



Drug Allergies in Primary Immunodeficiency

Thursday, November 3, 2022



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MISSION

Improving the diagnosis, treatment, and quality of life of people affected by primary immunodeficiency through fostering a community empowered by advocacy, education, and research.

Questions?



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Virtual groups exclusively for individuals & families living with PI



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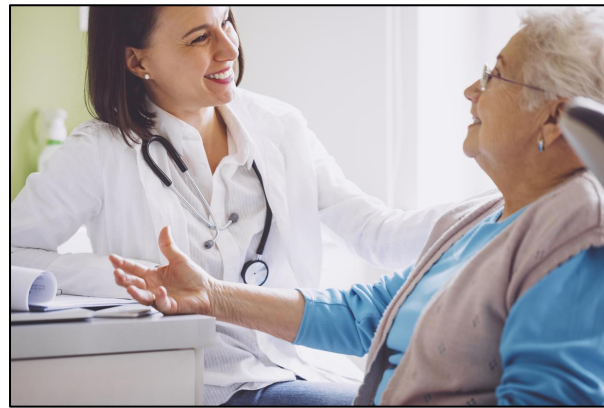
Drug Allergies in Primary Immunodeficiencies

Yesim Yilmaz Demirdag, MD
University of California in Irvine
November 3, 2022

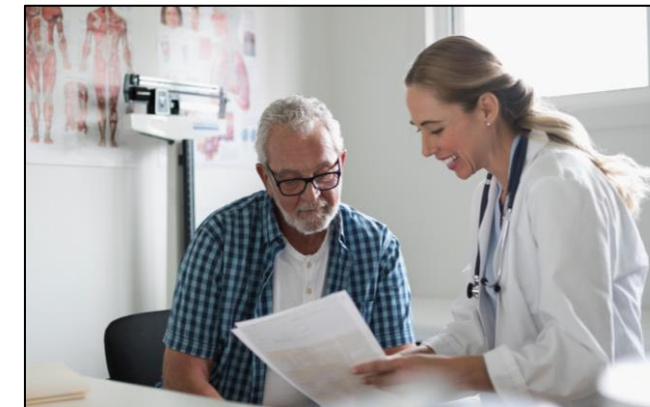
Outline

- What is a true allergic reaction?
- How common is drug allergy in primary immunodeficiencies?
- How important it is to confirm (or rule out) drug allergy?
- How do we diagnose a drug allergy?
- Can we still take the medication we are allergic to?

Mrs. Smith and Mr. Jones

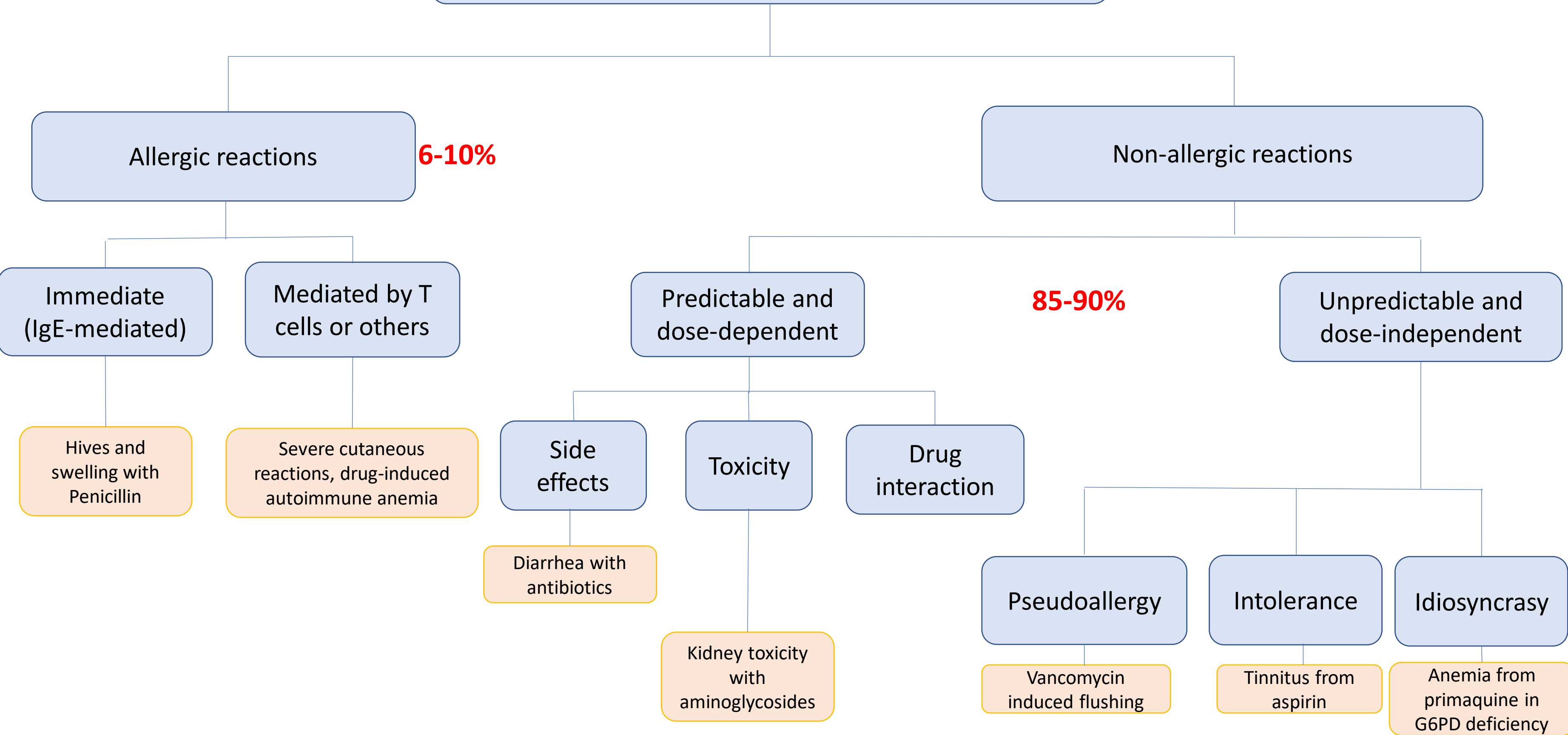


- Mrs. Smith is a 65-year-old woman with common variable immunodeficiency
- “Penicillin allergy” has been on her medical records for many years
- She had a rash when as an infant and her parents were told that she should never receive penicillin again



- Mr. Jones is a 65-year-old man with hypogammaglobulinemia
- He had hives within hours of taking Amoxicillin for a sinus infection several years ago
- Amoxicillin allergy as well as beta lactam allergy was entered on his health records

Adverse Drug Reactions



Adverse Drug Reactions

Allergic reactions

Non-allergic reactions

Immediate
(IgE-mediated)

Mediated by T
cells or others

Predictable and
dose-dependent

Unpredictable and
dose-independent

Hives and
swelling with
Penicillin

Severe cutaneous
reactions, drug-induced
autoimmune anemia

Side
effects

Toxicity

Drug
interaction

Pseudoallergy

Intolerance

Idiosyncrasy

Diarrhea with
antibiotics

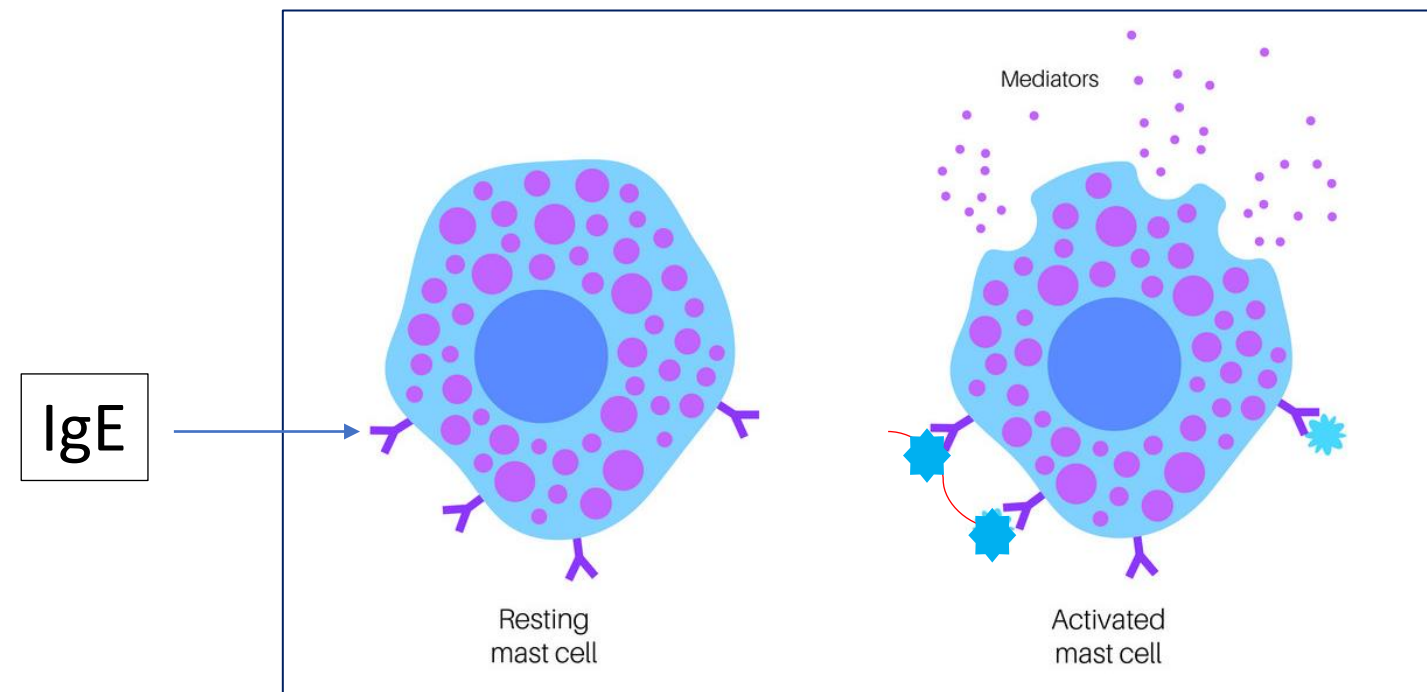
Kidney toxicity
with
aminoglycosides

Vancomycin
induced flushing

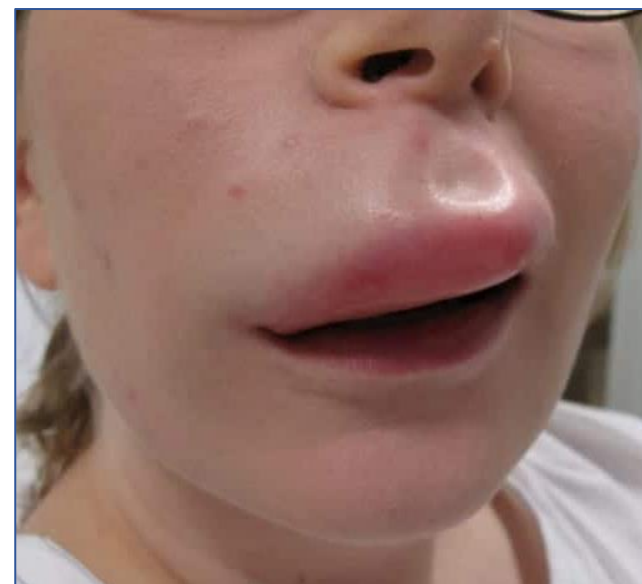
Tinnitus from
aspirin

Anemia from
primaquine in
G6PD deficiency

IgE-mediated allergic reaction



- Occurs within minutes to hours (usually < 1 hr)
- Anaphylaxis is the most severe form
- Fatality may be up to 10%



Common drugs causing IgE-mediated reactions

- Antibiotics, most commonly beta-lactam drugs (penicillins and cephalosporins)
- Neuromuscular blocking agents
- Chemotherapeutic agents
- Biologics
- NSAIDs

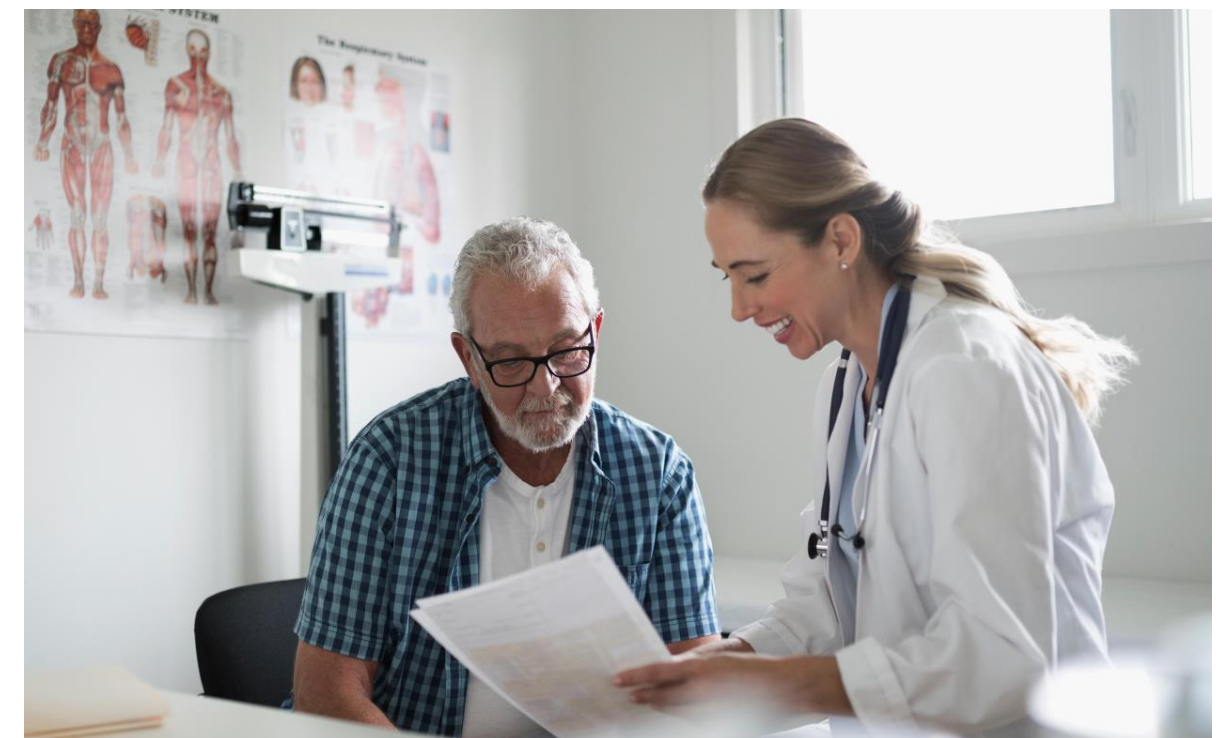
Risk factors for drug allergy

- Recurrent drug exposure
- Route of exposure (IV)
- Female sex
- Prior history of allergic reaction to drug

- Genetic factors - for delayed type of drug allergies such as Stevens Johnson syndrome

Mrs. Smith and Mr. Jones

- Mr. Smith and Mr. Jones are now admitted to the hospital with pneumonia
- Because of the “penicillin allergy” label, they were given an alternative antibiotic



Is it important to determine if I am allergic to Penicillin?

Increased risk of

- Delay in antibiotic treatment
- Usage of alternative and broader spectrum antibiotics
- Inadequate treatment of bacterial infections
- Longer hospital stay
- Frequent infections with drug-resistant microorganisms
- Adverse drug reactions, c. diff infection, and readmission
- Health care cost

Penicillin Allergy in General Population



10%

Why?



1%

Why is >9% of population think they allergic to PCN?

- Non-allergic reactions
- People can lose their allergies over time (80% after 10 yrs)
- Allergy was reported solely based on family history
- Initial symptoms were not symptoms of allergy



Rash during a viral illness



Headache due to sinus infection



Fatigue due to viral illness

Self-reported drug allergies in primary immunodeficiencies

- Autosomal dominant hyper IgE syndrome – 41%
(USIDNET registry, Gernez et al, 2018)
- Common variable immunodeficiency – 35%
(USIDNET registry, Hartman et al, 2017)
- 22q11.2 deletion syndrome – 19%
(Morsheimer MM et al, 2017)
- DOCK8 deficiency – 9%
(multicenter, Aydin et al, 2015)
- All PIDs – PCN allergy: 24.3%
(UCI data – unpublished)

9-41%

Penicillin Allergy in Common Variable Immunodeficiency

Hartman et al J Clin Immunol, 2017

- 100 patients with CVID
 - 33 self-reported penicillin allergy (33%)
 - 4 had nausea only or local irritation from IV infusion
 - 2 already evaluated and cleared
 - 15 patients underwent skin testing and office challenge – all tolerated PCN except one patient developed delayed nausea and vomiting
- Bjelac et al Ann Allergy Asthma Immunol 2018
 - 34/160 patients reported penicillin allergy (21.2%)
 - 11/11 -> negative skin test
 - 9/9 -> tolerated amoxicillin during challenge

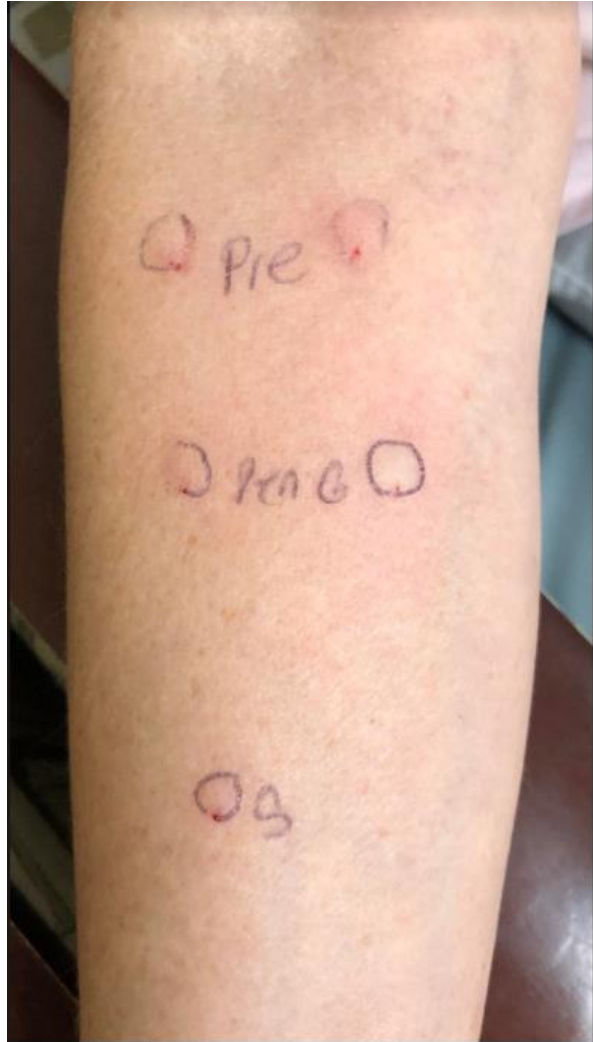
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TRUE PENICILLIN ALLERGY IS EXTREMELY RARE IN CVID

How is the drug allergy label removed from health records? (How is drug allergy diagnosed?)



- **History**

- Why was the antibiotic prescribed?
- How was it administered?
- When was the onset of the reaction?
- How many doses had you taken before the reaction?
- Have you taken that antibiotic since the reaction? If yes, what happened?

- **Skin testing**

- Penicillin, perioperative agents, insulin, radiocontrast agents

- **Drug challenge**

- Gold standard
- Contraindications – drug-induced liver disease, Stevens Johnson syndrome

Drug Challenge



Amount	Observation time
1/10 th of the dose (if tablet 1.4 th of the tablet)	30-60 min
Full dose	60 min

or

Amount	Observation time
Full dose	60 min

Management of Drug allergy

- Avoidance of the culprit drug
 - Alternative drugs
- Rapid drug desensitization
 - Antibiotics
 - Chemotherapeutics
 - Biologics

Mrs. Smith

- Mrs. Smith underwent 1-step challenge with full IV dose of Penicillin drug and tolerated well
- Penicillin/Amoxicillin allergy removed from allergy list



Mr. Jones

- Mr. Jones (who had hives within hours of taking Amoxicillin)
- Treated with cephalosporins
- Underwent outpatient penicillin skin testing (negative) and then Amoxicillin challenge and tolerated well
- Penicillin allergy removed from health records



Take home points

- Not all adverse drug reactions are allergic reactions
- Once the drug allergy is entered on medical records, it stays there forever
- Penicillin allergy is by far the most reported drug allergy (10% of Americans), and having “penicillin allergy” label on medical records has negative consequences
- The good news is that 95% of these people are able to tolerate penicillin without any allergic reaction
- Removing penicillin allergy label can be done by clinical history and, in some cases, by drug testing and/or challenge
- Reported penicillin allergy is much more common in PIDs but true penicillin allergy may be extremely rare

THANK YOU



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THANK YOU!

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YOUR QUESTIONS ANSWERED

THANK YOU!

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From all of us at IDF

Thank You!

- Abe
- Frances
- CHRIS
- Lorraine
- Jarey
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- Katherine
- Rachel
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- Clyde
- Chuck
- Fci
- Stephanie
- Karen
- Zach
- Emma
- Kathy
- Missy
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