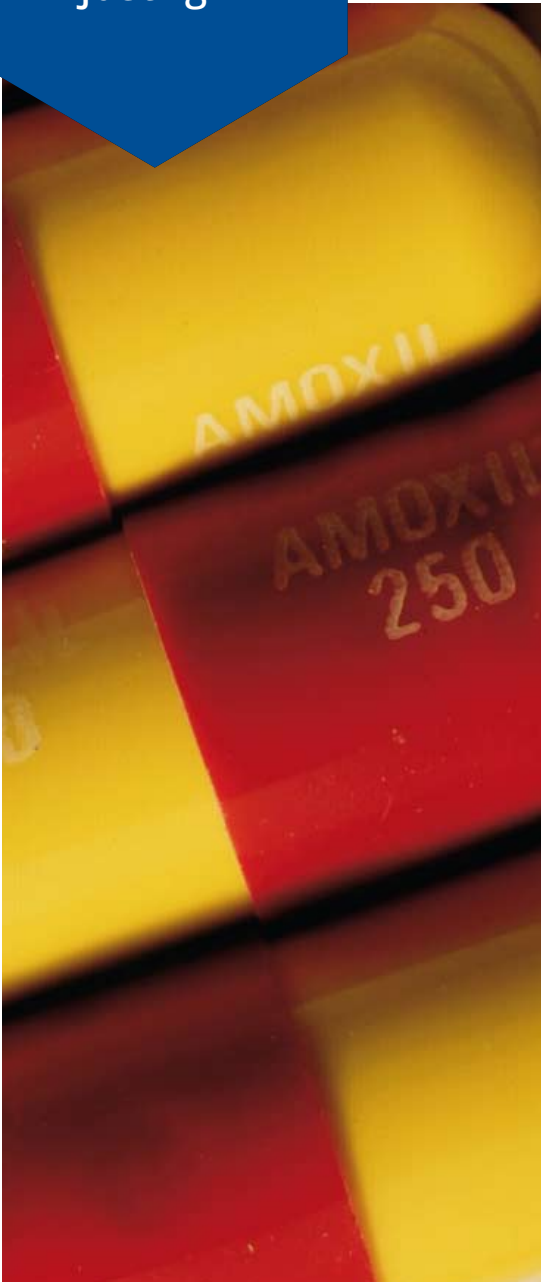


# Cellular Allergy Diagnosis

$\beta$ -Lactam antibiotics  
CAST<sup>®</sup> assays

There is more  
to allergy than  
just IgE



## „CAST<sup>®</sup> FIRST“

Clearly superior to sIgE -  
highest sensitivity of all *in vitro*  
tests

88% sensitivity in combination  
with skin tests

Clear allergy diagnosis in 70% of  
falsely negative patients

# Diagnosis of $\beta$ -lactam allergies

## $\beta$ -lactam allergy

About 12% of Europeans are affected by allergies to  $\beta$ -lactam antibiotics, the most frequent cause of immediate allergic reactions to drugs. These IgE mediated allergies can be induced by all  $\beta$ -lactam structures currently available, ranging from benzylpenicillin (BP) to modern  $\beta$ -lactam antibiotics. BP has been progressively replaced by amoxicillin (AX) and to a lesser extent by cephalosporins (CS) or other  $\beta$ -lactam antibiotics [4, 5].



**Figure 1:** Reaction to penicillin on the skin of a patient.

## Antigen selection

The selection of the allergen to be tested is important for a successful diagnosis: The European Network for Drug Allergy (ENDA) recommends to test not only the culprit allergen but also PPL and MDM. PPL contains major determinants and MDM minor determinants against BP and related antibiotics that cross react with penicillin derivatives. Therefore, their application is useful to confirm a suspected  $\beta$ -lactam allergy. MDM and PPL are not available for *in vitro* sIgE tests. Therefore only BÜHLMANN CAST<sup>®</sup> assays offer you a complete and clear diagnosis of immediate allergic reactions to  $\beta$ -lactam. We offer up to 12 different  $\beta$ -lactam allergen.

## Diagnosis of allergies to $\beta$ -lactam antibiotics

The ENDA has developed a diagnostic algorithm for diagnosis of immediate allergic reactions to  $\beta$ -lactam. This algorithm comprises the patients' anamnesis, skin tests (ST), *in vitro* tests (sIgE and CAST<sup>®</sup> assays) and a provocation test (PT). Thereby the following aspects are important:

- Skin tests can induce systemic reaction [7].
- Skin tests including PB, PPL, MDM, CS, AX and ampicillin don't surpass 70% of sensitivity. [12].
- Sensitivity of sIgE ranges only from 12.5%-25% [8].
- sIgE tests give a poor overall diagnostic performance even with two different cut-offs (0.10 & 0.35 kUA/L) [9].
- Specificity of sIgE declines progressively with increase of total IgE [14].

**A clear confirmation of  $\beta$ -lactam allergies can neither be achieved with skin test nor with sIgE alone; provocation tests are necessary in approximately 20% of cases.**

*In vitro* tests, especially Basophil Activation Test (e.g. Flow CAST<sup>®</sup>), should be the first choice for the diagnostic evaluation, for patients suffering from severe allergies. This is emphasized in the position paper of the ENDA group [3]. Furthermore, pseudo-allergic reactions for drugs are often not detectable by sIgE tests [12].

## ENDA $\beta$ -lactam study

Multicenter Study encompassing 10 European Centers including 181 patients with a history of  $\beta$ -lactam allergy and 81 controls evaluated the diagnostic efficiency of ST, sIgEs and CAST assays.

### Sensitivity & Specificity of diagnostic test methods

	Sens.[%]	Spec.[%]
Skin Tests	70	100
sIgE	30	86
CAST <sup>®</sup> ELISA / Flow CAST <sup>®</sup>	41	86

### Cumulative Sensitivity & Specificity

	Sens.%	Spec.%
Skin Tests	70	100
+ sIgE	76	86
+ Flow CAST <sup>®</sup>	86	87
Flow CAST <sup>®</sup> / CAST <sup>®</sup> ELISA	91 (88*)	67 (75*)

(\*Cumulative sensitivity and specificity of skin and cellular tests without sIgE)

The results show that the CAST<sup>®</sup> assays have clearly a higher sensitivity than sIgE tests which has recently been confirmed by Eberlein et al. Furthermore in up to 70% of patients negative to skin and sIgE test a provocation test could be avoided.

## Conclusion:

**CAST<sup>®</sup> assays are a decisive and powerful *in vitro* tool for clear diagnosis of  $\beta$ -lactam allergies ahead of sIgE:**

**"CAST<sup>®</sup> FIRST"**

# Clinical case reports

## Amoxicillin Allergy:

Patient: 46 years, male

Anamnesis: Developed severe urticaria in reaction to Amoxicillin in February 2007

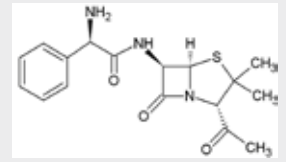
Skin Test: Negative

sIgE: Negative

Flow CAST®: Positive for PPL, MDM, Amoxicillin

(Data courtesy of Prof.M.Blanca, Dr.L.Mayorga, Carlos Haya Hospital, Malaga, ES)

The only *in vitro* test detecting the true culprit allergens for severe urticaria was Flow CAST®.



Patient: 59 years, male

Anamnesis: Anaphylactic shock after Amoxicillin intake in August 2005

Skin Test: Negative

sIgE: Negative

Flow CAST®: Positive for PPL, MDM, Amoxicillin

Provocation Test: Positive for Amoxicillin; anaphylactic reaction after 30 sec

(Data courtesy of Prof.A.Romano, Columbus Institute, Rome, IT)

Although an anaphylactic shock emerged, neither skin test nor sIgE could detect any of the tested antibiotics. Only Flow CAST® showed positive results and confirmed the anamnesis as well as the provocation test.

## Cefuroxim Allergy:

Patient: 61 years, female

Anamnesis: Anaphylactic shock after Cefuroxim intake

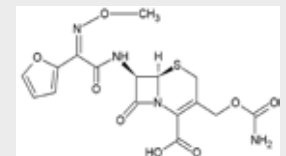
Skin Test: Positive for Cefuroxim, Ciprofloxacin

sIgE: Negative

Flow CAST®: Positive for Cefuroxim, Ciprofloxacin

(Data courtesy of Prof.B.Eberlein, TU München, DE)

Although an anaphylactic shock emerged, sIgE could not be detected for any of the tested antibiotics. Only skin test and Flow CAST® showed positive results and confirmed the anamnesis.



## Ceflacor Allergy:

Patient: 19 years, male

Anamnesis: Anaphylactic shock after Ceflacor intake

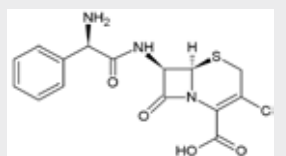
Skin Test: Positive for Ceflacor

sIgE: Negative

Flow CAST®: Positive for Ceflacor

(Data courtesy of Prof.A.Romano, Columbus Institute, Rome, IT)

Although an anaphylactic shock emerged, sIgE could not be detected for any of the tested antibiotics. Only skin test and Flow CAST® showed positive results and confirmed the anamnesis.



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