, 8.7%), headaches (1, 4.3%), decreased appetite (1, 4.3%), weight loss (1, 4.3%), fatigue (1, 4.3%), congestion (1, 4.3%), abdominal discomfort (1, 4.3%), "feeling hot" (1, 4.3%), increased pruritus (1, 4.3%)
Adalimumab	11	7.5	Mean Median Range	15.3 16.5 7.0–18.0	2.4 2.5 0.5–4.0	0.7 0.5 0.0–1.7	1.7 2.0	2.0 1.5 0.5–4.0	0.4 1.0	Cutaneous vasculitis with no systemic involvement (1, 9.1%), temporal headaches (1, 9.1%), verrucous papule (1, 9.1%), chest pain (1, 9.1%), nasal congestion (1, 9.1%), abdominal pain (1, 9.1%), hot flashes (1, 9.1%), photosensitivity (1, 9.1%)
Ustekinumab	6	4.9	Mean Median Range	14.8 16.5 7.0–18.0	2.6 3.0 1.5–4.0	1.5 0.5 0.0–4.0	1.1 2.5	N/A N/A N/A	N/A N/A	None
Methotrexate	14	11.1	Mean Median Range	13.9 15.5 7.0–18.0	2.4 2.3 1.0–4.0	1.4 1.0 0.0–3.5	1.0 1.3	1.5 1.3 0.0–3.5	0.9 1.0	Fatigue (1, 7.1%), productive/persistent cough (1, 7.1%), decreased white blood count (1, 7.1%), shortness of breath (1, 7.1%), verrucous papule (1, 7.1%), increased menstrual periods (1, 7.1%), increased liver function tests (1, 7.1%)
Cyclosporine	5	0.9	Mean Median Range	14.0 14.0 13.0–16.0	3.3 3.5 2.3–4.0	1.3 1.3 N/A	2.0 2.2	N/A N/A N/A	N/A N/A	Nausea (2, 40.0%), neuropathy (1, 20.0%), hair loss (1, 20.0%), bloating/abdominal discomfort (1, 20.0%)
Acitretin	1	0.3	Mean Median Range	15.0 15.0 N/A	N/A N/A N/A	N/A N/A N/A	N/A N/A	N/A N/A N/A	N/A N/A	Dry, chapped lips
Etanercept + methotrexate	5	1.3	Mean Median Range	15.2 15.0 13.0–17.0	3.1 3.3 2.5–3.5	1.8 2.0 0.0–3.0	1.3 1.3	N/A N/A N/A	N/A N/A	None
Adalimumab + methotrexate	9	8.4	Mean Median Range	14.7 15.0 11.0–17.0	2.4 2.5 1.3–3.5	1.0 0.5 0.0–3.0	1.4 2.0	0.3 0.0 0.0–1.0	2.1 2.5	Fatigue (2, 22.2%), injection site pain (1, 11.1%), injection site reaction (1, 11.1%), back pain (1, 11.1%), joint pain (1, 11.1%), tinea versicolor (1, 11.1%), worsening of psoriasis (1, 11.1%)
Ustekinumab + methotrexate	2	0.3	Mean Median Range	16.5 16.5 16.0–17.0	3.8 3.8 3.5–4.0	1.3 1.3 0.5–2.0	2.5 2.5	N/A N/A N/A	N/A N/A	None None
Adalimumab + methotrexate + prednisone	1	0.5	Mean Median Range	8.5 8.5 N/A	1.0 1.0 N/A	N/A N/A N/A	N/A N/A	N/A N/A N/A	N/A N/A	None
Adalimumab + cyclosporine	1	0.1	Mean Median Range	14.0 14.0 N/A	1.3 1.3 N/A	N/A N/A N/A	N/A N/A	N/A N/A N/A	N/A N/A	Mild hypertension, fatigue, malaise, dizziness, nausea, vomiting
Methotrexate + prednisone	1	0.1	Mean Median Range	8.0 8.0 N/A	N/A N/A N/A	N/A N/A N/A	N/A N/A	N/A N/A N/A	N/A N/A	None
Methotrexate + cyclosporine	1	0.2	Mean Median Range	13.0 13.0 N/A	N/A N/A N/A	N/A N/A N/A	N/A N/A	N/A N/A N/A	N/A N/A	Fatigue

Treatment of Moderate to Severe Pediatric Psoriasis: A Retrospective Case Series

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The decision to place a child with psoriasis on biologic or immunomodulatory therapy should be done on a case-by-case basis, with strong consideration of the effect of the disease on the patient and family.



Pediatric considerations: cyclosporine

1

Cyclosporine is not approved for use in pediatric psoriasis1

2

Data on the efficacy of cyclosporine in pediatric psoriasis are limited and ambiguous^{2,3}

3

Safety issues in children are also only sparsely described²

4

Due to the potential for major side effects (hypertension, renal dysfunction), its use in children and adolescents should be reserved for the most severe and therapy-resistant cases^{3,4}

→ It is not considered the systemic therapy of choice in pediatric psoriasis²

5

Usually administered daily, tapered gradually to lowest dose for disease control³

→ Children may require higher doses than adults as they have a higher body surface area (BSA) in relation to body weight – dose calculations based on mg/kg rather than BSA may result in lower efficacy¹



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doi: 10.3109/09546634.2015.1120852

Abstract

Cyclosporine (CysA) is effective for psoriasis in adult patients but little data exist about its efficacy and safety in childhood and adolescence psoriasis.

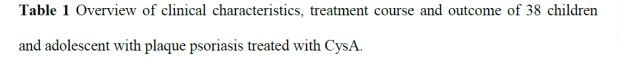
Objectives. To assess the effectiveness and safety of CysA for childhood and adolescence psoriasis.

Methods. Retrospective analysis of a group of children and adolescents (age< 17 years) with plaque psoriasis treated with CysA at several Italian dermatology clinics.

Results. Our study population consisted of 38 patients. The median age at the start of treatment was 12,3 years. Therapy duration varied from 1 to 36

months. The median maintenance dosage per day was 3,2 mg/kg (range 2–5 mg/kg). Fifteen patients (39,4 %) achieved a complete clearance or a good improvement of their psoriasis defined by an improvement from baseline of ≥75% in the Psoriasis Area and Severity Index at week 16. Eight patients (21.05%) discontinued the treatment due to laboratory anomalies or adverse events. Serious events were not recorded.

Conclusions. In this case series CysA was effective and well tolerated treatment in a significant quote of children. CysA, when carefully monitored, may represent a therapeutic alternative to the currently used systemic immunosuppressive agents for severe childhood psoriasis.



Number of patients	38
Males	13 (34.2%)
Females	25 (65.7%)
Family history	17 (44.7%)
Previous phototherapy	18 (47.3%)
Previous systemic treatments	8 (21.05%)
Age at start of CysA	5-17 years (median 12.3)
Daily dose at start of CysA	2.1-3.5 mg/kg
Maintenance daily dose of CysA	2-5 mg/kg (median 3.2)
Duration of treatment	1-24 months (median 5.7)
Response	15 (39.47%)
Adverse Events	8 (21.05%)





ΑII

patients were commenced on Cys-A for moderate to severe psoriasis recalcitrant to topical treatment and/or narrowband ultraviolet B (nbUVB) or other systemic treatments. All patients had received topical treatment before. Eighteen patients (47.3%) had previously been treated with nbUVB. One patients had previously been treated with methotrexate, one with etanercept, two with acitretin, four with psoralen UVA. Thus in 30 patients (78.9%) Cys-A had been administered as first line systemic treatment.



Consequently, etanercept, and ustekinumab should be administered following off-label use of other drugs, such as methotrexate, acitretin and Cys-A, since all these have not been registered for the treatment of childhood psoriasis. Adalimumab could be used as first choice systemic treatment, but only in severe form of the disease.

Treatment of moderate to severe psoriasis in childhood is often challenging. The Food and Drug Administration has not approved any of the available treatments of moderate to severe plaque psoriasis in adults (phototherapy, methotrexate, cyclosporine, retinoids, biologic agents) for use in children. Conversely, the European Medicines Agency approved etanercept and more recently adalimumab and ustekinumab. In particular, etanercept is licensed for the treatment of chronic severe plaque psoriasis in children ages 6 years and older who are inadequately controlled by or are intolerant to other systemic therapies or phototherapies. The European Commission has approved adalimumab for the treatment of severe chronic plaque psoriasis in children and adolescents ages 4 years and older who have had inadequate response to or are inappropriate candidates for topical therapy and phototherapy. Ustekinumab has been approved for the treatment of moderate to severe plaque psoriasis in adolescents ages 12 years and older who are inadequately controlled by or are intolerant to other systemic therapies and phototherapy.

Farmaci biologici

Etanercept (Enbrel®)	Approvato da EMA nel 2009 Trattamento della psoriasi a placche cronica grave nei bambini ed adolescenti a partire da 6 anni d'età che non sono controllati in maniera adeguata da altre terapie sistemiche o fototerapie o che sono intolleranti ad esse
Adalimumab (Humira®)	Approvato da EMA nel 2015per il trattamento della psoriasi cronica a placche grave in bambini e adolescenti dai 4 anni di età che abbiano avuto una risposta inadeguata, o siano candidati inappropriati alla terapia topica e alle fototerapie
Ustekinumab (Stelara®)	Approvato da EMA nel 2015 il trattamento della psoriasi a placche di grado da moderato a severo in pazienti adolescenti a partire dai 12 anni di età che non sono adeguatamente controllati da altre terapie sistemiche o fototerapia o ne sono intolleranti
Infliximab (Remicade®)	Non Approvato. L'uso in pediatria è limitato a evidenze anedottiche e case report

Psoriasi pediatrica: terapie biologiche

	Adalimumab ¹	Etanercept ²	Ustekinumab ³
Indicazione	Si	Si	si
Rimborsabilità	Si	Si	no
Somministrazione	sottocutanea	sottocutanea	sottocutanea
Età	4 anni	6 anni	12 anni
Dosaggi	0,8 mg/kg eow max 40 mg	0,8 mg/kg ew max 50 mg (24 settimane)	0,75 mg/kg e12w fino a 60 Kg_45 mg fino a 100kg, poi 90 mg
Induzione	Si	no	si
Terapie precedenti	fototerapia, topico	fototerapia, sistemico tradizionale	fototerapia, sistemico tradizionale
Studi fase III	vs MTX	vs Placebo	vs Placebo

Update on Pediatric Psoriasis

Nanette B. Silverberg, MD

Table 2.

Selected Areas of Unmet Needs in Pediatric Psoriasis

Comorbidities of pediatric psoriasis, especially long-term cardiovascular and metabolic disorders

Therapies for pediatric psoriasis, specifically the development of nonsteroidal agents and biologic therapies with US Food and Drug Administration approval for pediatric psoriasis

Dietary modification and weight loss for care of and prevention of psoriasis

Psychological concerns and quality of life for patients and caregivers

Safety of topical corticosteroids and addressing corticophobia

Comorbid and long-term development of autoimmunity in pediatric psoriasis

Ongoing monitoring guidelines for health and comorbidities





Grazie per l'attenzione!

Prof. Annalisa Patrizi