UWTASP

tele-antimicrobial stewardship program

September 10, 2019

Noon Session

Agenda

- Didactic
- Case Discussions
- Open Discussion

UWTASP

tele-antimicrobial stewardship program

September 10th, 2019

Penicillin Allergy

John Lynch, MD, MPH

UW Medicine | Harborview Medical Center

PODCAST Alert!

Breakpoints: The SIDP Podcast

Sidp.org/Podcasts

MIC'ed Up: A Podcast Miniseries on Leadership and Advocacy in Antimicrobial Stewardship

In this 3-episode podcast miniseries, Lisa Dumkow, Elizabeth Dodds-Ashley, and Jamie Kisgen talk leadership and advocacy in antimicrobial stewardship with moderator Erin McCreary

LISTEN

Straight Outta Amsterdam: An ECCMID Recap

In this 4-episode podcast miniseries, Ryan Shields and Erin McCreary review key posters, presentations, and other data from the 2019 European Congress of Clinical Microbiology & Infectious Diseases

LISTEN

The Itch: A Podcast Miniseries on Penicillin Allergy

In this 3-episode podcast miniseries, Julie Ann Justo, Bruce M. Jones, and Mary L. Staicu discuss all things penicillin allergy with moderator Jason Pogue

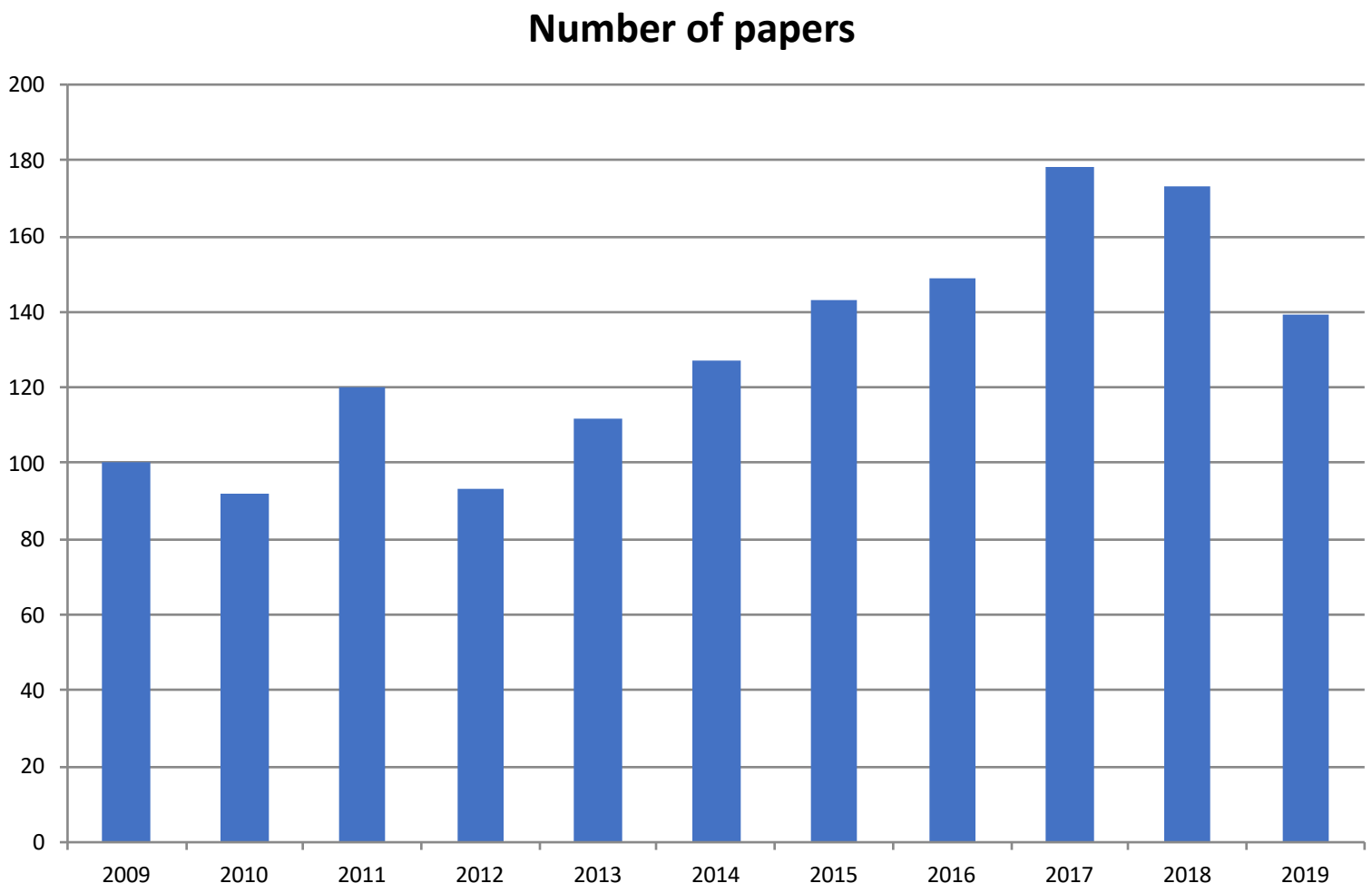
Question

How many people have ever been told or have said that they have a penicillin allergy?

A. Yes

B. No

“Penicillin Allergy” Papers



Penicillin Allergy Evaluations: An Emerging Component of Comprehensive Cancer Care

Allison Ramsey MD and Mary L. Staicu PharmD

Journal of Allergy and Clinical Immunology: In Practice, 2019-09-01, Volume 7, Issue 7, Pages 2192-2193, Copyright © 2019 American Academy of Allergy, Asthma & Immunology

Review

Penicillin Allergy Skin Testing in the Inpatient Setting

Julie Ann Justo [1,2], Wesley D. Kufel [3,4,5], Lisa Avery [6,7] and P. Brandon Bookstaver [1,2,*]

Antibiotic Allergy in Children: More than Just a Label

Elissa Abrams[a] Elena Netchiporouk[b] Barbara Miedzybrodzki[c]
Moshe Ben-Shoshan[c]

“Penicillin Allergy”

- True prevalence of penicillin allergy is ~1%
- 10-15% of inpatients and 9-12% of outpatients report an allergy
- 90% of the above are not allergic and of those who were, most are no longer
- Why so much confusion?
  - Allergenic impurities in penicillin in ’70s
  - Penicillin contamination of cephalosporins pre-1980

Why is This a Problem?

- Removes options for effective treatment
- Increases resistance and *C. difficile* disease as clinicians reach for vancomycin and fluoroquinolones
- At some sites, most vancomycin use due to reported allergy
- May require multiple antimicrobials to substitute

Dr. Bob Pelz, WSHA ASP, September 2016

Why is This a Problem?

Inferior patient outcomes

- Adverse effects
- Risk of drug resistance
- *C. difficile* infection

Increased costs

- 40% higher antibiotic cost
- Increased length of stay

Outcomes with MSSA

	All	Reported Penicillin Allergy	No Reported Penicillin Allergy	P Value*
Primary Outcome	(n = 456)	(n = 59)	(n = 397)	
Optimal Therapy Trial, n (%)	346 (76)	28 (47)	318 (80)	<0.001
	All	Reported Penicillin Allergy	No Reported Penicillin Allergy	P Value*
Secondary Outcome	(n = 440)	(n = 57)	(n = 383)	
Adequate Therapy Completion, n (%)	391 (89) †	48 (84)	343 (90)	0.26
Predominantly first-line therapy	302 (77)	26 (54)	276 (80)	<0.001‡
Predominantly second line therapy	50 (13)	19 (40)	31 (9)	
Combination of first-line and second-line therapies	39 (10)	3 (6)	36 (11)	

* Wilcoxon rank-sum or Fisher's exact test unless specified

† Of the 49 patients not receiving adequate therapy, 33 were discharged within 10 days without adequate therapy to complete their course, 16 were hospitalized for at least 10 days and not treated with adequate antibiotic therapy for MSSA bacteremia.

‡ Cochran-Armitage trend test

doi:10.1371/journal.pone.0159406.t002

- Hazard for mortality 0.57 for vanco vs beta-lactam for MSSA (McDaniel, CID, 2015)
- Recurrence higher for vanco (20% vs 4%) (Change, Medicine, 2003)

Blumenthal, PLoS, 2016

Outcomes with MSSA

Table 1. Summary of Published Studies Evaluating Empirical Therapy for Methicillin-Susceptible *Staphylococcus aureus* Bacteremia

Study	Year	Design	Study Size, No.	Outcome	Vancomycin vs β-Lactam	Result[a]
Vancomycin therapy vs β-lactam therapy[b]						
Chang et al [19]	2003	Prospective cohort	505	Bacteriologic failure[c]	19% vs 0%	OR, 6.5 (1.0–53)
Khatib et al [20]	2006	Prospective cohort	120	Overall mortality	27% vs 12%	HR, 2.3 (1.1–4.9)
Stryjewski et al [21][d]	2007	Prospective cohort	123	Treatment failure	31% vs 13%	OR, 3.5 (1.2–13)
Lodise et al [6][e]	2007	Retrospective cohort	84	Infection-related mortality	39% vs 11%	OR, 6.5 (1.4–29)
Kim et al [22]	2008	Retrospective case-control	27	Infection-related mortality	37% vs 11%	OR, 3.3 (1.2–9.5)
Schweizer et al [23]	2011	Retrospective	267	30-day in-hospital mortality	20% vs 3%	HR, 4.8 (2.1–11)[f]
Chan et al [24]	2012	Retrospective cohort	293 094	Hospitalization rate	12.5 vs 7.2[g]	HR, 1.6 (1.2–2.2)[f]
Vancomycin therapy vs vancomycin therapy de-escalated to β-lactam						
Lodise et al [6][e]	2007	Retrospective cohort	84	Infection-related mortality	33% vs 41%	NS
Schweizer et al [23]	2011	Retrospective cohort	267	30-day in-hospital mortality	20% vs 7%	HR, 3.2 (1–10)
Vancomycin therapy de-escalated to β-lactam therapy vs β-lactam therapy						
Khatib et al [25]	2006	Prospective cohort	168	Persistent bacteremia	56% vs 37%	$P = .03$
Lodise et al [6][e]	2007	Retrospective cohort	84	Infection-related mortality	41% vs 11%	Not reported

McDaniel, CID, 2015

2014 Kaiser CA Study

- Allergic patients had 0.59 day longer LOS, 23.4% more C. diff, 14% more MRSA, 30% more VRE
- Estimated cost increase: $64 million/3yr
- More vancomycin, fluoroquinolones, clindamycin

Macy, J Allergy Clin Immuno, 2014

Barriers

- Easier for busy clinicians to order alternative antibiotics
- Lack of knowledge and exaggerated risk perception (patients and providers)
- ID, FP, Peds and IM docs not trained
- Missed opportunity for emphasis in ID and ASPs

Dr. Bob Pelz, WSHA ASP, September 2016

Strategies

- Ask patient if PCN or ceph tolerated since allergy. If yes, OK to use.
- If not an allergy (ex. nausea), OK to use
- OK to use cephalosporin if allergy is not anaphylaxis, SJS, TEN, etc.
- PCN allergy testing
- Graded challenge, desensitization

Question

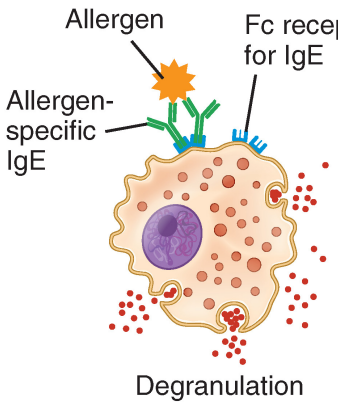
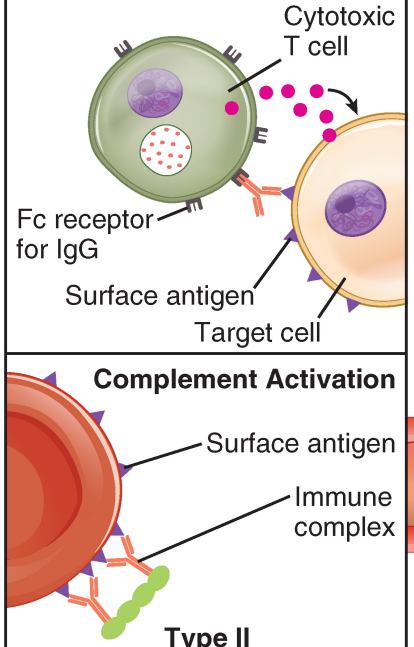
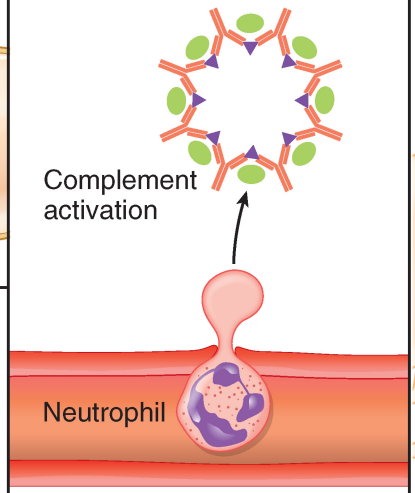
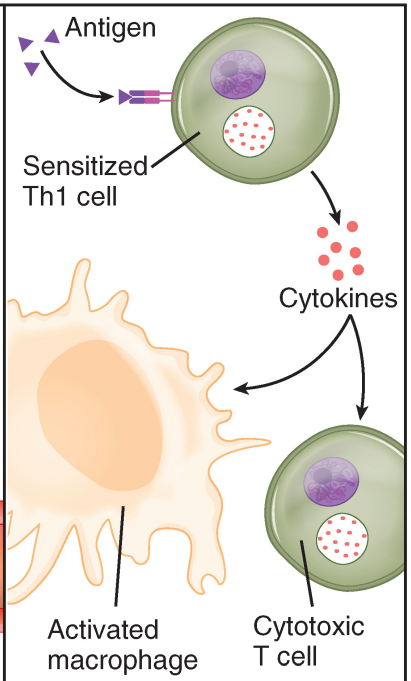
Does your facility have a process for skin testing patients with a reported allergy to penicillin?

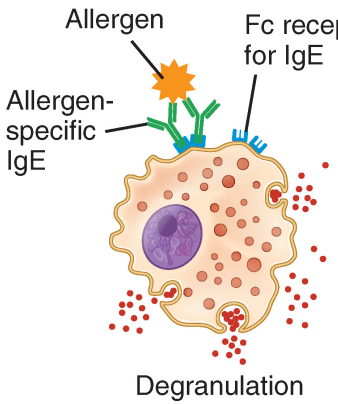
A. Yes

B. No

Penicillin Skin Testing (PST)

- Identifies only Type I, IgE-mediated allergy

Type I	Type II	Type III	Type IV
			
IgE-Mediated Hypersensitivity	**IgG-Mediated Cytotoxic Hypersensitivity**	**Immune Complex-Mediated Hypersensitivity**	**Cell-Mediated Hypersensitivity**
IgE is bound to mast cells via its Fc portion. When an allergen binds to these antibodies, crosslinking of IgE induces degranulation.	Cells are destroyed by bound antibody, either by activation of complement or by a cytotoxic T cell with an Fc receptor for the antibody (ADCC)	Antigen–antibody complexes are deposited in tissues, causing activation of complement, which attracts neutrophils to the site	Th1 cells secrete cytokines, which activate macrophages and cytotoxic T cells and can cause macrophage accumulation at the site
Causes localized and systemic anaphylaxis, seasonal allergies including hay fever, food allergies such as those to shellfish and peanuts, hives, and eczema	Red blood cells destroyed by complement and antibody during a transfusion of mismatched blood type or during erythroblastosis fetalis	Most common forms of immune complex disease are seen in glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus	Most common forms are contact dermatitis, tuberculin reaction, autoimmune diseases such as diabetes mellitus type I, multiple sclerosis, and rheumatoid arthritis

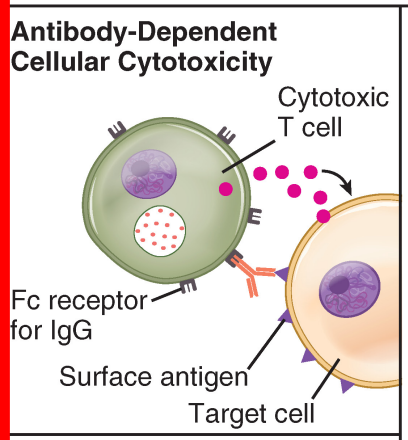


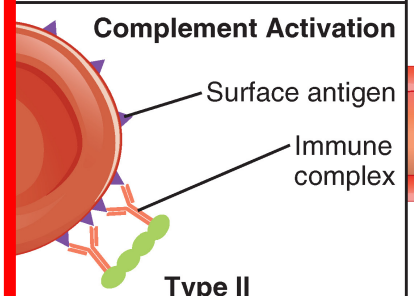
Type I

IgE-Mediated Hypersensitivity

IgE is bound to mast cells via its Fc portion. When an allergen binds to these antibodies, crosslinking of IgE induces degranulation.

Causes localized and systemic anaphylaxis, seasonal allergies including hay fever, food allergies such as those to shellfish and peanuts, hives, and eczema



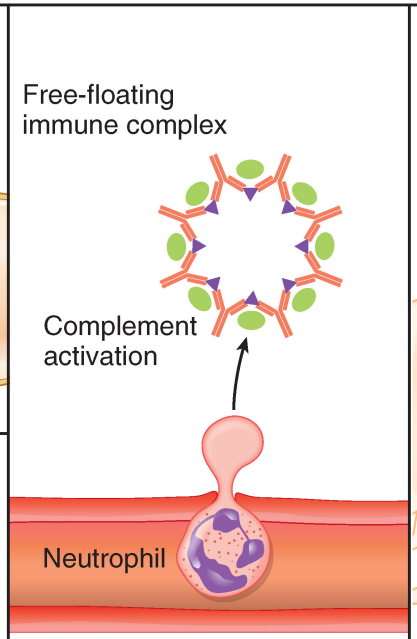


Type II

IgG-Mediated Cytotoxic Hypersensitivity

Cells are destroyed by bound antibody, either by activation of complement or by a cytotoxic T cell with an Fc receptor for the antibody (ADCC)

Red blood cells destroyed by complement and antibody during a transfusion of mismatched blood type or during erythroblastosis fetalis

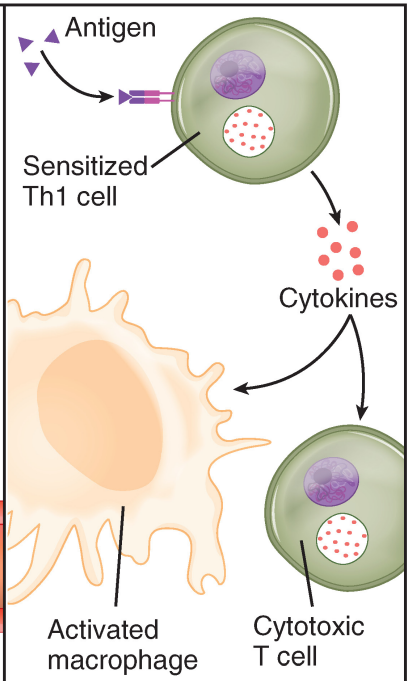


Type III

Immune Complex-Mediated Hypersensitivity

Antigen–antibody complexes are deposited in tissues, causing activation of complement, which attracts neutrophils to the site

Most common forms of immune complex disease are seen in glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus



Type IV

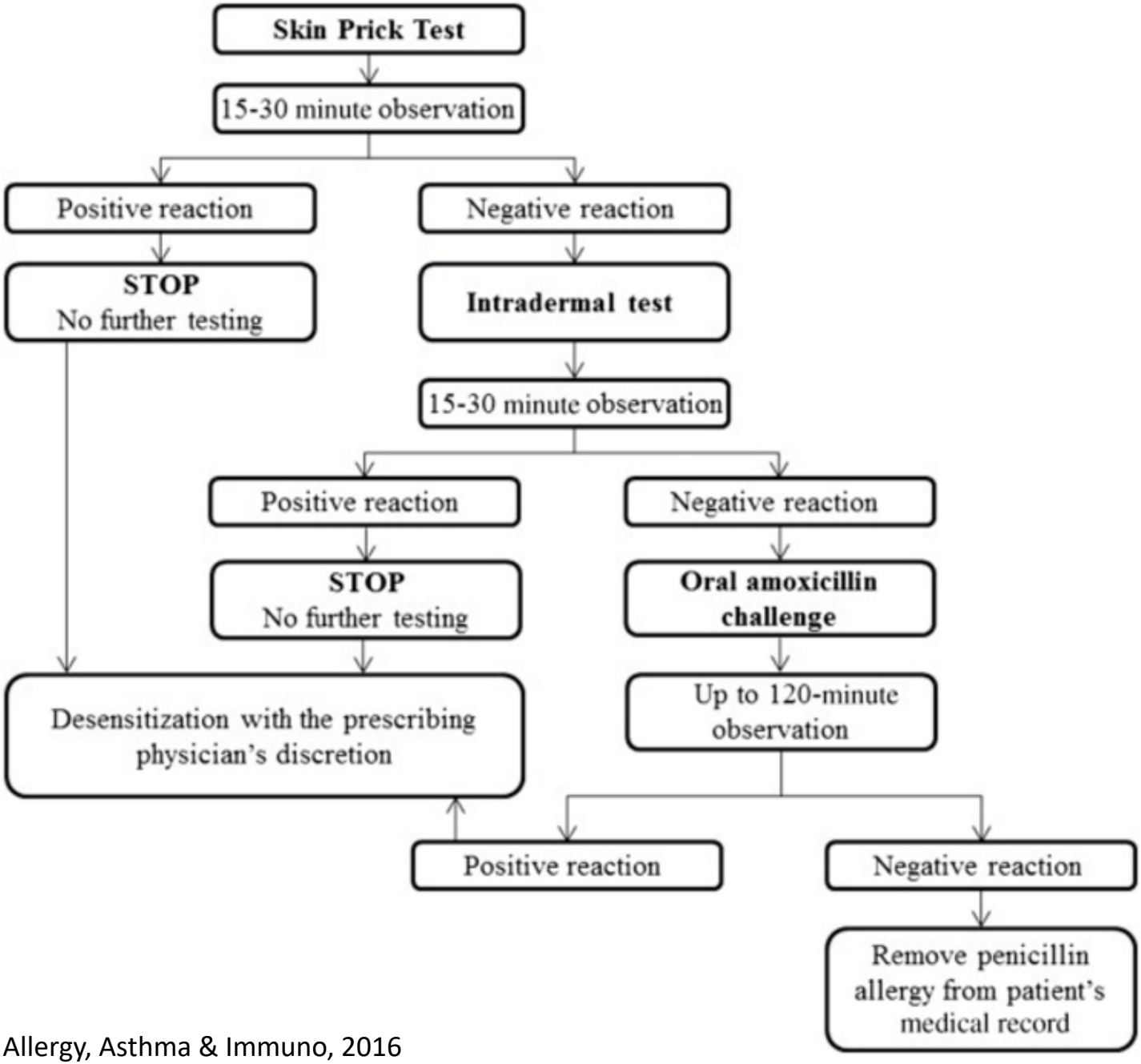
Cell-Mediated Hypersensitivity

Th1 cells secrete cytokines, which activate macrophages and cytotoxic T cells and can cause macrophage accumulation at the site

Most common forms are contact dermatitis, tuberculin reaction, autoimmune diseases such as diabetes mellitus type I, multiple sclerosis, and rheumatoid arthritis

Penicillin Skin Testing (PST)

- Identifies only Type I, IgE-mediated allergy
  - Benzylpenicilloyl polylysine
  - Urticaria, anaphylaxis, bronchospasm, angioedema
  - Usually within 1 hour of dose
- No antihistamines
- DO NOT skin test patients with h/o non-IgE allergy (TEN/SJS, DRESS, AIN, hemolysis, etc)
- Can be RN or pharmacist driven



King, Annals of Allergy, Asthma & Immuno, 2016

Penicillin Allergy Testing

- Pretest probability of not having an allergy is ~90%
- NPV of negative test is >99% (better than general population)
- Up to 3% of allergic pts missed with testing but can be safely identified with oral challenge
- **PST programs = cost savings + improved patient outcomes**

References and Reading

Esposito, S., Castellazzi, L., Tagliabue, C. & Principi, N. Allergy to antibiotics in children: an overestimated problem. *Int. J. Antimicrob. Agents* **48,** 361–366 (2016).

Sacco, K. A., Bates, A., Brigham, T. J., Saadi Imam, J. & Caroline Burton, M. Clinical outcomes following inpatient penicillin allergy testing: A systematic review and meta-analysis. *Allergy* (2017). doi:10.1111/all.13168

King, E. A., Challa, S., Curtin, P. & Bielory, L. Penicillin skin testing in hospitalized patients with β-lactam allergies: Effect on antibiotic selection and cost. *Ann. Allergy Asthma Immunol.* **117,** 67–71 (2016).

Jones, B. M. & Bland, C. M. Penicillin skin testing as an antimicrobial stewardship initiative. *Am. J. Health. Syst. Pharm.* **74,** 232–237 (2017).