DERMATITE ATOPICA

Approfondimenti su meccanismi patogenetici e terapia

DERMATITE ATOPICA

- Infiammazione cronica della cute
- Caratterizzata da periodi di remissione e periodi di riacutizzazione
- Secchezza cutanea, prurito, eczema, eritema, edema, escoriazioni, lichenificazione, essudato
- Prevalenza: 10% nei bambini
- Risolve nel 50% dei bambini con l'adolescenza
- Prevalenza e costi in aumento

BACKGROUND GENETICO

- Familiarità per atopia
- Diversi geni candidati: diverse forme di malattia

  early onset (< 6m),

  AD-childhood

  AD adolthood (late-onset),

  IgE mediata

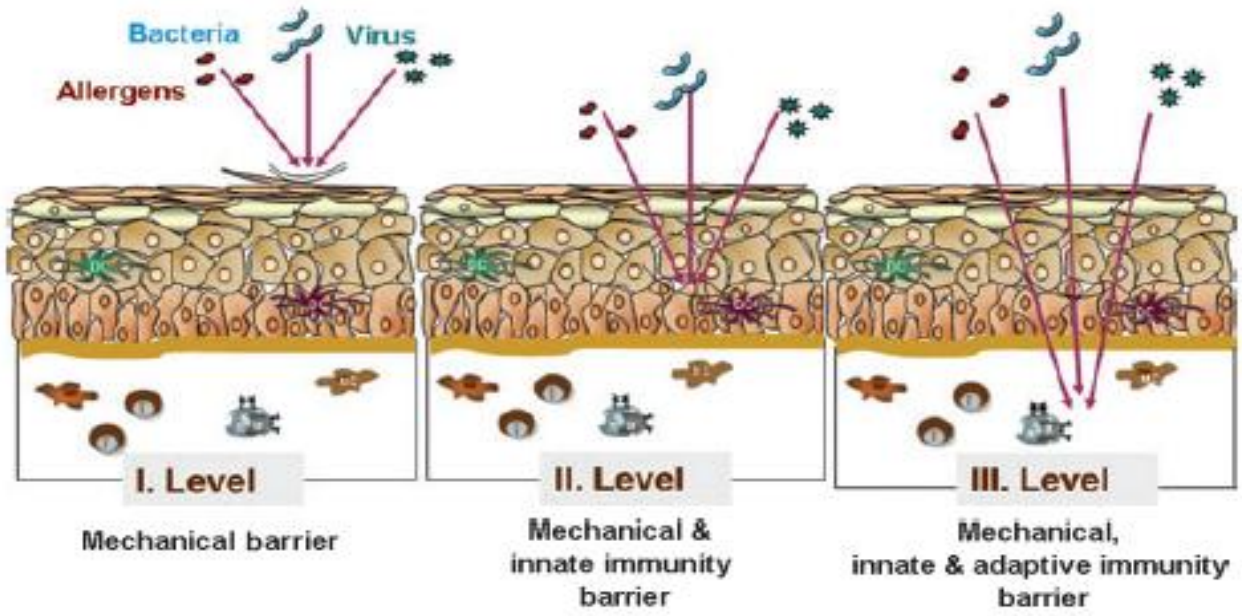

Figure 1. Deficiencies on the level of the skin barrier function as well as the innate and adaptive immune system contribute to the pathophysiological puzzle of atopic dermatitis (AD). The first level of the barrier is the mechanical skin barrier represented by the stratum corneum and the upper part of the skin. The second level of the skin barrier is represented by structures of the innate immune system such as pattern recognition receptors expressed by skin cells or antimicrobial peptides. The third level of the skin barrier is represented by the cellular defense of components of the adaptive immune system. DC, dendritic cell; M, mast cell; MC, macrophage; T, T cell.

DIFETTI DELLA BARRIERA CUTANEA

- Filaggrina
- SPINK5 (inibitore serino-proteasi)
- Alterazione enzima chimotriptico dello strato corneo
- Fattori non geneticamente determinati:

  Alterazioni del pH della cute

  variazioni del pH (da 5.0 a 5.5) ⟶ aumento dell'attività serino-proteasi e della perdita transcutanea di liquidi

IMMUNITÀ INNATA

- PRR (TLR, NOD, LPS receptor CD14)

Recettori espressi da diverse cellule della cute, riconoscono molecole patogene

- Dimostrata associazione con polimorfismi di TLR2, TLR9 e NOD1

- Dimostrata down-regulation di peptidi antimicrobici su cute infiammata

(indotta da alti livelli di IL-10 e citochine Th2)

IMMUNITÀ ADATTATIVA

Geni predisponenti alla DA

- 5q31-33

Citochine Th2: IL-3, IL-4, IL-5, IL-13, GMCS

- Mutazioni funzionali regione promoter di RANTES (citochina della superfamiglia dell'IL-8)
- Polimorfismi nella regione IL4-RA (16q12)
- Polimorfismi gene IL-18

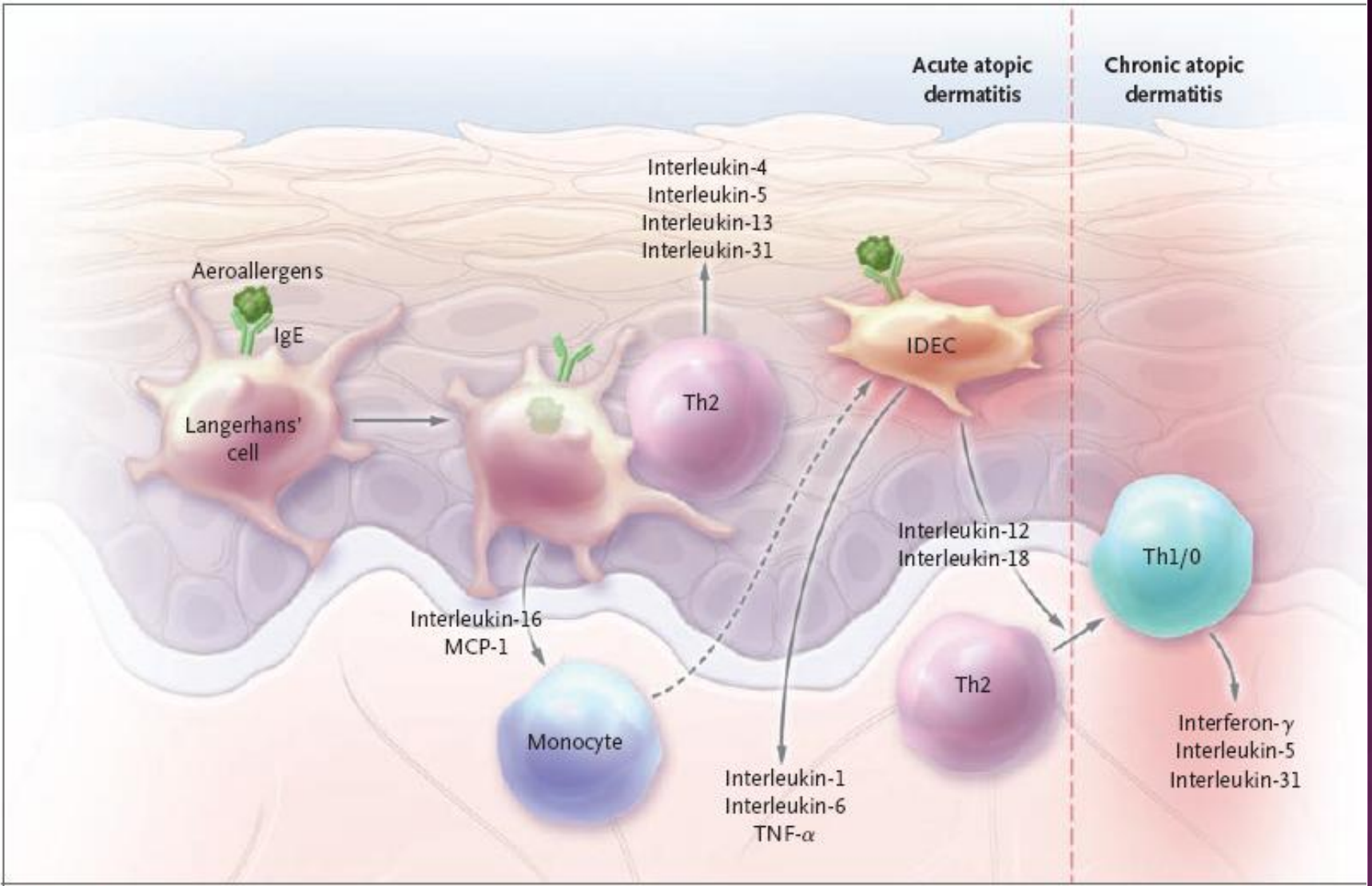

Figure 3. Acute and Chronic Phases of IgE and T-Cell–Mediated Atopic Dermatitis.

In the acute phase of atopic dermatitis, Langerhans' cells are activated on binding of allergens by means of specific IgE and FcεRI. They produce monocyte chemotactic protein 1 (MCP-1) and interleukin-16. Allergen-derived peptides are presented to T cells by Langerhans' cells that induce a Th2 profile. After migration into the skin, the recruited monocytes differentiate into inflammatory dendritic epidermal cells (IDEC) and produce the proinflammatory cytokines interleukin-1, interleukin-6, and tumor necrosis factor α (TNF-α). Their secretion of interleukin-12 and interleukin-18 contributes to the switch from Th2 to Th1/0 and thereby leads to the chronic phase of the disease.

Thomas Bieber, Atopic Dermatitis, NEngl J Med 2008;358:1483-94.

Box 1 Criteria for diagnosing atopic eczema in children

Itching plus three or more of:

- Visible flexural dermatitis involving skin creases (or involvement of cheeks and/or extensor surfaces in children aged up to 18 months)
- History of flexural dermatitis (or involvement of cheeks and/or extensor surfaces in children aged up to 18 months)
- History of dry skin in past 12 months
- History of asthma or allergic rhinitis (or history of atopic disease in a first degree relative in children aged under 4 years)
- Onset under the age of 2 years (but this criterion should be used only for children aged 4 years or more at time of diagnosis)

Box 2 Categorisation of physical severity of atopic eczema

Clear—Normal skin, with no evidence of active atopic eczema

Mild—Areas of dry skin, infrequent itching (with or without small areas of redness)

Moderate—Areas of dry skin, frequent itching, redness (with or without excoriation and localised skin thickening)

Severe—Widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking, and alteration of pigmentation)

TERAPIA

- Glucocorticosteroidi per uso topico
- Emollienti
- Antistaminici
- Antibiotici e/o antisettici se sovrainfezioni

Box 4 Stepped approach to management of atopic eczema

- Tailor treatment to severity
- Step treatment up or down according to clinical response. Always use emollients, even when the skin is clear, and add other treatments when required, with specialist advice where recommended

Mild atopic eczema—Use mild potency topical corticosteroids

Moderate atopic eczema—Use moderate potency topical corticosteroids, topical calcineurin inhibitors, bandages

Severe atopic eczema—Use potent topical corticosteroids (short periods only except under specialist supervision), topical calcineurin inhibitors, bandages, phototherapy, systemic therapy

Box 5 Indications for referral for specialist dermatological advice*

Immediate (same-day) referral

- If eczema herpeticum is suspected

Urgent referral (seen within two weeks)

- If the atopic eczema is severe and has not responded to optimal topical therapy after 1 week
- If treatment of bacterially infected atopic eczema has failed

Routine (non-urgent) referral

If any of the following apply:

- The diagnosis is or has become uncertain
- Atopic eczema on the face has not responded to appropriate treatment
- The atopic eczema is associated with severe and recurrent infections
- Contact allergic dermatitis is suspected
- The atopic eczema is giving rise to serious social or psychological problems for the child, parent, or carer
- The child, parent, or carer might benefit from specialist advice on treatment application
- Management has not controlled the atopic eczema satisfactorily according to a subjective assessment by the child, parent, or carer