ATOPIC DERMATITIS

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Reference

DERMATOLOGY Text Book. 3rd Edition 2012. Eds: Jean L Bologna, Joseph L Jorizzo, Julie V Schaffer. ElSevier Publishing

DEFINITION OF ATOPY

The term “atopy” is tightly linked to the presence of allergen-specific IgE antibodies in the serum, as documented by positive fluorescence enzyme immunoassays (previously radioallergosorbent [RAST] tests) or skin prick tests.

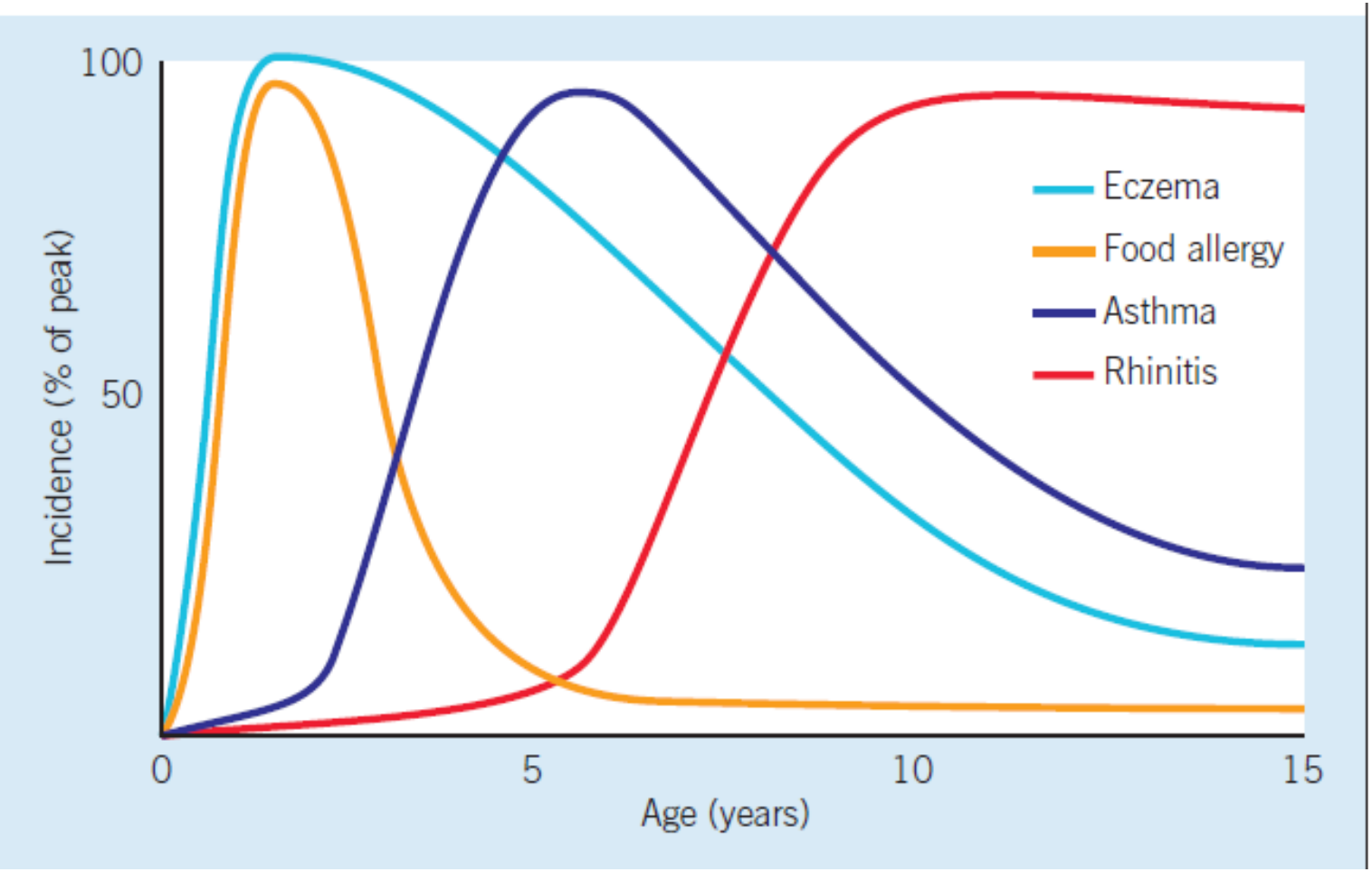
SPECTRUM OF AD

Spectrum of AD

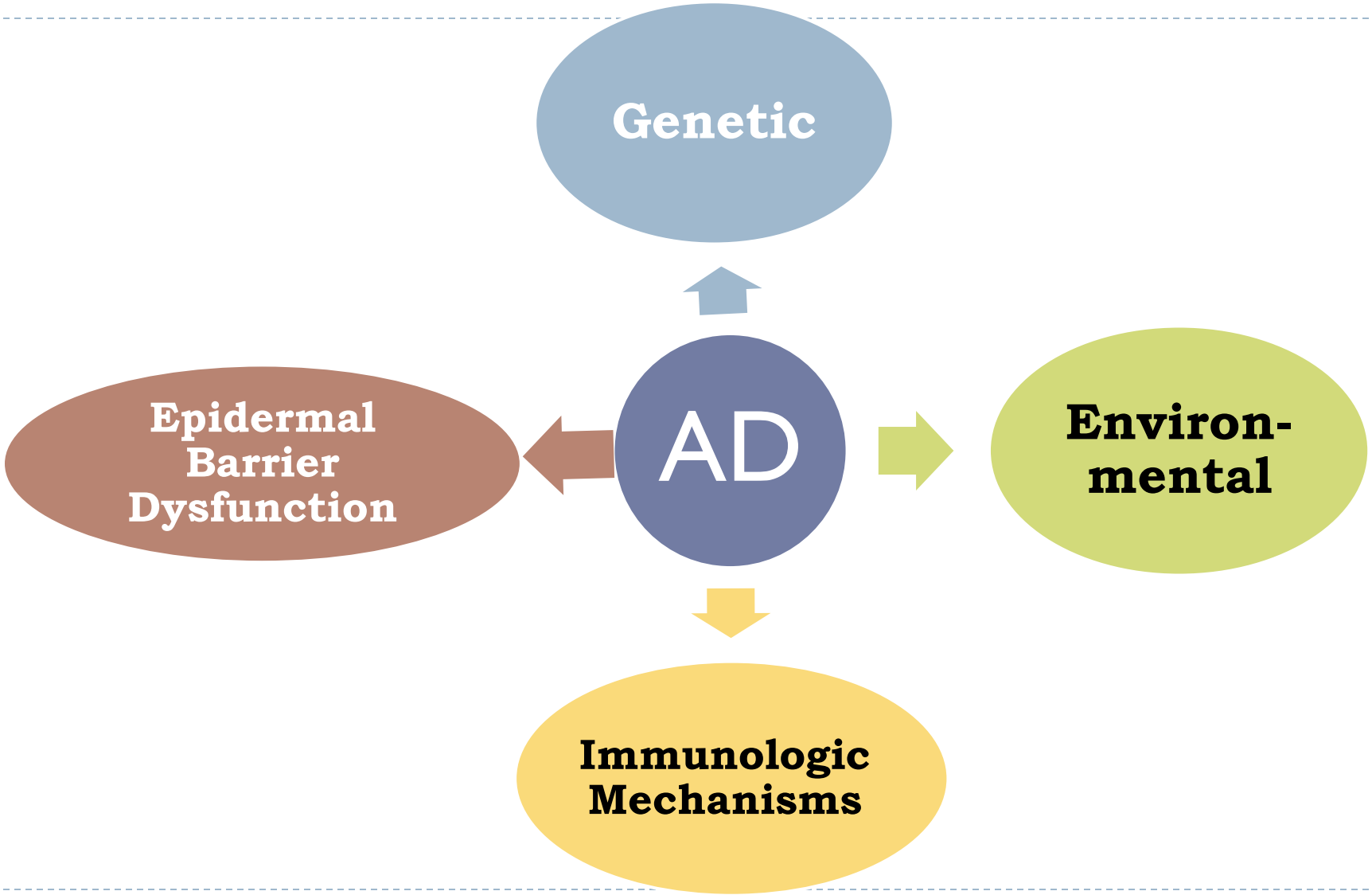
An *IgE associated* or *allergic* form of dermatitis corresponds to AD in the strict sense (formerly known as *extrinsic AD*

The remaining 20–30% of patients with the clinical phenotype of AD who have no evidence of IgE-sensitization are categorized as having a *non-IgE-associated* or *non-allergic* form of dermatitis (formerly known as *intrinsic AD*).

THE ATOPIC MARCH



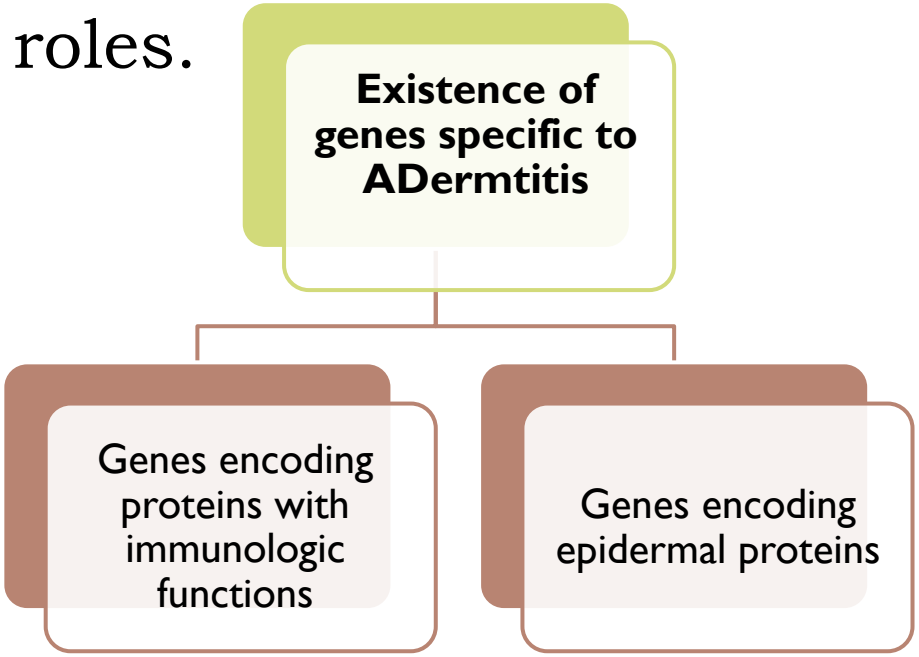
PATHOGENESIS of Atopic Dermatitis



GENETICS

The entities in the atopic triad cluster together in families.

AD is a complex genetic disease, and both gene–gene and gene–environment interactions have pathogenic roles.



Filaggrin

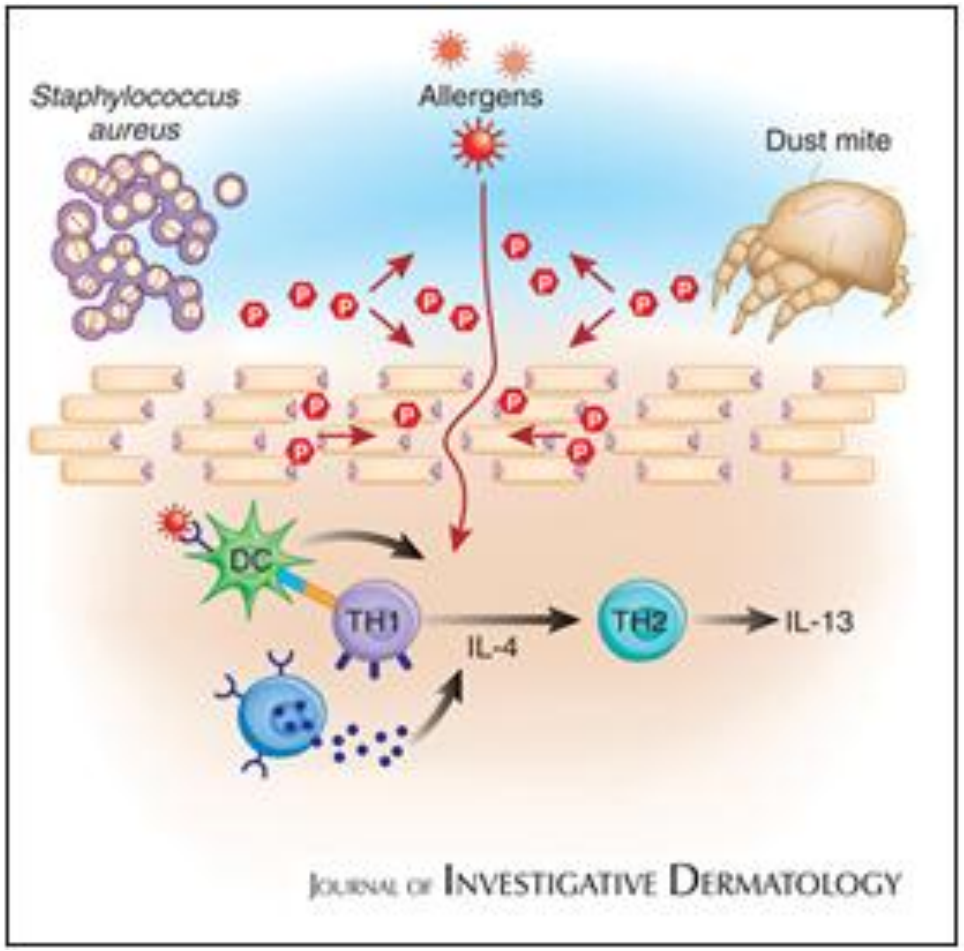
Mutations in the filaggrin gene (*FLG*), which encodes a protein that aggregates keratin filaments during terminal differentiation of the epidermis.

The presence of the filaggrin variants is correlated with early-onset, relatively severe, "extrinsic" (specific IgE-associated) AD that tends to persist into adulthood.

Affected individuals have an increased risk of eczema herpeticum and peanut allergies as well as a propensity to later develop asthma

Epidermal Barrier Dysfunction

The consequence of epidermal barrier dysfunction and an altered stratum corneum leading to increased transepidermal water loss



Cork et al. Journal of Investigative Dermatology (2009) **129:** 1892–1908

IMMUNOLOGIC MECHANISMS

Disturbed Item	Main component/player
Impairment Of The Epidermal Barrier	Degradation of corneodesmosomes, deficiency of Filaggrin
Mechanisms Of Inflammation In The Absence Of IgE-mediated Sensitization	Increased epidermal protease activity, dyscohesion
Epicutaneous Sensitization	high levels of thymic stromal lymphopoietin (TSLP) by keratinocytes leads to Th2 polarization
Role Of Dendritic Cells (Dcs)	*Langerhans cells* (*LCs*) and *inflammatory dendritic epidermal cells:* *present* allergens to Th1/Th2 cells
T-cell Responses, Cytokines And Chemokines	TH 2 predoninates in acute, Th1 in chronic
Role Of Microbial Colonization	decreased levels of antimicrobial peptides, *S. aureus adherence to skin*
Role Of Autoimmunity	circulating IgE antibodies

PRURITUS & IL-31

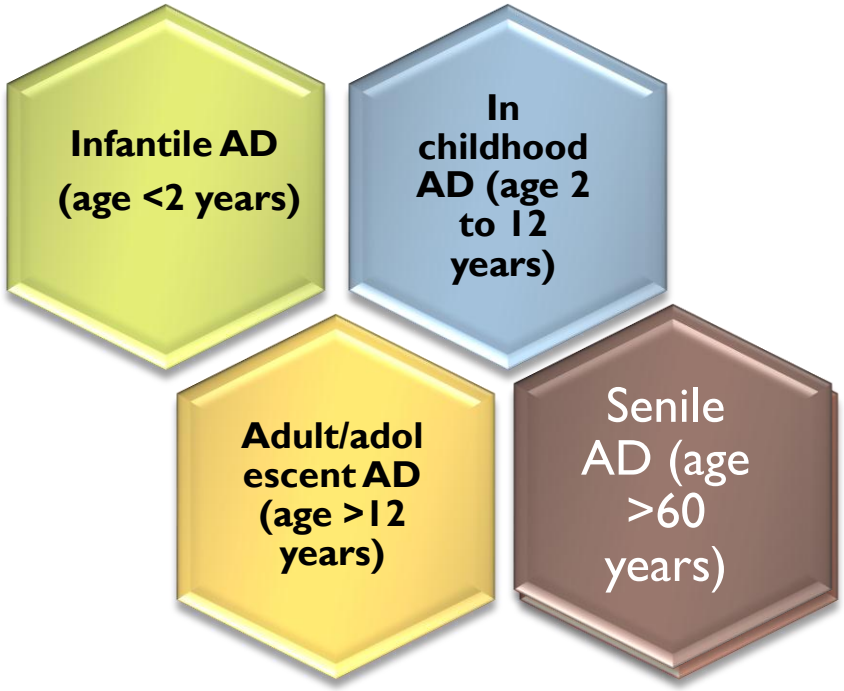
Classic antihistamines are ineffective in AD

neuropeptides, proteases, kinins, and cytokines such as interleukin (IL)-31 are known to induce itch.

IL-31 is strongly pruritogenic and exerts its biologic activity through a heterodimeric receptor composed of the IL-31 receptor A and oncostatin M receptor β protein, both of which are overexpressed in lesional skin of AD.

CLINICAL FEATURES

Disease Course



Clinical diagnosis of AD

- Pruritus
- eczematous skin lesions in typical age-specific distribution patterns,
- a chronic or chronically relapsing course,
- Early age at onset,
- A personal and/or family history of atopy.

Atopic stigmata

1. Xerosis
2. Keratosis Pilaris
3. Ichthyosis Vulgaris
4. Dennie Morgan lines
5. Periorbital darkening
6. White dermoographism

Associated Features

- Pityriasis Alba
- Pruritus
- Atopic Stigmata

Associated Complications

- Infections, esp eczema herpeticum
- Occular complications

Pathology: mainly to exclude other mimics (as MF).

Differential Diagnosis

- Seborrheic dermatitis in infants.
- Allergic Contact Dermatitis
- Mycosis Fungoides

Diagnostic criteria of AD

Validated scores to assess the severity of AD

1. EASI (Eczema Area Scoring Index)
2. SCORAD (SCORing Atopic Dermatitis)
3. POEM (Patient-Oriented Eczema Measure

MANAGEMENT CONCEPTS

- Avoidance of trigger factors, including irritants, relevant allergens and microbial agents.
- Skin care that aims to compensate for the genetically determined impaired epidermal barrier function.
- Anti-inflammatory therapy to control subclinical inflammation as well as overt flares.
- In selected cases, adjunctive or complementary modalities.

Avoidance of Trigger Factors

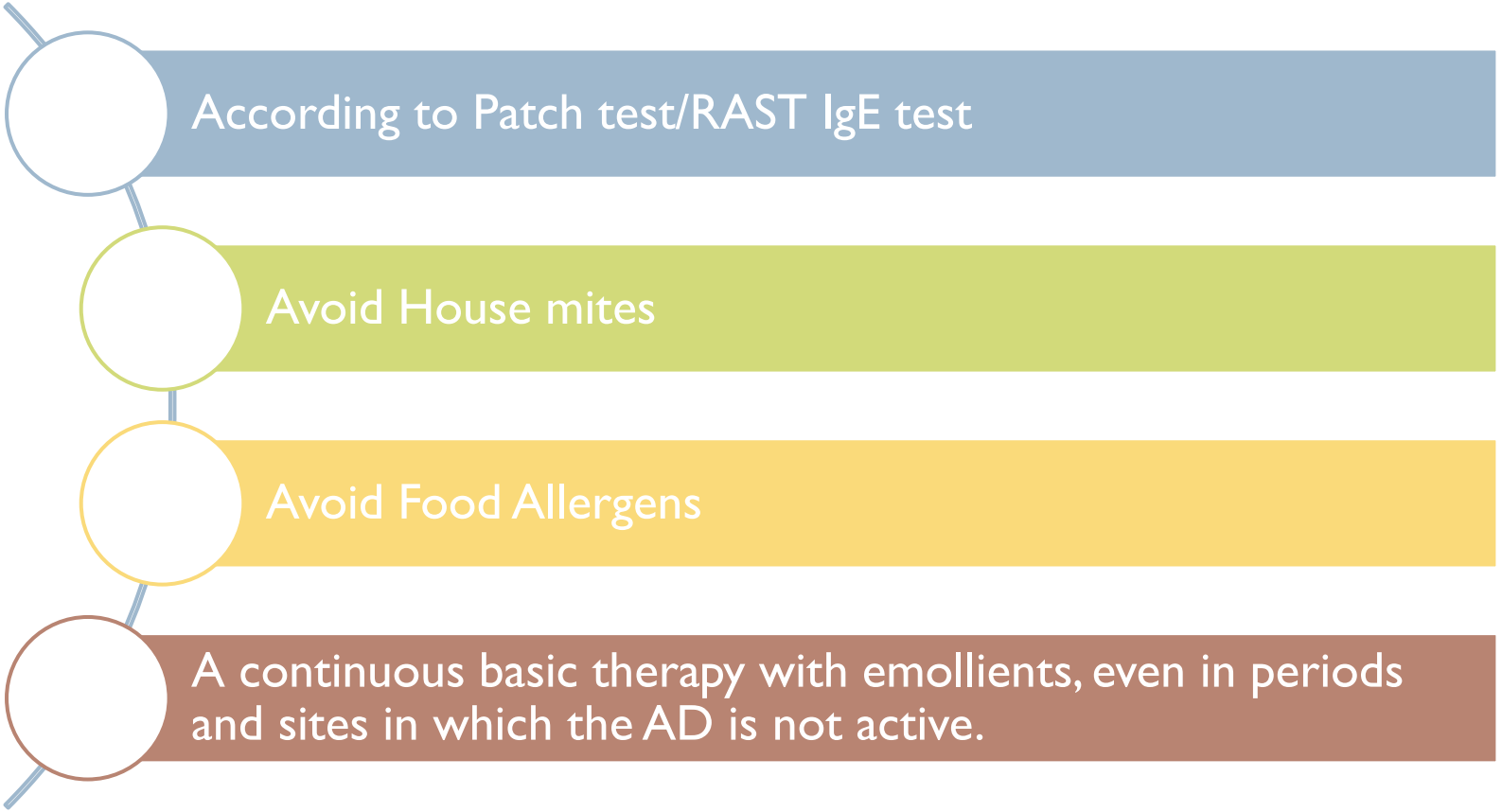
Intermittent use of intranasal mupirocin ointment over a 1- to 3-month

S. aureus strains that colonize and superinfect patients with AD are more likely to be susceptible to first-generation cephalosporins (e.g.cephalexin)

Cleansers and emollients containing antiseptics???

use mild, non-alkaline cleansers

Avoidance of Trigger Factors



Topical Anti-inflammatory Therapy

The corticosteroid with appropriate potency to quickly gain control of the flare, continuation of daily therapy until active dermatitis minimized.

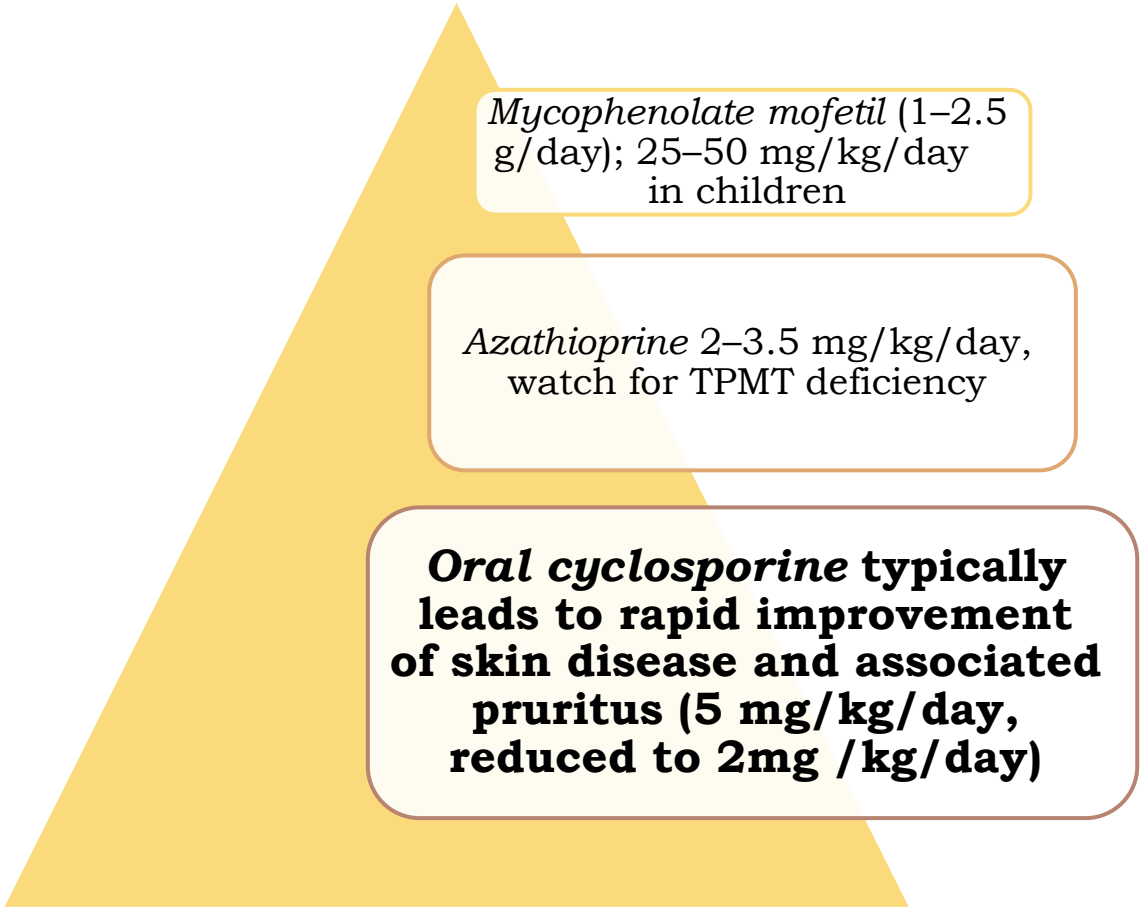
In moderate to severe AD, risk of relapse can be significantly reduced by proactive maintenance with twice-weekly application of a mid-potency topical corticosteroid.

Topical calcineurin inhibitors (TCIs)

Phototherapy: *UVA1, UVA combined with UVB*, and *narrowband UVB*

- Narrowband UVB and high-dose UVA1 can both be helpful for chronic AD, and UVA1 may also be useful in the treatment of acute flares.
- T cell apoptosis, reduction of dendritic cells, and modified cytokine expression, (e.g. decreased IL-5, IL-13 and IL-31 with UVA1).
- UVB reduces *S. aureus* colonization of the skin in AD patients.

Systemic Anti-inflammatory Therapy



Systemic corticosteroids should be avoided

Adjunctive Pharmacologic Therapy

- Sedating antihistamines (e.g. hydroxyzine)
- Non-Sedating antihistamines in very high doses.
- Leukotriene inhibitors
- Antimicrobial agents

Alternative/Complementary Therapy

- Dietary lipid supplements (e.g. evening primrose and borage oils)
- Chinese herbal therapy
- Hypnotherapy

Targeted Molecular Therapy ("Biologics")

- Anti-IgE monoclonal antibody ***omalizumab***, which inhibits the binding of IgE to its high-affinity receptor (FcεRI), is FDA-approved for the treatment of asthma in patients ≥12 years.
- The anti-CD20 monoclonal antibody ***rituximab*** (administered via 2 IV infusions separated by 2 weeks), which inhibits mature B cells
- ***mepolizumab*** inhibits IL-5, a crucial factor for growth and differentiation of eosinophils. Although mepolizumab can decrease the eosinophil count in patients with AD, it failed to lead to a significant clinical improvement

Emerging Therapies

- Goals of blocking factors such as cytokines involved in the regulation of IgE synthesis (e.g. IL-4) or chemoattractant receptor-homologous molecule expressed

on Th2 cells (CRTH2).

Primary Prevention

- For infants with a family history of atopy, exclusive breastfeeding during the first 4-6 months.
- Administration of probiotics (e.g. lactobacilli) or prebiotics (nondigestible oligosaccharides that promote the growth of desirable bacteria) to pregnant mothers and infants led to decreased frequencies of AD at 1 to 4 years of age.

Educational Programs

- Accepting "control" rather than a "cure"
- Parents are anxious about corticosteroid use, which often leads to delayed, inadequate treatment

Resumé: The APPROACH TO AD

Management should not be concentrated solely on the treatment of acute flares, but also be directed towards improving the underlying genetically determined epidermal barrier dysfunction and preventing active dermatitis (e.g. via maintenance therapy).

Such an approach could potentially block the sensitizations and ongoing inflammation that drive the atopic march forward