New Developments in Food Allergies, Prevention & Treatment

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Disclosures

- I have nothing to disclose relative to this presentation
- I will mention off-label use of medications and treatments that are in clinical trials but not approved for use
- I will try not to use any branded names when discussing treatments

Knowing how to edit

Chapter 1. The Boy Who Lived.

Mr. and Mrs. Dursley, of number four, Privet Drive, were proud to say that they were perfectly normal, thank you very much. They were the last people you'd expect to be involved in anything strange or mysterious, because they just didn't hold with such nonsense…

1,084,170 total words for all the HP books

Minimalism

- Snape kills Dumbledore
- Voldemort dies

What should we talk about?

- Overview of food allergies
- Immune mechanisms of food allergies
- Diagnostic testing for food allergies
- Current treatment options for food allergies
- New developments in prevention and treatment

Anaphylaxis:

Killer Allergy

MR. PEA
PLANTERS
PLANTERS
Mr. Peanut's
HOTROD

Miller
Lite
PINT

Food Allergy Basics

- A food allergy is an abnormal response by the immune system to a food protein
- When the food is eaten, the immune system releases histamine and other chemicals to “attack” the food
- This inappropriate immune response can lead to systemic reactions including death

Adverse reactions to foods

Allergy (hypersensitivity)

- Reactions to food proteins
- Classically IgE mediated
- Occasional non-IgE mediated

Intolerance

–non-immune
–toxic
–pharmacological
–metabolic
–psychogenic

Food allergy statistics

- 8% of children experience food intolerances. 2 to 4% appear to have allergic reactions to food.
- More than 150 people die annually from anaphylaxis to food.

Food Allergy Basics

Eight foods cause 90% of the allergic reactions in the United States:

Milk	Wheat
Eggs	Soy
Peanuts	Fish
Tree Nuts	Shellfish

Food Allergy Basics

- Foods that cause the majority of severe or anaphylactic reactions:
  - Peanuts
  - Tree Nuts
  - Fish
  - Shellfish

Prevalence of Food Allergies in the U.S.

Food	Young Children	Adults
Milk	2.5%	0.3%
Egg	1.3%	0.2%
Peanut	0.8%	0.6%
Tree nuts	0.2%	0.5%
Fish	0.1%	0.4%
Shellfish	0.1%	2.0%
Overall	**6%**	**4%**

Sampson, 2004

Natural history

- Egg
  - 60-80% of infants with egg allergy are tolerant of egg by 5 years of age
  - High risk for development of asthma later in life
- Milk, Soy
  - Enterocolitis
    - Vast majority become tolerant within 2 years
  - IgE mediated
    - **Host A. 1994**: Prospective study of milk hypersensitivity in children infancy through 3years:
    - Outgrown:
      - 50% by age 1 year
      - 70% by age 2 years
      - 85% by age 3 years
    - 3-4 fold increase risk of developing asthma or eczema
    - Allergen avoidance appears to hasten development of tolerance

Natural History of Peanut Allergy

- **Resolvers (~20%)**
  - Milder initial reaction
  - Initial reaction < 5 years
  - less allergic to other foods
  - <6mm wheal on SPT
  - much less likely to have asthma or other nut allergy

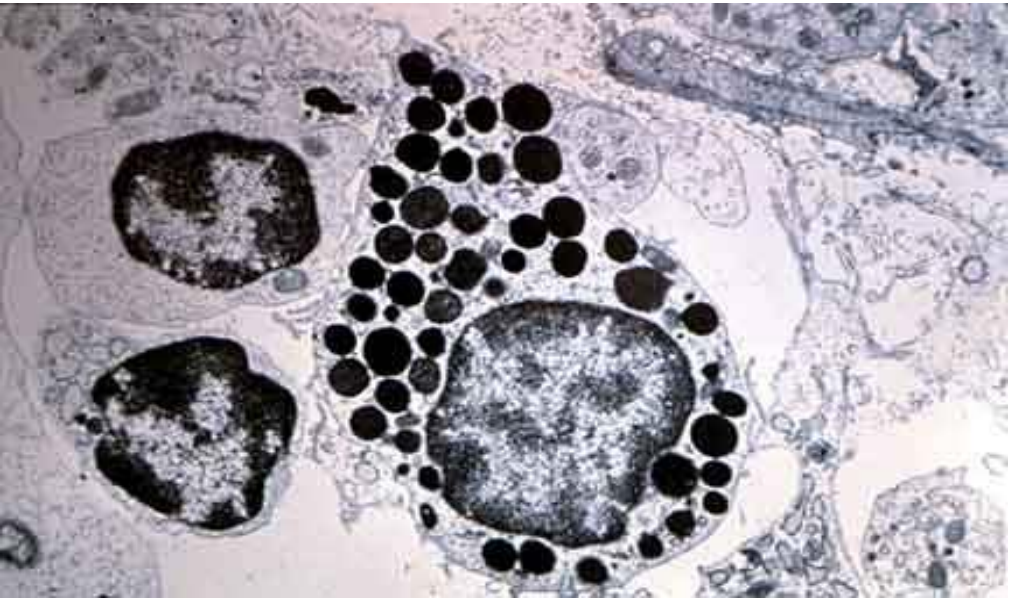
- *SPT predicted reactivity but not severity*

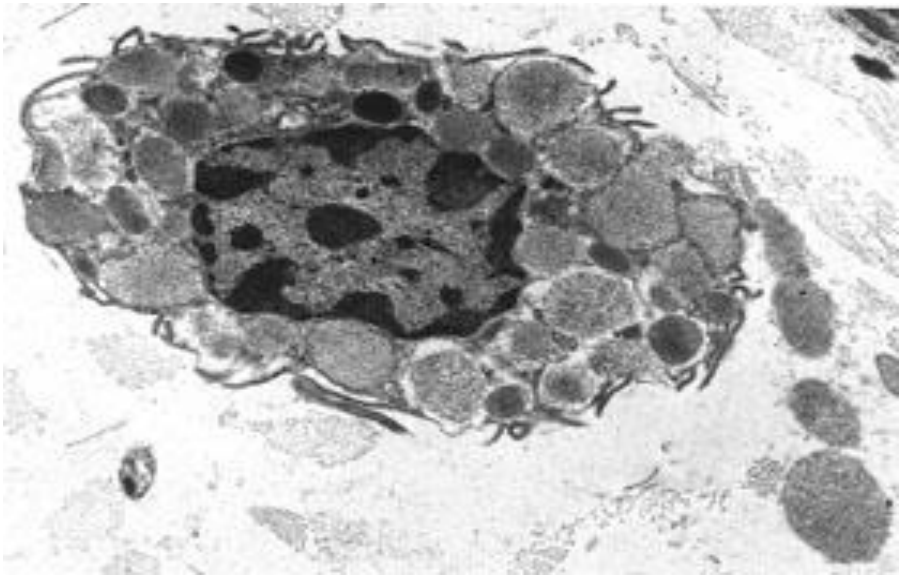
Methods for detecting IgE mediated disease processes

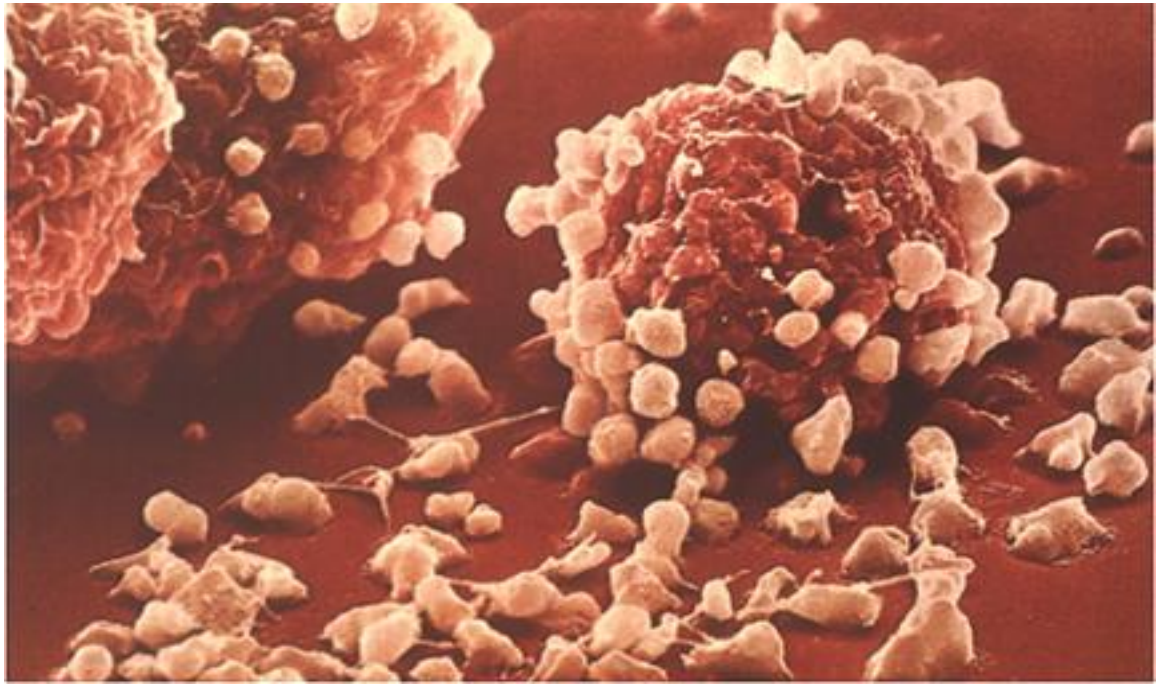
- PK reaction
- RAST testing
- Skinprick testing
- Intradermal skin testing

TABLE 1
Levels of Specific IgE-Yielding Predictive Values (kU_A/L) for CAP-RAST Tests[19]

Food	95% Positive Predictive Value	95% Negative Predictive Value
Milk	32	0.8
Egg	6	90% at 0.6
Peanut	15	85% at <0.35
Soy	50% at 65	2
Wheat	75% at >100	5
Fish	20	0.9







Class of product	Examples	Biological effects
Enzyme	Tryptase, chymase, cathepsin G, carboxypeptidase	Remodel connective tissue matrix
Toxic mediator	Histamine, heparin	Toxic to parasites Increase vascular permeability Cause smooth muscle contraction
Cytokine	IL-4, IL-13	Stimulate and amplify T_H2 cell response
	IL-3, IL-5, GM-CSF	Promote eosinophil production and activation
	TNF-α (some stored preformed in granules)	Promotes inflammation, stimulates cytokine production by many cell types, activates endothelium
Chemokine	CCL3 (MIP-1α)	Attracts monocytes, macrophages, and neutrophils
Lipid mediator	Leukotrienes C4, D4, E4	Cause smooth muscle contraction Increase vascular permeability Stimulate mucus secretion
	Platelet-activating factor	Attracts leukocytes Amplifies production of lipid mediators Activates neutrophils, eosinophils, and platelets

Figure 12-12 Immunobiology, 6/e. (© Garland Science 2005)

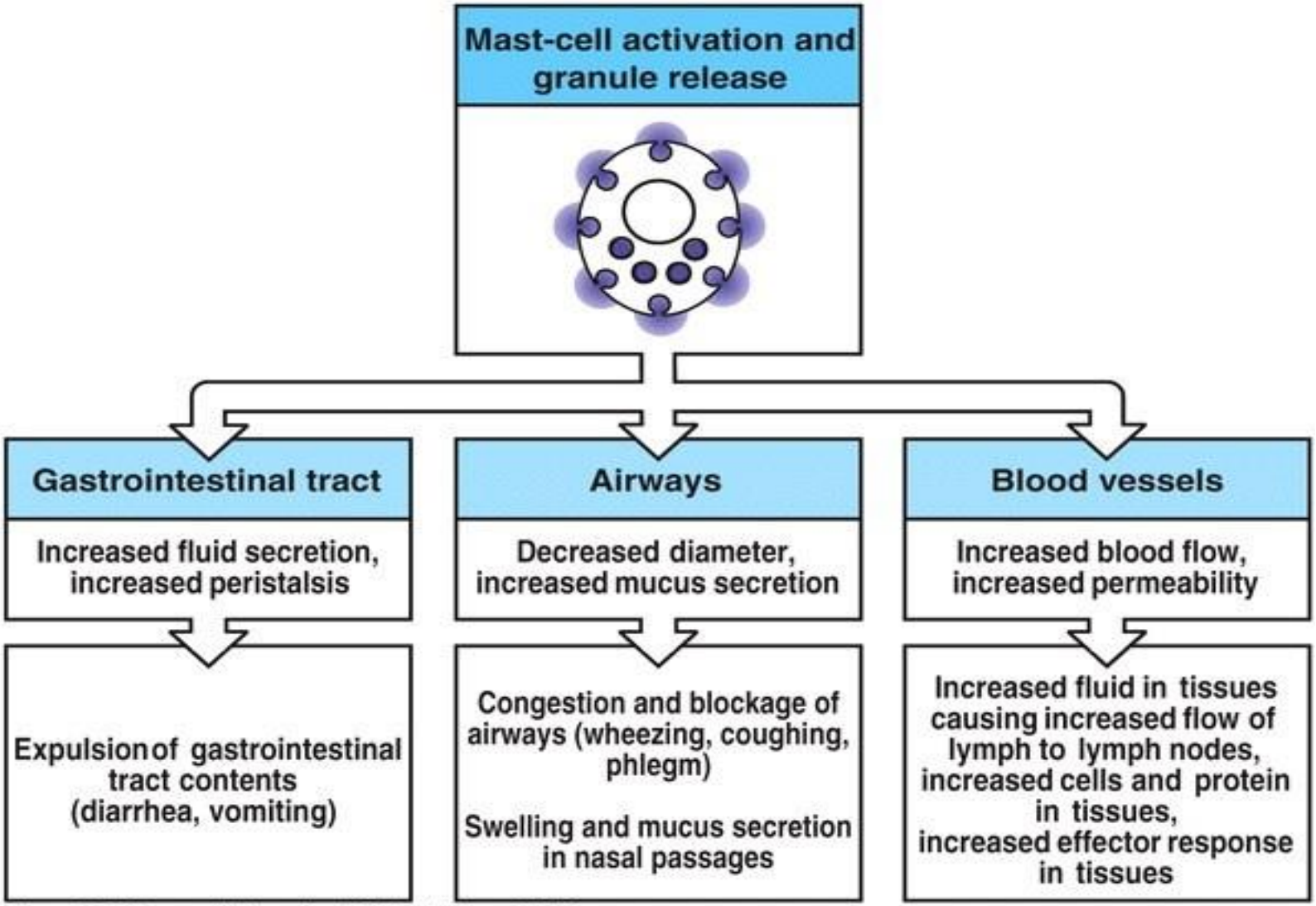
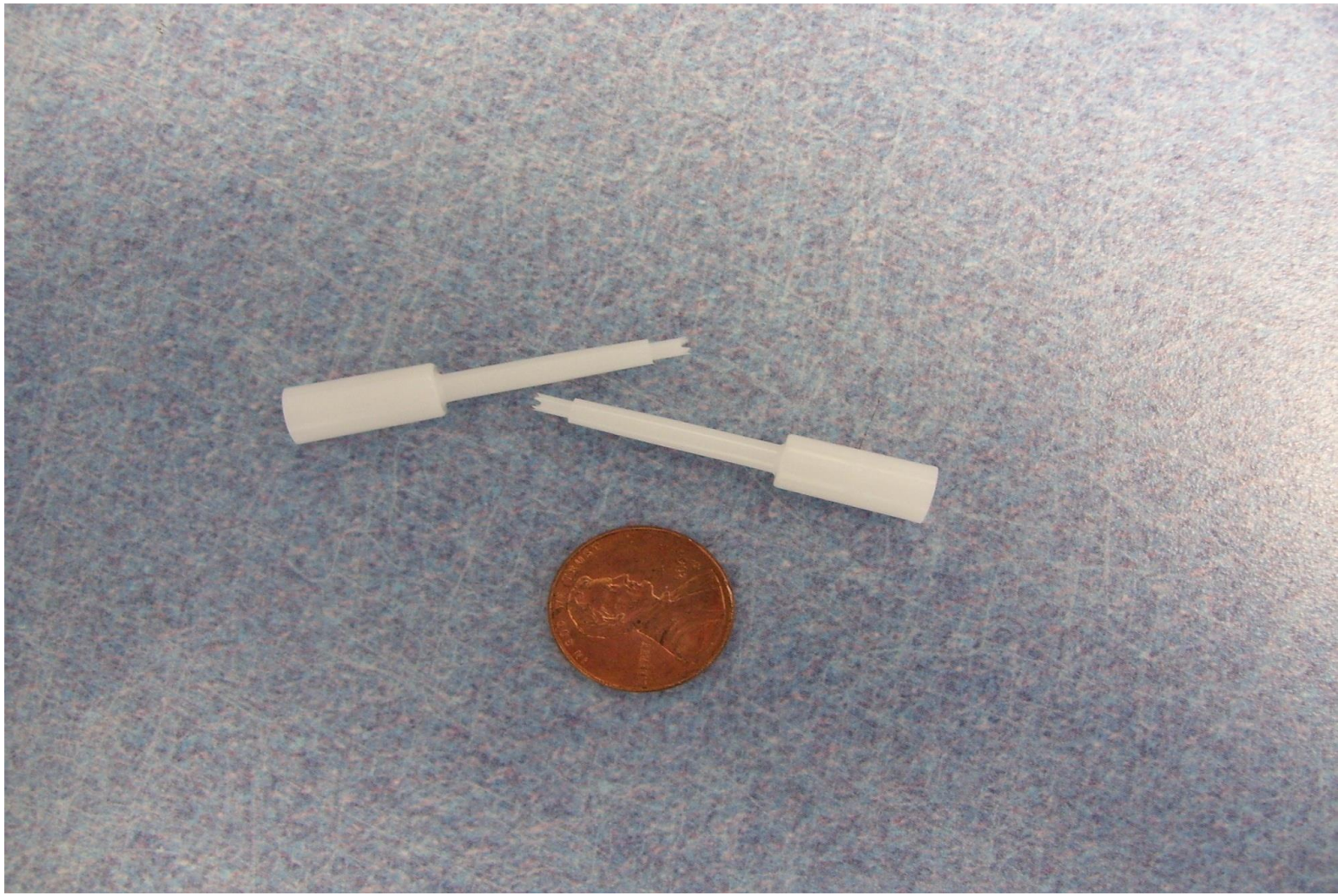


Figure 12-11 Immunobiology, 6/e. (© Garland Science 2005)



Four Types of Hypersensitivities

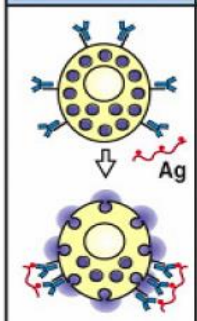
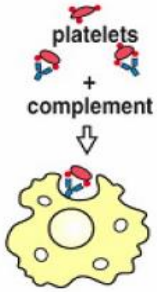
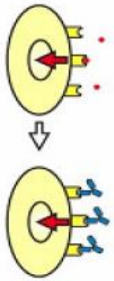
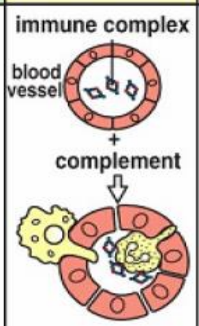
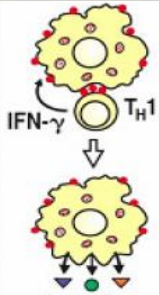
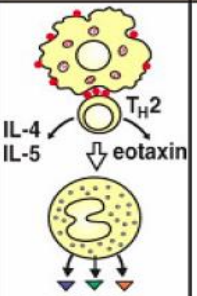
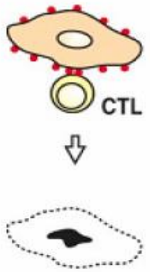
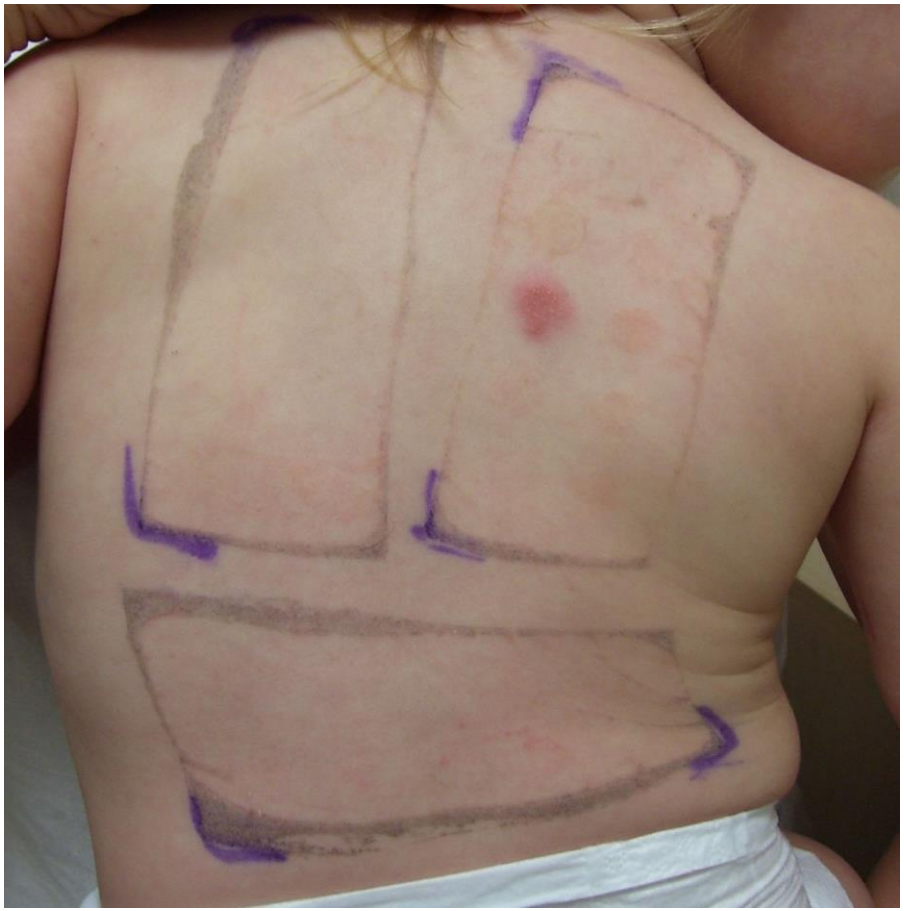
	Type I	Type II		Type III	Type IV		
Immune reactant	IgE	IgG		IgG	T_H1 cells	T_H2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcR^+ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, Phagocytes	Macrophage activation	IgE production, Eosinophil activation, Mastocytosis	Cytotoxicity
							
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Some drug allergies (eg, penicillin)	Chronic urticaria (antibody against FCεR1α)	Serum sickness, Arthus reaction	Contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Contact dermatitis

Figure 12-2 Immunobiology, 6/e. (© Garland Science 2005)

Finn Chamber Tray
Epitest Ltd Oy
LOT



Treatment: avoidance

- Peanuts won't jump out and get you
- Washing and wiping techniques effective to eliminate residual peanut
- Education of patient and parents
  - Reading labels, avoiding high risk situations
    - Hidden ingredients (eg peanuts in sauces and eggrolls)
    - Cross contamination
    - Buffets, peanut butter in home
    - School management plans
  - Early recognition of allergic symptoms
  - Early management of a severe reaction

WARNING:
May contain
traces of top
cane, monocle,
and spats.

What does it mean to have a Food Allergy?

- Strict avoidance of that food
- Constant vigilance
- Just one little bite can hurt!

Food Allergy Basics

- Symptoms may occur within minutes to two hours after ingestion
- Almost any food can cause a reaction
- There is no cure for food allergy-yet
- Complete and strict avoidance is the only way to prevent a reaction

Symptoms of a Mild Food-Allergic Reaction

Respiratory tract:

- Itchy, watery eyes, running or stuffy nose, sneezing, cough, itching or swelling of the lips, wheezing

GI tract:

- abdominal cramps, nausea, vomiting, diarrhea

Skin:

- hives, eczema, itchy red rash, swelling

Symptoms sometimes progress rapidly to severe reactions

Symptoms of a Severe Food-Allergic Reaction

Respiratory

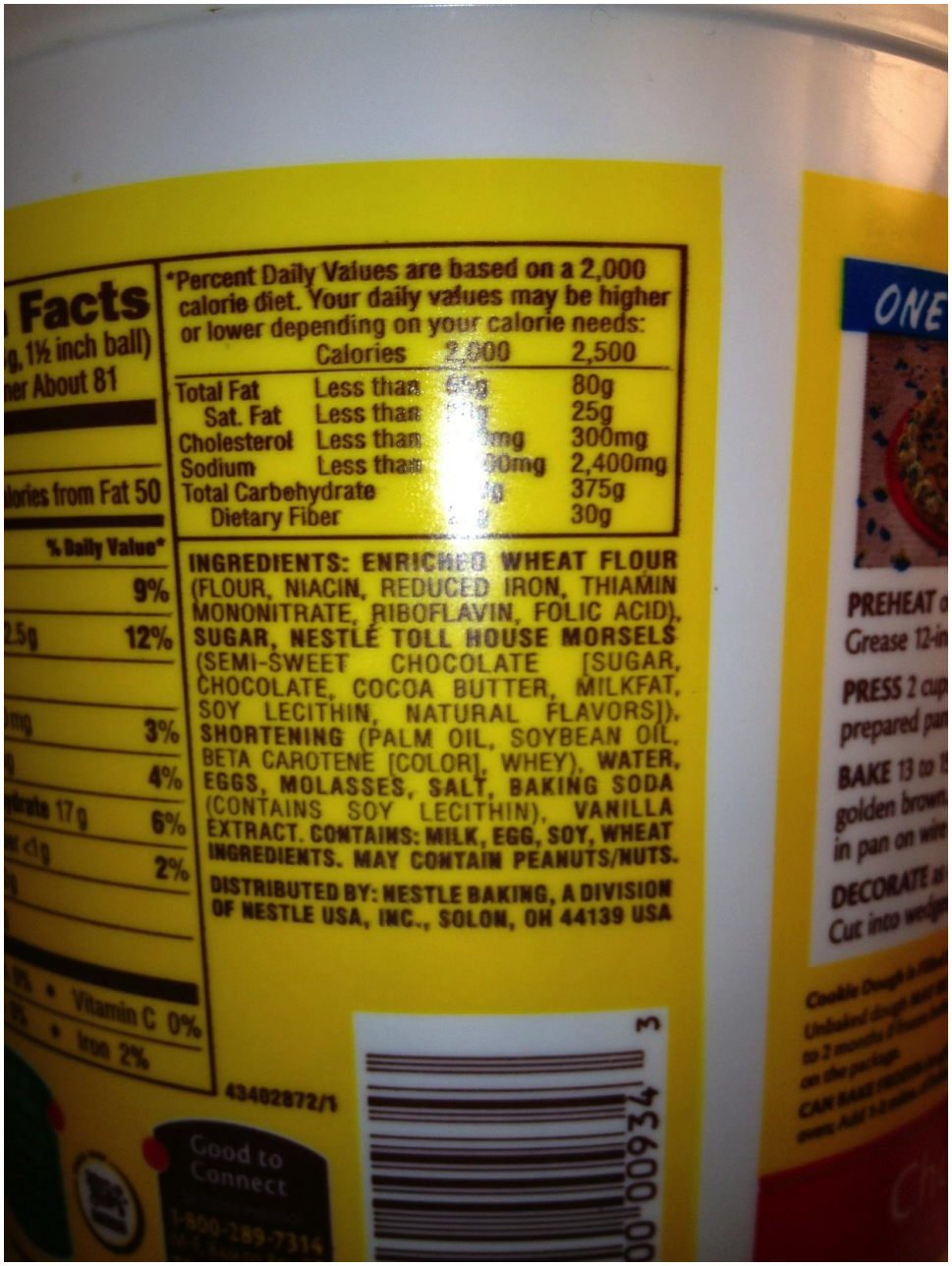
- shortness of breath, difficulty swallowing, chest tightness, tingling of the mouth, itching or swelling of the mouth or throat, change in voice

Cardiovascular

- Drop in blood pressure, loss of consciousness/fainting, shock

Causes of Accidental Exposures

- Not reading ingredient label to be sure food is allergen-free
- Food trading
- Inaccurate labeling
- Contamination from other foods from improperly cleaned utensils and table surfaces


Facts
g, 1½ inch ball)
ner About 81
lories from Fat 50
% Daily Value*
9%
2.5g 12%
mg 3%
4%
ydrate 17 g 6%
er <1 g 2%
Vitamin C 0%
Iron 2%
*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:
Calories 2,000 2,500
Total Fat Less than 80g
Sat. Fat Less than 25g
Cholesterol Less than mg 300mg
Sodium Less than 0mg 2,400mg
Total Carbohydrate 375g
Dietary Fiber 30g
INGREDIENTS: ENRICHED WHEAT FLOUR (FLOUR, NIACIN, REDUCED IRON, THIAMIN MONONITRATE, RIBOFLAVIN, FOLIC ACID), SUGAR, NESTLÉ TOLL HOUSE MORSELS (SEMI-SWEET CHOCOLATE [SUGAR, CHOCOLATE, COCOA BUTTER, MILKFAT, SOY LECITHIN, NATURAL FLAVORS]), SHORTENING (PALM OIL, SOYBEAN OIL, BETA CAROTENE [COLOR], WHEY), WATER, EGGS, MOLASSES, SALT, BAKING SODA (CONTAINS SOY LECITHIN), VANILLA EXTRACT. CONTAINS: MILK, EGG, SOY, WHEAT INGREDIENTS. MAY CONTAIN PEANUTS/NUTS.
DISTRIBUTED BY: NESTLE BAKING, A DIVISION OF NESTLE USA, INC., SOLON, OH 44139 USA
43402872/1
Good to Connect
1-800-289-7314
ONE
PREHEAT
Grease 12-in
PRESS 2 cup
prepared pan
BAKE 13 to 1
golden brown
in pan on wire
DECORATE
Cut into wedge

Treatment: Epinephrine

- Jr (.15mg) and regular (.3mg)
  - <30 kg: Jr
  - >30 kg: regular
- for anyone with a reaction to peanuts, nuts, seafood, seeds
- anyone with a serious reaction to milk, egg, kiwi, banana, carrot ect...
- Delayed use associated with poor outcomes
- Useless without training

Treatment: Acute

- Antihistamines
  - Oral allergy syndrome
  - Skin manifestations
  - *No systemic effects*
- Epinephrine (IM)
- Short acting bronchodilators
- Systemic corticosteroids
  - May protect against protracted or late phase anaphylaxis (biphasic)
- IV fluids, respiratory support, inotropic agents, H2 blockers
- Observe in ER for 6 hours

There is no way to know how serious a reaction will become, so it is important to treat all reactions quickly.

Food Allergy Facts

- The same food can cause different symptoms from one child to another
- Not all children have severe reactions to a food
- Some mild reactions may become severe
- A food allergy management plan is needed for all students with a food allergy, and may include the need for an epinephrine autoinjecter

Food allergy plan for schools

- Discuss “allowed” foods with the parents and child
- Form a food allergy awareness team
- Allow the allergic student to provide his/her own snacks and foods
- Allow only commercially-prepared food with a preprinted ingredient statement
- Medical alert bracelet, epinephrine injecter available

How to manage in school/daycare

- Wipe all surfaces thoroughly between uses
- Have designated “peanut free” table or section in the cafeteria where any student with a peanut free lunch is able to sit
- Implement a “No food trading” rule

What can schools contribute?

- Use books, music and other non-food items for celebrations
- Have parents provide stickers or other trinkets for goody bags instead of candy
- Use stickers to reward good behavior
- Eliminate food items in class lesson plans
- Review arts and crafts projects and avoid using common allergens

Food additives and behavior, GM foods,

- **Feingold, 1970's**
  - attributed 50% of hyperactivity and impulsive, disruptive destructive behavior to food additives
  - subsequently, a number of DBPC studies were conducted that refuted these reports
  - food additives NOT considered to play a role in cognitive/behavioral alterations

- **Sugar**
  - controlled trials have failed to demonstrate any significant change in children's behavior or cognitive function attributable to ingestion of sugar, or aspartame (Wolraich, NEJM, 1994; Mahan, Ann Allergy,1988)

- **Genetically modified foods**
  - Lots of people are allergic to foods
  - Very very very few are allergic to transgenes in GM foods

Current guidelines

- Expose children to a broad range of foods during the magic window of tolerance
- Consider evaluating for nut allergy in very high risk kids before introducing
- If there are symptoms of an IgE reaction to a specific food, test for an allergy to that food
- If allergic to a food, avoid that food and keep an epinephrine injector available in case of accidental exposures

Future things

- None of these are FDA approved
- I would not recommend that they be done outside of a clinical trial
- Most of these have been studied in peanuts, milk, and eggs
- Similar approaches may work with other allergens but have not been studied

Future things

- Allergy shots for foods (SCIT)
- Oral Desensitization (OIT)
- Sublingual Desensitization (SLIT)
- Epicutaneous Desensitization
- Biological treatments (monoclonal antibodies blocking specific targets in food allergy responses)

Allergy Shots (SCIT)

- Works really well for environmental allergies, asthma
- Probably can desensitize some food allergies
  - BUT!
- Severe systemic reactions, life threatening reactions, and a death in clinical trials

Oral Desensitization (OIT)

- Controlled exposure via GI tract is a relatively safe procedure because of GI tolerance
- Patients undergoing OIT ingest a mixture of protein powder in a vehicle food such as apple sauce
- Treatments are initiated in a controlled setting where gradually increasing doses of allergen are given, up to a targeted dose.
- Follow up dosing is done at home.

OIT

- Data can be hard to interpret
  - Many studies eliminate severely allergic subjects
  - Spontaneous remission of food allergies in kids
- Side effects occurred in 45% of daily food allergen doses compared to only 11% of placebos
- 10% of all OIT doses required treatment (1% in placebo)with an antihistamine
- 0.2% (4 allergen doses) required epinephrine (0 in placebo group)
- 10-15% stop therapy due to abdominal complaints
- New onset EoE in about 3 percent
- Success rates vary with different studies between 21 and 93 percent

Sublingual Immune Therapy (SLIT)

- Patients undergoing SLIT generally put a small amount of liquid extract under their tongue
- Smaller amounts of allergen used
- No digestion of allergenic proteins
- Probably less reactions to treatment, but less robust desensitization

Epicutaneous desensitization

- A ‘band-aid’ solution
- Small adhesive strip with a chamber containing food protein
- Food proteins released epicutaneously in a gradual, controlled manner
- Induces tolerance and increases amount of allergen exposure needed for allergic reaction

Biologicals

- Similar immune pathways involved in food allergies, asthma, etc
- Omalizumab significantly increases the exposure threshold for a food allergen to cause an allergic reaction
- Other biologicals have not been directly studied but may have some benefits

Modifying food allergens

- Genetic manipulation of allergenic foods to either eliminate the most common food allergen or alter it to reduce its allergenic effects
- Altering how foods are prepared
  - More soluble=less allergenic

Conclusions