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REVIEW ARTICLE

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Malassezia-associated skin diseases in the pediatric population

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Abstract

Malassezia are yeast species that commonly colonize healthy skin. However, they have been associated with or implicated in the pathogenesis of numerous skin disorders, particularly in the setting of pediatric populations. In this review, we will focus on several *Malassezia*-associated skin conditions manifesting in infants, children, and adolescents: pityriasis versicolor, *Malassezia* folliculitis, infantile and adolescent seborrheic dermatitis, head and neck dermatitis, and neonatal cephalic pustulosis. We examine the literature and provide an overview of these conditions, including clinical presentation in diverse skin colors, diagnosis, risk factors, and treatment and management. Additionally, we summarize and highlight some of the proposed theories on the role of *Malassezia* spp. in the pathogenesis of these skin conditions.

KEYWORDS
head and neck dermatitis, *Malassezia*, *Malassezia* folliculitis, pityriasis versicolor, seborrheic dermatitis

1 | INTRODUCTION

The human skin microbiota encompass a diverse set of commensal microorganisms that inhabit the skin.[1] Microbial diversity of bacteria and fungi have been implicated in the stability and maintenance of the skin.[1] *Malassezia* is a lipophilic yeast of particular interest as it is the most abundant fungal genus present on healthy skin of nearly all body areas.[1] The colonization period is theorized to begin soon after birth.[1–3] A study done in Japan revealed that *Malassezia* spp. were detected in 89% of 27 neonate samples on Day 0 and 100% of the samples on day 1. At least 14 species have been classified within the *Malassezia* genus, and 8 of them have been isolated in humans.[2] *Malassezia restricta* and *Malassezia globosa* predominate at the species level for both infants and adults.[2,3]

Both composition and distribution of *Malassezia* spp. in healthy skin can vary significantly based on age, gender, and geography.[2] However, alterations in the skin microbiome involving *Malassezia* spp. have also been linked with several dermatological disorders, most prominently in hot and humid environments.[2] The warmth and moisture provide a favorable environment for *Malassezia* proliferation.[4] Additionally, the lipophilicity of *Malassezia* spp. accounts for their tendency to distribute on sebum-rich areas of the skin such as the scalp and face.[2] Host factors, including immunosuppression, antibiotic usage, and underlying disorders such as diabetes, can impact the incidence and prevalence of skin conditions associated with *Malassezia* spp.[2] This review will provide an overview of common skin disorders in the pediatric population in which *Malassezia* may play a role in pathogenesis: pityriasis versicolor (PV), *Malassezia* folliculitis (MaF), seborrheic dermatitis (SD), head and neck dermatitis (HND), and neonatal cephalic pustulosis (NCP, Table 1). We will also explore current treatment regimens (Table 2), and examine the proposed theories and controversies surrounding *Malassezia*'s role in each condition.

2 | PITYRIASIS VERSICOLOR

PV, also known as tinea versicolor, is a superficial fungal infection of the skin caused by *Malassezia* spp.[5] The term "versicolor" refers to

TABLE 1 Summary of selected *Malassezia*-associated skin conditions.

Skin condition	Patient demographics	Skin presentation and distribution	Key differential diagnoses	Risk factors
Pityriasis versicolor	More common in adolescents than children[5,6]	Pink, hypo- or hyperpigmented macules and patches with fine scale.[5] Affects trunk, neck, and proximal upper extremities; hairline in infants and children	Vitiligo, pityriasis alba, confluent and reticulated papillomatosis, pityriasis rosea[5]	Hot, humid weather[7]; diabetes, pregnancy, immunosuppression[5]
Malassezia folliculitis	Adolescents, more common in males[8]	Pruritic follicular monomorphic papules and pustules on the chest, shoulders, and back[8]; rarely scalp and hairline	Acne vulgaris,[8] keratosis pilaris, bacterial folliculiti	Hot, humid weather; increased sebum production, sweating, antibiotic usage, and immunocompromise[9]
Infantile seborrheic dermatitis	Infants, generally onset by 3–6 months[10]	Thick, greasy white or yellow scales with underlying erythema distributed on the scalp, face, and less often torso.[10] Skin folds with bright erythema. Notable postinflammatory hypopigmentation in skin of color	Atopic dermatitis, inverse psoriasis	Maybe increased sebaceous activity in neonatal period or other host factors[9,11]
Adolescent seborrheic dermatitis	Adolescents; rarely in preadolescent children	Variable presentation. Ranges from dry flaky scalp (dandruff) to greasy adherent scalp scale with or without underlying erythema; erythematous to violaceous to hypopigmented scaly plaques on face, ears, neck, chest[10]	Psoriasis, atopic dermatitis, rosacea, lupus erythematosus[10]	Increased sebum production and other host factors[10,12]
Head and neck dermatitis	Adolescents mostly[13]	Scaly, eczematous plaques with erythema on the scalp, face, neck, and upper chest[14]	Rosacea, atopic dermatitis, seborrheic dermatitis, contact dermatitis[15]	Elevated IgE against *Malasseziae*,[14] dupilumab usage[15]
Neonatal cephalic pustulosis	Onset within the first 3 weeks of life[16]	Pustules and small papules with variable erythema on cheeks, chin, forehead, scalp, and neck[16]	Miliaria pustulosa, pustular psoriasis, folliculitis, neonatal herpes simplex[16]	Host factors in the setting of presumed increased maternal androgen and sebum production driving *Malassezia* growth[16–18]

the variability in the color of the skin lesions. The eruption is usually asymptomatic, though pruritus may accompany the skin findings.[5] Multiple hypo- or hyperpigmented coalescing rounded macules and patches with fine scale are typically distributed on the trunk, neck, and proximal upper extremities, and less commonly on the face, axillae, groin, and scalp.[5] The lighter the background skin pigmentation, the more pink or "salmon-colored" the patches appear (Figure 1).[7] In more darkly pigmented skin, the patches vary between hypopigmented and hyperpigmented against the background skin color (Figure 2A,B).[32] The predilection for specific areas of the body is a result of the increased sebum production in these regions, which harbor the lipophilic *Malassezia* spp, and varies by age group.[5] While typically more prevalent in adolescents and young adults due to increased sebum production generally, PV can also present in infants and children, though more often limited to along the hairline on the face and neck.[6] PV is more common during the summer season and may account for up to 40% of pediatric skin infections in tropical regions.[5] Other factors increasing the incidence of PV include pregnancy, diabetes, immunosuppression, and the use of systemic corticosteroids.

Wood lamp examination may aid diagnosis with hypopigmented lesions fluorescing gold-yellow or green—sometimes beyond the visible boundaries, indicating spreading involvement.[5] However, it is important to note that lesions may not reliably fluoresce, possibly due to recent bathing. Dermoscopy is another useful tool that may reveal a "contrast halo" sign with either a hyperpigmented ring surrounding a primary hypopigmented lesion or a hypopigmented ring surrounding a primary hyperpigmented lesion.[5] The differential diagnosis depends on the presentation. In the setting of hypopigmented lesions, diagnoses such as vitiligo, pityriasis alba, progressive macular hypomelanosis and postinflammatory hypopigmentation may be considered. In the setting of hyperpigmented lesions, it may be important to distinguish other inflammatory conditions including confluent and reticulated papillomatosis, tinea corporis, and pityriasis rosea.

TABLE 2 Treatment regimens for selected *Malassezia*-associated skin conditions.

Skin Condition	Treatment Regimen	Prevention
Pityriasis versicolor	• Ketoconazole 2% cream once daily for 2 weeks OR Selenium sulfide 2.5% lotion on affected areas for 10 min once daily for 2 weeks OR topical terbinafine 1% cream once daily for 2 weeks[5,19,20] • Fluconazole 300 mg once weekly for 2–4 weeks[5]	• Ketoconazole 2% shampoo monthly[5] • Two doses of oral itraconazole 200 mg taken 12 h apart once a month[5]
Malassezia folliculitis	• Ketoconazole 2% cream twice daily for 4 weeks OR Ketoconazole 2% wash every other day for 2–3 months[11,21–23] • Oral fluconazole 100–200 mg daily for 1–3 weeks[3]	• Ketoconazole 2% wash twice weekly[9,12]
Infantile seborrheic dermatitis	• *Scalp*: Mineral oil and petroleum jelly to loosen scales and gently remove with infant hairbrush or cloth.[24] • *Nonscalp area*: keep skin folds as dry as possible; if severely inflamed, low potency topical corticosteroid (hydrocortisone 1%–2.5% cream or ointment) and/or ketoconazole cream for 1–2 weeks[25,43]	• Self-limited
Adolescent seborrheic dermatitis	• *Scalp*: Ketoconazole 1%–2% shampoo twice weekly for 1 month[19] or as foam for coily or curly hair[26] • *Nonscalp area*: ketoconazole 2% cream twice daily for 4 weeks and as needed[19] • Short Courses (1–2 weeks) of topical corticosteroids (e.g., clobetasol, fluocinonide, fluocinolone, hydrocortisone) to relieve severe itch and scaling[27]; vehicle can be adjusted to patient preferences • Roflumilast foam 0.3% once daily for 8 weeks[26]	• Ketoconazole 2% shampoo once weekly[28]
Head and neck dermatitis	• Oral fluconazole 150 mg weekly for 2–4 weeks[15] • Topical calcineurin inhibitors (e.g., pimecrolimus 1% and tacrolimus 0.03% or 0.1%) twice daily or as needed[29,30]	• Topical calcineurin inhibitors (e.g. pimecrolimus 1% and tacrolimus 0.03% or 0.1%) twice daily or as needed[29,30]
Neonatal cephalic pustulosis	• Self-limited; topical ketoconazole 2% cream twice daily for one week[31]	• Self-limited

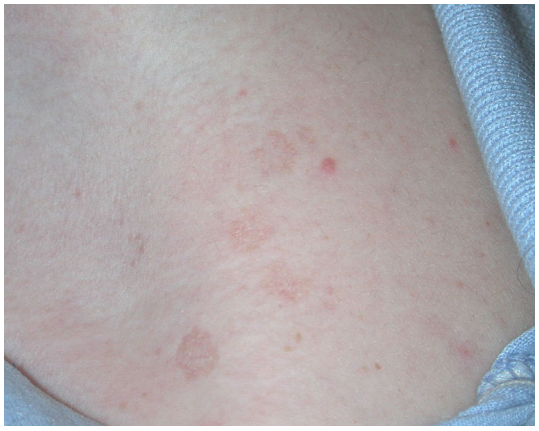

FIGURE 1 Salmon-colored plaques of pityriasis versicolor on a 13-year-old.

The causal relationship between *Malassezia* spp. and PV is suggested by the presence of *Malassezia* on cultured samples taken from lesional PV skin.[5,7] *Malassezia* spp. are grown more consistently in cultures taken from lesional skin of PV compared with cultures from the skin of matched healthy controls.[7] The yeast can be identified under direct microscopy of superficial scrapings from skin lesions, appearing in the characteristic "spaghetti and meatballs" configuration.[5] This pattern illustrates the clusters of yeast spores mixed with short pseudohyphae (Figure 3). *Malassezia globosa* is the predominant species detected in culture studies of lesional skin, isolated in more than 90% of PV patients.[7] *Malassezia sympodialis* and *Malassezia furfur* have also been identified in these cultures.[7]

The conversion of yeast into the filamentous phase is suggested to play a pathogenic role in PV, contributing to the discoloration that characterizes the disorder.[5,7,33] There are several proposed mechanisms for the pigmentary changes. Dicarboxylic acids produced by *Malassezia* spp. act as competitive inhibitors to tyrosinase, interfering with melanin synthesis.[5,34] Furthermore, pityriacitrin produced by *M. furfur* may act as a UV filter, causing the appearance of hypopigmented lesions in tanned skin.[34] Theories to explain the brown or hyperpigmented presentation include an increased thickness of the keratin layer, and the effect of an inflammatory response to the organism, stimulating pigment formation, similar to postinflammatory hyperpigmentation.[34]

PV has an excellent response to treatment, though normalization of the pigmentary changes is a gradual process even after successfully eradicating the yeast.[35] Topical antifungal agents can provide successful outcomes when the eruption is limited in extent. Ketoconazole 2% cream once daily for 2 weeks has a clearance rate of 80%–90% based on a systematic review including seven studies with 689 participants.[19] Selenium sulfide 2.5% lotion on affected areas for 10 min

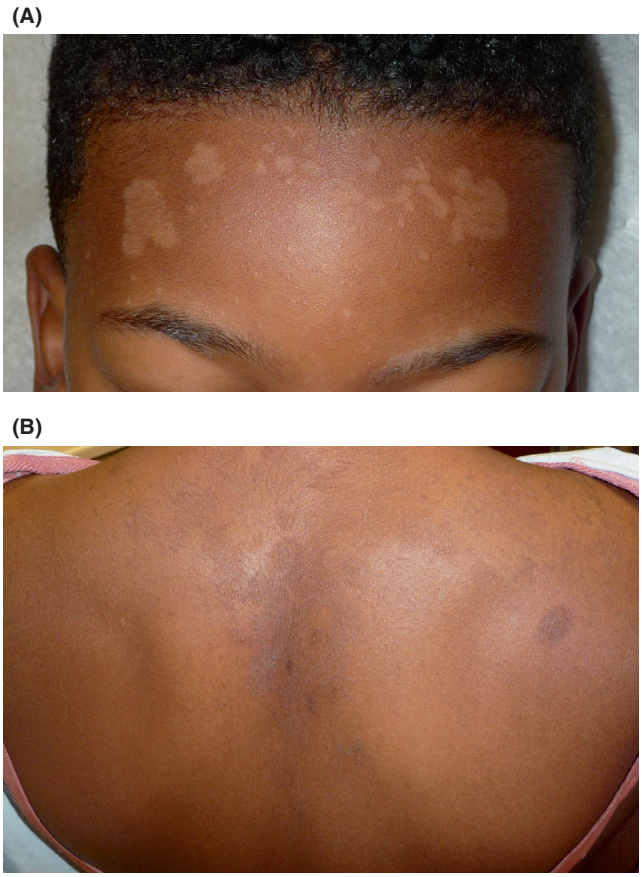

FIGURE 2 (A) Hypopigmented lesions of pityriasis versicolor on a 6-year-old. (B) Hyperpigmented lesions of pityriasis versicolor on a 13-year-old.

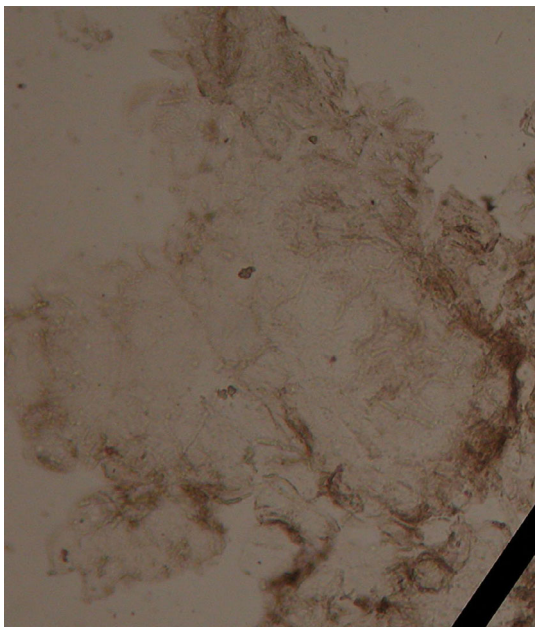

FIGURE 3 KOH prepared skin scrapings of pityriasis versicolor demonstrating pseudohyphae (spaghetti) and round spores (meatballs).

daily for 2 weeks has also been considered a longstanding, effective treatment measure.[20] Additionally, terbinafine 1% cream once daily for 2 weeks has shown comparable efficacy and a lower recurrence rate compared with ketoconazole 2% cream.[5]

Oral fluconazole 300 mg once weekly for 2–4 weeks or oral itraconazole 200 mg daily for 5–7 days may also be considered for extensive skin involvement or lesions refractory to topical therapy.[5] Fluconazole is generally considered as first choice systemic therapy due to the adverse side effect profile of itraconazole and black box warning for congestive heart failure. It is important to note that oral terbinafine is not effective against PV due to its inability to reach effective concentrations in the stratum corneum.[5] Although treatments are quite effective, the relapse rate for PV is high, with many relapses noted during the summer months. Topical agents, such as ketoconazole 2% shampoo applied to the body, may be useful as preventative treatment when applied on a regular monthly schedule.[5] Finally, improving overall hygiene, such as bathing daily to every other day when sweating significantly, may also play a role in controlling reoccurrences. It is important to remind patients that the pigmentary changes will resolve gradually over several weeks to months after treatment is complete, with skin of color often requiring a longer time to achieve pigmentary normalization. Consequently, frequently recurrent cycles of PV can make it difficult to regain baseline skin pigmentation.

2.1 | *Malassezia* folliculitis

MaF, previously known as pityrosporum folliculitis, also commonly affects adolescents and has a well-established relationship with *Malassezia* spp., including *M. globosa*, *M. sympodialis*, *M. restricta*, and *M. furfur*.[36] In 1969, Weary et al.[37] first described MaF as an acneiform eruption in response to antibiotic usage. The eruption consists of a relatively sudden onset of numerous small, monomorphic follicular papules intermixed with small pustules most commonly distributed on the chest, shoulders, and back (Figure 4A,B).[8] The scalp, hairline, upper arms, and neck can also be involved. Pruritus is a key feature noted in a majority of patients with MaF.[21]

The pathogenesis appears to stem from disruptive mechanisms affecting the pilosebaceous unit.[9] It is proposed that initial occlusion of the hair follicle allows for subsequent overgrowth of *Malassezia* yeast, leading to an inflammatory response to yeast metabolites.[8,9] Predisposing factors include increased sebum production, sweating, skin dysbiosis from antibiotics, and immunocompromise.[8] Systemic steroid treatment courses for other conditions may also precipitate an eruption.[8] Similar to PV, MaF flares are also associated with hot and humid climates, occurring more often in the summer months.[9] These factors are suspected to favor proliferation of *Malassezia* yeast and associated inflammation, resulting in follicular papules and pustules. The higher prevalence in teens, especially males, may be reflective of the increased activity of sebaceous glands during adolescence.[8]

In light of the distribution, patient population, and morphology, MaF is often misdiagnosed as acne vulgaris (AV).[8] Features that

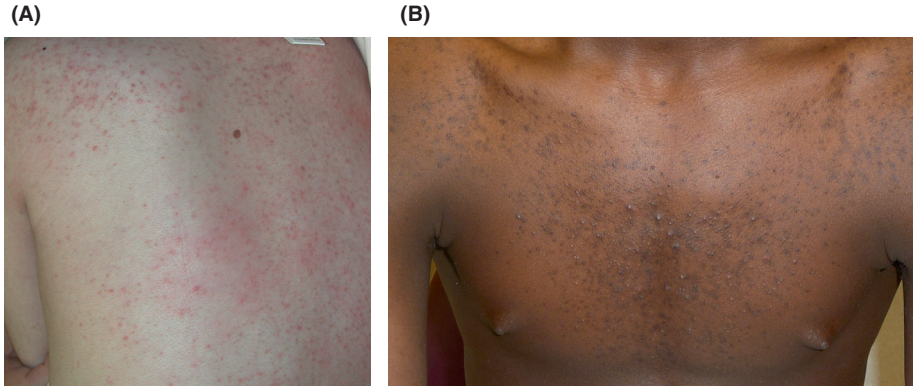

FIGURE 4 (A) Malassezia folliculitis on the back of a pediatric patient. (B) Malassezia folliculitis on the chest of a 13-year-old.

distinguish MaF from AV include the lack of comedones and cysts, presence of frontal hairline and scalp involvement without central facial involvement and the presence of pruritus. However, MaF can also coexist in the setting of AV, complicating the diagnosis and treatment.[21,38] A study that sampled the contents of pustules and papules from patients clinically diagnosed with AV revealed that 79 out of 320 (24.7%) AV patients had methylene blue-stained cytology smears demonstrating high density of *Malassezia* spores and bacillus bacteria, suggesting the coexistence of MF and AV.[38] Given that high sebum production and follicular occlusion predisposes to both conditions, it is not unexpected to have a combined presentation.[21] Additionally, the antibiotic treatments frequently used to treat AV may contribute to a shift in the microbiome allowing for excess proliferation of *Malassezia* species.[8]

Other differential diagnoses to consider in the setting of a pruritic, papulopustular eruption, include forms of folliculitis such as pseudomonal, staphylococcal, and invasive fungal folliculitis and other follicular disorders such as keratosis pilaris. Diagnosis of MaF frequently involves the integration of clinical findings, direct microscopic examination, and response to antifungal treatment.[2] Culture is not routinely performed due to special media requirements and frequent false positives given the presence of *Malassezia* spp. within the normal skin flora.[9] Dermoscopy may be helpful, showing papules or pustules with associated erythema, scaling, and hypopigmentation surrounding the hair shaft; notably absent are inflammatory comedones which characterize acne.[9] Direct microscopy of skin scrapings with potassium hydroxide (KOH) preparation can be used to visualize the unipolar, budding *Malassezia* spp. Unlike in the setting of PV, the organism does not typically present with the pseudohyphae morphology.[9] Obtaining several scrapings may increase sensitivity. Skin biopsy can also confirm the diagnosis; histopathology, enhanced by periodic acid-Schiff staining, demonstrates many *Malassezia* spores in dilated hair follicles plugged with keratinous material and an associated inflammatory infiltrate in the perifollicular regions.[9]

Ketoconazole 2% cream or shampoo are common agents used to treat MaF, though most of the clinical trials are based on adult populations.[8,9,11,21] Suzuki et al. studied the use of ketoconazole 2% cream twice daily and revealed improvement in all 37 adult patients after a mean treatment duration of 27 days.[11] In another study of MaF patients 0–21 years of age, all 48 patients (excluding 17 patients lost to follow-up) treated with ketoconazole 2% shampoo as a body wash every other day for 2–3 months demonstrated treatment success.[21] However, MaF is prone to recurrence with treatment cessation, so maintenance use of ketoconazole 2% wash twice weekly is recommended.[9,12,21] Systemic antifungal regimens can be considered to more comprehensively treat widespread eruptions, for immunocompromised patients and for those refractory to topical approaches.[9] Several treatment regimens have been published, including oral itraconazole 200 mg daily for 2–4 weeks yielding clinical improvement rates ranging from 87.2% to 100%[11,22,23] and oral fluconazole 100 mg daily for 1 week or 200 mg daily for 3 weeks ($N = 16$ with 1 lost to follow-up) with clinical improvement in 100%.[21] However, long-term continuous use of systemic azoles is not generally recommended based on the risk of adverse effects including hepatoxicity, drug interactions, and adrenal hormone imbalances.[9,39] Fluconazole is typically preferred first line due to risk of cardiac toxicity with itraconazole.

3 | SEBORRHEIC DERMATITIS

SD is a form of inflammatory eczema with incidence peaks in infants and adolescents.[10] Skin findings demonstrate a uniquely greasy type of scale that preferentially affects body sites with greater sebum production and sweat concentration.[10] Infantile and adolescent SD are discussed separately to address the differences in proposed etiologies, skin presentation and distribution, and treatments. Both variants have *Malassezia* associations, but causality remains unconfirmed and is frequently disputed.

3.1 | Infantile seborrheic dermatitis

Infantile seborrheic dermatitis (ISD) peaks in incidence during the first 3 months of life and may affect up to 70% of infants <3 months of age.[10,40] "Cradle-cap" is a common variant with thick, greasy yellow or white scales overlying confluent, erythematous patches on the crown of the scalp (Figure 5).[10] It can spread beyond the scalp as a variably itchy eruption of erythematous thin plaques with greasy scale on the face and bright erythema of body folds (Figure 6A,B).[10]

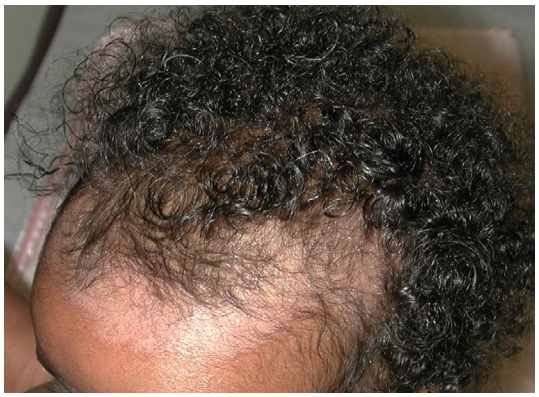

FIGURE 5 Infantile seborrheic dermatitis of the scalp on a 6-month-old.

Involvement of the trunk as thin oval well-demarcated to coalescing pink plaques can be prominent (Figure 6C). The pink rash progresses through a stage of postinflammatory hypopigmentation, especially notable in skin of color, that can be extensive and alarming to parents and caregivers. Families can be reassured that the discoloration will gradually normalize over weeks to a few months.

The pathogenesis of ISD is still not well-understood. Some suspect that maternal androgens drive excess sebaceous gland activity at birth.[10,41] Alterations of the cutaneous microbiome are also implicated, including *Malassezia* spp., but the exact mechanism is not known.[10] The differential diagnosis of ISD includes infectious forms of intertrigo, due to organisms such as *Streptococcus*, *Staphylococcus*, and *Candida*, when skin folds such as the neck and axillary creases are involved, and can be difficult to differentiate from infantile atopic dermatitis (AD) and inverse psoriasis as these conditions may overlap. Based on a retrospective analysis of 87 infants, the coexistence of ISD and AD at the time of ISD onset was 8%, with subsequent progression of ISD to AD in 34.4%.[42] However, as compared with AD, ISD tends to be less prominently itchy, and is more localized to the skin folds and scalp.[10] ISD is generally self-limited within a few weeks or months and can often be adequately managed with gentle skin care and use of moisturizers. For scalp involvement, emollients like mineral oil and petroleum jelly can help loosen scales, which can subsequently be removed by using an infant hair brush or cloth.[24] Low potency topical corticosteroids and antifungal creams such as hydrocortisone 1%–2.5% and ketoconazole 2% for 1–2 weeks can accelerate healing when the rash is particularly inflamed.[25,43]

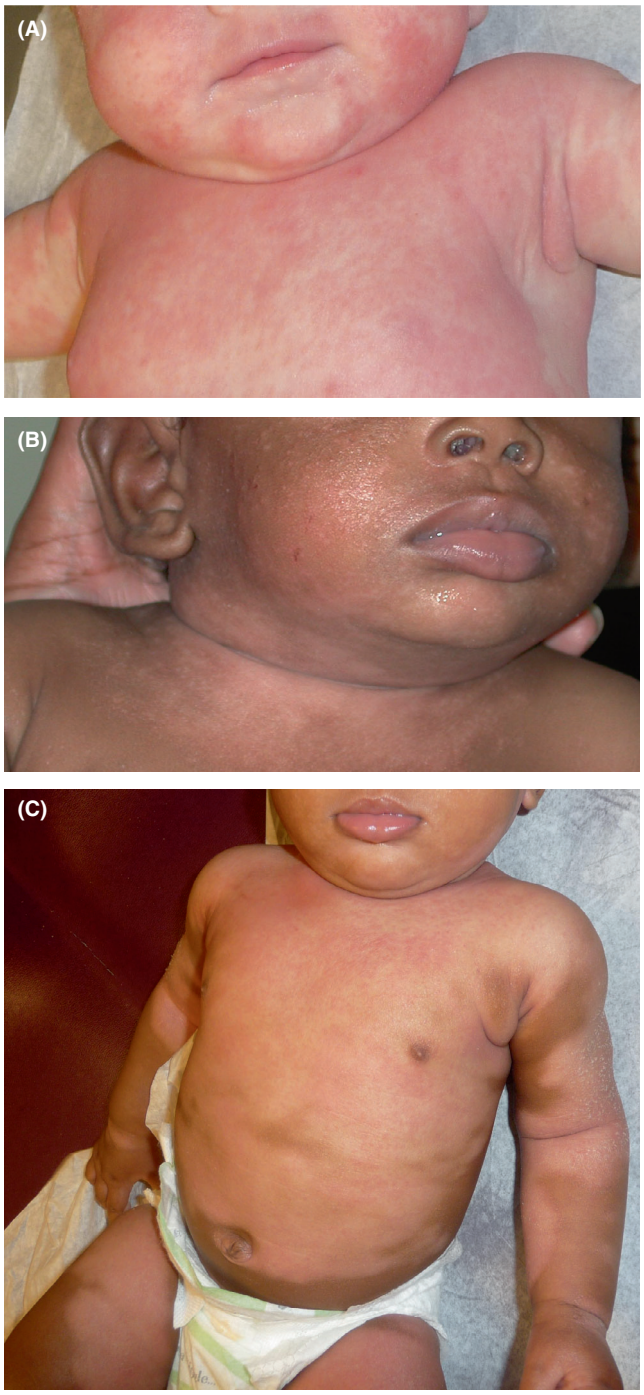

FIGURE 6 (A) Infantile seborrheic dermatitis on a 4-month-old. (B) Infantile seborrheic dermatitis affecting the face and neck with hypopigmentation. (C) Infantile seborrheic dermatitis on a 5-month-old with extensive hypopigmentation on the trunk and arms.

3.2 | Adolescent seborrheic dermatitis

Adolescent, like adult-type, SD follows a chronic, recurring course that can range from mild to severe.[10,44] SD of the scalp, commonly referred to as dandruff, presents variably as fine white loose scale or thicker greasier adherent scaling with or without underlying erythema.[10] Scaling and erythema may extend from the scalp to the forehead border which is referred to "corona seborrheica" (Figure 7A).[10] SD may also involve other sebum-rich areas including the face (commonly appearing on the forehead, eyebrows, and in the nasolabial folds), ears, upper chest, and body folds. The term "petaloid" variant may be used to describe coalescing scaly macules and patches resembling flower petals (Figure 7B).[10] The associated erythema may be harder to assess in patients of color, while

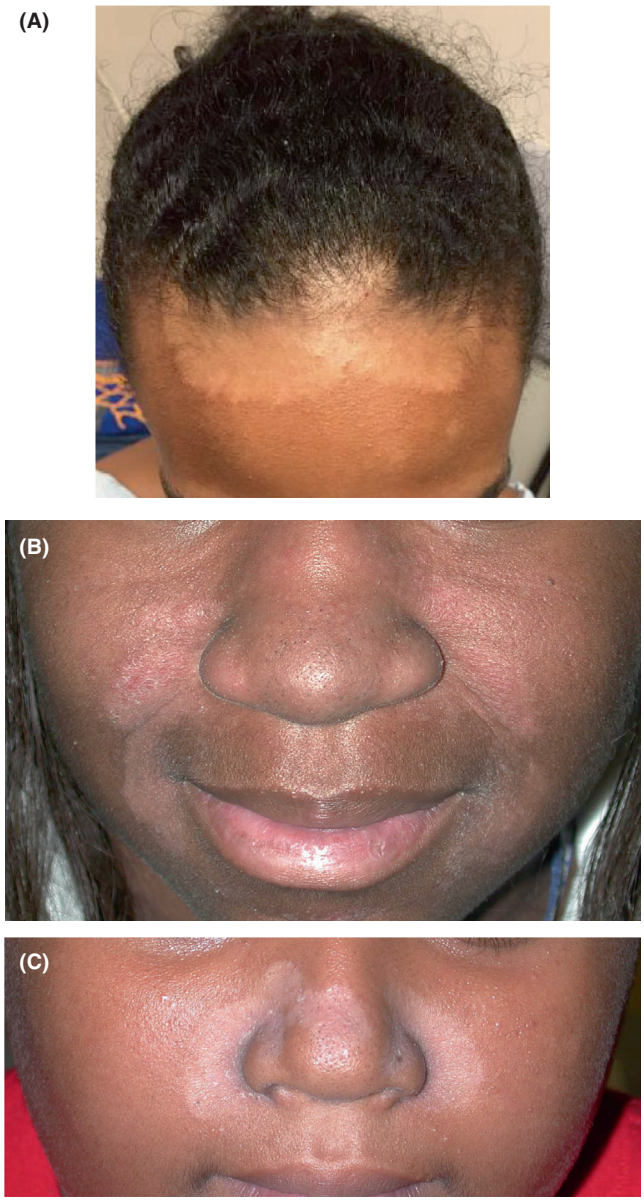

FIGURE 7 (A) Seborrheic dermatitis on the scalp and forehead of a 13-year-old. (B) Petaloid variant of seborrheic dermatitis on the face. (C) Seborrheic dermatitis with postinflammatory hypopigmentation around the nasolabial folds.

postinflammatory hypopigmentation can be marked (Figure 7C).[32] Diagnosis is usually determined based on history and physical examination of the skin—skin biopsies are rarely performed.[10] In adolescents, key differential diagnoses include psoriasis, AD, rosacea, and more rarely lupus erythematous.

The association of *Malassezia* spp. with SD has long been recognized.[2,10,44] However, its precise role is controversial. Some authors suggest that higher densities of *Malassezia* yeast observed in cases of SD are due to increased sebum production and correlate with increased severity of disease.[12] However, other studies were unable to replicate these results, and while the skin eruptions improved after antifungal treatment, this clinical improvement did not correlate with lower *Malassezia* counts in vivo.[2,44] Researchers also theorize that the intrinsic lipase activity generated by *Malassezia* breaks down sebum triglycerides into inflammatory metabolites such as oleic and arachidonic acids, which are suspected to damage the epidermal skin barrier and trigger cytokine cascades.[44]

Some also hypothesize that a *Malassezia*-focused etiology may not represent a complete picture.[44] The pathogenesis is likely multifactorial, involving disruptions in skin barrier, skin hygiene, genetic factors, and host-immune response.[10,44] Similar to other *Malassezia*-related disorders, some populations are at higher risk for SD, such as immunosuppressed individuals, particularly from advanced HIV infection with incidence ranging from 30% to 83%.[10] Neurological disorders, including depression, Parkinson's disease (PD), spinal cord injury, and other severe neurological insults have also been associated with a higher incidence of SD.[10] The prevalence was 36.1% in one of the limited studies examining the prevalence of SD in PD patients, and patients with more severe motor symptoms had 1.8 times higher risk of developing SD compared with those with mild motor symptoms, which fell within previously reported range of 18%–9%.[45] The etiology of this phenomenon is not known.[44] Investigations involving PD patients have suggested that altered neuroendocrine signaling in combination with relative facial immobility may increase sebum accumulation leading to SD.[10]

Management of SD in adolescents focuses on reducing inflammation and associated pruritus.[10] Despite uncertainty regarding the role of *Malassezia* in the mechanism of disease, antifungal therapies are considered a mainstay of therapy and appear to be beneficial in many cases. Topical antifungal agents, low-potency corticosteroids, calcineurin-inhibitors, and other anti-inflammatory and keratolytic agents such as sulfacetamide and pyrithione are often first-line treatments.[46] For children and adolescent scalp SD, ketoconazole 1%–2% shampoo twice weekly for 1 month is quite effective with treatment response ranging from 71% to 89% without significant side effects.[19] Once weekly for maintenance therapy is recommended as an effective way to prevent relapse.[28]

Based on adult studies, moderate-to-severe SD patients may have more significant treatment success by alternating twice weekly clobetasol propionate 0.05% shampoo with a regimen of twice weekly ketoconazole 2% shampoo for 4 weeks and once weekly ketoconazole 2% shampoo maintenance for a subsequent 4 weeks.[47] Severe scalp scaling and itch are also relieved with use of topical corticosteroids in foam, spray, lotion, solution, or even oil vehicles (typical agents include clobetasol, fluocinonide and fluocinolone in decreasing order of potency) for 1–2 weeks at a time and then intermittently as needed to maintain control.[27]

For face and trunk SD, ketoconazole 2% cream twice daily for 4 weeks demonstrated clinical efficacy ranging from 63.4% to 90% in six studies with a total pool of 275 participants aged 12–78 years.[19] Short courses (1–2 weeks) of low-potency topical corticosteroid creams (such as hydrocortisone 1%–2.5% or

desonide) in combination with the antifungal cream are helpful when the rash is more severe and inflamed to achieve more rapid control.[27] Roflumilast 0.3% foam, a selective phosphodiesterase-4 inhibitor, has recently been approved for the treatment of SD in patients ≥9 years of age. Based on phase 3 clinical trial data, once daily treatment with roflumilast 0.3% foam for involved scalp and body sites was well-tolerated and led to treatment success in 79.5% of 304 participants in the treatment group by Week 8 and 76.5% of 17 participants in the adolescent subgroup (ages 9–17).[26] However, more studies are needed to understand long-term efficacy and tolerability of this drug.

Given the high recurrence rates, episodic and maintenance treatment schedules are important to recommend.[41] Daily cleaning of affected areas can assist with management of sebum production and buildup.[41,46] This requires sensitivity to individual hair care practices which may impact choices regarding frequency of hair washing. Curly and coiled hair is naturally more dry and brittle, therefore hair washing less frequently, once a week or less, is preferred; similarly, many braided and twisted styles preclude frequent washing to preserve the style.[48] Management adjustments include the application of medicated shampoos directly on the scalp rather than coating the hair shafts, using foam vehicles when possible to minimize the need for water application,[48] and offering oil vehicles for topical corticosteroids when patients are accustomed to using hair oils as a standard component of their hair care regimen.

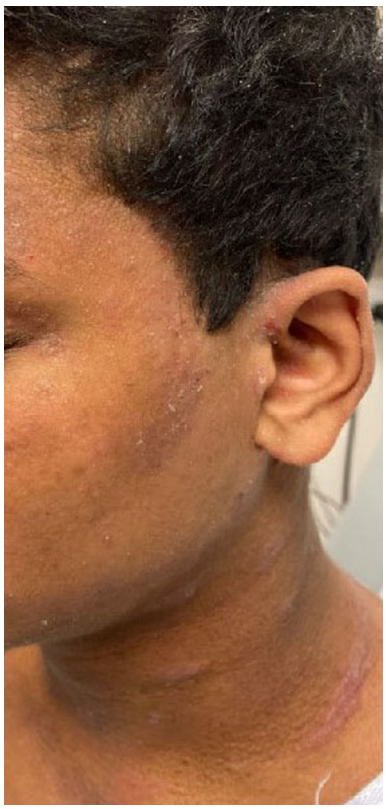

FIGURE 8 Head and neck dermatitis on the face of a 16-year-old.

Finally, postinflammatory discoloration can be notable, especially in patients with skin of color. It is important to discuss this stage of healing with patients and families and provide anticipatory guidance regarding the expectation for gradual normalization of pigmentation once active SD is well controlled.

4 | HEAD AND NECK DERMATITIS

HND describes eczematous plaques and diffuse erythema localized to the head, face, neck, and upper trunk region (Figure 8).[14] While some consider HND to be a variant of AD, it tends to be uniquely treatment-resistant, suggesting a different etiology.[49] *Malassezia* spp. have been proposed as a factor in HND, though its pathogenic role remains controversial.[14,50] HND is more common in adolescents and young adults, suggesting a role for the growth of sebaceous glands during puberty and subsequent overgrowth of *Malassezia* spp.[13] In addition to AD, the differential diagnosis of HND also includes rosacea, psoriasis, SD, and contact dermatitis.[15]

One theory regarding the pathogenesis of HND is that it represents a hypersensitivity reaction to *Malassezia*-specific allergens. A study done in Korea revealed that 36 out of 80 patients with a positive skin-prick test *to M. furfur* not only had higher total IgE levels, but higher severity scores for both HND and overall AD.[14] 67.5% (54/80) of HND participants also had anti-*M. furfur*-specific IgE antibodies; suggesting that HND may result from an allergy-like reaction to *Malassezia*. Although this sensitization study was done in adolescents and adults with HND between the ages of 12 and 42 years,[14] *Malassezia*-specific IgE was also found in 15.2% (9/58) of AD infants under 12 months of age and 18.1% (15/83) of children aged 12 months to 16 years.[50] *Malassezia* allergens may penetrate the defective skin barrier in AD skin more effectively than healthy skin, contributing to immune system sensitization and a subsequent inflammatory response.[4]

In the age of biologic therapies for AD, HND has been observed in a subset of patients on treatment with dupilumab (Figure 9). Dupilumab is an interleukin-4 receptor alpha inhibitor that blocks IL-4 and

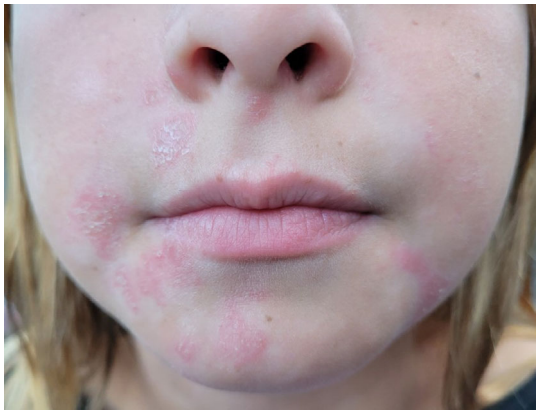

FIGURE 9 Head and neck dermatitis on a 9-year-old who is on dupilumab therapy for atopic dermatitis.

IL-13 cytokines.[15] Since its introduction, there have been multiple case reports of new-onset or worsening HND in both children and adolescents.[15] In a retrospective review of 24 patients with AD younger than 18 years treated with dupilumab, the incidence of dupilumab-associated HND was 29% (7/24).[51] A dupilumab trial for AD patients aged 3 to 18 reported an incidence of 5.4% (6/111).[52] Given the range, more studies are needed to evaluate the true incidence rates in pediatric populations. The cause of this phenomenon is poorly understood, but *Malassezia* hypersensitivity has been indicated as a possible pathway.[15,53] It is hypothesized that since dupilumab downregulates the T_H2 immune pathway, a shift in favor of T_H17-induced immune activation occurs.[15] The T_H17 pathway has been implicated in *Malassezia*-associated skin inflammation.

At this time, published management approaches for pediatric patients with HND while on dupilumab are based on a limited case series involving few patients.[15] A study of five adolescents with HND treated with fluconazole 150 mg weekly demonstrated significant improvement in four patients with 4 weeks of treatment and another patient treated for 2 weeks. However, in some cases, HND reappeared after treatment cessation, requiring continued treatment. Topical calcineurin inhibitors including pimecrolimus 1% cream and tacrolimus 0.03% or 0.1% ointment twice daily, may also be effective measures for treatment and prevention of HND.[29,30]

5 | NEONATAL CEPHALIC PUSTULOSIS

NCP is an eruption of primarily small pustules on the face that generally presents during the first 3 weeks of life. It is considered synonymous with neonatal acne but is the preferred term because of the lack of comedones. It appears as multiple pustules and small red papules often surrounded by a halo of erythema most commonly on the cheeks, chin, and forehead, but other sebaceous areas such as the scalp and neck may be affected as well (Figure 10A,B).[16] These lesions may mimic other non-infectious skin conditions such as miliaria pustulosa and pustular psoriasis, or infectious causes including folliculitis and neonatal herpes simplex.[16]

It is still widely debated if *Malassezia* spp. is a causal agent of this skin disorder. Some suggest that it may be a neonatal form of MaF.[16] Given that maternal androgens affect sebum production in neonates,[17,18] it may be inferred that sebum production can lead to yeast overgrowth similar to the potential etiopathogenesis of ISD. Additionally, as previously mentioned, *Malassezia* spp. skin transmission from mother to neonate may occur as early as Day 0.[3] Smears of the contents of some pustules demonstrate *Malassezia* spp. yeast on direct microscopy or culture.[16,54,55] However, as not all studies have been able to correlate disease severity with culture positivity or positive yeast findings, *Malassezia*'s role is not well-defined or established in NCP.[55] NCP is usually self-limited within 3 months without residual scarring, but topical antifungal creams, such as ketoconazole, may speed up clearance.[16,31]

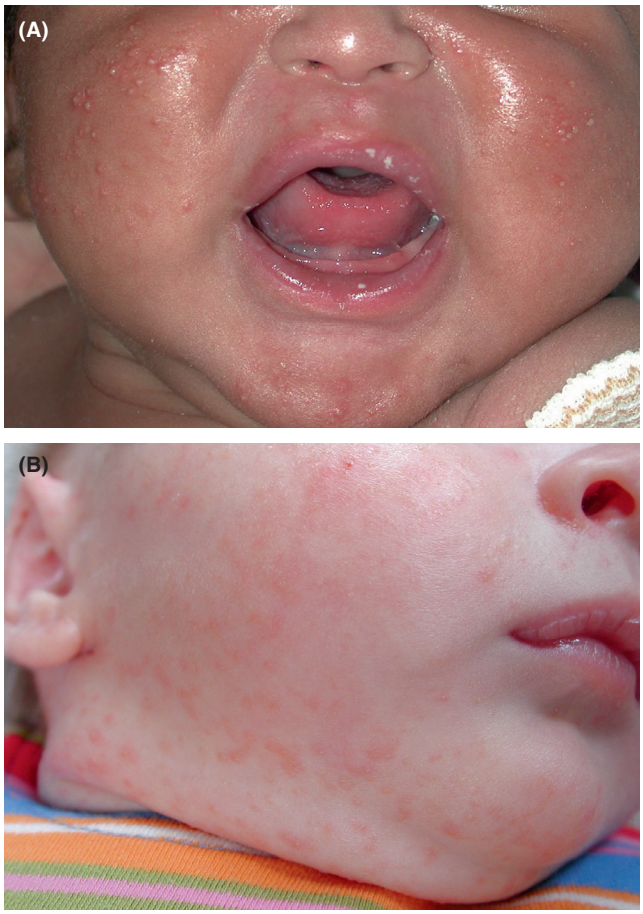

FIGURE 10 (A) Neonatal cephalic pustulosis on the face of a 2-week-old. (B) Neonatal cephalic pustulosis on the face of a 5-week-old.

6 | CONCLUSION

Malassezia spp. are a normal component of the human microbiome. It is still unclear why some individuals have a greater propensity to develop these *Malassezia*-associated skin conditions, and whether *Malassezia* is truly causative for all. Genetic and other environmental factors likely contribute toward the pathogenesis. Skin barrier defects from genetic predisposition and progression of inflammatory skin conditions such as atopic dermatitis may increase penetration of *Malassezia* and susceptibility to host inflammatory response. Recognition and diagnosis of these common pediatric dermatoses and understanding their natural history will improve management. Future investigations to clarify the causative role of *Malassezia* and its impact on cutaneous inflammation may allow for optimized treatments and improved patient satisfaction.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during this study.

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