

# Pederm Insights



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## Editor's Prologue

*Dear Colleagues,*

*Season's greetings and a very Happy New Year to all!*

*As we step into a new year, I want to take a moment to appreciate the stellar work of Dr. Sahana Srinivas and the entire editorial team for curating such informative and well-received issues over the past year. Taking the helm from someone so capable is both a privilege and a responsibility, and hope to do it to the best of my capacity.*

*I am delighted that we have continued with the format of a newsletter—designed as a source of concise, up-to-date information delivered in a format that is engaging yet not overwhelming. Our aim is to create a companion that stimulates the mind over a cup of coffee, teases it with challenges like the photo quiz, and enriches it with sections on therapeutics and clinical case vignettes.*

*In this issue, the Journal Review section focuses on the treatment of pediatric vitiligo, presenting key advances from the most recent articles on the topic. A focused review of key topics in vitiligo treatment has been conducted, incorporating expert consensus on topical therapies, non-surgical combination treatments, narrowband UVB phototherapy, 308-nm excimer laser therapy, and the role of JAK inhibitors.*

*This is followed by a highly relevant Clinical Vignette in the context of the current surge in dengue and chikungunya cases. For those who enjoy a challenge, we have an exciting Photo Quiz, along with a detailed discussion of the previous quiz's answer. The Therapeutics section offers practical tips to simplify the use of cyclosporine, an indispensable drug in pediatric dermatology. And finally, we wrap up this issue with a creative touch in Resident's corner—a beautiful poem on syndromes.*

*I extend my heartfelt gratitude to all our contributors and the editorial team for their hard work in bringing out this issue on time.*

*I hope you enjoy reading this edition as much as we enjoyed putting it together.*

*Warm regards,*

*Resham Vasani*

*Editor-in-Chief*

**Renert-Yuval Y, Ezzedine K, Grimes P, Rosmarin D, Eichenfield LF, Castelo-Soccio L, et al. Expert Recommendations on Use of Topical Therapeutics for Vitiligo in Pediatric, Adolescent, and Young Adult Patients. JAMA Dermatol. 2024;160:453-61.**

This is an evidence- and consensus-based expert recommendation document on the diagnosis and treatment of vitiligo in children, adolescents, and young adults. The grading was done using the Strength of Recommendation Taxonomy (SORT) and Oxford Centre for Evidence-based Medicine's Levels of Evidence and Grades of Recommendation.

The expert consensus for diagnosis of vitiligo included Woods lamp examination demonstrating enhancement as the first step to confirm the clinical diagnosis. Biopsy needs to be done only in doubtful cases where the Woods lamp enhancement is negative.

The expert consensus on high-risk features requiring close observation for progression and aggressive therapy include - involvement of more than 5 body sites, leucotrichia, halo nevi, trichrome vitiligo, confetti depigmentation, Koebner phenomenon, non-hair-bearing anatomical site, and young age with diffuse nonsegmental disease.

The general recommendations for management of vitiligo based on expert consensus were - topical corticosteroids (TCS), topical calcineurin inhibitors (TCI) and UV-B light therapy (phototherapy or excimer laser). The use of topical JAK inhibitors for nonsegmental vitiligo appears promising. Combination of phototherapy with TCS or TCI enhances the repigmentation response. Nevertheless, counseling for risk of carcinogenesis and long-term monitoring for skin cancers is required in such cases. For children, an outdoor sunlight exposure of 10-15 minutes would suffice in enhancing response to topical therapy.

The TCIs, tacrolimus and pimecrolimus, twice daily application for a minimum of three months are recommended as first-line therapy for vitiligo in children (> 2 years), adolescents, and young adults. If evidence of repigmentation is observed, it is recommended to continue for 6-12 months while in the absence of repigmentation by 3 months, it is recommended to switch to alternate agents. Risk of burning, stinging, itching in the first month needs to be explained. TCIs for vitiligo in children less than 2 years has limited evidence. TCIs are more effective in darker skin types, most effective in head and neck, intermediate response in trunk and extremities, and limited response in hands and feet. Biweekly maintenance therapy in areas at risk of

relapse. Despite the lack of evidence to suggest increase in lymphoma and skin cancer with TCI therapy, counseling on this regard has been recommended.

TCSs may be considered as first-line therapy with daily class 2 TCS for short-term continuous use or intermittent class 1 TCS. The best response with TCS is seen on face followed by trunk, arms and legs, and hands and feet. To prevent atrophy, short term usage of TCS or overlap with TCI has been recommended along with counselling and monitoring for atrophy. Addition of calcipotriene to TCS for increased efficacy has only limited evidence. Expert consensus on choice of steroids recommends the choice based on site and duration of treatment. TCS are used as a second line treatment for areas with thin skin (face, groin, intertriginous) and on eyelids for risk of atrophy and glaucoma.

Topical JAK inhibitor (tJAKi) ruxolitinib (1.5%) cream twice daily application limited to 10% BSA involvement for children  $\geq 12$  years has demonstrated promising response in childhood vitiligo. Hence tJAKi can be considered as first-line or second-line therapy for vitiligo in children  $\geq 12$  years of age especially in areas with risk of atrophy including face, eyelids, and groin ; and at younger ages there is limited evidence. Onset of repigmentation might take 3 months and maximal repigmentation might take more than a year. Based on data from adult studies, combination with phototherapy might be synergistic. Expert consensus recommends counseling patients regarding adverse events associated with systemic absorption of JAK inhibitors like acne and application site reactions.

Other therapies like topical pseudocatalase and microdermabrasion as adjunctive to enhance absorption of topical drugs have insufficient evidence to be recommended in children.

To summarize, for segmental vitiligo in children, the first line therapy is TCI or TCS and phototherapy; and for nonsegmental vitiligo in children  $\leq 12$  years, TCI or TCS are the first line agents while for those  $\geq 12$  years with < 10% BSA involvement, topical JAK inhibitors are the first line agents. For those  $\geq 12$  years with >10% BSA a combination of tJAKi, TCI, TCS can be given and for those with BSA>10%, more than 5 sites, or high-risk features, adjunctive phototherapy or systemic agents can be recommended. If no response to first line therapies, second line therapies include other sources of UVB therapy and systemic agents.

### Topical JAK inhibitors in childhood vitiligo: (Comments)

Apart from well-known and well-established therapies for management of childhood vitiligo that includes TCS and TCI, tJAKi are the newer kids in the block that have a potential to change the landscape of vitiligo management and have found a place as first or second line agents in the recommendations for management of vitiligo in the pediatric population.

The tJAKi studied in vitiligo include ruxolitinib (1.5%) cream, tofacitinib (2%) ointment, delgocitinib (0.5%) ointment, cerdulinib (0.37%) gel, and ifidancitinib (0.46%) solution. Of these, ruxolitinib (1.5%) cream is the first and only FDA approved agent (2022) approved for treatment of nonsegmental vitiligo in adult and pediatric patients  $\geq 12$  years of age with 10% BSA involvement. Apart from this, tofacitinib (2%) ointment has been reported to be used in pediatric vitiligo in few case reports and case series. Rest of the agents are under trial in adults. Combining tJAKi with NB-UVB or sun exposure was found to be beneficial for melanocyte stimulation.

Ruxolitinib 1.5% cream when applied twice daily, demonstrated onset of response (repigmentation) within four weeks which were more pronounced in facial lesions and demonstrated significant repigmentation by 32 weeks. Combination of ruxolitinib (1.5%) twice daily along with NB-UVB was found to have increased efficacy. Topical Ruxolitinib has been reported to have a steady-state epidermal concentration nearly 2000-fold higher than that of oral Ruxolitinib while the plasma concentration achieved with topical therapy was only one-thirtieth of oral therapy indicating that topical ruxolitinib effectively reaches skin, without affecting other organ systems. Adverse events reported include acne and itching at the application site, and

nasopharyngitis. Further clinical trials are required to understand its efficacy and safety in children  $< 12$  years of age and those with  $> 10\%$  BSA involvement.

Topical tofacitinib (2%) ointment has been tried in children and adolescents for bilateral upper eyelid vitiligo associated with eyelash leukotrichia, refractory acrofacial vitiligo, and chin and neck lesions with good results. Topical tofacitinib has also been used in combination with TCI or TCS for refractory vitiligo, which showed better improvement in face. Topical tofacitinib was found to have enhanced efficacy only in combination with NB-UVB (thrice a week) for 8 – 16 weeks in many cases. Younger age, darker skin type, and focal disease were favorable prognostic indicators of response to combination therapy. Future RCTs need to be undertaken to establish the efficacy of topical tofacitinib monotherapy or combination therapy with phototherapy in pediatric vitiligo along with drug penetration studies.

#### References:

1. Inoue S, Suzuki T, Sano S, Katayama I. JAK inhibitors for the treatment of vitiligo. *J Dermatol Sci.* 2024;113:86-92.
2. Qi F, Liu F, Gao L. Janus Kinase Inhibitors in the Treatment of Vitiligo: A Review. *Front Immunol.* 2021;12:790125.
3. Utama A, Wijesinghe R, Thng S. Janus kinase inhibitors and the changing landscape of vitiligo management: a scoping review. *Int J Dermatol.* 2024;63:1020-35.

**(Submitted by Malathi Munisamy)**

**Metko D, Mehta S, Lam J. Pediatric Vitiligo Treatment with JAK Inhibitors: A Scoping Review. Journal of Cutaneous Medicine and Surgery. 2024;0(0).**

Half of the reported cases of vitiligo have their onset in the first 2 decades of life. JAK inhibitors, both oral and topical, have been used in adults. However, there is a definite need to evaluate their efficacy and safety in the pediatric age group.

Metko D et al, conducted a scoping review on the current literature backing the use of JAK inhibitors in the treatment of vitiligo in children above and below the age of 12 years. The search was done on MEDLINE and Embase with the search terms vitiligo and JAK inhibitors as per PRISMA ScR guidelines. The study cohort included 22 patients.

Eleven children were less than 12 years whereas 10 children were above the age of 12 years. Mean age was 12.4 years. Boys made up 71.4% of the study population. Non-segmental vitiligo comprised 66.7% cases, 27.7 % had segmental vitiligo and 5.56% had a mixed type. Before the use of JAK inhibitors, topical calcineurin inhibitors, corticosteroids, phototherapy were used in equal measure, particularly in children above 12 years. Only one child less than 12 years had used topical corticosteroids.

In this study, majority of the patients used topical ruxolitinib (59.1%), followed by both oral and topical tofacitinib (27.3%), oral upadacitinib (9.09%) and oral baricitinib (4.54%). Topical therapy was favored by a majority 81.8%, whereas oral JAK inhibitors were given to 18.9% of the patients. All children of less than 12 years were on topical route of therapy. Above 12 years, 7 were on topical therapy and 4 were given oral JAKi.

Concomitant vitiligo therapy was ongoing for all children above 12 years and only one child of less than 12 years (who took UVB). Phototherapy was the most widely used auxiliary therapy (60%); topical calcineurin inhibitors and topical corticosteroids were used concomitantly in 10% of the patients each.

Results with topical JAK inhibitors were as follows: full repigmentation was achieved in 40.9% of patients (7 children less than 12 years and 2 above 12 years); near complete repigmentation achieved in 9.09% of patients (2 children above 12 years); partial repigmentation in 45.5% (3 children each in both age categories) no repigmentation in 9.1% (1 child of less than 12 years). However, only 18.2% reported partial repigmentation while on oral JAK inhibitor.

Comments:

The treatment targets of vitiligo are first to stabilize the condition, cause repigmentation and thereafter to maintain the repigmentation. The use of JAK inhibitors in vitiligo under the age of 12 years is not yet FDA approved (although they are recommended as first and second line of therapy

vitiligo in patients above 12 years).

In this study we can observe that full repigmentation was seen in 7 children less than 12 years, who were all on topical medications, with no concomitant therapy except for only one child who took phototherapy alongside. Partial repigmentation was observed in all the four kids who were taking JAK systemically. Near complete pigmentation was seen in 2 kids taking JAK orally. This study indicates similar repigmentation outcomes when JAKi s were used above and below 12 years of age and hence supports the off label use in the absence of discernable safety concerns or contraindications. Limitation of this study include a small sample size and unclear risk of bias of the included literature. Large scale studies are needed to confirm the purported safety and efficacy of the offlabel use of JAKi in the age below 12 years, though topical use seems safe and efficacious especially with the use of concomitant phototherapy.

**(Submitted by Preeti Sheth)**

**Editor's Note :**

The two articles above discuss the use of topical Janus kinase inhibitors (JAK inhibitors) in the treatment of vitiligo. Among the available options, topical tofacitinib is currently the only JAK inhibitor accessible in India and is becoming increasingly affordable. However, it is important to note that its use in vitiligo is currently off-label.

When comparing topical ruxolitinib (FDA-approved) and topical tofacitinib (not FDA-approved for vitiligo), key differences lie in their mechanisms of action and the evidence supporting their use. Topical ruxolitinib is a JAK1/JAK2 inhibitor, whereas tofacitinib primarily inhibits JAK1/JAK3 with some activity on JAK2. Similar to ruxolitinib, tofacitinib blocks cytokines in the IFN $\gamma$  pathway but exerts broader effects due to its additional inhibition of JAK3, which impacts T-cell signaling and adaptive immunity. This broader inhibition may theoretically lead to higher systemic absorption, potentially increasing the risk of side effects.

The current evidence regarding the safety and efficacy of topical tofacitinib in vitiligo is limited to small studies and case reports. As such, its use should be approached with caution and judicious clinical decision-making. Nevertheless, tofacitinib represents a promising addition to the therapeutic options available for vitiligo. It has a distinct advantage in situations where we would want to avoid the use of long term topical corticosteroids and the consequent side effects and in addition it avoids the stinging sensation associated with TCIs.



**Yuan-Yuan Liu, Jun-Feng Zhou, Yu Zhen, Yan Cui, Yang Song, Lei Yao and Shan-Shan Li. Clinical efficacy analysis of 110 cases of childhood vitiligo with non-surgical combined therapy. J Dermatolog Treat. 2022 Nov;33(7):3034-3038**

This article on childhood vitiligo evaluated the clinical efficacy of long term, non-surgical, combination modalities of treatment and looked at various factors that may affect the treatment efficacy. The current study was done in a retrospective manner which included 110 children of <12 years of age, with a clinical diagnosis of vitiligo who were treated with various combination modalities for >12 months. The various treatment options included topical corticosteroids (TCS, desonide 0.05% cream in <2 years and mometasone furoate 0.1% cream in older children), topical calcineurin inhibitors (TCI, Tacrolimus 0.03% ointment or pimecrolimus 1% cream), systemic corticosteroids (SC, oral prednisolone @0.3 mg/kg daily or prednisolone @1 mg/kg body weight twice weekly on 2 consecutive days until the disease was stable) and narrowband UVB phototherapy (NBUVB) with combinations tailored to individual patient's disease condition. In progressive vitiligo, TCI/TCS along with NBUVB was given with a short course of SC added in rapidly progressive disease. In stable disease or in maintenance phase, TCI twice weekly with NBUVB or NBUVB alone (in <2 years) was used. Repigmentation of depigmentation areas and adverse effects were noted at monthly intervals and photographic evidence documented every 3 months. Statistical analysis was carried out using chi-square test and Fisher's exact probability test.

Out of 110 children with vitiligo, 51 (46.4%) were boys and 59 (53.6%) were girls, with a male-to-female ratio of 1:1.16. The age range was 1.5-12 years with a mean age of  $7.1 \pm 3.0$  years. The median duration of the disease was 5 months. Non segmental vitiligo (NSV) was the most common type followed by segmental vitiligo (SV), undetermined vitiligo (UDV) and mixed type. All 110 patients underwent continuous medical treatment ranging from 5 to 86 months (mean- 23.13 ), of which >50%, and >90% repigmentation rates were seen in 64.5% (71/110), and 15.5% (17/110), respectively. The repigmentation rates after treatment for 3, 6, 9, and 12 months were assessed in all the patients and they concluded that longer duration of treatment was significantly associated with a higher repigmentation rates.

They also looked at the correlation between the VIDA score and the treatment efficacy and found that a higher initial VIDA score was associated with a higher overall repigmentation rate, which indicated that the rapid progressive stage of vitiligo was an excellent time for intervention. However, there was no significant correlation between the duration of disease and the overall repigmentation effect. The present study also showed no

significant difference among SV, NSV, and UDV in patients with respect to > 50% and >90% therapeutic response. However, there was a significantly better >25% response in SV group when compared to other groups indicating that SV is not more difficult to treat medically before it turns stable.

The total relapse rate in this study was 30.9% (34/110) with UDV group showing the highest rate of 42.1% (8/19). SV and NSV showed a relapse rate of 18.8% and 33.3% respectively. Adverse effects were seen in 32 patients during therapy with itching seen in 6 patients with TCI, telangiectasias in 5 patients with TC, weight gain in 3 patients on SC, erythema in 11 patients and blisters in 7 patients on NBUVB. No patients with Cushings or adrenal suppression were reported with either TCS or SC.

#### Comments

Childhood vitiligo, as we all know has a lot of negative impact on the mental health of the affected children and parents alike. The therapeutic armamentarium includes topicals medications, systemic immunosuppressants, phototherapy and surgical modalities. However, treatment of childhood vitiligo is still challenging as there is no single effective treatment modality.

The authors of this study concluded that rapid progressive stage of vitiligo is the optimal time to intervene with non-surgical combined treatment options. A longer duration of the treatment (atleast 12 months in childhood vitiligo) is advocated for better repigmentation response. They also found that SC although effective in stabilising the disease activity, did not significantly affect the repigmentation. Rath et al also showed that SCs alone produced lower repigmentation effects than SCs combined with NB-UVB therapy.<sup>1</sup> Therefore it is important to note that, although SCs are better in stabilizing the disease activity, it is always better to combine with phototherapy for effective repigmentation. Additionally, SV also responds significantly to medical treatment in the initial progressive phase. It is of interest to note that even SV can relapse after stabilising with treatment as seen by the relapse rate of 18.8% in the present study.

Further prospective long term comparative studies between various treatment modalities in childhood vitiligo is the need of the hour to decide effectively on the right and safe treatment choices.

1. Rath N, Kar HK, Sabhnani S. An open labeled, comparative clinical study on efficacy and tolerability of oral minipulse of steroid (OMP) alone, OMP with PUVA and broad/narrow band UVB phototherapy in progressive vitiligo. Indian J Dermatol Venereol Leprol. 2008;74(4):357–360.

**(Submitted by Sirisha Varala)**

**Garza-Mayers AC, Paquette GM, Harris JE, Wiss K. Narrowband ultraviolet B phototherapy in pediatric vitiligo: A retrospective study. J Am Acad Dermatol. 2023;89:135-6.**

Narrowband UV-B phototherapy (nbUV-B) is considered a first-line treatment in the management of vitiligo while there exist concerns regarding safety and practicality regarding its use in childhood vitiligo despite proving to be efficacious. This retrospective study (2009-2020) was undertaken to assess the prevalence, efficacy, and safety of nbUV-B, in pediatric patients with vitiligo. A total of 324 patients were included out of which 126 patients (38.9%) received phototherapy. Home based nbUV-B therapy was received by 46% patients. The median age at first visit was 8.7 years and the median follow-up was 20 months. There was no gender predilection and the youngest patient that received phototherapy was 3 years old.

The odds of improvement or resolution of vitiligo was 6.3 times higher in those who received nbUV-B versus those who did not with nonsegmental vitiligo, fewer signs of active disease, involvement of the face, head, neck, and extremities, and more areas of involvement being favorable prognostic factors.

Side effects like sunburns were observed in 29% of patients out of which 7.9% were those who used home based units and blistering was observed in 3.5% of patients while none of them developed scarring or skin cancer. One fourth (24.6%) of children discontinued therapy predominantly due to visit inconvenience, COVID-19 pandemic, or satisfaction or dissatisfaction with response to treatment and only one patient discontinued due to adverse effects like pruritus. Few who experienced erythema and blistering resumed treatment with counseling. Patients receiving home-based phototherapy experienced less side effects deeming it to be safer.

Based on the observations, it was concluded that nbUV-B is a well-tolerated and effective therapeutic option in the management of pediatric vitiligo supporting consensus guidelines.

#### **Narrowband UV-B phototherapy in childhood vitiligo: (Comments)**

Despite phototherapy being one of the most preferred treatment modalities for vitiligo owing to its safety and efficacy, literature on its efficacy in childhood vitiligo is limited probably owing to long-term effects of major concern like premature aging of the skin and increased risk of carcinogenesis. The role of nbUV-B in childhood vitiligo was first evaluated in 2000 by Nijoo but since then few studies have only been undertaken. With a promising role of combination therapy of nbUV-B with the existing (TCI, TCS) and newer topical therapies for childhood vitiligo (tJAKi), more studies exploring the beneficial role of nbUV-B are being undertaken.

In an open, uncontrolled study by Percivalle et al on 28 children with vitiligo receiving nbUV-B, twice a week for a mean (SD) duration of 10 (3.4) months, 14% had excellent

response, 28.6% had good response, 25% had moderate response, 28.6% had mild response and only 3.5% had no response. Except for a mild erythema requiring a dosage reduction, no side effects were reported.

Sen et al in their retrospective study on narrow-band ultraviolet B phototherapy in childhood in 77 children had received phototherapy and vitiligo was the most common indication (n=36). Median age of the patients with vitiligo was 12.5 years (range 6–16 years). Complete response was seen 16.7%; good response in 27.8%; partial response in 27.8%; poor response in 13.9%; and no response in 13.9%. nbUV-B phototherapy was found to be well tolerated with only minimal side effects like erythema, pruritus, etc. Thus nbUV-B can be considered a good alternative instead of systemic therapies associated with serious adverse effects.

Repigmentation of vitiligo requires an immunomodulator to halt the disease process (TCS, TCI, tJAKi) and requires phototherapy to stimulate the proliferation and migration of melanoblasts. These two combined modalities have synergistic action with their combination having higher efficacy.

In an open-label study by Dayal et al in 20 children, to study the efficacy of the synergistic combination of nbUV-B phototherapy with topical tacrolimus, it was observed that combination therapy resulted in higher proportion of those receiving combination therapy to have more than 50% repigmentation with few adverse events proving combination therapy to be a highly effective and promising therapeutic option for vitiligo in children.

Similarly, combining tJAKi with phototherapy or 308nm excimer LASER was found to increase the pigmentation in childhood vitiligo than when used alone but most available data are from adults and only few case series or case reports exist with regards to childhood vitiligo. Vehicle-controlled clinical trials of tJAKi with and without narrowband ultraviolet B light sources for segmental and non-segmental vitiligo for children aged < 12 years is required.

Thus, phototherapy needs to be considered a safe and effective first line option especially as combination therapy with topical agents for the management of childhood vitiligo.

#### **References:**

1. Percivalle S, Piccinno R, Caccialanza M, Forti S. Narrowband ultraviolet B phototherapy in childhood vitiligo: evaluation of results in 28 patients. *Pediatr Dermatol.* 2012;29:160-5.
2. Sen BB, Rifaioğlu EN, Ekiz O, Sen T, Celik E, Dogramaci AC. Narrow-band ultraviolet B phototherapy in childhood. *Cutan Ocul Toxicol.* 2014;33:189-91.
3. Dayal S, Sahu P, Gupta N. Treatment of Childhood Vitiligo Using Tacrolimus Ointment with Narrowband Ultraviolet B Phototherapy. *Pediatr Dermatol.* 2016;33:646-51.
4. Meister HM, Lebwohl M, Silverberg N. Case series of topical 1.5% ruxolitinib cream for pediatric vitiligo. *JAAD Case Rep.* 2024;54:27-30.

**(Submitted by Malathi Munisamy)**

**Sethi S, Silverberg N. Short and Long-Term Outcomes of 308-nm Laser for Pediatric Vitiligo. J Drugs Dermatol. 2022 Jul 1;21(7):773-775.**

The long-term outcome of therapeutics used to treat pediatric vitiligo has been poorly documented in the literature. It is, therefore, hard to counsel patients on the expected long-term results of therapy. We sought to address outcomes in pediatric vitiligo treated with a 308-nm laser. An IRB-exempt chart review was conducted in June of 2016 of children undergoing active 308-nm laser in the first half of 2016. Demographic data, location of disease, therapeutic parameters of the 308-nm laser, and outcomes were recorded at that time. In 2021, the long-term outcomes were analysed through chart review addressing pigmentation retained at later office visits. Initial repigmentation was noted in 86.7% of the face, 80% of the body, and 61.7% of the extremities. An average of 3.38 years of follow-up was recorded. Scoring extent of vitiligo using 18 site-scoring was helpful in identifying individuals who are less likely to respond to 308-nm laser, but needs broader evaluation. During that time, repigmentation was noted to be retained in 80% of facial, 40% of the body, and 20% of extremity lesions. Pediatric vitiligo responds well to the 308-nm laser, with the best retention of repigmentation for facial lesions. Patients and parents should be counselled on the likelihood of long-term retention of repigmentation and regarding the need for the ongoing management of vitiligo even after repigmentation is initially achieved after 308-nm laser therapy.

**Comments**

Excimer laser has emerged as an effective and non-invasive option for treating vitiligo. Unlike conventional UVB phototherapy, which involves broad-spectrum exposure, excimer laser treatment delivers targeted UVB radiation (308nm) to smaller, localized areas including difficult to access places like post auricular regions and the genitals. It is indicated for depigmented body surface areas (BSA) <10% and has the advantage of not affecting the surrounding skin.<sup>1</sup>

Current literature have shown superior repigmentation for combination therapy of excimer laser with calcineurin inhibitors (as described in this study) in localized, non-segmental and segmental vitiligo. However, insufficient evidence was found for combination therapy with topical vitamin D3 analogues and corticosteroids.<sup>2</sup>

There is insufficient evidence about the optimal regimen of excimer therapy. A minimum of 20 treatments is usually recommended, with a frequency of 2-3 sessions per week. Repigmentation is faster with three sessions per week, but the final response depends on the total number of sessions and not the frequency. Dosing usually starts at 100 mJ/cm<sup>2</sup>. and is gradually increased weekly by 10%–25%.<sup>3</sup> The average dose of laser energy used in this study was lesser for the face

(332.9mJ/cm<sup>2</sup>) and body (496mJ/cm<sup>2</sup>) than that used for extremity lesions (955mJ/cm<sup>2</sup>). The degree of repigmentation depends upon the sites treated, with face, trunk, arms, and legs being high response-sites; and elbow, wrists, knees, ankles, and dorsum of hands/feet being low response-sites (>75% repigmentation rates being 25% and 2% in two groups, respectively, at 10 weeks)<sup>4</sup>. Initial repigmentation can be seen in the first few treatment sessions itself with facial lesions showing signs of repigmentation even in the first couple sessions.<sup>5</sup>

Segmental vitiligo is usually refractory to treatment and surgical intervention is the preferred intervention modality. There are variable reports regarding the superiority of excimer laser for segmental vitiligo. Literature search has demonstrated excimer laser therapy to be effective in treating segmental vitiligo in combination with a topical steroid or topical calcineurin inhibitor. Facial lesions respond better.<sup>6</sup> In this study, the authors reported complete repigmentation of facial segmental lesions in 2 patients, except for the eyebrows, which remained white.

Longer disease duration, presence of poliosis, lesions on hands and feet and a plurisegmental pattern are poor prognostic indicators of excimer response. Facial lesions and younger patients have better and faster outcomes. The authors have used the 18 score number of lesion sites (by adding the number of body sites with a maximum of 18 sites) as a prognostic indicator. Children with >5 lesion sites had a lower response to 308-nm laser therapy while those with 1–5 locations involved tended to have better response to 308-nm laser and better long-term retention of repigmentation. It can be calculated easily but the clinical usage and eligibility of this criteria as a prognostic indicator of disease severity has to be validated by further research.

The long-term outcome of excimer laser in treating pediatric vitiligo has been poorly documented in the literature. In this study, the authors analysed the long-term outcomes through chart review addressing pigmentation retained at later office visits. An average of 3.38 years of follow-up was recorded. During that time, repigmentation was noted to be retained in 80% of facial, 40% of the body, and 20% of extremity lesions.

In general excimer phototherapy is well tolerated by patients with fewer (most common being erythema and blistering) to no side effects. Excimer laser usually requires a smaller number of treatment sessions and thus a smaller amount of cumulative UVB exposure, potentially reducing the patient's risk of developing major long-term side effects like carcinoma.

Larger, high-quality, multicenter RCTs are required to validate the long term effects of excimer therapy in treating childhood vitiligo.

## REFERENCES

1. Rodrigues M, Ezzedine K, Hamzavi I et al. Vitiligo Working Group. Current and emerging treatments for vitiligo. *J Am Acad Dermatol* 2017; 77: 17–29.)
2. Post, N., Ezekwe, N., Narayan, V., Bekkenk, M., Geel, N. V., Hamzavi, I., Passeron, T., & Wolkerstorfer, A. (2022). The use of lasers in vitiligo, an overview. *Journal of the European Academy of Dermatology and Venereology*, 36(6), 779.
3. Seneschal, J., Speeckaert, R., Taïeb, A., Wolkerstorfer, A., Passeron, T., Pandya, A. G., Lim, H. W., Ezzedine, K., Zhou, Y., Xiang, F., Thng, S., Tanemura, A., Suzuki, T., Rosmarin, D., Rodrigues, M., Raboobee, N., Pliszewski, G., Parsad, D., Oiso, N., Picardo, M. (2023). Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the international Vitiligo Task Force—Part 2: Specific treatment recommendations. *Journal of the European Academy of Dermatology and Venereology*, 37(11), 2185–2195
4. Bishnoi, A., & Parsad, D. (2024). Phototherapy for vitiligo: A narrative review on the clinical and molecular aspects, and recent literature. *Photodermatology, Photoimmunology & Photomedicine*, 40(3), e12968.
5. G. Leone, P. Iacovelli, A. Paro Vidolin, M. Picardo. Monochromatic excimer light 308 nm in the treatment of vitiligo: a pilot study. *J Eur Acad Dermatol Venereol*, 17 (2003), pp. 531-537
6. Shah, S., Sakhiya, J., Deshpande, P., Sakhiya, D., & Inamadar, A. C. (2020). Safety and Efficacy of the Combination of 308-nm Monochromatic Excimer Light and Topical 0.1% Tacrolimus Ointment in Segmental Vitiligo: An Open-label Study. *The Journal of Clinical and Aesthetic Dermatology*, 13(2), E69.

**(Submitted by – Rashmi Agarwal )**

## Editor's Note :

The findings of three studies discussed above hold significant practical value for counseling parents of children with pediatric vitiligo. The initiation of systemic immunosuppressants for vitiligo should be a shared decision between the healthcare provider and the parents, following a thorough discussion of the potential benefits and risks. It is crucial to set realistic treatment expectations before beginning therapy, emphasizing that systemic immunosuppressants aim to stabilize disease activity rather than guarantee complete repigmentation. Parents should also be made aware of the potential for disease relapse and the need for prolonged treatment in cases of unstable vitiligo.

Furthermore, the study underscores the importance of incorporating phototherapy into the treatment plan to enhance the likelihood of repigmentation. For pediatric patients, phototherapy should be prioritized as the first-line treatment to stabilize the disease, promote repigmentation, and sustain the achieved results. This approach may be complemented by topical therapies as needed to manage unstable vitiligo vulgaris effectively. In cases where phototherapy is inaccessible, home based phototherapy should be explored as an option. Excimer laser should be considered in the treatment of limited, difficult to access body areas in conjunction with topical treatment.



### Neonatal Chik sign with Maternal Dengue

Author - Shibhani S. Hegde

#### Introduction:

Chik sign is a very well-known and documented entity seen in chikungunya.<sup>1</sup> Similar pigmentation has also been reported with Dengue.<sup>2</sup> We report a case of facial pigmentation in a neonate born to a mother with documented dengue and discuss the intricacies in reaching the correct diagnosis.

#### Case Report:

Eleven-day-old neonate born at-term through normal vaginal delivery was referred to the department of dermatology with pigmentation over the face and scrotal erosions. The cutaneous presentation was preceded by fever that started on day 4 of birth, was low-grade, biphasic without any associated systemic symptoms.

Mother had history of fever 3-days post-partum and was detected with IgM and IgG antibody positive for Dengue virus 7-days later. Mother did not demonstrate any cutaneous pigmentary changes.

Cutaneous examination of the neonate showed mottled and reticulate pigmentation on the face with accentuation on the nose and perioral area; suggestive of chik sign [Figure 1]. Dermoscopy showed brown coloured globules over a background of brownish pigmentation [Figure 2].

A timeline of maternal and neonatal illness is shown in Figure 3.

Laboratory evaluation of the baby revealed a normal total leucocyte count of 7,600/cumm. with lymphocytosis (60%) and thrombocytopenia (86,000/cumm). Packed cell volume (PCV), prothrombin time (PT) and activated partial thromboplastin time (aPTT) were normal. Blood and urine cultures yielded no growth by the end of 5-days of incubation.

Since serology is not a standard diagnostic practice within the first week of neonatal illness, a tropical fever panel RT-PCR (reverse transcription- polymerase chain reaction) was sent. It tested negative for dengue and other tropical fever organisms but tested positive for chikungunya virus (CHIKV) confirming the diagnosis of chikungunya in the neonate without a co-infection with dengue.

Retrospectively when the mother was tested for chikungunya antibodies, she tested negative thus ruling out a serological oversight. Molecular diagnosis in the mother was not opted due to cost constraints and duration of illness.

Over the next few days of monitoring, child continued to have thrombocytopenia with levels dropping to about 30,000/cumm but by day-11 of illness, platelet counts rose up to 2,44,000/cumm. Throughout this period, baby continued to be better symptomatically and PCV continued to be normal. Scrotal erosions resolved within 2 weeks of its onset and discoloration resolved over the next 6-weeks.



**Fig 1: Irregular, blotchy hyperpigmentation over face particularly over the nasal tip**



**Fig 2: Dermoscopy of nose showing brown hyperpigmentation with a few brown globules (magnification 10X)**

## Discussion:

Both dengue and chikungunya are arboviral illnesses characterized by fever, rash and systemic features.<sup>3,4</sup> Maculopapular rash can be seen in both but petechiae are seen in dengue and pigmentation and vasculitic lesions are predominant features of chikungunya.<sup>5</sup> Although chik sign (brownish pigmentation on the tip of the nose) has been reported in dengue,<sup>2</sup> it could also indicate a co-occurrence of both infections or a possible misdiagnosis due to cross-reaction on serology.<sup>5</sup> We however found a third explanation with occurrence of two different arboviral illnesses in both mother and child.

Timing of confirmatory lab evaluation is paramount. Molecular diagnostic techniques are important in the first week of illness when viremia is pertinent and after the first week of illness is when serology becomes positive.<sup>3</sup> Our case posed a particular challenge as the mother had a serological diagnosis of dengue and neonate had a molecular diagnosis of chikungunya. In a quest to ascertain if this case had a missed overlap of the two arboviral infections, retrospective serology of the mother was conducted for chikungunya. Molecular diagnoses override serology to provide a definitive diagnosis in such bemusing cases within the first week of illness.<sup>3</sup> and molecular diagnosis of neonate conclusively ruled out dengue. With the mother testing negative for CHIKV, we concluded that two simultaneous arboviral infections affected both the mother and child.

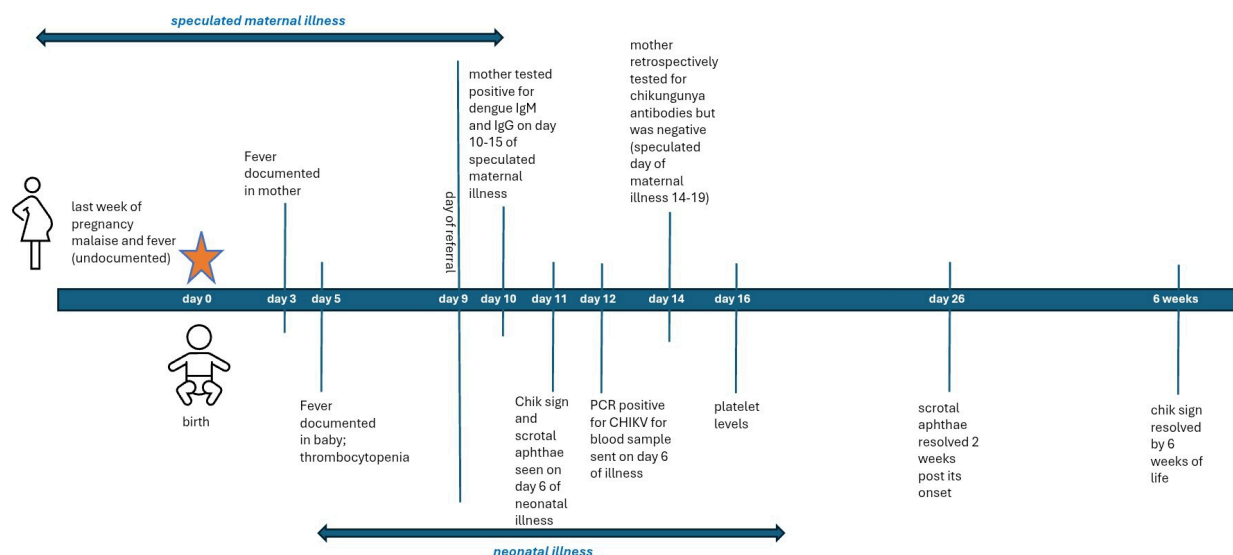
With maternal serology being positive for dengue and neonatal thrombocytopenia with fever, an assumption of neonatal dengue could be made. But it was the characteristic chik sign and scrotal aphthae that led us to probe for chikungunya, although it did pose another conundrum as chik sign has been reported in dengue as well.<sup>2,6</sup> Molecular diagnosis conducted on the child came to our rescue confirming chikungunya infection, thus drastically reducing worrisome monitoring and squashing the diagnostic dilemma. There are also diagnostic dermoscopic differences in chik sign seen in dengue with that of chikungunya.<sup>6</sup>

In resource poor settings, cost constraints limit the use of molecular diagnosis; serology after 1<sup>st</sup>-week of illness may be preferred but in cases like ours, early RT-PCR helped solve the predicament. Since serology in neonates is already futile, RT-PCR outweighed maternal serology thus avoiding any uncertainty. Our cases were neither an overlap of both infections, nor an oversight of cross-reaction on serology.

This case was unconventional as both mother and neonate were affected with two different arboviral infections at the same time. Although treatment of both infections are primarily symptomatic, the relative higher mortality of dengue over chikungunya still makes it important to distinguish one from another in especially vulnerable ages such as a neonate.<sup>3,4</sup>

## References:

1. Sheth PK, Vasani R. Chik Sign. Indian Journal of Paediatric Dermatology. 2022; 23(3):258-9.
2. Bhatia SS, Shenoi SD, Hebbar SA, Kayarkatte MN. The chik sign in dengue. Pediatr Dermatol. 2019;36(5):737-8.
3. National Centre for Vector Borne Diseases Control National guidelines for Clinical Management of Chikungunya Fever 2023 © [Internet]. ncvbdc.mohfw.gov.in. [cited 2024 Dec 18]. Available from: <https://ncvbdc.mohfw.gov.in/index1.php?lang=1&level=1&sublinkid=5899&lid=3686>
4. National Centre for Vector Borne Diseases Control National guidelines for Clinical Management of Dengue Fever 2023 © [Internet]. ncvbdc.mohfw.gov.in. [cited 2024 Dec 18]. Available from: <https://ncvbdc.mohfw.gov.in/index1.php?lang=1&level=1&sublinkid=5899&lid=3686>
5. Joob B, Wiwanitkit V. Comment on "Chik sign and dengue". Pediatr Dermatol. 2019;36(6):1022.
6. Sangal B, Barnwal S, Priya D, Pant A, Vashisht A. Chik Sign With Dermoscopic Findings in 10 Patients With Dengue: Case Series. Dermatol Pract Concept. 2024;14(3):e2024187.



**Figure 3: Timeline of maternal and neonatal illness**

**Editor's Note :**

An important takeaway from this case is that the Chik sign can be observed not only in Chikungunya but also in Dengue.

## Pediatric Dermatology Foundation



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## Answer to PDF - Photoquiz 3

Authors: Manjot Gautam, Akanksha Ghodke

### Clinical data

A sixteen-year-old boy, presented with a mildly painful lesion on right upper back noted since 4 months. The lesion was small to begin with and gradually progressed to the current size. The patient denied any history of trauma prior to this lesion. There was no history of any pre-existing mole at the site of this lesion. Cutaneous examination revealed a single, well-defined, oval hyperpigmented plaque measuring 2.5cm x 1.5 cm with elevated erythematous margin and atrophy in the centre, situated over the right scapula (figure 1a,1b). It was mildly tender.



**Fig 1a**



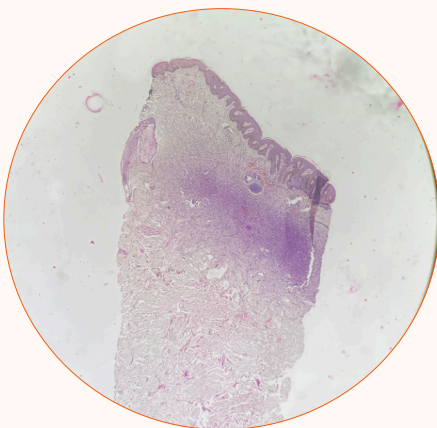
**Fig 1b**



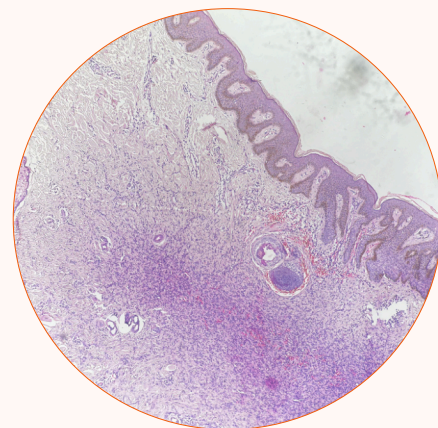
**Fig 2 On Dermoscopy- central irregular white scar like patch with pseudofollicular openings and peripheral erythematous homogenous macules is seen.**

Dermoscopy of the lesion showed central irregular white scar like patch with pseudofollicular openings and peripheral erythematous homogenous macules (figure 2).

A 4mm punch biopsy was done and sent for histopathological examination. (figure 3a,3b,3c,3d)

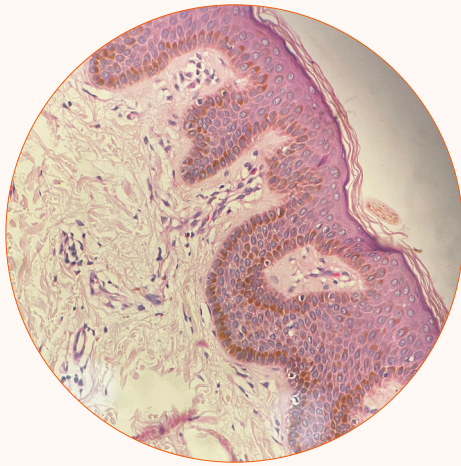


**Figure 3a**-Scanner view [H&E 4X] showed acanthosis in the epidermis with elongation of rete ridges and an infiltrate was noticed in the papillary and mid dermis.

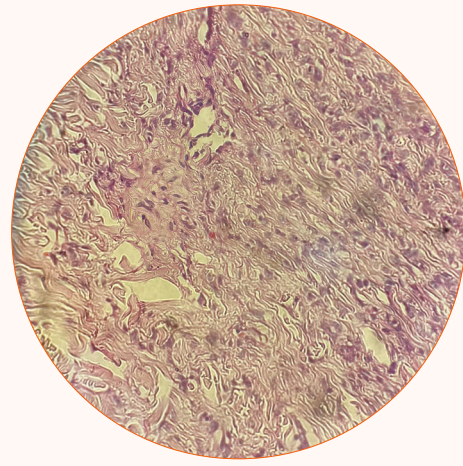


**Figure 3b**-A higher magnification confirmed an acanthotic epidermis with hyperpigmented basal keratinocytes known as 'dirty feet sign'. A clear Grenz zone is seen in the papillary dermis with spindle cells entrapping collagen bundles. [H&E 10X]





**Figure 3c-** Acanthotic epidermis with scanty perivascular infiltrate in the papillary dermis and hyperpigmentation of basal keratinocytes (Dirty feet sign).[H&E 40X]



**Figure 3d-** Storiform arrangement of spindle cells with entrapment of collagen bundles in the papillary and mid dermis. [H&E 40X]

#### Differential diagnosis considered were as follows

1. Dermatofibroma
2. Melanoma
3. Seborrheic Keratosis
4. Basal cell carcinoma
5. Lichen planus like keratosis
6. Melanocytic Naevi

#### Investigations

Histopathological examination showed an acanthotic epidermis with elongation of rete ridges and hyperpigmented basal keratinocytes, a feature referred to as the "dirty-feet sign." Examination of dermis revealed a clear Grenz zone followed by localized proliferation of spindle-shaped fibrous cells mixed with histiocytoid cells arranged in a storiform pattern with entrapment of collagen bundles in between the cells.

#### Final diagnosis- Dermatofibroma.

#### Treatment

Complete excision of the lesion was performed under local anaesthesia.

#### Discussion:

Dermatofibroma is a benign cutaneous lesion which generally occurs as a solitary reddish-brown or dark-brown firm papule or nodule over the extremities.<sup>1</sup> Dermatofibromas are prevalent across all age groups; however, they are more frequently observed in individuals aged 20 to 50, with a slight female preponderance.

The lesions represent a benign dermal proliferation of fibroblasts. They are usually asymptomatic but may sometimes cause pain, tenderness, or itchiness. Firm-hard lesions that adhere to the overlying epidermis may result in a depression over the nodule known as the 'dimple sign' or 'Fitzpatrick sign'.<sup>2</sup> Clinical variants include atrophic, atypical polypoid, giant, subungual, erosive, lichenoid, ulcerated dermatofibromas, and grouped palmoplantar histiocytoma.<sup>3</sup> Several histological variants have been described, including cellular, aneurysmal, epithelioid, atypical, and myxoid, as well as "subcutaneous" and "deep-penetrating dermatofibroma".

The aetiology of dermatofibroma remains a subject of debate, with some considering it a reactive process and others viewing it as a true neoplasm. Despite the unclear aetiology, many patients give history of local trauma, such as an insect bite, minor injury or superficial puncture wound prior to the onset of the lesions. However, dermatofibromas may develop spontaneously without any apparent triggering event or trauma.

Dermatofibromas can be differentiated from other conditions (as mentioned above) on the basis of dermoscopy and histopathological findings. Dermoscopy shows a variety of patterns with central irregular white scar like patch with pseudofollicular openings and peripheral erythematous homogenous macules being one of them.<sup>4</sup> Histopathology shows a localized proliferation of spindle-shaped fibrous cells mixed with histiocytoid cells within the dermis, these spindle cells may form a focal storiform pattern characterized by a multicentric whorling appearance of elongated nuclei.<sup>5</sup> Intermixed capillaries, lymphocytes, or multinucleated giant cells may also be present. A distinguishing characteristic of dermatofibroma is the presence of trapped collagen bundles or collagen balls within and between the fascicles of spindled fibrous cells.

Hence a diagnosis can be made of dermatofibroma with ease.

Treatment for dermatofibromas is typically not necessary unless the lesion causes symptoms. Excision biopsy is recommended if the lesion looks atypical, is irregular or grows rapidly to rule out malignant transformation. Atypical variants have a higher chance of recurrence and, in rare cases, can metastasize. Therefore, complete excision with clear margins is advised. Surgical excision for mere cosmetic reasons is not recommended as the resultant scar might be more conspicuous than the original lesion, especially on the lower extremities. Cryotherapy and lasers are associated with a higher chance of recurrence due to incomplete excision.

The correct answers to the PDF Photoquiz 3 were given by

1. Dr Shashidhar KC, Senior resident, Department of Dermatology, JJM Medical College, Davangere, Karnataka
2. Dr. Selvakumar P, Final year postgraduate, Institute of DVL, Madras medical College, Chennai
3. Anisha Amarnath

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

### 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).

**Q1) What is your diagnosis?**

**Q2) Name the special stain depicted in Fig 3.**

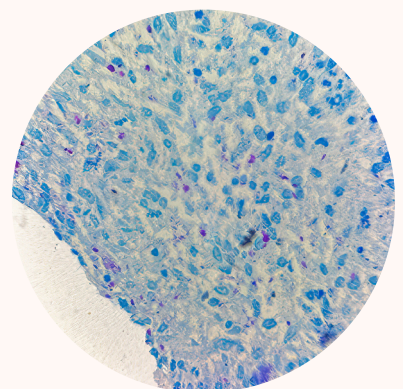
{Kindly mail your answers along with your affiliation to [peddermfoundation@gmail.com](mailto:peddermfoundation@gmail.com) before 20<sup>th</sup> February 2025. The winners of Photoquiz 4 will be announced in the next issue}



**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)**

# Drug dosing in children: Tips and tricks

## Cyclosporine in Pediatric Dermatology

Author: Dr Jeta Buch

### Introduction

Cyclosporine (CsA) is a highly effective and rapidly acting immunosuppressant effective in many dermatological conditions. Concern over the adverse effects of CsA has largely limited its use in children suffering with off-label indications.

### Pharmacokinetics

CsA is better tolerated in children than adults due to following pharmacokinetic differences<sup>1</sup> -

1. Lower oral absorption, rapid clearance and increased volume of distribution of CsA at steady state
2. Lower bioavailability due to shorter bowel length
3. Polymorphism in cytochrome P450 isoenzymes (CYP3A) responsible for systemic clearance of CsA in African Americans

### Off label indications:

Indication	Dose
Lichen Planus	3 mg/kg/day ( In case of Hypertrophic lesions 5mg/kg/day may be necessary)
Psoriasis	4 mg/kg/day
Atopic Dermatitis	3 to 5 mg/kg/day

### Others

1.Chronic urticaria
2. Steven Johnson Syndrome/ Toxic Epidermal Necrolysis
3. Dyshidrotic eczema
4. Photodermatoses like polymorphic light eruption, chronic actinic dermatitis, solar urticaria
5. Palmoplantar pustulosis
6. Pityriasis Rubra Pilaris
7. Pyoderma gangrenosum
8. Behcet's disease



### Optional therapy

1. Autoimmune connective tissue disorders – juvenile scleroderma, juvenile dermatomyositis
2. Autoimmune blistering disorders – bullous pemphigoid, epidermolysis bullosa acquisita, benign familial pemphigus
3. Alopecia Areata
4. Prurigo nodularis
5. Ofuji disease
6. Hidradenitis Suppurativa

### Adverse effects

Most of the adverse effects of CsA are dose and duration dependent and are reversible on discontinuation, except the structural renal abnormalities<sup>1</sup>.

- Hypertrichosis, keratosis pilaris, folliculitis, sebaceous hyperplasia are few cutaneous side effects especially at doses used in transplant therapy.
- Gingival hyperplasia associated with CsA has been related to poor oral hygiene which resolves within 6 months to 1 year.
- Paraesthesia, tremors, and headache are self-limiting side effects.
- CsA induced hypertension is a rare phenomenon in children and is less often dose – dependent.
- Children are less susceptible to CsA induced nephropathy than adults.
- Hyperbilirubinemia due to competitive inhibition of bilirubin transport, rather than direct hepatotoxicity, can occur.
- CsA associated hyperlipidemia seen in obese normalizes on drug discontinuation but may require active management in psoriasis, as it involves metabolic syndrome.
- Risk of cutaneous tumors and lymphomas is not found in dermatological use of CsA in children.

### Dosing

3-5 mg/kg/day in divided doses which is tailored according to the severity of disease and other co-morbidities. Higher than 5 mg/kg/day dose for a duration exceeding 1 year leads to vasculopathy and tubulopathy with structural changes that are irreversible and chronic. Hence not warranted. Bodyweight – independent regimens are safe and effective in dermatological conditions because of the lower doses involved.<sup>1</sup>

### Formulations available

Cyclosporine capsules (50 mg and 100 mg)

Cyclosporine oral solutions (100 mg/ml)

### Tips and Tricks for Administration :

The major drawbacks of using cyclosporine in liquid form are –

1. Difficulty in obtaining accurate dosage measurements
2. Poor taste leading to noncompliance

To overcome these challenges-

1. Cyclosporine Syringe - Cyclosporine (CsA) is the only drug which is dispensed in such a concentrated form. An error of just 1 ml will mean a difference of 100 mg. So utmost care needs to be taken while calculating the proper dose of CsA particularly in underweight infants. Use of insulin syringe is thus recommended for dose titration. In an insulin syringe, 40 units correspond to 1 ml, which is equivalent to 100 mg of cyclosporine. So, 1 unit is precisely 0.025 ml, amounting to 2.5 mg of CsA.<sup>2</sup> A 100 unit insulin syringe can also be used where 1 unit of the syringe is equal to 1mg of cyclosporine and hence is easier to dispense the required dose.
2. Modulation - If the oral solution must be used, it should be diluted with regular or chocolate milk or orange or apple juice. This will make it more palatable and also provide a more soluble vehicle. Use the same drink each time. Stir it well. To prevent any contamination, the desired weight dependent dose of the formulation should be administered within 10 minutes of preparation. After drinking, rinse the glass with a little more of the same liquid and have the child drink this as well so that they get the full dose of the medicine.<sup>3</sup> Avoid grapefruit, grapefruit juice, pineapple or papaya juice while on cyclosporine.

Safety instructions to parents <sup>3,4</sup> :

1. Give CsA at the same time every day. Divided doses should be administered at least 12 hours apart.
2. If the child spits the dose within 20-30 minutes of taking cyclosporine, repeat the dose. If it's longer than 30 minutes, do not repeat the dose but take a note of the missed dose.
3. If fewer than 3 hours have passed since the missed dose, give the missed dose and get back on schedule.
4. Do not double or increase the next dose to keep up for the missed dose.
5. If your child is sick, stop giving cyclosporine and contact your treating physician. Restart cyclosporine only when directed by the treating physician.
6. Room temperature should be maintained for both the oral solution and the diluents.
7. Glass cups, bottles and utensils must be preferred. Avoid plastic or paper container.
8. If syringe is used, wipe it dry after use, don't rinse with water.
9. If CsA is given with food, try to keep the amount and type of food same. Changes in the diet may influence the absorption of cyclosporine.
10. Do not change the brand of CsA.
11. Avoid crowded places while on CsA. Care should be taken when brushing or flossing the child's teeth. Avoid touching eyes or nose picking.

Monitoring <sup>5</sup> :

Blood pressure & baseline complete blood count, Liver function test, Renal function test, Magnesium, S. Fasting lipid profile. Repeat investigations after 1 month and then 3 monthly.

Note : Repeat blood test within 2 weeks if creatinine levels increase by > 30% from baseline.

Vaccination:

Live Vaccines to be administered at an interval of minimum 4 weeks before beginning CsA and 3 months after discontinuing CsA.<sup>6</sup>

Non - live vaccines can be given without restriction, but 2 weeks are generally required for the development of immune response following primary immunization and around 1 week following booster immunization.<sup>6</sup>

## References:

1. Al-Mutairi N. Cyclosporine in pediatric dermatology. 2016. doi:10.1007/978-3-319-32159-2\_25.
2. Dhar S, Ganjoo S. The Cyclosporine Syringe: A pragmatic approach for accurate calibration of cyclosporine dosing in children. Indian J Paediatr Dermatol. 2021;22(2):179-80.
3. Cyclosporine (Sandimmune). Children's Hospital of Pittsburgh. Available from: <https://www.chp.edu/our-services/transplant/liver/education/medications/cyclosporine-sandimmune-oral>.
4. Cyclosporine. AboutKidsHealth. Available from: <https://www.aboutkidshealth.ca/cyclosporine>.
5. Yee J, Orchard D. Monitoring recommendations for oral azathioprine, methotrexate, and cyclosporine in pediatric dermatology clinic and literature review. Australas J Dermatol. 2016;59(1):31-40.
6. Blanchard-Rohner G. Vaccination in children with autoimmune disorders and treated with various immunosuppressive regimens: A comprehensive review and practical guide. Front Immunol. 2021 Aug 2;12:711637.

## Editor's Note :

### Practical Considerations in the Use of Cyclosporine

- Certain side effects of cyclosporine require specific monitoring, particularly in pediatric patients, as they can differ in frequency and severity compared to adults. Notably, **hypertrichosis** and **gingival hyperplasia** are more common in children. Hypertrichosis, while benign and self-limiting upon discontinuation of cyclosporine, can be distressing to both parents and children. It is crucial to counsel parents about the transient nature of this side effect to alleviate concerns. Additionally, maintaining **good oral hygiene** is essential to minimize the risk of gingival hyperplasia, especially during prolonged cyclosporine therapy.
- While grapes and grapefruit may sound similar, they are entirely different fruits. Grapefruit and grapefruit juice should be avoided during cyclosporine treatment as they can significantly elevate blood cyclosporine levels. This occurs due to the inhibition of the enzyme cytochrome P450 3A4, which metabolizes cyclosporine, and P-glycoprotein, leading to increased drug absorption and potential toxicity.
- Cyclosporine should be given only in glass cups or other non-reactive materials. This precaution is necessary because cyclosporine can interact with certain plastics, compromising the drug's stability, efficacy, and safety. The oil-based solvents or emulsifiers in cyclosporine solutions can dissolve components of plastic cups, potentially degrading the medication or producing harmful byproducts.

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## Residents Column

### A Genetic Symphony

Author: Dr Neha Gogia

Junior Resident, D Y Patil Medical College, Nerul, Navi Mumbai

#### Tuberous Sclerosis Complex (Bourneville's Disease)

TSC1 and TSC2 disrupt cellular ease,  
Tumors and nodules on organs and knees.  
Ash-leaf spots, angiofibromas appear,  
Epilepsy storms bring challenges near.

#### Peutz-Jeghers Syndrome

STK11 crafts its polyp-laden tale,  
Pigment on lips and fingers prevail.  
Polyps within and cancer's thread,  
Vigilance needed for lives ahead.

#### Xeroderma Pigmentosum

Repair genes falter, UV becomes foe,  
Skin cancers blossom where rays do glow.  
Freckling young and dry skin hue,  
Nucleotide excision repair fails them too,  
In shadowed worlds, they journey through.

#### Cockayne Syndrome

With ERCC6 or ERCC8 astray,  
Growth and repair begin to sway.  
Thin, aged faces with photosensitivity,  
Shortened lives lived with dignity.

#### Dyskeratosis Congenita

With TERT and DKC1, telomeres fray,  
Nail dystrophy and skin tone gray.  
Marrow fails, cancer risks loom,  
Fragility etched, yet hearts still bloom.

#### Pachydermoperiostosis

HPGD shapes thick skin and bone,  
Clubbed fingers in a form all its own.  
Joints ache as the skin grows rough,  
A genetic puzzle, resilient and tough.

#### Bloom Syndrome

BLM gene falters, DNA unwinds,  
Short stature and breaks in genetic lines.  
Sun-sensitivity, cancers may start,  
A small frame holding a mighty heart.

#### Kindler Syndrome

FERMT1 lets skin split and tear,  
Fragile beneath a life of care.  
Blisters arise, photosensitivity stays,  
In strength and love, they find their ways.

Each syndrome tells a genetic tale,  
Through trials and triumphs, we prevail.  
With science and care, hope takes its flight,  
In the tapestry of genes, life shines bright.



# Pediatric Dermatology Foundation



Organizes

## Pediatric Dermatology Updates 2025

**Date: 23rd and 24th August 2025**

**Venue:** CIDCO Exhibition and  
Convention Center,  
Sector 30, Vashi,  
Navi Mumbai-400703

**Registration will open on 10th April 2025**

**Will apply for MMC points**

For Registration visit website:

[www.peddermfoundation.org](http://www.peddermfoundation.org)