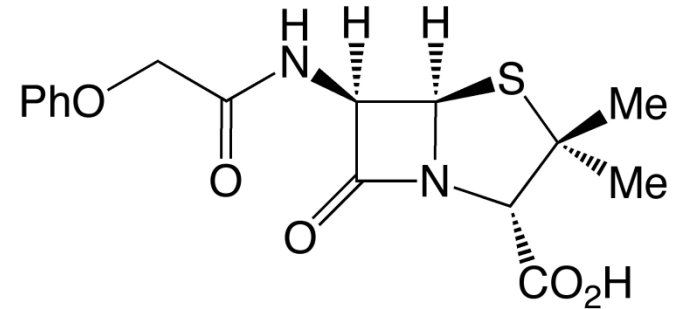


Update: Drug Allergy

CAOM Winter Conference
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UH Regional Hospitals

Outline

- History
- Introduction
- Epidemiology
- Burden of Drug Allergy
- Diagnosis
- Prognosis
- Management
- Summary



Penicillin V (1)

History...



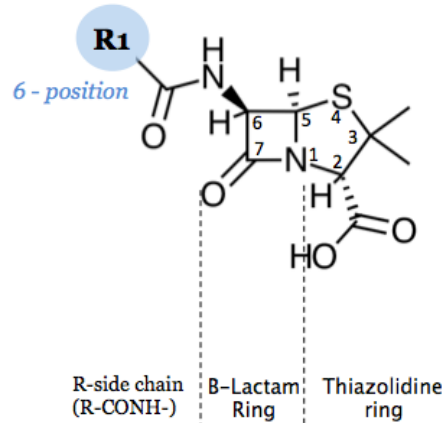
- **Alexander Fleming** discovered **penicillin**:
 - “When I woke up just after dawn on September 28, **1928**, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic... But I suppose that was exactly what I did.”
- Saved millions of lives since it came into use during WWII
- **Allergic reactions** to penicillin were described soon after its debut; today it remains the most commonly self-reported medication allergy, with a prevalence of **~10%**

Introduction to Adverse Drug Reactions

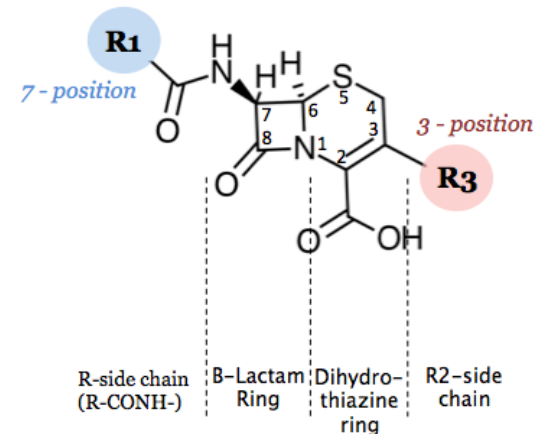
- Adverse drug reactions:

- Type A (85-90%):
Predictable, from known drug properties (i.e. side effects)
- Type B (10-15%):
Unpredictable or unexpected (i.e. DRUG ALLERGY)

- Most common drug groups causing hypersensitivity are β -lactam antibiotics and NSAIDs



Penicillins



Cephalosporins

Epidemiology

Most Common

- Cutaneous reactions – maculopapular eruptions and urticaria
- Acute angioedema, anaphylaxis, dyspnea, rhinitis



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Most severe

- Toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome (SJS), immune hepatitis, drug-induced hypersensitivity syndrome (DiHS) one of which is drug reaction with eosinophilia and systemic symptoms (DRESS)

Burden of Drug Hypersensitivity

- A study of hospital practice showed that penicillin-allergic patients had higher medical costs related to the use of alternative antibiotics
 - Alternative treatment is more expensive & more toxic than 1st-line
- Fleming's 1945 Nobel Peace Prize lecture cautioned against **antibiotic resistance**
 - Drug allergy contributes to resistance by use of broad spectrum antibiotics when penicillin alone could be used



Prognosis

- Hypersensitivity decreases with time.
 - IgE antibodies present in 90% of patients 1 year after allergic reaction, but only in 20-30% after 10 years
- Patients who have anaphylactic reactions are **more likely** to retain antibodies to the drug longer.



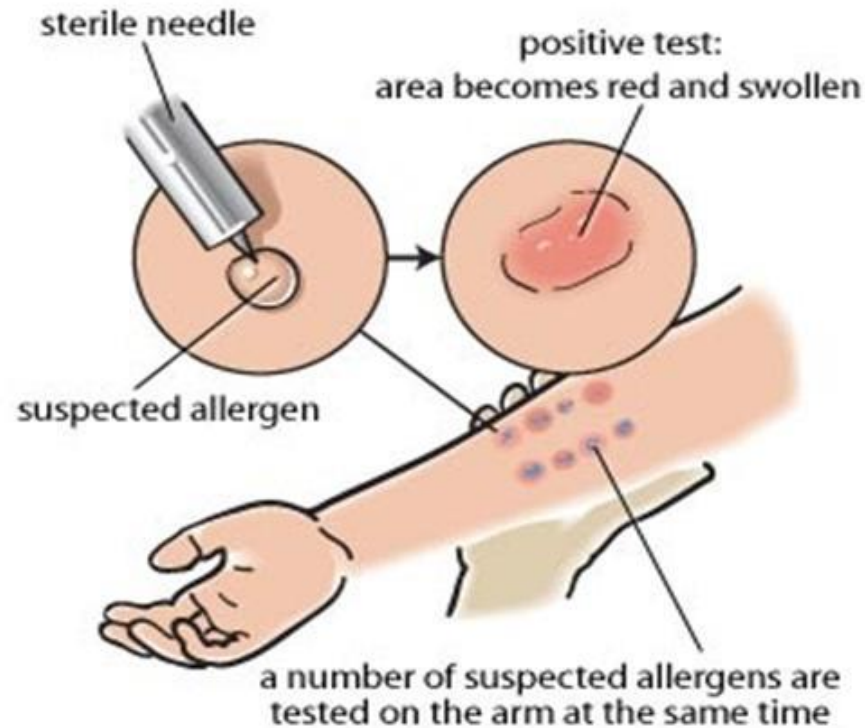
Diagnosis of Drug Allergy

- History is paramount
 - Consider TIMING, Immunogenicity of drugs
 - Immediate reactions (within 1 hour) usually indicate IgE-mediated
 - Delayed reactions usually indicate T-cell mediated
- Skin Testing
- In Vitro Testing
- Provocative Drug Testing (drug challenge)



Diagnosis: Skin Testing

- Skin prick & Intradermal
 - Skin prick first
 - ID if skin prick negative
- ONLY validated for penicillin
 - Safe & effective for children/adults with history of penicillin allergy
 - Often extrapolated for other drugs
- 90% of patients “penicillin allergic” are not.
 - Could safely receive β -lactam antibiotics



Predictive Value of Penicillin Skin Testing

• Prior Reaction PCN Skin Tests		IgE–Dependent Reaction (%)	Any Immunologic Rxn (%)
• Any	Pos	50-80*	—
• All histories	Neg	2.6†	5.4
• Anaphylaxis		3.6	7.1
• Urticaria		4.7	7.1
• Exanthem		2.0	6.8
• Other/unknown		1.1	3.0
• None	Pos	<50‡	—
	Neg	0.4†	1.0

Diagnosis: Provocative Drug Testing, i.e. Drug Challenge

- Provides definitive diagnosis
- *Few subjects* with + history have positive challenge
- Consider risk-benefit ratio (still risky)
- Graded challenge, completed within 1 day
 - Starting dose between 1:10,000 & 1:10 of therapeutic dose
 - Sequential doses q30-60 minutes
 - 4-5 incremental doses to reach max.
- Re-challenge is **contraindicated** for history of *severe* reactions (SJS, DRESS, TEN, DiHS, AGEP)



Management of Drug Allergy

- Supportive treatment for acute reactions
 - O2, epinephrine, H1 & H2 antihistamines, steroids
- Stop offending agent
- Alternatives for Drug-Allergic patients
 - Unrelated med
 - Potentially Cross-reactive med
 - Re-administer Offending drug
 - (desensitization)



Risks

- Risks of second line therapy
 - Treatment failure with antibiotics
 - Toxicity of alternative medication
 - Cost of alternative medication

Drug Desensitization

- Graduated exposure of the allergen can create a temporary state of tolerance to the agent → this is desensitization
 - Incremental doses given, side effects controlled with steroids, epi and H blockers in a controlled setting
 - Patients who undergo desensitization tend to tolerate the offending drug without major adverse events
 - Desensitization is an underutilized process

Drug Desensitization Protocol

- Obtain skin test to determine degree of sensitivity
- Establish baseline monitoring in medical setting with IV
- Prepare drug in 10 fold dilutions from full therapeutic dose (1/10, 1/100, 1/1000)
- If skin test negative, begin with 0.1 mL of 1/100 dilution (1/1000 in severe reactions)
- If skin test positive, begin 100-fold below dose that produces midpoint reaction (5-8 mm wheal)
- Dosing interval every 20 min
- Repeat dose for mild to moderate systemic reactions; drop back 2 doses for reactions producing HD change
- Dose escalation by 2-fold increments until target dose achieved
- Proceed with standard therapy – avoid lapses in therapeutic doses
- Repeat above for every new administration of offending agent

Summary



- Drug Allergy to Penicillin is common
- Drug allergy is a burden to the healthcare system
 - High cost, morbidity & mortality
 - Toxic effects of alternative meds, antibiotic resistance, treatment failure
- 90% of patients are not truly allergic and could safely receive β -lactam antibiotics
- Penicillin skin testing is safe and effective for children & adults with a history of penicillin allergy
- Provocative Drug Challenge can be done safely the same day
- Even if patient is allergic, drug desensitization is always possible

Thank you!