Atopic Dermatitis and Eczematous Eruptions

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Atopic Dermatitis

Clinical Features of the Disorder

Atopic dermatitis (AD) is a common, chronic, relapsing, pruritic inflammatory skin condition affecting approximately 10–20 % of children in several industrialized countries, and is increasing in prevalence in many parts of the world. The majority of cases begin before age 5, but onset may occur at any age [1–3]. Due to the unrelenting pruritus associated with the inflammatory skin lesions, sleep is often disturbed. Studies reveal the quality of life of children with AD is similar or worse than many chronic diseases of childhood such as asthma. Chronic itching and lack of proper sleep lead to measurable psychological, behavioral, and emotional consequences [4]. Having a child with AD often impacts the entire family, with one study finding that having a child with AD in the family to be comparable to having a child with type I diabetes [5]. The development of AD often heralds the onset of allergic comorbidities, specifically asthma, allergic rhinitis, and food allergy. Children with AD are also at higher risk of developing skin infections and neurodevelopmental disorders such as attention-deficit-hyperactivity disorder [6].

Clinical criteria aid in the diagnosis of AD and were proposed by Hanifin and Rajka in 1980 [7]. Key features that should be present to make a diagnosis of AD are shown in Table 3.1. The distribution of skin lesions varies with age. In infants, AD affects the cheeks and extensor surfaces of the limbs most commonly, while in older children and adults, lesions typically involve flexor surfaces (Figs. 3.1, 3.2, and 3.3). The groin and axillae are typically spared at all ages. A diagnosis should only be made when other conditions have been considered, such as scabies or contact dermatitis [8]. The presence of atypical morphology or distribution, or a history of repeated severe sino-pulmonary infections, should prompt the consideration of an immunodeficiency syndrome [8].

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Management Strategies

Management begins with disease education, followed by the creation of an individualized treatment plan using a sequential approach, primarily based on disease severity. Key educational points to deliver during the initial encounter with a patient and family include information on pathogenesis, the role of food allergy, topical steroid risks and benefits, prognosis, proper skin care, and avoidance of triggers (Table 3.2). Families should be asked about the presence of immediate hypersensitivity symptoms to foods such as lip swelling, urticaria, abdominal pain, or vomiting within 2 h after food consumption. If these are not present, there are few data to support the idea that foods contribute to the eczematous lesions, and food avoidance should not be routinely recommended [9].

Treatment Overview

Management can be roughly thought of in two parts—a *Clearance Phase* where inflammation becomes controlled rapidly and a *Maintenance Phase*, where therapy choices should consider long-term safety. If flares occur during maintenance therapy, an abbreviated *Clearance Phase* protocol may be needed.

Clearance Phase

Very mild disease may be managed with emollients alone. For mild to moderate disease, topical steroids should be prescribed in adequate quantities and potency to achieve near

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Table 3.1 American Academy of Dermatology Criteria for AD

Essential features:
Pruritus
Eczema (acute, subacute, chronic)
Typical morphology and age-specific patterns[a]
Chronic or relapsing history
Important features—seen in most cases, adding support to the diagnosis:
Early age of onset
Atopy
Personal and/or family history
Immunoglobulin E reactivity
Xerosis
Associated features—these clinical associations help to suggest the diagnosis of atopic dermatitis but are too nonspecific to be used for diagnosing AD in isolation:
Atypical vascular responses (e.g., facial pallor, white dermatographism, delayed blanch response)
Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis, ocular/periorbital changes
Other regional findings (e.g., perioral changes/periauricular lesions), perifollicular accentuation/lichenification/prurigo lesions
Exclusionary conditions—it should be noted that a diagnosis of atopic dermatitis depends on excluding conditions, such as:
Scabies
Seborrheic dermatitis
Contact dermatitis (irritant or allergic)
Iichthyoses
Cutaneous T-cell lymphoma
Psoriasis
Photosensitivity dermatoses
Immune deficiency diseases
Erythroderma of other causes

Adapted from AAD Consensus Conference on AD, 2003

[a]Patterns include: (1) Facial, neck, and extensor involvement in infants and children (2) Current or previous flexural lesions in any age group (3) Sparing of the groin and axillary regions

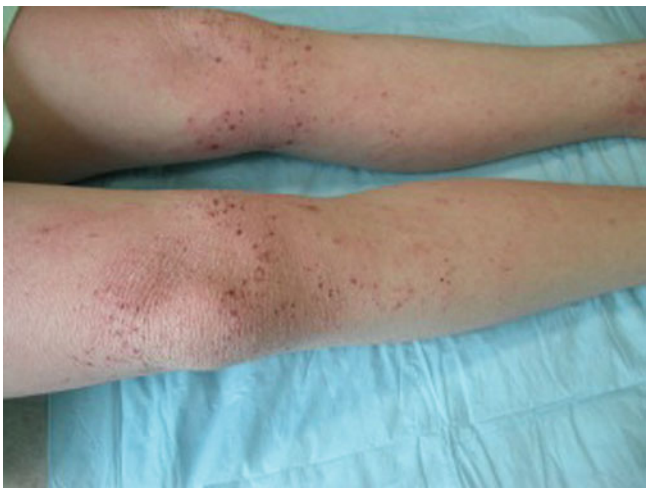

Fig. 3.1 Typical erythematous crusted and excoriated plaques with lichenification in two children with atopic dermatitis

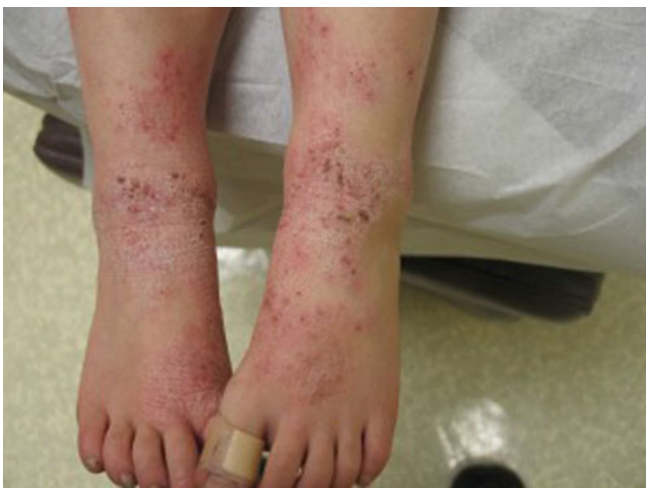

Fig. 3.2 Typical erythematous crusted and excoriated plaques with lichenification in two children with atopic dermatitis

clearance of the disease within 1–3 weeks. Topical steroids may be applied once or twice daily, with data showing little clinical difference between the two frequencies [10]. Ointment preparations are generally preferred over creams and lotions because of their enhanced efficacy and reduced possibility of causing stinging or contact dermatitis. One small study found that daily bathing followed immediately by topical steroid ointments ("soak and seal") led to 95 % of patients with moderate to severe disease achieving mild disease or better after 1–2 weeks of treatment [11]. Another study found 3 days of a medium-potency topical steroid was just as effective as 2 weeks of low-strength steroid [12].

Clinically relevant hypothalamic-pituitary-adrenal axis suppression typically occurs only in the setting of inappropriate use (i.e., prolonged duration with daily application). The short-term use of daily topical steroids has proven to be safe, but topical steroid therapy should not be used daily for long-term control [13, 14]. Topical calcineurin inhibitors may be used as first-line treatment in areas of the body prone to steroid side effects such as the face, but are not often tolerated when skin is flaring due to burning and stinging (Table 3.3).

Maintenance Phase

After achieving disease control in the Clearance Phase with topical steroids, the Maintenance Phase begins. The Maintenance Phase involves reducing topical steroid use to twice-weekly application to newly active or residual lesions. This reduction in steroid frequency prevents potential side effects such as skin atrophy, telangiectasias, and striae. Topical calcineurin inhibitors may be added at this stage if twice-weekly application of topical steroids is not adequate to maintain disease control [13]. Daily use of topical steroids to the same areas of skin for longer than 4–6 weeks should be avoided. For patients with severe disease that frequently relapses, intermittent topical steroid (two times per week) or calcineurin inhibitors (three times per week) may be used on *normal-appearing skin* at sites that frequently flare, so-called "proactive therapy," to reduce the probability of relapse [15, 16].

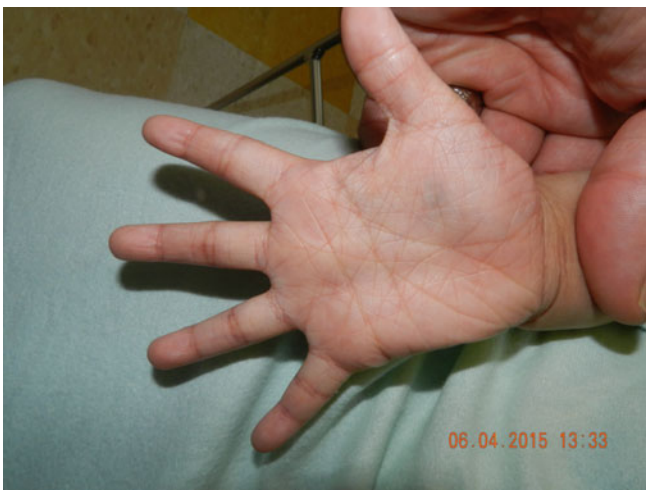

Fig. 3.3 Hyperlinear palms are a common finding in patients with AD (Photo courtesy of Alfons Krol, MD)

Rescue of Flares

If a patient experiences a disease flare, the cause of the flare, such as a bacterial infection of the skin, should be identified and treated. Other common causes of flares include upper respiratory viral infections, change in season, and non-adherence to the prescribed skin care or maintenance regimen. A shortened version of the Clearance Phase may then be instituted, such as 3–7 days of daily topical steroid.

Adjunctive Interventions

Twice-weekly dilute sodium hypochlorite baths (1/4 to ½ cup of household bleach to a full standard tub) may improve the severity of AD when added to routine therapy; their use may be especially helpful in patients with moderate-to-severe disease who experience frequent bacterial infections [17]. Some controlled studies also support oral vitamin D3 supplementation [18]. While oral antihistamines may be useful for treating allergic comorbidities, or may be needed as a short-term sleep aid, there are little data supporting their effectiveness in treating the itch or inflammation of atopic dermatitis [19]. Some data support the use of acupressure as an adjunctive treatment for itch [20]. Narrowband ultraviolet B phototherapy may be added if topical therapy does not achieve satisfactory results [21]. Topical calcineurin inhibitors should be discontinued during phototherapy, given the theoretical photocarcinogenesis potential of these two interventions used concomitantly.

Table 3.2 Key educational points to be delivered in first visit

The cause of the disease	The cause of AD may be thought of as a disease driven by genetic and environmentally derived alterations in both the skin barrier and immune regulation
The prognosis and disease course	Parents should be informed that AD is a chronic disease that needs continued management. Early aggressive control of the inflammation will improve a patient's itch and quality of life
Role of food allergy	Patients with atopic dermatitis are more likely to have immediate reactions to foods like egg, milk, and peanut. However, in the absence of immediate hypersensitivity symptoms, there are no convincing data that altering a child's diet will improve the eczema
Avoiding triggers and exacerbating factors	Avoid common triggers to reduce itch such as contact with wool, a warm environment, harsh soaps, or lotions with fragrance
Steroid phobia and steroid side effects	A thorough explanation of the risks and benefits of topical steroids should take place with a discussion on how those risks may be mitigated
Patient support and education	Written instructions and information regarding patient support organizations such as the National Eczema Association (nationaleczema.org) are important resources for patients
Skin care	Gentle skin care should be encouraged with the use of mild cleansers and the daily use of emollients (moisturizers)

Refractory Disease

Patients with moderate or severe disease that fail to respond adequately to intensive topical therapy are candidates for systemic therapy. The diagnosis in patients failing intensive topical therapy should be reconsidered, with consideration given to scabies infection, skin infection, contact dermatitis, cutaneous T-cell lymphoma, or other dermatosis. Oral immunosuppressive/immunomodulatory medications are the current mainstay of treatment for this subset of patients, with cyclosporine being the treatment of choice for acute disease control given its rapid onset of action and well-documented efficacy. Cyclosporine is normally started at a dose of 3–6 mg/kg/day, with higher initial doses likely leading to more rapid clinical response [21]. Once disease control is obtained with cyclosporine, patients may be transitioned to safer longer-term options such as phototherapy, methotrexate, azathioprine, or mycophenolate mofetil (Tables 3.4, 3.5).

Table 3.3 First line therapies [8, 13, 22, 23]

Topical corticosteroids	A
Emollients	A
Topical calcineurin inhibitors	A

Table 3.4 Second line therapies [17, 18, 21]

Sodium hypochlorite baths	A
Vitamin D3 supplementation	A
Phototherapy (NBUVB, UVA1, PUVA)	A

Table 3.5 Third line therapies [21, 24–29]

Cyclosporine	A
Methotrexate	A
Azathioprine	B/A*
Mycophenolate mofetil	C/A*
Interferon-gamma	A*
Apremilast	C*
Ustekinumab	E
Rituximab	D

Specific Investigations Recommended

No routine investigations are required. The diagnosis is primarily clinical and based on the presence of the criteria listed in Table 3.1. If symptoms of immediate hypersensitivity are present, referral to an allergist for allergy testing may be needed to confirm the history. Referral to an allergist may also be useful for supervised oral food challenges if children are on overly restrictive diets based on the results of allergy testing. Biopsy, immunologic evaluation, KOH preparation, or genetic testing may rarely be needed if an alternative diagnosis is suspected, or in cases of severe refractory disease.

Topical corticosteroids remain the mainstay of acute therapy in AD in evidence-based guidelines supported by extensive literature review. Evidence-based guidelines also strongly support topical calcineurin inhibitors as a proven option for long-term control. A systematic review of "proactive" therapy (i.e., intermittently treating normal-appearing skin that frequently flares to prevent flares) reported that both topical steroids and topical tacrolimus trials showed efficacy, with twice-weekly topical steroids possibly being slightly superior to tacrolimus.

Huang et al. published the first controlled trial showing the effectiveness of twice-weekly sodium hypochlorite, or dilute bleach baths, in reducing AD severity in 2009; prior to this, only anecdotal evidence was available. A randomized trial of oral calciferol (1,000 IU/day) showed improved disease severity at 1 month over placebo in children aged 2–17 years. Strong evidence is also available supporting various light modalities in AD, with narrowband UVB representing the treatment of choice.

Multiple studies document the efficacy and safety of cyclosporine in pediatric and adult patients with atopic dermatitis, with a systematic review of controlled trials revealing cyclosporine consistently improves AD severity by greater than 30–50 %. Methotrexate in controlled trials also has been found to be safe and effective in both the pediatric and adult population; one study in adults reported comparable efficacy of both methotrexate and azathioprine, but with fewer side effects, especially hematological abnormalities, in the methotrexate group. Mycophenolate mofetil has also been shown effective and safe in adult and pediatric patients; however, response can often be delayed. A randomized, controlled study in which adult patients were cleared with 6 weeks of 5 mg/kg cyclosporine, then randomized to maintenance therapy with either 3 mg/kg cyclosporine or mycophenolate sodium, showed equivalent responses; however several patients in the MMF group received oral steroid rescue, while none in the CsA group needed rescue during the treatment phase. In an adult randomized controlled trial, almost half of patients treated with interferon gamma achieved more than 50 % clearance.

Pityriasis Alba

Clinical Features of the Disorder

Pityriasis alba (PA) is characterized by ill-defined, oval, hypopigmented to pink macules, small patches or very thin plaques with fine overlying scale (Fig. 3.4). The hypopigmented lesions are typically not preceded by obvious signs of inflammation. Multiple lesions are normally present and distributed most often over the cheeks, forehead, perioral

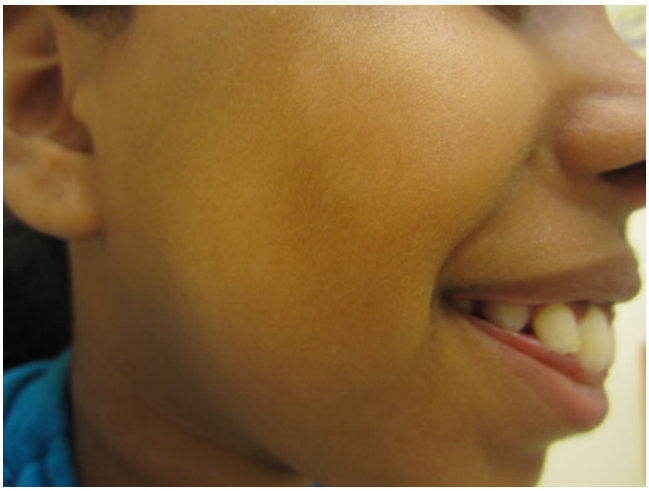

Fig. 3.4 Pityriasis alba characterized by round hypopigmented macules of the cheeks (Photo courtesy of Sabra Leitenberger, MD)

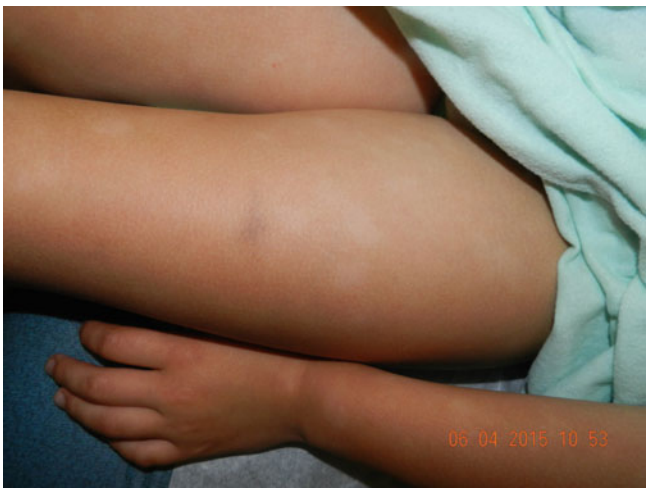

Fig. 3.5 Pityriasis alba involving the arms and legs of a young girl with atopic dermatitis (Photo courtesy of Alfons Krol, MD)

skin, and proximal arms. Less commonly, involvement of the trunk and legs can be seen (Fig. 3.5) [30–32].

PA is frequently associated with atopic dermatitis, and in these patients likely represents a form of post-inflammatory hypopigmentation. PA has been described in an endemic form associated with poor hygiene, parental income, and more siblings [33, 34]. The role of exposure to sunlight is controversial, as it has been reported to both improve PA as well as exacerbate it. A portion of the change seen with sunlight could be due to increasing pigment of skin surrounding the PA lesions. This condition is more readily apparent in children of darker skin types. The lesions are most often asymptomatic, although mild itching may be present. Histologically, PA shows spongiotic dermatitis and, less often, hyperkeratosis and acanthosis [35].

Management Strategies

Treatment can be frustrating, and in some cases may not be necessary, as lesions often resolve spontaneously over months to years. Very few controlled studies have been performed evaluating the treatment of PA. The most often recommended treatments include gentle skin care with mild cleansers, emollients, and sunscreen (Table 3.6). The efficacy of these recommendations has not been thoroughly evaluated, but they likely counteract possible causative factors. The gentle skin care combats any role xerosis and inflammation may be playing, and the sunscreen is helpful in that it lessens the contrast between involved and uninvolved skin and may help prevent new lesions. In cases with suspected dermatitis, low-potency topical corticosteroids (such as hydrocortisone 1 % or 2.5 %) and calcineurin inhibitors may be of benefit. Calcineurin inhibitors have been the most studied treatments, suggesting the role of subclinical inflammation in the etiology of PA.

Specific Investigations Recommended

PA in most cases is diagnosed clinically. Biopsy may be necessary to rule out hypopigmented mycosis fungoides if the lesions are extensive with significant involvement off of the face [36]. Testing for a loss of sensitivity to light touch, pinprick, or temperature can be useful in patients in which leprosy is suspected [37].

Biopsy if hypopigmented MF is suspected
Skin scraping for KOH to exclude dermatophyte infection or tinea versicolor
Testing for loss of sensitivity if patient is at risk for leprosy

In a review of 67 cases seen at the Mayo Clinic, bland lubricants such as white petrolatum were equivalent in effectiveness when compared to 5 % ammoniated mercury in petrolatum, 2 % crude coal tar in petrolatum, Whitfield's ointment, and Myconef ointment. A randomized, controlled study of tacrolimus 0.1 % ointment versus placebo showed improvement over the 9-week study period in hypopigmentation, pruritus, and scaling, with significantly greater improvement in pruritus and hypopigmentation in the tacrolimus group at all three time points. A similar study randomizing to three groups—tacrolimus 0.1 % ointment, calcipotriol 0.0003 % ointment, and petrolatum ointment for 8 weeks—showed improvement in all groups, but the improvement in the tacrolimus and calcipotriol groups was superior to petrolatum. A study using pimecrolimus 1 % cream also showed efficacy in pediatric and adult subjects, with clearance of scaling for most patients by week 3 and evening of pigmentation by week 12.

A study of 12 patients (skin types III–V) reported complete clearance of PA lesions with twice-weekly for 12 weeks with Excimer. Another study reported clearance or marked improvement in five of six patients treated with 4 weeks of oral methoxsalen, followed by exposure to midday summer sun or exposure to UVA cabinet.

Contact Dermatitis

Clinical Features of the Disorder

Contact with various exogenous compounds can induce an eczematous dermatitis either by delayed type IV hypersensitivity (allergic contact dermatitis), or through direct injury to skin cells (irritant contact dermatitis).

Allergic contact dermatitis (ACD) is becoming increasingly recognized as a cause of dermatitis in children and may be under-recognized, as children are not often patch tested [2, 3, 44]. ACD is classically characterized in its acute form by well-demarcated erythematous edematous and often vesicular plaques that are quite pruritic (Fig. 3.6) Chronic ACD appears as lichenified scaling plaques and can be more difficult to distinguish from irritant contact dermatitis (ICD) and atopic dermatitis (AD) (Fig. 3.7). The distribution of ACD depends on the contactant, and can be major clue to the diagnosis and likely causative agent. Geometric angular streaks raise the possibility of exposure to plants, usually of the toxicodendron family. Involvement of the eyelids, face, and anterior neck is typical for airborne allergens such as fragrances or sesquiterpene lactones. Pruritic eczematous dermatitis of the plantar and dorsal feet should raise suspicion of an ACD to a component of shoes. ACD should also be considered in patients with AD that have a sudden worsening of their disease or that is difficult to treat, especially when the flare involves areas of the body not typically involved in AD. Any asymmetric dermatitis or eruption limited to one area of the body (i.e., feet, eyelids, buttocks) should also raise suspicion for contact dermatitis. Patch testing is the standard for establishing the diagnosis of ACD and should be done when the history and clinical exam supports a diagnosis of ACD. Positive reactions must be interpreted in the clinical context to identify those that are truly relevant to the patient. The most common allergens causing ACD in children are shown in Table 3.8, below.

Table 3.6 First line therapies [38–41]

Low potency topical corticosteroids	C
Topical calcineurin inhibitors	A
Emollients	B
Sunscreen	B

Table 3.7 Second line therapies [40, 42, 43]

Excimer laser	D
Calcitriol 0.0003 %	C
PUVA	D

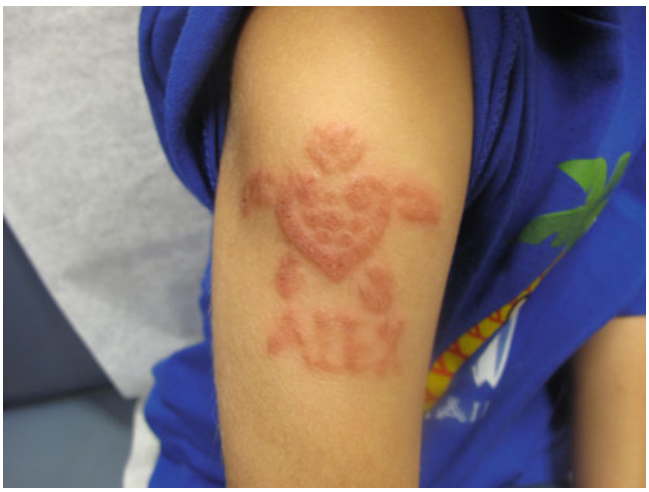

Fig. 3.6 Young boy with ACD to p-Phenylenediamine in a temporary tattoo (Photo courtesy of Patricia Norris, MD)

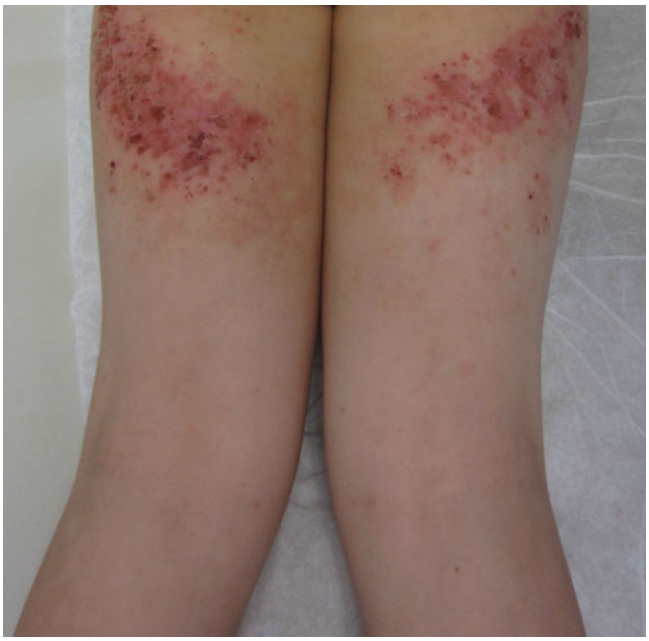

Fig. 3.7 ICD or ACD from household cleaners used on toilet seats between uses. So-called "toilet seat" dermatitis (Photo courtesy of Julianne Mann, MD)

Management Strategies

The principal goal in treating contact dermatitis is removal and avoidance of the causative agent. For irritant contact dermatitis, the offending agent is often obvious such as soap and

Table 3.8 Most common allergens causing allergic contact dermatitis in children

Allergen	Most common source
Nickel	Jewelry
Cobalt	Jewelry
Neomycin sulfate	Topical antibiotics
Balsam of Peru	Fragrance in perfumes and toiletries; flavoring in food and drink
Lanolin	Pharmaceutical preparations, cosmetics, and toiletries
Fragrance mix	Cosmetics, toiletries
Bacitracin	Topical antibiotics
Formaldehyde	Cosmetics, toiletries, and skin- and health-care products
Quaternium-15	Cosmetics, toiletries, and skin- and health-care products
p-Phenylenediamine	Hair dyes, temporary tattoos

Adapted from Zug et al. [48]

water for hand dermatitis. See Chap. 2 for a discussion of diaper dermatitis, another form of irritant contact dermatitis. Identification of the causative agent in allergic contact dermatitis is not always straightforward and depends on correct identification of the contactant, with a careful comprehensive history and patch testing. Parents and patients must be thoroughly educated about the compounds responsible for their ACD. Handouts describing common products containing the suspected contactant as well as suggesting alternative products that do not contain them can be helpful in educating parents and patients. For acute ACD, or in cases when avoidance alone does not lead to improvement, topical steroids can be helpful. Topical calcineurin inhibitors are often useful for treating the face or intertriginous areas [45]. In severe acute ACD, systemic therapy with oral corticosteroids or other immunosuppressants may be necessary (Table 3.9). Many authors recommend systemic treatment for acute severe ACD (such as seen with rhus dermatitis) covering greater than 10 % of the skin surface. A common regimen involves prednisone, 1 or 2 mg/kg/d, as a single morning dose for 7–10 days, with the dose tapered over an additional 7–10 days. Premature cessation may result in rebound dermatitis. Barrier creams and specialized soaps also exist for occasions when exposure cannot always be avoided, such as when outdoors in areas with poison oak/ivy. If the causative allergen can be successfully identified and avoided, long-term treatment is usually not necessary. As is the case with many pediatric conditions, research specifically evaluating the treatment of contact dermatitis in children is lacking.

Table 3.9 First line therapies [45]

Patch testing and removal of contactant	Expert opinion
Topical corticosteroids	A*
Avoidance of irritants	C*
Emollients (lipid rich moisturizers)	A*
Barrier creams (dimethicone or perfluoropolyethers)	B*

Specific Investigations Recommended [46–49]

For diagnosis

Patch testing

Multiple studies have been performed using patch testing in symptomatic children and adolescents. Most showed one or more positive patch test reaction in 62–83 % of patients (one study was only 25.1 % of those tested), of which 55–77 % were considered to be relevant. The most common sensitizers were metals, fragrances, and hair dyes.

A thorough systematic review of 49 studies (pulled from 413 initial articles) of adult patients was performed with multiple evidence-based findings. Barrier creams containing dimethicone or perfluoropolyethers, cotton liners, and softened fabrics were able to prevent irritant CD. Lipid-rich moisturizers both prevent and treat irritant CD. Topical skin protectant and quaternium 18 bentonite (organoclay) can prevent rhus dermatitis. Diethylenetriamine pentaacetic acid (chelator) cream prevents nickel, chrome, and copper dermatitis. Potent or moderately potent steroids (fluticasone propionate 0.05 %, clobetasone butyrate 0.05 %, and clobetasol propionate 0.05 %) effectively treat allergic CD.

Multiple studies report statistically significant improvement in adult patients with ACD with tacrolimus 0.1 % ointment when compared with petrolatum or vehicle alone. In studies comparing tacrolimus 0.1 % ointment and mometasone ointment, both showed efficacy. Tacrolimus 0.1 % ointment in the treatment of eyelid ACD led to improvement in erythema, edema, scaling, and lichenification at 30 days of treatment, though fissuring did not improve. In a study of adult patients with nickel-induced ACD, pimecrolimus 0.6 % cream was comparable to betamethasone-17-valerate 0.1 % cream and was more effective than the vehicle.

Several authors recommend oral prednisone in cases of widespread and/or severe reactions. Dosing recommendations include 1 mg/kg/day for 10–14 days (>10 % body

Table 3.10 Second line therapies [50–54]

Topical calcineurin inhibitors	A*

Table 3.11 Third line therapies [44, 55–58]

UVB/PUVA for CD of hands	B
Systemic corticosteroids	Expert opinion

surface area) up to >3 weeks (severe reactions, such as from poison ivy exposure).

Studies show treatment with UVB or PUVA can lead to improvement in ACD, though amount and duration of improvement varied. One study of ten patients treated with UVB led to complete resolution of hand ACD; however, treatment duration was lengthy at 5 months) and maintenance therapy was required. Two studies compared UVB and PUVA. One using left–right comparison of the two modalities showed no significant different between the two, though side effects were seen more often in the PUVA group. The other study showed significant improvement but not clearance in UVB-treated patients, whereas all patients treated with PUVA has clearance of their dermatitis, but over half experienced relapse within 3 months.

Juvenile Plantar Dermatosis

Clinical Features of the Disorder

Juvenile plantar dermatosis (JPD) is characterized by shiny erythema and superficial scaling primarily involving the weight-bearing surfaces of the forefoot, toes (especially great toes), and the heel (Fig. 3.8). In more extensive cases, painful fissures may develop. JPD presents in school-age children and early adolescents and typically resolves by age 12–16. Pruritus is variably present. The etiology is unclear but it is often associated with a personal or family history of atopy. There may also be a relationship with excessive sweating and occlusive footwear [2, 3].

Management Strategies

Interventions are aimed at preventing maceration and irritation from repeated moistening and drying of the plantar skin. This is accomplished by wearing breathable footwear, cotton socks, and application of barrier emollients such as white petrolatum. Changing out damp socks with a fresh dry pair after applying white petrolatum to the affected skin can be a useful strategy. In more severe cases with significant pruritus and fissures, mid- to high-potency topical steroids may be helpful (Table 3.12). Topical tacrolimus 0.1 % used in combination with emollients has also been reported to be helpful (Table 3.13). In patients with significant hyperhidrosis, aluminum chloride can be helpful.

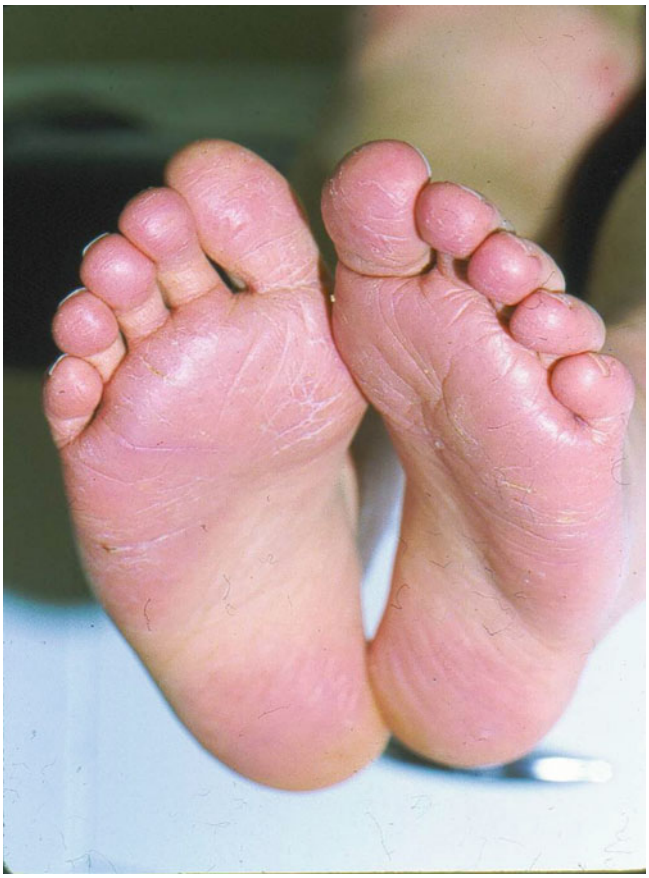

Fig. 3.8 Shiny erythema and superficial scaling on the weight-bearing surfaces of the forefoot (Photo courtesy of Alfons Krol, MD)

Specific Investigations Recommended [59]

For diagnosis
Skin scraping for KOH to exclude dermatophyte infection
Biopsy rarely necessary but can be useful if psoriasis is suspected
Patch testing if ACD is suspected

The diagnosis is primarily clinical. Potassium hydroxide preparation can be useful to evaluate for tinea pedis, although the absence of interdigital involvement supports a diagnosis of juvenile plantar dermatosis. Patch testing is helpful in cases where allergic contact dermatitis (ACD) is suspected. ACD involving the feet typically is more pruritic than JPD and often involves the dorsal aspects of the feet. Palmoplantar psoriasis can involve the soles but tends to be more sharply demarcated, have thicker scale, and typically extends beyond the weight-bearing surfaces.

Table 3.12 First line therapies [60–62]

Corticosteroids	D
Emollients	D
Cotton socks	D
Breathable footwear	
Reducing friction	

Table 3.13 Second line therapies [63]

Topical calcineurin inhibitors	E

Retrospective reviews of patients with JPD have reported disease duration averaging 4.5–8.4 years. Patient report of associated factors varied, including friction, wearing cotton socks, and switching from sporting footwear or "trainers" to leather shoes. Response to any treatment also varied, with one study showing only 54 % of patients felt that treatment had any effect on their condition. Improvement was reported with the use of emollients alone in 22–57 %, and with topical steroids in 20–34 % of patients.

A single case report of an 8-year-old boy with JPD, treated with BID application of 0.1 % tacrolimus ointment as well as regular emollients, reported improvement within 4 weeks.

Lichen Simplex Chronicus

Clinical Features of the Disorder

Lichen simplex chronicus (LSC), also called neurodermatitis, is characterized by pruritic ill-defined hyperpigmented thickened lichenified plaques. It is rarely seen in infants or young children but can be seen in older children and adolescents. Locations that tend to be involved are the nape of the neck, ankles, wrists, genitalia, and pretibial skin. LSC results from repetitive rubbing and scratching of the skin, most often in response to localized pruritus. The lesion may be found in isolation with no apparent inciting event, or may be seen in the setting of atopic dermatitis, or other pruritic skin disease. Insect bites or poison ivy exposure have also been reported to initiate pruritus leading to LSC. Scratching can increase c-fiber responsiveness, which in turn leads to increased pruritus and further scratching. This cycle can cause intensifying pruritus, repetitive rubbing and, ultimately, LSC [2, 3].

Management Strategies

No evidence-based guidelines for the treatment of LSC in children exist. Most treatment recommendations are based on studies in adults. Key to management of LSC is breaking the itch–scratch cycle. This is most often accomplished with high-potency topical steroids, with or without occlusion, and patient behavior modification. Improvement is not seen if the rubbing continues. Occlusion can play a dual purpose in that it increases penetration of the topical steroid while also acting as a protective barrier. Flurandrenolide-impregnated tape can be used to provide occlusion as well as deliver corticosteroid. Intralesional triamcinolone is often used and effective in adults, but is frequently not tolerated by children. Any xerosis should be managed with emollients and optimizing bathing habits. Oral antihistamines may be of some benefit and are potentially helpful with nighttime sedation when pruritus is often at its peak. Menthol preparations can provide a cooling sensation that can help alleviate itch. Topical pimecrolimus and tacrolimus can be used as alternatives to topical steroids. Topical doxepin cream has also been shown to be effective, including use in a 3-year-old child. Its use however, has been limited by transcutaneous absorption leading to sedation, as well as development of allergic contact dermatitis. Topical aspirin has also been used with success in treatment of recalcitrant LSC.

Specific Investigations Recommended

In the absence of generalized pruritus, no specific investigations needed. Patients with new-onset generalized pruritus should undergo evaluation for systemic illnesses associated with pruritus.

A randomized, controlled trial of two topical corticosteroids, 0.05 % halobetasol propionate ointment and 0.05 % clobetasol 17-propionate ointment, showed significant improvement in adults with chronic, localized AD or LSC. One pediatric case report documents successful treatment of LSC on the forehead with tacrolimus 0.1 % ointment. A case series of adult female patients with vulvar LSC treated with pimecrolimus 1 % cream showed improved signs and symptoms in all patients.

In a small study of 18 patients with LSC, 10 treated with flurandrenolone tape and 8 with topical steroid without occlusion, lasting remission was seen in a greater number (70 %) of patients using flurandrenolone tape versus topical steroid alone (25 %). Topical doxepin cream showed significantly greater pruritus relief than those treated with vehicle in all efficacy parameters measured in a large multicenter double-blind trial of mostly adult patients (aged 12–65, mean age 38 years) with different eczematous conditions, of which 136 had LSC. Doxepin 5 % cream also was successful in treating persistent lichenification in a 3-year-old patient. A small double-blind study of 29 patients with LSC treated with either topical aspirin/dichloromethane or placebo showed significant therapeutic response in 46 % of treatment group compared to 12 % in the placebo group.

Table 3.14 First line therapies [64–66]

Corticosteroids	A*
Topical calcineurin inhibitors	C*

Table 3.15 Second line therapies [67–70]

Flurandrenolone tape	C
Topical 5 % doxepin cream	E/A*
Topical aspirin	A*

Table 3.16 Third line therapies [71–77]

Biofeedback, cognitive behavioral therapy, hypnosis	D
Gabapentin	E*
Botulinum toxin type A injection	E*
Acupuncture	C*
Ketotifen	C

There is some evidence to support modalities such as biofeedback, cognitive-behavioral methods, and hypnosis in the treatment of LSC and other aspects of dermatology. A case series of four patients, including one 16-year-old, reported significant improvement in neurodermatitis with a single treatment session using the "habit-reversal" technique. Another case report showed temporary, partial response of LSC to gabapentin. A case series of three patients receiving Botulinum toxin type A injections directly into chronic LSC lesions showed pruritus subsided within 3–7 days in all patients. Small clinical studies also show improvement in neurodermatitis with electro-acupuncture (with needles inserted around diseased areas) in adults and with ketotifen in children.

Lichen Striatus

Clinical Features of the Disorder

Lichen striatus presents as a transient linear eruption consisting of erythematous and lichenoid papules following the lines of Blaschko (Fig. 3.9) It most commonly presents on the extremities, but can be seen on the trunk and face. Lesions can be a few centimeters or extend over an entire limb. Involvement of a digit can lead to nail dystrophy, which may precede skin findings (Fig. 3.10) This is a self-limited condition that can persist for several weeks to 2–3 years, with occasional relapses [78, 79]. Post-inflammatory pigmentary changes can follow inflammatory lesions (Fig. 3.11) [2, 3]. Biopsy of lesions typically shows a mixed lichenoid and spongiotic pattern. This can vary depending on the age of the lesion biopsied. The etiology is unclear, but the Blaschko-linear distribution suggests genetic mosaicism with inflammation caused by loss of tolerance to a keratinocytic clone [78]. Several possible

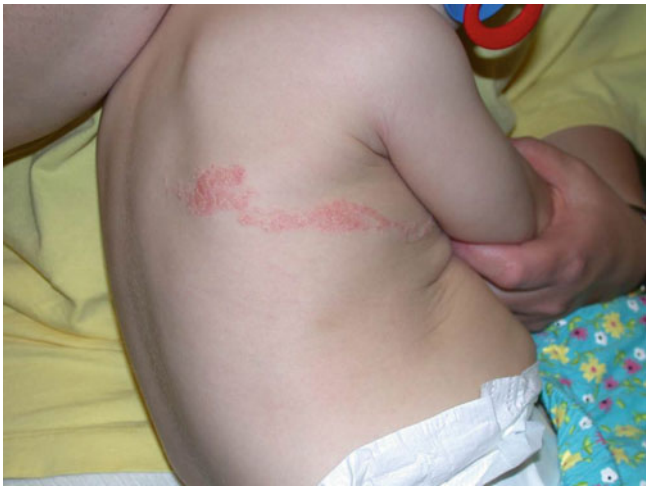

Fig. 3.9 Erythematous and psoriasiform papules following the lines of Blaschko on the back (Photo courtesy of Alfons Krol, MD)

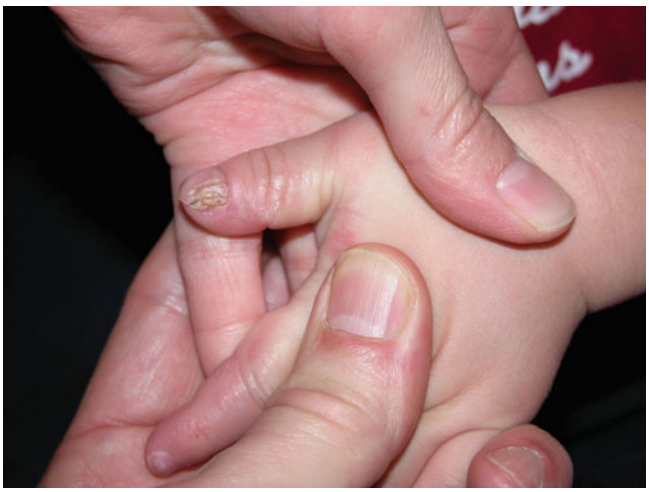

Fig. 3.10 Lichen striatus causing nail dystrophy (Photo courtesy of Alfons Krol, MD)

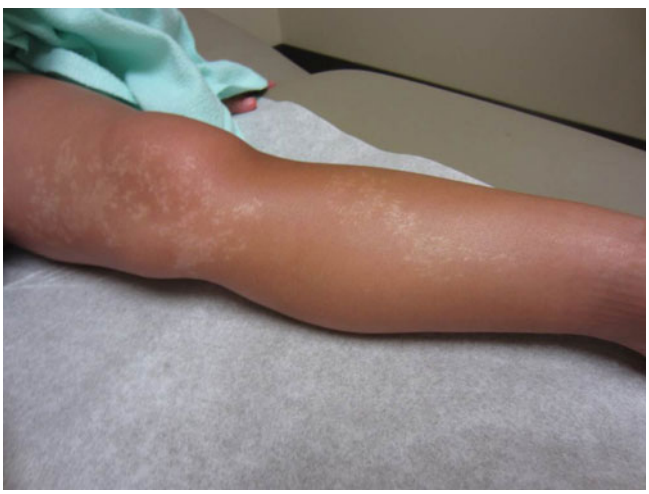

Fig. 3.11 Hypopigmented stage of lichen striatus on the leg (Photo courtesy of Sabra Lietenberger, MD)

Table 3.17 First line therapies [78–81]

Observation	Expert opinion
Topical corticosteroids	D
Emollients	D
Topical calcineurin inhibitors	E

Table 3.18 Second line therapies [82]

Hydroxychloroquine	E

triggers for a loss of tolerance have been proposed, including viral infection, atopic dermatitis, contact dermatitis, and ultraviolet light.

Management Strategies

Intervention is rarely necessary for this self-limited process. For the minority of patients with associated pruritus, mid potency topical steroids can be helpful. Topical tacrolimus may hasten resolution and possibly reduce hypopigmentation.

Specific Investigations Recommended

In cases where the diagnosis is unclear, biopsy may be needed to differentiate from other linear inflammatory skin conditions such as linear lichen planus, linear lichen nitidus, linear psoriasis, and inflammatory linear verrucous epidermal nevus.

In a series of 18 patients, mean duration of eruption was 9.5 months without treatment. A review of 61 patients with LS also reported eventual resolution without treatment, though they did note that several patients treated with medium-strength topical corticosteroids seemed to have faster resolution of inflammatory lesions, with lesions becoming non-erythematous within 2–4 weeks of commencing treatment. Case reports also have found improvement in erythema and hyperpigmentation with topical tacrolimus.

Case series of four patients initially thought to have a lupus erythematosus LS overlap. Three were treated with hydroxychloroquine, with resolution of lesions in 3–15 months. The fourth patient was treated with prednisolone valerate cream, with improvement after 9 months.

Nummular Dermatitis (Discoid Eczema)

Clinical Features of the Disorder

The term nummular is used to describe the round "coin-shaped" eczematous lesions characteristic of this condition. The round eczematous plaques often begin with the coalescence of pruritic exudative papules or papulovesicles. The distribution is less predictable than nummular dermatitis seen in adults, but tends to first involve extensor surfaces of the extremities then spread to trunk and dorsal hands. Nummular dermatitis is often associated with atopic dermatitis, and in these children may represent a nummular form of atopic dermatitis, but it can be seen independently. Xerosis seems to be a major predisposing factor. The eruption tends to last for several months with flares in the winter. It can be worsened by use of harsh soaps and other irritants [2, 3]. Medications including isotretinoin, interferon, ribavirin, gold, and anti-tumor necrosis factor inhibitors, are reported to induce nummular dermatitis [83]. Occult infections (dental infections, H. pylori) have rarely been reported in association with nummular dermatitis in adults [84].

Management Strategies

Nummular dermatitis can be challenging to treat, and response to treatment is often slow. Treating xerosis with regular emollients and gentle bathing is important. Crusted or exudative lesions should be cultured and the patient treated with topical or oral antibiotics if superinfection is present. Mid- to high-potency topical steroids are often needed. Antihistamines such as hydroxyzine have also been recommended. No evidence-based guidelines exist for the treatment of this condition in children.

Specific Investigations Recommended [83–86]

Consider patch testing
Skin scraping for KOH examination
Bacterial culture of skin lesions
Consider other infections (dental, H.pylori) in persistent cases
Consider causative medications

In a retrospective review of 48 adult patients who underwent patch testing, 33 % had positive patch tests thought to be clinically relevant. The most common allergens were rubber chemicals, formaldehyde, neomycin, chrome, and nickel. In a larger review of 1,022 patients (including some children), 35 % had at least one positive patch test, of which 69 % of these were thought to be relevant. The most common allergens were nickel sulfate, potassium dichromate, cobalt chloride, paraphenylenediamine, and ethylenediamine.

Most studies group nummular eczema with other forms of eczema, making it difficult to judge specific responses and form evidence-based treatment recommendations. For patients with a discoid/nummular variant of AD, evidence-based treatment recommendations for AD can be used (see previous AD section).

Table 3.19 First line therapies [87]

Topical corticosteroids	C*
Topical calcineurin inhibitors	C
Topical antibiotics	C
Emollients	C
Oral antibiotics if infection present	C
Oral antihistamines	E

Table 3.20 Second line therapies [88, 89]

Phototherapy	C*
Methotrexate	C

Mid- to high-potency topical corticosteroids are the normal first line treatment for this condition. These can be used with or without occlusion. Caution should be used when using potent corticosteroids under occlusion in children, given the risk of atrophy. Emollients and gentle skin care practices should be employed in conjunction. Any superinfection should be treated with topical or oral antibiotics. In one adult study, patients with "nummular eczema" cleared after 8 days of once-weekly clobetasol propionate lotion left under Duoderm occlusive patches.

In a case series of 25 children with refractory nummular eczema treated with methotrexate (dose range 5–15 mg), 16 patients (64 %) completely cleared after an average of 10.5 months of treatment. No serious adverse events were reported.

Seborrheic Dermatitis

Clinical Features of the Disorder

Seborrheic dermatitis is characterized by erythematous plaques with thick adherent yellow scale. The distribution depends on the age of presentation. This condition has two major forms, an infantile form and an adolescent form. Unlike many forms of eczema, pruritus is usually not a prominent feature of seborrheic dermatitis. These forms may represent two separate clinical entities, but share the same name and often respond to similar treatments [2, 3, 90]. Despite how commonly this condition is encountered, the exact etiology remains unclear. Many propose that commensal Malassezia yeasts (formerly called *Pityrosporum ovale*) are involved in the pathogenesis given the presence of this organism on affected skin as well as the response to treatment with antifungal agents. However, the total levels of Malassezia on affected skin do not seem to correlate with disease severity. This finding suggests an important role of host susceptibility in the etiology. The pathogenesis of infantile seborrheic dermatitis may have a similar etiology. In one study Malassezia was isolated more frequently from the skin of patients with infantile seborrheic dermatitis (ISD) than patients with atopic dermatitis (AD) and unaffected controls [91]. ISD also responds to antifungal treatments.

Infantile seborrheic dermatitis (ISD) presents most commonly in the first 4–6 weeks of life, and is characterized by erythema and thick scale over the frontal and vertex scalp, as well as intertriginous areas. The scalp is typically the first area of involvement, and has been colloquially referred to as "cradle-cap."

Adolescent seborrheic dermatitis presents with erythematous scaly plaques, with a greasy yellow scale over the seborrheic areas are the head, neck, and upper trunk. On the face it tends to be most prominent over the forehead, eyebrows, and alar creases. The retro-auricular folds and auditory canal are also often involved [2, 3].

Management Strategies

ISD tends to be self-resolving and does not always require treatment, but when necessary, conservative treatment will usually suffice. For the scalp, gentle removal of scale can be accomplished after softening with oil preparations or white petrolatum. After softening, the scale can be gently removed while washing with a gentle shampoo. A soft washcloth or baby toothbrush can be used to aid in removal of scalp scale, but over-vigorous scrubbing or brushing should be avoided. If the above is not helpful, addition of a mild topical corticosteroid or shampoo containing 2 % ketoconazole, selenium sulfide, or zinc pyrithione, may be necessary.

ISD involving the trunk and intertriginous areas tends to respond well to topical treatment with mild corticosteroids, as well as antifungal agents such as ketoconazole cream. Treatments containing tar and salicylic acid should be avoided in infants. TCIs have been shown effective as well, but they are not approved for use in children younger than 2 years of age.

Adolescent SD can be treated similarly to adult SD. Conventional treatment of the scalp in adolescent SD is comprised of intermittent use (two to three times weekly) of a medicated shampoo containing zinc pyrithione, selenium sulfide, coal tar, ketoconazole, or ciclopirox olamine. A shampoo with 5 % solution of maleluca oil may be effective, but many cases of allergic contact dermatitis have been reported to this botanical extract. Addition of a corticosteroid lotion or foam is occasionally needed in patients with significant erythema or pruritus. Adolescent SD involving the face is usually treated with hydrocortisone, ketoconazole, or a combination of the two. Pimecrolimus and tacrolimus creams may serve as an alternative to mild topical steroids. Other options with some evidence of effectiveness include other formulations of ketoconazole including gel and foam, metronidazole 0.75 % gel, ciclopiroxolamine 1 % cream, and

lithium gluconate 8 % ointment. Oral antifungals have been shown to be effective, but likely should be reserved for cases of severe refractory SD.

Specific Investigations Recommended

Biopsy to r/o LCH if the patient has refractory disease or an atypical presentation
HIV serology in adolescents with risk factors and severe refractory SD
Consider biopsy to distinguish from psoriasis or AD
Serum zinc levels

The differential for ISD includes AD, psoriasis, acrodermatitis enteropathica, and Langerhans histiocytosis (LCH). In early infancy, differentiating these conditions clinically can be challenging, as there can be significant overlap. Over time, however, the clinical features become more characteristic. The presence of xerosis and pruritus can be helpful in making the diagnosis of AD. AD also tends to involve the forearms and shins, in contrast to ISD, which is found more in the axillae and diaper area. Psoriasis can begin with erythematous well-demarcated scaly plaques in the diaper area. The presence or absence of greasy scale in the scalp can be helpful in making the distinction between psoriasis and ISD, as well as more characteristic lesions that tend to appear on the trunk. A family history of psoriasis can also be informative. The presence of crusting, atrophy, or hemorrhage should prompt the clinician to rule out LCH. Skin biopsy can easily differentiate LCH and ISD, and should be performed if LCH is suspected. The primary differential for adolescent SD is psoriasis. This can be a difficult differential, especially if only the scalp and face are affected. The presence of more typical psoriatic plaques elsewhere on the body, or nail changes, can be helpful in making this distinction [2, 3].

Multiple randomized studies of ketoconazole 2 % in various formulations (cream, foam, shampoo) show superior results, with less scale and less pruritus, when compared to placebo. One of these, a large multicenter double-blind study, compared cream and foam formulations and did not show a significant difference between them. Another large multicenter double-blind study showed the need for periodic prophylactic treatment and efficacy of ketoconazole shampoo as prophylactic treatment. In this study, 47 % of the patients using placebo relapsed, compared to 19 % of patients treating once weekly and 31 % of patients treating once every other week with ketoconazole 2 % shampoo. Studies of zinc pyrithione shampoo and selenium sulfide shampoo have also shown significant improvement compared to placebo. Studies in adult and pediatric populations of ketoconazole cream (2 % adult study, 1 % pediatric study) versus hydrocortisone 1 % cream showed significant improvement, with no significant difference between the two groups in global assessment at 4 weeks in the adult study. In the pediatric study of children age 2 months to 2 years old, all patients showed significant improvement at 1 week and complete clearance by 2 weeks. An adult study comparing ketoconazole 2 % foaming gel with betamethasone dipropionate 0.05 % lotion showed the response rate for ketoconazole was higher than for betamethasone, according to the global evaluation by the physician and the patient.

In a double-blind study of 96 adults with seborrheic dermatitis, pimecrolimus 1 % cream showed only slightly greater improvement when compared to placebo, and this improvement was significant only in the per protocol analysis and not significant in the intent-to-treat analysis. A randomized study of pimecrolimus 1 % cream versus betamethasone valerate 0.1 % cream showed significant improvement; betamethasone was slightly quicker in action, but patients in that group had more relapses and more pruritus upon treatment discontinuation. A study of 18 consecutive adult patients using tacrolimus 0.1 % ointment showed either clearance or 75–99 % improvement in all treated. Tacrolimus 0.1 % ointment also compared favorably to hydrocortisone 1 % ointment, with statistically significant improvement in both groups. A large, randomized double-blind study comparing ciclopirox shampoo to vehicle showed rates of "effective treatment"(global score of 0 or 1) with ciclopirox 1 % shampoo twice and once weekly were 57.9 % and 45.4 %, respectively, compared with 31.6 % for vehicle. As a prophylactic treatment, relapses occurred in 14.7 % of patients shampooing once weekly, in 22.1 % of

Table 3.21 First line therapies [92–100]

Corticosteroids-low potency	A
Topical ketoconazole foam/shampoo/cream	A
Topical calcineurin inhibitors	A
Zinc pyrithione shampoo	B
Selenium sulfide shampoo	A

Table 3.22 Second line therapies [101–106]

Topical calcineurin inhibitors	A*
Ciclopirox shampoo/cream	A*

Table 3.23 Third line therapies [107–117]

5 % Tee tree oil shampoo	B
Metronidazole gel	B
Lithium succinate/gluconate	A*
Bifonazole shampoo/cream	B*
Oral terbinafine	B*
Oral itraconazole	B*
Moisturizer containing 0.025 % licochalcone	A

those shampooing once every 2 weeks, and in 35.5 % of the vehicle group. In another large, randomized double-blind study, this time comparing ciclopirox 1 % cream to vehicle, responders at 1 and 2 months were 44 % and 63 % in the treatment group versus 15 % and 34 % in the vehicle group.

A randomized study of adolescents and adults reported greater improvement in the severity of seborrheic dermatitis with 5 % tea tree oil shampoo (41 %) versus placebo (11 %). Metronidazole 1 % gel showed statistically significant improvement versus placebo in adult patients over an 8-week treatment period, and a randomized, double-blind study comparing metronidazole 0.75 % gel versus ketoconazole 2 % cream in adolescent and adult patients showed improvement with decrease in clinical severity scores from baseline in both groups. Lithium succinate ointment also showed significant improvement compared to placebo in a double-blind trial of 227 adult patients. In adult patients, randomized studies of bifonazole shampoo (three times a week) and bifonazole 1 % cream (once daily) versus placebo showed significantly greater improvement in patients in the treatment groups. Both oral terbinafine and itraconazole have also shown efficacy in smaller studies, with oral terbinafine leading to statistically significant improvement in erythema, scaling and pruritus at 4 and 12 weeks.

Two studies have been performed in infants and young children. A study of bifonazole 1 % shampoo for scalp seborrhea in 34 infants and younger children also showed improvement or cure without any serious side effects noted. A randomized, prospective, split-side, double-blind study of 75 infants found that moisturizer containing 0.025 % licochalcone had a higher cure rate compared to 1 % hydrocortisone for the treatment of infantile SD at days 3–4; however, by the end of the first week, this difference was no longer significant, and both treatments led to significant improvement.

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