

Beta-Lactam Hypersensitivity Reaction: CROSS-REACTIVITY

Daniel Yerly, PhD

Drug Allergy Research Laboratory
University-hospital, Bern – Switzerland
WAO – Cancun December 7th 2011

Beta-Lactam Hypersensitivity Reactions

Immediate-type

- IgE mediated
- Symptoms
- Urticaria
- Anaphylaxis
- First encounter: silent sensitization
- Re-exposition: rapid occurrence of the symptoms



Beta-Lactam Hypersensitivity Reactions

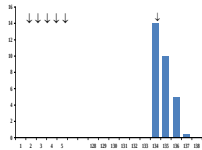
Delayed-type

- T cell mediated
- Symptoms:
 - Maculo-papular Erythema
 - Skin-Rash
 - Severe reaction: Bullae, SJS / TEN, DRESS, AGEP
 - Lesions in intern organs
- Occurance after 8-12 days after starting the therapy

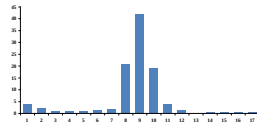


Immediate Hypersensitivity

- First Encounter: silent sensitization
- Reexposition: rapid occurrence of symptoms

**Delayed-type Hypersensitivity**

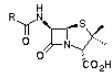
- Occurrence after 8-12 days therapy
- Expansion of drug reacting T cells



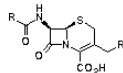
β-lactam Antibiotika

Core Structure Defines The Class

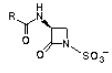
Penicillin G
Penicillin V
Amoxicillin



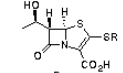
Cephalosporins



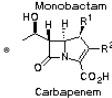
Aztreonam
Azactam ®



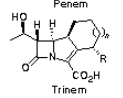
Ertapenem INVANZ ®



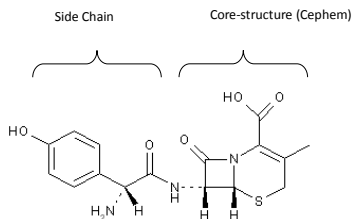
Imipenem Tienam ®
Meropenem Meronem ®
Ertapenem Inva ®



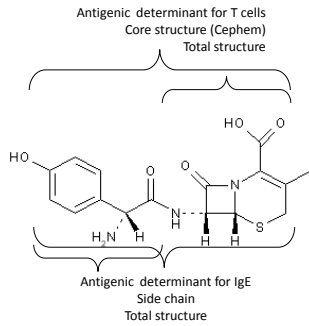
Sanfetrinem



Core-structure and Side-chain

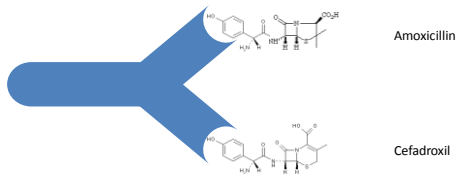


Antigenic determinant in β -Lactams



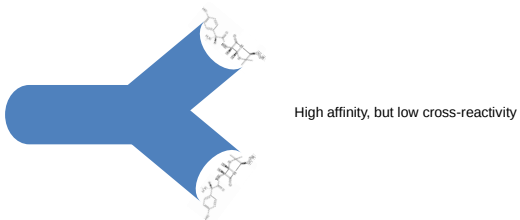
Possible cross-reactivity between different classes

Antibodies (IgE) are able to recognize very tiny determinants on a molecule.



Cave: Possible cross-reactivity between penicillin and cephalosporin due to identical side chain

Possible cross-reactivity between different classes



Crossreactivity

- Concepts
 - Type of the involved immune mechanism
T cell mediated? IgE mediated
 - Analysis of the chemical structure of the culprit β -lactam
Identical core structure?
Delayed type DHR $\rightarrow$ Switch to another β -lactam class
Identical side chain?
Immediate reaction $\rightarrow$ Choose a molecule with another side chain
- Clinic
 - Skin test
 - By negative skin test $\rightarrow$ Provocation test
 - Cave anaphylaxis!

Cephalosporin Challenges in Penicillin ST-Positive (IgE) Patients

Reference (Year)	# of Patients	# (%) of Reactions	Comment
Girard (1968)	23	2 (8.7)	Both reactions to cephaloridine*
Assem (1974)	3	3 (100)	All reactions to cephaloridine*
Warrington (1978)	3	0	
Solley (1982)	27	0	
Saxon (1987)	62	1 (1.6)	Specific cephalosporin not noted
Blanca (1989) cefamandole*	16	2 (12.5)	Both reactions to
Shepherd (1993)	9	0	
Audicana (1994)	12	0	
Novalbos (2001)	23	0	
Macy (2002)	42	1 (2.4)	Reaction to cefixime
TOTAL	220	9 (4.1)	

* These cephalosporins have R-group side chains similar to benzylpenicillin.

Cross-reactivity Penicillin - Cephalosporin

- Cross-reactivity between Penicillin and Cephalosporin is probably over-evaluated
- Cross-reactivity is rare (only 4.1% of skin tests with positive IgE)
 - z.T. bedingt durch Kontaminationen des Cphalosporins mit Penizillinen
 - z.T. bedingt durch gleiche Seitenkette

Case # 1

- Patient mit Urtikaria 2 hr nach Amoxicillin:
- Kann er Cephalosporine 3. Generation haben?

Hautteste	prick/i.d.
– mit PPL	+++
– mit Amoxicillin	++
– Cephadroxil	-

Case # 2

- Patient with a severe exanthem after 7 days of Amoxicillin treatment
- May he receive a Cephalosporine of 3rd generation?

Skintest	i.d.	Epicutan
– PPL	-	nd
– Amoxicillin	-	++
– Cephadroxil	nd	-
– Kefrol (Cefazolin)	nd	-

Aknowledgements



Division of Allergologie,
Inselspital

Prof. Dr. Werner PICHLER

Jacqueline ADAM

Klara K. ERIKSSON

Heidi JAMIN

Karin SCHNYDER

Steve WATKINS

Natascha WUILLEMIN

James YUN

ADR-AC:

Adverse Drug Reactions - Analysis & Consulting

Monika KELLER

Barbara Monika Gertrud Gudrun DAUBNER

Thomas GENTINETTA

Tatjana PETKOVIC

Yuttana SRINOULPRASERT



Swiss Centre for Applied Human Toxicology
Schweizerisches Zentrum für Angewandte Humantoxikologie
Centre Suisse de Toxicologie Humaine Appliquée
Centro Svizzero di Tossicologia Umana Applicata



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