

Improving People's Lives Through Innovations in Personalized Health Care

Curbside Consultations
Allergy Immunology

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Disclosure

- None

Objectives

- Review the current recommendations for influenza vaccination for Health Care Providers
- Understand the implications of egg allergy on those who are to receive the influenza vaccination
- Discuss the state of the art in evaluating penicillin allergy

It begins sometime in October…

- In the Physician's lounge a colleague comes up to you and says:
  - "Bryan: I'm allergic to eggs and can't take the flu vaccine. Can you sign an excuse for me so that I don't have to get the flu vaccination this year?"

- The real questions:
  - Is egg allergy a contraindication to influenza vaccination?
  - Do I really have to take the influenza vaccination?

Why is Influenza vaccination for Healthcare providers an issue?

- Annual influenza vaccination is recommended for health care personnel, including physicians, nurses and other workings in inpatient and outpatient care settings, medical emergency response workers such as paramedics and EMTs, and employees of nursing home and long term care facilities who have contact with patients or residents.
- Many facilities now have **requirements** for annual influenza vaccination for **credentialing**.
  - Thus…. The request for a medical exemption.

How do we approach this potentially spurious request?

- This is a friend who we have known for years… We share patients.
- Ask if s/he has ever had a reaction to an influenza vaccination
- And conversely, if s/he has ever received an influenza vaccination without having a reaction.
  - "A previous severe allergic reaction to influenza vaccine, regardless of the component suspected of being responsible for the reaction, is a contraindication to future receipt of the vaccine."*

Grohskopf LA, Sokolow LZ, Broder KR, et al. MMWR Recommendations and Reports. 2017;66(2):1-20.

Egg allergy and influenza vaccination

- If s/he has not had a reaction to the Influenza vaccine…
  - For the sake of collegiality, ask the details of the reaction to egg
    - Severe reaction to egg AND to egg baked into other items; evaluated and verified
    - Moderate to severe reaction to egg, but able to tolerate egg baked into other items
    - Mild reaction to egg

Egg Allergy and Influenza vaccination

- CDC recommendations (2017-2018):
  - Egg allergy (only hives after exposure to eggs); should receive any licensed and recommended flu vaccine.
  - Egg allergy involving symptoms other than hives (angioedema, respiratory distress, lightheadedness, or recurrent emesis; or who required epinephrine) may similarly receive any licensed and recommended flu vaccine. The selected vaccine should be administered in an inpatient or outpatient medical setting and supervised by a health care provider who is able to recognize and manage severe allergic conditions.

Egg Allergy and Influenza vaccination

Ann Allergy Asthma Immunol 120 (2018) 49–52

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ELSEVIER

Practice Parameters

Administration of influenza vaccines to egg allergic recipients: A practice parameter update 2017☆

Matthew Greenhawt, MD, MBA, MSc; Paul J. Turner, BM, BcH, FRACP, PhD; John M. Kelso, MD

- "Influenza vaccine recipients with egg allergy are at no greater risk for a systemic allergic reaction than those without egg allergy. Precautions, such as choice of a particular vaccine, special observation periods, or restriction of administration to particular medical settings, are not warranted and constitute an unnecessary barrier to immunization. Vaccine providers and screening questionnaires do not need to ask about egg allergy status of recipients of influenza vaccine."

Time Magazine

- February 5, 2018
- “Flu complacency is killing us.”
- “…less than half of young Americans get the flu shot, and 1 in 5 millennials believes the long disproved myth that vaccines can cause autism.”

We need to take flu outbreaks far more seriously

By Jonathan D. Quick

Overflow flu patients are placed in a tent outside a hospital in California

GINA FERAZZI—LOS ANGELES TIMES/POLARIS

FLU COMPLACENCY IS KILLING US. The usual response to the annual flu is not enough to combat the risks we currently face, let alone prepare us for an even deadlier pandemic flu that most experts agree will come in the future. Yes, we have an annual vaccine, and everyone eligible should get it without question. The reality, however, is that we largely remain stuck at immunization rates of under 50%. And the flu vaccines we have are only 60% effective in the best years and 10% effective in the worst years. The current flu vaccine is better than nothing. We urgently need a much, much more effective flu vaccine.

People suffer and die needlessly. In the U.S. alone, seasonal flu can cause up to 36 million infections, three-quarters of a million hospitalizations and 56,000 deaths. We are not taking the time and investing the resources needed to protect ourselves, our loved ones and our communities.

Why not? We haven’t been hit by a truly devastating pandemic in a long time. So as individuals, we let down our guard as our leaders quietly defund and destaff the services we need to protect us.

The risk to humanity of continued foot dragging is huge. In a severe pandemic, the U.S. health care system could be overwhelmed in just weeks. Millions of people would be felled by the virus, and hundreds of thousands—including newborn babies, toddlers and adults—would die in the weeks and months following the initial outbreak.

Inadequate preparedness programs—and the investments required to fund and sustain them—mean that even with some of the best available health care there is, the U.S. remains woefully susceptible to a major future flu epidemic. Since 2003, the federal government has cut per capita funding by 60% for the U.S. Public Health Emergency Preparedness program that it created in the aftermath of the 9/11 attacks to protect against bioterrorism, pandemics and other public health emergencies. This has contributed to the loss of more than 45,700 jobs at state and local health departments since 2008. And the Trump Administration has called for even more draconian budget cuts.

The cost of preventing epidemics is roughly a tenth of what it costs to cope with them when they hit. In 2012, renowned professor Michael Osterholm from the University of Minnesota issued a clarion call for an annual billion-dollar U.S. commitment to the development of a universal flu vaccine. Six years later, the search for a universal vaccine remains seriously underfunded, even as the seasonal flu costs the U.S. economy an estimated $87 billion a year.

Why do we as a nation continue to leave ourselves vulnerable? The simple answer lies in our collective complacency. As soon as headlines about the flu are gone, hospitals are emptied of flu patients, schools are back in session and workplace absenteeism declines, we go back to business as usual.

> The cost of preventing epidemics is roughly a tenth of what it costs to cope with them when they hit

AT THE PERSONAL LEVEL, you can learn the essentials of reducing flu transmission in your family and local community. You can make sure that everyone in your family receives the flu shot; today less than half of young Americans get the flu shot, and 1 in 5 millennials believes the long-disproved myth that vaccines can cause autism. And you can reach out to your congressional representatives to encourage them to support funding that strengthens local, state and national pandemic-preparedness programs.

Leading scientists and public health officials have the capability to keep us much safer from devastating influenza pandemics. They need your prompt and decisive support to succeed. Your action today may be a matter of life and death for you and your loved ones.

Quick is a senior fellow at Management Sciences for Health and an instructor at Harvard Medical School. His new book, The End of Epidemics: The Looming Threat to Humanity and How to Stop It, *is out on Jan. 30.*

Vaccination Hesitancy

- There is still an incredible distrust of vaccinations, in spite of all the good they do.
- Many people, even physicians, want to avoid vaccinations if possible.
- We need to be prepared to discuss these vaccine questions and myths appropriately and with science.
- Google “vaccines”: ~26M hits
- Google “vaccines no”: ~17.2M hits

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American Academy of Allergy, Asthma & Immunology

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Five More Things Physicians and Patients Should Question

9

Don't routinely avoid influenza vaccination in egg-allergic patients.

Of the vaccines that may contain egg protein (measles, mumps, rabies, influenza and yellow fever), measles, mumps and rabies vaccines have at most negligible egg protein; consequently no special precautions need to be followed in egg-allergic patients for these vaccines. Studies in egg-allergic patients receiving egg-based inactivated influenza vaccine have not reported reactions; consequently egg-allergic patients should be given either egg-free influenza vaccine or should receive egg-based influenza vaccine with a 30-minute post-vaccine observation period. Egg-allergic patients receiving the yellow fever vaccine should be skin tested with the vaccine and receive the vaccine with a 30-minute observation period if the skin test is negative. If positive, the vaccine may be given in graded doses with appropriate medical observation.

Egg protein is present in influenza and yellow fever vaccines and in theory could cause reactions in egg-allergic patients. However, in 27 published studies collectively 4,172 patients with egg allergy received 4,729 doses of egg-based inactivated influenza vaccine (IIV) with no cases of anaphylaxis, including 513 with severe egg allergy who uneventfully received 597 doses. The CDC's Advisory Committee on Immunization Practices recommends that egg-allergic persons receive IIV as a single dose without prior vaccine skin testing and be observed for 30 minutes afterwards for any possible allergic reaction. If the reaction to the ingestion of eggs was hives only, the vaccine can be administered in a primary care setting, whereas if the reaction to the ingestion of eggs was more severe, the vaccine should be administered in an allergist/immunologist's office. Two new IIVs not grown in eggs have been approved for patients 18 years and older: Flucelvax, prepared from virus propagated in cell culture, and Flublok, recombinant hemagglutinin proteins produced in an insect cell line. For egg-allergic patients 18 years of age and older, either egg-based IIV can be used with the precautions above or egg-free IIV can be used.

Measles and mumps vaccines (and Purified Chick Embryo Cell [PCEC] rabies vaccine) are grown in chick embryo fibroblast cultures and contain negligible or no egg protein. Thus, MMR and PCEC rabies vaccine can be administered to egg-allergic recipients in the usual manner.

Per the Yellow Fever vaccine package insert, egg-allergic recipients should be skin tested with the vaccine prior to administration. If negative, the vaccine can be given in the usual manner, but the patient should be observed for 30 minutes afterward. If the vaccine skin test is positive, the vaccine can be given in graded doses under appropriate medical observation.

As you get a cup of coffee

- One of the orthopedic surgeons asks you about his patient with a history of allergy to penicillin
- He asks:
  - I have a patient who needs prophylactic antibiotics but has a history of penicillin allergy.
  - Is it safe to use a cephalosporin?
- He goes on to say that he has many patients with a history of penicillin allergy – is there some way you can help me with these patients.

What is the reality of the history of allergy to penicillin

- There is much confusion regarding the patient with a history of allergy to penicillin.
- There are two specific questions here:
  1. Can penicillin allergic patients take cephalosporin?
  2. What can be done about the large number of patients with penicillin allergy on their charts?
     - Is this real or spurious?
     - How can I tell the difference?

Background

Beta Lactam antibiotics are common

- 2011: PCN & Cephalosporins are top 2 classes of antibiotics in US
  - 60% in US; 55% Globally
- 2017: 34 Beta Lactam compounds approved by FDA, including 18 cephalosporins
- Patient reported allergy to PCN is reported to be from 8-15%

Penicillin Allergy is Poorly Understood

- PCN allergy is over-reported
  - PCN allergy testing has shown that approximately 90% of patients with reported history of PCN allergy can safely take penicillin.
- On the other hand
  - Allergy Vigilance Network: European Registry of recorded drug induced severe anaphylaxis reports:
    - 42.6% of cases between 2002-2016 were from beta-lactams
- Take home point: beta-lactam allergy is over reported, BUT can cause life threatening allergic reactions

Your patient says s/he has a PCN allergy

- The diagnosis of PCN allergy is like used bubble gum:
  - Often carelessly placed where it doesn't belong
  - Difficult to scrape off once it is there.
  - We often don't understand how it got there.

Pro/Con Review

Are Cephalosporins Safe for Use in Penicillin Allergy without Prior Allergy Evaluation?

Eric Macy, MD, MS, FAAAAI[a], and Kimberly G. Blumenthal, MD, MSc[b,c,d] *San Diego, Calif; and Boston, Mass*

INTRODUCTION

At the American Academy of Allergy, Asthma, and Immunology 2017 Annual Meeting in Atlanta, Georgia, the following issue was debated: "Cephalosporins are safe for use in penicillin allergy (without prior allergy evaluation)." The pro position was presented by Eric Macy, and the con position was presented by Kimberly Blumenthal. Each position considered the existing data on the safety of using cephalosporins in patients with a history of penicillin allergy, without prior allergy evaluation to confirm acute tolerance to that cephalosporin. The present article is an account of the pro/con debate and does not constitute a systematic review of the literature.

THE PRO POSITION—DR MACY

The basic argument for the pro position relies on the underappreciation of the risks of avoiding a needed therapeutic cephalosporin when it is the drug of choice for a documented bacterial infection, versus the dramatically exaggerated risk of serious immunologically mediated reactions to cephalosporins in one could not treat a patient with a cephalosporin before removing the penicillin *allergy* or confirming a penicillin allergy (ie, a clinically significant IgE-mediated reaction). Penicillin allergy testing supports effective antibiotic stewardship and helps reduce health care expenditure, specifically excess hospital days.[5] Additional testing to document acute tolerance to a cephalosporin in the setting of a penicillin *allergy*, before therapeutic use of the cephalosporin, is not clinically useful because it has such a high number needed to treat for even a minimal hypothetical benefit.[6] Recommending that cephalosporin tolerance testing must occur does not improve overall patient safety or clinical outcomes because of the high number needed to treat, time, expense, and the low likelihood of such testing occurring, and will potentially result in ever greater use of less effective non—beta-lactam antibiotics.

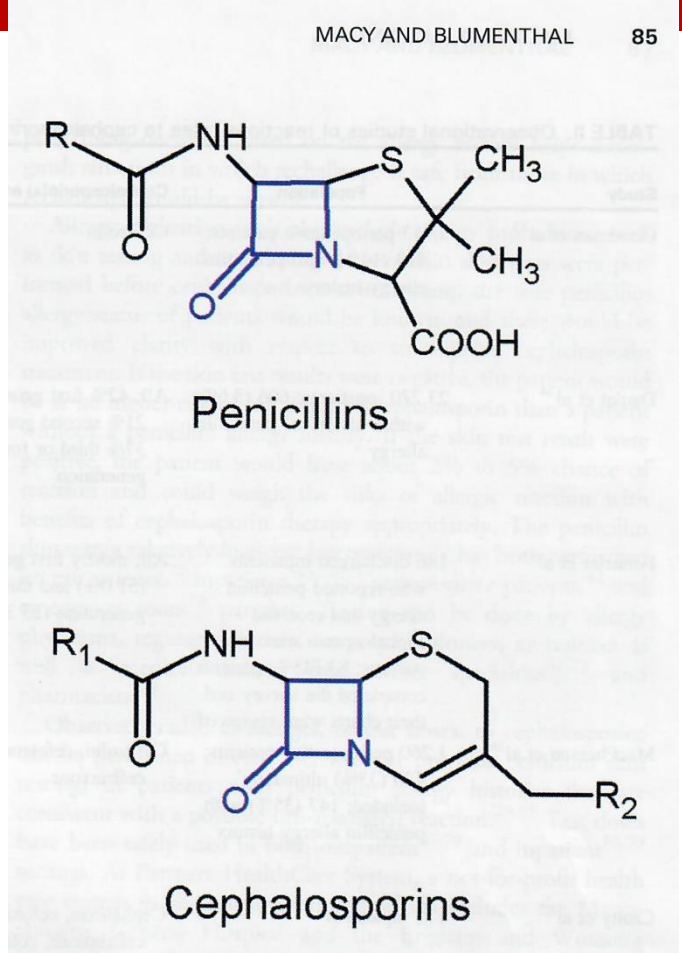
Epidemiology

About 9.0% of the US population that uses health care carries a history of a penicillin *allergy* and about 1.3% carries a history of any cephalosporin allergy.[7] The adverse reaction rate reported in the

Macy E and Blumenthal KG. The Journal of Allergy and Clinical Immunology: In Practice. 2018. 6:1;82-89.

Beta-Lactam X-reactivity

- Penicillin and Cephalosporins share a beta-lactam ring (shown in blue)
- What is known & still unknown
  - Early studies: Penicillin physically contaminated cephalosporins leading to falsely high cross reactivity estimates
    - Leads to current FDA estimate of up to 10%
  - Current data support 2-5% cross reactivity



Macy E and Blumenthal KG. The Journal of Allergy and Clinical Immunology: In Practice. 2018. 6:1;82-89.

West J Med. May 2000;172:341

Medical Myth

Ten percent of patients who are allergic to penicillin will have serious reactions if exposed to cephalosporins

Cephalosporins and penicillins share a common beta-lactam ring. It is commonly taught that at least 10% of patients who are allergic to penicillin will have an adverse reaction to cephalosporins. This potential cross-reactivity has extremely important therapeutic implications because many serious infections are best treated with cephalosporins as first-line therapy.

viewed data from published series and postmarketing reports from drug manufacturers. Serious allergic reactions to cephalosporins occur in about 0.02% of patients who take the antibiotic. The rate of serious reactions in patients with a penicillin allergy appears to be twofold to fourfold this baseline rate. However, a threefold baseline rate of serious reactions is seen in patients with penicillin

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- "The myth that a high rate of cross-allergy between PCN and cephalosporins needs to be exposed so that patients who need cephalosporins will be given them whether or not they have a history of PCN allergy." Physicians should note that patients with true PCN allergy are at slightly increased risk of an allergic reaction when given any antibiotic."

Zagursky RJ & Pichichero ME. The Journal of Allergy and Clinical Immunology: In Practice. 2018. 6:1;72-81.

Clinical Commentary Review

Cross-reactivity in β-Lactam Allergy

Robert J. Zagursky, PhD, and Michael E. Pichichero, MD *Rochester, NY*

β-Lactam drugs (penicillins, amoxicillin, and cephalosporins) account for 42.6% of all severe drug-induced anaphylaxis. In this review, we focus on clinically significant immunologic cross-reactivity in patients with confirmed penicillin allergy to cephalosporins, and the structural involvement of the R_1 and R_2 chemical side chains of the cephalosporins causing IgE-mediated cross-reactivity with penicillin and other cephalosporins. Skin tests predict IgE-mediated reactions and showed cross-reactivity between penicillins and early generation cephalosporins that shared side chains, but confirmatory challenge data are lacking. Later-generation cephalosporins, which have distinct side chains, do not have any skin test cross-reactivity with penicillin/amoxicillin. There is debate as to the involvement of R_2 side chains as the antigenic determinants that cause IgE-mediated hypersensitivity with various cephalosporins. Avoidance of cephalosporins, when they are the drug of choice in a penicillin-allergic individual, results in significant morbidity that outweighs the low risk of anaphylaxis. We conclude that there is ample evidence to allow the safe use of cephalosporins in patients with isolated confirmed penicillin or amoxicillin allergy. **(J Allergy Clin Immunol Pract 2018;6:72-81)**

Key words: *Anaphylaxis; β-Lactam allergy; Penicillin;*

Performance of penicillin allergy testing has shown that approximately 90% of patients with a reported history of penicillin are not allergic to penicillin. This has important ramifications because increased usage of non−β-lactam drugs encourages the development of antibiotic-resistant organisms and use of alternative antibiotics that have serious side effects.[5] The same concern should be applied to patients with a reported history of cephalosporin allergy.

The 2013 American Academy of Pediatrics Sinusitis Guideline[6] endorsed the use of specific cephalosporin antibiotics for the treatment of patients even if there is a report of type I (IgE-mediated) allergy or non−type I penicillin reactions; however, for unclear reasons the endorsement in older guidelines excludes penicillin reactions that are type I allergic reactions (2004 American Academy of Pediatrics and American Academy of Family Physicians,[7] 2013 American Academy of Pediatrics Acute Otitis Media Guidelines, and the 2010 Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology[8]). Our previous review focused on the immunologic cross-reactivity of patients with a penicillin allergy to certain cephalosporins and the structural involvement of the R_1 cephalosporin site for this cross-reactivity.[9] Here, we include type I allergy reactions with penicillins and cephalosporins including

Cross reactivity among beta-lactams

- Cross reactivity can be on the basis of the beta-lactam ring OR on the R1 or R2 side chain.
  - Ampicillin and cephalexin have identical R1 side chains
- Carbapenems are unlikely to cross react with PCN or cephalosporins
- Monobactams do not cross react to PCN or most cephalosporins
  - Aztreonam and Ceftazidine have an identical R1 side chain

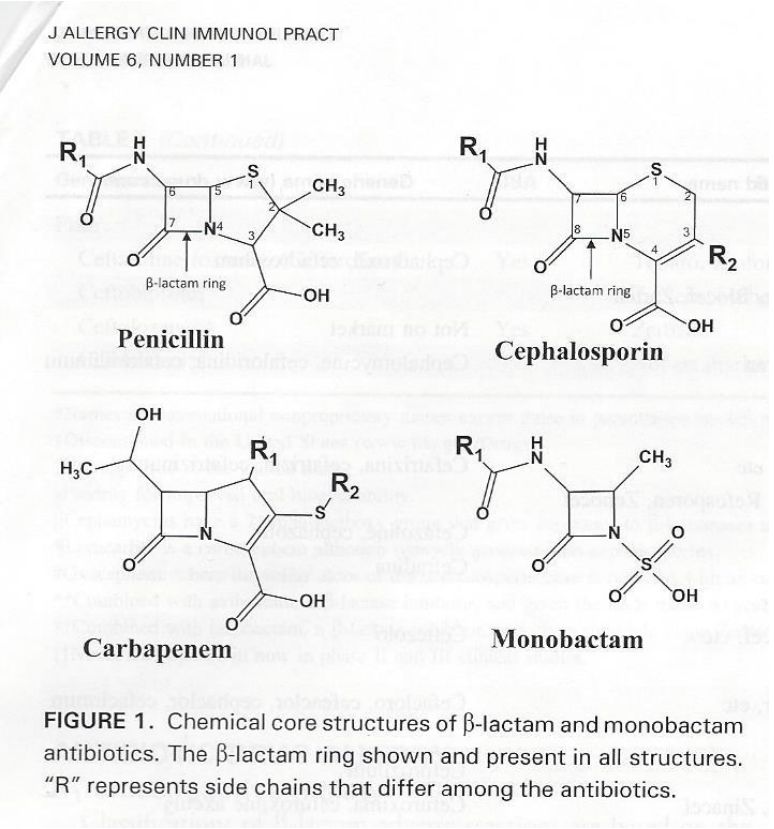


FIGURE 1. Chemical core structures of β-lactam and monobactam antibiotics. The β-lactam ring shown and present in all structures. "R" represents side chains that differ among the antibiotics.

Zagursky RJ & Pichichero ME. The Journal of Allergy and Clinical Immunology: In Practice. 2018. 6:1;72-81

R1 and R2 Structural Similarities

		Penicillins							1st							2nd							3rd									4th		5th			Mono
		Nafcillin	Oxacillin	Dicloxacillin	Penicillin G / V	Piperacillin	Ampicillin	Amoxicillin	Cefadroxil	Cefatrizine	Cephalexin	Cefazolin	Ceftezole	Cephalothin	Cephapirin	Cefoxitin	Cefuroxime	Cefotetan	Cefprozil	Cefaclor	Cefonicid	Cefamandole	Cefoperazone	Ceftibuten	Cefdinir	Cefixime	Ceftriaxone	Cefditoren	Cefodizime	Cefotaxime	Cefpodoxime	Ceftazidime	Cefepime	Cefpirome	Ceftaroline fosamil	Ceftolozane	Cefiderocol	Aztreonam
PCN	Nafcillin	■																																				
	Oxacillin		■	r1																																		
	Dicloxacillin		r1	■																																		
	Penicillin G / V				■	r1'	r1'	r1'	r1	r1	r1								r1	r1	r1	r1	r1'															
	Piperacillin				r1'	■	R1'	r1'	r1'	r1'	R1'								r1'	R1'	r1'	r1'	R1"															
	Ampicillin				r1'	R1'	■	r1'	r1	r1	R1								r1	R1	r1	r1	r1'															
	Amoxicillin				r1'	r1'	r1'	■	R1	R1	r1'								R1	r1	r1	r1	R1'															
1st	Cefadroxil				r1	r1	r1	R1	■	R1	r1								R1	r1	r1	r1	R1'															
	Cefatrizine				r1	r1'	r1	R1	R1	■	r1								R1	r1	r1	r1	R1'															
	Cephalexin				r1	R1'	R1	r1	r1	r1	■								r1	R1	r1	r1	r1'															
	Cefazolin											■	R1r2																									
	Ceftezole											R1r2	■																									
	Cephalothin													■	R2	R1r2	r1'r2													R2								
	Cephapirin													R2	■	r2	r2													R2								
2nd	Cefoxitin													R1r2	r2	■	r1'R2													r2								
	Cefuroxime													r1'r2	r2	r1'R2	■									r1"	R1"	R1"	R1"	R1"r2	R1"		R1"	R1"	r1"			
	Cefotetan																	■			r2	R2	R2															
	Cefprozil				r1	r1	r1	R1	R1	R1	r1								■	r1	r1	r1	R1'															
	Cefaclor				r1	R1'	R1	r1	r1	r1	R1								r1	■	r1	r1	r1'															
	Cefonicid				r1	r1	r1	r1	r1	r1	r1							r2	r1	r1	■	R1r2	r1'r2															
	Cefamandole				r1	r1	r1	r1	r1	r1	r1							R2	r1	r1	R1r2	■	r1'R2															
3rd	Cefoperazone				r1'	R1"	r1'	R1'	R1'	R1'	r1'							R2	R1'	r1'	r1'r2	r1'R2	■															
	Ceftibuten																							■	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	r1'	r1'	R1'	R1'
	Cefdinir																							R1'	■	R1'R2	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	r1'	r1'	R1'	R1'
	Cefixime																r1"							R1'	R1'R2	■	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	r1	r1	R1'	R1'
	Ceftriaxone																R1"							R1'	R1'	R1'	■	R1	R1	R1	R1	R1'	R1	R1	r1	r1	R1'	R1'
	Cefditoren																R1"							R1'	R1'	R1'	R1	■	R1	R1	R1	R1'	R1	R1	r1	r1	R1'	R1'
	Cefodizime																R1"							R1'	R1'	R1'	R1	R1	■	R1	R1	R1'	R1	R1	r1	r1	R1'	R1'
	Cefotaxime													R2	R2	r2	R1"r2							R1'	R1'	R1'	R1	R1	R1	■	R1	R1'	R1	R1	r1	r1	R1'	R1'
	Cefpodoxime																R1"							R1'	R1'	R1'	R1	R1	R1	R1	■	R1'	R1	R1	r1	r1	R1'	R1'
	Ceftazidime																							R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	■	R1'	R1'r2	r1	R1'	R1	R1
4th	Cefepime																R1"							R1'	R1'	R1'	R1	R1	R1	R1	R1	R1'	■	R1	r1	r1	R1'r2	R1'
	Cefpirome																R1"							R1'	R1'	R1'	R1	R1	R1	R1	R1	R1'r2	R1	■	r1	r1'	R1'	R1'
5th	Ceftaroline fosamil																r1"							r1'	r1'	r1'	r1	r1	r1	r1	r1	r1	r1	r1	■	R1'	r1	r1'
	Ceftolozane																							r1'	r1'	r1'	r1'	r1'	r1'	r1'	r1'	R1'	r1'	r1'	R1'	■	R1'	R1'
	Cefiderocol																							R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1	R1'r2	R1'	r1	R1'	■	R1
Mono	Aztreonam																							R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1'	R1	R1'	R1'	r1'	R1'	R1	■

FIGURE 3. Comparison of R_1 and R_2 structural similarities between β-lactam drugs. Drugs that have identical R_1 or R_2 structures are listed as R1 (red cell) or R2 (gold cell). If only the ring or branch chain moiety of the R_1 structure is identical, it is listed as R1′ or R1″, respectively. Drugs that have similar R_1 or R_2 structures are listed as r1 or r2. If only the ring or branch chain moiety of the R_1 structure is similar, it is listed as r1′ or r1″, respectively. Blank cells imply no R_1 or R_2 structural similarities.

Is it safe to use a cephalosporin in a PCN allergic patient?

- "The notion that PCN-allergic patients must avoid all cephalosporins because of potential cross-reactivity should be dismissed as a myth. Cross-reactivity between PCN and cephalosporins occurs rarely and when it occurs it is due to similarity in the R1 side chain of the molecules."
- "Carbapenem and monobactams are beta-lactams but their molecular structure is sufficiently dissimilar from thos of penicillins and cephalosporins that cross-allergy among these molecules would not be predicted."

Zagursky RJ & Pichichero ME. The Journal of Allergy and Clinical Immunology: In Practice. 2018. 6:1;72-81

Side Note: Cephalosporin Allergy

- Must this patient avoid all cephalosporins? All beta-lactams?
- "The notion that a patient allergic to a specific cephalosporin must avoid all cephalosporins because of cross reactivity among the molecules should be dismissed as a myth. Cross-reactivity between cephalosporins occurs rarely and when it occurs it is due to similarity in the R1 or R2 side chain of the molecules."

Approach PCN allergic history

- Approach #1: All to often used – accept history of PCN allergy at face value. Write PCN allergy in the chart. Avoid all beta-lactams
- Approach #2: Get a good allergic history and review its implications with the patient
  - What was the reaction?
  - What was the drug in question (as specifically as possible)
  - When was the reaction? How long ago AND how long after starting to take the medication?
  - Has the patient taken the drug since the original reaction? What happened?
    - Has the patient taken related drugs? What happened?

Results of your history of allergies

- If it is clear that this is not a history consistent PCN allergy, don't document PCN allergy in the chart.
  - For example: Patient says s/he had GI upset with PCN or headaches after taking PCN
  - Explain to the patient the consequences of having such an allergy listed in the chart, and explain why you do not believe it is an actual allergy
  - Document your thinking and the discussion with the patient in the chart.
- If the patient had a clear anaphylactic reaction to a beta-lactam, don't just document PCN allergy or beta-lactam allergy.
  - Document specific medication and reaction

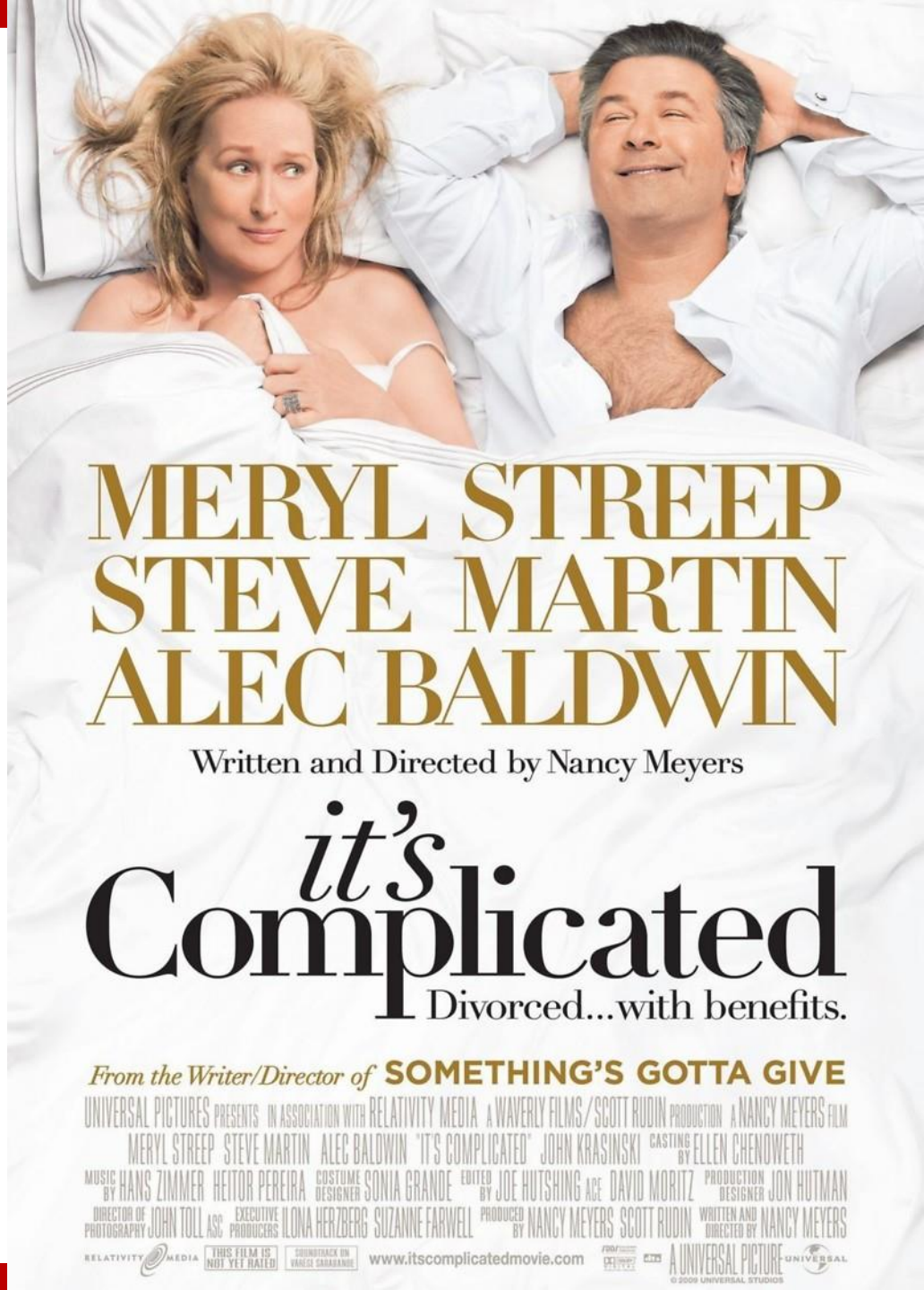
Medicolegal risks are a concern

- "The risks of medicolegal prosecution are always a concern for clinicians and part of the decision-making paradigm. It should be recognized that patients with a bona fide allergy to a beta-lactam antibiotic may experience an allergic reaction to a different beta-lactam antibiotic as an independent hypersensitivity reaction that is not related by cross-allergy. The old adage, 'true, true and unrelated' can and does occur in patients."
- Important to explain your thinking to your patient

Zagursky RJ & Pichichero ME. The Journal of Allergy and Clinical Immunology: In Practice. 2018. 6:1;72-81

PCN Allergy

1. Is clinically important
2. Is common
3. Is over diagnosed (over documented)
4. It can cause serious reactions
5. Can cause longer hospital stays, higher costs and worse outcomes for patients
6. Skin testing is available and has high negative predictive value



How can an allergist help?

- Well trained allergy immunology specialists have varying levels of comfort with drug allergy.
- Talk to your local allergists to find one who is comfortable with PCN and cephalosporin drug testing and challenge.
  - PCN skin testing available
    - Pre-Pen FDA approved in September 2009
    - Negative testing followed by oral challenge with amoxicillin
  - Cephalosporin skin testing can be done, but is not FDA approved or standardized

Routine Allergy Consult for evaluation of PCN allergy

- Your allergist should:
  - Take and document a very good allergy history
- IF PCN allergy is spurious, provide the documentation to take the diagnosis off the chart.
- IF PCN allergy is possible:
  - Skin testing
    - Negative: oral amoxicillin challenge
      - Challenge negative – remove PCN allergy
      - Explain to patient what a negative test means
        - s/he is not allergic to PCN or cephalosporins
        - But could still have a reaction – there is no guarantee that s/he won't develop a new allergy
    - Positive Document the reaction

American Academy of
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Penicillin Allergy Testing Should Be Performed Routinely in Patients with Self-Reported Penicillin Allergy

Approved by the AAAAI Board of Directors, July 2016

Adverse reactions to medications are frequently observed. Among the drugs associated with IgE-mediated allergic reactions, penicillins are most commonly implicated.[1] Penicillin allergy is estimated to affect 7% to 10% of community populations and up to 20% of hospitalized patients.[1,2] However, when penicillin allergy testing is performed in individuals who report a history of

Systemic reactions have been reported, although rarely; for this reason, penicillin allergy testing should be performed in a health care setting only by clinicians with the knowledge, training, and experience to select appropriate patients for this procedure, interpret test results, and manage a systemic allergic reaction should it occur.[1,2] Patients with negative skin testing to

Emergency Consult for Evaluation of PCN Allergy

- Your hospitalized patient needs PCN, but has PCN allergy on the chart.
- What can an allergy consult provide?
  - Good history and the potential to take the allergy off the chart.
  - If there is time, possibility of inpatient PCN skin testing and oral challenge with amoxicillin – take the allergy off the chart.
  - Confirm allergy: positive test
  - Confirm potential allergy: consistent history without being able to do testing

PCN allergic patient who must have PCN

- Allergist will nearly always request an ID consult to verify that the patient must have PCN and there are no viable alternative antibiotics.
  - If alternative is used, patient should have skin testing on routine basis after discharge
- Verified allergy or consistent history
  - PCN desensitization (done in a matter of hours)
    - Begin with very dilute drug, gradually build to therapeutic dose, then continue normally
    - Protects only as long as drug is given at least daily; it conveys no long term protection
    - Patient should have skin testing on routine basis after discharge

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Five More Things Physicians and Patients Should Question

10

Don't overuse non-beta lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation.

While about 10 percent of the population reports a history of penicillin allergy, studies show that 90 percent on more of these patients are not allergic to penicillins and are able to take these antibiotics safely. The main reason for this observation is that penicillin allergy is often misdiagnosed and when present wanes over time in most (but not all) individuals. Patients labeled penicillin-allergic are more likely to be treated with alternative antibiotics (such as vancomycin and quinolones), have higher medical costs, experience longer hospital stays, and are more likely to develop complications such as infections with vancomycin-resistant enterococcus (VRE) and Clostridium difficile.

Evaluation for specific IgE to penicillin can be carried out by skin testing. Ideally, penicillin skin testing should be performed with both major and minor determinants. The negative predictive value of penicillin skin testing for immediate reactions approaches 100 percent, whereas the positive predictive value is between 40 and 100 percent. The usefulness of in vitro tests for penicillin-specific IgE is limited by their uncertain predictive value. They are not suitable substitutes for penicillin skin testing.

By identifying the overwhelming majority of individuals who can safely receive penicillin and penicillin-like drugs, we can improve the appropriateness of antibiotic therapy and clinical care outcomes.

Summary

- Influenza vaccinations are important and can be given to egg allergic individuals
- Penicillin allergy is still complicated
  - Over diagnosed and over documented
  - Potential cross reactivity between PCN and cephalosporins is overstated in the older literature
    - Side chain cross reactivity must be taken into account
  - PCN skin testing is available and provides high negative predictive value
  - PCN allergy history should be evaluated and potentially removed in order to provide better antibiotic stewardship and better clinical outcomes

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