

5 Common Errors in Outpatient Antimicrobial Prescribing

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Presenter Disclosure

- Relationships with commercial interests:
 - **Grants/Research Support:** Merck, Gilead, Abbvie, ViiV
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 - **Advisory Boards:** Gilead, Avir Pharma, ViiV, Merck
 - **Other:** N/A

Objectives

- At the completion of this presentation participants should be aware of the following recommendations:
- 1) Don't treat sore throats with antibiotics unless proven Group A streptococcus
- 2) Don't treat rhinosinusitis with antibiotics unless ↑fever/facial pain or persistence x 10days
- 3) Don't treat mild otitis media in otherwise healthy children >6 months of age
- 4) Don't treat AECOPD exacerbations with antibiotic unless ↑cough and sputum volume/purulence
- 5) Use cephalosporins with a different side chain for patients with penicillin allergy

Do you need that antibiotic?

Canadians filled
25 million +
prescriptions
for antibiotics in 2015.

These drugs are prescribed more frequently in Canada than in many of our peer countries, and **twice as often as in the Netherlands**, the country that prescribes the fewest antibiotics.

Antibiotics

are often overused and misused, and antibiotic resistance is one of the biggest threats to global health.ⁱ

Antibiotics should not be prescribed to treat common colds and related symptoms (e.g., cough, sore throat).ⁱⁱ

i. World Health Organization.
ii. Choosing Wisely Canada.



Daily dose

per 1,000 population
per day, 2015



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For provincial values and more prescribing data, see CIHI's OECD Interactive Tool.

Outpatient Antibiotic Prescribing in Canada

- > 25 million courses of oral antibiotic prescribed in 2015
- Equivalent to one prescription for every adult between age 20-69
- Every day 20/1000 Canadians are taking antibiotic therapy
- 3/5 prescriptions given for diagnoses where antibiotics are unnecessary

Antibiotic Prescribing For Acute URTI Common in Canadian Elderly

- Retrospective study of patients >65 in Ontario
- 8990 primary care MD's and 185,014 patients
- Common cold (53.4%), acute bronchitis (31.3%), acute sinusitis (13.6%), acute laryngitis (1.6%)
- 46% received antibiotic (70% broad spectrum)
- Prescribers more likely to be:
 - Mid-late career
 - Foreign medical graduates
 - High volume practices



Government of Canada Gouvernement du Canada

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

Human Antimicrobial Use Report

2011

ICD-9 diagnostic class diagnostic code	Number of antimicrobial recommendations / 10,000 inhabitants				
	2007	2008	2009	2010	2011
Diseases of the genitourinary system					
0788 Other disease due to virus and <i>Chlamydia</i>	48	47	77	57	62
0999 Venereal diseases-unspecific	11	26	22	31	26
6110 Inflammatory disorder of breast	30	43	20	40	22
6049 Orchitis epididymitis, w ithout abscess	19	18	26	17	18
6010 Acute prostatitis	24	18	15	11	15
Other diagnostic codes	115	85	92	106	93
Total	247	236	251	262	237
Diseases of the respiratory system					
4660 Bronchitis-acute	683	674	620	627	640
4619 Sinusitis acute-unspecified	504	498	482	426	470
4659 Acute upper respiratory infections-unspecified site	404	338	381	275	365
4860 Pneumonia-organism unspecified	287	310	290	320	304
4620 Pharyngitis-acute	445	367	371	372	304
Other diagnostic codes	1,510	1,556	1,416	1,292	1,276
Total	3,833	3,743	3,560	3,312	3,360
Infections of the urinary tract					
5990 Urinary tract infection-site unspecified	801	845	790	726	619
5950 Acute cystitis	211	160	190	160	196
5959 Cystitis-unspecified	60	30	65	43	48
7881 Dysuria	11	20	14	15	15
5901 Acute pyelonephritis and pyelonephrosis	21	16	21	19	12
Other diagnostic codes	54	80	84	51	58
Total	1,158	1,151	1,163	1,014	949

Diagnostic class	Recommended antimicrobial	Number of antimicrobial recommendations / 10,000 inhabitants				
		2007	2008	2009	2010	2011
Diseases of the respiratory system	Amoxicillin	1,002	952	970	894	969
	Clarithromycin	972	919	948	916	843
	Azithromycin	532	566	404	437	464
	Moxifloxacin	354	359	321	339	366
	Penicillin v	183	170	151	150	127
	Other antimicrobial drugs	790	777	766	576	591
	Total	3,833	3,743	3,560	3,312	3,360

Tonsillopharyngitis

- 25% of pediatric and 10 % of adult acute pharyngitis is due to Group A Streptococcus
- Don't culture if cough, coryza and conjunctivitis
- Send swab for antigen testing (done routinely in patients ≤ 18)
- Culture done reflexively if rapid screen (-)



Tonsillopharyngitis

- Early treatment reduces symptom severity/duration, reduces suppurative/non-suppurative complications and reduces transmission
- 10% are resistant to macrolides
- Sulfonamides and tetracyclines are of minimal value
- 10 days of Penicillin V usually recommended

Amoxicillin is superior to Penicillin

- Superior bacteriologic eradication
- It is more effective if concurrent otitis media (15% of children)
- Tastes better than Penicillin V
- Once daily amoxicillin equivalent to BID

(Pediatr Infect Dis Journal 2006;25:761)

- 20 mg/kg/dose bid to maximum of 500 mg x 10 days
- 50 mg/kg od to a maximum of 1 gm x 10 days

Prescribing Error #1

Don't Treat Sore Throats With Antibiotic

- Send throat swab if acute pharyngitis and no symptoms of viral URTI → only treat if positive
- Penicillin or amoxicillin is the drug of choice

**Choosing
Wisely
Canada**



8 Don't use antibiotics in adults and children with uncomplicated sore throats.



Acute Rhinosinusitis

- 99% are viral
- Adults have 2 – 4 episodes/yr (children have 6 – 10)
- 175 million episodes per year in Canada
- Diagnostic testing unnecessary
- Treatment:
 - Saline rinses
 - Analgesics
 - Decongestants if eustachian tube dysfunction
 - Dextromethorphan if cough

Acute Bacterial Rhinosinusitis

- 1% of rhinosinusitis
- Diagnostic features :
 - Fever + facial pain lasting ≥ 3 days
 - OR
 - Symptoms persist/worsen after ≥ 10 days
- *S. pneumoniae, H. influenza, M. catarrhalis*
(anaerobes if extension of dental root infection)
- Diagnostic testing unnecessary
- Doxycycline 100 mg po q12h x 5 days

Prescribing Error #2

Do Not Prescribe Antimicrobials For Rhinosinusitis Unless High Fever With Facial Pain x 3 Days or Persistent/Worsening Symptoms x 10 Days

Otitis media

- The most common dx in sick pediatric visits to GP
- 85% resolve spontaneously
- 80% are prescribed antibiotic
- Does your patient even have AOM?
 - Otalgia + middle ear effusion + middle ear inflammation (bulging TM or perforation)
- Does your patient with AOM even require antibiotic?

Observation Appropriate For AOM Except For The Following Circumstances:

- Age < 6 months
- Fever ≥ 39
- Moderate-severe systemic illness
- Severe otalgia
- Significant symptoms > 48 hrs
- Acute symptomatic perforation
- Complicated AOM (mastoiditis, cranial nerve palsy, meningitis etc.)
- Craniofacial abnormalities, immunocompromised, recurrent AOM

Otitis media

Amoxicillin is the Drug of Choice

	S. pneumoniae	H. influenzae	M. catarrhalis	Viruses
Expected pathogens (%)	40	20	10	30
Amoxicillin resistance (%)	10	30	90	100
Expected resistance (%)	4	6	9	30
Expected spontaneous resolution rate by day 5 (%)	20	50	75	30
Expected clinical failures due to resistant organisms not resolving spontaneously	3	3	2	9

80-90 mg/Kg/day divided q12h
x 10 days if < 2 yo, perforated TM or recurrent
x 5 days if \geq 2 yo

When Amoxicillin is Not The Drug of Choice in AOM:

- Otitis-conjunctivitis syndrome: amoxicillin-clavulanate
- Recent amoxicillin in past 30 days: amoxicillin-clavulanate
- Recurrent AOM: amoxicillin-clavulanate
- Hypersensitivity reaction to penicillin:
 - Mild: cefuroxime
 - Severe: macrolide

WASP for Children Aged 6-12 Months Visiting ER With Otitis Media

	Wait and See Prescription	Standard Prescription
Number Enrolled	132	133
Did not fill Rx	82 (62%)	17 (13%) (p<0.001)

Spiro et al. JAMA 2006;296(10):1235-1241

Prescribing Error #3

- a) **Do Not Prescribe Antibiotic For Mild Acute Otitis Media in Otherwise Healthy Children > 6 Months of Age**
- b) **Amoxicillin is the Drug of Choice For Majority of Uncomplicated AOM**

Exacerbations of Chronic Bronchitis

- 40% viral, 20% bacterial, 10% environmental, 30% idiopathic
- Risk Fx for poor outcome:
 - FEV₁ <50%
 - >4 exacerbations per year
 - Cardiovascular disease
 - Recent steroid or antibiotic use
 - Home O₂

Anthonisen Staging Criteria

- Type I – ↑ sputum volume
 ↑ sputum purulence
 ↑ dyspnea
- Type II – two of the above
- Type III – one of the above

Outcome of Exacerbation Treatment by Staging Criteria

	Placebo (%)			Antibiotic (%)		
Stage	I	II	III	I	II	III
Success	43.0	60.0	69.7	62.9	70.1	74.2
No Resolution	22.2	26.7	18.2	20.0	20.8	11.4
Deterioration	30.5	10.7	12.1	14.3	5.2	11.4

Ann Int Med 1987; 100: 196

AECOPD Treatment According to Risk Stratification

Group	State	Pathogens	Treatment
0	Acute tracheobronchitis	Viral	None
1	Simple Chronic Bronchitis	S. pneumoniae H. influenzae M. catarrhalis	Doxycycline
2	Complicated Chronic Bronchitis	Organisms above Gram negative rods	Amoxicillin- Clavulanate
3	Chronic Suppurative Bronchitis	Organisms above Pseudomonas sp.	Based on culture

Prescribing Error #4

- a) **Never Treat Acute Bronchitis With Antibiotic**
- b) **Only Treat AECOPD With Antibiotic If Anthonisen Type I or II Symptoms**

Clinical Case

- 1 yo girl presents with 48 hrs of severe otalgia and new onset fever
- Hx of rash with amoxicillin when treated for AOM 4 weeks ago
- Has bilateral, red, bulging tympanic membranes

What would you do?

Penicillin Allergy

- 10% of all patients have a penicillin allergy label
- >90% of these patients do not actually have penicillin allergy
- 50% of allergy labels are either unknown or non-allergic
- Once a label is removed it frequently reappears
- Associated with poor outcomes

Outcomes



**Increased
Broad-
Spectrum
Antibiotics**



**Increased
Cost**



**Increased
Length
Of Stay**



**Increased
Adverse
Events**

Charneski et al *Pharmacother* 2011;31(8):742
Macy et al *J Allergy Clin Immunol* 2014;133:790

Adverse Reactions Associated with Oral and Parenteral Use of Cephalosporins: A Retrospective Population-Based Analysis

- Retrospective Population-Based Analysis (3.9 million patients) over 3 years
- Objective: For patients receiving a cephalosporin: determine the occurrence of reports of new cephalosporin “allergy” or serious adverse reaction
- Results:
 - Cephalosporin use was common in patients with unconfirmed penicillin allergy with low rate of new reported allergy (1.13% vs 0.37%)
 - Anaphylaxis was rare (.0005-.001%) and not ↑ in patients with unconfirmed penicillin allergy
 - Only 3 cases of serious cutaneous reactions in 1.4 million treatment courses
 - *C. difficile* was the most common adverse drug reaction

Lack of Allergic Cross-Reactivity to Cephalosporins Among Patients Allergic to Penicillins (Novalbos *et al.* Clin Exper Allergy 2000; 31:438-443)

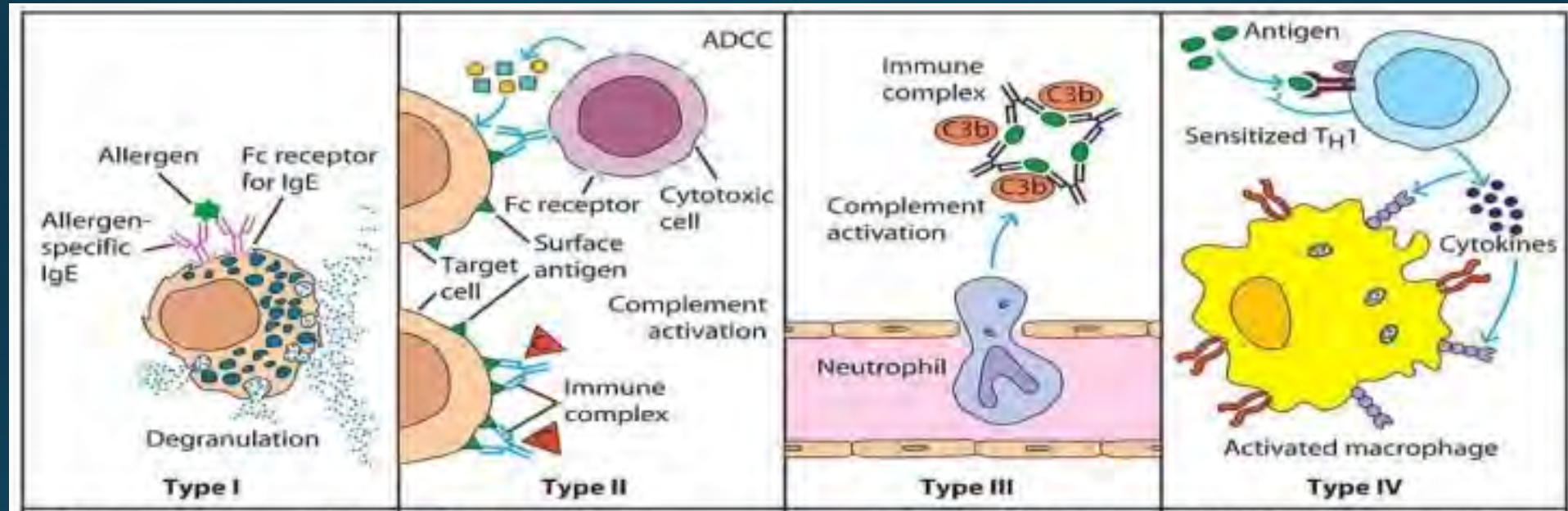
- **No ↑ risk of anaphylaxis when pen allergic patients given cephalosporins**
- **The risk of true IgE-mediated cross-reactivity between penicillins and cephalosporins is extremely low (0.4%) and is related to similar side chains**
- **This risk of cross-reactivity is low compared to the high risk of inappropriate antibiotic Rx, ↑ cost, ↑LOS, ↑*C.diff* infection, ↑ ARBO and ↑mortality.**

- All patients subsequently received therapeutic doses of each agent without any reactions

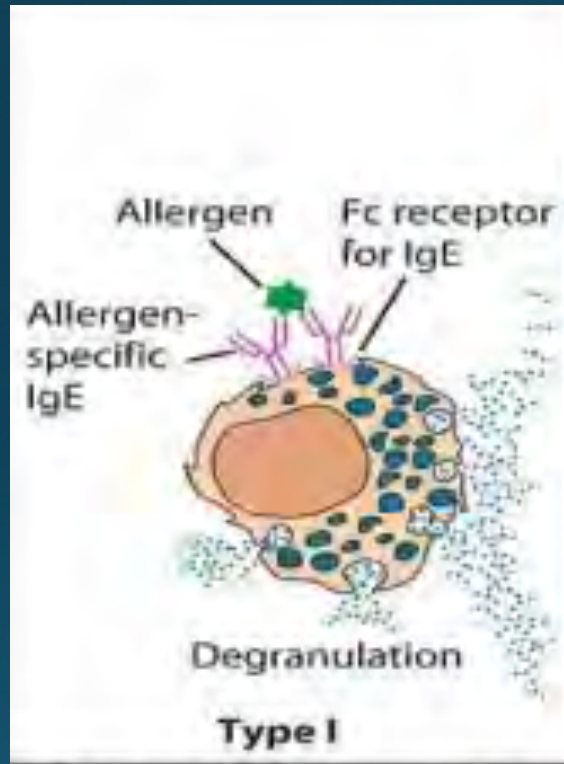
- Conclusion:

- Risk of cross-reactivity between penicillins and cephalosporins is very low, provided that the cephalosporin used has a dissimilar side chain to the penicillin which caused the reaction

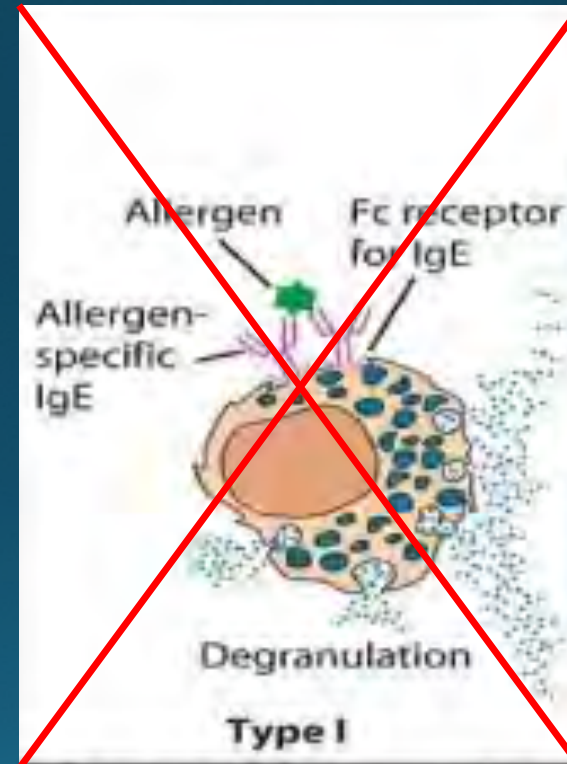
Gell and Coombs Classification of Hypersensitivity Reactions



Classification of Hypersensitivity Reactions

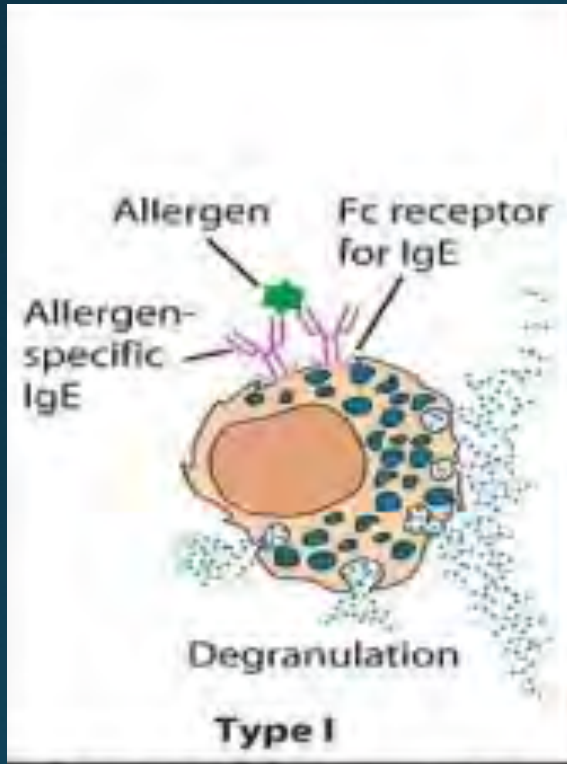


IgE

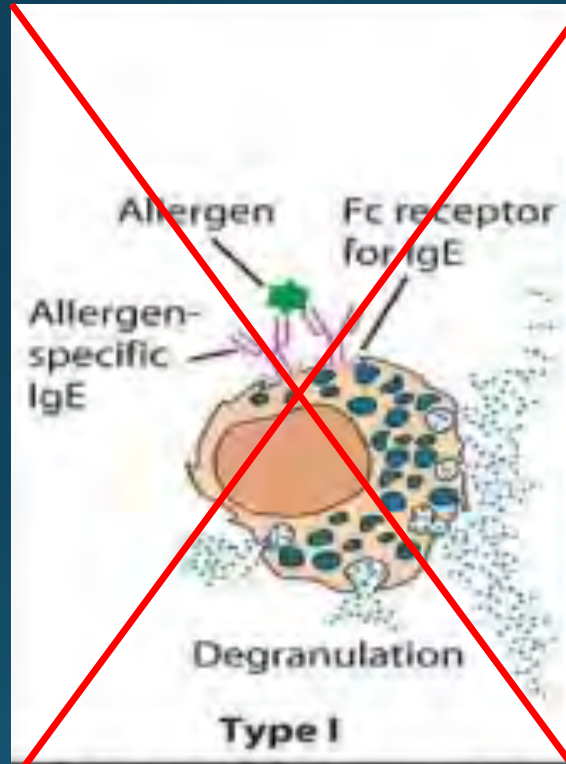


Non-IgE

Classification of Adverse Antibiotic Reactions



IgE



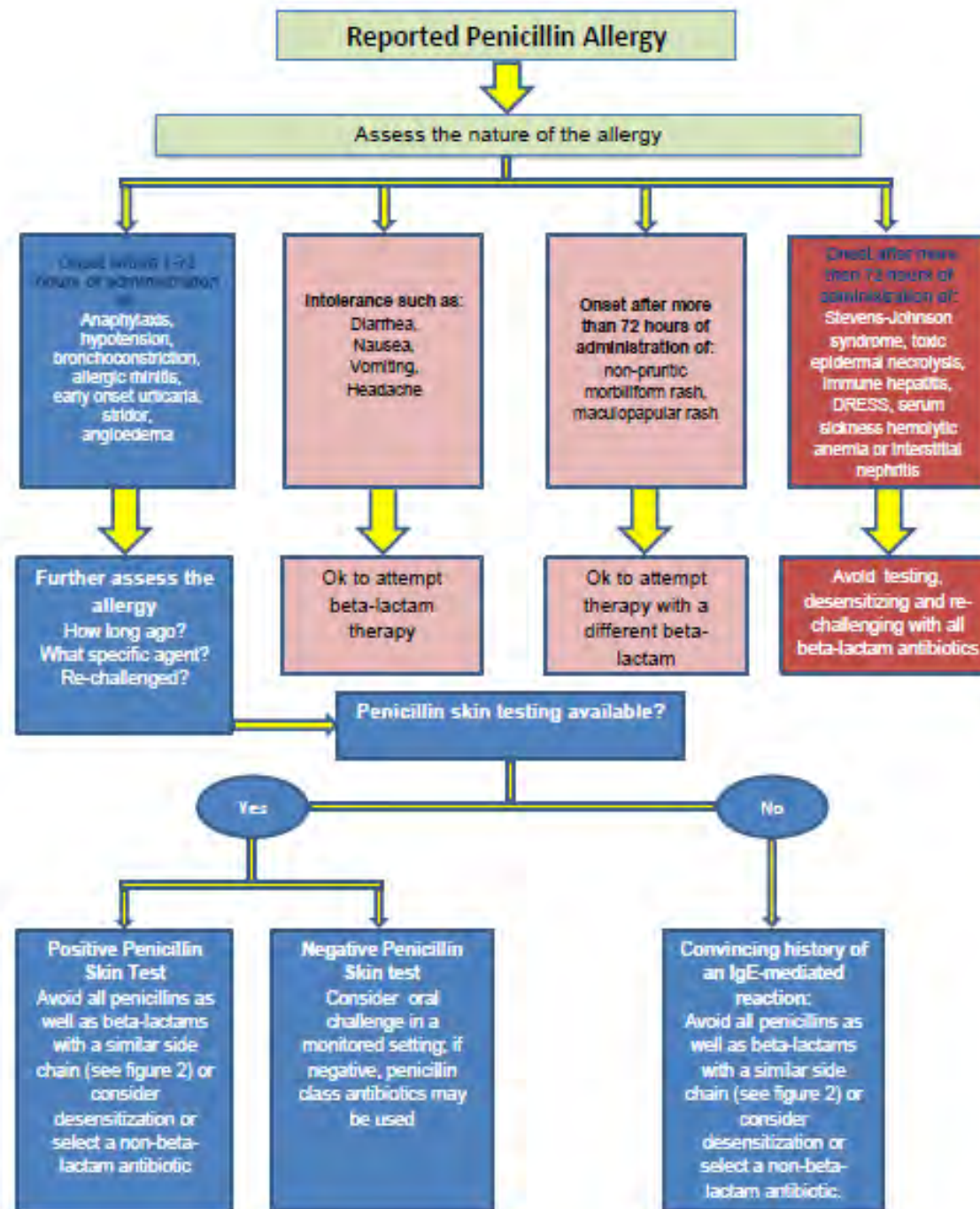
Non-IgE



Unknown



Non-Allergic



Matrix of Beta-Lactam Cross Allergy

		penicillin	amoxicillin	ampicillin	cloxacillin	piperacillin	ticarcillin	cefadroxil	ceFAZolin	cephalexin	cephalothin	cefactor	cefprozil	cefuroxime	cefOXitin	cefixime	cefotaxime	cefTAZidime	cefTRIAxone	cefepime	meropenem	imipenem	ertapenem	aztreonam	
PENICILLINS	penicillin	■	*	*	*	*	*				*				*										
	amoxicillin	*	■	*	*	*	*	*		*		*	*												
	ampicillin	*	*	■	*	*	*	*		*		*	*												
	cloxacillin	*	*	*	■	*	*																		
	piperacillin	*	*	*	*	■	*																		
	ticarcillin	*	*	*	*	*	■																		
1ST GENERATION CEPHALOSPORIN	cefadroxil		*	*				■		*		*	*												
	ceFAZolin								■																
	cephalexin		*	*				*		■		*	*												
	cephalothin	*									■				*		*								
2ND GENERATION CEPHALOSPORIN	cefactor		*	*				*	*			■	*												
	cefprozil		*	*				*	*			*	■												
	cefuroxime													■	*										
	cefOXitin	*									*			*	■										
3RD GENERATION CEPHALOSPORIN	cefixime															■									
	cefotaxime										*						■	*	*						
	cefTAZidime																	■	*				*		
	cefTRIAxone															*			■	*				*	
4TH GEN CEPH	cefepime														*		*		■						
CARBAPENEMS	meropenem																				■	*	*		
	imipenem																				*	■	*		
	ertapenem																			*	*	■	*		
Monobactam	aztreonam																*							■	

NB Provincial Health Authorities Anti-infective Stewardship Committee. Antimicrobial Treatment Guidelines for Common Infections - Management of Penicillin and Beta-Lactam Allergy - June 2016. Available at: <http://en.horizonnb.ca/home/careers-and-education/learning/antimicrobial-use.aspx> (accessed July 4, 2017)

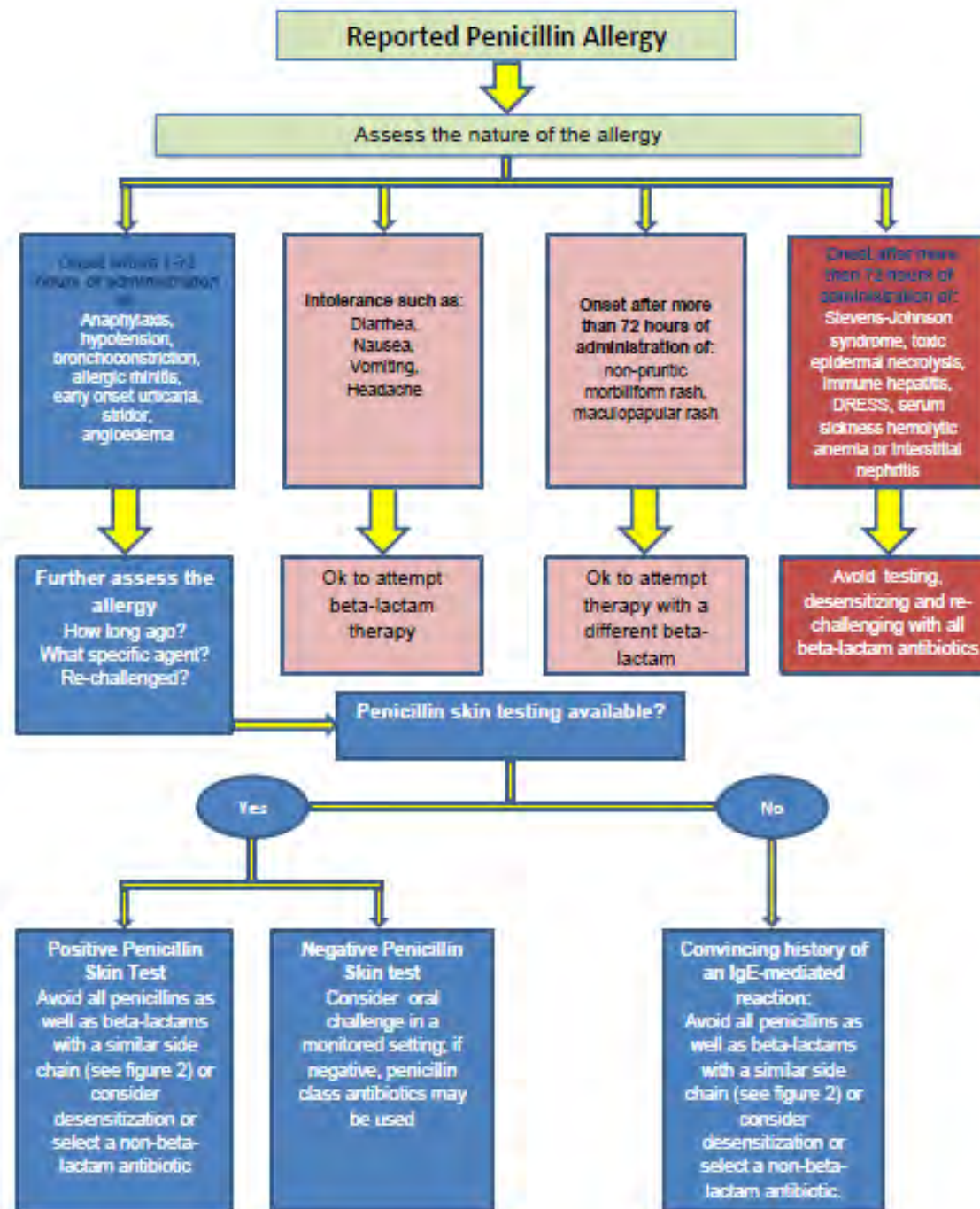
Clinical Case

- 1 yo girl presents with 48 hrs of severe otalgia and new onset fever
- Hx of rash with amoxicillin when treated for AOM 4 weeks ago
- Has bilateral, red, bulging tympanic membranes

What would you do?

Take a history:

Developed pruritic hives within 24 hours of first dose



Matrix of Beta-Lactam Cross Allergy

		penicillin	amoxicillin	ampicillin	cloxacillin	piperacillin	ticarcillin	cefadroxil	ceFAZolin	cephalexin	cephalothin	cefactor	cefprozil	cefuroxime	cefOXitin	cefixime	cefotaxime	cefTAZidime	cefTRIAxone	cefepime	meropenem	imipenem	ertapenem	aztreonam	
PENICILLINS	penicillin	■	*	*	*	*	*				*				*										
	amoxicillin	*	■	*	*	*	*	*		*		*	*												
	ampicillin	*	*	■	*	*	*	*		*		*	*												
	cloxacillin	*	*	*	■	*	*																		
	piperacillin	*	*	*	*	■	*																		
	ticarcillin	*	*	*	*	*	■																		
1ST GENERATION CEPHALOSPORIN	cefadroxil		*	*				■		*		*	*												
	ceFAZolin								■																
	cephalexin		*	*				*		■		*	*												
	cephalothin	*									■				*		*								
2ND GENERATION CEPHALOSPORIN	cefactor		*	*				*	*			■	*												
	cefprozil		*	*				*	*			*	■												
	cefuroxime													■	*										
	cefOXitin	*									*			*	■										
3RD GENERATION CEPHALOSPORIN	cefixime															■									
	cefotaxime										*						■	*	*						
	cefTAZidime																	■	*	*				*	
	cefTRIAxone															*		■	*	*					
4TH GEN CEPH	cefepime														*		*	■	*						
CARBAPENEMS	meropenem																			■	*	*			
	imipenem																			*	■	*			
	ertapenem																			*	*	■			
Monobactam	aztreonam																*							■	

NB Provincial Health Authorities Anti-infective Stewardship Committee. Antimicrobial Treatment Guidelines for Common Infections - Management of Penicillin and Beta-Lactam Allergy - June 2016. Available at: <http://en.horizonnb.ca/home/careers-and-education/learning/antimicrobial-use.aspx> (accessed July 4, 2017)

Prescribing Error #5

- a) Always take an allergy history to classify type of adverse antibiotic reaction (4 types)
- b) Safe to use a beta-lactam with a different side chain for mild immediate / delayed allergic reactions

Summary

1. Prove that your patient has streptococcal pharyngitis before you treat it.
2. Do not prescribe antibiotic for acute rhinosinusitis unless severe (fever+facial pain) or prolonged (x 10 days)
3. Provide WASP or monitor mild AOM in otherwise healthy children > 6 months of age
4. Only prescribe antibiotic for AECOPD if patient has ↑SOB +↑sputum volume/purulence.
5. Cephalosporins with a different side-chain are safe for patients with non-severe penicillin allergy