

# Drug allergy and Skin Disorders

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Distinguished Educator  
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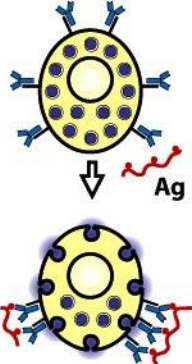
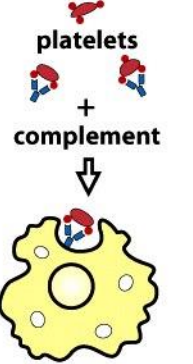
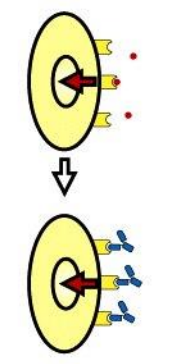
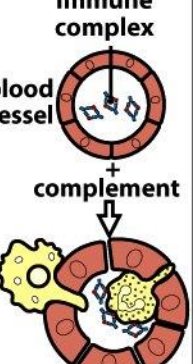
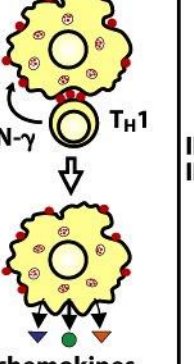
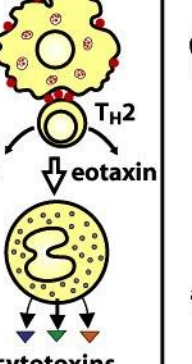
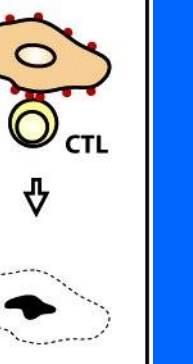
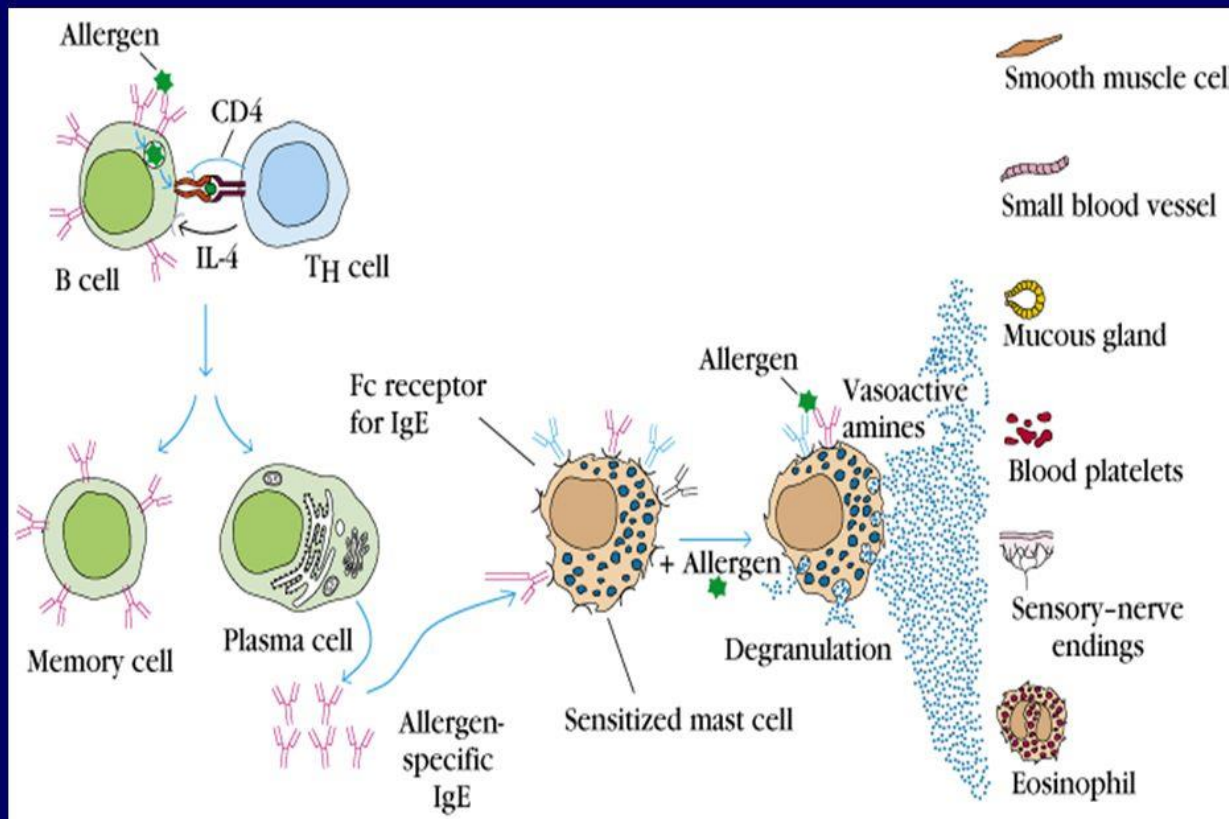
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Figure 13-1 Immunobiology, 7ed. (© Garland Science 2008)

# Type 1 H/S. ( immediate hypersensitivity ).



# The best screening test for anaphylaxis is?

- A. histamine
  - B. IL-5
  - C. tryptase
  - D. C-3
- 
- Ans:

# The best screening test for anaphylaxis is?

- A. histamine
  - B. IL-5
  - C. tryptase
  - D. C-3
- 
- Ans: C

Treatment of choice for immediate hypersensitivity is?

- A. diphenhydramine
- B. prednisone
- C. combination of diphenhydramine and prednisone
- D. epinephrine

Treatment of choice for immediate hypersensitivity is?

- A. diphenhydramine
  - B. prednisone
  - C. combination of diphenhydramine and prednisone
  - D. epinephrine
- 
- Answer: D



**EpiPen<sup>®</sup>**  
**TRAINING DEVICE**

CONTAINS NO DRUG - PRODUCE THE NOISE

**1** Pull off blue safety release.

**2** Swing and firmly push orange tip against outer thigh so it clicks AND HOLD on thigh several secs to simulate drug delivery.

**3** Tip extends upon use.

**TO RESET, SEE OTHER SIDE**

Fringidula versu  
Eli Lilly Pharmazeutische Werke AG  
Messeplatz 1, D-57074 Sprockhöbel  
Germany

EpiPen is a registered trademark of Nydan, Inc. Licensed to Day, L.P. of Napa, CA



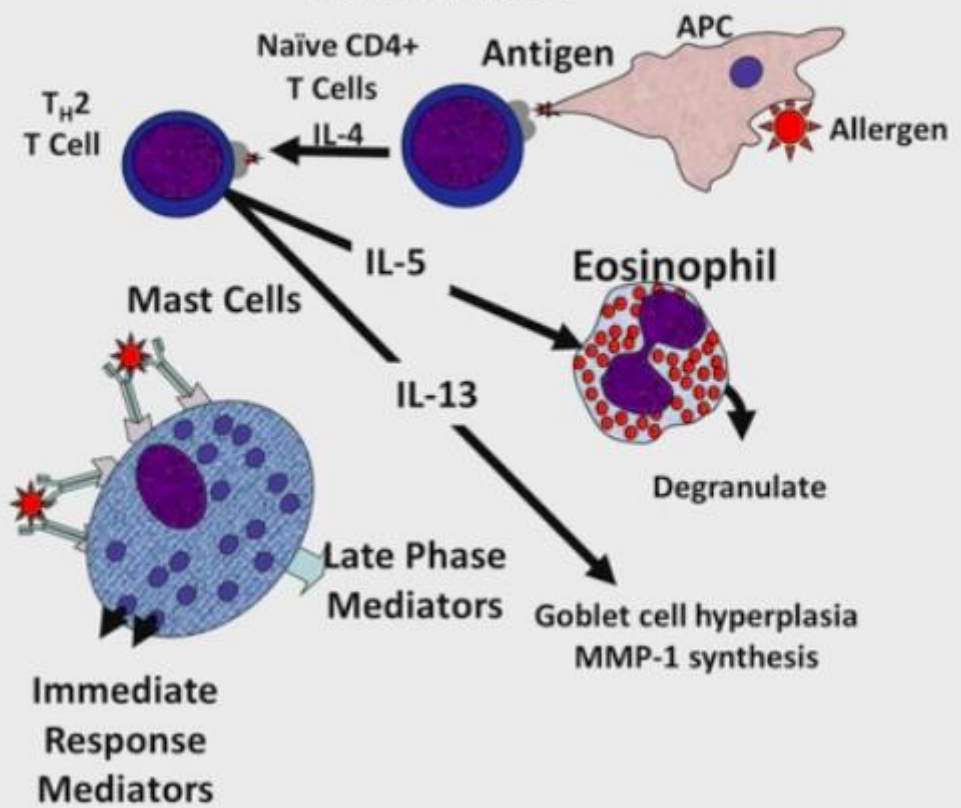
The late phase of immediate hypersensitivity is mainly due to what cell?

- A. Neutrophils
- B. Eosinophils
- C. Mast cells
- D. T helper cells
  
- Answer:

The late phase of immediate hypersensitivity is mainly due to what cell?

- A. Neutrophils
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  - C. Mast cells
  - D. T helper cells
- 
- Answer: B

# Late Phase



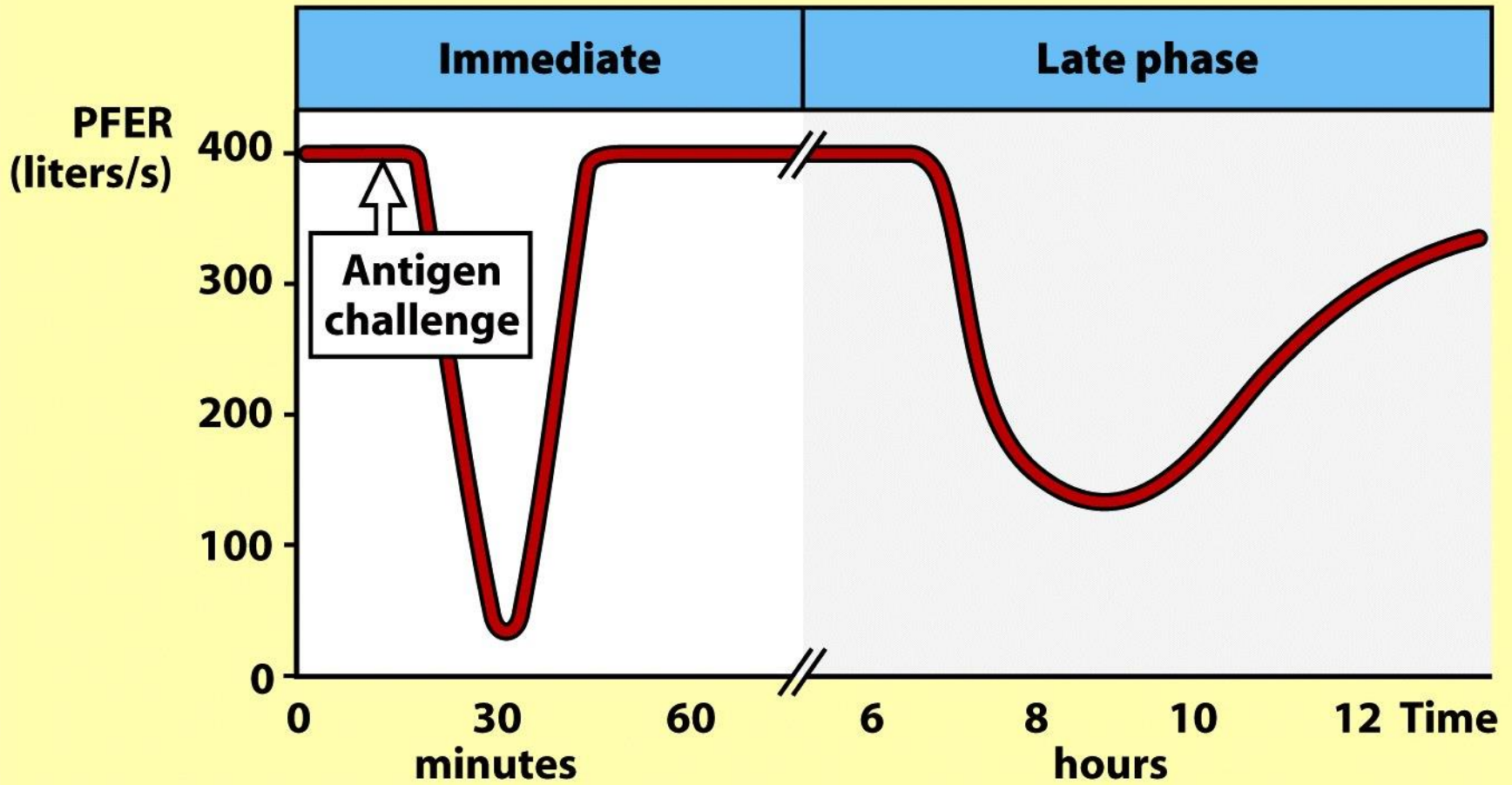
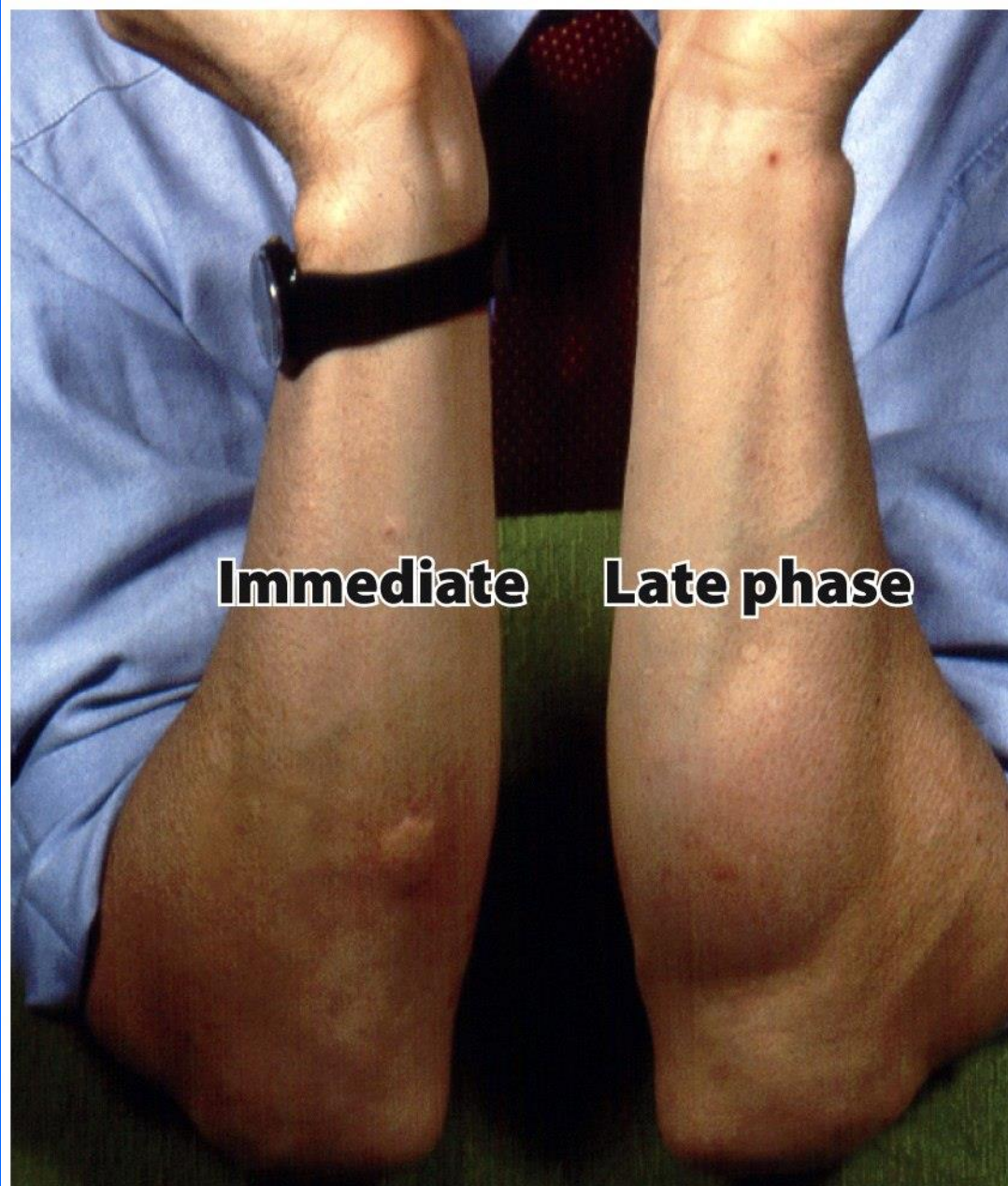


Figure 13-14 part 1 of 2 Immunobiology, 7ed. (© Garland Science 2008)



**Immediate      Late phase**

Figure 13-14 part 2 of 2 Immunobiology, 7ed. (© Garland Science 2008)

# Penicillin Skin Test for type 1 hypersensitivity

## Practical Insights On Penicillin Skin Testing



ID STEWARDSHIP

Penicillin allergy: 10% state they have penicillin allergy.

90% of these do not.

98% predictive value if skin tests to Pen G  
and penicilloyl polylysine are negative.

Because of the 2% missed oral challenge is  
given.

If positive you can desensitize.



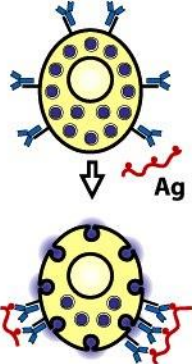
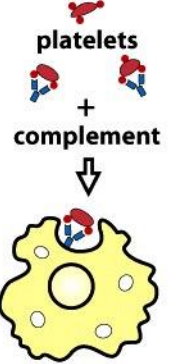
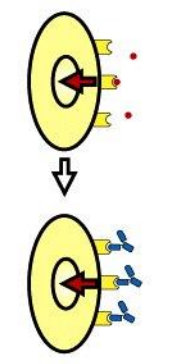
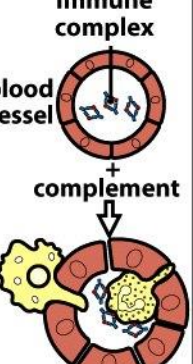
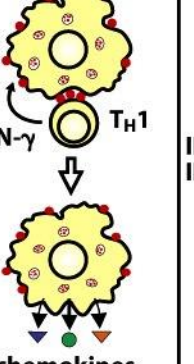
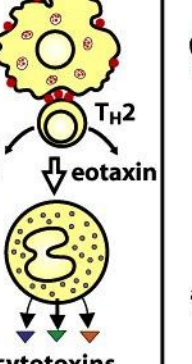
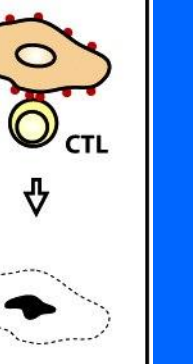
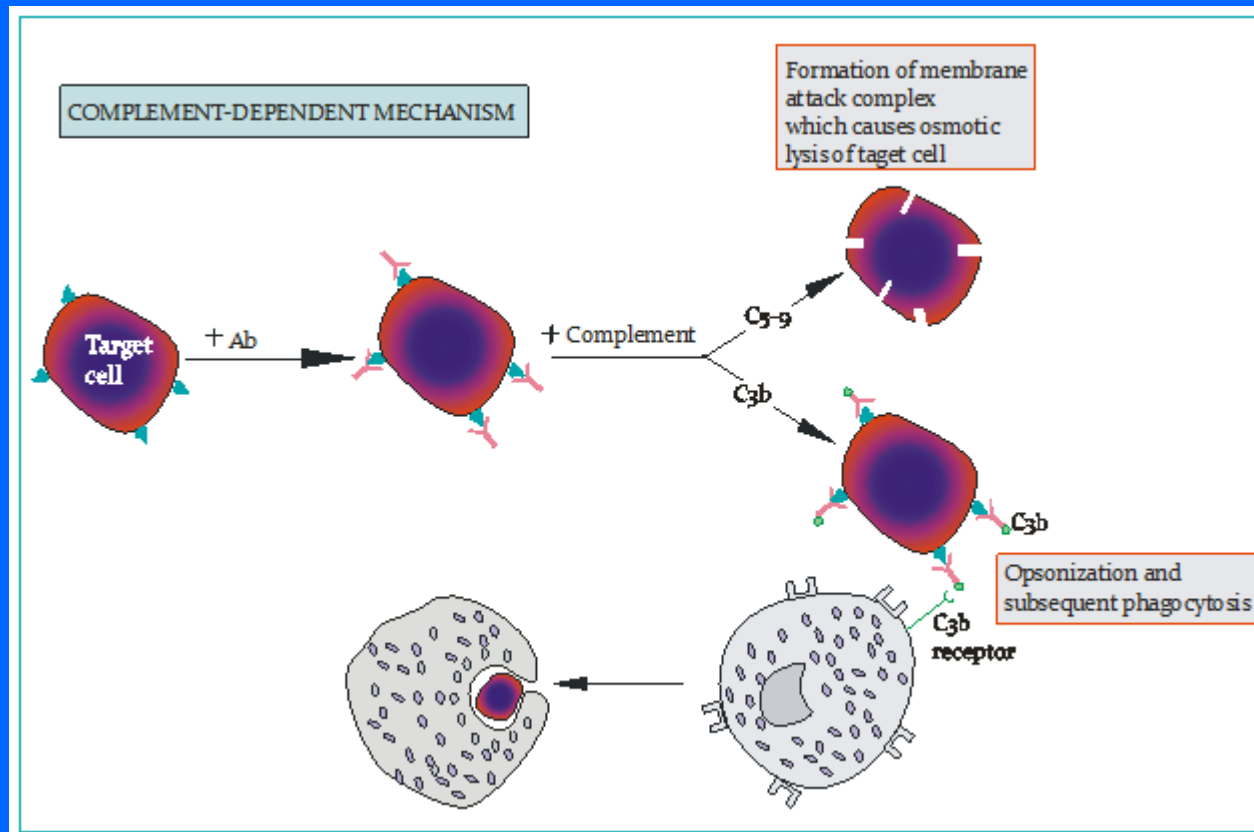
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Figure 13-1 Immunobiology, 7ed. (© Garland Science 2008)

# Type 2 hypersensitivity





## Type 2 hypersensitivity

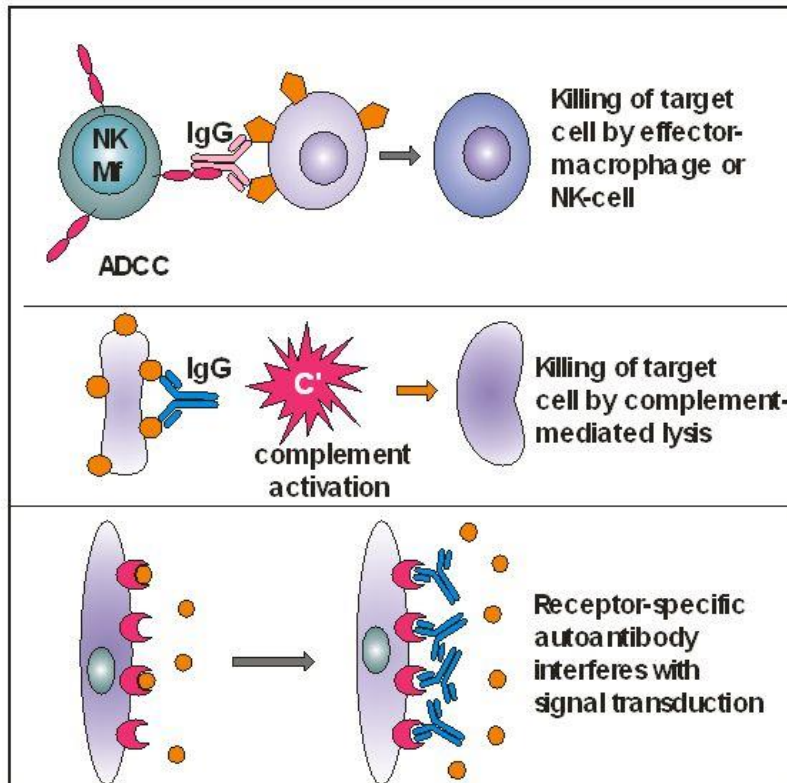
- 26 year old female admitted for Neisseria sepsis.
  - Last hospitalization she develop hemolytic anemia from penicillin
  - What would you do at this admission?
- A. desensitize to penicillin
  - B. Avoid penicillin at all costs
  - C. pretreat with steroids and antihistamines before penicillin
  - D. Skin test to penicillin first

## Type 2 hypersensitivity

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  - C. pretreat with steroids and antihistamines before penicillin
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Common Causes: cephalosporins, penicillin,  
NSAID, quinine/quinidine.  
Only treatment is avoidance.

## MECHANISMS OF TYPE II HYPERSENSITIVITY REACTIONS



Hemolytic anemia of newborns

*Erythroblastosis fetalis*

ABO blood transfusion

Drug induced

Hemolytic anemia

Trombocytopenia

Agranulocytosis

**Penicillin-based antibiotics**

**Anti-arythmic quinidin**

Goodpasture syndrome  
(type IV collagen)

Pemphigus vulgaris

(desmosomal antigens)

*Damage of epidermal and mucosal junctions, acantholysis*

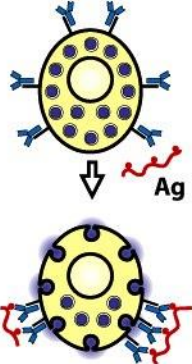
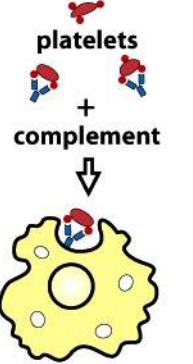
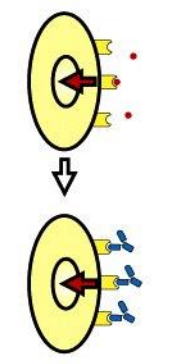
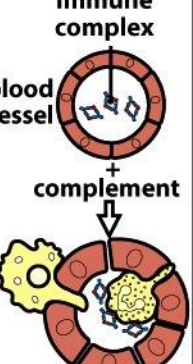
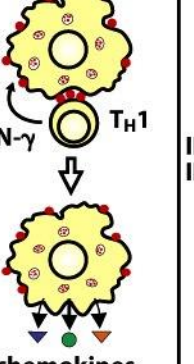
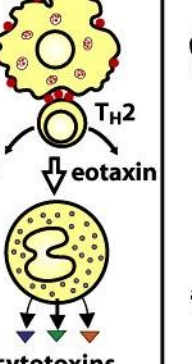
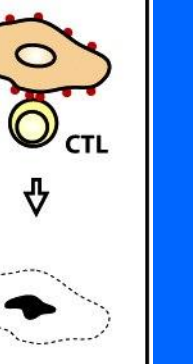
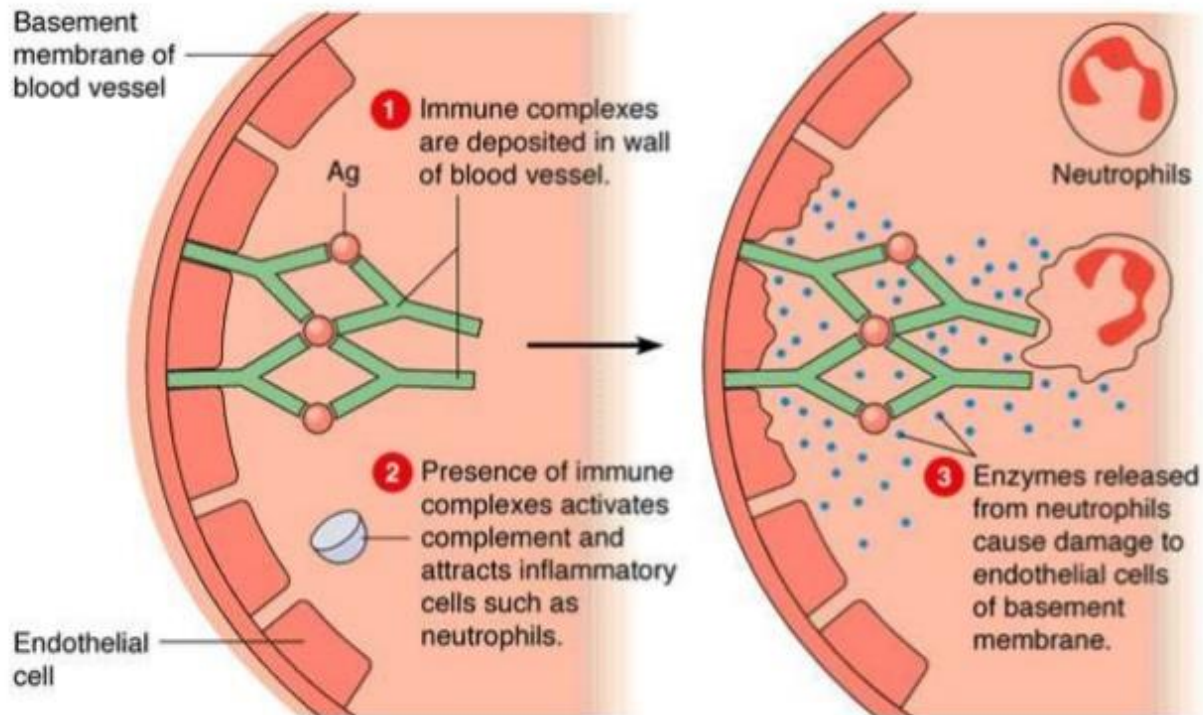
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Figure 13-1 Immunobiology, 7ed. (© Garland Science 2008)

# Type three hypersensitivity





# TYPE III HYPERSENSITIVITY

- symptoms caused by type III hypersensitivity reactions depend on the site of immune complex deposition
- serum sickness – intravenous immunocomplexes  
(horse antiserum against snake/spider venom)
- Arthus reaction – localized, skin
- Farmer's lung – localized, lungs

Route	Resulting disease	Site of immunocomplex deposition
Intravenous (high dose)	Vasculitis	Blood vessel walls
	Nephritis	Renal glomeruli
	Arthritis	Joint spaces
Subcutaneous	Arthus reaction	Perivascular area
Inhaled	Farmer's lung	Alveolar/capillary interface



Figure 12.33 The Immune System, 3ed. (© Garland Science 2009)

# Type three hypersensitivity

- 22 year old given amoxicillin for a presumed sinusitis 4 days after developing sore throat, nasal congestion and cough.
- On day 10 of therapy he developed a fever, arthralgias, itchy rash and fatigue.
- **The diagnosis is?**
  - A. serum sickness
  - B. Stevens-Johnson Syndrome
  - C. Type 4 hypersensitivity reaction
  - D. Anaphylaxis



# Type three hypersensitivity

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  - C. Type 4 hypersensitivity reaction
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# Type III hypersensitivity

- Type III hypersensitivity is also known as immune complex hypersensitivity. The reaction may be general (*e.g.*, serum sickness) or may involve individual organs including skin (*e.g.*, systemic lupus erythematosus, Arthurs reaction), kidneys (*e.g.*, lupus nephritis), lungs (*e.g.*, [Aspergillosis](#)), blood vessels (*e.g.*, [polyarteritis](#)), joints (*e.g.*, rheumatoid arthritis) or other organs. This reaction may be the pathogenic mechanism of diseases caused by many microorganism

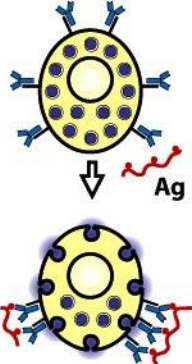
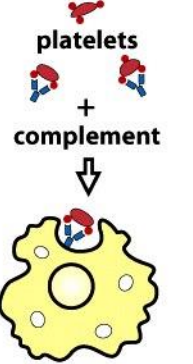
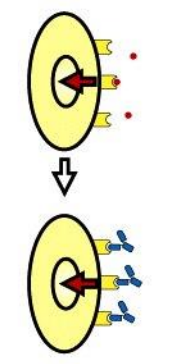
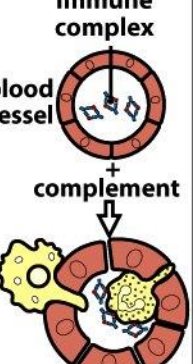
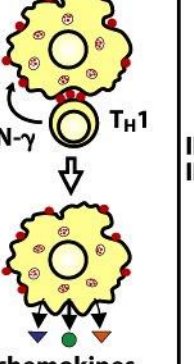
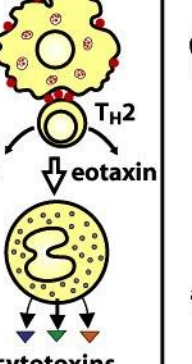
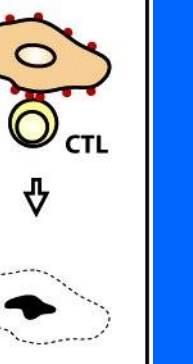
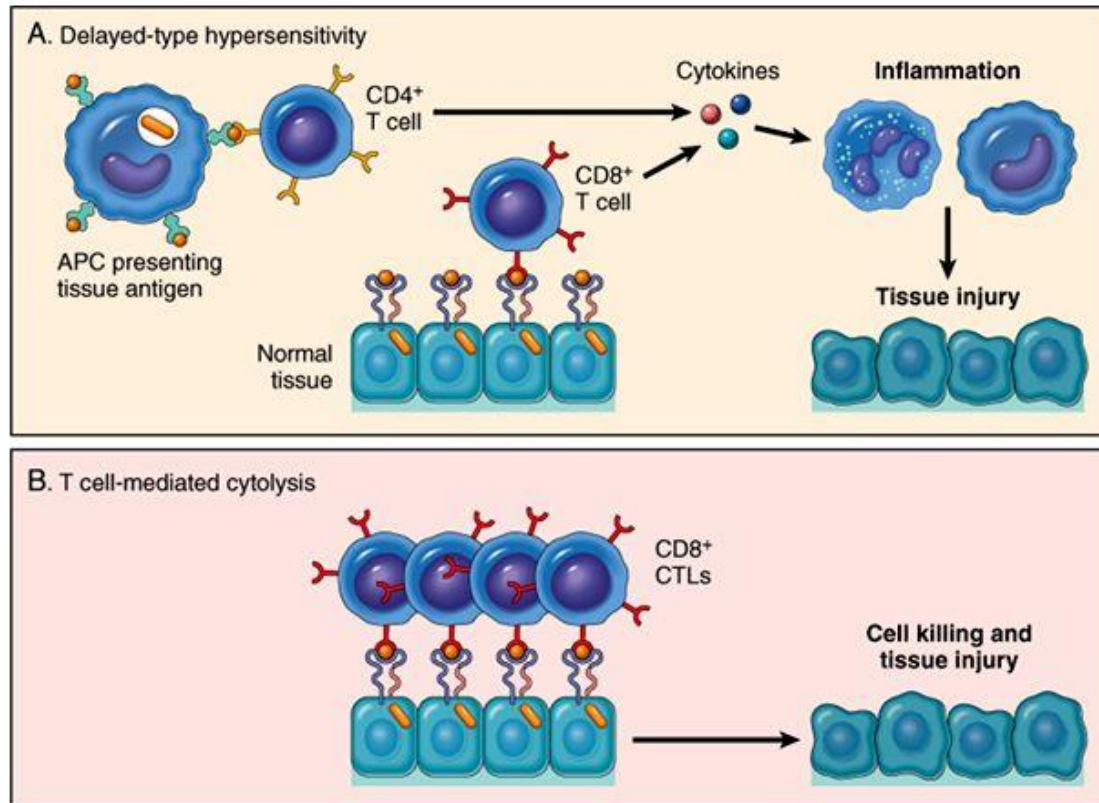
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Figure 13-1 Immunobiology, 7ed. (© Garland Science 2008)

# Type IV Hypersensitivity

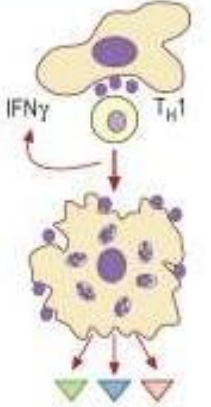
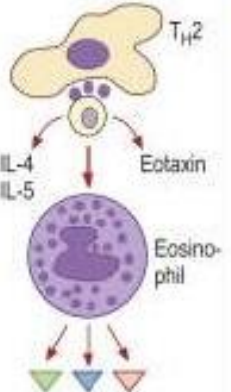
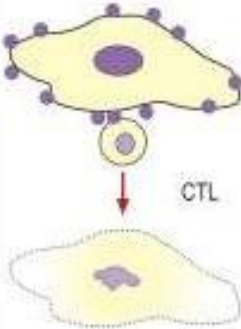
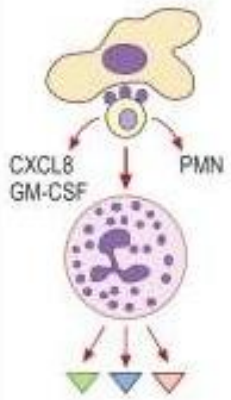


© Elsevier. Kumar et al: Robbins Basic Pathology 8e - www.studentconsult.com

- **Delayed-type hypersensitivity** (e.g. tuberculin reaction, dermatitis) – T<sub>H</sub>1 cells presented with antigen release IFN- $\gamma$  and other cytokines causing inflammation and tissue injury
- **Direct cell cytotoxicity** (e.g. T1DM, MS, RA) – T-cytotoxic cells react to antigens displayed by host cells



## T cell orchestrated hypersensitivity reactions (Gell and Coomb's types IVa–d)

Type	Type IVa	Type IVb	Type IVc	Type IVd
Cytokines	IFN $\gamma$ , TNF $\alpha$ (T <sub>H</sub> 1 cells)	IL-5, IL-4/IL-13 (T <sub>H</sub> 2 cells)	Perforin/granzyme B (CTL)	CXCL8, GM-CSF (T cells)
Antigen	Antigen presented by cells or direct T cell stimulation	Antigen presented by cells or direct T cell stimulation	Cell-associated antigen or direct T cell stimulation	Antigen presented by cells or direct T cell stimulation
Cells	Macrophage activation	Eosinophils	T cells	Neutrophils
Pathomechanism	 <p>Chemokines, cytokines, cytotoxins</p>	 <p>Cytokines, inflammatory mediators</p>	 <p>CTL</p>	 <p>Cytokines, inflammatory mediators</p>
Example	Tuberculin reaction, contact dermatitis (with IVc)	Chronic asthma, chronic allergic rhinitis Maculopapular exanthema with eosinophilia	Contact dermatitis Maculopapular and bullous exanthema hepatitis	AGEP Behçet disease

Middleton's allergy. Seventh edition.

# Type IV (Cell Mediated) Hypersensitivity



## Type IV (Delayed or Cell-Mediated) Hypersensitivity

- Delayed hypersensitivity is a function of **T Lymphocytes, not antibody.**
- It starts hours (or Days) after contact with the antigen and often lasts for days.
- It can be transferred by immunologically committed (Sensitized) T cells, not by serum.
- Principal pattern of immunologic response to variety of intra cellular microbiologic agents
  - i.e.: Mycobacterium Tuberculosis
  - Viruses
  - Fungi
  - Parasites

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**Also includes: IV-a- contact dermatitis, TB skin testing**  
**IV-b- asthma, rhinitis, nasal polyyps, DRESS**  
**IV-c- some bullous skin disorders**  
**IV-d- Behcet' s and AGEP**

Treatment:  
avoidance and  
corticosteroids

21 year old with itchy rash.  
Worse in winter and summer.  
Worried about food allergies.  
Presented for diagnosis and therapy.



Your patient with the this rash should be treated with?

- A. topical antibiotics
- B. topical corticosteroids
- C. oral steroids
- D. dapsonsone
- E. famciclovir

• Ans:



Your patient with the this rash should be treated with?

- A. topical antibiotics
- B. topical corticosteroids
- C. oral steroids
- D. dapsonsone
- E. famciclovir
  
- Ans: B





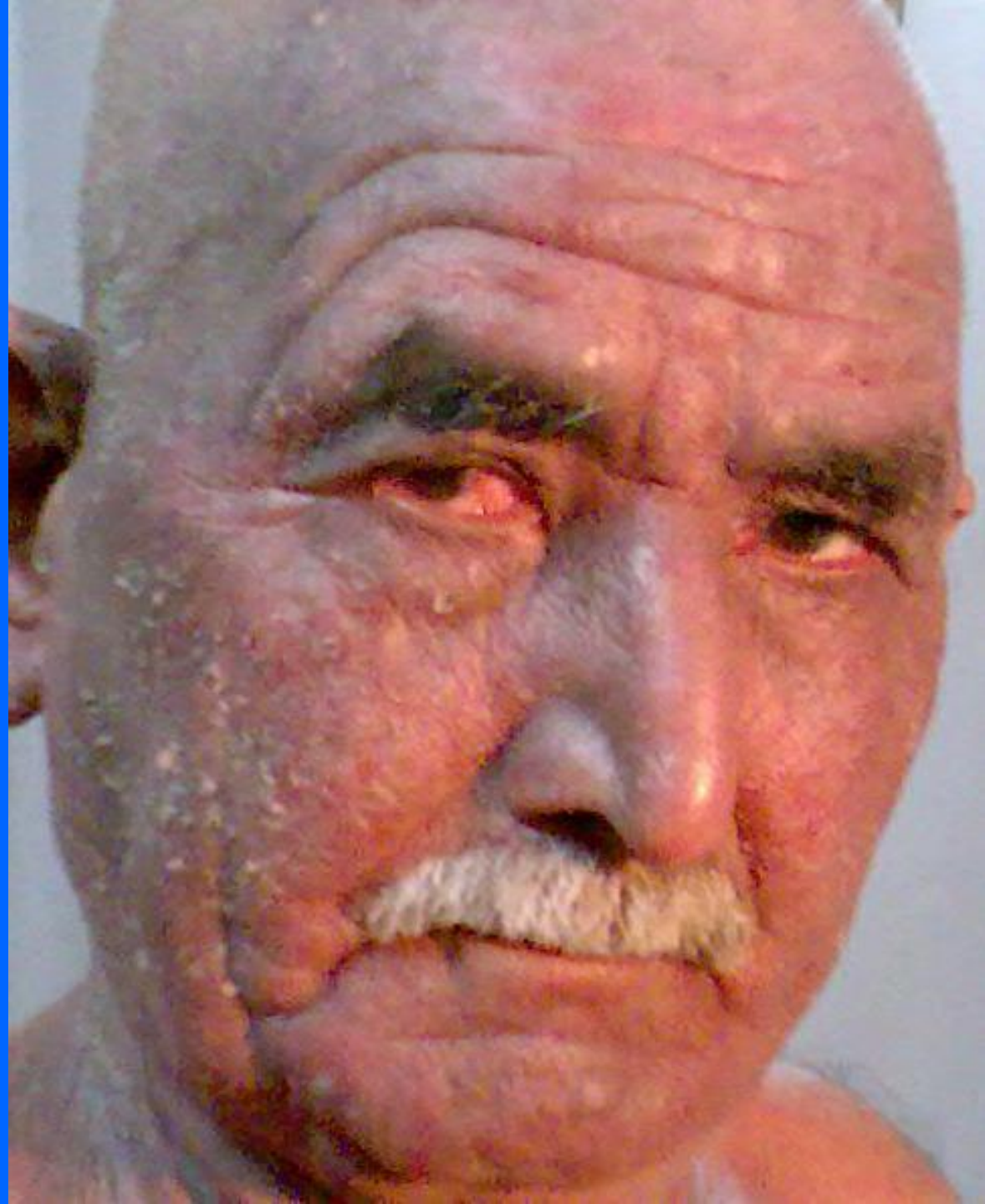
# Infantile AD











# Atopic Dermatitis

- Adults - flexure areas, hands
- Eyes- think atopic keratoconjunctivitis
- Exacerbations – think Staph or Herpes simplex
- 30% with food allergy (frequent false positives)
- Anergy: decreased TH-1 cell and decreased interferon predispose to skin infections
- increase IgE, IL<sub>4</sub> , IL<sub>5</sub>, GM-CSF, IL<sub>13</sub>,  
(lymphocytes T helper type 2 phenotype)
- Filaggrin gene defect is very important
- Rx - lubricants, topical steroids, pimecrolimus and tacrolimus and phosphodiesterase 4 inhibitor



# IMPORTANT INFORMATION ABOUT TOPICAL CORTICOSTEROID THERAPY

- Potency- ointments > creams > lotions
- Limit use of high potency on face, breasts and genitals
- Skin side effects
  - Atrophy
  - Telangiectasia
  - Striae
  - Perioral dermatitis

# TOPICAL IMMUNE MODULATORS

- Tacrolimus (Protopic) ointment
- Pimecrolimus (Elidel) cream
  
- Derived from fungal polypeptides and Inhibit T-lymphocyte activation
- Potent immunosuppressive if given systemically
- Slow acting anti-inflammatory
- Great substitute for potent steroids on face
- Questionable risk of lymphoma with chronic use



# TOPICAL IMMUNE MODULATORS

(Tacrolimus (Protopic) ointment  
Pimecrolimus (Elidel) cream)

- Effective in childhood and adult AD
- No skin atrophy / steroid side effects
- Stinging and burning at initiation of therapy
- Slight increase in skin infections ?
- ? Risk of neoplasms?
- Long-term safety seems safe

20 year old male with isolated itchy rash below. WHAT IS THIS?



# The preferred test to exclude the diagnosis is?

- A. Patch testing
- B. Delayed hypersensitivity intradermal skin testing
- C. IgE mediated skin tests
- D. No testing is effective
  
- Answer:

# The preferred test to exclude the diagnosis is?

- A. Patch testing
- B. Delayed hypersensitivity intradermal skin testing
- C. IgE mediated skin tests
- D. No testing is effective
  
- Answer: A

# Allergic Contact Dermatitis

- Type 4 cell mediated reaction with T-helper-type 1- lymphocytes
- delayed 48 hours
- Rhus is the best example
- patch test for diagnosis
- nickel, rubber additives (not latex protein), thimerosal (eye gtt), benzocaine, neomycin, topical doxepin
- Rx - avoidance, topical steroids, or 2 weeks of oral steroids



L1-L2  
T12-L1  
L1-L2

48h

L1-L2  
T12-L1

L1-L2  
T12-L1

L1-L2  
T12-L1

L1-L2  
T12-L1

L1-L2  
T12-L1

L1-L2  
T12-L1

L1-L2  
T12-L1

L1-L2  
T12-L1



- For questions or concerns please contact me at 717-531-6525 or Email me at [tcraig@psu.edu](mailto:tcraig@psu.edu)
- Good luck with your boards!