Drug allergy and Skin Disorders

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<table>
<thead>
<tr>
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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
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• Answer: D
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
- B. Eosinophils
- C. Mast cells
- D. T helper cells

• Answer: B
Late Phase

T_H2 T Cell

Naïve CD4+ T Cells

IL-4

Antigen

APC

Allergen

Mast Cells

IL-5

Eosinophil

IL-13

Late Phase Mediators

Degranulate

Goblet cell hyperplasia

MMP-1 synthesis

Immediate Response Mediators
Immediate    Late phase

Figure 13-14 part 2 of 2 Immunobiology, 7th ed. (© Garland Science 2008)
Penicillin Skin Test for type 1 hypersensitivity

Penicillin allergy: 10% state they have penicillin allergy. 90% of these do not. 98% predictive valve 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

COMPLEMENT-DEPENDENT MECHANISM

Target cell + Ab + Complement

Formation of membrane attack complex which causes osmotic lysis of target cell

Opsonization and subsequent phagocytosis

C3b

C5-9

C3b
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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- What would you do at this admission?
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Common Causes: cephalosporins, penicillin, NSAID, quinine/quinidine. Only treatment is avoidance.
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Figure 13-1 Immunobiology, 7th ed. (© Garland Science 2008)
Type three hypersensitivity

1. Immune complexes are deposited in the wall of the blood vessel.
2. Presence of immune complexes activates complement and attracts inflammatory cells such as neutrophils.
3. Enzymes released from neutrophils cause damage to endothelial cells of the basement membrane.
TYPE III HYPERSENSITIVITY

- Symptoms caused by type III hypersensitivity reactions depend on the site of immune complex deposition.

- Serum sickness – intravenous immune complexes (horse antiserum against snake/spider venom)

- Arthus reaction – localized, skin
- Farmer’s lung – localized, lungs
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

- 22 year old given amoxicillin for a presumed sinusitis 4 days after developing sore throat, nasal congestion and cough.
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- The diagnosis is?
  - A. serum sickness *
  - B. Stevens-Johnson Syndrome
  - C. Type 4 hypersensitivity reaction
  - D. Anaphylaxis
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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<td><img src="image3" alt="Antibody alters signaling" /></td>
<td><img src="image4" alt="Complement, phagocytes" /></td>
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<td>Example of hypersensitivity reaction</td>
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<td>Chronic urticaria (antibody against FcεR1)</td>
<td>Serum sickness, Arthus reaction</td>
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<td></td>
<td>Contact dermatitis, tuberculin reaction</td>
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<td>IgE production, eosinophil activation, mastocytosis</td>
<td>Chronic asthma, chronic allergic rhinitis</td>
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Figure 13-1 Immunobiology, 7ed. (© Garland Science 2008)
Type IV Hypersensitivity

- **Delayed-type hypersensitivity** (e.g. tuberculin reaction, dermatitis) – $T_{\text{H}1}$ 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)

<table>
<thead>
<tr>
<th>Type</th>
<th>Type IVa</th>
<th>Type IVb</th>
<th>Type IVc</th>
<th>Type IVd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokines</td>
<td>IFNγ, TNFα (Th1 cells)</td>
<td>IL-5, IL-4/IL-13 (Th2 cells)</td>
<td>Perforin/granzyme B (CTL)</td>
<td>CXCL8, GM-CSF (T cells)</td>
</tr>
<tr>
<td>Antigen</td>
<td>Antigen presented by cells or direct T cell stimulation</td>
<td>Antigen presented by cells or direct T cell stimulation</td>
<td>Cell-associated antigen or direct T cell stimulation</td>
<td>Antigen presented by cells or direct T cell stimulation</td>
</tr>
<tr>
<td>Cells</td>
<td>Macrophage activation</td>
<td>Eosinophils</td>
<td>T cells</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>Pathomechanism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IFNγ</td>
<td>IL-4, IL-5, Eotaxin</td>
<td>IL-12</td>
<td>CXCL8, GM-CSF, PMN</td>
</tr>
<tr>
<td></td>
<td>Th1</td>
<td>Il-2, Eosinophil</td>
<td>CTL</td>
<td></td>
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<tr>
<td>Example</td>
<td>Tuberculin reaction, contact dermatitis (with IVc)</td>
<td>Chronic asthma, chronic allergic rhinitis Maculopapular exanthema with eosinophilia</td>
<td>Contact dermatitis Maculopapular and bullous exanthema hepatitis</td>
<td>AGEP Behcet disease</td>
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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

Also includes:
- IV-a- contact dermatitis, TB skin testing
- IV-b- asthma, rhinitis, nasal polyps, 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 this rash should be treated with:

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

Ans:
Your patient with the this rash should be treated with?

- A. topical antibiotics
- B. topical corticosteroids
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• 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_4, IL_5, GM-CSF, IL_{13}, (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
For questions or concerns please contact me at 717-531-6525 or Email me at tcraig@psu.edu

Good luck with your boards!