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Pederm Insights

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In this Issue

Editor's Note

Dear Colleagues,

*Welcome to the sixth edition of the **Paediatric Dermatology Foundation** newsletter. This issue focuses on Psoriasis and Psoriasiform Disorders.*

*We begin with a **journal review** that addresses key clinical conundrums encountered in the routine management of **paediatric psoriasis.** This review explores:*

- *When, how, and to what extent pediatric psoriasis should be investigated in the context of underlying metabolic abnormalities?*
- *We face a common situation, where the clinical features of pediatric psoriasis and atopic dermatitis overlap. What is this entity?*
- *How to manage pediatric nail psoriasis?*
- *What are the guidelines in the management of pediatric psoriasis?*

*Following this, we present an interesting clinical vignette on erythroderma in an infant. The **answer to the PDF Photoquiz 4** is also revealed, along with a detailed explanation.*

*This edition features an exciting **crossword on psoriasiform dermatoses** and concludes with the **Residents' Corner,** where we delve into an important theoretical topic—palmoplantar keratoderma. Remembering its classifications and nomenclature can be challenging, but we have simplified it using mnemonics.*

We hope this newsletter provides valuable insights and enhances your clinical knowledge and practice. Your feedback is always welcome and can be sent to dr.resham@gmail.com.

Until next time,

Resham Vasani

Editor-in-Chief

Journal Review

In this section we review three clinical conundrums, followed by the concise review of the current guidelines in the treatment of pediatric psoriasis.

Clinical conundrum 1 - When, how, and to what extent pediatric psoriasis should be investigated in the context of underlying metabolic abnormalities?

Journal review by Dr. Sirisha Varala

Osier E, Wang AS, Tollefson MM, Cordoro KM, Daniels SR, Eichenfield A, et al. Pediatric Psoriasis Comorbidity Screening Guidelines. JAMA Dermatol. 2017 Jul 1;153(7):698-704.

The above cited article is a consensus statement on 'pediatric psoriasis comorbidity screening guidelines' based on current evidence by an expert panel in psoriasis, pediatric dermatology, pediatric rheumatology, pediatric gastroenterology, pediatric endocrinology, and adult and pediatric cardiology. The strength of the panel's recommendations is classified as 'SORT level C expert consensus recommendations' due to paucity of studies on comorbidities in pediatric psoriasis. These recommendations are directed towards all pediatric patients with psoriasis irrespective of the type, severity, or duration of disease.

They came up with the following recommendations and monitoring guidelines-

- Overweight or obesity- It has been confirmed by several studies around the world that pediatric psoriasis is clearly associated with obesity as compared to controls. Screening recommendations include **calculating BMI percentile yearly, starting at 2 years of age.**

- Type 2 diabetes mellitus (DM)- Although the risk of DM in children with psoriasis needs to be established conclusively, screening recommendations include **testing with fasting serum glucose every 3 years starting at 10 years of age or at the onset of puberty** in overweight children with other risk factors for DM and in all obese children irrespective of risk factors.

- Dyslipidemias- Although there is evidence for early metabolic and lipid abnormalities in children with psoriasis, screening for dyslipidemia is **indicated only in age ranges of 9-11 years and 17-21 years and in children with other cardiovascular risk factors with a fasting lipid panel.**

- Hypertension- A retrospective study by Michalek et al supports the association between pediatric psoriasis and hypertension.[1] **Screening for hypertension yearly starting at 3 years of age, using age, sex, and height reference charts is recommended.**

- Non alcoholic fatty liver disease (NAFLD)- Children with obesity or overweight with additional risk factors for NAFLD should be **screened with alanine aminotransferase (ALT) measurement starting at 9 to 11 years of age with repetition every 2 to 3 years if risk factors remain unchanged**

- Polycystic ovary syndrome- Association of PCOS with adult psoriasis is well established, however there are no studies in pediatric population. Although routine screening is not recommended, the possibility of this association should be kept in mind by health care providers.

- Psoriatic arthritis- Children should be screened for arthritis by a directed review of systems and physical examination at the time of diagnosis of psoriasis itself and periodically thereafter although the optimal time for repeat screening is yet to be determined.

- Uveitis- Routine ophthalmology examinations for uveitis is only warranted for patients with psoriatic arthritis.

- Mood disorders and substance abuse- Recommendations include **screening yearly for anxiety and depression regardless of the age using Patient Health Questionnaire (PHQ)-4 tool and screening for substance abuse yearly starting from 11 years of age.**

- Quality of life- The QOL of both children with psoriasis and their parents is impacted equally with younger children and those with arthritis being significantly affected. Hence **evaluation using Children's Dermatology Life Quality Index is recommended.**

- Systemic therapy- looking for associated comorbidities prior to initiation of systemic therapy will impact the choice of medication, tolerability, and adverse effects especially with drugs like methotrexate and cyclosporine.

2.

Phan K, Lee G, Fischer G. Pediatric psoriasis and association with cardiovascular and metabolic comorbidities: Systematic review and meta-analysis. Pediatr Dermatol. 2020 Jul;37(4):661-669.

This is an updated systematic review and meta-analysis where they have found a statistically significant association between pediatric psoriasis and overweight/obesity, waist: height ratio >0.5, metabolic syndrome, diabetes, hyperlipidemia, hypertension, and cardiac ischemia and failure. It is of interest to note that, calculation of waist-to-height ratio with a cut off of >0.5 provides a more objective and convenient way to look for central adiposity in children with psoriasis and it has also been shown to predict risk in adolescence. Pallor et al also demonstrated that waist-to-height ratio is elevated in psoriasis overall as well as for the severe psoriasis subgroup as compared to mild psoriasis subgroup.[2] While some studies have reported no significant association between pediatric psoriasis and cardiovascular and metabolic comorbidities, the current review states that pediatric psoriasis patients appear to be at greater risk of metabolic and cardiovascular comorbidities as compared to valvular heart disease and arrhythmias. Furthermore, this risk is greater in children <9 years of age. Hence they have stated that children with psoriasis may benefit from early and frequent monitoring for cardiovascular and metabolic risk especially in those with elevated waist:height ratio and have recommended the same screening guidelines given

Moudgil S, Mahajan R, Narang T, Sachdeva N, Dayal D, Dogra S. Central obesity and dyslipidemia in pediatric patients with psoriasis: An observational study from India. J Am Acad Dermatol. 2021 Dec;85(6):1655-1657.

This is a single centre cross-sectional study where they included 114 children (6-17 years) with psoriasis and 50 age and sex-matched controls. They looked at the frequency of metabolic syndrome and its components in children with psoriasis and compared with healthy controls. Waist circumference, body mass index, blood pressure, fasting blood sugar, lipid profile, and serum leptin levels were measured and the results showed that children with psoriasis had a significantly higher prevalence of central obesity, low high density lipoprotein (HDL) levels and high leptin levels. The severity of the disease correlated with higher body mass index, higher waist circumference and lower HDL levels. Findings from this study establish the relation between pediatric psoriasis and obesity and also support the notion that psoriasis predisposes to atherogenic profile early in the course of the disease which warrants frequent monitoring and maintaining a healthy weight and lifestyle.

Conclusion:

Metabolic syndrome and various other comorbidities in psoriasis are well established in adults but there is paucity of prospective long-term studies in children. Obesity/overweight, especially central adiposity is significantly associated with pediatric psoriasis uniformly across various studies. Measurement of waist:height ratio is an easy and objective method to look for central obesity in children.

In addition, various cardio metabolic abnormalities have been reported in children with psoriasis calling for proper screening using the above-mentioned guidelines, counselling regarding maintaining a healthy lifestyle and preventing obesity. These guidelines also help in rationale use of drugs like acitretin and cyclosporine which have direct impact on these comorbidities.

References:

a) Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017; 31(2):205–212.

b) Paller AS, Mercy K, Kwasny MJ, et al. Association of pediatric psoriasis severity with excess and central adiposity: an international cross-sectional study. JAMA Dermatol. 2013;149:166-176.

Clinical conundrum 2: We often encounter pediatric patients where the clinical features of atopic dermatitis and Psoriasis overlap. What is this entity?

Journal Review by Dr. Malathi Munisamy

Pediatric psoriasiform dermatitis (PD) describes children with overlapping clinical features of atopic dermatitis (AD) and pediatric psoriasis (PP). These children do not fully meet the diagnostic criteria for AD or PP but often show poor response to AD treatments and significant improvement with psoriasis-specific therapies. We review 3 articles relevant to this entity.

Forward E, Lee G, Fischer G. Shades of grey: what is paediatric psoriasiform dermatitis and what does it have in common with childhood psoriasis? Clin Exp Dermatol. 2021 Jan;46(1):65-73. - Australasian Study

- **Objective:** Identify clinical features distinguishing PD from AD and PP.
- **Methods:** Cross-sectional study comparing 109 children with PP, 49 with AD, and 43 with unclassified dermatitis. Twenty-one clinical features were evaluated, and patients with ≥4 psoriasis-associated features were classified as PD and treated with psoriasis-specific therapy.
- **Results:**

§ Eight key features distinguishing PD:

1. History of cradle cap
2. Nappy rash
3. Post-streptococcal/viral exacerbation
4. Weather-related flare-ups
5. Absence of pruritic insomnia
6. Family history of psoriasis (first-degree relative)
7. Scalp scaling
8. Dorsal lichenification or papules on elbows/knees

§ Patients with ≥4 of these features improved significantly on psoriasis-specific treatments (85% PASI reduction in 6 weeks).

- ***Conclusion:*** *PD exists on a spectrum between AD and PP. Children with dermatitis unresponsive to AD treatment and meeting ≥4 psoriasis-associated criteria should be considered for psoriasis-specific management.*

Docampo-Simón A, Belinchón I, Sánchez-Pujol MJ, Berbegal L, Miralles J, Lucas A, et al. Psoriasis dermatitis, a common phenotype of early forms of both psoriasis and atopic dermatitis in children: A prospective multicenter study. Int J Dermatol. 2024 Oct;63(10):1392-1397. (Spanish Multicenter Study)

- **Objective:** Evaluate the progression of PD in children and identify factors predicting disease evolution.
- **Methods:** Prospective study of 24 children (median age: 7 years) diagnosed with PD across six Spanish hospitals, followed for a median of 31 months.
- **Results:**

§ 83.3% of children with PD evolved into a definitive diagnosis of AD (38.9%) or PP (44.4%).

§ Only 11.1% retained the PD diagnosis, and 5.6% had spontaneous resolution.

§ Children who developed AD were younger than those who progressed to PP.

§ Paradoxical association: Children with a family history of psoriasis were more likely to develop AD.

- ***Conclusion:*** *PD may represent an early, undifferentiated phase of AD or PP due to immune system immaturity. Long-term follow-up is essential for accurate diagnosis and treatment adjustment.*

Kouwenhoven TA, Bronckers IMGJ, van de Kerkhof PCM, Kamsteeg M, Seyger MMB. Psoriasis dermatitis: an overlap condition of psoriasis and atopic dermatitis in children. J Eur Acad Dermatol Venereol. 2019 Feb;33(2):e74-e76. (Dutch Study)

- **Objective**: Analyse the clinical characteristics of PD and its overlap with PP and AD.
- **Methods:** Single-centre cohort study comparing 15 children with PD (median age: 7.4 years) to children with confirmed psoriasis from the ChildCAPTURE registry.

- **Results:**

§ PD accounted for 3.7% of pediatric dermatology referrals.

§ PD was associated with:

§ Female predominance (86.7%)

§ Earlier age of onset

§ Positive family history of atopy

§ Higher facial involvement and less frequent scalp involvement

§ PD cases met more AD criteria but retained mixed clinical features over a 1.2-year follow-up.

- **Conclusion:** PD is a distinct subtype with overlapping AD and PP features. Recognizing PD can guide appropriate treatment strategies.

- **Clinical Implications:**

- Diagnostic Considerations:

PD should be suspected in children with chronic dermatitis unresponsive to AD treatment and presenting ≥4 psoriasis-associated features.

Diagnosis aids when classic PP signs (e.g., nail dystrophy, genital rash) are absent but psoriasiform traits persist.

- Pathophysiology:

Emerging evidence suggests that AD and PP exist on an inflammatory disease spectrum, sharing immunologic pathways (e.g., Th17 and Th22 responses).

- Treatment Approaches:

PD cases often require psoriasis-specific therapies when AD treatments fail.

Promising therapies include IL-17 and IL-23 inhibitors, with ongoing investigation into JAK and PDE4 inhibitors.

Long-term monitoring is essential as PD may evolve into either AD or PP with age.

Conclusion:

Pediatric psoriasiform dermatitis represents a clinically significant overlap between AD and PP. Diagnosis relies on identifying psoriasis-associated features in treatment-resistant dermatitis. Longitudinal follow-up is crucial as PD may evolve into AD or PP over time. Further research is needed to refine diagnostic criteria and optimize management strategies.

Clinical conundrum 3: Management of Pediatric Nail Psoriasis

Journal Review by Dr. Shibhani Hegde

Psoriasis with a total prevalence in children and adolescents of approximately 0.7%. Prevalence of nail psoriasis in children (6-17 years) is 0.6% thus reiterating that nail psoriasis is indeed rare in pediatric age group and resultant therapeutic studies are also sparse. Extrapolated data from isolated case reports and case series can be taken. Additionally, complementary information about improvement of nail psoriasis from studies on plaque psoriasis and psoriatic arthritis can also be considered. With adalimumab being approved in adult nail psoriasis, future studies could see approval of pharmacological molecules being approved for pediatric psoriatic nail disease.

Plachouri KM, Mulita F, Georgiou S. Management of Pediatric Nail Psoriasis. Cutis. 2021;108(5):292-4.38.

Nail psoriasis can cause physical discomfort, functional impairment, and psychological distress due to cosmetic concerns. There is a lack clinical trials: most data come from case reports and case series.

Topical therapies:

Topical agents are the first line therapies that can have limited efficacy because of limited penetration of the actives through the nail plate. Hence these therapies need to be combined with mechanical interventions such as grinding, clipping or drilling or the use of keratolytics such urea to thin the nail.

Calcipotriene (Calcipotriol) has been reported to be effective as a monotherapy in a 8- year old patient with pustular nail psoriasis. It must be applied twice daily on the nail and the surrounding tissues.

Topical corticosteroids (clobetasol propionate, mometasone furoate and betamethasone dipropionate in combination with calcipotriene) with or without occlusion have been used with satisfactory results. These have be to used with caution on account of risk of skin atrophy if used long term.

Intralesional corticosteroids, although useful and effective, are less likely to be tolerated by pediatric population on account of pain and hematoma formation.

A 6-year-old with isolated nail psoriasis showed improvement with topical tazarotene gel (0.05%) applied once daily to nail plates and periungual areas.

Systemic therapy

Systemic treatments are indicated in cases of severe nail psoriasis causing functional impairment, cases refractory to the topical treatment and those with psoriatic arthritis.

Two case reports of systemic methotrexate use in pediatric nail psoriasis showed one case with 20 nail dystrophy reporting improvement in one month versus the other case where concomitant psoriasis lesions showed improvement well before the nail lesions. Low dose regime with 5mg/week has shown improvement beginning in a month with complete resolution between 9- 13 months (for finger and toe nails)

Acitretin in pustular psoriasis with nail changes in a 5-year-old boy showed partial improvement when on acitretin within the first 6 weeks of treatment. Dosage mentioned for the same is initial dosage of 0.8 mg/kg/day for 6-weeks, followed by maintenance dose of 0.3 mg/kg/day for 4 weeks.

Biological agents used in isolated nail psoriasis is scarce. They can be considered in severe cases where there is no response to conventional treatment.

Adalimumab is the only FDA approved agent in nail psoriasis. The initial dose is 80 mg followed by 40 mg after 1 week, then every 2 weeks. Clearance starts within 8 weeks.

One case report of an 8-year-old girl with nail psoriasis, plaque psoriasis and psoriatic arthritis with resistance to multiple therapies was successfully treated after 3-months of secukinumab (150 mg monthly).

Cases in which infliximab was used (5 mg/kg at weeks 0, 2, and 6 with maintenance every 8 weeks) resulted in rapid (within 2 weeks) yet transient improvement of psoriatic nail disease.

Ixekizumab, a monoclonal antibody that selectively targets interleukin (IL)-17A, is approved for use in pediatric psoriasis. In a phase III multicentre, double-blind, randomized, placebo-controlled study of ixekizumab use in moderate-to-severe psoriasis, 50% of patients randomized to IXE at baseline achieved complete clearance by week 48.

Phototherapy can be an adjunctive or alternative therapy in cases with localized involvement/mild cases where systemic drugs are contraindicated. Narrowband UVB (311 nm) has been used as targeted therapy for isolated nail involvement where partial improvement was noted after 36 sessions. Broadband UVB + Thalidomide has been used as a combination therapy in case of a 2-year -old with acrodermatitis continua of Hallopeau involving 19 digits and marked improvement was seen within 2 months.

Wang X, Sun Y, Xie W, Liu H, Liu G. Case report: Intralesional secukinumab injection for pediatric nail psoriasis: does it have to be a positive outcome? Front Immunol. 2024;15:1435141.

In a case series of 3 pediatric children (all aged ≤8-years) under regional anesthesia, intralesional secukinumab (30mg on each finger nail) was injected on either sides of proximal nail fold and on either sides of anterior nail plate on the distal end. The patients were injected once every 2 weeks for 3 months. They were then shifted to receive 150mg subcutaneous injection of secukinumab monthly for 9 months. With long term follow-up on both patients, improvement of nail psoriasis were noted in all.

Conclusion:

The severity of nail psoriasis in childhood does not correlate with that of the skin psoriatic lesion and its diagnosis could be difficult and overestimated. Nail pitting, onycholysis and subungual hyperkeratosis are seen in most studies. Nail psoriasis appearing as trachyonychia can itself pose to be a diagnostic and therapeutic challenge.[a]

Nail disease in pediatric population is typically limited to topical treatment options, such as topical corticosteroids, tazarotene, vitamin D analogues and calcineurin inhibitors. Systemic medications are usually not recommended. However, for severe nail disease, systemic agents can be indicated based on cost constraints, parent preference, contraindications to said agent.

Although apremilast is used in a few studies on adult nail psoriasis,[b] *and a phase 2 open-label study of apremilast in adolescent plaque psoriasis,*[c] *no trials of apremilast use in pediatric nail psoriasis are reported in literature. Intralesional injections of triamcinolone, methotrexate and secukinumab are reported but pain can heavily limit the use of intralesional injections in pediatric population.*

References:

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b. Oak ASW, Ho-Pham H, Elewski BE. Improvement of 11 patients with nail psoriasis with apremilast: Results of an investigator-initiated open-label study. J Am Acad Dermatol. 2020;83(6):1830-32.

c. Paller AS, Hong Y, Becker EM, de Lucas R, Paris M, Zhang W, et al. Pharmacokinetics and safety of apremilast in pediatric patients with moderate to severe plaque psoriasis: Results from a phase 2 open-label study. J Am Acad Dermatol. 2020;82(2):389-97.

Current guidelines in the treatment of Pediatric psoriasis

Journal Review by Dr. Rashmi Agarwal

Menter A, Cordoro KM, Davis DMR, Kroshinsky D, Paller AS, Armstrong AW, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. J Am Acad Dermatol. 2020;82(1):161-201.

- The American Academy of Dermatology and the National Psoriasis Foundation provide evidence-based recommendations for pediatric psoriasis, considering unique physiological, pharmacokinetic, and psychosocial factors in children.

- **Assessing Psoriasis Severity in Children**

  Body Surface Area (BSA):

  - Mild: <3%
  - Moderate: 3–10%
  - Severe: >10%

- Psoriasis Area Severity Index (PASI): Used but less practical in pediatric dermatology.

- Quality of Life (QOL) Assessments: Recommended to capture the psychosocial burden (e.g., Children's Dermatology Life Quality Index, CDLQI).

- **Comorbidities in Pediatric Psoriasis**

  a. Psoriatic Arthritis (PsA): Develops in 80% of affected children before skin involvement, with peak onset at ages 2–3 and 10–12 years. Uveitis is a possible complication.

  b. Obesity: Central obesity often develops around age 8years. Routine assessment for hypertension, dyslipidemia, and insulin resistance is advised.

  c. Cardio-metabolic & Inflammatory Bowel Disease (IBD): 3–4 times higher risk than non-psoriatic children. Cardiovascular risk (without obesity) remains inconclusive.

  d. Mental Health: Increased risk of social isolation, depression, and anxiety.

  e. Asthma: Emerging as a potential comorbidity.

  f. Screening Recommendations:

  IBD screening for children with GI symptoms, poor growth, or weight loss.

  Regular assessment for obesity-related conditions.

- **Non-Biologic Systemic Treatments**

  <u>Phototherapy (NB-UVB)</u>

  -Indications: First-line for extensive psoriasis (>15–20% BSA), refractory plaque/guttate/pustular psoriasis, or cases unsuitable for systemic therapy.

  -Contraindications: PUVA is not recommended for children <12 due to ingestion-related toxicity and cancer risks.

  <u>Methotrexate (MTX)</u>

  -Indications: Moderate-to-severe plaque psoriasis, PsA, erythrodermic, pustular, or disabling palmoplantar psoriasis.

-Dosing:
Children <13 years: 0.2–0.3 mg/kg/week (max 25 mg/week).
Preferred administration: Subcutaneous (better bioavailability, fewer GI effects).

-Monitoring: CBC, liver enzymes, creatinine (baseline & monthly for 3 months, then every 3–6 months).

-Side Effects: Nausea, vomiting, transient liver enzyme elevations, rare hepatotoxicity.

-Vaccine Considerations:
Live vaccines (MMR, VZV) can be given to MTX patients.
Primary immunization requires a 2 to 4-week gap before MTX initiation.

Cyclosporine (CsA)

-Indications: Severe, unstable plaque, pustular, or erythrodermic psoriasis. Effective in infants.

-Dosing: 3–5 mg/kg/day in divided doses.

-Monitoring: Kidney function, blood pressure, CBC, cholesterol, triglycerides.

-Adverse Effects:
Renal toxicity, hypertension, electrolyte imbalances, hypertrichosis, rare malignancy risk.

-Limitations:
Treatment beyond 12 months is not recommended due to toxicity.
Live vaccines contraindicated.

Acitretin

-Indications: Guttate, pustular, moderate-to-severe plaque, and palmoplantar psoriasis. Safe for children as young as 6 weeks.

-Dosing: ≤0.5–1 mg/kg/day.

-Side Effects: Dry skin, pruritus, epistaxis, hyperlipidemia, liver enzyme elevations.

-Special Considerations:
Teratogenicity: Pregnancy must be avoided for 3 years post-treatment.
Bone Toxicity: Low-dose therapy minimizes risk; periodic X-rays recommended for musculoskeletal symptoms.

Apremilast

-FDA Approved (2024) for children ≥6 years and ≥20 kg needing systemic therapy.

-Dosing:
•35–70 kg: 20 mg BID
•>70 kg: 30 mg BID

-Advantages: No lab monitoring required, well-tolerated with minor GI and headache side effects.

- **Biologic Therapies**

Biologics target specific inflammatory pathways and are effective in moderate-to-severe pediatric psoriasis.

Biologic	**Target**	**Key features**
Etanercept	TNF-α	Longest pediatric use, mild injection site reactions
Adalimumab	TNF-α	Similar safety to MTX, lower cost improves accessibility
Ustekinumab	IL-12/23	Less frequent dosing enhances compliance
Ixekizumab	IL-17A	Fastest acting, may worsen IBD
Secukinumab	IL-17A	Less injection site reaction, more injections required

Biologic Therapy Considerations

• Pre-Treatment Screening:
- TB screening before initiation, annual TB monitoring.
- Hepatitis & HIV screening based on risk factors.

• Vaccination Guidelines:
- Live vaccines (MMR, VZV) should be avoided.
- Household members should be fully vaccinated.

• Infection Monitoring:
- Higher risk of respiratory infections; close surveillance required.

Note: Lack of response to one biologic does not rule out success with another, even within the same class.

Conclusion

Pediatric psoriasis requires individualized treatment approaches, balancing efficacy, safety, and long-term management. Non-biologic systemic treatments, phototherapy, and biologics each have distinct roles based on disease severity and comorbidities. Continuous monitoring and personalized adjustments ensure optimal patient outcomes.

Bronckers IMGJ, Paller AS, West DP, et al. A Comparison of Psoriasis Severity in Pediatric Patients Treated With Methotrexate vs Biologic Agents. JAMA Dermatol. 2020;156(4):384–392.

A multicenter, retrospective cohort study across 20 sites in Europe and North America assessed the real-world effectiveness and long-term drug survival of methotrexate compared to biologic agents in pediatric plaque psoriasis. Children with moderate to severe psoriasis treated between December 1990 and September 2014 were included, provided they received at least three months of systemic therapy and had adequate data for analysis.

Study Cohort and Methodology

Of the 234 pediatric patients (mean age: 11.6 years for methotrexate, 13.3 years for biologics), 163 received methotrexate alone, 47 received only biologics, and 24 were treated sequentially with both. Treatment response was measured using Psoriasis Area and Severity Index (PASI) and/or Physician Global Assessment (PGA) scores at baseline and within the first 6 months.

Efficacy Outcomes

Biologic therapies, predominantly etanercept (73.2%), demonstrated superior short-term efficacy. At 6 months:

PASI75 (≥75% improvement): Achieved by 40.0% of patients on methotrexate vs. 71.4% on biologics.

PGA of clear/almost clear (score 0/1): Achieved by 35.6% on methotrexate vs. 48.6% on biologics.

The likelihood of achieving PASI75 was significantly higher with biologics (OR: 4.56; 95% CI: 2.02–10.27; $p < .001$). PGA improvement trended in favor of biologics (OR: 2.00; 95% CI: 0.98–4.00; $p = .06$), though not statistically significant.

Drug Survival and Safety

At 1, 3, and 5 years, biologics showed greater drug survival than methotrexate (HR: 2.23; 95% CI: 1.21–4.10; $p = .01$). Discontinuation due to lack of efficacy was similar between groups. Methotrexate was more often discontinued due to adverse effects such as gastrointestinal symptoms, infections, and liver function abnormalities. In contrast, biologics were associated with fewer and generally milder adverse effects.

Clinical Context and Implications

Systemic therapy—including methotrexate, cyclosporine, acitretin, and phototherapy—is indicated for pediatric patients with moderate to severe psoriasis (PASI >10, BSA >10%, CDLQI >10), particularly in cases refractory to topical treatment or those presenting with erythrodermic or pustular subtypes. The limited availability of approved systemic agents and paucity of head-to-head comparative trials make treatment decisions challenging.

Biologics are increasingly considered first-line options due to their favorable safety profile, ease of use, and efficacy. Current EMA and FDA-approved biologics for pediatric psoriasis include:

- Etanercept (≥6 years)
- Adalimumab (≥4 years)
- Ustekinumab (≥6 years)
- Ixekizumab and Secukinumab (both ≥6 years)

Despite the higher cost, biologics offer a compelling risk-benefit profile, especially for patients requiring long-term systemic therapy. Methotrexate, however, remains the most commonly prescribed and cost-effective agent, with meaningful clinical responses observed in a subset of patients.

Combination Therapy and Future Directions

Although methotrexate is commonly used in combination with biologics for rheumatoid arthritis, its role in combination regimens for psoriasis and psoriatic arthritis remains less defined. Some evidence suggests that methotrexate may enhance the efficacy of TNF-α inhibitors by reducing immunogenicity, though its benefit in combination with newer biologic classes such as IL-17 or IL-12/23 inhibitors warrants further investigation.

A recent randomized study found that adalimumab (0.8 mg/kg) resulted in a PASI75 response in 58% of pediatric patients by week 16, compared to 32% with methotrexate. These findings support the increasing adoption of biologics as the preferred long-term therapy, particularly for patients with inadequate response or intolerance to conventional agents.

Conclusion

This retrospective study reinforces the growing consensus that biologic therapies offer superior efficacy and drug survival with a favorable safety profile compared to methotrexate in children with moderate to severe psoriasis. While methotrexate remains a valid and accessible option, biologics represent a pivotal advancement in pediatric psoriasis management. Further real-world and long-term studies are needed to solidify the optimal positioning of biologics in treatment algorithms and evaluate their use in combination with traditional agents.

It is important to note that the majority of studies have been conducted in Europe and North America, with a significant lack of data from Indian populations. We are also aware that genetic predisposition, cardiometabolic factors, climate, socioeconomic conditions, dietary habits, and lifestyle differ considerably between Indian and Western populations. Moreover, while insurance coverage and access to biologics are more readily available in Europe and the U.S., these treatments remain less accessible to Indian patients. In our setting, methotrexate continues to be a time-tested option for pediatric psoriasis, despite the limited formal studies evaluating its use in this population.

References:

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Case Vignette

Erythroderma in a 3 month old infant

Author - Dr Ajit Barve, Consultant Dermatologist, Dr. Ajit Skin Clinic, Thane

A 3-month-old infant presented with widespread erythema and generalized scaling persisting for six weeks. The child was born at term via normal vaginal delivery to non-consanguineous parents, with no notable postnatal complications and normal skin at birth.

The child had received topical halobetasol propionate with salicylic acid in a lotion base for application, prescribed by a local practitioner, which was continued for a month prior to presentation.

Upon examination, the child was well-nourished and not in distress. Vital signs were within normal limits: heart rate 140 bpm, respiratory rate 40 breaths per minute, weight 6 kg, and height 60 cm. There was diffuse erythema accompanied by thick white scales covering the entire body [Figure 1], including the palms [Figure 2], soles [Figure 3], and scalp . The scales were larger and more detachable over the dorsa of hands [Figure 4] and feet and revealed a base of erythema. All nails exhibited dystrophy with subungual hyperkeratosis [Figure 5] . The rest of the systemic examination was normal.

Given the absence of skin lesions or a collodion membrane at birth, congenital causes of erythroderma were considered less likely. Differential diagnoses included infantile erythrodermic psoriasis and crusted scabies (Norwegian scabies).

Complete blood count, differential count, T-cell and B-cell subsets, quantitative immunoglobulins, and HIV test were all within normal limits.

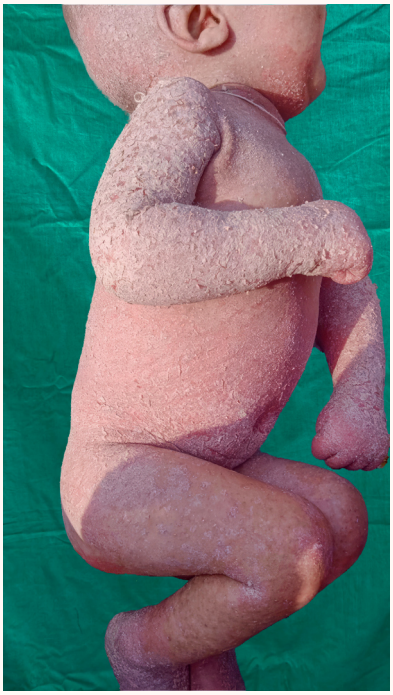

Fig 1: Generalised erythema and scaling

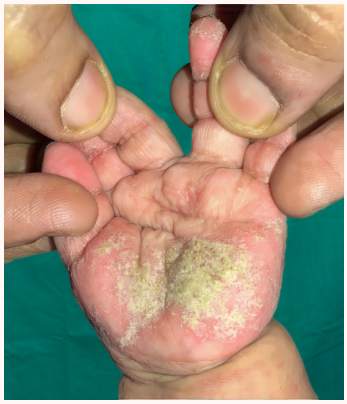

Fig 2: Psoriasiform scaling seen on the palms

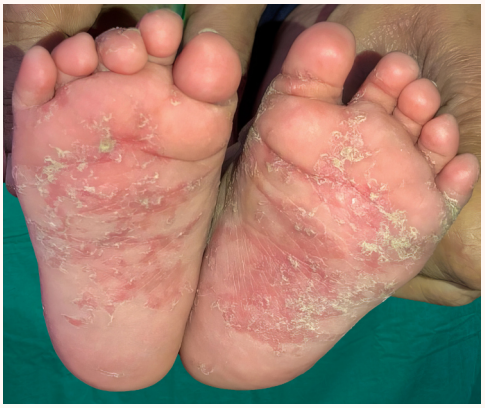

Fig 3: Psoriasiform scaling over a background of erythema seen on the soles

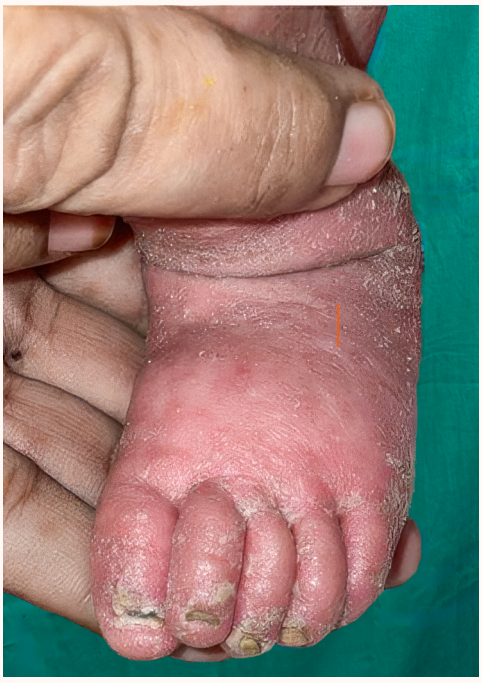

Fig 4: Brownish discoloration with subungal hyperkeratosis involving all the toe nails

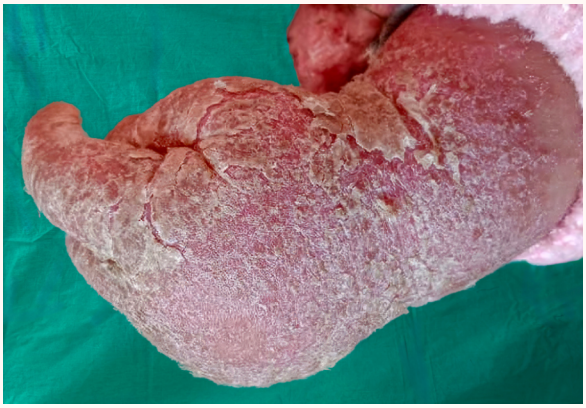

Fig 4: Thick white large loosely adherent scales seen on the dorsa of hand over a background of erythema

Dermoscopy revealed numerous burrows in a noodle-like pattern with multiple brownish triangular structures (delta glider sign) [Figure 6]. Potassium hydroxide (KOH) preparation of skin scrapings confirmed the presence of numerous Sarcoptes scabiei mites , eggs and scybala [Figure 7], establishing a diagnosis of crusted scabies.

Retrospective history-taking revealed that multiple family members experienced pruritic lesions consistent with scabies. The infant was treated with permethrin 5% cream applied twice weekly, along with daily liberal application of emollients. After three weeks, there was a substantial reduction in erythema and scaling, and the affected nails were shed. Family members received simultaneous treatment to prevent reinfestation.

Crusted scabies is a rare, extremely contagious form of scabies characterized by infestation by extremely large number of Sarcoptes scabiei mites in contrast to typical scabies, where an intact type IV hypersensitivity reaction limits the extent of the infestation.[1,2] Risk factors include neurological disease (difficulty in scratching), intellectual disability, malignant neoplasms, malnutrition, immune disorders and use of topical and systemic steroids. The eruption in crusted scabies is characterized by diffuse hyperkeratosis, associated with a variable degree of underlying erythema. The entire body may be affected, including the face and scalp. Pruritus may or may not be present. Nail dystrophy can be present. Due to its hyperkeratotic appearance, the disease is often confused with other entities such as psoriasis, eczema or keratoderma which can lead to a delay in diagnosis and erroneous treatment with topical corticosteroids.

Family history is a pertinent clue in majority of cases. Dermoscopy features include the well described hang glider sign and a noodle-like pattern due to several burrows on top of each other. [3]

Multiple case reports have highlighted mistreatment with topical steroids as a factor leading to crusted scabies. Potent topical steroids can cause local immunosuppression and also mask the clinical features of the disease.

In a recent case series of 20 children with crusted scabies, prior topical steroid use was noted in 12 cases (60%).[4,5]

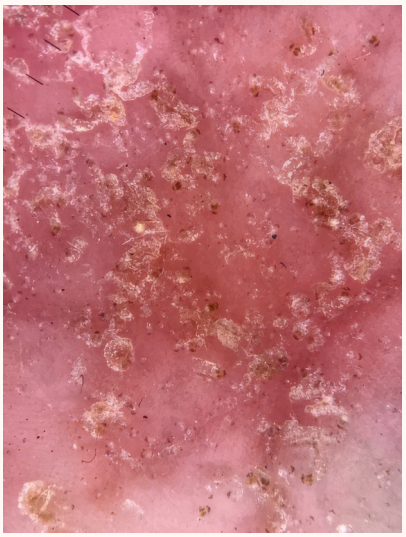

Fig 6: Dermoscopy using Dermlite 4N, Polarised mode, showing numerous burrows in a noodle-like pattern with multiple brownish triangular structures (delta glider sign)

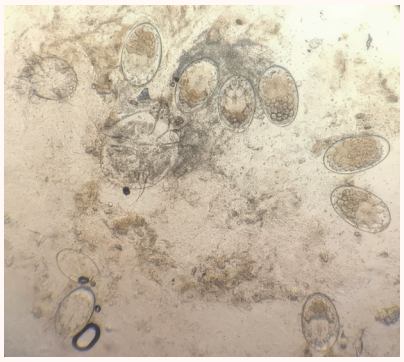

Fig 7: Potassium Hydroxide mount – 40x Magnification – Showing Adult mites, eggs and scybala.

For crusted scabies, a more aggressive treatment regimen has been recommended with administration of oral ivermectin repeated doses at days 1, 2 and 8 depending on the severity of the infestation. Concomitant topical permethrin every 2–3 days for the first 1–2 weeks is recommended.[2] Oral ivermectin has been recommended only for adults or those weighing > 15 kg. The use of ivermectin among young children has been limited by safety concerns related to potential central nervous system side effects of ivermectin due to an immature blood–brain barrier. [6]

However, a recent study of 170 infants aged 1–64 months found oral ivermectin to be effective, with no severe adverse effects.[7] Studies have shown that clearance of ivermectin is higher in children than adults, therefore higher weight-based doses are needed to achieve a similar drug exposure. A multicentre, phase 2 trial enrolled 100 children with scabies. They evaluated 3 mg ivermectin dose in these children with scabies, aged 2–4 years and weighing 10–14 kg. Complete resolution of scabies occurred in 90/99 children by day 14. Adverse effects were mild and occurred in 7/99, the majority of which were gastrointestinal.[6]

Salicylic acid is used in the treatment of crusted scabies in adults but its use in extensive areas in infants can cause salicylate poisoning.[8]

Take Home Points-

- Crusted scabies can present as erythroderma
- Timely diagnosis is essential to avoid mistreatment as psoriasis or atopic dermatitis.
- Good history taking and dermoscopy can be a valuable aid to confirm the clinical diagnosis.

References (Clickable links)

1. Segado Sánchez et al
2. Rehmus et al
3. Chavez-Alvarez et al
4. Grodner et al
5. Leung et al
6. Gwee et al
7. Levy et al
8. Fil et al

Answer to PDF - Photoquiz 4

Author: Dr Vasudha Belgaumkar

Clinical data-

A 6 -year-old boy is a known case of common variable immunodeficiency disorder (CVID) with autoimmune hemolytic anemia (AIHA) on monthly intravenous immunoglobulins (IVIG) since the age of 4 years. He presented with a painful swelling over lateral side of left upper arm, gradually increasing in size since 7 months with pus discharge since past one month. There was history of recurrent upper and lower respiratory tract infection associated with fever on and off along with weight loss since one year. The child had received injection rituximab (4 doses) a year ago for AIHA. He was appropriately vaccinated for age. There was no history of prior trauma at the site. Family history was non-contributory.

On dermatological examination, an erythematous, fleshy ulcerated nodule of size 3cm x 2cm was noted over lateral aspect of left upper arm (deltoid area) with pus discharge (Figure 1) . Tenderness and local rise of temperature were present. Ipsilateral axillary and cervical lymph nodes were palpable (1-2 cm sized), tender, discrete with normal overlying skin. He had white adherent lesions with erythema over tongue and buccal mucosa suggestive of oral candidiasis (Figure 2). Nails and other mucosae were unremarkable.

His haemoglobin was 7.9g/dl, white blood count 7000/cumm, platelet count-1.91 lakh/cumm. Liver and renal function tests were within normal limits. CRP and ESR were elevated with negative fever profile .Chest X-ray showed right parahilar consolidation with prominent bronchovascular markings but sputum Cartridge-based nucleic acid amplification test (CBNAAT) for mycobacterium tuberculosis (M.TB) was negative. Local ultrasonography of lesion site showed 4 x1.1 mm heterogenous, hypoechoic collection in subcutaneous plane with hyperechoic content within with minimal peripheral vascularity on colour doppler suggestive of infective aetiology. Surrounding tissue and bones were normal. Ultrasonography (USG) abdomen and pelvis was unremarkable while USG neck found subcentimetric lymph nodes with maintained fatty hilum at bilateral 1,2a and 2b level. HIV and Mantoux tests were negative.

A punch biopsy was taken from the nodule and sent for histopathological examination with special stain (figure 3).

Answers:

A. BCGitis

B. Ziehl Neelson Stain

Discussion

A differential diagnosis of reactivation of BCG (BCGitis), opportunistic deep fungal infection (Aspergillosis and Sporotrichosis) atypical mycobacterial infection and lupus vulgaris were considered in the background of immunosuppressed state.

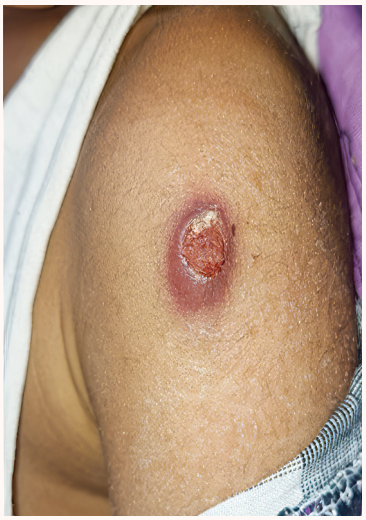

Figure 1- Erythematous ulcerated nodule over left deltoid area in a child with CVID

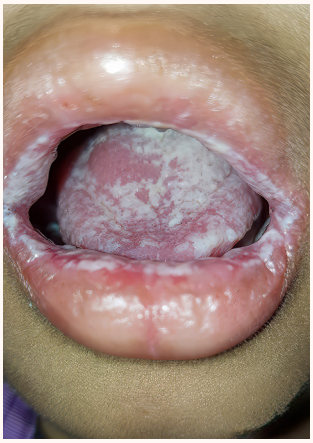

Figure 2 -Curdy white plaques over tongue and lips (Oral candidiasis)

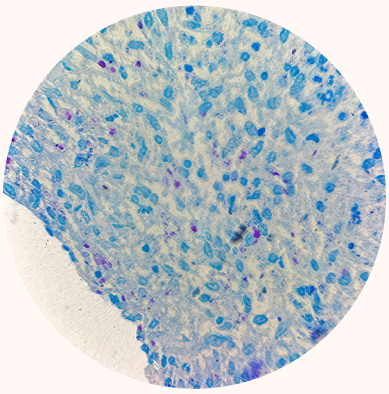

Figure 3 - Photomicrograph of biopsy from nodule (40 x with special stain)

Histopathology from the nodule showed hyperkeratinized epidermis with regular elongation of rete ridges. Dermis showed collection of epitheloid cells, caseating necrosis along with acute on chronic inflammatory infiltrate. **Ziehl Neelson staining** was positive for Mycobacteria (figure3). Tissue specimen was positive by CBNAAT for Mycobacteria with rifampicin sensitivity. KOH mount, bacterial and fungal cultures were negative.

Final diagnosis was Localised BCGitis with oral candidiasis in a child with common variable immunodeficiency disorder.

According to the Revised National Tuberculosis Control Program (RNTCP) guidelines, the child was treated with fixed dose combination of antitubercular treatment (ATT) regimen for weight which comprises 4 drug regimen of Tab Isoniazid (120 mg) PO OD, Tab Rifampicin 180 mg PO OD, Tab Pyranzinamide (420mg) PO OD, Tab Ethambutol (300mg) PO OD, Tab Pyridoxine (10mg0 PO OD for intensive phase of 2 months followed by 3 drug regimen of Tab Isoniazid (120 mg) PO OD, Tab Rifampicin (180 mg) PO OD, Tab Ethambutol (300mg) PO OD for continuation phase of 4 months. The patient was continued with monthly IVIG. Oral and topical antifungals were added for oral candidiasis. The skin lesion resolved with marked weight gain and improvement in general condition.

Common variable immunodeficiency disorder (CVID) is the most frequently encountered primary immunodeficiency disorder mainly affecting humoral immunity. Clinical features are seen in late childhood and adults are frequent lower and upper respiratory tract infections like chronic sinusitis, pneumonias, gastrointestinal tract infections with autoimmunity (1). In our case, the child was diagnosed at the age of four years for recurrent respiratory tract infection and autoimmune haemolytic anaemia. Previous data suggest that almost all patients with BCGiosis and half of those with BCGitis had a documented primary immune deficiency disorder (2).Thus immunological evaluation is recommended in individuals with BCG vaccine complications (3).

Tuberculosis (TB) is a leading infectious cause of death worldwide. BCG is a live vaccine made by sequential culture of virulent Mycobacterium bovis strain which has been modified to its non- virulent form for vaccine use. It helps in preventing serious complications like childhood TB meningitis or miliary TB (4). WHO recommends BCG vaccination to all neonates immediately after birth, preferably within 28 days. As BCG is a live vaccine it is not recommended in individuals with HIV infection, congenital immunodeficiency such as chronic granulomatous disease or interferon gamma receptor deficiency, leukemia, lymphoma or family history of the listed conditions. It is to be avoided in patients on immunosupressants like corticosteroids, alkylating agents, antimetabolites or radiation (5).

As immunodeficiency is usually not diagnosed during neonatal period, this leads to inadvertent vaccination. Our child was vaccinated as per protocol till he was diagnosed as a case of CVID with AIHA for which he received four doses of injection rituximab along with monthly IVIG which probably led to severe immunosuppression predisposing to BCGitis.

Complications secondary to BCG vaccination are subdivided into: i) local (vaccine site) or regional (vaccine site draining) lymph-node which is referred as BCGitis ii) distant (site away from vaccination) or disseminated (affecting > 1 site or blood) namely BCGiosis (6). Incidence of BCGitis and BCGiosis is 1:10 000 and 1: 1 000 000 respectively with BCGiosis being more severe (2).

Clinically, dermatological manifestations include erythema, edema, pustulation/abscess formation at the BCG site with/ without regional lymphadenopathy (as observed in our case), keloid formation, erythema nodosum, diffuse maculopapular rash. Systemic involvement presents as generalised lymphadenopathy, pulmonary or hepatic/splenic infiltrates, osteitis or military lesions with multi-organ dissemination (2).

A diagnosis of BCGitis can be validated by direct staining (Ziehl-Neelsen or auramine-rhodamine), histological observation (presence of a granulomatous pattern with or without caseous necrosis) or polymerase-chain reaction (PCR) assays. However, the reliability of all these investigations is low, leading to increasing difficulty in establishing the diagnosis. In our case, appearance of lesion at site of old BCG scar, characteristic histopathology, positive AFB staining and CBNAAT with dramatic response to ATT favours the diagnosis of BCGitis. Treatment of BCGitis in immunocompromised children comprises first line drugs, isoniazid 15–20 mg/kg/day, rifampicin 20 mg/kg/day, ethambutol 20–25 mg/kg/day and pyrazinamide 20–25 mg/kg/day (to be given for 2 months until Mycobacterium tuberculosis is excluded, as M. bovis is inherently resistant to pyrazinamide). Second- line drugs like ofloxacin 15 mg/kg/day or ciprofloxacin 30 mg/kg/day can be added if required. Duration of treatment varies from 6 to 9 months (5).

Early recognition and treatment of BCGitis in immunocompromised children can significantly impact disease progression. Timely intervention is crucial to improving the prognosis in such vulnerable populations.

Conflict of interest: None

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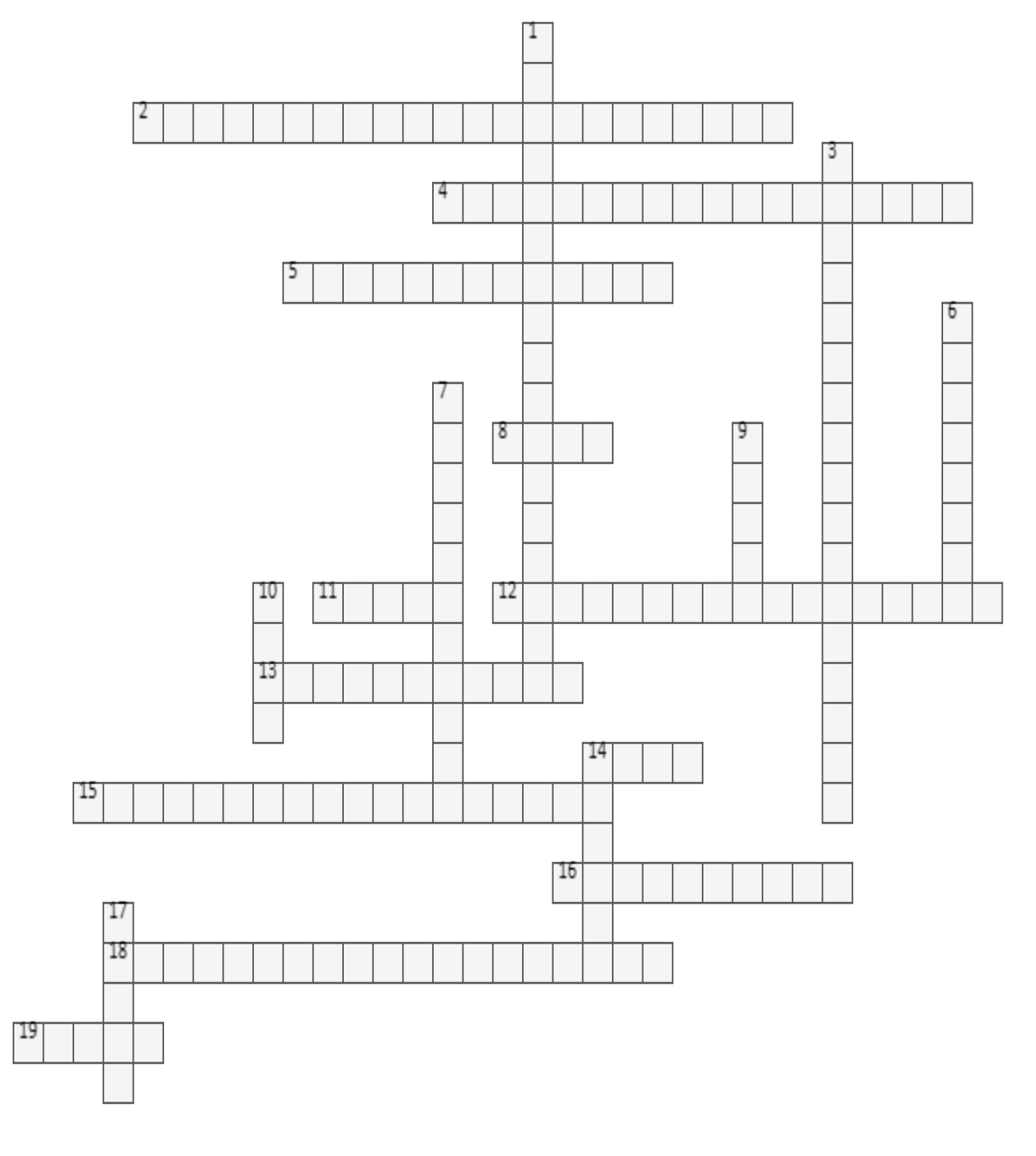
The correct answer to the PDF Photoquiz 4 were given by

Dr. Jeta Buch, Shardaben General Hospital, Ahmedabad, Gujarat

The Editorial board congratulates the winner. Free complimentary registration will be provided to the winners for the upcoming 'Pediatric Dermatology Updates 2025' conference, Mumbai. Further information will be emailed.

Crossword on Pediatric Psoriasiform dermatoses

Formulated by – Dr Jeta Buch



Across

2. Dysfunctional branched-chain amino acids metabolism yields a characteristic aromatic byproduct, masking severe neurologic sequelae. Though its name suggests a breakfast topping, its effects are far from a treat. Name the condition (5,5,5,7)
4. A secondary immunologic host response that occurs following a primary eczematous process (18)
5. A dermatologic condition, starting with digitate scaly patches >5cm, harboring the potential for a malignant transformation. What am I? (13)
8. Name the sign on ultrasound biomicroscopy which refers to the appearance of alternating echogenic layers in Bowen's disease (4)
11. A tropical treponematosis that mainly affects the skin, causing mottled pigmentation in later stages, historically found in Central and South America (5)
12. An 8 year old girl presented with mono-articular oligo-arthritis and conjunctivitis, 2-3 weeks after an episode of diarrhoea. Name the condition (8,9)
13. First and only FDA approved topical PDE-4 inhibitor for the treatment of plaque psoriasis. (11)
14. A new entity with clinical features that overlap between psoriasis and pityriasis rubra pilaris, has autosomal dominant inheritance and is resistant to conventional therapies. The name of the condition is an abbreviation derived from its genetic association. Identify the condition (4)
15. The physician and poet who gained fame from his work - " Syphilis sive morbus gallicus " (8,10)
16. Humanized monoclonal antibody targeting IL-36 receptor approved for the treatment of generalized pustular psoriasis (10)
18. The condition mimics lichen nitidus and keratosis pilaris, but is distinguished by perifollicular granulomas and a positive tuberculin test (6,13)
19. This psoriasiform eruption is a paraneoplastic phenomenon associated with upper aerodigestive tract malignancies. What is the eponymous name of this syndrome? (5)

Down

1. The histological pattern in psoriasis located within the parakeratotic areas of the cornified layer consisting of accumulation of neutrophils and pyknotic nuclei of neutrophils that have migrated from capillaries in the papillae through the supra-papillary epidermis (5,12)
3. Following the initiation of antibiotic treatment for Lyme disease, a patient develops fever, chills and muscle aches. Name the reaction (7,10)
6. Inflammation at the BCG inoculation site is the pathognomic feature of this disease. Name the disease (8)
7. A rare and severe form of secondary syphilis common in immunosuppressed particularly in HIV / AIDS. Name the condition (4,7)
9. Autosomal recessive condition where IL-36 fades, recurrent pustules rise, as family history cascades. What is the acronym for this condition? (5)
10. Gene-edited living drugs that target cancer cells for therapeutic purposes in precision medicine primarily refers to _____ cell therapy.(4)
14. Name the trace element which is deficient on long term high dose supplementation of zinc in acrodermatitis enteropathica (6)
17. A mosaic, inflammatory, pruritic, treatment resistant nevus characterized histologically by alternate orthokeratosis and parakeratosis. Mention the acronym for this condition (5)

Kindly mail your answers along with your affiliation to peddermfoundation@gmail.com before 30th June 2025. The winners of Crossword will be announced in the next issue.

Apremilast

Author: Dr Preeti Sheth

Introduction

Apremilast has been extensively utilized in managing various dermatological conditions. Due to its immunomodulatory properties, minimal immunosuppressive effects, and favourable side effect profile, it serves as a valuable addition to the dermatologist's therapeutic arsenal. Primarily approved for treating adult patients with psoriasis and psoriatic arthritis, its use in the paediatric population is not widely established. However, emerging studies have begun to explore its potential in children and adolescents.

Mechanism of Action

Apremilast is a selective inhibitor of the enzyme phosphodiesterase 4 (PDE4). It functions intracellularly by inhibiting the conversion of cyclic adenosine monophosphate (cAMP) to AMP, thereby increasing cAMP levels. This elevation leads to the suppression of pro-inflammatory markers such as TNF-α, IFN-γ, IL-12, IL-17, IL-22, and IL-23, while promoting anti-inflammatory markers like IL-6 and IL-10. Consequently, inflammation is reduced, leading to an improvement in clinical symptoms and signs.

Pharmacokinetics

Studies in adults indicate that apremilast has a bioavailability of 73% following oral administration of a 20 mg tablet, with 68% binding to human plasma proteins. The elimination half-life ranges from 6 to 9 hours. In cases of severe renal impairment, drug clearance is reduced by approximately 47%, necessitating a dose reduction. Food intake does not significantly affect absorption.

Indications

FDA-Approved Indications:

- Moderate to Severe Plaque Psoriasis: Approved for children aged 6 years and older, weighing over 20 kg.
- Behçet's Disease: Approved in adults for the treatment of oral ulcers associated with Behçet's disease. A phase 3 trial is ongoing for children aged 2 to 17 years, with results expected in 2028.

Off-Label Indications (Literature Limited to Case Reports in Children):

- Alopecia Areata
- Vitiligo
- Atopic Dermatitis
- Lichen Planus
- Hidradenitis Suppurativa (HS)

Dosing and Formulation

Optimal dosing regimens for pediatric patients have not been firmly established. Dosing is adjusted based on the patient's weight:

- 20 mg twice daily for patients weighing between 20–50 kg.
- 30 mg twice daily for those weighing over 50 kg, subject to drug tolerability.

Apremilast is available in oral tablet form in 10 mg, 20 mg, and 30 mg strengths. To minimize gastrointestinal adverse effects, it is advisable to initiate therapy with 10 mg once daily, increasing by 10 mg daily to reach the optimal dose of 30 mg twice daily by day 6. Titration can be adjusted on a case-by-case basis, with close monitoring during therapy initiation.

- The tablets can be taken with or without food but should not be crushed, chewed, or split to ensure proper absorption. This may pose a challenge for young children unable to swallow pills. Enteric-coated tablets are preferred to mitigate gastrointestinal side effects.

Side Effects

The safety profile of apremilast in pediatric patients appears consistent with that observed in adults. Common adverse effects include:

- Gastrointestinal symptoms (diarrhoea, nausea, vomiting)
- Headache
- Weight loss, which may be particularly concerning to parents
- Other potential side effects include upper respiratory tract infections, nasopharyngitis, upper abdominal pain, dyspepsia, decreased appetite, fatigue, insomnia, back pain, migraine, mood disorders, suicidal ideation, and arthralgia. No new safety concerns have been identified in the limited pediatric studies available.

Contraindications

- Apremilast is contraindicated in pregnant and lactating women.
- In patients with impaired renal function (creatinine clearance <30 mL/min), a modified dosing regimen is recommended: 10 mg once daily on days 1 to 3 followed by 20 mg once daily on days 4 and 5 & maintenance dose of 30 mg once daily in the morning thereafter
- Moderate to severe hepatic impairments do not necessitate dose adjustments.

Monitoring

- While apremilast does not require intensive laboratory monitoring compared to traditional immunosuppressants, baseline and periodic assessments are recommended to ensure safety, especially considering the unique physiological aspects of pediatric patients.
- Baseline documentation should include weight, height, and laboratory evaluations such as complete blood count, liver, and renal function tests.
- Ongoing monitoring should focus on weight, gastrointestinal symptoms, and mental health. Periodic laboratory assessments can be considered based on clinical judgment, particularly if the patient presents with symptoms.
- Dose reduction or treatment interruption may be necessary depending on the severity of adverse effects. In cases of gastrointestinal symptoms, a slower titration, or supportive treatments like antiemetics for vomiting or analgesics for headaches may help manage side effects and allow continuation of therapy. Weight loss up to 10% is acceptable; discontinuation should be considered if weight loss exceeds this threshold. Adolescents with psychiatric disturbances should be monitored closely, as apremilast may exacerbate depressive symptoms and suicidal ideation.

Vaccination

- Regarding vaccinations, no specific guidelines exist for apremilast use in pediatric patients. However, vaccination schedules remained uninterrupted in clinical trials, and as apremilast is an immunomodulatory (rather than immunosuppressive) agent, live vaccines may be administered during treatment.

Drug Interactions

- Apremilast interacts with potent CYP450 inducers such as rifampicin, phenytoin, and phenobarbital, which may reduce its efficacy. However, no clinically significant interactions have been reported with CYP450 inhibitors such as ketoconazole or methotrexate.

Current evidence available for use of Apremilast in the Paediatric psoriasis

- **Paller AS, Hong Y, Becker EM, et al. Pharmacokinetics and safety of apremilast in pediatric patients with moderate to severe plaque psoriasis: results from a phase 2 open-label study. J Am Acad Dermatol 2020; 82(2): 389-397.**
    - A phase 2, multicentre and open label study was conducted in pediatric patients with psoriasis. Apremilast was given to 42 patients, 21 children (age group 6-11 years) were given 20mg bd and 21 children (age bracket 11-17 years) were given 20mg or 30mg depending on their weight. Duration of the study was 2 weeks with 48 weeks extension. This study was conducted to assess primary endpoints of pharmacokinetics, safety and to determine doses for phase 3 study.
    - Conclusion of the study: Apremilast reaches maximum concentration in 2-3 hours after intake. Improvements in PASI score was seen as early as 2 weeks in 79% children and 68% adolescents. The medication was given according to their body weight but was not titrated; hence, gastrointestinal side

effects were observed. Children less than 20kg were not enrolled. Most of the children found the taste of the medicine to be acceptable.

- **Fiorillo L, Becker M, Lucas RD, et al. Efficacy and safety of apremilast in pediatric patients with moderate-to severe plaque psoriasis: 16-week results from SPROUT, a randomized controlled trial. J Am Acad Dermatol 2024; 90: 1232-9.**
    - A phase 3 multicentre, double blinded randomized study (SPROUT) was conducted in 221 patients to evaluate the efficacy and safety of apremilast in children. Apremilast was given to 149 children of which 13o were adolescents (72 were given placebo). Duration of study was 16 weeks with 52 weeks extension. Here dose was titrated slowly to reach the final dose of 20mg for children between 20-50kg and 30mg for children above 50kg.
    - Conclusion of the study: Apremilast was tolerated well. Gastrointestinal side effects were less than previous phase 2 study because of titration. More than 75% reduction in PASI score was achieved. However, children less than 20kg were not involved.
    - Based upon the findings of the above study, FDA approved apremilast in children between 6-17 years, weighing at least 20kg with moderate to severe plaque psoriasis and who are candidates for systemic therapy or phototherapy, not controlled by or intolerant to treatment.

Our experience with Apremilast

- *In our clinical practice, we have found apremilast to be a 'hit or miss' treatment for various conditions, including psoriasis. While it proves highly effective in some cases, it may show little to no response in others, with no reliable way to predict which patients will benefit.*
- *Notably, we have observed good results in palmoplantar, scalp, and nail psoriasis.*
- *In cases of psoriasis vulgaris, we have noticed a moderate response where the condition may not clear completely, it often becomes more manageable with the addition of topical treatments. However, it has a slow onset of action (4–6 weeks), requiring a minimum of 24 weeks for optimal results. Thus, systemic therapies can initially be employed to manage flares, with apremilast introduced later to maintain remission.*
- *We have also used it in severe cases of alopecia areata as a maintenance therapy after control of disease activity is achieved with immunosuppressive drugs such as cyclosporine or tofacitinib.*
- *The most common side effects we have observed were gastrointestinal. Other occasional side effects we have observed include headaches and weight loss, the latter being of particular concern for parents and requiring careful monitoring.*

When treating paediatric skin conditions, two key concerns often arise: safety and the need for frequent blood tests, which can be undesirable in children. Apremilast stands out in this regard—it has a well-established safety profile and does not require routine blood monitoring. It can also be safely combined with other immunosuppressives to have an additive benefit and sparing effect in the maintenance therapies. Given these advantages, we believe it is worth considering as a treatment option in appropriately selected cases.

Cracking the Classification of Palmoplantar Keratoderma (PPK) with Easy Mnemonics

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Palmoplantar Keratoderma (PPK) is a commonly tested topic in postgraduate dermatology exams. However, remembering the extensive classification can be quite a challenge! Here, we present a fun and easy way to retain the various types of PPK using mnemonics.

Definition

PPK refers to a group of disorders characterized by abnormal thickening of the skin on the palms and soles, which can be either inherited or acquired.

Classification of PPK

Broadly classified into:

1. **Inherited PPK**
2. **Acquired PPK**

Inherited PPK (Mnemonic - PDF)

- **P**unctate
- **D**iffuse
- **F**ocal

Diffuse PPK (Subdivided into Transgradient and Non-Transgradient types)

Non-Transgradient PPK (Mnemonic - VOH NA UTRA "He did not come down")

- **V**oner
- **N**axos
- **U**nna-Thost

Transgradient PPK (Mnemonic - Camisa Nagashima, went to Clouston Hurriedly to meet Papillon Bu(r)t was instead Greeted with a wink by Meleda)

- **Camisa**
- **Nagashima**
- **Clouston**
- **Huriez**
- **Papillon-Lefevre**
- **Bart-Pumphrey**
- **Greither**
- **Vohwinkel**
- **Mal de Meleda**

Focal PPK

- **With systemic associations (Mnemonic - Rich PC Has Car)**
    - **R**ichner-Hanhart
    - **P**achyonychia congenita
    - **H**owel-Evans
    - **C**arvajal syndrome

- **Without systemic associations**
    - Focal epidermolytic PPK
    - Striate PPK

Punctate PPK

- **Without systemic associations**
    - Punctate keratoderma of palms and soles
    - Punctate keratoderma of palmar creases
    - Marginal punctate keratoderma
- **With systemic associations (Mnemonic - LASS)**
    - **L**ipomata
    - **A**nkylosing Spondylitis
    - **S**ebaceous hyperplasia
    - **S**pastic paralysis
    - **S**chopf-Schulz-Passarge syndrome

Acquired PPK (Mnemonic - KERATOTIC PALMS)

K **Keratoderma climactericum**

E **Endocrine disorders (Hypothyroidism, Diabetes)**

R **Reactive arthritis**

A **Arsenic poisoning**

T **Tylosis**

O **Occupational PPK**

T **Tinea manuum/pedis**

I **Internal malignancy (Paraneoplastic)**

C **Chronic inflammatory conditions (Psoriasis, Lichen Planus, Eczema)**

P **Pityriasis rubra pilaris**

A **Acrokeratosis paraneoplastica (Bazex syndrome)**

L **Leprosy, Lymphoma, Leukemia**

M **Medication-induced PPK (lithium, fluorouracil, BRAF inhibitors**

S **Scabies, Scleroderma, Systemic connective tissue disorders**

Visual Aids for Quick Recall

Flowchart: Classification of PPK

PPK
├── Inherited (PDF)
│ ├── Diffuse
│ │ ├── Non-Transgradient (VOH NA UTRA)
│ │ ├── Transgradient (Camisa...Meleda)
│ ├── Focal
│ │ ├── With systemic (RICH PC HAS CAR)
│ │ ├── Without systemic (Epidermolytic, Striate)
│ ├── Punctate
│ │ ├── Without systemic
│ │ ├── With systemic (LASS)
└── Acquired (KERATOTIC PALMS)

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