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If you cannot see the wood for the birches

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About every second allergic person in Germany suffers from a so-called "early bloomer allergy", a little scientific description of the tree pollen allergy [2]. And almost every allergic person knows the specific tree, which he or she is allergic to, the hazel, the alder, the birch, the ash, the plane tree, and finally the most German of all the trees, the oak. This knowledge has been burned into the minds of our patients. So, it comes to a revolution, when a German-Danish research group around the lateral thinker Jörg Kleine-Tebbe in their article "Is allergy immunotherapy with birch sufficient to treat patients allergic to pollen of tree species of the birch homologous group?" now speaks out, that most trees from an allergological point of view are actually birches [1]. Or at least those of the Fagales homologous group. They shed light on this from various aspects, the regulatory, the immunological and finally the clinical perspective, and with this knowledge, they have the intention to give recommendations for diagnosis and change current treatment habits.

Indeed, they have strong arguments on their side:

Already in 2008, the European Medicine Agency EMA defined homologous allergen groups and subsumed not only birch, hazel, alder, hornbeam and oak, but also hop hornbeam, beech and sweet chestnut among the birch group. All this is based on strong scientific evidence, which comes from the field of molecular

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allergy, rather than from the previous botanical view of taxonomical classes. It started with the characterization of the PR-10 like molecule Bet v 1, as the major allergen in birch. All trees of the Fagales group display a high degree of structural homology in their major allergens. This is in line with results from the immunological diagnosis of numerous allergen immunotherapy studies. In these studies high levels of cross-reactivity of birch specific IgE towards allergens of the birch homologous trees were observed with correlation coefficients ranging from 0.83 for birch/oak to 0.98 for birch/hazel. They report similar findings also for the changes in allergen-specific IgG4, a factor which is often interpreted as a biomarker of the treatment effects of AIT. Here the correlation coefficients reached from 0.72 for birch/oak to 0.95 for birch/alder.

In their own studies from Northern and Central Europe the overlap of birch sensitization with alder or hazel was almost complete and a patient reaction to alder or hazel but not displaying a birch sensitization was an extremely rare exception.

The article quotes surprising sensitization data from the Mediterranean Italy [3]. High rates of birch sensitization were also found in the Italian South. This is not just about cross-reactivity. Birch pollen can spread with the wind over thousands of kilometres and also sensitize atopic people, where a birch has never been spotted. Even there, IgE reactivity to Bet v 1 seems to be a fine marker of Fagales sensitization.

But the strongest argument for the paradigm shift comes from the recently presented clinical trials with the birch tablet. "He who heals is right" said our predecessors in the pre-evident era. The birch tablet not only demonstrated symptom improvements in birch, alder and hazel patients, but also showed highly significant and clinically relevant improvements for patients who were shown to be sensitized exclusively to oak allergen. Moreover, they cite studies with recombinant Bet v 1 which were efficacious, thereby demonstrating that this major allergen is the main driver of the disease.

The authors attribute the effects which they have observed to the long-term induction of birch-specific IgG4 and especially to the appearance of birch-specific IgE Blocking Factor in the blood of successfully treated patients as the underlying mechanism.

The work of Kleine-Tebbe and colleagues propagates a novel, minimalist approach for both, the diagnosis and the treatment of tree allergy:

Their simple algorithm recommends for allergy sufferers who develop symptoms before the grass pollen period, that it is usually sufficient to test only for birch allergen and to treat the patient in a positive case

with the birch tablet. If this approach proves to be effective on a broad basis, it would at least partially reduce the continuous discussion about the constant shortage of diagnostic allergens. Because then we could dispose properly of the diagnostic solutions for hazel, for alder, for beech and for oak. And space would be created in the refrigerator because the twofold and threefold combinations of tree pollen therapy allergens have become obsolete. I think this is a conceivable scenario, but I find it difficult and time-consuming to communicate these new findings to our well informed and highly motivated allergy patients polysensitized to various tree pollen.

Conflict of interest statement:

Prof. Mösges reports personal fees from ALK, grants from ASIT biotech, personal fees from allergopharma, personal fees from Allergy Therapeutics, grants and personal fees from Bencard, grants from Leti, grants, personal fees and non-financial support from Lofarma, non-financial support from Roxall, grants and personal fees from Stallergenes, grants from Optima, personal fees from Friulchem, personal fees from Hexal, personal fees from Servier, personal fees from Klosterfrau, non-financial support from Atmos, personal fees from Bayer, non-financial support from Bionorica, personal fees from FAES, personal fees from GSK, personal fees from MSD, personal fees from Johnson&Johnson, personal fees from Meda, personal fees and non-financial support from Novartis, non-financial support from Otonomy, personal fees from Stada, personal fees from UCB, non-financial support from Ferrero, grants from BitopAG, grants from Hulka, personal fees from Nuvo, grants from Ursapharm, personal fees from Menarini, personal fees from Mundipharma, personal fees from Pohl-Boskamp, grants from Immunotek, personal fees from Hikma, personal fees from Sandoz, grants and personal fees from Lek, grants and personal fees from Cassella, outside the submitted work.

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