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DIAGNOSTIC FEATURES OF ATOPIC DERMATITIS

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Establishment of diagnostic guidelines for atopic dermatitis derives from the need for clear delineation of the clinical populations that are subjects of investigative studies. There is no objective laboratory marker for the disease. The nomenclature varies from one speciality to another and from a country to another (Table I). Until a distinctive diagnostic test becomes available, it is important to apply uniform criteria in diagnosing atopic dermatitis. Diagnostic guidelines can be of especial value for non-dermatologists who lack familiarity with subtle cutaneous features. Atopic dermatitis has manifestations which span many biomedical disciplines and attract the research interest of allergists, immunologists, geneticists and pediatricians.

Diagnostic criteria are also important for ruling out the diagnosis of atopic dermatitis. An example of confusion is the hyperimmunoglobulinemia-E syndrome which is seen primarily by pediatricians and studied by immunologists. The first 2 cases were reported by Buckley et al. who were unable to state with certainty that the patients did not have atopic dermatitis (2). Subsequent case reports have mentioned eczema in describing patients with this syndrome. Recently Dr Buckley has clarified the situation; patients have "dermatitis at the time of their evaluation or, more often, a history of pruritic dermatitis earlier in life. Although the lesions resembled those of an eczematoid dermatitis and the skin was often lichenified, the distribution and characteristics of the lesions were not those of typical atopic eczema" (3).

Obviously there continue to be terminological problems with the word "eczema" which is derived from the Greek "eczeo", "a boiling over". Thus eczema or "eczematoid" properly refer to a weeping or vesiculated dermatitis. The terms are non-specific and do not adequately describe the lesions of atopic dermatitis but the word "eczema" is widely used and interpreted by physicians and patients to indicate atopic dermatitis. The term "atopic dermatitis" may itself be criticized because it has caused many physicians to assume an allergic causation similar to asthma and allergic rhinitis. In the practical sense, terminology is less importance than is uniform definition of the disease.

In previous publications we have independently suggested diagnostic criteria for atopic dermatitis (5, 11). Subsequently we have made revisions based on practical experience, suggestions by various individuals and discussions during this symposium. The result is a unified outline of diagnostic criteria which we hope will be useful to practitioners and investigators in all parts of the world.

Basic features

Firm diagnosis of atopic dermatitis would require the presence of at least 3 basic features: (Table II):

1) Pruritus. The diagnosis of active atopic dermatitis cannot be made if there is no history of itching. Indeed, since a primary cutaneous lesions has never been firmly established, it may be that all the cutaneous changes are secondary to itch-induced scratching as suggested by Jacquet at the beginning of this century (8).

2) Lichenification. This is a hallmark of the disease when seen in typical locations. Obviously other skin diseases may manifest lichenified skin (e.g. lichen simplex chronicus) without any evidence of atopic dermatitis.

3) Chronically relapsing course. Atopic dermatitis is remarkable for its chronicity and for flares and relapses

Table I. *Synonyms for atopic dermatitis*

Atopic eczema
Infantile eczema
Prurigo Besnier
Lichen Vidal
Endogenous eczema
Spätexudatives Ekzematoid
Neurodermatitis (constitutionalis)

Table II. *Guidelines for the diagnosis of atopic dermatitis*

Must have 3 or more basic features:
Pruritus
Typical morphology and distribution:
Flexural lichenification or linearity in adults
Facial and extensor involvement in infants and children
Chronic or chronically-relapsing dermatitis
Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)
Plus 3 or more minor features:
Xerosis
Ichthyosis/palmar hyperlinearity/keratosis pilaris
Immediate (type I) skin test reactivity
Elevated serum IgE
Early age of onset
Tendency toward cutaneous infections (esp. *Staph. aureus* and *Herpes simplex*)/impaired cell-mediated immunity
Tendency toward non-specific hand or foot dermatitis
Nipple eczema
Cheilitis
Recurrent conjunctivitis
Dennie-Morgan infraorbital fold
Keratoconus
Anterior subcapsular cataracts
Orbital darkening
Facial pallor/facial erythema
Pityriasis alba
Anterior neck folds
Itch when sweating
Intolerance to wool and lipid solvents
Perifollicular accentuation
Food intolerance
Course influenced by environmental/emotional factors
White dermographism/delayed blanch

which may occur as often as weekly during active disease. At the other extreme, relapses appear many years after seemingly complete remissions.

4) Atopic history

(*a*) Personal. Manifestations of allergic respiratory disease are present in roughly 50% of patients, though this figure varies with the age of the population; e.g. many infants with eczema may not develop respiratory symptoms until much later.

(*b*) Family members. Approximately 70% of patients with atopic dermatitis are aware of other family members who have one or more manifestations of atopy.

Minor or less characteristic features

In addition to having 3 of the basic features, a patient should manifest 3 "minor" features which are either less-specific or relatively rare. These characteristics might allow exclusion of, for example, a patient with chronic allergic contact dermatitis who has pruritus, lichenification and family history of atopy.

1) Xerosis. The presence of generalized dry skin is highly suggestive of atopic dermatitis. This feature tends to fluctuate with disease severity and during remissions may not be detectable.

2) Ichthyosis. This condition has been reported in from 2–6% of patients with atopic dermatitis and, if the associated features of palmar hyperlinearity, keratosis pilaris and xerosis were considered as evidence for the ichthyosis phenotype, the association would be much higher. Certainly atopic features are seen in at least 50% of patients with ichthyosis (11).

3) Immediate (type I) skin test reactions. Rajka showed that approximately 80% of patients with atopic dermatitis manifested Type I responses to skin test antigens (10). The test is quite non-specific however, and its usefulness is highly dependent upon antigen quality, concentration and proper standardization.

4) Elevated serum IgE. This is a very non-specific feature, seen in a number of disease states (9). A high level (e.g. >2 000 units/ml) may add considerable support to the diagnosis of atopic dermatitis but the serum concentration of IgE is normal in about 20% of patients.

5) Early age of onset. Though obviously non-specific, this can be a very helpful clue for accepting or rejecting the diagnosis of atopic dermatitis. Ninety per cent of patients have onset of their disease in the first 5 years and adult onset will always raise suspicions as to correctness of diagnosis.

6) Cutaneous infections. Although the majority of patients with atopic dermatitis have no problem with infections, recurrent, poorly controlled eruptions of Herpes simplex or warts may support the diagnosis. In addition superficial staphylococcal oozing or pustular lesions are seen in many patients (6). These indicate decreased cell-mediated immunity including impaired chemotaxis of monocytes and polymorphonuclears (6, 11).

7) Non-specific hand dermatitis. Agrup's study showed that hand eczema occurred in 70% of patients with atopic dermatitis and that the disease began on the hands in 1/3 of cases (1). The presence of dry, scaling inflammation, expecially on the dorsal hands and wrists may be indicative of atopic dermatitis.

8) Nipple eczema. Although not common, the presence of chronic lichenified, fissured or weeping dermatitis over one or both nipples is quite specific for atopic dermatitis.

9) Cheilitis. Chronic desquamation of the upper lip is perhaps most specific for atopic dermatitis but patients commonly may have involvement of both lips and even the perioral areas. An extreme variation of cheilitis is the furrowed mouth syndrome which is usually accompanied by scrotal tongue and is due to oral breathing in patients with chronic allergic rhinitis.

10) Recurrent conjunctivitis. This problem commonly coexists with allergic rhinitis and may be indicative of strong reaginic reactivity. It may also occur independently of rhinitis and many patients with atopic dermatitis have considerable conjunctival involvement which may progress to severe ectropion. Vernal conjunctivitis with fine papulation of the inner eyelids is due to lymphoid infiltration and may cause considerable corneal discomfort.

11) Dennie-Morgan infraorbital fold. This poorly-understood feature is present as a single fold in ever 70% of patients with atopic dermatitis and may be supportive of the diagnosis. However, the single crease is less specific and, as Dr Meenan has documented of this meeting, the more definitive doublefold is seen in only a small percentage of atopic dermatitis patients.

12) Keratoconus. This feature was prominently mentioned

in the past (12) but is not specific for atopic dermatitis and in our experience is not often seen in patients today.

13) Anterior subcapsular cataracts. Spontaneously developing, bilateral cataracts in the anterior lens are quite specific for atopic dermatitis. They may develop in the second decade or later and affect up to 16% of patients, most often those with severe dermatitis (7).

14) Orbital darkening. The so-called "allergic shiners" are seen in various atopic disorders and are present in the majority of patients with atopic dermatitis.

15) Facial pallor and facial erythema. These somewhat paradoxical features may be present simultaneously and both are frequently overlooked as features of atopic dermatitis.

16) *Pityriasis alba*. This mild, post-inflammatory hypopigmentation occurs most on sun-exposed areas of patients with darker skin. It is obviously seen in many patients with no evidence of atopy but the presence of pityriasis alba may be a clue to the disease in some patients.

17) Anterior neck folds. These horizontal creases are certainly not specific but are present in the majority of patients with atopic dermatitis.

18) Itch when sweating. This is an almost universal symptom among patients with atopic dermatitis. It may be precipitated by exertion, thermal or emotional sweating and occclusion from non-porous clothing or ointments.

19) Intolerance to wool and lipid solvents. This probably reflects the decreased itch threshold to irritants on atopic skin and is a very common feature.

20) Perifollicular accentuation. This feature, which gives the skin a pebbled appearance, is especially prominent among those patients with darker pigmentaton and can be almost pathognomonic of the disease.

21) Food intolerance. Cutaneous reactions to foods are seen in a considerable number of children with atopic dermatitis. While these reactions frequently subside during childhood, a small proportion of adult patients retain demonstrable food sensitivity, sometimes manifesting as contact urticaria to eggs, fish and other materials.

22) Course influenced by environmental and emotional factors. Perhaps no other dermatological condition is so prominently associated with stresses and environmental changes and the majority of patients are highly cognizant of these associations.

23) White dermographism and delayed blanch. Stroking the involved skin of patients with atopic dermatitis will produce a white line instead of the normal triple response. Injection of methacholine normally causes reddening, but produces blanching around the injection site in patients with atopic dermatitis. However, studies by Engelhardt (4) and more recently by Ofuji & Uehara (13) have shown that these reactions are non-specific and occur in other forms of dermatitis.

Most dermatologists find a number of patients who, at a given moment, may not present all the features necessary for a firm diagnosis of atopic dermatitis. Nevertheless, one or more of the above features may be present to provide a suggestive diagnosis. Usually, subsequent evaluations will provide a firm diagnosis. Conversely, in the clinical setting, these guidelines are frequently helpful for rejecting the diagnosis of atopic dermatitis in patients with ambiguous cutaneous inflammatory disease.

Purely clinical diagnostic features such as these are necessarily imprecise and may fail to distinguish between possible subgroups which are genetically and biochemically different. Hopefully future investigations will clarify whether there are distinct subgroups of atopic dermatitis patients and this possibility should be kept in mind when evaluating research data.

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DISCUSSION

Zachariae (Aarhus). Q: Early onset is an important diagnostic tool. I have seen some patients who got so-called atopic dermatitis as adults. They also had high IgE and several other things listed in your diagnostic table. However, the turned out to have Hodgkin's disease within some years, and I will

always be suspicious of this in adults who develop so-called atopic dermatitis at a later age.

Kelly (Los Angeles). Q: Some 20–40 % of all black patients with atopic eczema have follicular lesions. This is not the same as keratosis pilaris.

A: I agree with Dr Kelly. I think that as pigmentation increases in the skin, we tend to find more of that.

Voorhees (Ann Arbor). Q: we see prurigo nodularis in many of our black patients. Most of the prurigo that we see occurs in people who we believe have atopic dermatitis.

A: We have had only 2 or 3 patients in the past 6 years with definite prurigo nodularis. What most of the residents diagnose as prurigo nodularis usually turns out to be hypertrophic lichen planus.

Jones (Atlanta): I think it is important to us as dermatologists that we agree how to diagnose this disorder. I congratulate Dr Hanifin and Dr Rajka for their efforts to try to establish diagnostic criteria. Allergists seem to think that any patient who has respiratory atopy is exactly equivalent to a patient with atopic dermatitis. I think there is considerable evidence that that is not the case. What do you think about the patient with chronic lichenifying flexural dermatitis who has never wheezed or sneezed?

A: I think they can have atopic dermatitis without having other atopy.