# Penicillin – Diagnosis of Allergy

**Janni Hjortlund**
*Department of Dermatology and Allergy Centre, Odense University Hospital, DK-5000 Odense C, Denmark. E-mail: jannihg@hotmail.com*

**Janni Hjortlund defended her PhD thesis "Penicillin – diagnosis of Allergy (PEDAL)" at the University of Southern Denmark, Denmark, on September 3, 2014. The thesis was supervised by Professor Carsten Bindslev-Jensen, Associate Professor Charlotte Gotthard Mortz and Professor Per Stahl Skov, Department of Dermatology and Allergy Centre, Odense University Hospital, Denmark. The Opponents and Members of the Evaluation Committee were Professor Torben Barington, Clinical Immunology, Department of Clinical Research, Odense University Hospital, Denmark, Professor Knut Brockow, Department of Dermatology and Allergology Biederstein, Technishe Universität München, Germany and PhD Lene Heise Garvey, Department of Dermato-Allergology KAA-816, Gentofte Hospital, Denmark.**

The diagnosis of allergic reactions to beta-lactam antibiotics is based on the European Network for Drug Allergy (ENDA) guidelines. Many patients experience reactions during a course of penicillin treatment; however the ENDA guidelines proposed for diagnosing penicillin allergy do not include long-term challenge. Skin testing in duplicate, correlation between case history of immediate and non-immediate reactions (NIR), challenge outcome and 7-day oral challenge with penicillin in the diagnostic evaluation of allergic reactions to beta-lactams, mimicking real life situations, has only been addressed in few studies.

The thesis focuses on main aspects of allergic reactions to penicillin, with special emphasis on the diagnostic evaluation of penicillin allergy. The serum half-life (T½) of specific IgE in patients, sensitized to penicillin were also investigated in order to find out whether a previous positive specific IgE to penicillin always is accompanied by clinical disease.

A total of 747 patients were evaluated and in all, the extended penicillin diagnostic work up was positive in 208 patients (27.8%), 146 of the 747 patients (19.5%) were positive according to ENDA guidelines and additionally 62 patients (8.3%) reacted during the 7-day oral challenge (1, 2).

Skin testing were included with the major penicilloyl-polylysine (PPL) and minor (minor determinant mixture; MDM) penicillin determinant. Only 3 patients were positive to PPL and/or MDM, all also positive to penicillin G in intracutaneous test. No relation between case histories of immediate and non-immediate reactions, respectively, and reaction time during challenge was found. The data suggest that case history is often insufficient to discriminate between immediate and non-immediate reactions (2).

*Fig. 1.* Janni Hjortlund (second from left) defended her thesis on September 3, 2014 in the University of Southern Denmark. The Members of the Evaluation Committee were (from left) Professor Torben Barington, Professor Knut Brockow and PhD Lene Heise Garvey.

A total of 32 challenges with beta-lactams were performed in 24 patients with previous IgE sensitization to penicillin and negative skin tests. Four different challenge outcomes were obtained: 10 patients had negative clinical reaction to challenge and negative post-challenge IgE, 8 patients had negative clinical reaction to challenge, but positive post-challenge IgE

levels. Three patients were challenge positive and had positive post-challenge IgE whereas 3 patients were challenge positive, but had negative post-challenge IgE.

T½ varied from 1.6 months to 76.4 months and in approximately half of the patients T½ were less than one year (3).

We demonstrated that approximately 30% of all patients with positive outcome during penicillin challenge are found by adding a 7-day oral challenge with penicillin to the original ENDA guidelines. The extended protocol with identical work-up in patients with case histories of immediate and non-immediate reactions, respectively, and with 7-day oral challenge suggests a significant diagnostic improvement (1, 2). Specific IgE to penicillin declines over time stressing the importance of a close time relation between diagnostic work-up and clinical reaction. Reversal of previously positive serum specific IgE to penicillin may still be associated with positive penicillin challenges and/or re-boostering of serum specific IgE to positivity (3).

## Literature

1. Hjortlund J, Mortz CG, Skov PS, Eller E, Poulsen JM, Borch JE, et al. One-week oral challenge with penicillin in diagnosis of penicillin allergy. Acta Derm Venereol 2012; 92: 307–312.
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