Medical algorithm: Treatment of Atopic Dermatitis in Early Childhood (part II)

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None declared

The diagnostic work-up of atopic dermatitis (AD, atopic eczema) was discussed in part I[1]. This part of the medical algorithm focuses on the therapy of AD in early childhood and is based on international guidelines[2-4].

The management of AD is mainly based on the severity. Assessment of disease severity has already been discussed in part I. Basic therapy of the disturbed skin barrier is always necessary, i.e. also for children that do not suffer from active lesions. Normally, topical treatment is the first choice. If topical anti-inflammatory treatment fails, and patient adherence and compliance have been addressed, or in case of severe and very severe disease, phototherapy or systemic therapy are indicated (step-up approach, see Table 1[2,3]).

Basic therapy consists of emollients to moisturize the skin and improve barrier function, advice on daily skin care and hygiene/bathing, and avoidance of trigger factors (including allergens). Adherence to (basic) therapy and correct drug use have to be addressed. Counseling needs to be focused on allergen avoidance (if confirmed by allergy testing and deemed relevant [e.g. food]), possible cross reactions, and alimentary substitutes. In addition, also individual non-allergic trigger factors should be identified and patients and their parents need to be counseled in order to know how to cope with these factors (which are not always avoidable). Therapeutic patient education (e.g. 'eczema school') and written instruction plans are of great importance because many patients with AD can achieve disease control with optimized skin care and mild topical treatments[5].

Mild AD can usually be controlled with reactive therapy in addition to basic therapy. Moderate-severe AD often requires subsequent proactive therapy with topical corticosteroids (TCS) (with or without wet wraps) or topical calcineurin inhibitors (TCI). The choice for the best approach with regard to corticosteroid potency and class depends on age and body site (e.g. lower potency for the face versus higher potency for the trunk). The choice for vehicles (oil-in-water versus water-in-oil) for topical corticosteroids depends on lesion characteristics (moist versus dry), and patient preference/adherence. The fingertip unit (FTU) method should be used for optimal dosing: one fingertip of cream for an area of two adult palms. There is conflicting evidence on once versus twice-daily application[6]. TCI also can be used off-label in children <2 years[3]. The choice of topical anti-inflammatory drug depends on local cofactors (e.g. in moderate-severe AD it is recommended to start with TCS instead of TCI because the latter can evoke stinging in inflamed skin). Topical phosphodiesterase inhibitors are a treatment alternative.

For all patients, depending on the individual situation and disease course and severity, other non-pharmacological options can be used. Silver coated textiles can be used to decrease *Staphylococcus aureus* colonization on the skin (conflicting evidence). Psychological counseling should be considered with regard to individual family psychodynamics. Climate therapy at high altitude has shown beneficial effects on atopic dermatitis, probably due to UV exposure, avoidance of allergen exposure, and decreased stress[7].

For severe AD, or for cases that do not respond well to topical therapy, wet wrap therapy can be initiated in an inpatient or outpatient setting[8]. Ultraviolet (UV) therapy is used reluctantly in early childhood due to the cumulative UV dosage, time necessary, and anxiety in the UV cabin). If used, narrowband ultraviolet B (311 nm) or ultraviolet A1 is preferred. All other systemic medication is off-label in early childhood. However, there is ample clinical experience with use of cyclosporine A (fast-acting and approved in Europe from age 16 years) and methotrexate, which is a safe alternative but clinical improvement takes longer. Cyclosporine A is known for nephrotoxicity and risk for hypertension, so blood pressure and renal function have to be monitored. Methotrexate is known for hepatotoxicity. Other options are azathioprine (side effects: infection, nausea, cancer) and mycophenolate mofetil (side effects: infection, anemia, leukopenia, and diarrhea). Regular blood tests are necessary to screen for hematological, hepatic and renal side effects. The first biologic, the interleukin (IL)4/13 receptor antagonist dupilumab, has been approved in ages >=12 years and is sometimes used off-label in early childhood[9]. Its main side effects are eye inflammation (including non-infectious conjunctivitis and blepharitis), injection site reactions, and herpes simplex virus infections.

Systemic corticosteroids are not recommended because of side effects (e.g. growth impairment) and risk of rebound after discontinuation. Antibiotics should only be initiated systemically in cases of superinfection and not for the treatment of *Staphylococcusaureus* colonization. In cases of recurrent skin infections sodium hypochlorite can be added to the bathwater ('bleach bath' with 1 mL of 5% household bleach per 1 L of water), however, recent data on efficacy are conflicting [10]. Long-term daily use of sedating antihistamines in childhood may affect sleep quality and is not recommended. In some countries, melatonin is used to improve sleep quality. A therapeutic algorithm is presented in Figure I.

The algorithms (part I and part II) summarize the current standards for diagnosis and therapy of AD, however, the landscape is changing rapidly, especially for new therapeutic options. Dupilumab is currently the only biological approved for ages >= 12 years, with trials in younger children underway. Also, other drug classes are currently under investigation (e.g. janus-kinase and phosphodiesterase inhibitors for topical and

systemic use). Given the special pace of innovation in AD treatment, the future is bright for young children with severe atopic dermatitis!

Table 1 – Discussion of the therapeutic options mentioned in the algorithm for the treatment of Atopic Dermatitis (AD) in early childhood

Drug	**Comments**
	Topical
Corticosteroids	The mainstay of therapy; for reactive and proactive use. Extensive experience with the Fingertip U
Calcineurin inhibitors	Safe, also < 2 years of age (off-label).
PDE4 inhibitors	Not available in Europe.
Wet wraps	Good alternative to systemic medication for crisis intervention or averting hospitalization.
Antiseptics	Topical disinfectants (e.g. bleach) may be used but evidence is conflicting.
	Systemic
Phototherapy	Not commonly used in early childhood (feasibility). If used, preference for narrowband ultraviolet
Antibiotics	Topical antibiotics are not advised; in case of superinfection systemic antibiotics are warranted.
Cyclosporine A	Approved from the age of 16.
Methotrexate	Safe in children but off-label and effect takes longer than cyclosporine A. Folic acid suppletion rec
Azathioprine	Off label.
Mycophenolate mofetil	Off label.
Dupilumab	Biologic (injection). Approved from the age of 12.

PDE4 = phosphodiesterase 4

Green = on label; Yellow = off label

Figure legends

Figure 1 – Medical algorithm for the therapeutic management of Atopic Dermatitis (AD) in early childhood, based on severity. Adapted from: Wollenberg A et al, J Eur Acad Dermatol Venereol, 2018[3]

[A]For criteria, see part I of this medical algorithm.

[B]Disease severity scales can be used but might not be practical. Severity (global assessment) can alternatively be assessed by body surface area involvement, lesional features and locations, and disease impact on quality of life.

[C]Please refer to part I of this medical algorithm.

[1]In cases of recurrent skin infections sodium hypochlorite can be added to the bathwater (1mL of 5% household bleach per 1L of water) – conflicting data.

[2]Not commonly used in early childhood (feasibility). Preference for narrowband ultraviolet B (311 nm) or ultraviolet A1.

[3]Cyclosporine is licensed from age 16 and dupilumab from age 12 in Europe. All other systemic options are off-label.

[#]Choice depending on local cofactors. For moderate-severe AD it is recommended to start with a corticosteroid. Choice of corticosteroid class (European classification shown) depending on age and local cofactors.

[%]Off-label treatment option.

*Special attention if age <3 months or recurring infections: in early-onset severe AD, certain primary immunodeficiency syndromes such as Omenn syndrome, selective IgA-deficiency, Hyper-IgE-syndromes and Wiskott Aldrich syndrome, genetic disorders with an impaired barrier function, such as Comel-Netherton

syndrome and peeling skin syndrome, and some inherited metabolic diseases such as biotin deficiency or phenylketonuria should be considered as differential diagnoses.

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