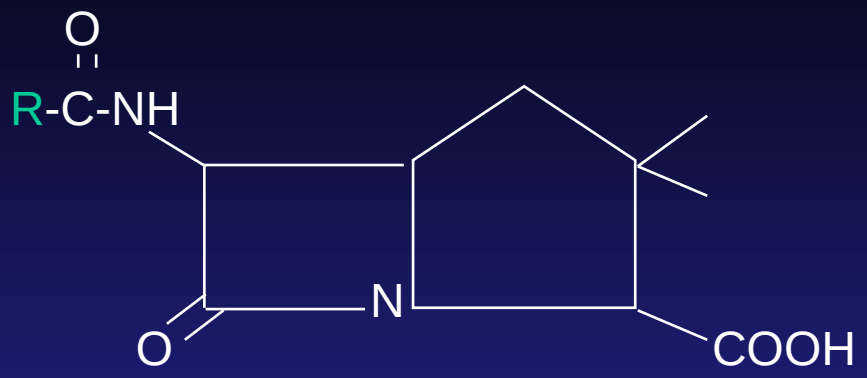
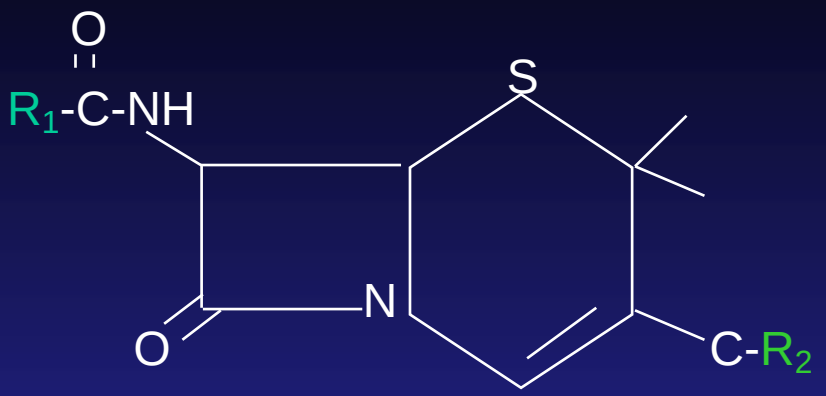
Diagnostica dell'allergia a β-lattamici: "up-to-date"

Antonino Romano
antoninoromano@h-columbus.it
Complesso Integrato Columbus – Roma
IRCCS Oasi Maria S.S. – Troina (EN)

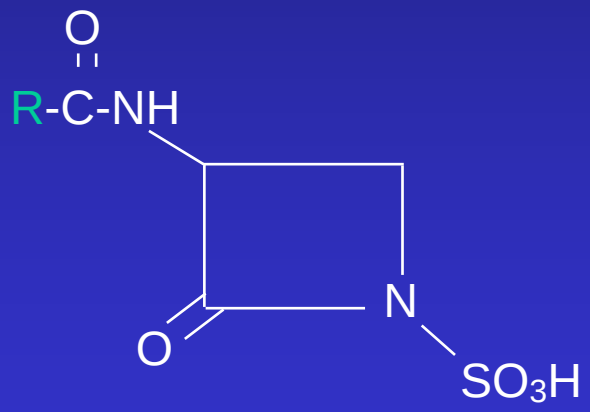
PENICILLINS



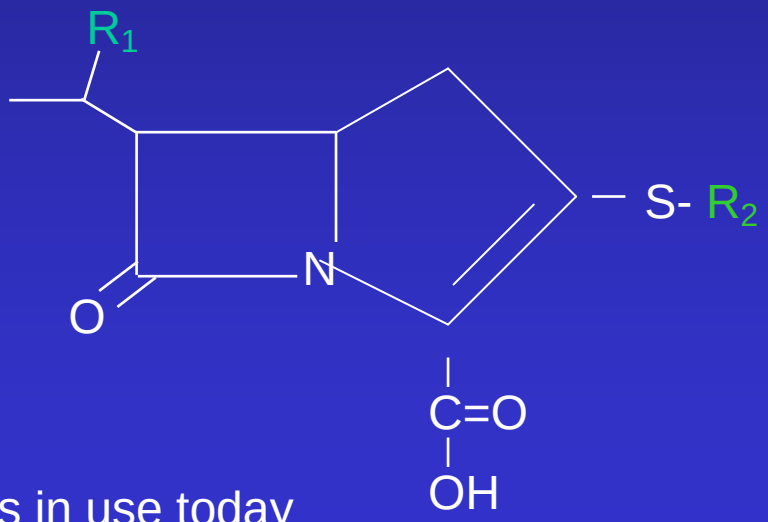
CEPHALOSPORINS



MONOBACTAMS



CARBAPENEMS



Structure of the four classes of betalactam antibiotics in use today

Allergy 2009: 64: 183–193

DOI: 10.1111/j.1398-9995.2008.01924.x

Review article

Update on the evaluation of hypersensitivity reactions to betalactams

Hypersensitivity reactions to betalactams (BLs) are classified as immediate or nonimmediate. The former usually appear within 1 h of drug-intake and are mediated by specific IgE-antibodies. Nonimmediate reactions are those occurring more than 1 h after drug-intake, and they can be T-cell mediated. The diagnostic evaluation of allergic reactions to BLs has changed over the last 5 years, for several reasons. Major and minor determinants are no longer commercially available for skin testing in many countries. In immediate allergic reactions, the sensitivity of skin testing and immunoassays is decreasing and new *in vitro* methods, such as the basophil activation test, are gaining importance for diagnosis. For nonimmediate reactions, skin testing appears to be less sensitive than previous results, although more studies need to be carried out in this direction. Nevertheless, the drug provocation test is still necessary for diagnosis.

M. Blanca[1], A. Romano[2], M. J. Torres[1], J. Férnandez[3], C. Mayorga[4], J. Rodriguez[5], P. Demoly[6], P. J. Bousquet[6], H. F. Merk[7], M. L. Sanz[8], H. Ott[7], M. Atanasković-Marković[9]

[1]Allergy Service, Carlos Haya Hospital, Malaga, Spain; [2]Department of Internal Medicine and Geriatrics, UCSC-Allergy Unit, Complesso Integrato Columbus, Rome and IRCCS Oasi Maria S.S., Troina, Italy; [3]Allergy Section, Department of Clinical Medicine, UMH, Elche, Spain; [4]Research Laboratory, Carlos Haya Hospital-Fundación IMABIS, Malaga, Spain; [5]Service of Immune-Allergology, Hospital S. João, E.P.E, Porto, Portugal; [6]Exploration des allergies et INSERM U454, Hopital Arnaud de Villeneuve, Montpellier Cedex, France; [7]Department of Dermatology and Allergology, Medical Faculty, Aachen, Germany; [8]Allergy and Clinical Immunology Department, Navarra University Hospital, Pamplona, Spain; [9]Department of Allergology and Pulmonology, University Children's Hospital, Belgrade, Serbia

Diagnostic tests of hypersensitivity reactions to drugs

Type of reaction		Type of test
Immediate	*In vitro*	Specific IgE assays
		Flow cytometric basophil activation tests
	In vivo	Skin tests
		Provocation tests

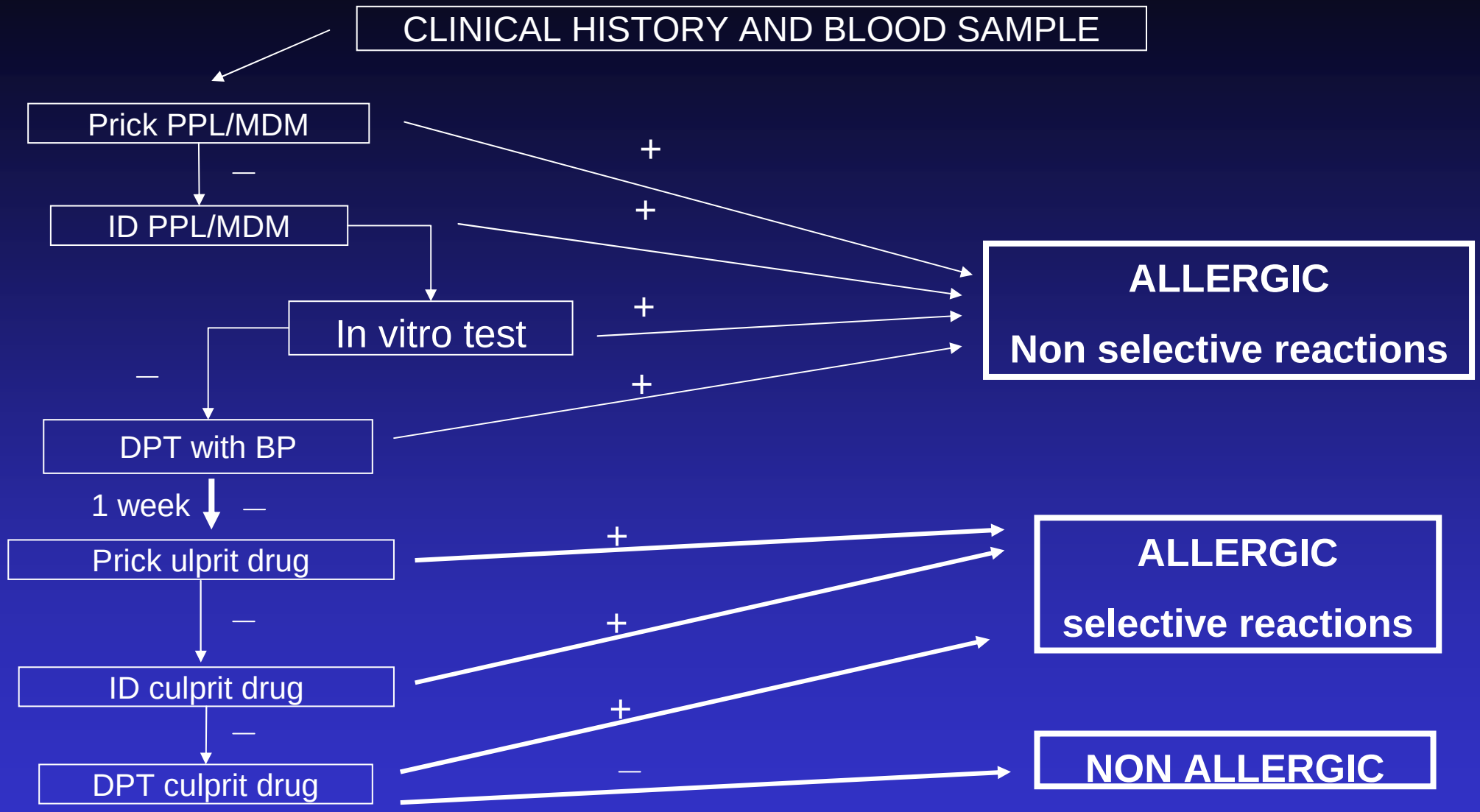
A Romano et al, J Allergy Clin Immunol 2011

Update on the evaluation of hypersensitivity reactions to betalactams

- Immunoassays remain an important diagnostic method
- The basophil activation test has emerged as a useful tool for the diagnosis of immediate allergic reactions to betalactams, especially cephalosporins, for most of which immunoassays are not available

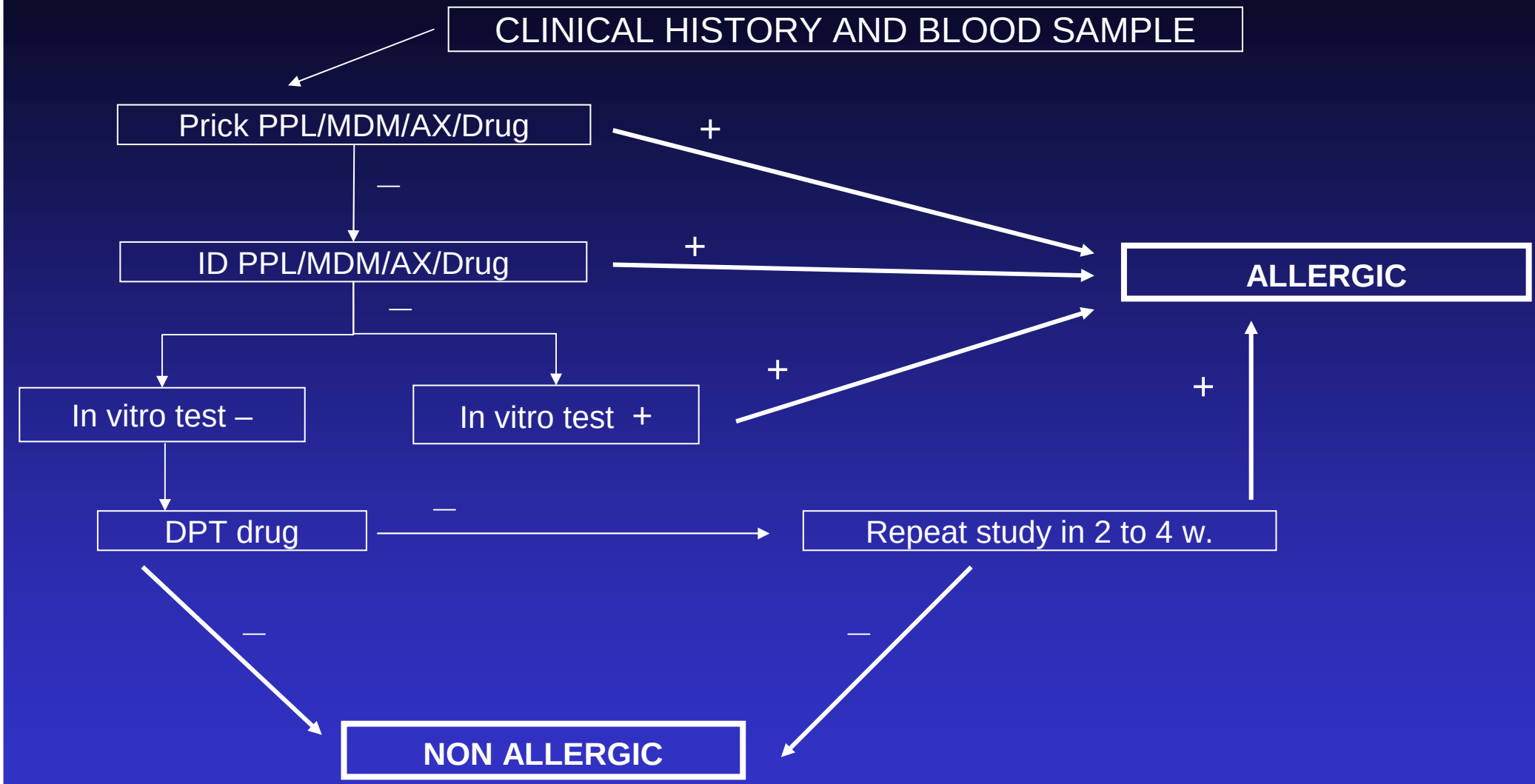
M Blanca et al, Allergy 2009

LONG ALGORITHM



M Blanca et al, Allergy 2009

SHORT ALGORITHM



M Blanca et al, Allergy 2009

The diagnostic interpretation of basophil activation test in immediate allergic reactions to betalactams

Of the 70 patients, 34 (48.6%) were positive to Basotest, 31 (44.3%) to CAP/RAST and 46 (65.7%) to either one or both

MJ Torres et al, Clin Exp Allergy 2004

The diagnostic interpretation of basophil activation test (BAT) in immediate allergic reactions to betalactams

	No. of patients	BAT-positive	%
Group A (ST+)	53	27	50.9%
Group B (ST- / CAP+)	10	6	60%
Group C (ST- / CAP- / DPT+)	7	1	14.3%

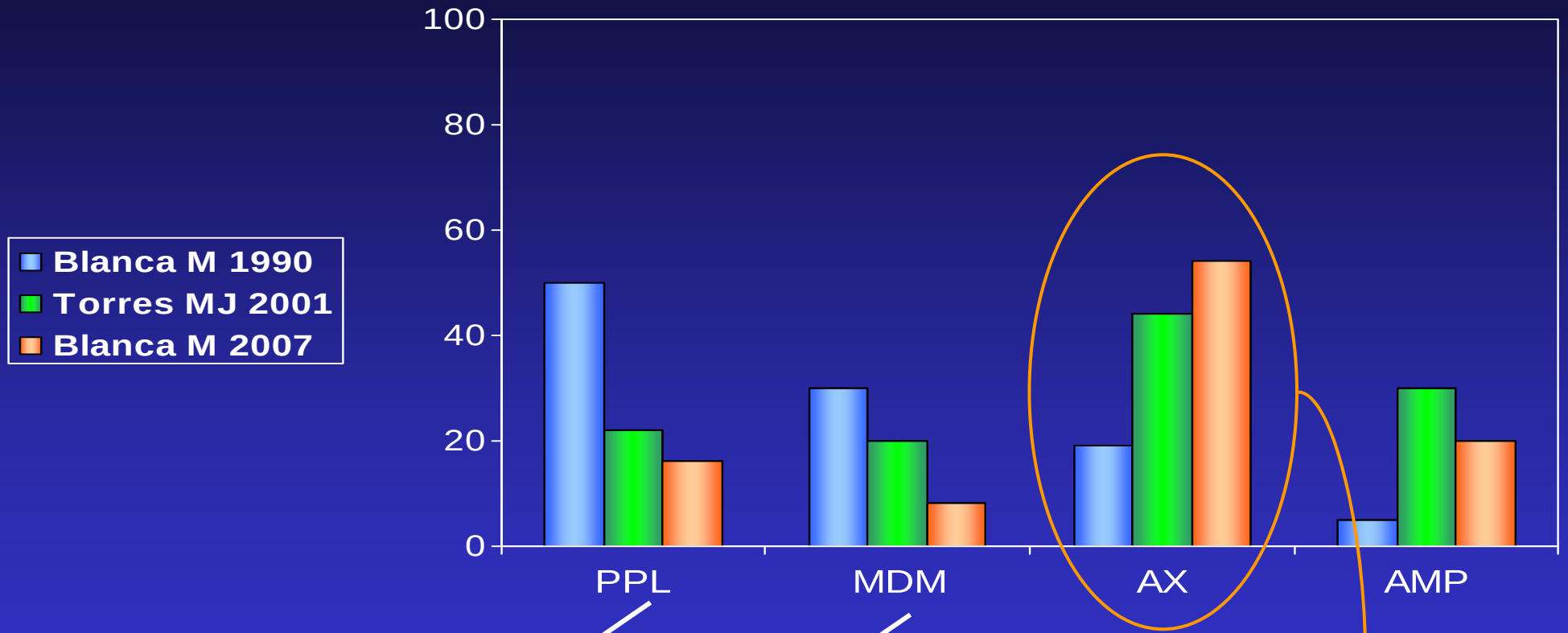
MJ Torres et al, Clin Exp Allergy 2004

Haptens and the highest concentrations recommended for prick and intradermal tests

HAPTEN	DOSE	UNIT
PPL	$5x10^{-5}$	mMol/l
MDM	$2x10^{-2}$	mMol/l
AMOXICILLIN	20	mg/ml
BENZYLPENICILLIN	10,000	IU/ml
CULPRIT DRUG		
• Cephalosporin	2	mg/ml
• Amoxicillin-clavulanic	20	mg/ml
• Ampicillin	20	mg/ml

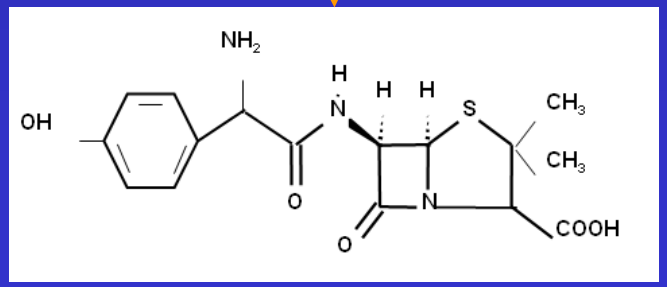
M Blanca et al, Allergy 2009

Which is the major determinant?



Benzylpenicilloil

Benzylpenicillin
Benzylpenicilloic acid
Benzylpenilloic



doi: 10.1111/j.1365-2222.2011.03834.x

Clinical & Experimental Allergy, 41, 1595–1601

ORIGINAL ARTICLE Clinical Allergy

Immunoglobulin E-mediated hypersensitivity to amoxicillin: *in vivo* and *in vitro* comparative studies between an injectable therapeutic compound and a new commercial compound

M. J. Torres[1], A. Romano[2], N. Blanca-Lopez[3], I. Doña[1], G. Canto[3], A. Ariza[1], A. Aranda[1], M. I. Montañez[1], C. Mayorga[1] and M. Blanca[1]

[1]*Research Unit For Allergic Diseases, Allergy Service, Carlos Haya Hospital, Málaga, Spain,* [2]*Allergy Unit, Complesso Integrato Columbus, Rome; IRCCS Oasi Maria S.S., Troina, Italy and* [3]*Allergy Service, Infanta Leonor Hospital, Madrid, Spain*

Haptens and the highest concentrations recommended for prick and intradermal tests

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M Blanca et al, Allergy 2009

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• Amoxicillin-clavulanic	20	mg/ml
• Ampicillin	20	mg/ml

M Blanca et al, Allergy 2009

Nonirritating concentrations for 15 commonly used antibiotics

Antimicrobial drug	Full-strength concentration	NIC (as dilution from full-strength concentration)	No. of patients tested
Cefotaxime	100 mg/mL	10^{-1}	25
Cefuroxime	100 mg/mL	10^{-1}	25
Cefazolin	330 mg/mL	10^{-1}	25
Ceftazidime	100 mg/mL	10^{-1}	25
Ceftriaxone	100 mg/mL	10^{-1}	30
Tobramycin	80 mg/2 mL	10^{-1}	25
Ticarcillin	200 mg/mL	10^{-1}	25
Clindamycin	150 mg/mL	10^{-1}	25

R Empedrad et al, J Allergy Clin Immunol 2003

Skin tests with cephalosporins at a concentration of 20 mg/mL

- **Nonirritating**

215 patients	Cefuroxime	Second-generation cephalosporin
31 patients	Ceftriaxone	Third-generation cephalosporin
24 patients	Cefotaxime	Third-generation cephalosporin
24 patients	Ceftazidime	Third-generation cephalosporin
5 patients	Cefazolin	First-generation cephalosporin

- **Irritating**

7 control subjects	Cefepime	Fourth-generation cephalosporin

S Testi et al, J Investig Allergol Clin Immunol 2010

Haptens and the highest concentrations recommended for prick and intradermal tests

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M Blanca et al, Allergy 2009

Clavulanic acid can be the component in amoxicillin-clavulanic acid responsible for immediate hypersensitivity reactions

HAPTEN	DOSE	UNIT
PPL	$5x10^{-5}$	mMol/l
MDM	$2x10^{-2}$	mMol/l
CLV	20	mg/ml
AMOXICILLIN	20	mg/ml
AMOXICILLIN+CLV	20+4	mg/ml

M J Torres et al, J Allergy Clin Immunol 2010

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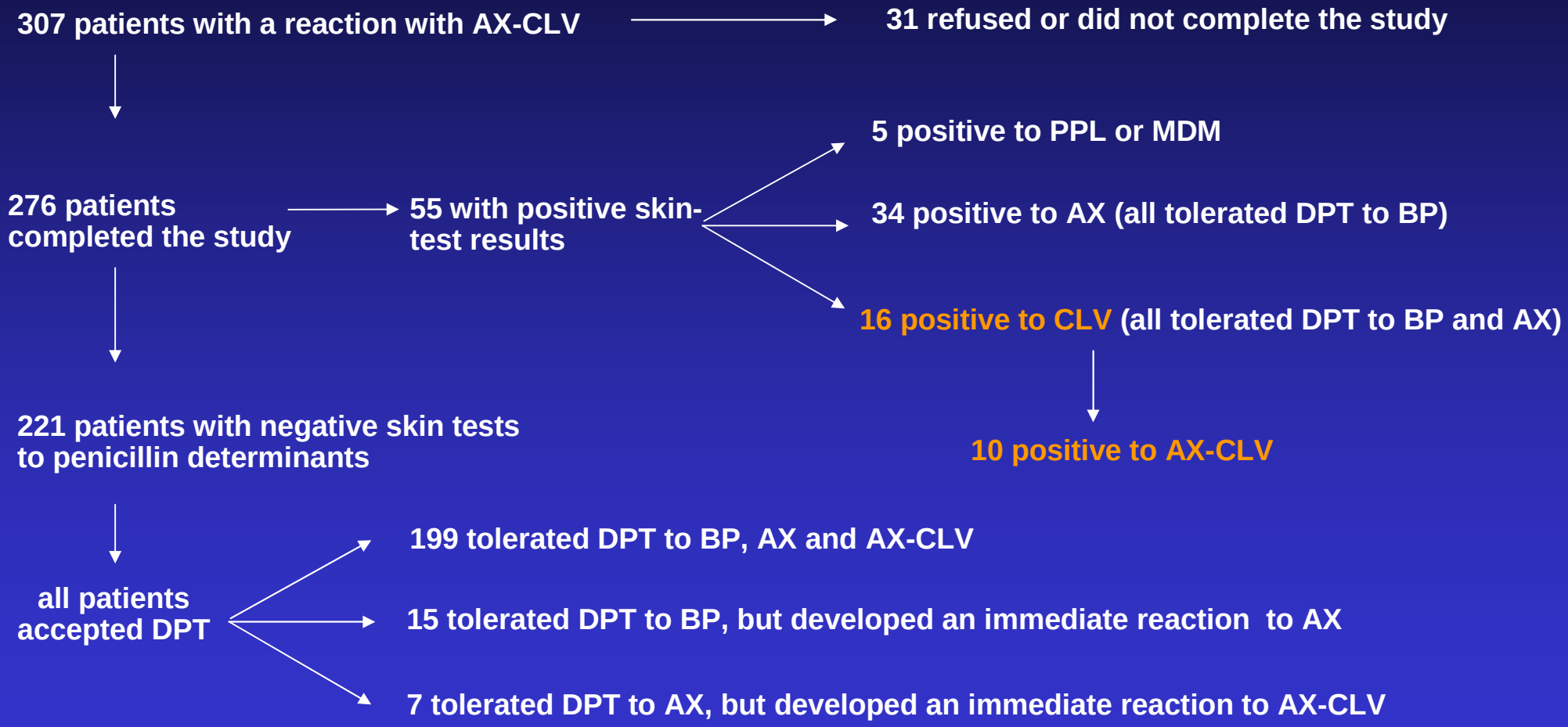
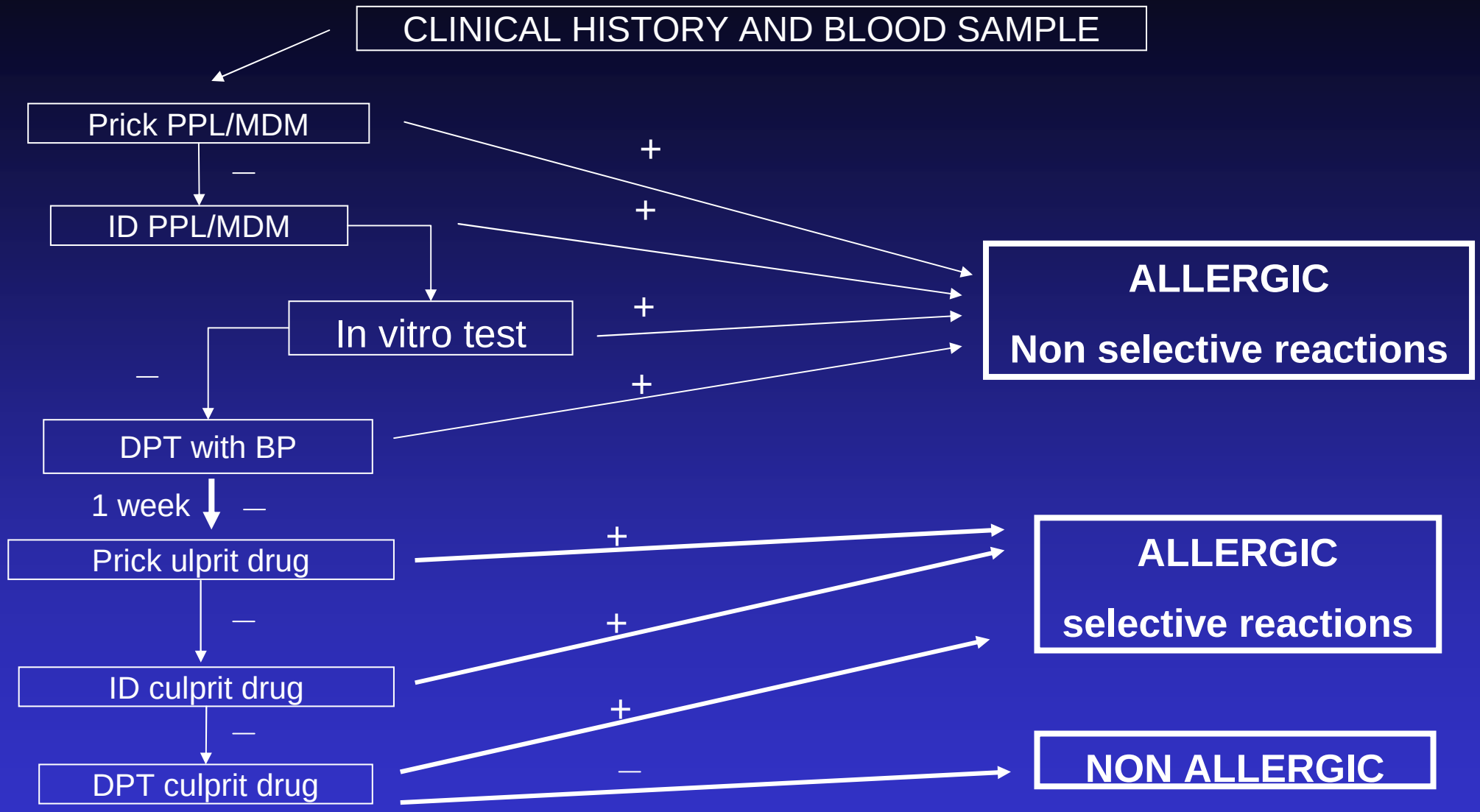


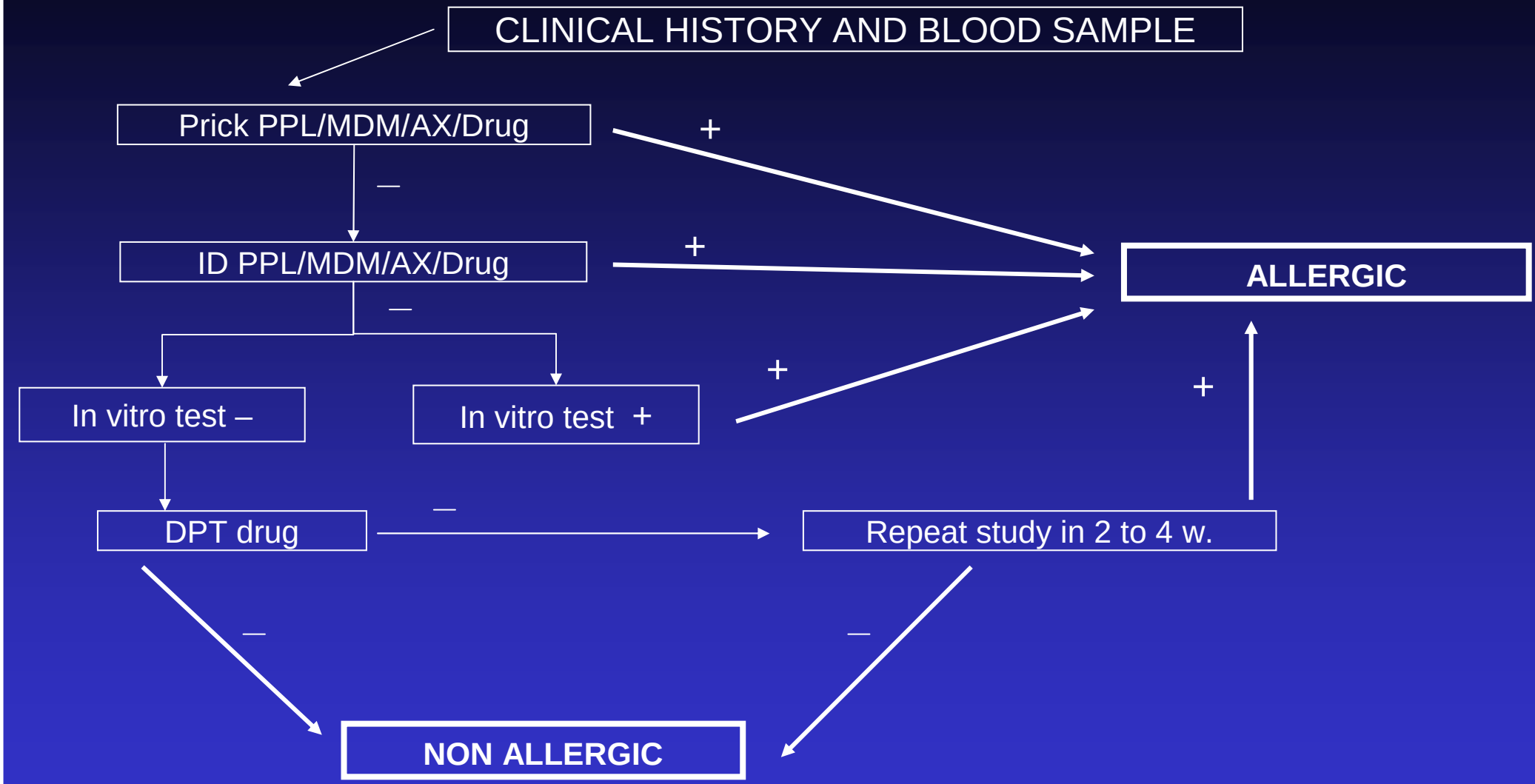
M J Torres et al, J Allergy Clin Immunol 2010

LONG ALGORITHM



M Blanca et al, Allergy 2009

SHORT ALGORITHM



M Blanca et al, Allergy 2009

Controlled administration of penicillin to patients with a positive history but negative skin and specific serum IgE tests

- ***Positive skin tests to at least one determinant observed in 203 (61.5%) out of the 330 subjects evaluated***

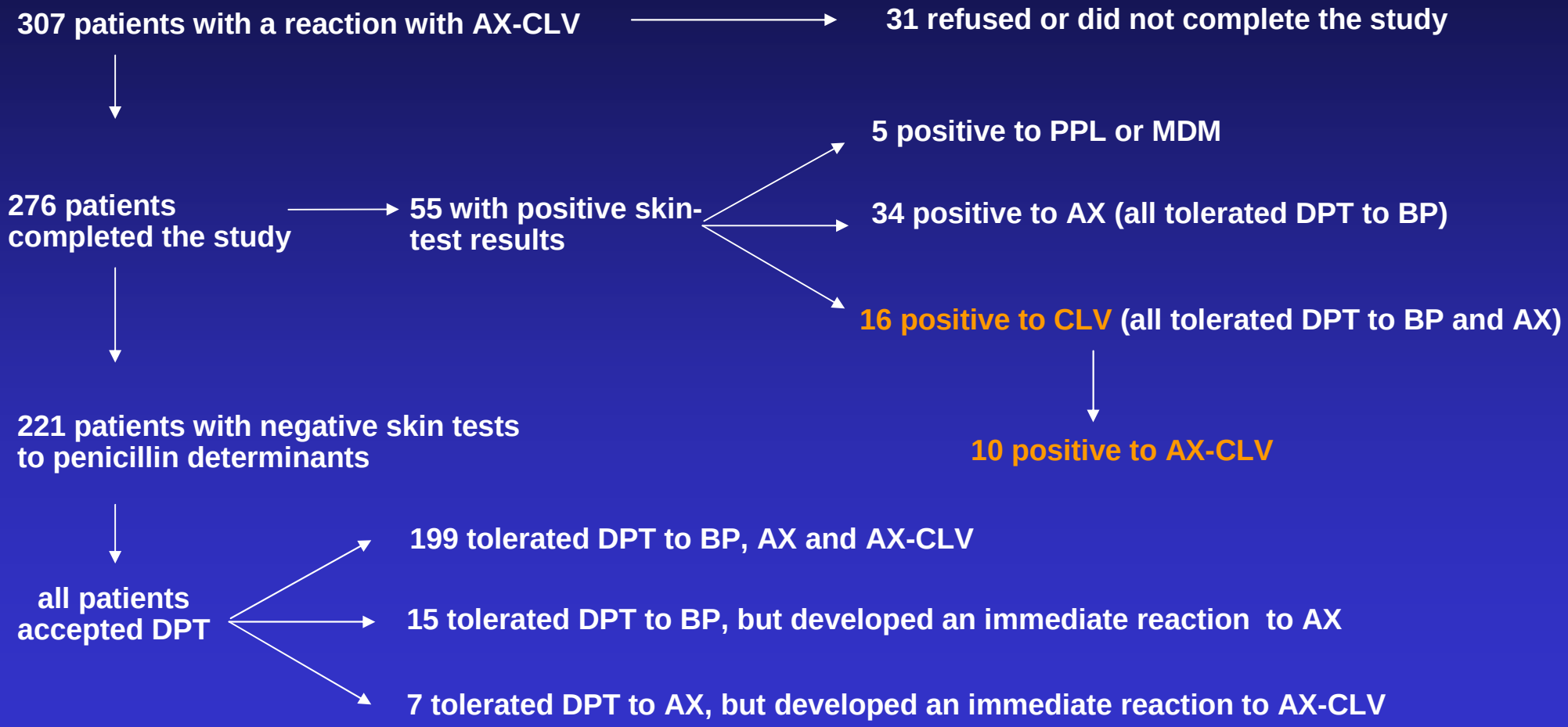
- 38 (11.5%) out of the 330 subjects were skin test negative and had positive benzylpenicilloyl and/or amoxicilloyl in vitro tests (CAP-FEIA)

- 49 (14.8%) out of the 330 subjects were skin test and CAP-FEIA negative and reacted to the controlled administration

- 40 (12.1%) out of the 330 subjects were negative in allergologic workups, including challenges

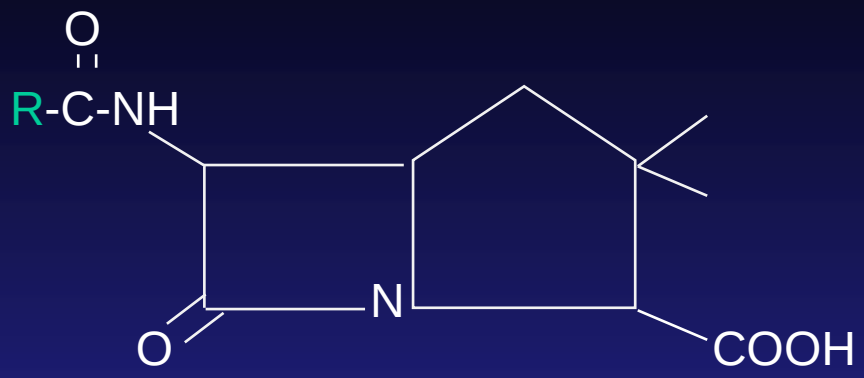
MJ Torres et al, Clin Exp Allergy 2002

Clavulanic acid can be the component in amoxicillin-clavulanic acid responsible for immediate hypersensitivity reactions

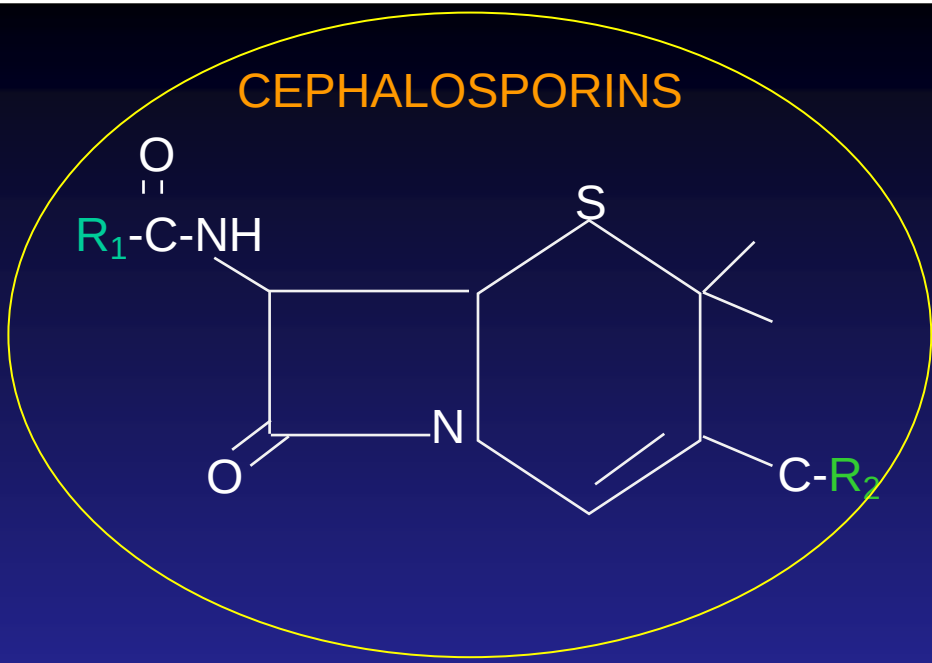


M J Torres et al, J Allergy Clin Immunol 2010

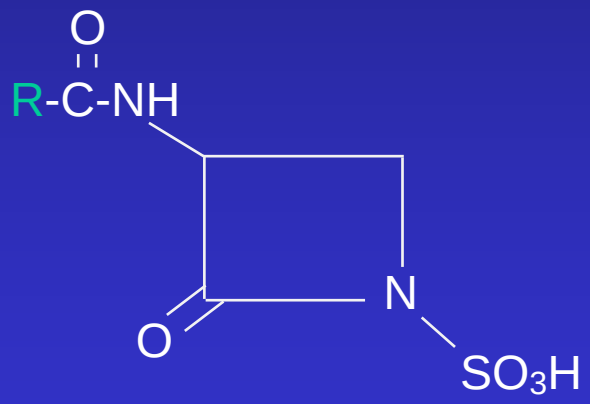
PENICILLINS



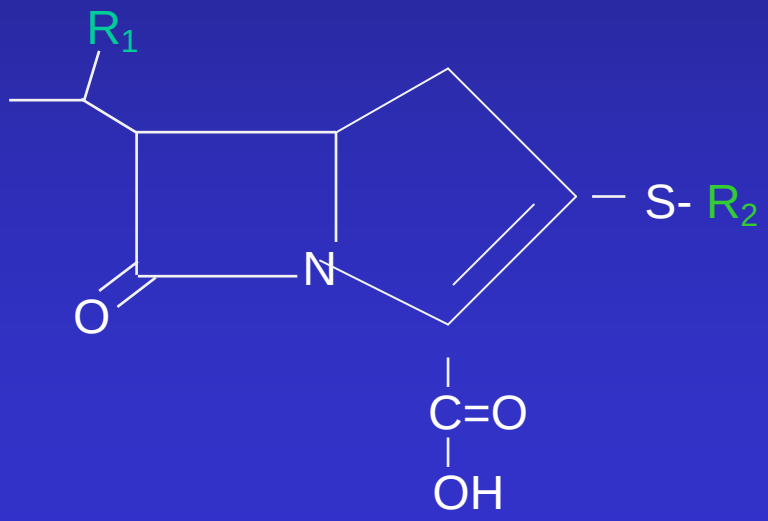
CEPHALOSPORINS



MONOBACTAMS



CARBAPENEMS



Clin Exp Allergy 2005; 35:1234–1242 doi:10.1111/j.1365-2222.2005.02317.x

Diagnosing immediate reactions to cephalosporins

A. Romano*†, R.-M. Guéant-Rodriguez‡§, M. Viola*, F. Amoghly‡, F. Gaeta*, J.-P. Nicolas‡ and J.-L. Guéant‡

*Department of Internal Medicine and Geriatrics, UCSC-Allergy Unit, Complesso Integrato Columbus, Rome, Italy, †IRCCS Oasi Maria S.S., Troina, Italy, ‡Laboratoire de Pathologie Cellulaire et Moléculaire en Nutrition, EMI INSERM 0014 et IFREMER 20, Faculté de Médecine, Vandoeuvre, France and §Service de Cardiologie, CHU de Nancy-Brabois, Vandoeuvre, France

Summary

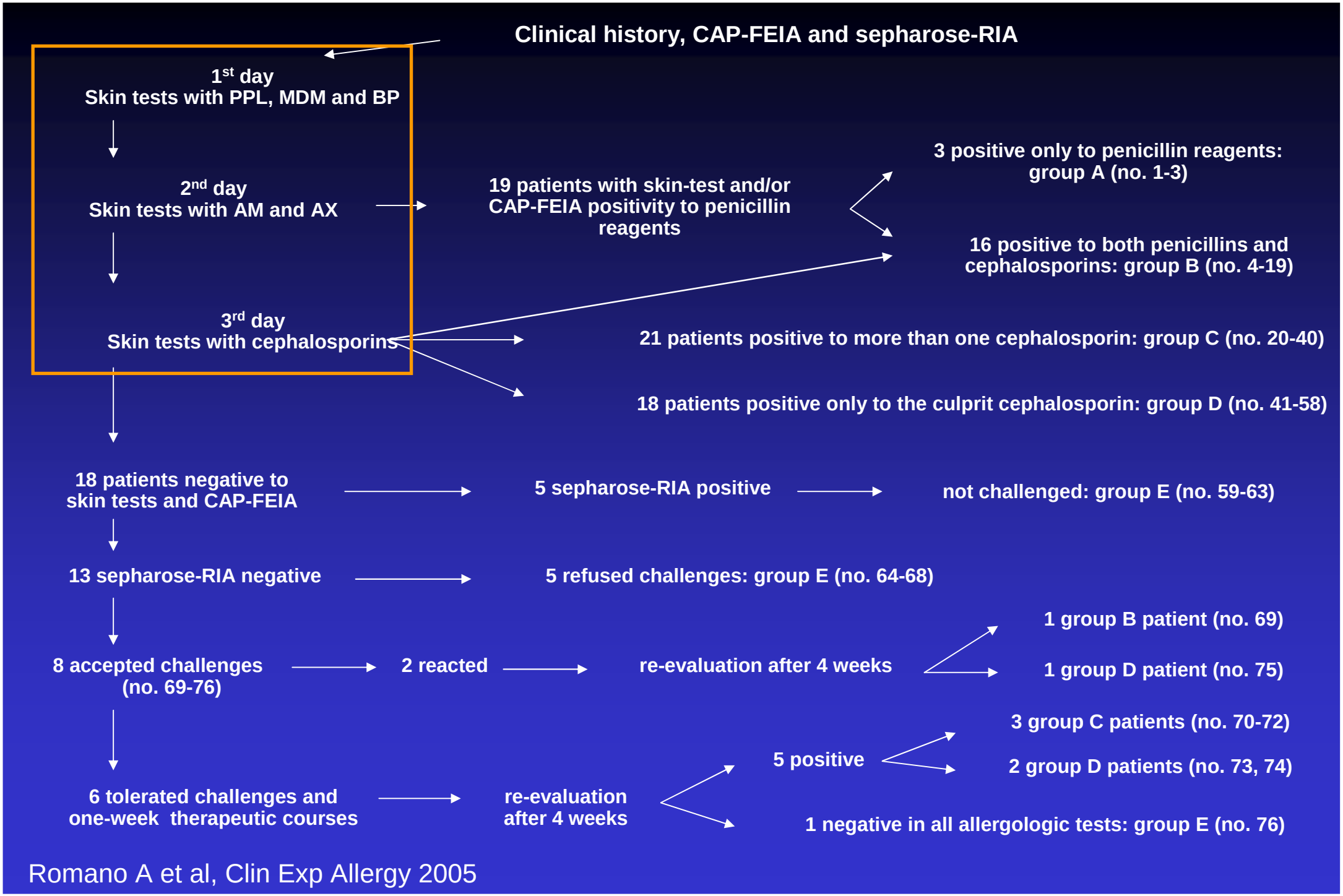
Background After penicillins, cephalosporins are the betalactams that most often induce IgE-mediated reactions. The development of diagnostic tests has been delayed, however, because the cephalosporin allergenic determinants have not been properly identified.

Objective To evaluate the usefulness of skin tests, serum specific IgE assays, and challenges in diagnosing immediate reactions to cephalosporins and to clarify the pathogenic mechanism of such reactions.

Methods We studied 76 adults with immediate reactions to cephalosporins, mainly ceftriaxone, cefotaxime, and ceftazidime. Skin tests and serum specific IgE assays were performed for culprit cephalosporins and cefaclor, as well as for penicillin, amoxicillin, and ampicillin. Some subjects with negative results underwent challenges and re-evaluations. Responses to cephalosporins other than the culprit ones were also studied.

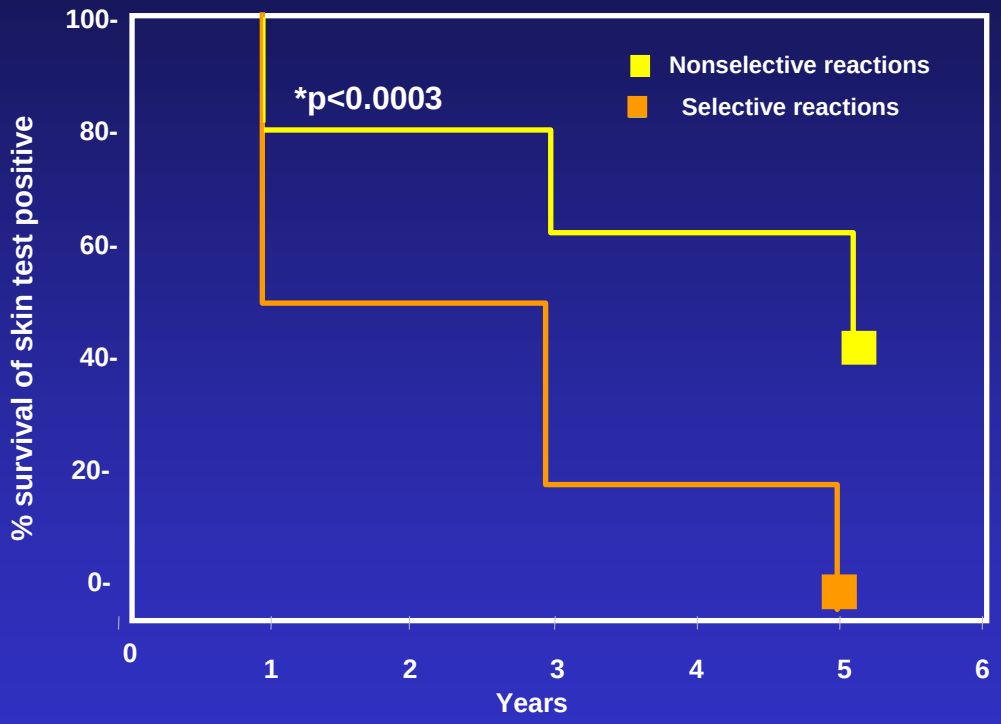
Results In the first allergologic work-up, an IgE-mediated hypersensitivity to penicillins and/or cephalosporins was diagnosed in 63 (82.9%) of the 76 patients on the basis of skin-test and/or specific IgE assay positivity. Of the 13 negative patients, eight accepted challenges and underwent re-evaluations. Considering both first- and second-evaluation results, the skin-test-positivity rate increased from 76.3% to 85.5% and that of sepharose-radioimmunoassay positivity from 67.1% to 74.3%. Overall, an IgE-mediated hypersensitivity was diagnosed in 70 patients (in seven after retesting). On the basis of skin-test and CAP-FEIA results, we classified our 76 patients into five groups: group A (three patients), positive only to penicillin reagents; B (17), positive to both cephalosporin and penicillin reagents; C (24), positive to more than one cephalosporin; D (21), positive only to the responsible cephalosporin; E (11) negative to skin tests and CAP-FEIA, including five sepharose-radioimmunoassay positive.

Conclusions Most immediate reactions to cephalosporins appear to be IgE-mediated. Cephalosporin skin testing and sepharose-radioimmunoassay are useful tools for evaluating these reactions. Cephalosporin IgE-mediated hypersensitivity may be a transient condition; therefore, allergologic exams should be repeated in patients with negative initial allergologic work-ups, including challenges.

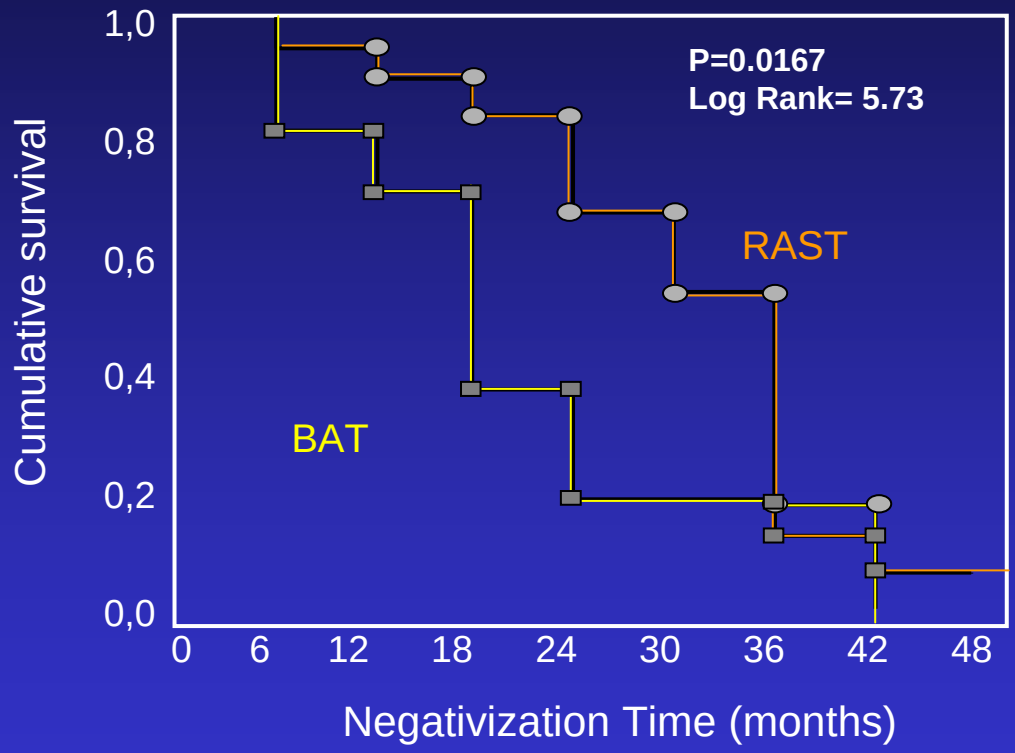


Romano A et al, Clin Exp Allergy 2005

Skin test, RAST, and BAT sensitivity over time



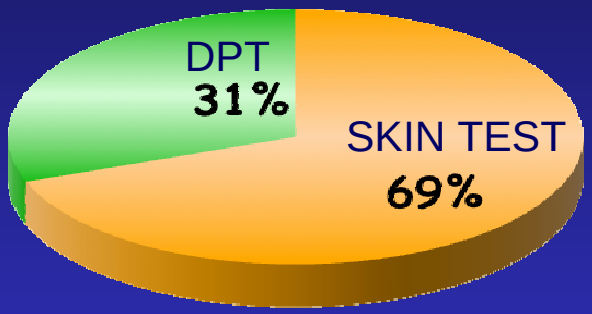
M Blanca et al, J Allergy Clin Immunol 1999



TD Fernández et al, Clin Exp Allergy 2008

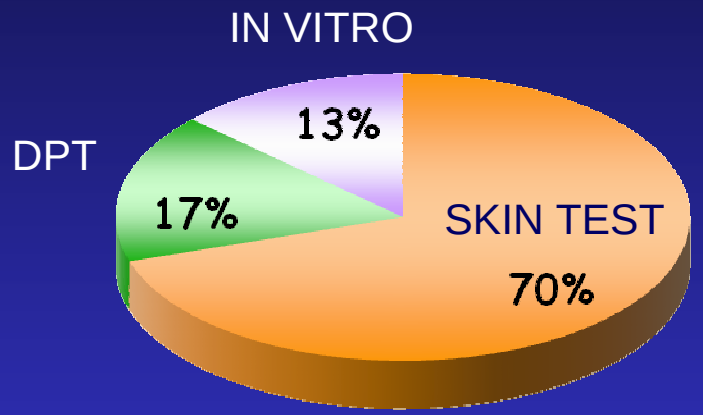
SENSITIVITY OF THE DIAGNOSTIC METHODS

N= 257
Confirmed BL allergy



Bousquet PJ et al, Clin Exp Allergy 2008

N= 290
Confirmed BL allergy



Torres MJ et al, Allergy 2001

DPT is still needed for confirming the diagnosis and has to be performed in patients with suspected antibiotic allergy

Haptens and doses recommended for drug provocation tests

DRUG	Benzylpenicillin	Penicillin V	Amoxicillin
DOSE	10^3 IU/ml 10^4 IU/ml 10^5 IU/ml $5x10^5$ IU/ml	5 mg 50 mg 150 mg 200 mg	5 mg 50 mg 100 mg 150 mg 200 mg
CUMULATIVE DOSE	$6x10^5$ IU/ml	400 mg	500 mg
ROUTE	IM	Oral	Oral
INTERVAL	45-60 min	45-60 min	45-60 min

M Blanca et al, Allergy 2009

Allergy 2009: 64: 183–193

DOI: 10.1111/j.1398-9995.2008.01924.x

Review article

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Diagnostic tests of hypersensitivity reactions to drugs

Type of reaction		Type of test
Nonimmediate	*In vitro*	Lymphocyte transformation or activation tests
		Enzyme-linked immunospot assays for analysis of antigen-specific, cytokine-producing cells
	In vivo	Delayed-reading intradermal tests
		Patch tests
		Provocation tests

A Romano et al, J Allergy Clin Immunol 2011

Original article

CD69 upregulation on T cells as an *in vitro* marker for delayed-type drug hypersensitivity

A. Beeler et al, Allergy 2008

Patients' characteristics

Patient	Age/sex	Culprit drug	Disease	LTT	Patch test	Duration*
AS	35 years/f	AMX	MPE	Positive†	−/−‡	14 months
BK	35 years/m	AMX	MPE	Positive	−/−	8 months
LDM	57 years/f	AMX	MPE	Positive	−/−	5 months
HH	47 years/m	AMX	SJS	Positive	++/+++	9 months
SF	26 years/f	AMX	MPE	Positive	++/++	2 months
ES	82 years/f	AMX, CLA	E.L.E.§, fever, thrombocytosis	Positive	n.d./n.d.¶	5 months
WZ	64 years/m	AMX, PHE, SMX	DRESS, MPE, erythrodermia	Positive	−/−	19 months
UNO	45 years/m	SMX	MPE, malaise	Positive	++/++	12 years
HB	71 years/m	SMX	SJS	Positive	−/−	2 months
AA	48 years/m	SP	DRESS	Positive	−/−	13 months
EK	19 years/m	CFX	MPE, fever	Positive	−/−	8 months
GR	80 years/f	MXFX	MPE	Positive	+/+	10 months
VG	31 years/f	VCM	AGEP	Positive	+++/n.d.	14 months
CS	35 years/f	CBZ	DRESS	positive	−/−	14 months
GO	45 years/f	CBZ	AGEP, erythrodermia	positive	+++/n.d.	2 months

*Time interval between acute allergy and testing.
†SI_{LTT} >2.
‡−, no reaction; +, exanthema and sparse induration; ++, exanthema with well-defined induration; +++, exanthema, induration and vesicles after 48 h/72 h respectively.
§Elevated liver enzymes.
¶Not determined.

A. Beeler et al, Allergy 2008

Detection and quantification of drug-specific T cells in penicillin allergy

- The frequency of circulating specific T cells was analyzed by IFN-γ enzyme-linked immunospot (ELISPOT) in 22 patients with an allergic maculo-papular exanthema caused by amoxicillin

- Amoxicillin-specific circulating T cells were detected in 20 of 22 patients with frequencies ranging from 1:8,000 to 1:30,000 circulating leucocytes

A Rozieres et al, Allergy 2009

Detection and quantification of drug-specific T cells in penicillin allergy

- No reactivity was observed in 46 control patients, including 15 with IgE-mediated hypersensitivity to amoxicillin
- Amoxicillin-specific T cells were still detectable several years after the occurrence of allergic reactions

A Rozieres et al, Allergy 2009

Allergy 2004: 59: 1153–1160
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ALLERGY
DOI: 10.1111/j.1398-9995.2004.00678.x

Review article

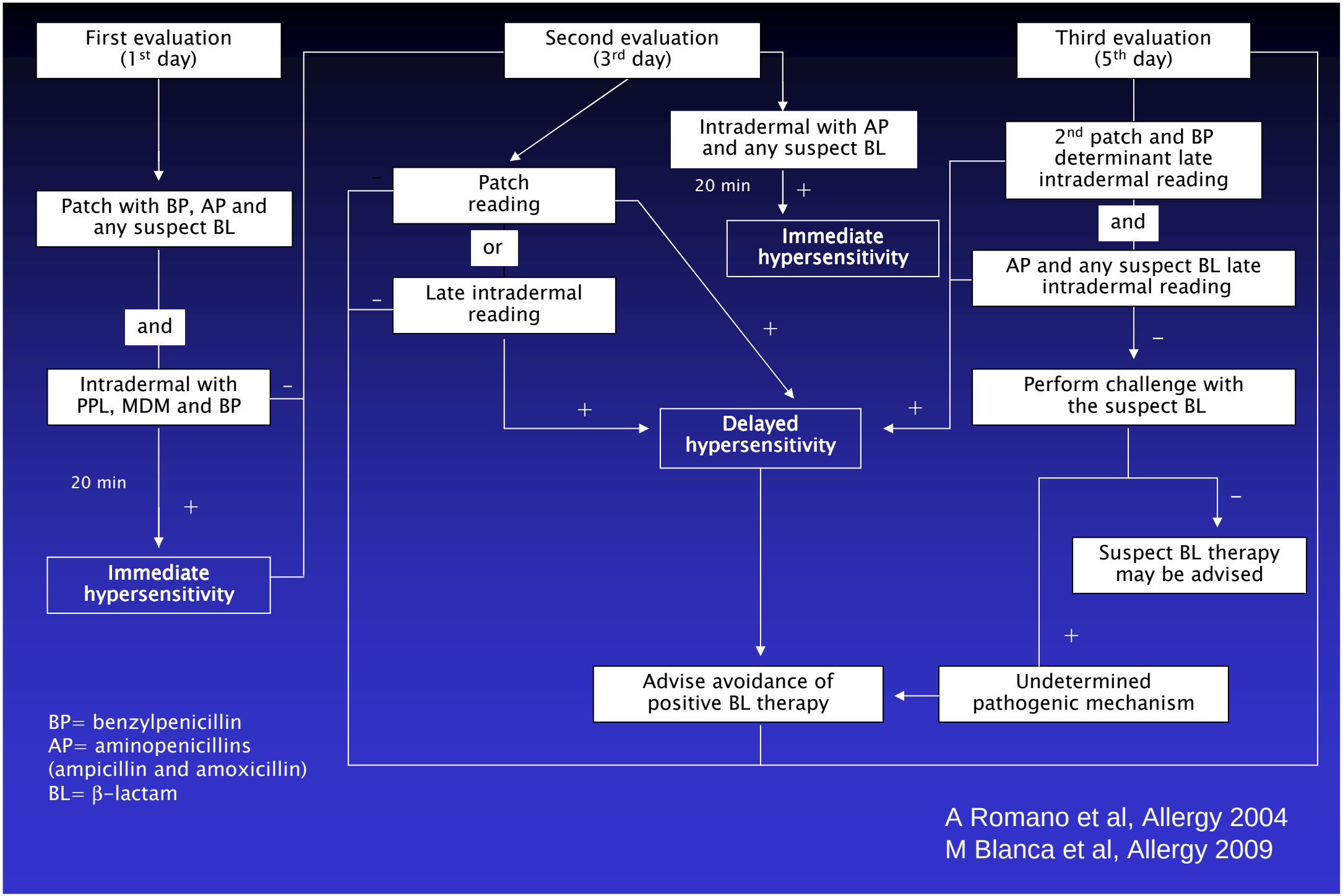
Diagnosis of nonimmediate reactions to β-lactam antibiotics

Nonimmediate manifestations (i.e. occurring more than 1 h after drug administration), particularly maculopapular and urticarial eruptions, are common during β-lactam treatment. The mechanisms involved in most nonimmediate reactions seem to be heterogeneous and are not yet completely understood. However, clinical and immunohistological studies, as well as analysis of drug-specific T-cell clones obtained from the circulating blood and the skin, suggest that a type-IV (cell-mediated) pathogenic mechanism may be involved in some nonimmediate reactions such as maculopapular or bullous rashes and acute generalized exanthematous pustulosis. In the diagnostic work-up, the patient's history is fundamental; patch testing is useful, together with delayed-reading intradermal testing. The latter appears to be somewhat more sensitive than patch testing, but also less specific. In case of negative allergologic tests, consideration should be given to provocation tests, and the careful administration of the suspect agents. With regard to *in vitro* tests, the lymphocyte transformation test may contribute to the identification of the responsible drug.Under the aegis of the European Academy of Allergology and Clinical Immunology (EAACI) interest group on drug hypersensitivity and the European Network for Drug Allergy (ENDA), in this review we describe the general guidelines for evaluating subjects with nonimmediate reactions to β-lactams.

A. Romano[1], M. Blanca[2], M. J. Torres[2], A. Bircher[3], W. Aberer[4], K. Brockow[5], W. J. Pichler[6], P. Demoly[7], for ENDA and the EAACI interest group on drug hypersensitivity*

[1]Oasi Maria SS, Troina, and C. I. Columbus, Rome, Italy; [2]Research Unit for Allergic Diseases, Carlos Haya Hospital, Malaga, Spain; [3]Department of Dermatology, Basel, Switzerland; [4]Department of Environmental Dermatology, Graz, Austria; [5]Klinik und Poliklinik für Dermatologie und Allergologie, Muenchen, Germany; [6]Clinic for Rheumatology and Clinical Immunology/Allergology, Inselspital, Bern, Switzerland; [7]Maladies Respiratoires-INSERM U454, Hôpital Arnaud de Villeneuve, Montpellier, France

*ENDA and the EAACI interest group on drug hypersensitivity are given in Appendix.


First evaluation (1st day)
Second evaluation (3rd day)
Third evaluation (5th day)
Patch with BP, AP and any suspect BL
and
Intradermal with PPL, MDM and BP
20 min
+
Immediate hypersensitivity
−
Patch reading
or
Late intradermal reading
−
+
Intradermal with AP and any suspect BL
20 min
+
Immediate hypersensitivity
+
Delayed hypersensitivity
+
2nd patch and BP determinant late intradermal reading
and
AP and any suspect BL late intradermal reading
−
Perform challenge with the suspect BL
−
Suspect BL therapy may be advised
+
Undetermined pathogenic mechanism
Advise avoidance of positive BL therapy
BP= benzylpenicillin
AP= aminopenicillins (ampicillin and amoxicillin)
BL= β-lactam
A Romano et al, Allergy 2004
M Blanca et al, Allergy 2009

Manifestations reported by the subjects and results of allergologic evaluation

Symptoms	Patients	Patients with DH	Patients with IH
Maculopapular rash	173	93 (53.7%)	1 (0.6%)
Urticaria	33	-	1 (3%)
Erythema	22	4 (18.2%)	1 (4.5%)
Angioedema	13	-	-
Urticaria/angioedema	13	-	-
Local reaction	1	1 (100%)	-
Other manifestations	4	-	-
Total	259	98 (37.8%)	3 (1.1%)

A Romano et al, Int Arch Allergy Immunol 2002

Allergy

ORIGINAL ARTICLE

BIOTECHNOLOGY AND *IN VITRO* DIAGNOSTICS

The very limited usefulness of skin testing with penicilloyl-polylysine and the minor determinant mixture in evaluating nonimmediate reactions to penicillins

A. Romano[1,2], F. Gaeta[1], R. L. Valluzzi[1], C. Caruso[1], G. Rumi[1] & P. J. Bousquet[3,4]

[1]Allergy Unit, Complesso Integrato Columbus, Rome, Italy; [2]IRCCS Oasi Maria S.S., Troina, Italy; [3]Département de Biostatistique, Epidemiologie, Recherche Clinique, Santé Publique et Information Médicale, Hôpital Carémeau, BESPIM, GHU Caremau, Nimes, France; [4]Exploration des Allergies, Hôpital Arnaud de Villeneuve, Montpellier Cedex, France

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Table 2 Patterns of skin test and patch test reactivity in 162 patients allergic to penicillins

Patch test results, *n* (%)				Skin test results, *n* (%)						
BP	AM	AX	Responsible[§]	PPL	MDM	BP	AM	AX	Responsible[§]	Pattern, *n* (%)
−	+	+	+	−	−	−	+	+	+	74 (45.7)
+	+	+	+	−	−	+	+	+	+	24 (14.8)
−	+	+	+	−	−	+	+	+	+	23 (14.3)
+	+	+	+	−	+	+	+	+	+	13 (8)
−	−	−	−	−	−	−	+	+	+	6 (3.7)
−	−	−	−	+[¶]	−	−	−	−	−	4[¶] (2.5)
−	+	−	−	−	−	−	+	+	+	2 (1.3)
−	+	+	+	+*	−	−	+	+	+	2 (1.3)
+	+	+	+	+*	−	+	+	+	+	1 (0.6)
+	+	+	−	−	−	+	+	+	+	1 (0.6)
+	−	−	+	−	+	+	+	+	+	1 (0.6)
−	+	+	+	−	−	−	−	+	+	1 (0.6)
−	+	+	+	−	+	+	+	+	+	1 (0.6)
−	+	+	+	−	+	−	+	+	+	1 (0.6)
−	+	−	+	−	−	−	+	+	+	1 (0.6)
−	+	−	+	−	−	+	+	+	+	1 (0.6)
−	+	+	−	−	−	−	+	+	+	1 (0.6)
−	−	−	+	−	−	−	−	−	+	1 (0.6)
−	−	−	−	−	−	+	−	−	+*	1 (0.6)
−	−	−	−	+*	−	−	+	+	+	1 (0.6)
−	−	−	−	+*	+*	−	+	+	+	1 (0.6)
−	−	−	−	−	−	−	−	+[¶]	+*	1 (0.6)
40 (24.7)	146 (89.5)	141 (87)	144 (88.9)	9 (5.5)	17 (10.5)	66 (40.7)	154 (95.1)	156 (96.3)	158[†] (97.5)	162

Challenges in subjects with non-immediate reactions during penicillin therapy

	No. of patients tested	Results	
		negative	positive
Maculopapular rashes negative in allergologic tests (total number of patients: 78)	67	66	1
Non-maculopapular reactions negative in allergologic tests (total number of patients: 76)	58	56	2

A Romano et al, Int Arch Allergy Immunol 2002

Oral provocation tests and positive challenge reactions to drugs from 1975 to 2000

Agent tested	*n*	+ (%)	Challenge reactions		
			Exanthema	Urticaria	FDE
ß-Lactams	324	24 (7.4)	23	1	
Other antibiotics	357	66 (18.5)	47	8	11
Aspirin	68	7 (10.3)		5	2
Other NSAIDs	40	10 (25)	2	5	3
Anti-epileptics	18	12 (66.6)	9		3
Other	194	17 (8.8)	16	1	
Total	**1,001**	**136 (13.6)**	**97**	**20**	**19**

K Lammintausta and O Kortekangas-Savolainen, Acta Derm Venereol 2005 (modified)

False negative results in skin and/or patch tested subjects with nonimmediate reactions to betalactams

Author	**No. of patients** (total challenged, %)	**Culprit drug**	**Type of reaction**	**Method**
S Terrados et al, *Allergy 1995*	**10**	Penicillins	Exanthema	Intradermal test
C Ponvert et al, *Pediatrics 1999*	**14** (270, 5.2)	Penicillins, cephalosporins	Exanthema, urticaria, angioedema	Intradermal test
I Luque et al, *Allergy 2001*	**12**	Aminopenicillins, benzylpenicillin	Urticaria, exanthema	Intradermal test (LTT)
A Romano et al, *Int Arch Allergy Immunol 2002*	**3** (125, 2.4)	Aminopenicillins	Maculopapular rash, oral and vaginal ulcers, linear IgA bullous dermatosis	Intradermal test, patch test

False negative results in skin and/or patch tested subjects with nonimmediate reactions to betalactams

Author	**No. of patients** (total challenged, %)	**Culprit drug**	**Type of reaction**	**Method**
K Lammintausta & O Kortekangas-Savolainen, *Acta Derm Venereol 2005*	**24** (324, 7.4)	Penicillins, cephalosporins	Urticaria, exanthema	Prick test, patch test
A Padial et al, *Clin Exp Allergy 2008*	**20**	Penicillins, cephalosporins	Urticaria, exanthema	Intradermal test, patch test
N Blanca-López et al, *Allergy 2009*	**19**	Aminopenicillins	Urticaria, exanthema, SSLS	Intradermal test, patch test
JC Caubet et al, *J Allergy Clin Immunol 2011*	**2** (77, 2.6)	Penicillins, cephalosporins	Urticaria, exanthema	Intradermal test, patch test

Diagnosing nonimmediate reactions to cephalosporins

- 105 patients with histories of nonimmediate reactions to cephalosporins were evaluated
- 7 (6.6%) out of the 105 subjects displayed positive results in in cephalosporin allergologic tests
- Of the 98 subjects with negative results in in cephalosporin allergologic tests, 86 accepted challenges (91 in all) with the suspect cephalosporins and tolerated them

A Romano et al, J Allergy Clin Immunol 2012

Diagnosing nonimmediate reactions to cephalosporins

Pt. No.	*Responsible drugs*	*Type of reaction*	*Delayed-reading skin tests*						*Patch tests*			
			PPL	*MDM*	*BP*	*AM*	*AX*	*Culprit*	*BP*	*AM*	*AX*	*Culprit*
1	Cephalexin	MP	-	-	-	+	+	+/-	-	+	+	-
2	Cephalexin	MP	-	-	+	+	+	+	+	+	+	+
3	Ceftriaxone	MP	-	-	-	-	-	+	-	-	-	-
4	Cefaclor	ED	-	-	-	-	-	+	-	-	-	-
5	Ceftriaxone	MP	-	-	-	-	-	+	-	-	-	+
6	Cefodizime Unknown penicillin	LR ER	+ (i)	-	-	+	+	+ (i)	-	+	+	-
7	Ceftriaxone	MP	-	-	-	-	-	+	-	-	-	+

A Romano et al, J Allergy Clin Immunol 2012

The role of penicillin in benign skin rashes in childhood: A prospective study based on drug rechallenge

- 88 children with delayed-onset urticarial or maculo-papular rashes associated with β-lactam therapy were evaluated by skin tests, patch tests, and oral challenges
- There were 11 (12.5%) positive intradermal tests and no positive patch tests

JC Caubet et al, J Allergy Clin Immunol 2011

The role of penicillin in benign skin rashes in childhood: A prospective study based on drug rechallenge

- All 88 children underwent oral challenges: 6 (6.8%) reacted; 4 were intradermal-test positive, and 2 intradermal-test negative. No challenge reactions were more severe than the index event
- The sensitivity of intradermal testing was 66.7%, and the specificity was 91.5%

JC Caubet et al, J Allergy Clin Immunol 2011

The role of penicillin in benign skin rashes in childhood: A prospective study based on drug rechallenge

Clinical implications:

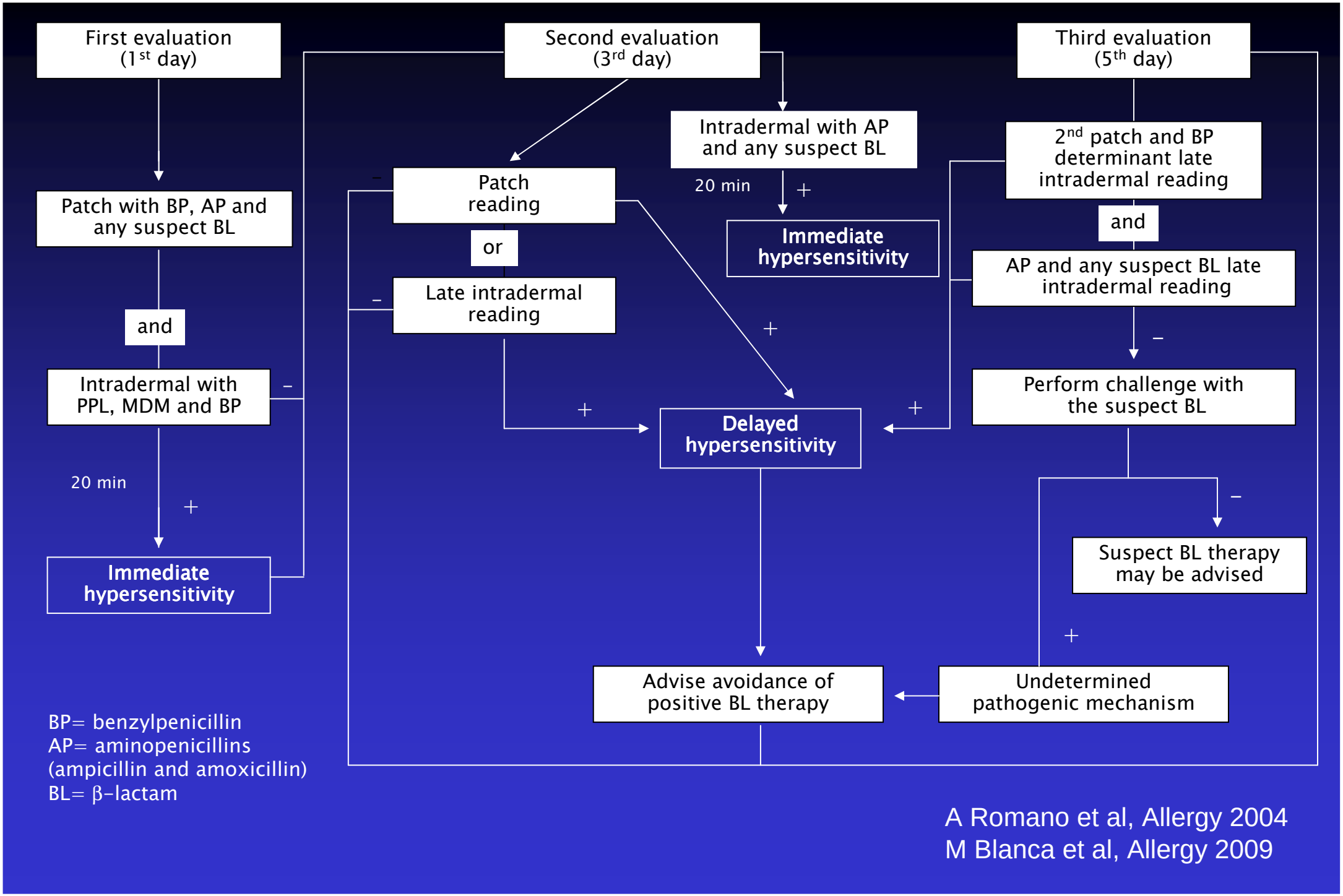
In children who develop a benign skin rash while on β-lactams, a physician-supervised oral challenge administered as 1 dose followed by standard dosing for 48 hours at home is a safe and efficient diagnostic procedure

JC Caubet et al, J Allergy Clin Immunol 2011

The role of penicillin in benign skin rashes in childhood: A prospective study based on drug rechallenge

Children with positive intradermal tests had a higher rate of positive oral challenges than those without (P <.05 by Fisher exact test)

JC Caubet et al, J Allergy Clin Immunol 2011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A Romano et al, Allergy 2004
M Blanca et al, Allergy 2009

Full-Course Drug Challenge Test in the Diagnosis of Delayed Allergic Reactions to Penicillin

- 22 patients with histories of nonimmediate reactions to penicillins displayed negative results in allergologic work-ups, including challenges, and underwent a 10-day therapeutic course

- 11 (50%) of the 22 patients experienced cutaneous reactions

JE Borch and C Bindslev-Jensen, Int Arch Allergy Immunol 2011

Determining the negative predictive value of provocation tests with beta-lactams

- A multicentre cohort study was conducted to assess the negative predictive value of provocation tests with beta-lactams in patients tested for a suspicion of drug allergy
- Of the 457 patients included, only 118 (25.8%) were re-exposed to the negatively tested beta-lactams
- 111 out of 118 (94.1%) patients tolerated the drug provocation test

P Demoly et al, Allergy 2010

Ringraziamenti

Malaga

M Blanca

C Mayorga

MJ Torres

Belgrado

M Atanasković-Marković

Montpellier

PJ Bousquet

P Demoly

Nancy

RM Guéant-Rodriguez

JL Guéant

Troina

R Pettinato

G Stella

Roma

C Alonzi

C Caruso

M Maggioletti

R Valluzzi

M Caringi

F Gaeta

G Rumi

M Viola


Unità di Allergologia
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