

Inpatient management of atopic dermatitis

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ABSTRACT: Atopic dermatitis (AD) is a common chronic inflammatory skin disease that is generally managed on an outpatient basis. However, a significant percentage of patients may develop complications severe enough to require inpatient treatment. The most common complications of AD that may require hospital admission include erythroderma, eczema herpeticum, and systemic bacterial infection. Hospital admission can also be useful for chronic and severe disease that has not responded to standard therapy or in situations where nonadherence is suspected as the cause of treatment failure. In these cases, inpatient treatment can offer an opportunity for caretaker education and allow for an objective evaluation of a patient's response to a structured treatment plan. This article will review the indications for inpatient management of AD and the therapies that can be used to acutely manage severe disease and associated complications.

KEYWORDS: atopic dermatitis, eczema herpeticum, erythroderma, hospitalized patient, wet wrap therapy

Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disease that affects approximately 17% of children and 1–3% of adults (1). Traditional therapy consists of emollients, mild to moderate potency topical corticosteroids, or topical calcineurin inhibitors, along with avoidance of irritants and allergens. Although this treatment strategy results in significant improvement for most patients, a small percentage will require more intensive therapy. The most common complications of AD that may require inpatient management include erythroderma, eczema herpeticum, and systemic or severe bacterial infection. Hospital admission can also be useful for chronic and severe disease that has not responded to standard therapy or in situations where nonadherence is suspected as the cause of treatment failure. In these cases, inpatient

treatment can offer an opportunity for caretaker education and allow for an objective evaluation of a patient's response to a structured treatment plan. This article will review the indications for inpatient management of AD and the therapies that can be used to acutely manage severe disease and associated complications.

Erythroderma

Acute decompensation of moderate to severe AD can lead to erythroderma, which is defined as the presence of erythema and scaling involving greater than 80% of the body surface area. AD is one of the more common causes of erythroderma, but many other causes exist (Table 1). Regardless of the underlying disease, complications of erythroderma can be life-threatening and can include temperature instability, hypoproteinemia, hypovolemia, hypernatremia, and high-output congestive heart failure. Inpatient management of erythroderma is often necessary.

The first step in the management of a patient presenting with erythroderma is a thorough

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Table 1. Differential diagnosis of common causes of erythroderma

Disease	Characteristic clinical features
Atopic dermatitis	Severe pruritus, lichenification, personal or family history of atopy, elevated immunoglobulin E, eosinophilia
Seborrheic dermatitis	Infants, greasy yellow scale, diaper area involved
Psoriasis	Silvery scale, preexisting psoriatic lesions, nail changes, + family history of psoriasis
Staphylococcal scalded skin syndrome	Infants and young children, superficial blisters, + Nikolsky's sign, skin fold and perioral accentuation, painful
Ichthyosis	Congenital, possible collodion membrane
Netherton syndrome	Onset in infancy, sparse hair (trichorrhexis invaginata), failure to thrive, atopy
Immunodeficiencies	Early onset, alopecia, failure to thrive, recurrent infections
Drug	History of medication intake
Cutaneous T cell lymphoma	Adults, severe pruritus, keratoderma
Pityriasis rubra pilaris	Keratoderma, islands of sparing, salmon-colored erythrema

workup to identify the underlying etiology. A careful history should be taken at presentation, giving special attention to preceding illnesses, recent fevers, new medications, and relevant past medical and family history. Physical examination should include evaluation of the mucosal surfaces, testing for a positive Nikolsky sign (sloughing of the epidermis with light lateral friction on the skin surface), and palpation of the lymph nodes. Baseline laboratory evaluation should consist of liver function tests, chemistry panel, and complete blood count. Preexisting dermatitic lesions, severe pruritus, lichenification, personal or family history of atopy, elevated serum levels of immunoglobulin E, or eosinophilia can be helpful features that support the diagnosis of AD. Helpful clues on histological examination include mild to moderate acanthosis and spongiosis, dermal eosinophils, and parakeratosis.

Although definitive treatment of erythroderma depends on the underlying cause, all patients

should be managed for fluid loss, electrolyte abnormalities, and temperature instability (2). Nutritional support is also critical. The large body-surface-to-body-mass ratio in children combined with an impaired skin barrier and cutaneous vasodilation leaves them especially vulnerable to hypernatremic dehydration, high-output cardiac failure and hypothermia (3). Secondary bacterial infection with *Staphylococcal aureus* is common in erythrodermic atopic patients and should be recognized and treated promptly. Once the cause of erythroderma has been established, proper treatment of the underlying condition can be initiated. In the case of AD, wet wrap therapy can achieve rapid improvement.

Wet wrap therapy

Wet wrap treatment is defined as any treatment consisting of the application of a topical agent with a double layer of bandages or gauze, first with a moist layer and then a dry second layer. The effectiveness of wet wrap therapy in AD is thought to be multifactorial. Wet wraps have been shown to heal the disrupted skin barrier of AD patients, repair the lamellar structure of intercellular lipid, and decrease transepidermal water loss (4). It is also suggested that the dressings create a physical barrier to scratching, which allows the skin to heal in addition to providing a moist environment in which topical medications are more easily absorbed (5). Although most regimens include the use of a topical corticosteroid, there are also reports of improvement with emollient alone. A trial by Schnopp et al. comparing wet wrap therapy with either mometasone or a bland emollient showed significant improvement in both arms of the study; however, the effect was significantly better in the mometasone-treated group (6). The effectiveness of steroid-free treatment does, however, lend support to the idea that improved penetration of topical medications is only one facet of the effectiveness of wet wrap therapy.

Regarding the practical details of wet wrap therapy, a basic protocol that includes the features common to most wet wrap regimens is presented in Table 2. A variation in which the first layer is soaked in warm steroid cream instead of water has also been reported to be effective; in this variation, the steroid-soaked wet layer replaces the application of a topical steroid (7). The steroid of choice as well as the frequency of wet wrap application also varies by institution. Table 3 shows several topical steroids and frequencies of application that have been reported effective. Regarding the duration of

Table 2. Wet wrap protocol

General wet wrap protocol

- Using tubular bandages, cut the appropriate size to cover the arms, trunk, legs, and (if needed) a mask for the face. You will need enough for two layers.
- Gently bathe skin with lukewarm water for 5–10 minutes. Pat dry gently.
- Apply steroid cream or ointment to the skin.
- Soak the first layer of bandages in lukewarm water, wring out, and apply to skin wrapping the extremities and trunk.
- Apply second layer of dry bandages.
- Leave in place at least 2 hours and repeat every 12 hours. Children may sleep overnight in dressings if tolerated.

therapy, all studies showed significant improvement of AD after 1 week of wet wrap therapy, with less improvement seen in the second week and thereafter (6–10). Therefore, the present authors recommend a treatment period of no more than 7 days to balance the risk of side effects while achieving the maximal benefit available with this therapy.

The major risk of wet wrap therapy is suppression of the hypothalamic-pituitary-adrenal (HPA) axis. Several studies have shown that wet wrap therapy can lead to a temporary drop in early morning serum cortisol levels (7,8). However, cortisol levels returned to normal within 2 weeks of discontinuing therapy, and no adverse events occurred in either study as a result of this suppression. Several investigators have examined the effect of dilution of steroid with emollient as a way to decrease the total amount of steroid delivered to the skin and have found that there was no difference in efficacy between various dilutions of fluticasone propionate (see Table 3 for dilutions studied) (8,9). Wolkerstorfer et al. also examined whether or not HPA axis suppression could be minimized if a more dilute steroid cream was applied (9). They found that more HPA axis suppression did occur in patients treated with higher steroid concentrations. Therefore, increasing the dilution of potent steroids appears to result in lower risk of HPA axis suppression while maintaining efficacy of higher steroid concentrations.

The two most common adverse effects associated with wet wrap treatments are poor tolerance of the process and folliculitis likely secondary to occlusion. Using creams instead of ointments may reduce the incidence of folliculitis. The increased risk of bacterial or herpetic infections with wet wrap therapy is controversial but appears to be rare. Although some studies report an increase in

the incidence of secondary bacterial infection, others actually report a decrease in the colonization of *S. aureus* on the skin of AD patients after wet wrap treatment (6,8). The present authors suggest that wet wraps not be applied to any obviously infected areas until proper antimicrobial treatment has been initiated and improvement is seen.

Eczema herpeticum (EH)

EH occurs when skin previously affected by AD becomes secondarily infected with herpes simplex virus (HSV). EH can lead to serious and even fatal complications, especially in the case of disseminated viremia and multiorgan involvement (11,12). For this reason, EH is another complication that can require inpatient management. Dissemination of the herpes virus in patients with AD is thought to be a result of the impaired skin barrier, which facilitates viral invasion and binding to cellular receptors (13). Children affected by EH will often have a history of a more severe disease, an earlier onset of AD, and a higher rate of coexistent food allergy or asthma (14). Elevated serum immunoglobulin E has also been implicated as a risk factor for EH (15). Although topical corticosteroids have been implicated in the past as a potential cause of this complication, further research has refuted this assertion (15).

EH presents as umbilicated vesicles progressing to punched-out crusted ulcers occurring primarily in skin affected by AD (FIG. 1). The head and neck are preferentially involved. The infection can be a result of either dissemination of recurrent HSV or a result of inoculation from an infected person (15). The skin lesions can be extremely painful and are at risk for secondary bacterial infection. New lesions typically appear for the first 7–10 days, and the lesions will typically resolve in 2–6 weeks (16). The primary episode is often associated with fever, lymphadenopathy, and malaise. Systemic viremia can lead to multiorgan involvement, most commonly the liver, lungs, central nervous system, and adrenal glands. The diagnosis can be confirmed with viral changes seen on skin biopsy, direct fluorescent antibody (DFA) staining, viral culture, or polymerase chain reaction for viral DNA on a smear or tissue sample. Diagnosis can also be made performing a Tzanck test. The Tzanck test refers to a procedure in which the base of a freshly unroofed vesicle is scraped and the cells are smeared onto a glass slide. After staining the slide with Wright or Giemsa stain, the presence of multinuclear viral cells or balloon cells with typical viral

Table 3. Topical steroids and frequency of steroid application in several reported regimens

Reference	Topical steroid	Frequency of wrap application Duration of wrap therapy (hours) Duration of treatment (weeks)
UAB Department of Dermatology	Triamcinolone 0.1% cream to body Desonide cream to face	Twice daily Two hours per wrap For 1 week
Devillers et al. (8)	Fluticasone propionate 0.05% cream 5% dilution to face Adults: 10 or 25% dilution to body Children: 5 or 10% dilution to body	Once daily Twenty-four hours per wrap, rewetting every 2–3 hours with water mist For 1 week
Wolkerstorfer et al. (9)	Fluticasone propionate 0.05% cream 0, 10, 25, or 50% dilution to body	Once daily Twenty-four hours per wrap, rewetting every 2 hours with water mist For 2 weeks
Goodyear et al. (7)	0.5% Hydrocortisone cream if <2 years 10% dilution of betamethasone valerate 0.01% cream if >2 years	Twice daily Twelve hours per wrap For 2–5 days
Schnopp et al. (6)	0.1% mometasone furoate	Twice daily Duration of wrap not given For 5 days
Pei et al. (10)	0.1% mometasone furoate diluted to 10% 0.005% fluticasone propionate diluted to 10%	Once daily Duration of wrap 8 hours For 2 weeks

cytopathic change, such as nuclear molding and condensed chromatin, confirms the diagnosis (17). DFA staining is the most rapid and reliable test if available in your local hospital lab. DFA also requires scraping the base of the lesions and smearing on a glass slide in six to eight different wells for the DFA technician to test with HSV and varicella zoster virus reagents.

The cornerstone of EH therapy is antiviral medication (Table 4). Intravenous acyclovir is preferred in EH because of the lower bioavailability (15–30%) of oral acyclovir (13). Therefore, oral acyclovir should be restricted to the treatment of mild disease. For children <12 years old, the recommended intravenous dose is 750 mg/m² given three times a day. For older children and adults, the recommended regimen is intravenous acyclovir 5–10 mg/kg/dose given three times a day. Although no studies have been done on the appropriate length of intravenous therapy prior to transition to oral antivirals, 3–7 days of intravenous therapy is common (13). For mild disease, oral antiviral medications (acyclovir, valacyclovir, and famciclovir) can be used (18). Oral dosing regimens for drugs other than acyclovir are not

well established in the pediatric population. The recommended dosage for acyclovir in children is 20 mg/kg/dose four times daily. The maximum dose is 800 mg four times a day. Recommended adult dosages are acyclovir 800 mg five times daily, valacyclovir 1 g three times daily, and famciclovir 500 mg three times daily (18). All medicines are continued for 7–10 days or until evidence of healing is noted.

Adjunctive treatment for EH consists of pain control, treatment of secondary bacterial infection, and avoidance of systemic or topical corticosteroids and topical calcineurin inhibitors during acute disease. Opioid analgesics may be necessary in some cases. Secondary bacterial infection is common and prior to antibiotic therapy was a common cause of mortality in EH. Any potentially infected areas should be cultured, and antibiotic therapy should be tailored accordingly. Infection with *S. aureus*, group A beta hemolytic streptococci, or *Pseudomonas aeruginosa* is most common. Normal saline or aluminum acetate (1 : 40) compresses may be useful. Bland emollients can be applied to the erosions, but topical or systemic immunosuppressives should be avoided until the



FIG. 1. Eczema herpeticum. Umbilicated vesicles and hemorrhagic-crust papules characteristic of eczema herpeticum. Note significant periorbital edema.



FIG. 2. Atopic dermatitis and secondary bacterial infection. Erosions and crusted papules superimposed over lichenified eczematous plaques.

acute phase has resolved. Another rare but potentially serious complication of EH is keratoconjunctivitis (19). Patients should receive an ophthalmologic examination, especially if there is facial involvement.

Bacterial infection

Bacterial colonization is a common complication of AD (FIG. 2). A study by Leyden et al. showed that 90% of patients with AD had *S. aureus* colonization of diseased skin (20). When compared with psoriatic plaques, which were colonized only 50% of the time in a similar study. This colonization rate may indicate a specific vulnerability of atopic skin to bacterial colonization (21). Although the reasons for this are not completely understood, decreased expression of endogenous antimicrobial peptides in atopic skin may cause a localized immunodeficiency in atopic skin (22). Chronic colonization with *S. aureus* can exacerbate disease and make disease clearance more difficult. Treatment with topical or oral antistaphylococcal antibiotics can facilitate recovery (23). Interestingly, patients with AD do not appear to be more likely than the general population to be carriers of resistant strains of *S. aureus* (23).

In addition to colonization, *S. aureus*, and less commonly streptococcus, can cause clinical infection. Active infection manifests as pustules, honey-crusted papules, abscesses, or cellulitis. Patients with AD are also at risk for serious infections including sepsis, endocarditis, septic arthritis, and osteomyelitis (24). Not surprisingly, patients with more severe AD are at greater risk for bacteremia. Invasive *S. aureus* infection should be considered in all atopic patients presenting with an acute

Table 4. Management of eczema herpeticum

Antiviral treatment^a

Intravenous acyclovir

<12 years of age: 750 mg/m²/dose every 8 hours

>12 years of age: 5–10 mg/kg/dose every 8 hours

Oral acyclovir^b

Child: 20 mg/kg/dose every 6 hours (maximum dose 800 mg)

Adults: 800 mg five times a day (treat children as adults when mg/kg dosing is $\geq$ 800 mg)

Other antivirals (dosing schedules not established in pediatric patients)

Valacyclovir 1 g three times a day

Famciclovir 500 mg three times a day

Adjunctive treatment

Pain control

Avoidance of topical corticosteroids and topical calcineurin inhibitors to active areas of infection

Avoidance of systemic immunosuppressives during acute infection

Identify and treat secondary bacterial infection

Normal saline or Burrow's compresses twice a day

Bland emollients

Ophthalmologic consult if facial involvement present

^aAll treatment is administered for a minimum of 7–10 days.

^bIntravenous acyclovir is preferred except in cases of mild disease.

unexplained febrile illness or fever and localized pain. In such cases, early recognition and treatment with appropriate antibiotics can be lifesaving.

Oral antibiotics can be used for most cases of active infection. The prevalence of methicillin-resistant *S. aureus* (MRSA) varies by community and makes the implementation of generalized treatment recommendations difficult. Empiric therapy should be based on local patterns of antibiotic resistance. Care should be taken to identify any fluctuant areas in need of surgical drainage. Cellulitis that fails oral treatment should be treated on an inpatient basis with intravenous antibiotics. Goals for discharge include decreasing size, redness, and tenderness of the affected area. A culture should be obtained whenever possible to help tailor antibiotic therapy. Depending on culture results, patients can be discharged on oral antibiotics or maintained on home intravenous infusions for a full course of treatment with the appropriate antibiotic. More serious infections will require hospital admission and treatment with intravenous antibiotics. Consultation with an infectious disease specialist may be beneficial. Empiric antibiotic therapy should provide coverage against MRSA until cultures and sensitivities are available. MRSA causes more serious and virulent infections compared with methicillin-sensitive *S. aureus* (MSSA). Patients requiring hospitalization for their staphylococcal infections were found to be more likely to grow MRSA than MSSA (25).

Conclusions

Inpatient treatment of AD can be a helpful and important part of long-term management of patients with this chronic condition. Erythroderma can be a life-threatening complication that requires careful attention to fluid status and rapid correction of the underlying dermatitis. Although many protocols for wet wrap therapy exist, the basic structure of steroid application under a wet and then a dry dressing has been shown in several studies to lead to rapid improvement of AD. EH is another serious complication of chronic AD requiring in most cases intravenous antiviral medication and inpatient monitoring for potential complications. Awareness of community-acquired MRSA is also important when treating AD patients. Although *S. aureus* colonization of atopic skin is a common occurrence, the existence of pathogenic strains capable of causing more severe infections

that are resistant to traditional therapies is a recent development complicating the management of these patients. Intravenous therapy should be considered for any AD patient with a severe bacterial skin infection that is resistant to oral antibiotics. Although most AD patients will not require acute inpatient therapy, it is important to recognize that there are certain subsets of our AD population who may benefit greatly from it. Prompt recognition of these patients and institution of the proper therapy can improve patient outcomes and prevent more serious complications.

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