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CANADIAN DERMATOLOGY TODAY

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- 118 patients were re-randomized to Ebglyss 250 mg Q4W[1]

81.7% (94/115) of patients who were EASI 75 responders at week 16 maintained their response through week 52.[1,3]

76.9% (59/77) of patients who were IGA 0,1 responders at week 16 maintained their response through week 52.[1,3]

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ADvocate 1 and ADvocate 2: Two identically designed, 52-week, randomized, double-blind, placebo-controlled, Phase 3 trials in adolescents and adults 12 years of age and older with moderate-to-severe AD not adequately controlled by topical medication(s) and who were candidates for systemic therapy. Patients received either Ebglyss 250 mg (with a loading dose of 500 mg at baseline and week 2, n=564) or placebo (n=287) Q2W up to week 16. Patients who responded at the end of this 16-week induction period were re-randomized to receive Ebglyss 250 mg Q2W (n=113), Ebglyss 250 mg Q4W (n=118), or placebo Q2W (n=60) for 36 additional weeks (maintenance period).
*Responder was defined as a subject with a 75% reduction in EASI, or an IGA 0 or 1 ("clear" or "almost clear") and a reduction of ≥2 points on a 0-4 IGA scale, from baseline to week 16, respectively.

EASI=Eczema Area and Severity Index; IGA=Investigator's Global Assessment; NRS=Numeric Rating Scale; Q2W=every 2 weeks; Q4W=every 4 weeks.

References: 1. Ebglyss™ (lebrikizumab). Product Monograph. Eli Lilly Canada, Inc. June 24, 2024. **2.** Silverberg JI, Guttman-Yassky E, Thaçi D, *et al*; for ADvocate1 and ADvocate2 Investigators. *N Engl J Med.* 2023;388(12):1080-1091. **3.** Blauvelt A, Thyssen JP, Guttman-Yassky E, *et al. Br J Dermatol.* 2023;188(6):740-748.

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Bare Realities: Uncovering the Life-Altering Impacts of Alopecia Areata

Anastasiya Muntyanu, MD, PhD, FRCPC, FAAD

Hair plays a pivotal role in shaping personal and group identity, conveying messages about age, gender, culture, ethnicity, and social status. The vast economic impact of the hair care industry—reflected in billions of dollars spent on products and hair salon treatments—highlights its cultural and societal importance.

The versatility of hair, in terms of style and appearance, has long symbolized power, transformation, and self-expression across various cultures and histories.[1] Whether through myths, religious texts, or modern media, well-groomed hair is celebrated and often equated with attractiveness and social status.

For patients with alopecia areata (AA), hair loss carries heavy public and self-imposed stigma. The impact on self-esteem and identity is profound, with many patients experiencing deep feelings of loss, grief, and shame. It is important to explore the impact of AA on a patient's life in many domains. Holistic management, which combines effective medical treatments with mental health support and effective camouflage strategies is needed, with the ultimate aim of improving the quality of life (QoL) for those affected by AA.

Introduction

AA is an autoimmune disease that targets hair follicles and affects approximately 2% of the population.[2] It can develop at any age and affects patients of any gender and ethnicity. Clinically, it presents in many different forms, including the patchy (or localized) subtype observed in approximately 70% of cases, alopecia totalis (loss of all scalp hair) or universalis (loss of all body hair) observed in 15–25% of cases, and more rare patterns such as diffuse, reticular (extensive confluent patches), ophiasis (band-like, peripheral pattern), and sisaipho forms. Nails are affected in approximately 30% of patients (e.g. pitting and trachyonychia), which confers a worse prognosis.[4]

The Severity of Alopecia Tool (SALT) is a commonly used tool in clinical trials to grade the extent of hair loss across the scalp, ranging between 0%–100%.[5] A SALT score of >50 is typically defined as severe disease and is often an indication for systemic therapy.[5] Although several other clinical assessment tools are available, most do not take into consideration the impact on a patient's QoL. The QoL is an important indicator, as two patients with identical SALT scores can experience significant differences in QoL impacts. Therefore, it is important to consider the patient's perspective when assessing disease severity.

Impact on Quality of Life

AA has a significant impact on QoL in both adults and children, with more than 75% of patients experiencing some level of impairment and up to a third reporting extremely severe effects.[6,7] Compared to conditions such as androgenetic alopecia and psoriasis, for example, AA shows a markedly worse impact on QoL. In addition to the loss of hair, functional impairments can also occur, such as increased sensitivity to weather with risk of sunburn to the scalp and ocular irritation from the loss of eyebrows and eyelashes.

The impact of AA on QoL is influenced by several demographic and clinical factors. Younger patients and women tend to experience a lower QoL. Factors such as the severity and extent of hair loss, including more widespread involvement, longer disease duration, multiple recurrences, and hair loss involving the eyebrows and eyelashes are associated with worse outcomes.[7] Interestingly, discrepancies between patient and physician assessments have been noted, with patients' self-rated severity being a more accurate predictor of QoL impairment. This indicates that the negative impact on self-image plays an important role in the patient's perceived burden of the disease.

The emotional and social dimensions of QoL metrics are particularly affected by AA. Both adults and children with AA often report challenges in mental health, social interactions, and familial relationships. This impact extends beyond the patient to family members, as seen by the significant impact on parental QoL.[8] AA patients often struggle with initiating and maintaining romantic relationships and may camouflage their condition due to fear of rejection or negative perceptions. In fact, up to a third of individuals have ended their relationships due to AA.[9] All of these factors contribute to social withdrawal and isolation, highlighting the need for improved disease awareness and support systems within both the medical community and society at large.

Psychiatric Comorbidities

AA carries a significant mental health burden, with numerous studies showing that 30%–68% of adult patients experience anxiety, depression, or other psychological symptoms, and these rates are significantly higher compared to those in age-and gender-matched controls.[7] Notably, receiving an AA diagnosis itself appears to be a risk factor for the development of depression,[10] with patients showing a 30%–38% higher risk of new-onset depression and increased use of antidepressants.[11] These findings are particularly pronounced among women and individuals aged 30–49 years. The severity of depression appears to correlate with the extent of hair loss. AA has also been associated with suicidal ideation in 13%–38.5% of patients and attempted suicide in 4.3%.[7,12]

In addition to depression, AA is associated with several anxiety disorders, including social anxiety (clinically significant in 47.5% of patients)

that often leads to significant social withdrawal and isolation.[13] This is associated with a higher rate of anxiolytic prescriptions. A survey-based study reported that all participants disclosed symptoms of anxiety and up to 66% rated it as extremely severe.[14] Pediatric patients with AA also exhibit separation anxiety, generalized anxiety, and social phobia compared to their unaffected peers. Additionally, this group exhibits higher rates of attention-deficit/hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) compared to controls.

In elderly patients, AA has been associated with an increased risk of dementia, possibly related to decreased social involvement.[15] These findings underscore the necessity for dermatologists to consider comprehensive mental health evaluations and support as part of the management strategy for patients with AA.

Impact on Work, School and Beyond

Over two-thirds of patients reported that AA influenced major life decisions, including choices related to relationships, education, and careers.[9] Adults with AA show significantly higher rates of work absenteeism (56%) and unemployment (82%) compared to controls.[9,16] AA also impacts patients' career choices and promotion opportunities. This can result from new-onset mental health disorders, social withdrawal, and the increased scheduling burden of appointments and treatments. Factors that contributed to higher rates of unemployment and work absenteeism include being a woman, having moderate-to-severe disease (as reported by the patient) and facial hair loss.[7] Decreased work productivity was found to be linked to the psychological burden of AA and to physical effects of hair loss (such as eye irritation from eyelash loss).

Similarly, children with AA face considerable challenges in their daily lives. Approximately half of affected children report missing school and experiencing academic difficulties due to the distress associated with their hair loss.[9] The condition also contributes to stigmatization and bullying, particularly among boys and those with localized disease, leading to diminished self-esteem and social isolation.[17] These educational and social setbacks often result in long-term impacts, such as altered career or education plans, as patients adjust their lifestyles to manage the condition.

Due to the burden of AA, most patients (90% of women and 72% of men) focus on camouflage techniques for their hair loss.[9] In fact, wigs are frequently used to mitigate the visible effects of AA, with 86.7% of patients reporting their use for social events and 55.9% wearing them continuously.[13] These strategies are often time-consuming, averaging 10.3 hours of preparation per week and increasing to 13.7 hours during peak disease activity.[9] Despite their utility in avoiding stigmatization, wigs and hairpieces are associated with physical discomfort, high costs, persistent worry about misplacement of the wig, and discovery by others. Additionally, the need to camouflage can lead to reduced physical activity and social engagement, as patients may avoid activities such as swimming, shopping, or simply going out due to anxiety about their appearance.

Financial Burden

Patients with AA face a substantial economic burden, with costs extending beyond direct medical expenses to include lost income (absenteeism), higher insurance premiums, transportation, and expenses for wigs, cosmetic products, and procedures. In the US, annual healthcare costs were estimated to exceed $11,000 USD with even higher costs for patients with alopecia totalis/universalis.[18] Out-of-pocket costs vary widely, with median annual spending of approximately $1,350 USD (medical appointments and supplements),[19] and additional expenses—averaging $2,000 per year—for hairpieces and psychotherapy.[9] Many patients reported using their savings or cutting back on essential expenses (including food and clothing) to manage these costs.

Conclusion

AA is not merely a matter of appearance—it is a life-altering autoimmune disease with wide-ranging impacts on psychological well-being, social functioning, professional and academic achievement, and financial stability. The burden extends across age groups and genders, often with underestimated consequences. Effective care for AA must combine access to evidence-based therapies with comprehensive support that reflects the condition's emotional, social, and financial impact. Only through such an integrative approach can we hope to meaningfully restore not just hair, but also confidence, and QoL for those affected.

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References

1. Wan SJ, Donovan J. Hair loss and identity-from Homer to Donne. J Cutan Med Surg. 2018;22(6):656. doi:10.1177/1203475418786211
2. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: a systematic review. Clin Cosmet Investig Dermatol. 2015;8:397-403. doi:10.2147/CCID.S53985
3. Finner AM. Alopecia areata: Clinical presentation, diagnosis, and unusual cases. Dermatol Ther. 2011;24(3):348-354. doi:10.1111/j.1529-8019.2011.01413.x
4. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. J Am Acad Dermatol. 2010;62(2):177-188, quiz 189-190. doi:10.1016/j.jaad.2009.10.032
5. King BA, Senna MM, Ohyama M, Tosti A, Sinclair RD, Ball S, et al. Defining severity in alopecia areata: current perspectives and a multidimensional framework. Dermatol Ther (Heidelb). 2022;12(4):825-834. doi:10.1007/s13555-022-00711-3
6. Liu LY, King BA, Craiglow BG. Alopecia areata is associated with impaired health-related quality of life: a survey of affected adults and children and their families. J Am Acad Dermatol. 2018;79(3):556-558 e551. doi:10.1016/j.jaad.2018.01.048
7. Muntyanu A, Gabrielli S, Donovan J, Gooderham M, Guenther L, Hanna S, et al. The burden of alopecia areata: a scoping review focusing on quality of life, mental health and work productivity. J Eur Acad Dermatol Venereol. 2023. doi:10.1111/jdv.18926
8. Matzer F, Egger JW, Kopera D. Psychosocial stress and coping in alopecia areata: a questionnaire survey and qualitative study among 45 patients. Acta Derm Venereol. 2011;91(3):318-327. doi:10.2340/00015555-1031
9. Mesinkovska N, King B, Mirmirani P, Ko J, Cassella J. Burden of illness in alopecia areata: a cross-sectional online survey study. J Investig Dermatol Symp Proc. 2020;20(1):S62-S68. doi:10.1016/j.jisp.2020.05.007
10. Tzur Bitan D, Berzin D, Kridin K, Sela Y, Cohen A. Alopecia areata as a proximal risk factor for the development of comorbid depression: a population-based study. Acta Derm Venereol. 2022;102:adv00669. doi:10.2340/actadv.v102.1622
11. People who develop alopecia areata have an increased risk for depression, anxiety, time off work and unemployment. British Journal of Dermatology. 2022;187(1):e49-e49. doi:10.1111/bjd.21283
12. Wang LH, Ma SH, Tai YH, Dai YX, Chang YT, Chen TJ, et al. Increased risk of suicide attempt in patients with alopecia areata: a nationwide population-based cohort study. Dermatology. 2023;239(5):712-719. doi:10.1159/000530076
13. Montgomery K, White C, Thompson A. A mixed methods survey of social anxiety, anxiety, depression and wig use in alopecia. BMJ Open. 2017;7(4):e015468. doi:10.1136/bmjopen-2016-015468
14. Rajoo Y, Wong J, Cooper G, Raj IS, Castle DJ, Chong AH, et al. The relationship between physical activity levels and symptoms of depression, anxiety and stress in individuals with alopecia Areata. BMC Psychol. 2019;7(1):48. doi:10.1186/s40359-019-0324-x
15. Li CY, Tai YH, Dai YX, Chang YT, Bai YM, Tsai SJ, et al. Association of alopecia areata and the risk of dementia: a nationwide cohort study. J Clin Psychiatry. 2021;82(6).21m13931 doi:10.4088/JCP.21m13931
16. Macbeth AE, Holmes S, Harries M, Chiu WS, Tziotzios C, de Lusignan S, et al. The associated burden of mental health conditions in alopecia areata: a population-based study in UK primary care. Br J Dermatol. 2022;187(1):73-81. doi:10.1111/bjd.21055
17. Christensen T, Yang JS, Castelo-Soccio L. Bullying and quality of life in pediatric alopecia areata. Skin Appendage Disord. 2017;3(3):115-118. doi:10.1159/000466704
18. Senna M, Ko J, Tosti A, Edson-Heredia E, Fenske DC, Ellinwood AK, et al. Alopecia areata treatment patterns, healthcare resource utilization, and comorbidities in the US population using insurance claims. Adv Ther. 2021;38(9):4646-4658. doi:10.1007/s12325-021-01845-0
19. Li SJ, Mostaghimi A, Tkachenko E, Huang KP. Association of out-of-pocket health care costs and financial burden for patients with alopecia areata. JAMA Dermatol. 2019;155(4):493-494. doi:10.1001/jamadermatol.2018.5218

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Management of Infantile Hemangioma in the Community

Lisa Flegel, MD, FRCPC, DABD

I practice as a general medical dermatologist in Northern British Columbia. During my first year of practice, I saw several infants requiring treatment for an infantile hemangioma, which required me to become familiar with topical and systemic therapies. The objective of this article is to provide an overview of the management of uncomplicated infantile hemangiomas in community settings, helping dermatologists become confident in prescribing first-line topical and systemic therapies.

Epidemiology, Clinical Presentation, and Natural History

Infantile Hemangiomas (IHs) are the most prevalent benign tumours in infancy, occurring in approximately 3% of infants.[1] Risk factors for IHs include female sex, multiple gestations, preterm birth, low birth weight, progesterone use in mothers, and a positive family history.[2]

IHs can be classified based on their depth (superficial, deep, and mixed) and their pattern of involvement (focal, multifocal, segmental, and indeterminate).[3] Superficial IHs typically present as red, lobulated papules or plaques, while deep IHs present as blue or skin-coloured subcutaneous lesions, often with overlying telangiectasia. Mixed IHs exhibit features of both superficial and deep types.

IHs appear within the first few weeks of life, and follow a characteristic growth pattern of proliferation then involution. Proliferation is most rapid within the first 3 to 5 months, during which the lesions reach approximately 80% of their final size, which is followed by slower growth up until 9 to 12 months of age, on average.[4] Involution typically begins at approximately 12 months of age, and continues for a period of 3 to 9 years.[4] It was previously thought that IHs regress by a rate of approximately 10% per year (i.e., 30% of IHs will involute by 3 years of age, 50% by 5 years, and 90% by 9 years).[5] However, more recent data shows that involution is complete by 4 years of age in 90% of patients.[6] Deep hemangiomas tend to present later and have a prolonged proliferative phase.[4] IHs with minimal or absent growth (IH-MAG), also known as Abortive Hemangiomas,

Morphologic or Anatomic feature(s)	Possible Associated Complication(s)
• Large or segmental infantile hemangiomas (IH) • Mixed IH • Lower lip, neck, anogenital area, 'biker glove' distribution	• Ulceration
• Segmental, especially face or scalp • Nasal tip, lip • Face ≥2 cm (>1 cm if ≤3 months of age) • Scalp, neck, trunk or extremity >2 cm • Breast (in females)	• Cosmetic deformity
• Periocular	• Astigmatism, visual axis obstruction, nasolacrimal duct obstruction, ptosis, amblyopia, strabismus
• 'Beard' distribution (preauricular, mandible, lower lip, chin, anterior neck)	• Airway hemangiomas, risk of airway obstruction
• Perioral	• Feeding difficulties
• ≥5 IHs	• Infantile hepatic hemangioma (may be associated with hypothyroidism)
• Large, segmental facial IH	• PHACES syndrome (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities, Sternal cleft)
• Segmental IH overlying lumbosacral spine or perineal	• LUMBAR syndrome (Lower body IH, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Renal anomalies, Arterial anomalies)

Table 1. Potential complications of infantile hemangiomas by morphologic and anatomic features[3,7]; *courtesy of Lisa Flegel, MD, FRCPC, DABD.*

represent a variant that has minimal to no proliferation but follows a similar involution pattern as other IHs.[5] After involution, patients may be left with telangiectasia, fibrofatty tissue, anetoderma, redundant skin, or scarring.[6]

Complications

Most IHs involute spontaneously and do not require intervention. Possible complications of IHs include cosmetic disfigurement, pain, ulceration, bleeding, infection, and functional impairment. IHs may also be associated with extracutaneous involvement, such as liver hemangiomas, and multi-system syndromes such as Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities, Sternal cleft (PHACES) and Lower body IH, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Renal anomalies, Arterial anomalies (LUMBAR) (**Table 1**).

Management

The decision to treat and selecting a treatment for IH requires consideration of several factors, including size, location, risk of complications, as well as caregivers' preference. The American Academy of Pediatrics (AAP) has established a clinical practice guideline for managing IH, which outlines recommendations for topical, systemic, and physical therapy modalities.[7]

The majority of IHs do not need treatment given their tendency for spontaneous involution.

Considering this, and their common occurrence, most infants born with an IH will not be referred to Dermatology. However, for those with IHs requiring treatment, due to the rapid growth in the proliferative phase, early intervention is important to limit potential complications. In my practice I aim to see infants before they are 1 month old. For IHs with a low risk of complications, active non-intervention may be appropriate. If observation is chosen, lesions can be monitored through serial measurements and/or photographs.

Treatment is indicated for IHs located in cosmetically sensitive areas or for those at risk for functional impairment or ulceration. The presence of clinical features suggestive of PHACES or LUMBAR syndrome, or concern for extracutaneous IH involvement, should prompt a referral for further evaluation and management recommendations.

Topical Therapy

Topical beta blockers are the preferred treatment for thin, superficial IHs where treatment is not medically necessary but is desired. The most commonly used agent is timolol maleate 0.5% gel-forming drops, administered as one drop twice daily.[7] Topical timolol is well tolerated and is an effective treatment for select IHs. The best response is observed in thin (<1 mm) superficial IH.[8] Adverse events are mild and uncommon, occurring in <3% of patients, with the most common being mild irritation and xerosis.[8] Timolol has been documented to have systemic absorption, therefore, it is recommended to limit usage to a maximum of two drops per day.[8] Caution is advised when using topical timolol on large or ulcerated IHs, as well as on mucosal surfaces or occluded areas (e.g., the diaper region), due to the potential for increased systemic absorption.

Oral Beta Blockers

Oral propranolol is the first-line therapy for IHs requiring systemic therapy and has been established as a safe and effective treatment. Its use is reviewed in two consensus guidelines: one by the British Association of Dermatologists (2018) and another by the Australasian College of Dermatologists (2017).[9,10] **Table 2** summarizes the treatment parameters for oral propranolol. If contraindications are present, referral to a pediatrician and/or pediatric dermatologist should be considered.

Systemic therapy is indicated for IHs that pose risks such as visual impairment, airway compromise, nasal obstruction, auditory canal involvement, ulceration, or those with a potential for permanent disfigurement.[9] In Canada, propranolol oral solution (3.75 mg/mL) is commercially available as *Pr* Hemangiol (Pierre Fabre Dermo-Cosmétique Canada Inc.) and has Health Canada approval for treating life- or function-threatening hemangiomas, ulcerated hemangiomas with pain and/or lack of response to simple wound care measures, and hemangiomas with a risk of permanent scarring or disfigurement.[11]

Prior to starting propranolol, a thorough history and physical exam, including infant heart rate, should be performed to assess for potential contraindications.[9,10] Outpatient initiation of propranolol is considered appropriate for term infants with a normal birth weight who are older than 4 weeks and have no significant comorbidities.[9,10] For younger or low weight (<2.5 kg) patients or those with comorbidities, consider a referral to Pediatrics or Pediatric Dermatology for treatment initiation. In such cases, a lower initial dose, three times daily dosing, and slower dose escalation may be warranted.[12]

During the COVID-19 pandemic, in-person evaluations were not always feasible, prompting the Hemangioma Investigator Group to develop consensus guidelines for managing IHs by telemedicine.[13] Propranolol initiation via telemedicine can be considered for infants older than 5 weeks with a normal birthweight, without ulceration or features concerning for PHACES or LUMBAR syndrome. Patients should have a recently documented weight (within 2 weeks) and a normal cardiovascular and respiratory exam within the previous 4 weeks.[13]

Propranolol therapy is typically initiated at 1 mg/kg/day, with an increase to 2 mg/kg/day

Indications	• Life or function-threatening • Ulcerated or high risk of ulceration • High risk of deformity or psychosocial impact
Contraindications	Consider specialist consultation for patients with contraindications **Relative** • Infants prone to hypoglycemia • Infants with cardiovascular disease (persistent bradycardia, aorta coarctation) • Bronchospasm • Intracranial arterial anomalies • Other systemic disease **Absolute** • Second or third degree heart block • Hypersensitivity to propranolol
Side effects	**More common** • Sleep disturbance • Cold extremities • Diarrhea **Less common** • Hypoglycemia • Bradycardia • Hypotension • Bronchospasm
Dose	Start at 1 mg/kg/day, given as twice daily dosing; increase the dose after 1 to 2 weeks to 2 mg/kg/day (unless the lower dose is clinically effective)
Monitoring	Clinical monitoring monthly until signs of involution, then every 3 months until discontinuation of therapy
Duration of therapy	At least 12 months of age for most patients
Instructions for parents	• Give propranolol twice a day, at least 8 hours apart • Give propranolol with feeds • Temporarily hold the dose if the child is feeling unwell (e.g., vomiting, decreased feeds, wheezing) until feeding normally • If a dose is missed do not give an extra dose, simply resume at the next scheduled time • Routine immunizations can be given during therapy

Table 2. Summary of oral propranolol for the treatment of infantile hemangiomas[9-11]; *courtesy of Lisa Flegel, MD, FRCPC, DABD.*

after 1 to 2 weeks.[9,10] The lowest clinically effective dose should be used. If there is no response, the dose may be increased up to 3 mg/kg/day if needed.[7,11] Clinical signs of response include softening, lightening in colour, a reduction or cessation in growth rate, and over time, a decrease in size.

Caregivers should be counselled on potential adverse effects and advised on when the medication should be held or medical consultation sought. Common side effects include sleep disturbances, peripheral vasoconstriction (manifesting as cold hands and feet), and diarrhea. More serious adverse events, though less frequent, include hypoglycemia, bradycardia, hypotension, and bronchospasm. If an infant is feeling unwell, has reduced oral intake or is wheezing, propranolol should be temporarily withheld until they are feeding normally.

Patients can be monitored monthly until clinical signs of involution are observed, with dose adjustments made based on weight, and then less frequently until treatment cessation. The duration of therapy varies among individuals and rebound growth may occur following discontinuation. A large multicentre retrospective cohort study found the lowest risk of rebound when treatment was discontinued between 12 to 15 months of age.[14] Consequently, many experts recommend continuing therapy until at least 12 months of age.[7,9] Propranolol can be discontinued at the end of treatment without any weaning.

Nadolol is an oral beta blocker that has also been used to treat IHs. While a full review of nadalol is beyond the scope of this article, a Canadian prospective study demonstrated that oral nadolol is non-inferior to propranolol and has a comparable safety profile.[15]

Other Therapies

With the use of oral and topical beta blockers for IHs, the need for alternative treatments has decreased.

Systemic corticosteroids were the standard treatment for IHs prior to the introduction of propranolol and remain an option in select cases, such as when beta blockers are contraindicated or ineffective.[7] Intralesional corticosteroids have been used to treat small, bulky IHs.[7]

Surgical intervention is generally reserved for older children requiring reconstruction for functional or cosmetic purposes, but it may be considered in select infant cases.[7] Laser therapy, including pulsed dye laser and long-pulse Nd:YAG laser, can be used for small, superficial IHs, although access to these treatments is limited in some communities.[12]

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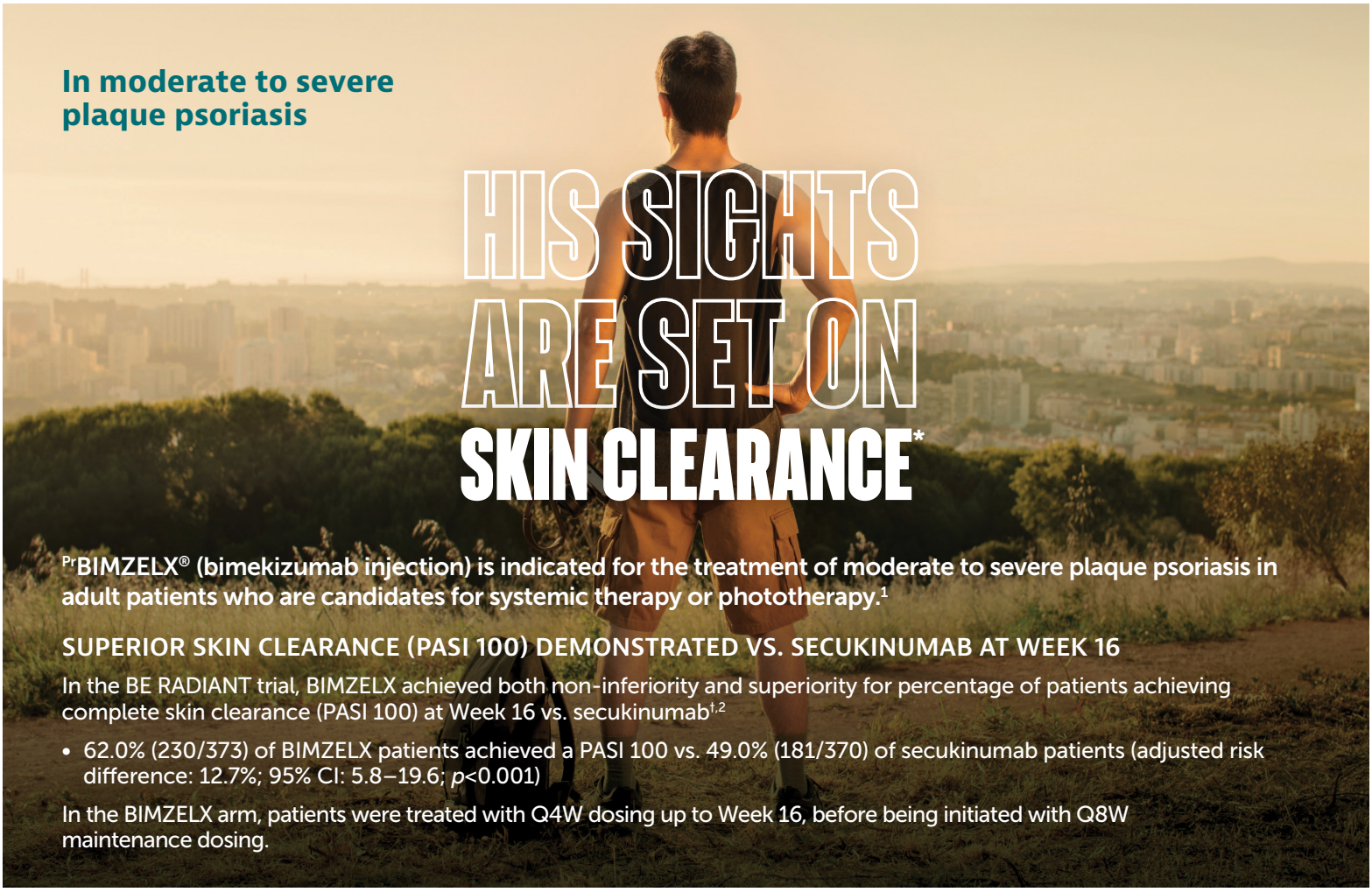
References

1. Sun Y, Zhao J, Meng Y, Luo W, Jiang C, Deng G, et al. The prevalence, complications, and risk factors for infantile hemangioma: a systematic review and meta-analysis. Int J Dermatol. 2024;63(6):737-746. doi:10.1111/ijd.17062
2. Ding Y, Zhang JZ, Yu SR, Xiang F, Kang XJ. Risk factors for infantile hemangioma: a meta-analysis. World J Pediatr. 2020;16(4):377-384. doi:10.1007/s12519-019-00327-2
3. Rodríguez Bandera AI, Sebaratnam DF, Wargon O, Wong LF. Infantile hemangioma. Part 1: Epidemiology, pathogenesis, clinical presentation and assessment. J Am Acad Dermatol. 2021;85(6):1379-1392. doi:10.1016/j.jaad.2021.08.019
4. Chang LC, Haggstrom AN, Drolet BA, Baselga E, Chamlin SL, Garzon MC, et al. Growth characteristics of infantile hemangiomas: implications for management. Pediatrics. 2008;122(2):360-367. doi:10.1542/peds.2007-2767
5. Paller AS, Mancini AJ. Infantile hemangiomas, vascular malformations, and other vascular disorders of infancy and childhood. In: Paller AS, Mancini AJ, editors. Hurwitz Clinical Pediatric Dermatology. 5th ed. Philadelphia: Elsevier; 2020. p. 326-368.e8.
6. Baselga E, Roe E, Coulie J, Munoz FZ, Boon LM, McCuaig C, et al. Risk factors for degree and type of sequelae after involution of untreated hemangiomas of infancy. JAMA Dermatol. 2016;152(11):1239-1243. doi:10.1001/jamadermatol.2016.2905
7. Krowchuk DP, Frieden IJ, Mancini AJ, Darrow DH, Blei F, Greene AK, et al. Clinical practice guideline for the management of infantile hemangiomas. Pediatrics. 2019;143(1):e20183475. doi:10.1542/peds.2018-3475
8. Püttgen K, Lucky A, Adams D, Pope E, McCuaig C, Powell J, et al. Topical timolol maleate treatment of infantile hemangiomas. Pediatrics. 2016;138(3):e20160355. doi:10.1542/peds.2016-0355
9. Solman L, Glover M, Beattie PE, Buckley H, Clark S, Gach JE, et al. Oral propranolol in the treatment of proliferating infantile haemangiomas: British Society for Paediatric Dermatology consensus guidelines. Br J Dermatol. 2018;179(3):582-589. doi:10.1111/bjd.16779
10. Smithson SL, Rademaker M, Adams S, Bade S, Bekhor P, Davidson S, et al. Consensus statement for the treatment of infantile haemangiomas with propranolol. Australas J Dermatol. 2017;58(2):155-159. doi:10.1111/ajd.12600
11. Pierre Fabre Dermo-Cosmétique Canada Inc. Product monograph including patient medication information Pr HEMANGIOL (propranolol solution). Oral solution, 3.75 mg/mL propranolol (as propranolol hydrochloride), oral use. Brossard, QC, Canada. [Authorization 2021 Jun 16, Revision 16 Jun 2021]. Available from: https://www.hemangiol.ca/pm/
12. Sebaratnam DF, Rodríguez Bandera AL, Wong LF, Wargon O. Infantile hemangioma. part 2: management. J Am Acad Dermatol. 2021;85(6):1395-1404. doi:10.1016/j.jaad.2021.08.020
13. Frieden IJ, Püttgen KB, Drolet BA, Garzon MC, Chamlin SL, Pope E, et al. Management of infantile hemangiomas during the COVID pandemic. Pediatr Dermatol. 2020;37(3):412-418. doi:10.1111/pde.14196
14. Shah SD, Baselga E, McCuaig C, Pope E, Coulie J, Boon LM, et al. Rebound growth of infantile hemangiomas after propranolol therapy. Pediatrics. 2016;137(4):e20151754.
15. Pope E, Lara-Corrales I, Sibbald C, Liy-Wong C, Kanigsberg N, Drolet B, et al. Noninferiority and safety of nadolol vs propranolol in infants with infantile hemangioma: a randomized clinical trial. JAMA Pediatrics. 2022;176(1):34-41. doi:10.1001/jamapediatrics.2021.4565



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References: 1. BIMZELX Product Monograph. UCB Canada Inc. March 11, 2024. **2.** Reich K, Warren RB, Lebwohl M, et al. Bimekizumab versus secukinumab in plaque psoriasis. *N Engl J Med.* 2021;385(2):142–152.

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The World Congress of Pediatric Dermatology: Key Sessions and Takeaways

Cathryn Sibbald, MSc, MD, FRCPC, DABD

The World Congress of Pediatric Dermatology, held in Buenos Aires, Argentina from April 8–11, 2025, offered a valuable opportunity to hear from experts and gain insights and perspectives on the field. Here are some key takeaways.

Atopic Dermatitis

Elaine Siegfried, based in Missouri, USA, shared some pearls on the workup and management of patients with atopic dermatitis. Based on her own experience, she provided a list of investigations that she considers at baseline for select patients. These include total IgE and eosinophil counts, albumin and protein (as markers of malnutrition), immunoglobulin levels (to screen for immunodeficiencies), anti-nuclear and anti-histone antibodies (as potential markers of predilection for anti-drug antibody formation), vitamin D levels, and a celiac screen. While not every patient requires this full panel, it provides a helpful checklist of tests to consider.

Carlston Flohr, from the United Kingdom, presented findings from the TREAT trial, which compared methotrexate 0.4 mg/kg/week to cyclosporine 4 mg/kg/day in 103 patients aged 2–16 years old with atopic dermatitis.[1] While cyclosporine demonstrated faster initial

	Hyper-IgE Syndrome[15]	Chronic Granulomatous Disease[16]	DIRA (*Deficiency of Interleukin (IL)1-RA*)[17]	DITRA (*Deficiency of IL36RA*)[18]
Gene	*STAT3, DOCK8, ZNF341, IL6ST, IL6R1*	*CYBB, NCF1/2/4, CYBA, CYBC1*	*IL1RN*	*IL36RN (PSORS14)*
Onset	Week 2	Week 4	Infancy	Infancy
Pustules	Localized	Localized	Disseminated	Disseminated
Symptoms	Abscess, Eczema	Lymphadenopathy, Hepatosplenomegaly	Fever, Arthropathy	Fever, Serositis

Table 1. Neonatal Pustular Eruptions; *courtesy of Cathryn Sibbald, MSc, MD, FRCPC, DABD.*

improvement than methotrexate at week 12, methotrexate showed superior efficacy by week 36. After stopping treatment, a higher proportion of patients who had received cyclosporine reported experiencing significant flaring compared to those treated with methotrexate (48% versus 35% by week 60). He reviewed his considerations for tapering off systemic treatments after disease control has been achieved and maintained. Key considerations include possible flaring of comorbidities that have been concurrently controlled by eczema treatments (e.g., asthma control with dupilumab), the importance of reinforcing diligent adherence to topical regimens when tapering systemic therapies, and the implementation of slow tapering either by dose or interval to allow early detection of disease worsening.

Immunodeficiencies

Peter Hoeger, from Germany, discussed immunodeficiencies that present in the neonatal period. He highlighted key differentiating factors in neonates with immunodeficiencies compared to those with atopic dermatitis, which includes erythroderma, pronounced lymphadenopathy, and severe infections. He also shared a helpful table outlining differentiating factors in pustular eruptions (**Table 1**).

He also referred to an interesting multicentre study demonstrating that certain features of eczema in infancy could help discriminate between atopic dermatitis and *DOCK8* or *STAT3* deficiencies.[2] These atypical presentations include rash onset in the neonatal period, and eczema localized to the retro-auricular, axillary, sacral, and genital areas. In the study, these features demonstrated high specificity, ranging between 73.4% and 94.1%, and positive descriptive values ranging between 55% and 93.1% in discriminating *DOCK8* and *STAT3* from atopic dermatitis. He concluded by encouraging us to use **online score calculators for hyper-IgE syndromes**.

Jennifer Huang, from Boston, discussed long-term effects of skin conditions in immunocompromised patients. She emphasized the dose-dependent risk for skin malignancies associated with voriconazole exposure in pediatric patients,[3] emphasizing that acute voriconazole-associated phototoxicity is a risk factor for voriconazole-related skin cancers later in life. As preventative measures, she recommended considering a switch to posaconazole for fungal prophylaxis when feasible, using sirolimus instead of systemic calcineurin inhibitor regimens, and finally incorporating adjunctive photoprotective agents such as nicotinamide, acitretin, and polypodium leucotomos.

John McGrath, from the United Kingdom, delivered a plenary session on genetic disorders. He reviewed a case involving an adolescent of Taiwanese background who presented with progressive hyperpigmentation. Laboratory findings revealed very low serum B12 levels and elevated levels of plasma homocysteine.[4] Genetic testing revealed a homozygous pathogenic mutation in the *ABCD4* gene, resulting in skin hyperpigmentation in this patient and, in other cases, an increased risk of neurologic findings including transient ischemic attacks. Treatment with 3 mg of systemic vitamin B12

daily led to reversal of the hyperpigmentation and is expected to prevent possible neurologic sequelae.[4] He highlighted the growing number of genetic mutations being associated with genodermatoses, using hyper-IgE syndrome (HIES) as a key example. In addition to the *STAT3* mutation, other genes associated with autosomal dominant HIES include *ERBB21P*, and *CARD11*. Conversely, mutations associated with autosomal recessive HIES now include *DOCK8*, *ZNF341*, *PGM3*, *IL6R* and *IL6ST*. Treatment options include intravenous immunoglobin (IVIG), omalizumab, dupilumab, N-acytelgalatosamine, with bone marrow transplant demonstrating disease altering advantages.[5]

He also discussed inflammatory linear verrucous epidermal nevi (ILVEN), highlighting a published case series in which genetic testing confirmed mosaic pathogenic mutations, allowing successful targeted treatments.[6] These treatments included ustekinumab for patients with *CARD14* mutations, topical statin and cholesterol formulations for those with *PMVK* and *NSDHL* mutations, and a Janus kinase (JAK) inhibitor for *ABCA12*-related cases.

Pierre Vabres, from France, presented on disorders of hyperpigmentation that warrant careful attention. He pointed out that in patients with Café au lait macules, "looking" for nevus anemicus can serve as another marker indicative of possible neurofibromatosis. He emphasized that these lesions are often located on the head and neck region and may be overlooked by primary care physicians.

Aarti Nanda, from Kuwait, provided an update on primary immunodeficiencies–now referred to as inborn errors of immunity. She highlighted a 2024 updated review that includes 555 distinct conditions associated with 504 gene defects.[7]

Rare Dermatoses in Pediatrics

Elena pope delivered an engaging review of some notable tumours in pediatric patients. For patients presenting with dermatofibroma sarcoma protuberans, she emphasized the importance of wide-margin excisions. Citing a large pediatric cohort from China, she noted that 14 of 49 patients with dermatofibrosarcoma protuberans experienced recurrence within a follow up of 12–161 months (median 60 months), all of whom had initially undergone marginal excisions.[8]

She also presented a case of a patient with xeroderma pigmentosa (XP) and discussed the use of cemipilimab, a PD-1 inhibitor, as a treatment strategy to improve survival in this population.[9] In addition, Jennifer Huang highlighted a study in which 18 patients with XP (aged 17±5 years) received daily supplementation with 960 mg of polypodium leucotomos and 10 mg of vitamin D, and were advised to apply sunscreen with a minimum SPF of 50 each day.[10] After 12 months, 61.1% of patients had not developed new lesions, suggesting potential benefit from this regimen without reported adverse effects.

Marc Koh provided an update on pediatric mycosis fungoides (MF) and introduced the new consensus recommendations for its diagnosis, staging, and treatment soon to be published in the *British Journal of Dermatology*. He reviewed key points, emphasizing that progression to advanced MF is rare in pediatric cases. For staging, he recommended ultrasound of peripheral lymph nodes, abdomen, and chest X-ray in early-stage MF, instead of CT/PET-CT. Lymphadenopathy should be observed for 3–4 weeks, with use of antibiotics if infection is suspected. If the lymphadenopathy has not resolved, a biopsy should be considered. Finally, flow cytometry should be included in the initial workup.

Shared Decision-Making

Kelly Cordoro, from San Francisco, outlined an approach to shared decision-making in pediatrics, noting its complexity because of the limited autonomy of the patient (being a minor), and the involvement of multiple stakeholders beyond the dyad between patient and clinician. She broke the process down into simple steps:

1. Share relevant information about the condition and treatment options in a clear and understandable manner (organize information, avoid jargon, assess understanding)
2. Solicit and understand the patient's and family's perspectives, preferences, and priorities (understand beliefs, concerns, and assumptions that may influence decisions)
3. Invite the patient and family in the shared decision-making conversation
4. Follow up frequently

She highlighted that there is no universal agreement on the age at which minors should be deemed competent to make health care decisions, as maturity is variable among patients of the same age. A helpful review article outlines that age, context, and development all play roles in decision-making competence.[11] Key capacities that should be demonstrated for decision-making include the ability to communicate a choice, demonstrate understanding, reason through options and appreciate the implications. In general, many adolescents achieve this capacity at the age of 12 years. It is also important to start encouraging autonomy in our adolescent patients at their appointments, such as addressing them directly throughout the visit, while involving accompanying caregivers as needed.

Genetic Syndromes

Jemima Mellerio, from the United Kingdom, delivered a plenary session on recent developments in genetics. She discussed a recent retrospective international multicentre study, published in the *British Journal of Dermatology*, that examined the use of biologics in patients with congenital ichthyoses, supplemented with reports from the literature.[12] The study included 98 patients receiving biologics targeting interleukin (IL)-17, IL-12/23, IL4 and, in a few cases, tumor necrosis factor (TNF)-alpha inhibitors. Among the findings, patients with Netherton's syndrome responded best to IL-12/23 blockade, followed by IL-4R blockade, whereas those with congenital ichthyosiform erythroderma responded best to IL-4R blockade, followed by IL-12/23 blockade.

She also reviewed earlier mouse data on the proposed mechanism of losartan in targeting fibrosis for epidermolysis bullosa, before presenting the results from a new study on its use in pediatric epidermolysis bullosa.[13,14] The study enrolled 27 children aged 2–16 years who received losartan starting at 0.4 mg/kg/day titrated over 16 weeks to a target dose of 1.4 mg/kg/day. This dose was continued for 24 weeks, followed by a 3-month follow-up after discontinuation. After 9 months, most patients showed improvements in disease activity, function, and patient reported outcomes, with no adverse cardiac or blood pressure indices.[14]

Conclusion

The conference was a resounding success, and the next congress, set to take place in Austria in four years, promises another exciting round of outstanding sessions!

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References

1. Flohr C, Rosala-Hallas A, Jones AP, Beattie P, Baron S, Browne F, et al. Efficacy and safety of ciclosporin versus methotrexate in the treatment of severe atopic dermatitis in children and young people (TREAT): a multicentre parallel group assessor-blinded clinical trial. Br J Dermatol. 2024 Jan 23;190(2):e13. doi: 10.1093/bjd/ljad442.] [published correction appears in Br J Dermatol. 2024 Jun 20;191(1):e1. doi: 10.1093/bjd/ljae157.] Br J Dermatol. 2023;189(6):674-684. doi:10.1093/bjd/ljad281
2. Kasap N, Kara A, Celik V, Bilgic Eltan S, Akay Haci I, Kose H, et al. Atypical localization of eczema discriminates DOCK8 or STAT3 deficiencies from atopic dermatitis. J Clin Immunol. 2023;43(8):1882-1890. doi:10.1007/s10875-023-01554-z
3. Huang JT, Coughlin CC, Hawryluk EB, Hook K, Humphrey SR, Kruse L, et al. Risk factors and outcomes of nonmelanoma skin cancer in children and young adults. J Pediatr. 2019;211:152-158. doi:10.1016/j.jpeds.2019.04.017
4. Takeichi T, Hsu CK, Yang HS, Chen HY, Wong TW, Tsai WL, et al. Progressive hyperpigmentation in a Taiwanese child due to an inborn error of vitamin B12 metabolism (cblJ). Br J Dermatol. 2015;172(4):1111-1115. doi:10.1111/bjd.13413
5. Gracci S, Novelli T, D'Elios S, Bernardini R, Peroni D. Hyper IgE syndromes. Curr Pediatr Rev. 2024;20(3):253-264. doi:10.2174/1573396320666230912103124
6. Atzmony L, Ugwu N, Hamilton C, Paller AS, Zech L, Antaya RJ, et al. Inflammatory linear verrucous epidermal nevus (ILVEN) encompasses a spectrum of inflammatory mosaic disorders. Pediatr Dermatol. 2022;39(6):903-907. doi:10.1111/pde.15094
7. IJspeert H, Edwards ESJ, O'Hehir RE, Dalm V, van Zelm MC. Update on inborn errors of immunity. J Allergy Clin Immunol. 2025;155(3):740-751. doi:10.1016/j.jaci.2024.12.1075
8. Zhang Z, Lu Y, Shi C, Chen M, He X, Zhang H. Pediatric dermatofibrosarcoma protuberans: a clinicopathologic and genetic analysis of 66 cases in the largest institution in Southwest China. Front Oncol. 2023;13:1017154. doi:10.3389/fonc.2023.1017154
9. Fernandez ER, Tamura D, Khan SG, Momen S, Fassihi H, Sarkany R, et al. Retrospective study of efficacy and adverse events of immune checkpoint inhibitors in 22 xeroderma pigmentosum patients with metastatic or unresectable cancers. Front Oncol. 2023;13:1282823. doi:10.3389/fonc.2023.1282823
10. El Mansouri M, Essaddouki S, Mouradi M, Oukerroum A, El Fatoiki FZ, Truchuela MT, et al. Evaluation of the effectiveness and safety of combined oral and topical photoprotection with a standardized extract of Polypodium leucotomos (Fernblock(R)) in a Moroccan population with xeroderma pigmentosum. Photodermatol Photoimmunol Photomed. 2023;39(6):607-612. doi:10.1111/phpp.12904
11. Grootens-Wiegers P, Hein IM, van den Broek JM, de Vries MC. Medical decision-making in children and adolescents: developmental and neuroscientific aspects. BMC Pediatr. 2017;17(1):120. doi:10.1186/s12887-017-0869-x
12. Mazereeuw-Hautier J, Granier Tournier C, Hernandez-Martin A, Milesi S, Texier H, Severino-Freire M, et al. Biologics in congenital ichthyosis: are they effective? Br J Dermatol. 2025;192(2):327-334. doi:10.1093/bjd/ljae420
13. Nystrom A, Thriene K, Mittapalli V, Kern JS, Kiritsi D, Dengjel J, et al. Losartan ameliorates dystrophic epidermolysis bullosa and uncovers new disease mechanisms. EMBO Mol Med. 2015;7(9):1211-1228. doi:10.15252/emmm.201505061
14. Kiritsi D, Schauer F, Gewert S, Reineker K, Reimer-Taschenbrecker A, Schwieger-Briel A, et al. Safety and tolerability of losartan to treat recessive dystrophic epidermolysis bullosa in children (REFLECT): an open-label, single-arm, phase 1/2 trial. EClinicalMedicine. 2024;77:102900. doi:10.1016/j.eclinm.2024.102900
15. Olaiwan A, Chandesris MO, Fraitag S, Lortholary O, Hermine O, Fischer A, et al. Cutaneous findings in sporadic and familial autosomal dominant hyper-IgE syndrome: a retrospective, single-center study of 21 patients diagnosed using molecular analysis. J Am Acad Dermatol. 2011;65(6):1167-1172. doi:10.1016/j.jaad.2010.09.714
16. Agarwal S. Chronic granulomatous disease. J Clin Diagn Res. 2015;9(5):SD01-SD2. doi:10.7860/JCDR/2015/12139.5945
17. Stenerson M, Dufendach K, Aksentijevich I, Brady J, Austin J, Reed AM. The first reported case of compound heterozygous IL1RN mutations causing deficiency of the interleukin-1 receptor antagonist. Arthritis Rheum. 2011;63(12):4018-4022. doi:10.1002/art.30565
18. Ellingford JM, Black GC, Clayton TH, Judge M, Griffiths CE, Warren RB. A novel mutation in IL36RN underpins childhood pustular dermatosis. J Eur Acad Dermatol Venereol. 2016;30(2):302-305. doi:10.1111/jdv.13034

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Update in Diagnosis and Management of Severe Cutaneous Adverse Reactions: Emerging Therapies and Evolving Presentations

Jennifer Lipson, MD

Introduction

Severe cutaneous adverse drug reactions (SCARs) represent some of the most critical and potentially life-threatening conditions encountered in dermatology. These reactions include Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)—also referred to as Drug-Induced Hypersensitivity Syndrome (DIHS), Acute Generalized Exanthematous Pustulosis (AGEP), and Generalized Bullous Fixed Drug Eruption (GBFDE). All of these are classified as T-cell mediated hypersensitivity reactions.[1]

The development of SCARs is influenced by a complex interplay of genetic predisposition, variations in drug metabolism, and, in some cases, concurrent infections. In this update, I will review the latest advances in the diagnosis and management of SCARs, highlighting emerging patterns of presentation, differential diagnoses, and therapeutic strategies that are impacting clinical practice.

Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN)

SJS and TEN are both diseases of drug-induced epidermal necrosis, differing mainly by the extent of cutaneous involvement. SJS and TEN are type IVa hypersensitivity reactions mediated primarily by type 1 cytotoxic lymphocytes and natural killer cells.[2] The global incidence of SJS and TEN remains relatively stable, with an estimated 1–2 cases per million individuals per year. Despite their rarity, these conditions carry significant morbidity and mortality, warranting careful attention to risk stratification. Several factors are associated with an increased risk of developing SJS/TEN. Immunosuppression is a notable risk factor—whether due to malignancy, acquired immunodeficiency syndrome, or immunosuppressive therapies. Advanced age and systemic lupus erythematosus have also been linked to a higher incidence of these conditions. In addition, certain populations, particularly individuals of Black and Asian descent, appear to have a heightened susceptibility, potentially due to genetic and pharmacogenomic factors.[1,3]

Co-trimoxazole and lamotrigine remain the drugs with the highest incidence rates of SJS/TEN. Although the onset typically occurs within 4 days to 4 weeks, it can extend up to 8 weeks for drugs with longer half-lives, such as allopurinol, phenytoin, carbamazepine, or lamotrigine.

Due to the ethical challenges of conducting randomized, double-blind, controlled clinical trials and the lack of standardized outcome measures, there are no consistent treatment guidelines for SJS/TEN. Consequently, consensus recommendations for therapy primarily focus on supportive care.[4] Over the years, corticosteroids, intravenous immunoglobulin (IVIG), and cyclosporine have been used for treating SJS and TEN, with clinical results remaining controversial. In 2017, a meta-analysis of immunomodulating therapies for SJS and TEN suggested that careful use of corticosteroids (administered early, pulsed and/or in particular populations) or cyclosporine appeared most promising, with a possible mortality benefit. However, IVIG did not show any mortality benefit.[5] In 2018, Chung et al. performed an impactful randomized controlled trial of 96 patients with SJS/TEN who were treated with etanercept or traditional corticosteroids.[6] This study found that etanercept shortened the time of skin healing in patients with moderate to severe disease compared with corticosteroids and resulted in fewer gastrointestinal side effects. A more recent network meta-analysis in 2021 showed that a combination of IVIG and corticosteroids reduced mortality in SJS/TEN and TEN. While other therapies and their combinations may also be effective, further evidence is required to confirm these findings.[7] Several studies have shown that TNF-alpha inhibitors, either alone or in combination with other therapies, can improve disease outcomes. In 2022, a small cohort study of 25 patients showed that etanercept combined with methylprednisolone (15 patients) decreased acute disease duration and accelerated the skin healing time compared to systemic steroids alone (10 patients).[8] Additionally, a Cochrane review in 2022 concluded that treating SJS/TEN with etanercept rather than systemic steroids may decrease mortality. However, there is currently insufficient evidence for cyclosporine, systemic steroids, and IVIG.[9] A recent and exciting therapeutic development in TEN was reported in a study published in Nature in November 2024. The study showed upregulation of the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway in TEN, then effectively treated mouse models of TEN using pan-JAK (tofacitinib) and JAK1 (abrocitinib, upatacitnib) inhibitors. They subsequently safely and effectively treated seven human patients with SJS/TEN and TEN using JAK inhibitors, with patients showing rapid cutaneous re-epithelialization and recovery.[4] While more studies are required, this represents a very exciting potential future application of JAK inhibitors.

Special Populations

Updates have been made for three specific special populations: the management of pediatric epidermal necrolysis, the diagnosis and management of epidermal necrolysis in patients on immune checkpoint inhibitors, and the management of epidermal necrolysis in pregnancy.

In the pediatric population, the incidence rates of SJS/TEN are reported to be slightly higher than in adults. However, this may be due to the erroneous inclusion of cases of erythema multiforme major and reactive infectious mucocutaneous eruption (RIME) misdiagnosed as SJS/TEN.[2] Ramien et al. described useful distinguishing features between RIME and epidermal SJS/TEN, stressing that mucous membranes are more severely affected than the skin in RIME, with 47% of cases showing sparse skin findings and 34% having absent skin findings.[10] Additionally, in children presenting with mucosal eruptions, prodromal respiratory symptoms, and lack of significant drug exposure the diagnosis is most likely RIME.[10] SJS/TEN generally has a better prognosis in children than in adults. TNF-alpha inhibitors, such as etanercept and infliximab, have been reported to be successful in treating SJS/TEN pediatric populations. These treatments have shown success both as monotherapy and in combination with IVIG, with IVIG and systemic corticosteroids, or with cyclosporine and systemic corticosteroids. A systematic review by Sachdeva et al. examined ten studies including 12 pediatric patients with a mean age of 9.5 years and mean body surface area involvement of 52.2%, all treated with TNF-alpha inhibitors for SJS/TEN.[9] The complete remission rates with infliximab and etanercept were 80% and 85.7%, respectively. Only one patient died (treated with infliximab and systemic corticosteroids) due to the severity of the disease. This mortality rate is lower than previously reported rates.[9]

SJS/TEN rarely occurs during pregnancy. While the effects of pregnancy on SJS/TEN are not well understood, it has been reported to have a milder course. The largest cohort study to date on SJS/TEN in pregnancy retrospectively identified 650 hospitalizations for SJS/TEN and compared them to pregnant patients admitted for reasons other than SJS/TEN. The findings were reassuring, showing milder disease and a higher survival rate compared to the general population with SJS/TEN. Additionally, apart from a higher preterm delivery rate, there was no difference in fetal outcomes, such as live birth and stillbirth. Risk factors for SJS/TEN in pregnancy included genitourinary infections, human immunodeficiency virus (HIV), herpes simplex virus (HSV), mycoplasma infection, malignancy, and cutaneous autoimmune conditions. Most episodes had occurred in the third trimester.[11]

Immune-check-point inhibitors (ICI), an emerging class of drugs for the treatment of cancer, have been found to have many potential cutaneous adverse reactions including SJS/TEN (<1% of reactions).[12] It is important for physicians to recognize that SJS/TEN induced by ICIs may have an atypical or blunted presentation. The latency period from drug initiation to eruption onset can span several months, and sudden desquamation may be preceded by a slowly progressing lichenoid or morbilliform eruption.[12] A 2023 retrospective cohort study looked at the differences between SJS/TEN induced by PD-1/PD-L1 inhibitors and those induced by gout and seizure medications. The study showed a delayed onset (4–7 weeks versus a 15-week median onset for PD-1/PD-L1 inhibitors). Additionally, the incidence was higher for PD-1/PD-L1 inhibitors (6.1 cases/10,000 starts in one year versus 1.9–2.8 cases/10,000 starts for other medications). Similar to studies with other drugs, non-white patients were more commonly affected. No significant difference in disease severity was identified.[13]

Molina et al. have proposed reclassifying these reactions as 'Progressive Immunotherapy Related Mucocutaneous Eruption (PIRME)' while others in the literature have referred to these reactions as 'TEN-like'.[14,15] In the PIRME concept introduces a '2-hit hypothesis' based on observations that all the patients in their case series first started an ICI and then had a second drug introduced. They suggest that the ICI reduces immune tolerance to the second drug, leading to a heightened sensitivity and development of a more severe eruption than would typically occur from a drug that would otherwise have had a more benign eruption. Given the '2-hit hypothesis', the group also proposed that in some situations, restarting the ICI may be considered.[14] There are reports of patients being rechallenged with ICIs without recurrence of the eruption; however, this approach must be taken with caution given the potentially life-threatening nature of SJS/TEN and the lack of evidence. Systemic therapies

reported for ICI-induced SJS/TEN reactions include corticosteroids, cyclosporine, and TNF-alpha inhibitors.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

DRESS is characterized by fever, rash (with typical facial edema), internal organ involvement, and the potential for subsequent onset of autoimmune disease. It is a potentially fatal type IVb hypersensitivity reaction primarily involving the activation of T helper 2 (Th2) lymphocytes and viral reactivation.[2,16]

Similar to SJS/TEN, high quality therapeutic studies for DRESS are lacking. The first step in management is drug discontinuation. If systemic therapy is required, corticosteroids remain the first-line treatment.[17] Steroid sparing agents with reported success include cyclosporine, IVIG, and anti-interleukin (IL-5) agents. Additionally, antiviral therapies may play a role in treatment based on the disease's pathophysiology if a viral reaction is suspected.

In the early stages of DRESS, the expansion of T-reg cells induces immunosuppression, which increases the risk of viral reactivation. Additionally, drugs such as valproic acid and amoxicillin can stimulate viral replication. Viruses that have been reported to have reactivated in DRESS include human herpesvirus 6 (HHV6), human herpesvirus 7 (HHV7), Epstein-Barr Virus, and cytomegalovirus.[17] Although the exact mechanism is unclear, viral reactivation in DRESS has been associated with a more severe disease course, prolonged disease, and severe internal organ involvement, as well as autoimmune sequelae such as myocarditis, hepatitis, and pancreatitis, among others. The viruses may modulate the immune response to the drugs or may directly infect and damage immune cells. If viral reactivation is suspected, antivirals such as intravenous ganciclovir or valganciclovir may be added to the more conventional systemic therapies for DRESS, which include systemic steroids, cyclosporine, or a combination of systemic steroids and IVIG.[17]

More recently JAK-STAT pathway activation has been identified in patients with DRESS and there have been case reports of tofacitinib successfully treating recalcitrant DRESS.[17,18]

Genetic polymorphisms are associated with increased risk of DRESS with specific drugs in specific populations. For many years, patients have been screened for *HLA-B5701* prior to initiating abacavir. Other organizations recommend screening for *HLA-3103* prior to initiating carbamazepine, *HLA-1301* prior to dapsone and *HLA-5801* prior to allopurinol. Additionally, *HLA-B*58:01* testing is routinely conducted in some Asian countries.[17]

An interesting article published in the *Journal of the American Academy of Dermatology* (JAAD) in 2024 pointed out the differences in the presentation of DRESS based on the culprit drug. Beta-lactams were found to have the shortest median latency, less than the classically reported 21 days, while allopurinol had the longest latency at 36 days. Sulfonamide-induced DRESS was almost always associated with a fever (87%), however, only 40% of patients exhibited eosinophilia. Cephalosporin-induced dress was found to have longer hospital stays with most patients requiring an ICU admission, whereas non-steroidal anti-inflammatory drug (NSAID)-induced DRESS had the shortest hospital stays. Cephalosporins and vancomycin had the highest fatality rates. Although vancomycin-induced DRESS is commonly known for renal involvement, this study found it is most commonly associated with liver involvement.[19]

Acute Generalized Exanthematous Pustulosis (AGEP)

AGEP is estimated to occur in 1–5 individuals per million each year and is characterized by an abrupt onset of numerous sterile pustules accompanied by erythema, typically appearing with a short latency period following antibiotic use. After antibiotics, hydroxychloroquine is the second most common culprit, with some cases presenting a delayed onset.[20] AGEP is felt to be a T-cell mediated disease in which CD8+ lymphocytes produce large quantities of IL-8. More recently, IL-36 has been implicated in its pathogenesis.[21] AGEP generally has a good prognosis, typically self-resolving in a couple of weeks, except in

the elderly or chronically ill patients. It is more commonly observed in women and patients with a higher body mass index.[20] A localized variant of AGEP, known as acute localized exanthematous pustulosis (ALEP), has been reported. In ALEP, the eruption is localized to one or a couple of locations, most often the face. This variant follows a similar time course and is triggered by the same drugs (most commonly antibiotics), however, it is less likely to have systemic involvement.[20]

If systemic treatment is required, oral corticosteroids are typically used first; however, cyclosporine has demonstrated similar efficacy. In recalcitrant cases, secukinumab and infliximab have been reported as successful options. Since 2024, there have been two case reports of AGEP being successfully treated with the anti-IL-36 receptor monoclonal antibody spesolimab.[21,22]

Generalized Bullous Fixed Drug Eruption (GBFDE)

GBFDE is commonly associated with the use of NSAIDs. While it can resemble SJS/TEN, diagnostic clues include the presence of islands of normal skin, previous exposures to the drug with milder reactions, shorter latency periods, milder mucosal involvement, and typically no ocular involvement.[2,23]

Conclusion

SCARs remain among the most critical and challenging conditions for dermatologists to manage. With the rapid development of new therapies, including immunotherapies, the clinical patterns of these reactions are evolving. Dermatologists must stay abreast of these changes to ensure safe, effective, and comprehensive patient care. The presentation of drug reactions can vary significantly depending on the offending agent and patient-specific factors. Despite advances in our understanding of these syndromes, there is still no consensus regarding the optimal first-line systemic therapies. Notably, JAK inhibitors have emerged as promising therapeutic candidates for severe drug reactions such as SJS, TEN, and DRESS, although further clinical studies are needed to validate their safety and efficacy.

Highlights

SJS/TEN

- Mainstay of care remains **early drug withdrawal + supportive measures.**
- Etanercept shows promising efficacy (faster healing, fewer gastrointestinal side effects versus corticosteroids).
- **JAK inhibitors** are emerging as a new therapeutic option with mechanistic support via JAK/STAT activation.

DRESS

- **HHV-6, HHV-7, EBV, CMV** are often reactivated—antiviral therapy should be considered.
- Genetic markers: *HLA-B57:01* (abacavir), *HLA-B58:01* (allopurinol), and others depending on the population.
- JAK inhibitors are also being explored for **recalcitrant DRESS**.

AGEP

- **IL-36** is emerging as a central cytokine; **spesolimab** (IL-36R antagonist) has shown early success in 2024 case reports.
- **Hydroxychloroquine**-induced cases may have longer latency.
- ***Localized variant:*** **ALEP** (e.g., facial involvement without systemic disease).

GBFDE

- Can mimic SJS/TEN.
- ***Key clues:*** islands of skin-sparing, milder mucosal/ocular involvement, prior mild episodes to same drug.

ICI-Induced Reactions / PIRME

1. May present as **blunted SJS/TEN**, with delayed onset, preceded by lichenoid eruptions.
2. "2-hit hypothesis": immune checkpoint inhibition followed by a second drug triggers SCAR.
3. Potential rechallenge with ICIs in very selected cases.

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Financial Disclosures

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References

1. Gibson A, Deshpande P, Campbell CN, Krantz MS, Mukherjee E, Mockenhaupt M, et al. Updates on the immunopathology and genomics of severe cutaneous adverse drug reactions. J Allergy Clin Immunol. 2023;151(2):289-300.e284. doi:10.1016/j.jaci.2022.12.005
2. Hung SI, Mockenhaupt M, Blumenthal KG, Abe R, Ueta M, Ingen-Housz-Oro S, et al. Severe cutaneous adverse reactions. Nat Rev Dis Primers. 2024;10(1):30. doi:10.1038/s41572-024-00514-0
3. Ubukata N, Nakatani E, Hashizume H, Sasaki H, Miyachi Y. Risk factors and drugs that trigger the onset of Stevens-Johnson syndrome and toxic epidermal necrolysis: a population-based cohort study using the Shizuoka Kokuho database. JAAD Int. 2023;11:24-32. doi:10.1016/j.jdin.2022.12.002
4. Nordmann TM, Anderton H, Hasegawa A, Schweizer L, Zhang P, Stadler PC, et al. Spatial proteomics identifies JAKi as treatment for a lethal skin disease. Nature. 2024;635(8040):1001-1009. doi:10.1038/s41586-024-08061-0
5. Zimmermann S, Sekula P, Venhoff M, Motschall E, Knaus J, Schumacher M, et al. Systemic immunomodulating therapies for Stevens-Johnson syndrome and toxic epidermal necrolysis: a systematic review and meta-analysis. JAMA Dermatol. 2017;153(6):514-522. doi:10.1001/jamadermatol.2016.5668
6. Wang CW, Yang LY, Chen CB, Ho HC, Hung SI, Yang CH, et al. Randomized, controlled trial of TNF-α antagonist in CTL-mediated severe cutaneous adverse reactions. J Clin Invest. 2018;128(3):985-996. doi:10.1172/jci93349
7. Tsai TY, Huang IH, Chao YC, Li H, Hsieh TS, Wang HH, et al. Treating toxic epidermal necrolysis with systemic immunomodulating therapies: a systematic review and network meta-analysis. J Am Acad Dermatol. 2021;84(2):390-397. doi:10.1016/j.jaad.2020.08.122
8. Ao S, Gao X, Zhan J, Ai L, Li M, Su H, et al. Inhibition of tumor necrosis factor improves conventional steroid therapy for Stevens-Johnson syndrome/toxic epidermal necrolysis in a cohort of patients. J Am Acad Dermatol. 2022;86(6):1236-1245. doi:10.1016/j.jaad.2022.01.039
9. Jacobsen A, Olabi B, Langley A, Beecker J, Mutter E, Shelley A, et al. Systemic interventions for treatment of Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and SJS/TEN overlap syndrome. Cochrane Database Syst Rev. 2022;3(3):Cd013130. doi:10.1002/14651858.CD013130.pub2
10. Tonkin R, Ladha M, Johnson N, Astle WF, Britton A, Shear NH, et al. Reactive infectious mucocutaneous eruption - repeat etanercept after intravenous immunoglobulin: a case report. SAGE Open Med Case Rep. 2022;10:2050313×221117887. doi:10.1177/2050313×221117887
11. Wasuwanich P, Egerman RS, Wen TS, Motaparthi K. A nationwide study of Stevens-Johnson syndrome and toxic epidermal necrolysis in hospitalized pregnant women in the United States, 2009-2020. JAAD Int. 2024;16:175-182. doi:10.1016/j.jdin.2024.04.002
12. Quach HT, Johnson DB, LeBoeuf NR, Zwerner JP, Dewan AK. Cutaneous adverse events caused by immune checkpoint inhibitors. J Am Acad Dermatol. 2021;85(4):956-966. doi:10.1016/j.jaad.2020.09.054
13. Chen A, Kolodney JA, Kolodney MS. Retrospective cohort study characterizing PD-1/PD-L1 checkpoint inhibition associated Stevens-Johnson syndrome and toxic epidermal necrolysis. J Am Acad Dermatol. 2024;91(5):948-949. doi:10.1016/j.jaad.2024.06.066
14. Molina GE, Yu Z, Foreman RK, Reynolds KL, Chen ST. Generalized bullous mucocutaneous eruption mimicking Stevens-Johnson syndrome in the setting of immune checkpoint inhibition: a multicenter case series. J Am Acad Dermatol. 2020;83(5):1475-1477. doi:10.1016/j.jaad.2020.03.029
15. Driscoll W, Yale K, Smith J. A case of pembrolizumab-induced toxic epidermal necrolysis with a delayed developmental timeline. JAAD Case Rep. 2024;53:27-29. doi:10.1016/j.jdcr.2024.08.011
16. Hama N, Abe R, Gibson A, Phillips EJ. Drug-induced hypersensitivity syndrome (DIHS)/drug reaction with eosinophilia and systemic symptoms (DRESS): clinical features and pathogenesis. J Allergy Clin Immunol Pract. 2022;10(5):1155-1167.e1155. doi:10.1016/j.jaip.2022.02.004
17. Wei BM, Fox LP, Kaffenberger BH, Korman AM, Micheletti RG, Mostaghimi A, et al. Drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms. Part I. Epidemiology, pathogenesis, clinicopathological features, and prognosis. J Am Acad Dermatol. 2024;90(5):885-908. doi:10.1016/j.jaad.2023.02.072
18. Kim D, Kobayashi T, Voisin B, Jo JH, Sakamoto K, Jin SP, et al. Targeted therapy guided by single-cell transcriptomic analysis in drug-induced hypersensitivity syndrome: a case report. Nat Med. 2020;26(2):236-243. doi:10.1038/s41591-019-0733-7
19. Blumenthal KG, Alvarez-Arango S, Kroshinsky D, Lo YC, Samarakoon U, Salem AR, et al. Drug reaction eosinophilia and systemic symptoms: clinical phenotypic patterns according to causative drug. J Am Acad Dermatol. 2024;90(6):1240-1242. doi:10.1016/j.jaad.2023.05.067
20. Parisi R, Shah H, Navarini AA, Muehleisen B, Ziv M, Shear NH, et al. Acute generalized exanthematous pustulosis: clinical features, differential diagnosis, and management. Am J Clin Dermatol. 2023;24(4):557-575. doi:10.1007/s40257-023-00779-3
21. Russo G, Dumont S, Menzinger S, Pastor D, Toutous Trellu L, Kaya G, et al. Severe acute generalized exanthematous pustulosis successfully treated by spesolimab. Acta Derm Venereol. 2024;104:adv41311. doi:10.2340/actadv.v104.41311
22. Xuan Y, Jin S, Zhang C, Wang S. Rapid improvement in refractory acute generalized exanthematous pustulosis with spesolimab. JAMA Dermatol. 2024;160(9):1009-1012. doi:10.1001/jamadermatol.2024.2311
23. Paulmann M, Reinkemeier F, Lehnhardt M, Mockenhaupt M. Case report: generalized bullous fixed drug eruption mimicking epidermal necrolysis. Front Med (Lausanne). 2023;10:1125754. doi:10.3389/fmed.2023.1125754

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Cicatricial Alopecias and the Role of Janus Kinase Inhibitors: A Novel Approach and Comprehensive Overview to a Challenging Problem

Marisa G. Ponzo, MD-PhD, FRCPC, FAAD

Cicatricial alopecias (CAs) represent a group of conditions that result in permanent hair loss due to the destruction of hair follicles and their replacement with scar tissue. Recently, Janus kinase (JAK) inhibitors have emerged as potential treatments for various alopecias, including scarring types. In this review, we will discuss CAs, their pathophysiology, diagnosis, and the evolving role of JAK inhibitors in their treatment.

Pathophysiology of Cicatricial Alopecia

The prevalence of cicatricial alopecias (CAs) is growing and is estimated to account for 7% of all alopecia cases.[1] These conditions include frontal fibrosing alopecia (FFA), lichen planopilaris (LPP), central centrifugal cicatricial alopecia (CCCA), discoid lupus erythematosus (DLE), and folliculitis decalvans. However, for the purpose of this review, we will focus on FFA, LPP and CCCA. Unlike non-CAs (e.g., alopecia areata, androgenetic alopecia, telogen effluvium), CAs result in irreversible follicular damage due to lymphocytic attack of the follicular bulge and scar tissue

formation, which prevents hair from regrowing due to irreversible damage to epithelial stem cells. Early diagnosis and treatment are imperative to help prevent scarring and the associated psychological burden.

The clinical presentation of CAs varies depending on the specific condition. However, patients will typically present with gradual hair loss, scarring, inflammation, perifollicular erythema, perifollicular hyperkeratosis, and follicular plugging. They may experience scalp dysesthesia and pruritus. The areas of the scalp affected develop shiny, smooth patches without visible follicular ostia. FFA primarily affects postmenopausal women and causes eyebrow loss and recession of the frontal hair line. Although distinct, LPP is thought to share an overlapping pathology and hence similar histological findings. LPP affects all genders and age groups, resulting in patchy hair loss throughout the scalp. Patients with LPP may experience more pruritis and scalp dysesthesia due to inflammation compared to those with FFA. CCCA is primarily observed in Afro-American women, and results in hair loss and tenderness at the vertex of the scalp.

The inflammatory process is central to the pathogenesis of these conditions. Some insights of this complex pathophysiological process can be gleaned. The inflammatory pathway is thought to involve the upregulation of T helper (Th) 1/interferon (IFN) g and fibrosis-related markers.[2-3] Studies have shown that the Th1 and Janus Kinase (JAK)/signal transducers and activators of transcription (STAT) pathways are upregulated in FFA.[4] Lesional skin of patients with CAs has shown enhanced fibrosis and STAT pathway-related genes.[5]

JAK Inhibitors: Mechanism of Action and Role in Cicatricial Alopecia

Treating CAs is challenging and aims to control inflammation and prevent further hair loss. Currently, there are no treatments approved by Health Canada or the Food and Drug Administration. While in-depth review of standard treatment protocols for CAs is reviewed elsewhere,[6] the focus of this review is on the novel use of JAK inhibitors (JAKi) for this condition. Previous treatment paradigms have shown inconsistent efficacy, which highlights an area of unmet need for CA therapies.

JAKi are a class of medications that target specific intracellular signalling pathways crucial for the immune response. JAKs are enzymes that mediate the activity of cytokines involved in immune responses. Specifically, they are critical for the signalling of interleukins and interferons, which are implicated in inflammation and autoimmunity. The most well-known JAKi include tofacitinib, ruxolitinib, upadacitinib, abrocitinib, and baricitinib. These medications are approved and are commercially available for other dermatologic conditions, namely nonsegmental vitiligo, atopic dermatitis, and alopecia areata. By blocking the signalling of pro-inflammatory cytokines, they help reduce the immune-mediated inflammation observed in various conditions, including autoimmune skin diseases such as alopecia. In conditions such as CAs, particularly those with autoimmune or inflammatory mechanisms such as LPP and DLE, JAKi have shown promise as novel treatments due to their ability to target the inflammatory pathways directly.

Clinical Evidence for JAK Inhibitors in Cicatricial Alopecias

Data from retrospective analyses, case series, and case reports show promising results in blocking the JAK pathway for CAs. Several clinical trial programs are underway to provide larger-scale datasets.

Interestingly, some early studies have reported the use of topical JAKi as an effective treatment option for CAs. Given the potential toxicity of systemic JAKi, this offers a valuable addition to our treatment armamentarium. A retrospective chart review with 41 patients demonstrated that topical tofacitinib, a JAK-1/3 inhibitor, applied as a 2% cream twice daily in patients with LPP and FFA, resulted in a 48% decrease in the Lichen Planopilaris Activity Index (LPPAI) score at 9 months.[6]

In 2024, Desai et al. published a case study on the use of topical ruxolitinib 1.5% cream in a 55-year-old male with FFA.[7] Ruxolitinib is a selective JAK1 and JAK2 inhibitor, approved in Canada and the US for treating atopic dermatitis and nonsegmental vitiligo. In this case report, the patient presented with a 4-year history of frontal hairline tenderness and recession, followed by eyebrow pruritus and loss, along with facial papules. The patient applied topical ruxolitinib 1.5% cream generously to the frontal scalp/forehead for 3 months. He reported an improvement in pain, stabilization of his frontal hair line, and resolution of his facial papules. These findings were confirmed by clinical evaluation and trichoscopy. A case series in 2023 has shown similar findings.[8] In 2025, a retrospective cohort study showed an average 34% improvement in the LPPAI after a mean usage period of 8.5 months.[9]

In a phase 2a randomized clinical trial, patients with CA (LPP/FFA/CCCA) were randomized in a 3:1 ratio to receive either brepocitinib, an oral JAK1/2 inhibitor, at a dose of 45 mg once daily for 24 weeks or a placebo. After this period, all participants were re-randomized to receive brepocitinib for another 24 weeks.[10] The coprimary endpoints were changes in lesional expression of C-C motif chemokine ligand (CCL5), changes in lesional expression of fibrosis-related markers, and safety at week 24. Patients receiving brepocitinib showed significant downregulation of CCL5 expression at week 24. Analysis of placebo patient data showed an enrichment of fibrosis-related markers. Brepocitinib was well tolerated. Key secondary clinical efficacy outcomes showed significantly improved clinical severity scores. Patients with LPP receiving brepocitinib showed a significant mean percent change in LPPAI of -51% (90% confidence interval [CI], -79.5, to -30.2) compared to baseline at week 24. Further improvement was noted at week 48 with a mean percent change of -79.2% (90% CI, -100 to -53.6). Similar improvements were noted in the FFA and CCCA groups. Phase III trials are underway and are expected to be informative.

Overall, emerging evidence suggests a role for JAKi in the treatment of CAs. However, it remains uncertain whether the results can be maintained once topical or systemic JAKi are discontinued.

Challenges and Future Directions

While JAKi show promise as a treatment option for CAs, several challenges and areas for further investigation remain. JAKi can cause side effects, including immunosuppression, which can increase the risk of infections, and potential adverse effects on cholesterol and liver function. The long-term effectiveness of JAKi for CAs is still under study. Given the chronic nature of many CAs, ongoing trials are essential to assess whether JAKi can provide sustained benefits. Due to the heterogeneous nature of CAs, personalized treatment approaches, including the use of JAKi, need to be tailored to each patient's specific condition and response to therapy.

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References

1. Whiting DA. Cicatricial alopecia: clinico-pathological findings and treatment. Clin Dermatol. 2001;19(2):211-225. https://doi.org/10.1016/s0738-081x(00)00132-2
2. Meyer KC, Tiede S, Harries MJ, Kloepper JE, Paus R. IFN-gamma induces bulge immunoprivilege collapse and may cause epithelial stem cell exhaust. J Invest Dermatol. 2010;130:S42-S42.
3. Moretti S, Amato L, Massi D, Bianchi B, Gallerani I, Fabbri P. Evaluation of inflammatory infiltrate and fibrogenic cytokines in pseudopelade of Brocq suggests the involvement of T-helper 2 and 3 cytokines. Br J Dermatol. 2004;151(1):84-90. doi:10.1111/j.1365-2133.2004.05976.x
4. Del Duca E, Ruano Ruiz J, Pavel A, Sanyal RD, Song T, Gay-Mimbrera J, et al. Frontal fibrosing alopecia shows robust T helper 1 and Janus kinase 3 skewing. Br J Dermatol. 2020;183(6):1083-1093. doi:10.1111/bjd.19040
5. Dubin C, Glickman JW, Del Duca E, Chennareddy S, Han J, Dahabreh D, et al. Scalp and serum profiling of frontal fibrosing alopecia reveals scalp immune and fibrosis dysregulation with no systemic involvement. J Am Acad Dermatol. 2022;86(3):551-562. doi:10.1016/j.jaad.2021.05.016
6. Chen LC, Ogbutor C, Kelley KJ, Senna MM. Topical tofacitinib for patients with lichen planopilaris and/or frontal fibrosing alopecia. J Am Acad Dermatol. 2024;90(6):1260-1262. doi:10.1016/j.jaad.2024.01.060
7. Desai D, Nohria A, Lo Sicco K, Shapiro J. The use of topical ruxolitinib 1.5% cream in frontal fibrosing alopecia: a case report. JAAD Case Rep. 2024;50:141–143. doi: 10.1016/j.jdcr.2024.04.034
8. Dunn C, Griffith V, Coican A, Dane A, Chow W, Aneja S, et al. Janus kinase inhibition for the treatment of refractory frontal fibrosing alopecia: a case series and review of the literature. JAAD Case Rep. 2023; 40:47-52. doi:10.1016/j.jdcr.2023.07.037
9. Williams KN, Perez SM, Burroway B, Tosti A. Topical ruxolitinib in the management of frontal fibrosing alopecia and/or lichen planopilaris: a single-center retrospective cohort study. J Am Acad Dermatol. 2025;92(1):170-172. doi: 10.1016/j.jaad.2024.09.032.
10. David E, Shokrian N, Del Duca E, Meariman M, Dubin C, Hawkins K, et al. A phase 2a trial of brepocitinib for cicatricial alopecia. J Am Acad Dermatol. 2024 Oct 24:S0190-9622(24)03043-3. doi: 10.1016/j.jaad.2024.09.073.

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