

# Drug allergy

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# Adverse drug reaction

- Adverse drug reactions are classified as predictable or unpredictable.
- A predictable drug reaction is related to the pharmacological actions of the drug.
- An unpredictable reactions are related to immunological response ( hypersensitivity reactions )

# Definition of drug allergy

- A specific immune response either directly to the drug or its metabolites, or to a drug bound to a body protein such as albumin.
- Such binding alters the structure of the drug/protein complex, rendering it antigenic.

# Distinctive features of allergic drug reactions

- No linear relationship with drug dosage
- Include a rash, angioedema, or anaphylaxis.
- Occur in a minority of people receiving the drug

# Distinctive features of allergic drug reactions

- Require an induction period on primary exposure but not on readministration
- Disappear on cessation of therapy and reappear after readministration of a small dose

# Classification of hypersensitivity

- The criteria of the classification

- 1) Time -- immediate and delayed hypersensitivity.

- 2) The nature of organ involvement.

- Fewer than 10 percent of adverse drug reactions are allergic.

# Types of hypersensitivity reactions caused by drugs

Type I	Immediate, IgE-mediated	Anaphylaxis, urticaria angioedema, bronchospasm, hypotension
Type II	IgG and IgM-dependent complement-mediated cytolysis	Leukopenia, vasculitis, rashes, interstitial nephritis

# Types of hypersensitivity reactions caused by drugs

Type III	Immune complexes with IgG and IgM	Serum sickness, vasculitis, rashes, fever
Type IV	T cell-mediated reactions	Contact sensitivity, delayed rashes



# The most common drug to cause allergy

- Analgesics such as nonsteroidal anti-inflammatory drugs
- Antibiotics such as penicillin, sulfa drugs, and tetracycline

# Risk factors for drug allergy

- Frequent exposure to the drug
- Drug given by injection rather than oral
- Family tendency to develop allergies like asthma.

# Most common allergic reactions

- Rash
- Fever
- Muscle and joint aches
- Lymph node swelling
- Inflammation of the kidney
- Anaphylactic shock

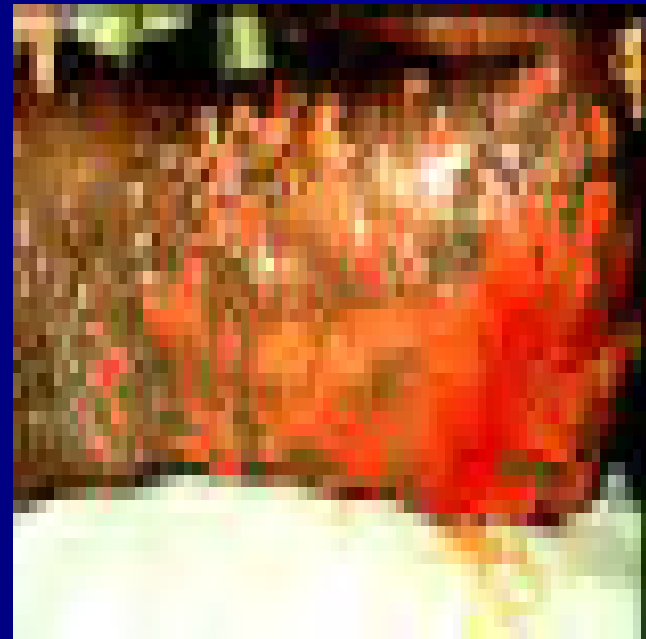
# Allergic reactions on skin

- Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)
- A manifestation of acute graft versus host disease
- Drugs with longer half-lives are more likely to pose a risk for SJS and TEN

# Stevens Johnson syndrome



# Toxic epidermal necrosis



# Toxic epidermal necrosis



# SJS & TEN

- SJS & TEN develop 1-3 weeks after the culprit medication is initiated
- Sulphonamides, antibiotics, NSAIDs, anticonvulsant and antiretroviral agents are the most common causative medications.
- Medications with longer half-lives are more likely than those with shorter half-lives to pose a risk for SJS and TEN



# Signs and Symptoms of SJS & TEN

SJS	TEN
Mucosal erosions	Mucosal erosions
Asymmetric skin involvement with blisters	Flaccid blisters and denuded skin
<10% total body surface area affected	> 30% total body surface area affected

# Signs and Symptoms of SJS & TEN

- Fluid and electrolyte imbalance
- Compromised cutaneous integrity promotes bacterial colonization and infection of the skin with the risk for sepsis.
- Debilitated, bedridden patients are susceptible to aspiration pneumonia, deep vein thrombosis and pulmonary embolism

# Guideline for Treatment of SJS & TEN

- Admit to intensive care or burn unit
- Discontinue culprit medication and all unnecessary medications
- Sterile technique in handling patient; reverse-isolation nursing techniques
- Place intravenous or central line in area of uninvolved skin if possible

# Anaphylactic reaction

- Life threatening
- Almost all anaphylactic reactions occur within 4 hours of the first dose. Most occur within 1 hour of taking the drug, and many occur within minutes or even seconds.

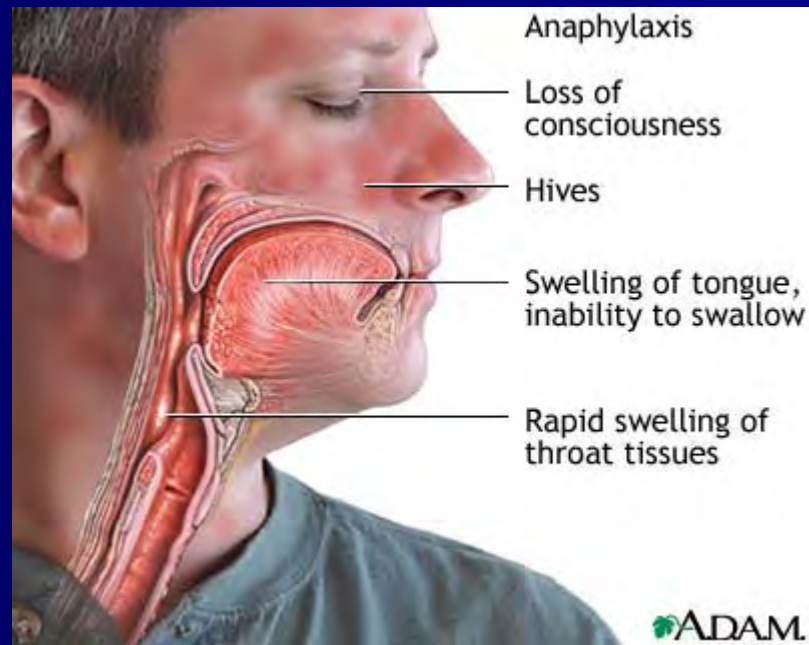
# Symptoms of anaphylactic shock

- Skin reaction - Hives, redness/flushing, sense of warmth, itching
- Difficulty breathing - Chest tightness, wheezing, throat tightness
- Fainting - Light-headedness or loss of consciousness due to drastic decrease in blood pressure ("shock")
- Rapid or irregular heart beat
- Swelling of face, tongue, lips, throat, joints, hands, or feet

# The causative antigens causing anaphylaxis

- Blood products
- $\beta$ -lactam antibiotics
- X-ray contrast agent
- Other drugs

# Anaphylaxis



# Treatment for anaphylaxis

- Immediate treatment with adrenaline is imperative
- Adrenaline is an antagonist to the effects of the chemical mediators on smooth muscle, blood vessels and other tissues.
- Treatment is based on the severity of the reactions



# Examples of Drug allergy

# Penicillin allergy

- Symptoms

Fever

Rash

Urticaria

Angioedema

Nephritis

Lymphadenopathy

Arthralgias

# Rash



# Urticaria

- It is local wheals and erythema in the superficial dermis
- Urticaria induced by drug is generally acute and is limited to the skin and subcutaneous tissues.

# Urticaria

## Signs and symptoms

- Pruritus (generally the first symptom)
- Crops of hives
- Lesion (if lesion persists more than 24 hours, the possibility of vasculitis should be considered)

# Urticaria



# Angioedema

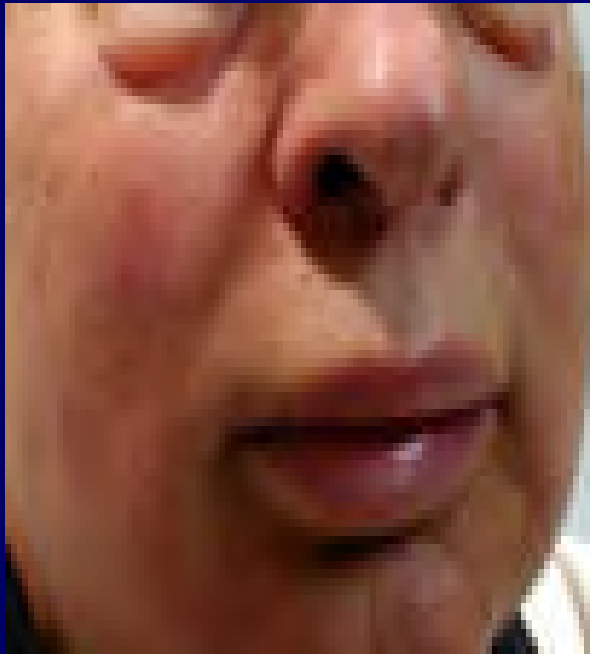
- It is a deeper swelling due to edematous areas in the deep dermis and subcutaneous tissue and may also involve mucous membranes.

# Signs & Symptoms of Angioedema

- Diffuse and painful swelling of loose subcutaneous tissue, dorsum of hands or feet, eyelids, lips, genitalia and mucous membranes.
- Edema of the upper airways may produce respiratory distress



# angioedema



# Mechanism of Penicillin allergy

- Only proteins and large polypeptide drugs can stimulate specific antibody production by straightforward immunologic mechanisms.
- The drug, or one of its metabolites must be chemically reactive with protein can act as haptens and bond covalently to proteins.

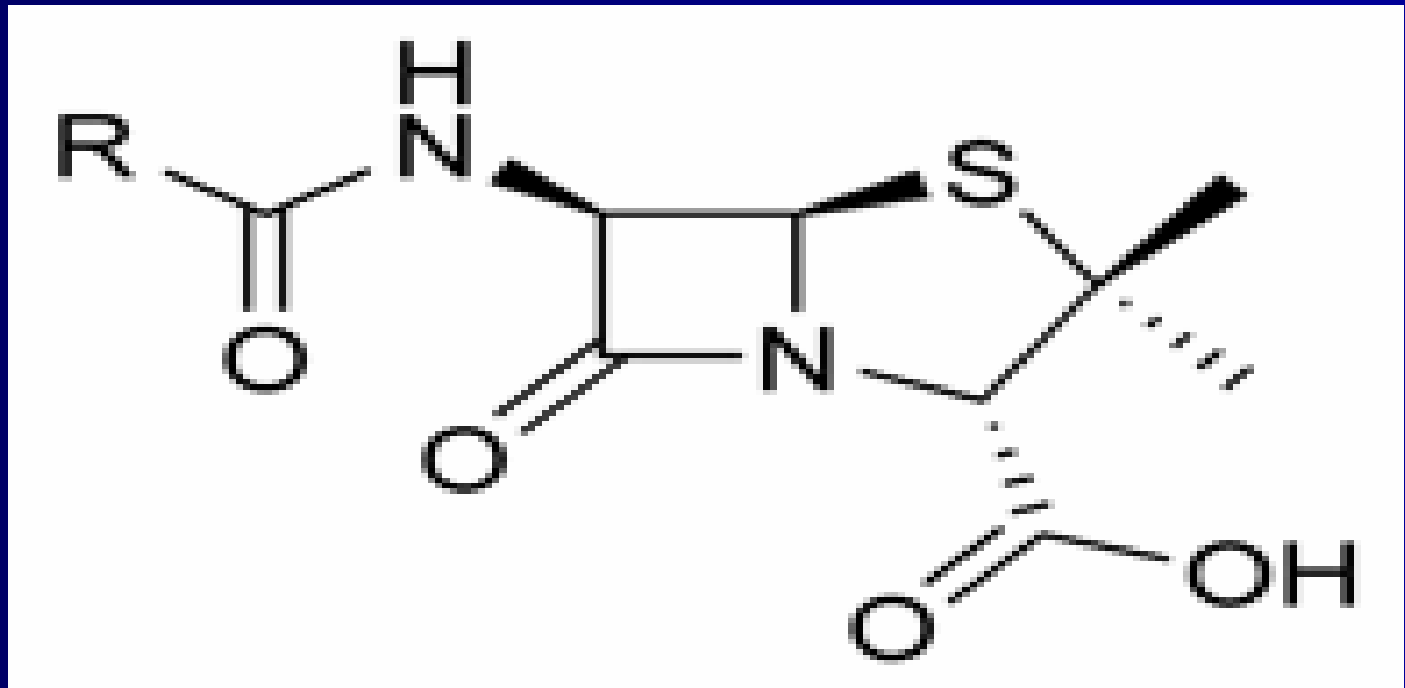
# Mechanism of Penicillin allergy

- The breakdown products can bond to  $\epsilon$ -amino groups of lysine residues, most importantly globulins.
- This binding leads to a spectrum of potentially immunologically active moieties on serum proteins that can cross-link with a variety of preformed anti-penicillin IgE bond to mast cells.

# Cross-reactivity

- The most important part of penicillin antigen appears to be the core structure
- The structure of the penicillin is a  $\beta$ -lactam ring with the five-membered thiazolidine ring

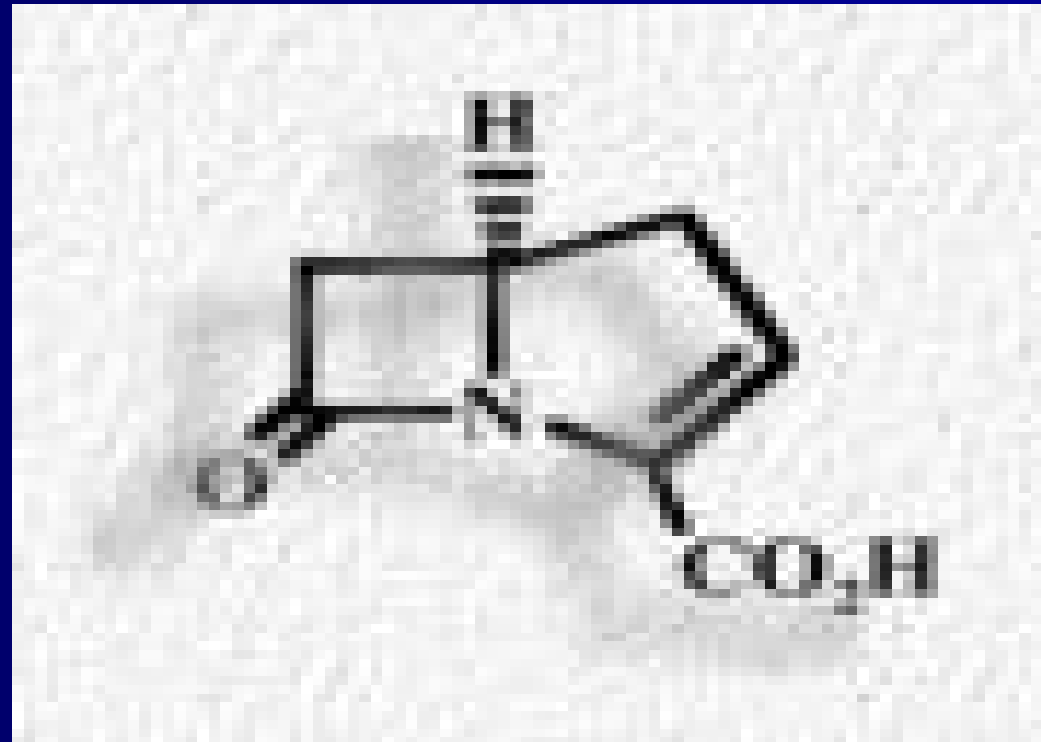
# The structure of penicillin



# Cross-reactivity

- Carbapenems have a bicyclic nucleus containing  $\beta$ -lactam ring and an adjacent five-membered ring.
- It showed 50% cross-reactivity in allergy skin testing
- Patients with positive penicillin skin test should withhold carbapenems

# The structure of carbapenem

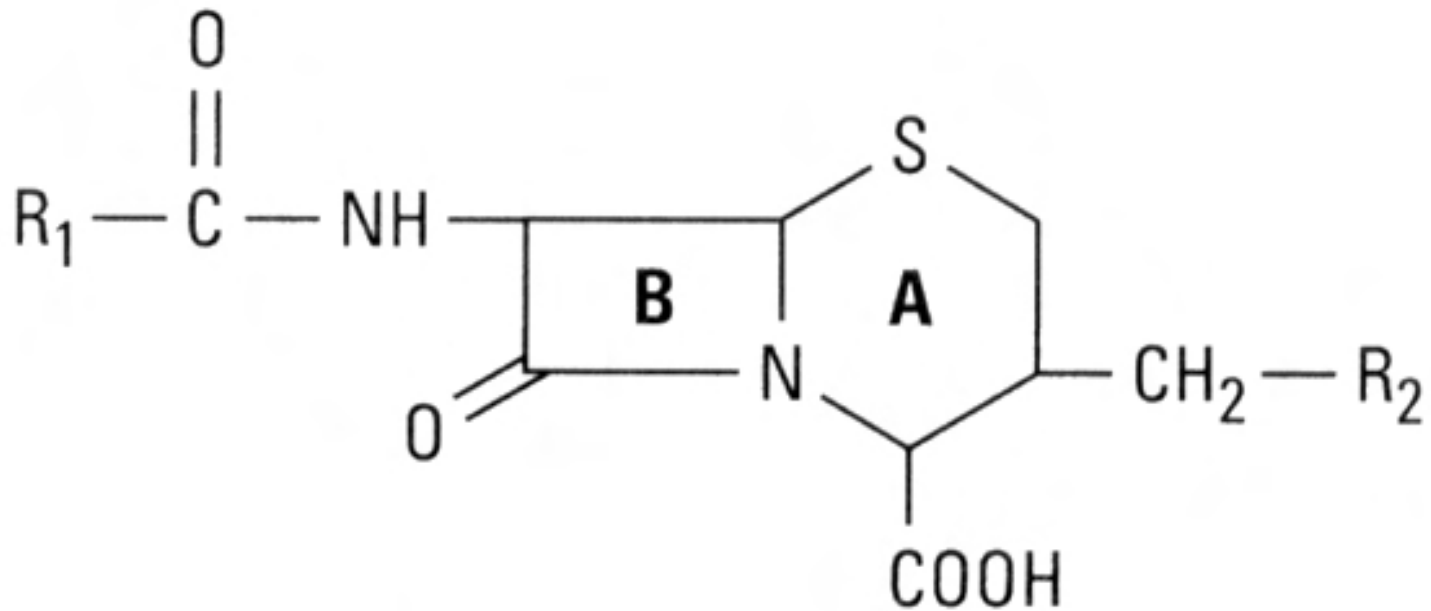


# Cross-reactivity

- The structure of cephalosporin contains a  $\beta$ -lactam ring with a six-membered dihydrothiazine ring.
- Cephalosporin had a cross reaction rate of 10%-20%



# The structure of cephalosporins



# Prophylaxis of penicillin allergy

- Skin test

Skin tests for immediate-type (IgE-mediated) hypersensitivity are very useful in diagnosis of reactions to penicillin, enzymes, and some vaccines.

# Prophylaxis of penicillin allergy

- Skin test

Performed in patients

With a history of penicillin allergy

$\beta$ -lactam antibiotic is indicated drug of choice.

# When will desensitization perform?

- When penicillin is the drug of choice.
- The alternate drugs fail, induce unacceptable side effects or are less effective.
- When anaphylaxis of the penicillin present

# Contraindication of desensitization

- Patients with a history of Stevens-Johnson syndrome and toxic epidermal necrolysis.

# The protocol of desensitization

## Oral desensitization protocol for patients with a positive skin test for penicillin

*(NEJM, 312:1229, 1985)*

Penicillin V suspension - dose increments every 15 minutes

dose#	units/ml	ml	units	cumulative dose
1	1,000	0.1	100	100
2	1,000	0.2	200	300
3	1,000	0.4	400	700
4	1,000	0.8	800	1,500
5	1,000	1.6	1,600	3,100
6	1,000	3.2	3,200	6,300
7	1,000	6.4	6,400	12,700
8	10,000	1.2	12,000	24,700
9	10,000	2.4	24,000	48,700
10	10,000	4.8	48,000	96,700
11	80,000	1.0	80,000	176,700
12	80,000	2.0	160,000	336,700
13	80,000	4.0	320,000	656,700
13	80,000	8.0	640,000	1,296,700

Desensitization completed after 4 hours - start therapy

# Allergic reactions to vaccines

- Sensitivity reactions can occur when egg-allergic patients are vaccinated with vaccines containing egg protein.
- Severe anaphylactic reactions to influenza vaccination have been reported to occur at a rate of 0.024 per 100,000 vaccinations

# Sign of serious allergic reaction

- Difficulty breathing
- Hoarseness or wheezing
- Hives
- Paleness
- Fast heart beat
- Dizziness



# Conclusion

- As drug allergy can pose risk to patients' health,
- Healthcare professions should...
- Be aware of patients' drug allergy history
- Record such information properly
- Double check patients' drug allergy history before drug administration

**Thank you!**