Received: 3 December 2019 | Revised: 29 September 2020 | Accepted: 14 October 2020

DOI: 10.1111/all.14638

NEWS & VIEWS

Algorithms in Allergy and Clinical Immunology

Medical algorithm: Diagnosis of atopic dermatitis in early childhood (part I)

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Keywords: algorithm, allergy, atopic, atopic dermatitis, childhood, children, diagnosis, eczema, immune system, medical algorithm, pediatric

Atopic dermatitis (AD, atopic eczema) is a chronic, relapsing, pruritic, noncommunicable inflammatory skin disease that affects children and adults.[1] It almost always has its debut in early life;[2,3] therefore, this medical algorithm focuses on diagnosis (part I) and therapy (part II[4]) of AD in early childhood, which is defined by UNESCO as "the period from birth to eight years old."

Several criteria were developed for the diagnosis, for example, by Hanifin and Rajka,[5] and by the United Kingdom (UK) Working Party.[6] These are useful in clinical trials and in academic settings, but may not be suitable for daily clinical practice. The American Academy of Dermatology (AAD) consensus criteria consist of useful clinical findings for clinicians, divided into three categories (Figure 1): *essential features* (must be present: pruritus, eczematous dermatitis with typical morphology and age-specific patterns, and chronic or relapsing history), *important features* (adding support to the diagnosis: early age of onset, personal or familial history of atopy, xerosis, and lichenification), and *associated features* (help to suggest the diagnosis but too nonspecific: eg, keratosis pilaris, pityriasis alba, hyperlinear palms, nipple involvement, perifollicular accentuation).[2,7]

In infancy (0-2 years), eruptions usually develop on the cheek or forehead and are worsened by scratching. The eruption may extend to the whole face including ears and lips. Other sites may be intertriginous zones (exudative erythema), the thoracoabdominal region, back, and extremities (including extensor sides). Rarely, lesions are nummular.

In early childhood (2-8 years), eruptions on the face decrease, and typical sites include the neck, axilla, cubital and popliteal fossa (flexural), and the limbs, especially the wrist and ankles.[3]

In early-onset severe AD (<3 months), 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.[1] In the first two years of life, the differential diagnosis includes cradle cap and seborrheic eczema, napkin dermatitis, irritative eczema, and scabies. In early childhood, important differential diagnoses include psoriasis inversa, Gianotti-Crosti syndrome, tinea corporis, and impetigo. There is no absolutely reliable in vitro test for AD.

Once the diagnosis of the disease is made, diagnostic workup includes assessment, and education and counseling of individual provocation factors (Figure 2). Individual provocation factors, of which some are not always avoidable, include inadequate hygiene practices/diapering, irritative factors (inadequate textiles such as wool), *Staphylococcus aureus* colonization, teething, sun exposure/climate, seasonal changes, tobacco smoke exposure, swimming, and (familial) stress and conflicts.[8] Vaccines should not be avoided. Allergy diagnostics should only be performed if indicated by medical history (eg, food-induced urticaria, which is an IgE-mediated immediate-type, noneczematous reaction). In cases of persistent moderate-severe AD despite optimal management, many experts advise testing for food/aeroallergen-induced aggravation of AD, which usually takes 24-48 hours to develop.[8] Because blindly allergy testing is generally not helpful, tests need to be chosen in the light of medical history and/or specific clinical findings. Clinical examination can reveal clues to possible

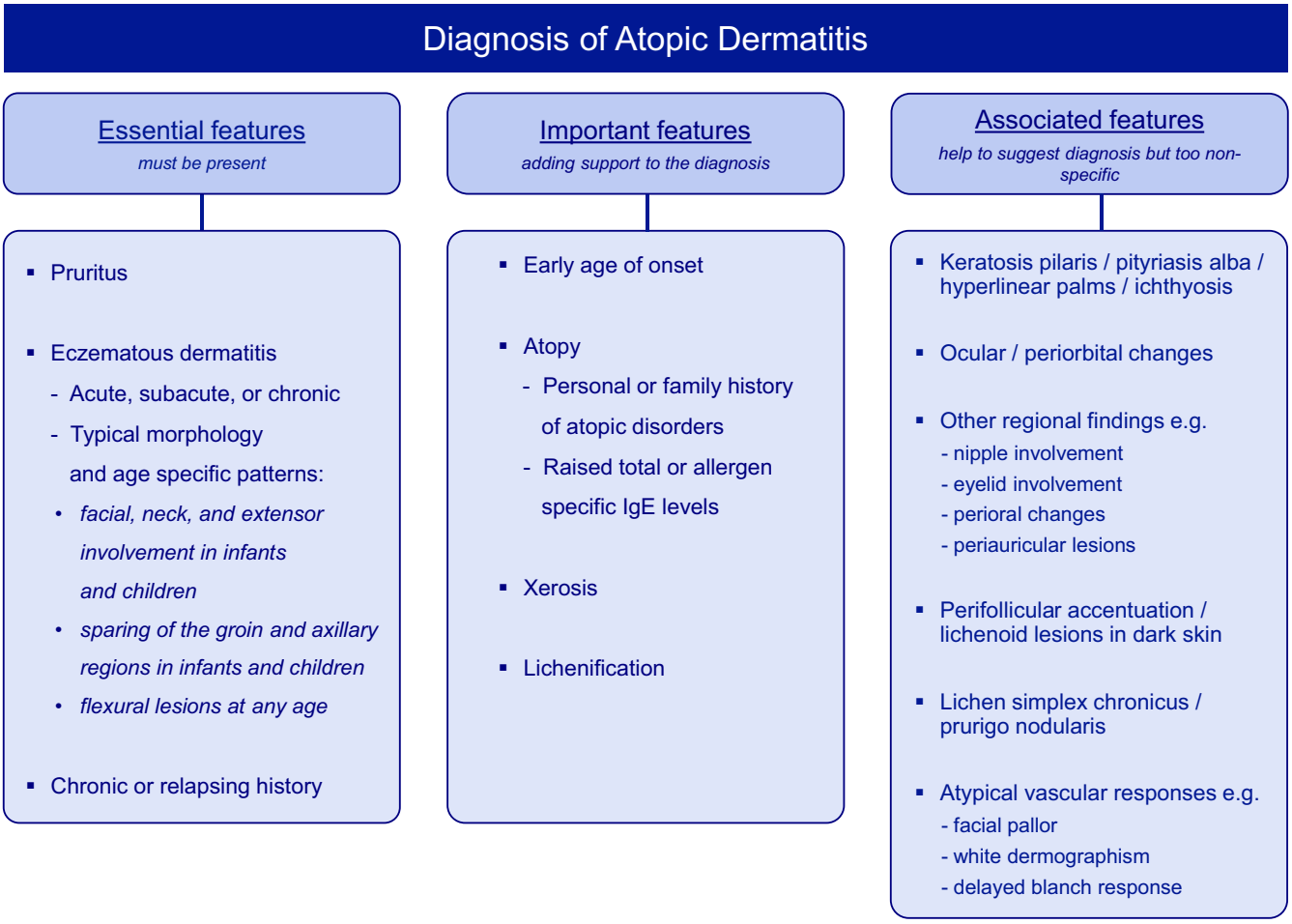

FIGURE 1 Diagnosis of atopic dermatitis (AD). Useful clinical findings for clinicians, outlined by the American Academy of Dermatology (AAD), divided into essential (must be present), important (adding support to the diagnosis), and associated (help to suggest the diagnosis but too nonspecific) features. Adapted from Eichenfield L et al, *J Am Acad Dermatol*, 2003[7]

allergens such as food allergy in infants with peri-oral AD (the area around the mouth is normally not involved except if there is an irritative eczema, eg, due to saliva) or worsening by specific food intake. In these cases, skin prick tests/serum-specific IgE tests followed by oral food challenges are recommended. Among food allergens, cow's milk, hen's egg, peanut, soya, nuts, and fish are most frequently associated with AD exacerbation in infants and toddlers. In older children (as well as in adolescents and adults), pollen-associated food allergy should also be considered. For patients with suspicion of contact dermatitis, persistent hand or foot lesions, or AD on earlobes or beneath the belly button (the latter is suggestive for a type IV allergy to Nickel), patch testing is indicated.

Finally, AD patients can develop complications. In early childhood, these include mainly bacterial (eg, impetigo) or viral (eg, eczema herpeticum, eczema molluscatum) infections. Figure 2 depicts an algorithm that can be followed for the diagnostic workup of AD in early childhood.

An important aspect, which is often omitted during AD consultations, is the assessment of disease severity and patients' quality of life (QoL). The most frequently used disease severity scales include the Eczema Area and Severity Index (EASI) and SCORing Atopic Dermatitis (SCORAD).[8] Patient- or parent-reported severity can be assessed by Patient-Oriented SCORAD (PO-SCORAD) and Patient-Oriented Eczema Measure (POEM), among others. The impact of AD on daily life may be different from what the clinician assumes and needs to be

FIGURE 2 Medical algorithm for the diagnosis of atopic dermatitis (AD) in early childhood. *For diagnostic criteria, Hanifin and Rajka's criteria, the United Kingdom (UK) Working Party's criteria, the American Academy of Dermatology (AAD) consensus criteria, or other criteria can be used. As a minimum, pruritus, eczematous dermatitis with typical morphology and age-specific patterns, and chronic or relapsing history must be present. **In early-onset severe AD (<3 months), 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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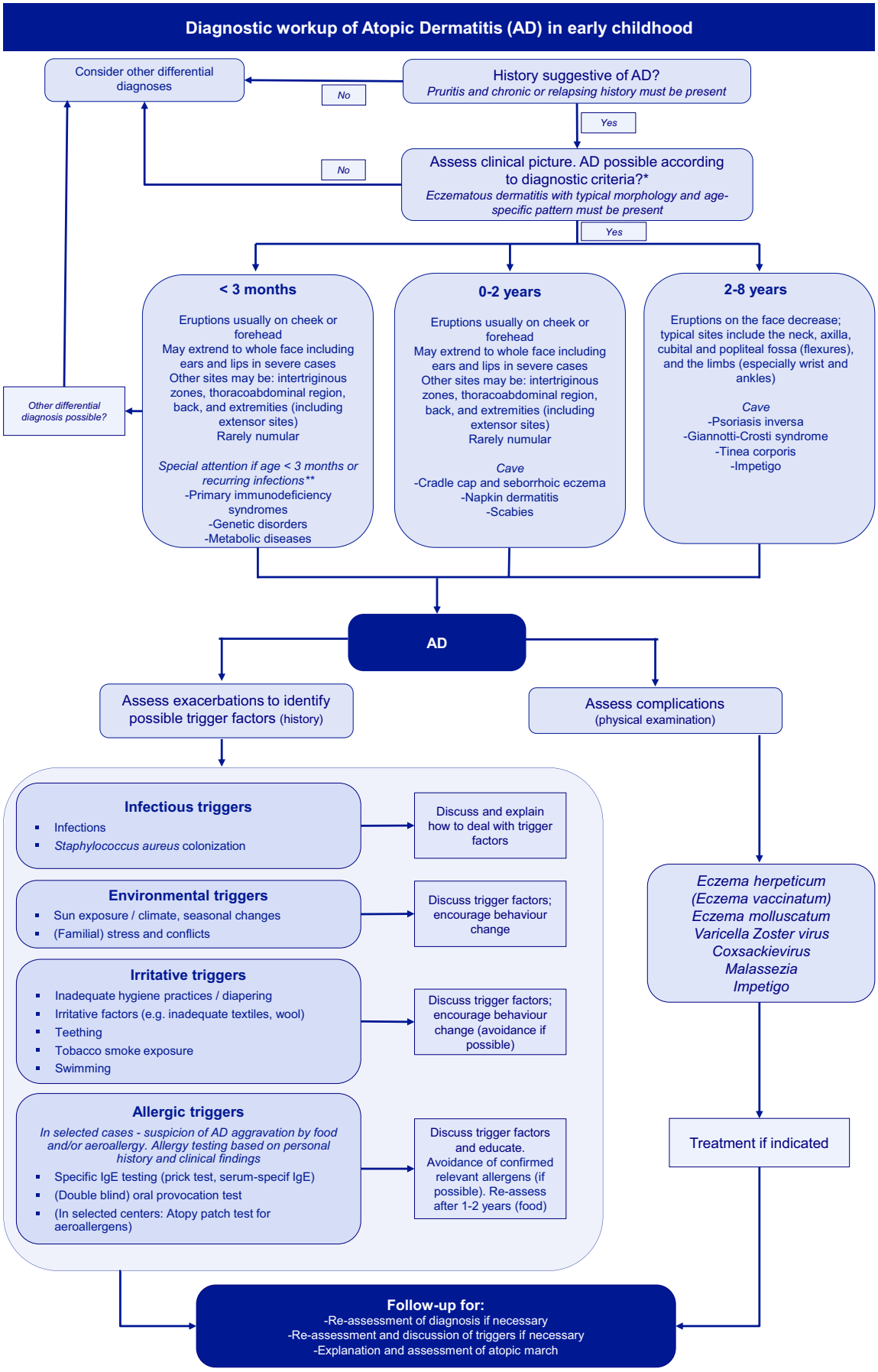

evaluated. Different age-adjusted tools exist for assessing QoL. These scores can be used for treatment planning and assessment of treatment response. Most scales are validated for use in clinical trials. In clinical practice, the use of scoring systems is useful in moderate and especially in severe cases, which require systemic treatment. In certain countries, reimbursement of some treatments requires documentation of disease severity. However, EASI and SCORAD are time-consuming for routine use in clinical practice. Therefore, a US-based expert group came to a consensus with global assessment scores to be used in a way from "clear" to "almost clear," "mild," "moderate," or "severe".[2] Furthermore, in global assessment, moderate-severe disease can also be defined by body surface area involvement (minimum 10%), individual lesions with moderate-severe features, involvement of highly visible areas or important for function, or significantly impaired QoL.[2] The differentiation between mild, moderate, and severe disease aids in choosing the optimal treatment regimen, which is among others based on AD severity as will be discussed in part II.

CONFLICT OF INTEREST

Dr Janmohamed reports personal fees from Pierre Fabre Benelux, outside the submitted work; Dr Grosber has nothing to disclose; Dr Eichenfield reports grants and personal fees from AbbVie, grants and personal fees from Allergan, grants and personal fees from Almirall, grants and personal fees from Amgen, grants and personal fees from Asana BioSciences, grants and personal fees from Dermavant, grants and personal fees from Dermira, Inc, grants and personal fees from DS Biopharma, grants and personal fees from Eli Lilly, grants and personal fees from Forté Pharma, grants and personal fees from Galderma, grants and personal fees from Glenmark, grants and personal fees from Incyte, grants and personal fees from LEO, grants and personal fees from MatriSys, grants and personal fees from Novartis, grants and personal fees from Ortho Dermatologics/Valeant, grants and personal fees from Pfizer, grants and personal fees from Sanofi-Genzyme/Regeneron, and grants and personal fees from UCB Pharma, outside the submitted work; Dr Ring reports personal fees from Sanofi-Genzyme/Regeneron, personal fees from AbbVie, personal fees from LEO, and personal fees from Allergika, outside the submitted work; and Dr Gutermuth reports grants, personal fees and other from Sanofi-Genzyme/Regeneron, personal fees and other from AbbVie, personal fees and other from Lilly, personal fees and other from LEO, personal fees and other from Pfizer, personal fees and other from L'Oreal, and personal fees from Pierre Fabre, outside the submitted work.

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