Atopic Dermatitis: Pathogenesis and Treatment

What is atopic dermatitis?

- Complex inflammatory skin disorder
  - intense pruritus
  - cutaneous hyperreactivity
  - immune dysregulation
- Chronic with exacerbations and remissions
- Affects all ages, but more common in kids
- **Major impact on quality of life**

AAD Consensus, 2003

- Atopic dermatitis is a syndrome

- Components:
  - Essential: must be present
  - Important: supportive
  - Associated: suggestive, nonspecific

Essential Features

1. Pruritus
2. Eczema
   - acute, subacute, or chronic
   - typical morphology for age
   - chronic or relapsing course

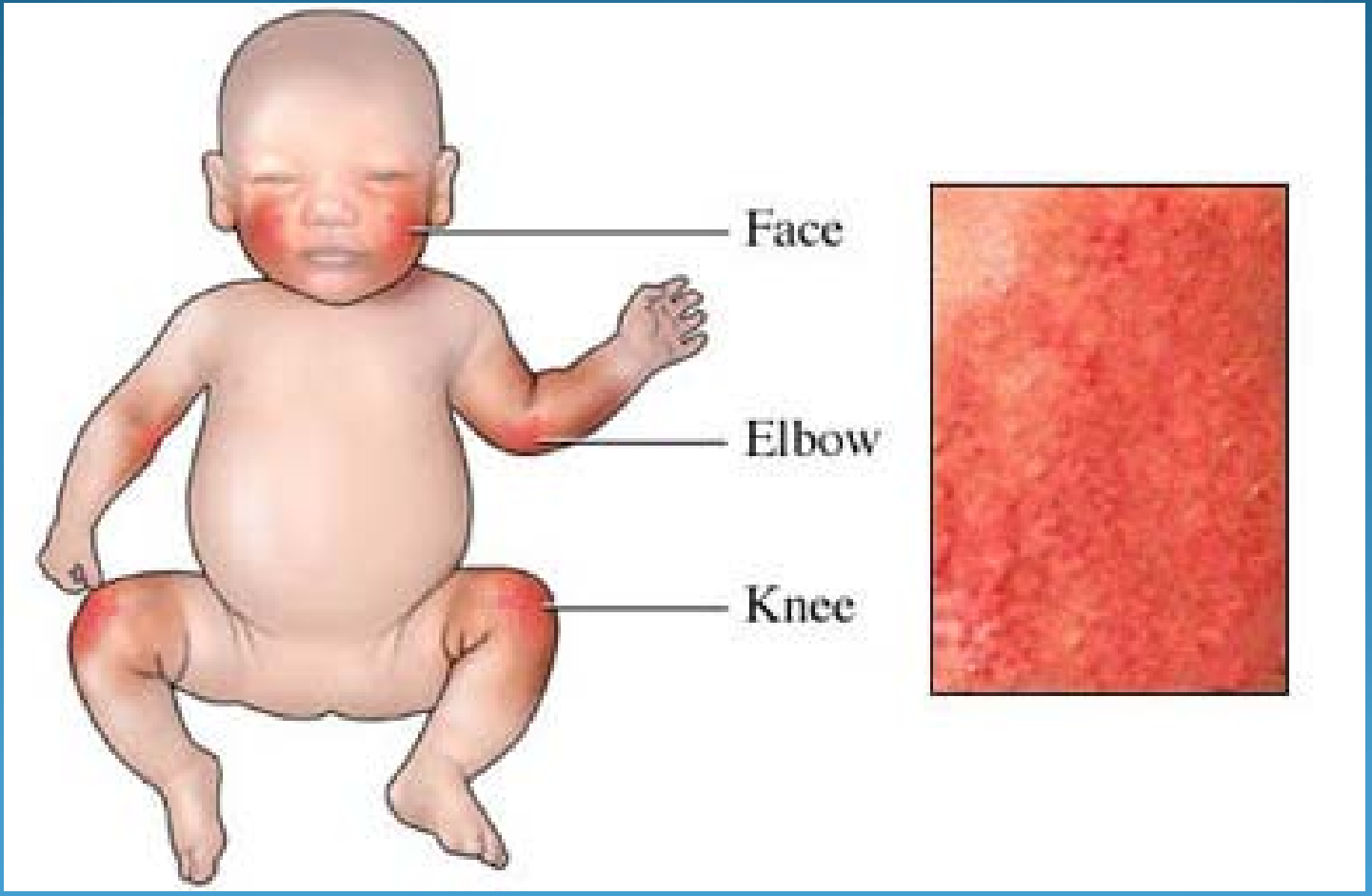
Pruritus

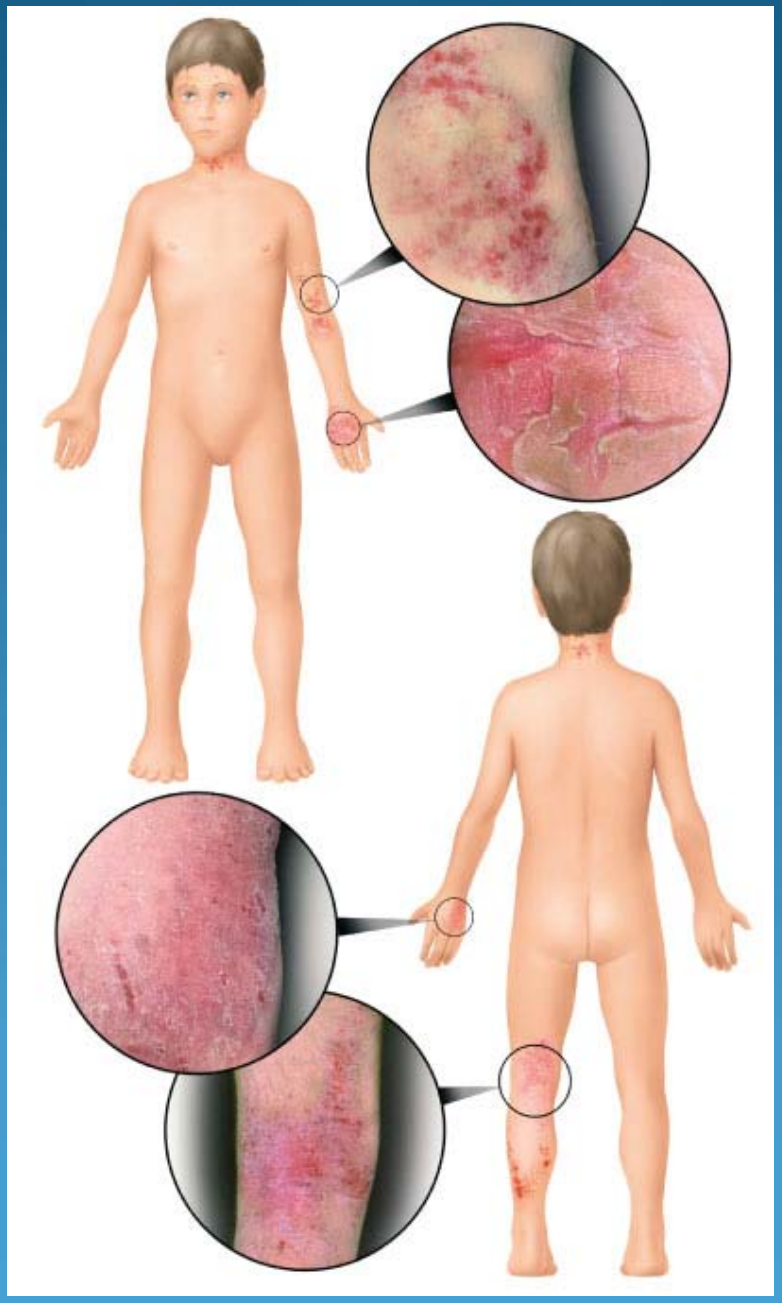
Acute

Subacute / Chronic

Chronic

Infantile Distribution



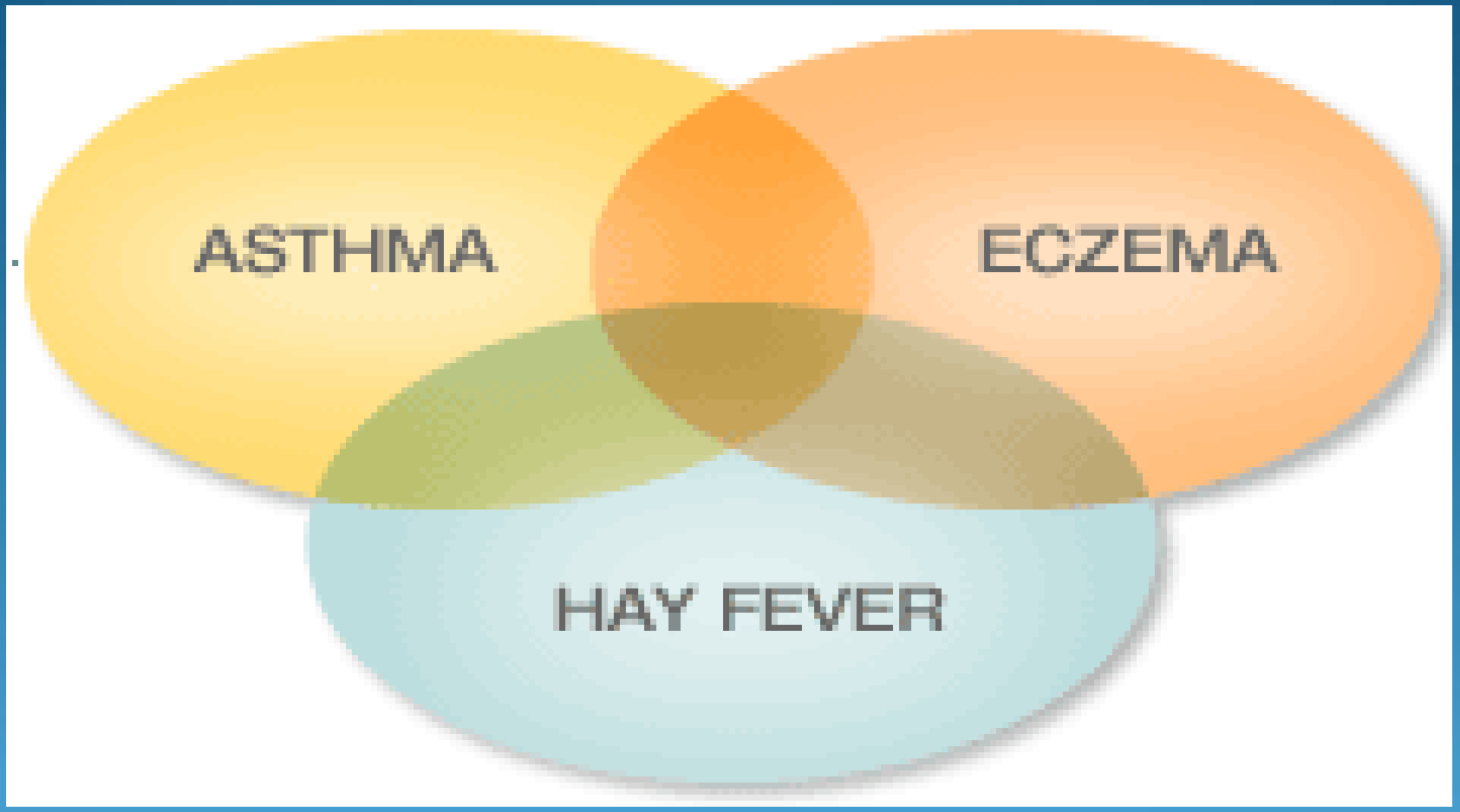


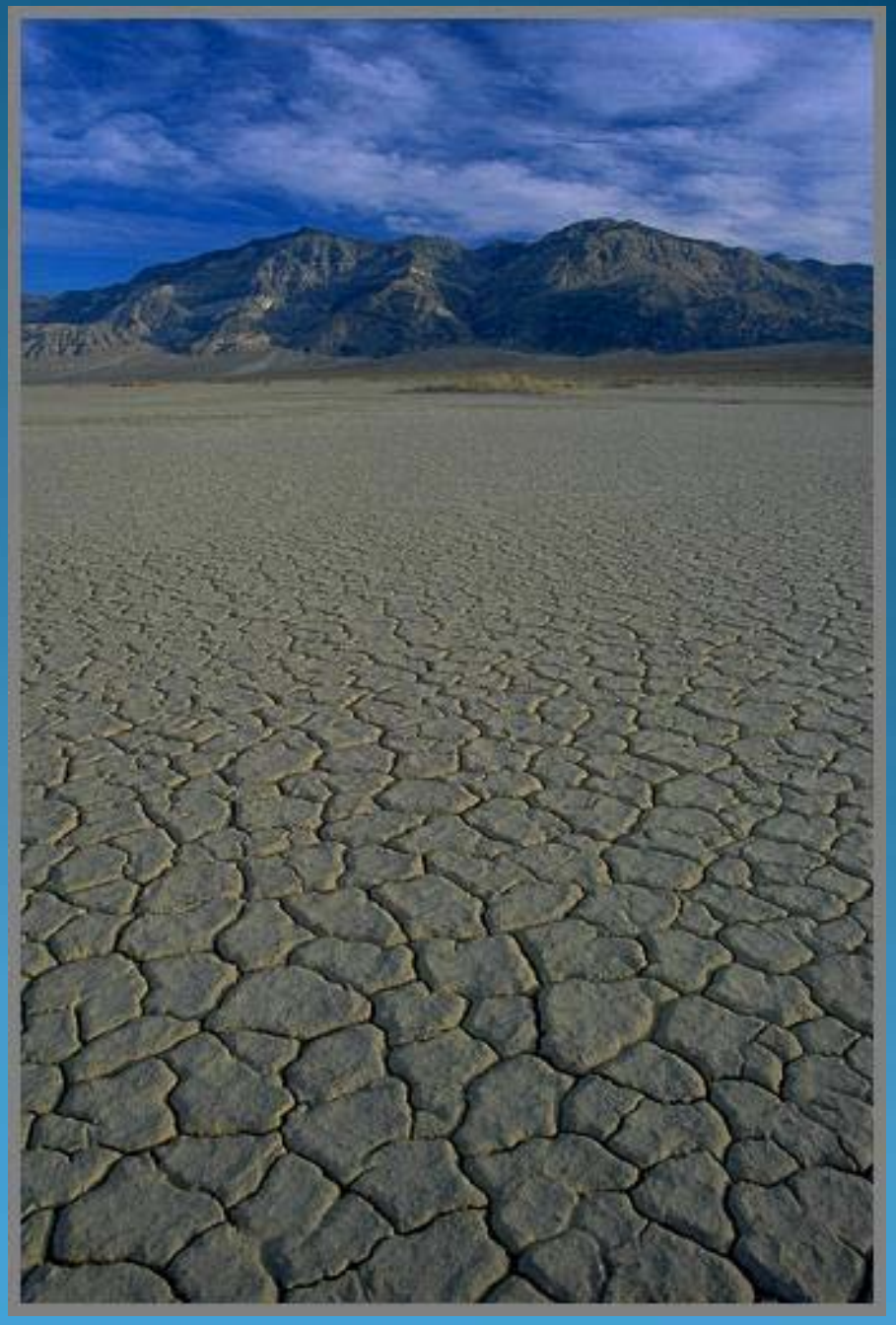
Important Features

1. Early age at onset:
   - 70-90% by age 5
   - 95% by age 15
2. Atopy
   - personal or family history
   - IgE reactivity
3. Xerosis

Early Age at Onset

History of Atopy





Associated Features

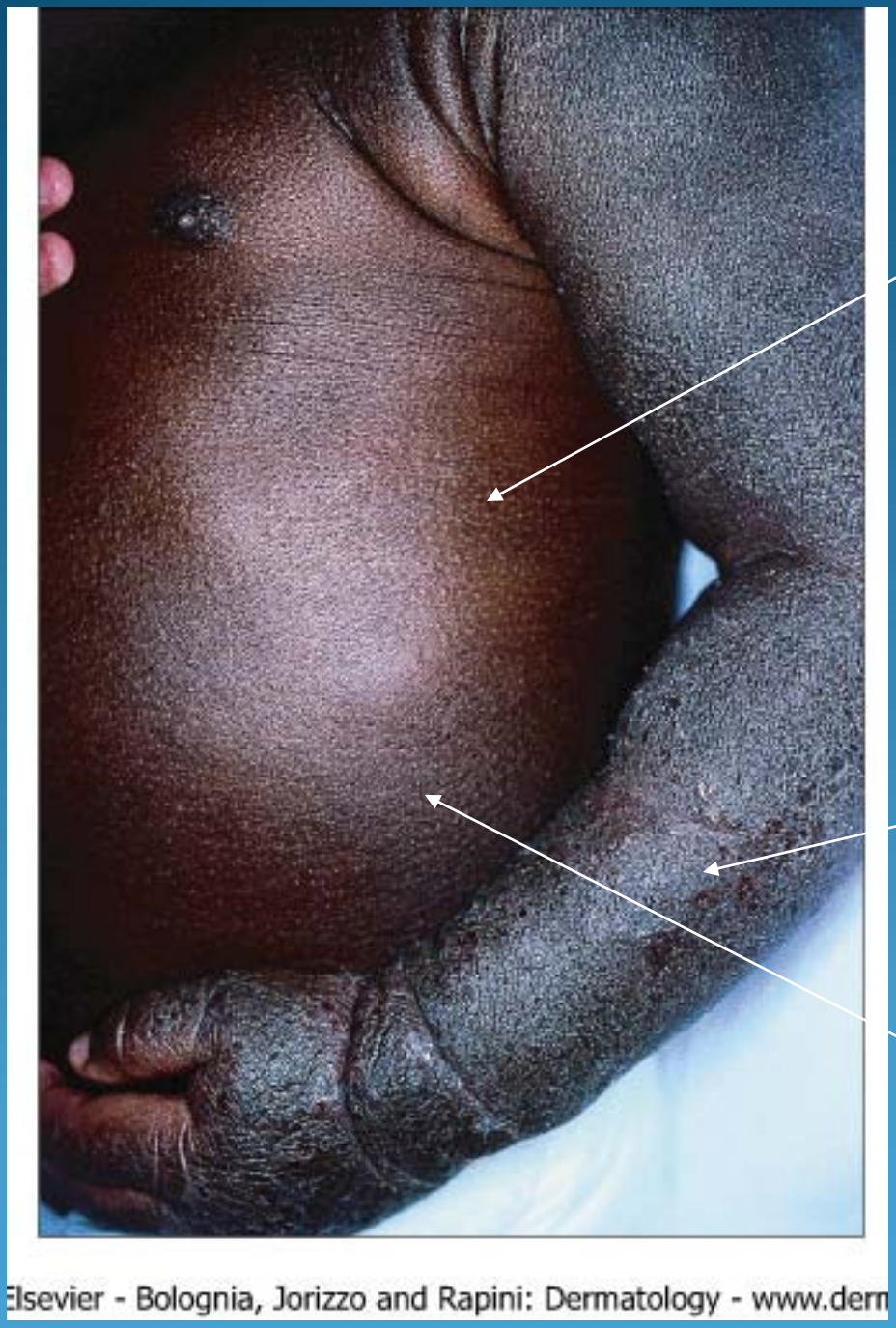
1. Atypical vascular response
2. Keratosis pilaris
3. Hyperlinear palms
4. Peri-ocular, auricular, oral findings
5. Lichenification


A.D.A.M.

Keratosis Pilaris

Infraorbital Folds


(c) University Erlangen,
Department of Dermatology
Phone: (+49) 9131 - 85 - 2727


Perifollicular
Accentuation
Lichenification
Xerosis
Elsevier - Bolognia, Jorizzo and Rapini: Dermatology - www.derm

Exclusionary Conditions

- Scabies
- Psoriasis
- Seborrheic dermatitis
- Allergic contact dermatitis
- Cutaneous lymphoma
- Immunodeficiency diseases

The bottom line…

the diagnosis is clinical

Epidemiology

- Trend:
  - prevalence is increasing in Western and developing countries worldwide

- Lifetime Prevalence in US:
  - Children: 10-20%
  - Adults: 1-3%

- Three-fold increase in industrialized nations
- Remains low in agricultural nations

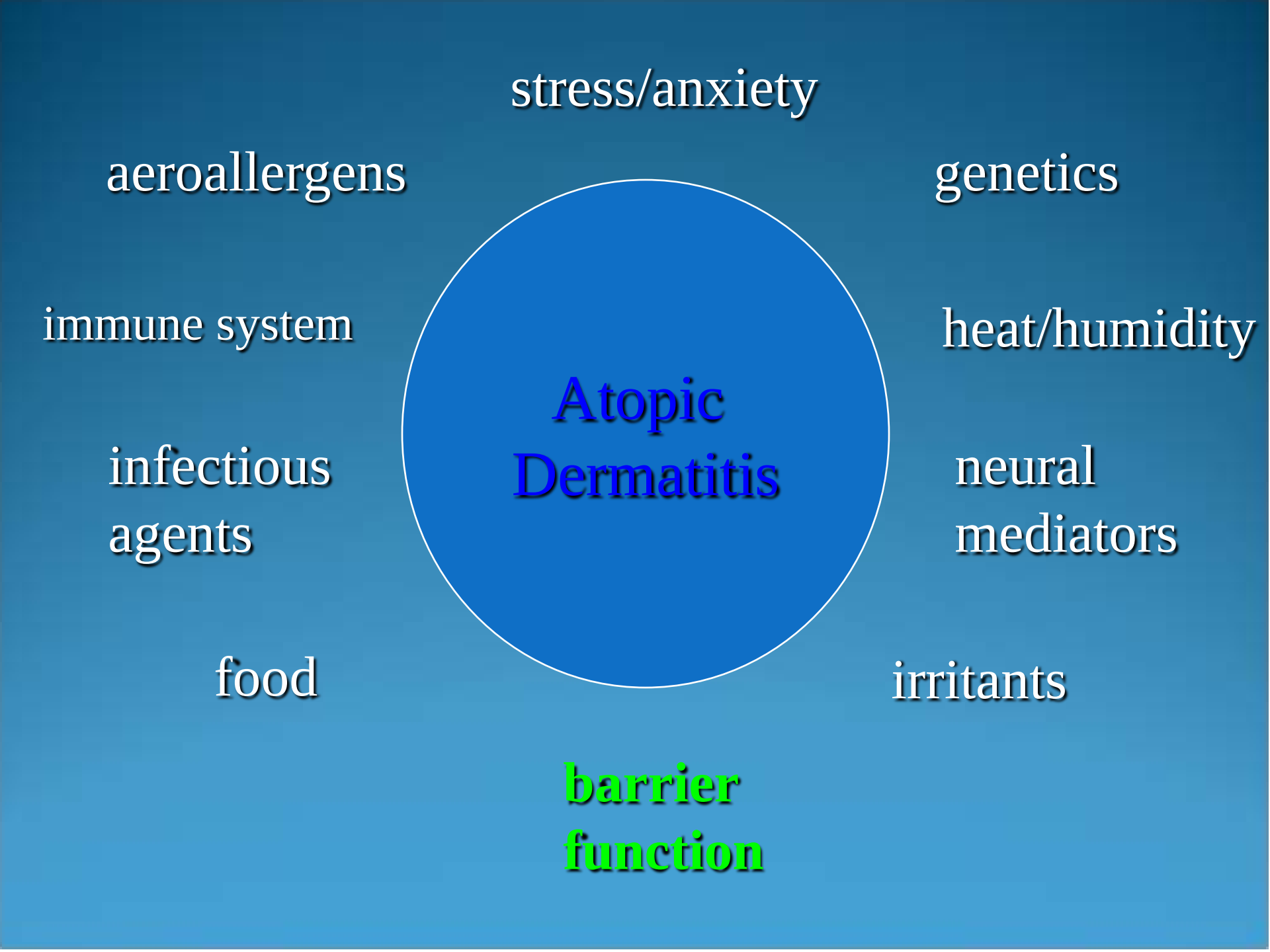
Environmental Influences

- **Western lifestyle**
  - Smaller families, urban environments
  - Increased education and income
  - Increased use of *antibiotics*
- **Hygiene Hypothesis**
  - Allergic diseases may be prevented by infection in *early* childhood
  - T_H1 antagonizes the development of T_H2

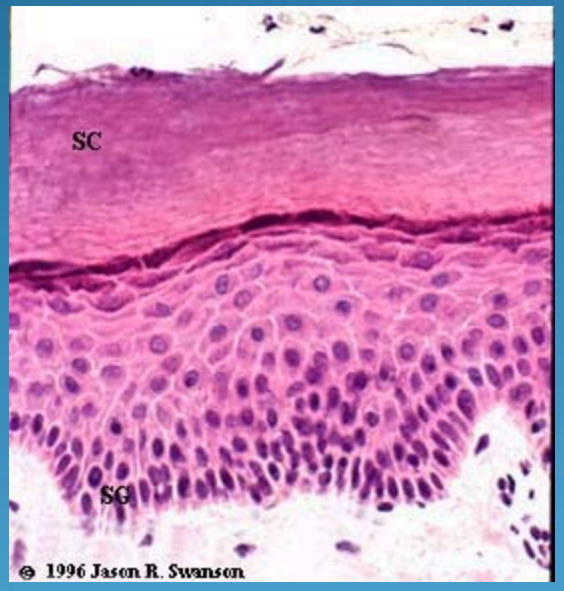
Evolution of Atopy

- AD often initiates the *atopic march*
- 50% outgrow AD by adolescence
- 50^{+} % develop respiratory allergy
- Co-existence marks more severe disease

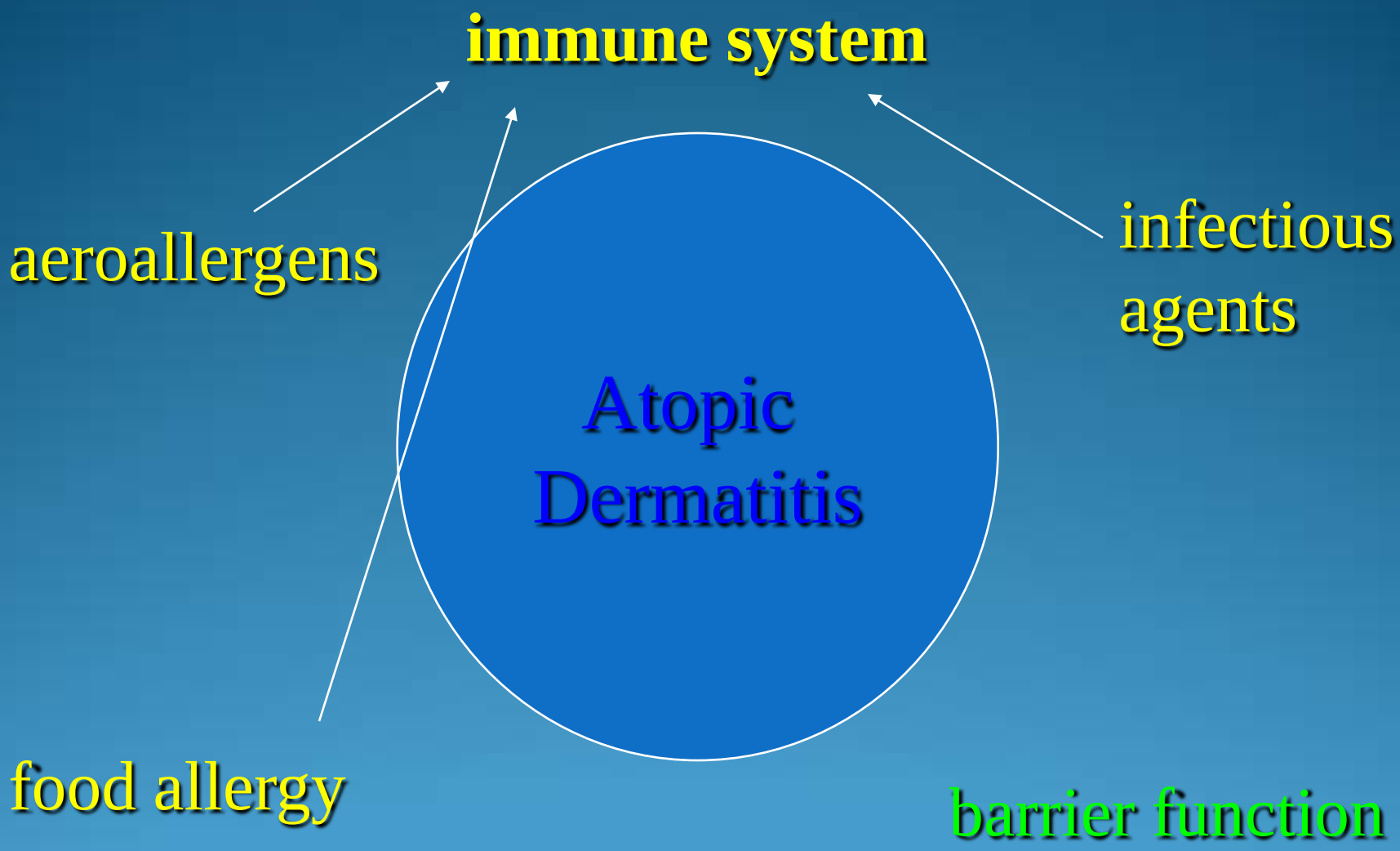
- Skin sensitization by allergens may augment the systemic allergic response


stress/anxiety
aeroallergens
genetics
immune system
heat/humidity
Atopic Dermatitis
infectious agents
neural mediators
food
irritants
barrier function

Stratum Corneum: The Permeability Barrier



- Keeps water in
  - Transepidermal water loss can be measured
- Keeps the world out


immune system
aeroallergens
infectious agents
Atopic Dermatitis
food allergy
barrier function

Food Allergy

- Food allergens can induce eczema
- 90%: milk, egg, peanut, soy, wheat, fish
- 80% outgrow by age 5
  - except peanut and shellfish

- Food allergy correlates with increased severity and younger age of onset of AD

Guillet G, 1992

Clinical Correlation is Key

- Positive Tests
  - clinical relevance must be verified
  - controlled elimination and food challenges
- Elimination of documented food allergens *may not* result in improvement
- Negative tests are the most useful

Aeroallergens

- Immune responses in atopic skin can be elicited by environmental aeroallergens
  - *dust mites, animal dander*

- Intranasal or bronchial challenge in sensitized AD patients can elicit *pruritus, skin lesions,* and *specific IgE*

Test if standard therapies fail or known triggers exist

Aeroallergens

- Avoidance is difficult, but effective in selected cases
  - dust mites

Microbes

- *Staphylococcus aureus*- disrupted skin
- Secretes toxins: superantigens
  - bind TCR: mass T cell activation
  - induce specific IgE on basophils, mast cells
- Itch-scratch cycle

Treatment Concepts

- Education
- Education
- Education
- Education
- Basic skin care
- Topical medications
- Systemic medications
- Lifestyle modification

Treatment Concepts

- Standardize your approach
- Individualize the care plan
  - Age
  - Severity
  - Prior therapy
  - Beliefs and expectations

Approach to the Patient

- #1: Repair the Skin
- #2: Control the Itch
- #3: Treat Secondary Infection
- #4: Educate & Follow-Up
- #5: Maintain Skin Integrity
- #6: Refractory Cases

#1: Repair the Skin

- Hydration and moisturization (soak & seal)
- Bath or shower followed by emollient
- Ointments or oils, avoid lotions and creams
- Petrolatum, aquaphor, elta, cetaphil

Water is not the enemy!

Rehydrate the skin!

This Is The Enemy

Topical Treatments: Corticosteroids

- First line therapy
  - Anti-inflammatory
  - Decrease Staph density
- Agent/Duration
  - severity, distribution, age, vehicle, occlusion
- Control disease, taper, and withdraw
- Write out the care plan!
- Close follow-up

steroids are essential and continue to be first line therapy in atopic dermatitis

the key is to use steroids adjunctively within the framework of a multi-modality care plan

Risk of atrophy?

Topical Treatments: Calcineurin Inhibitors

- Immunomodulators: ↓ IL-2 = ↓ T cells
- Tacrolimus Ointment, 0.03 and 0.1%
  - .03% approved for mod-severe AD in pts > 2
- Pimecrolimus 1% Cream
  - approved for mild-moderate AD in pts > 2

Topical Calcineurin Inhibitors in Clinical Practice

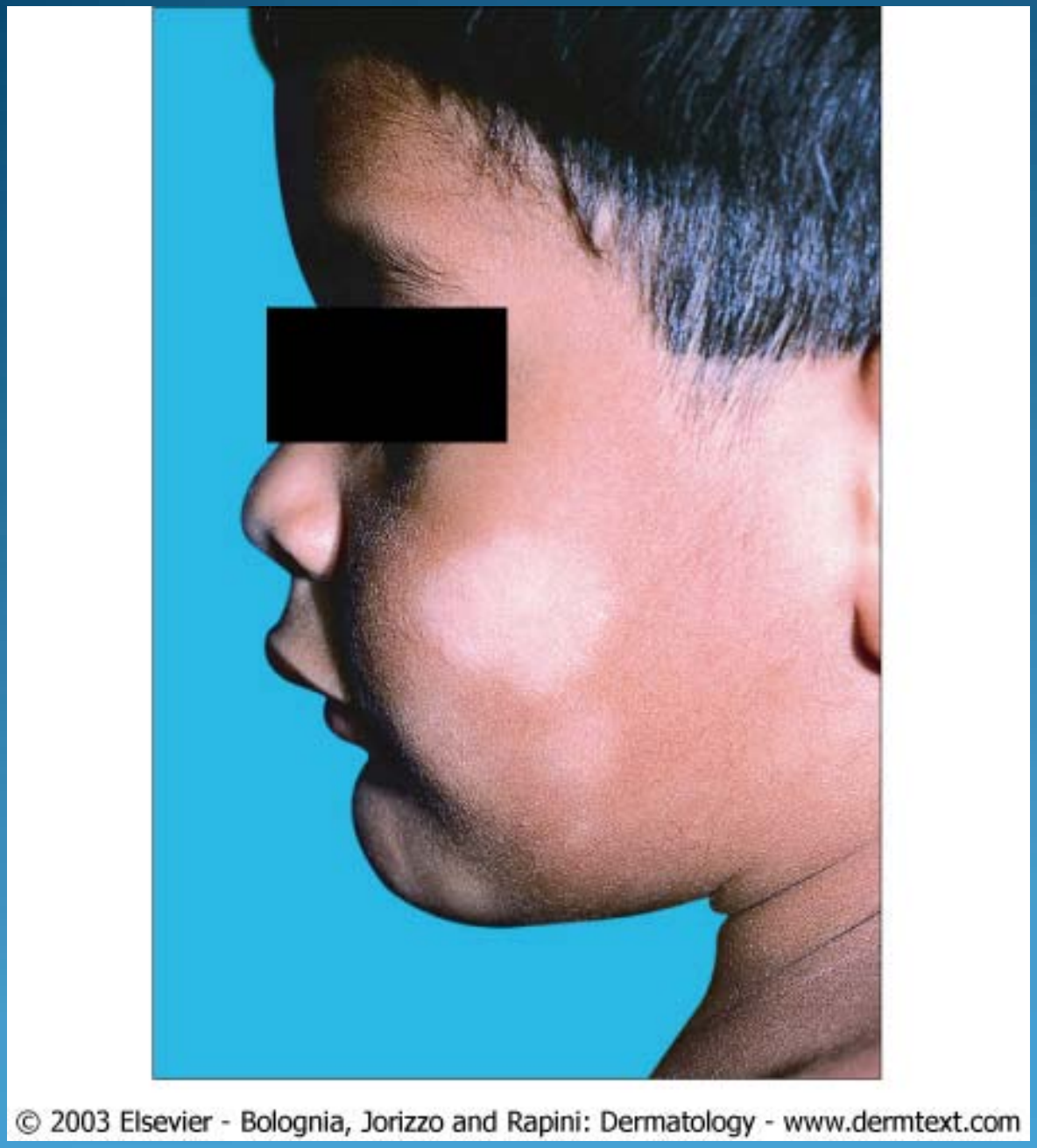
Efficacy:

- Mild, patchy eczema
- Eyelid involvement
- Combination with topical steroids
- Maintenance therapy

Topical Calcineurin Inhibitors in Clinical Practice

Safety:

- Risk of cutaneous malignancy
- FDA Alert: potential cancer risk
  - animal studies
  - case reports in small number of pts
  - mechanism of action
- No causal relationship in humans
- 2nd line Rx, only as indicated, time will tell



Tacrolimus
or
Pimecrolimus
BID

Tac or Pim QD
+
1% HC oint QD

#2: Control the Itch

- Systemic sedating antihistamines
  - Bedtime dosing to break the itch-scratch cycle
  - Diphenhydramine and Hydroxyzine
- Doxepin:
  - Tricyclic antidepressant/anti- H1 and H2
  - Reserved for recalcitrant pruritus
- Non-sedating antihistamines
  - If co-existent respiratory allergy

Follicular Eczema

#3: Treat Infection

- Secondary infection is common
- Treat early and aggressively
- Staphylococcus aureus:
  - cephalexin or dicloxacillin
- Herpes Simplex
  - systemic antiviral (acyclovir)
- Culture often for resistant strains (MRSA)

#4: Educate & Follow-Up

- Control versus cure
- Lifestyle modification
  - Trigger avoidance
  - Shared sleeping
  - Daily routine
- Risks/benefits: enhance compliance
- Frequent visits for tailoring and education

#5: Maintain Skin Integrity

- Implement a step-down regimen
- Treat early flares aggressively
- Keep a trigger diary
- Make one change at a time

4 year-old boy with diffuse, impetiginized eczema

Parents fearful, cautious

Refused steroids in past

Child shares bed with parents

Losing weight, excoriated, miserable

How did we get here from there?

Management

#1: Repair the Skin

#2: Control the Itch

#3: Treat Infection

#4: Educate & F/U

#5: Maintenance

1. Body: Tac 0.1% Oint
   Face: HC 2.5% Oint
   Scalp: Dermasmooth
   Petrolatum liberally
2. Hydroxizine qHS
3. Cephalexin x 10 days
4. Write plan, literature
5. Desonide, aquaphor, ceramide cream

#6: Refractory Cases

- Review regimen, determine compliance
- Culture
- Allergy testing
- Phototherapy
- Systemic immunomodulatory agents
  - cyclosporin, azathioprine, mycophenolate
  - avoid systemic steroids

It Takes a Village…

- Primary Care Physician
- Allergy/Immunology
- Dermatology
- Infectious Disease
- Endocrinology

A Final Thought

atopic skin…

treat it from the outside in