

August 2017 Issue

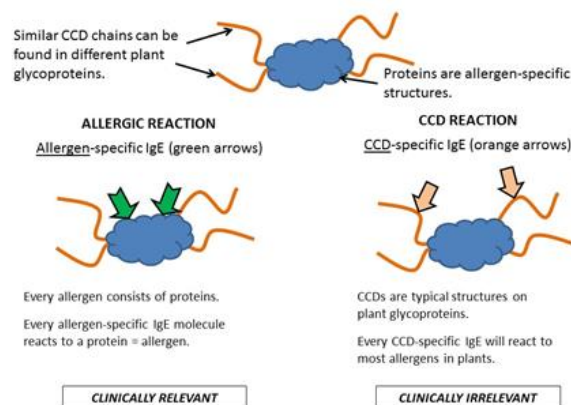
The influence of carbohydrate side chains on testing for seasonal allergens

CCD (cross-reactive carbohydrate determinant) – cross-reactive carbohydrate side chains

Some of you may have already heard about carbohydrate side chains and their influence on allergy testing. It is a phenomenon that has been known in human medicine for three decades. Now, research on it has also begun in veterinary medicine. Every now and then, you have certainly received a pollen allergy test which was positive for (nearly) all allergens. It is now known that some of these cases are so-called cross-reactions with carbohydrate chains from plants. Thus, the term cross-reactive carbohydrate side chains or carbohydrate determinants (**CCD**; cross-reactive carbohydrate determinant) was coined.

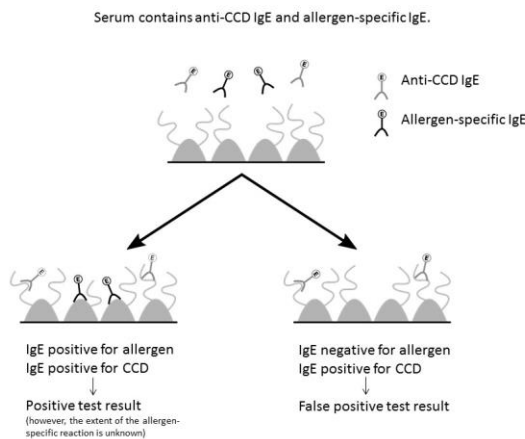
In these cases, the animal reacts specifically to carbohydrate side chains (CCD) from plants with a type 1 reaction, i. e. immunoglobulin E (IgE) against these carbohydrates is produced, which leads to positive results for (almost) all seasonal allergens. This problem is not linked to a certain test or a specific technology, but all IgE in vitro tests in humans and animals are affected. Once this phenomenon occurs, the correct or actual IgE reaction to seasonal pollen allergens can no longer be determined. This explains why selecting allergens for ASIT (allergen-specific immunotherapy, hyposensitisation) can also not be done accurately anymore.

During evolution, a specific glycosylation pattern (a set of enzymatic and chemical reactions in which, i. a., carbohydrates are bound) developed for plants and invertebrates. The main form for plants is the carbohydrate structure MMXF (core α 1,3-fucose and β 1,2-xylose molecule on the N-glycan). This epitope is identical in plants (pollen, vegetables, fruit), insects (especially hymenoptera), helminths, arthropods, molluscs and latex. Hence, a patient who has developed IgE to these CCD reacts to each of the allergens mentioned. As these modifications do not occur in mammals, they have a profound immunogenicity. Anti-CCD IgE antibodies can therefore be found in sera of patients sensitised to different allergens. Though it is unknown why some patients develop these anti-CCD IgE while others do not. **However, this anti-CCD IgE is not of clinical relevance!**



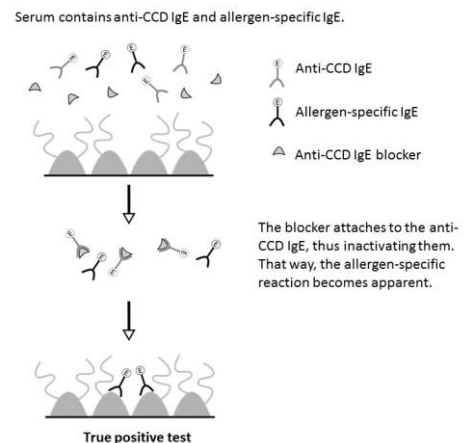
How can anti-CCD IgE alter the test?

There can be IgE to CCD in the serum and, additionally, IgE to specific proteins. Extremely positive results (positive results for nearly every allergen) in a seasonal allergy test indicate that not only IgE to proteins were developed but also IgE to CCD.



the allergens. By **blocking the CCD reaction**, it is possible to get a result with either a true positive reaction to the respective allergens or a true negative reaction. Thus, false positive reactions – caused by the CCD reaction – are eliminated.

The true positive serum sample



How do you recognise a CCD-positive case?

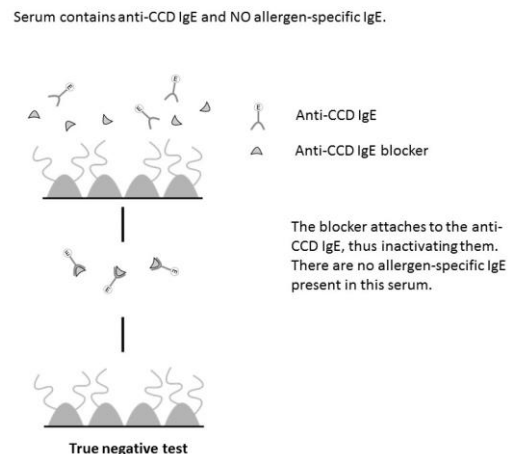
CCD reactivity can be identified with a special test, the so-called **CHO test**. The CHO test is an Fc-epsilon receptor test that identifies IgE to the CCD determinant.

In a study with 500 cases, 21% were tested positive for CCDs (sensitivity of > 88%, specificity of > 94%).

Is it possible to get a true specific IgE result when working with a CCD-affected sample?

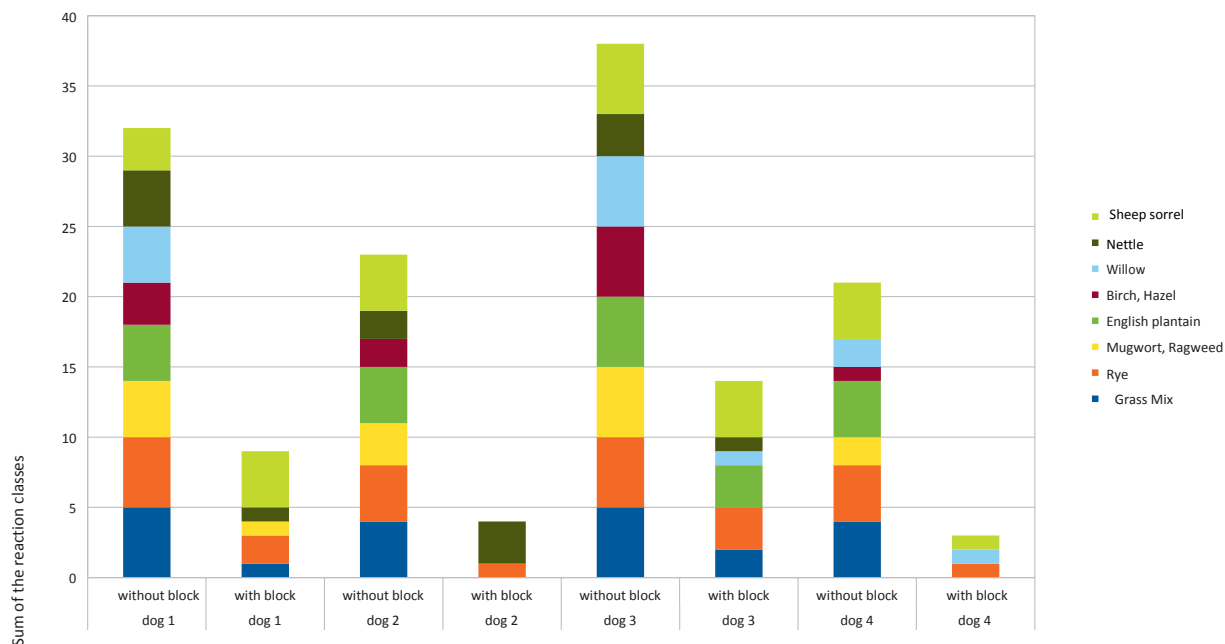
An inhibition was developed which prevents anti-CCD IgE from binding to

The true negative serum sample



Examples

	without CCD blocker dog A	with CCD blocker dog A	without CCD blocker dog B	with CCD blocker dog B
Grass Mix	RC 4	RC 0	RC 5	RC 1
Rye	RC 5	RC 0	RC 5	RC 2
Mugwort, Ragweed	RC 4	RC 0	RC 4	RC 1
English plantain	RC 4	RC 0	RC 4	RC 0
Birch, Hazel	RC 4	RC 0	RC 3	RC 0
Willow	RC 3	RC 0	RC 4	RC 0
Nettle	RC 4	RC 0	RC 4	RC 1
Sheep sorrel	RC 4	RC 1	RC 3	RC 4



Conclusion

So-called anti-CCD IgE (antibodies on carbohydrate side chains of plants) may cause false positive reactions in allergy tests for seasonal allergens. These results are, without exception, highly positive reactions to all seasonal allergens in the test. As it is impossible to know which results are false positive in such a case, too many or even wrong allergens might be selected for ASIT. Such samples can clearly be identified with the CHO test. By using a so-called blocker (blocking agent), this reaction can be blocked in vitro, thus getting a true positive result and therefore being able to only select the true positive allergens for ASIT. Many times, this also avoids producing a double set. Testing for perennial allergens (mites, moulds) is not influenced in any way by CCD as this phenomenon only affects seasonal allergens (grass, weed and tree pollen) and hymenoptera.

Our allergy test – the Fc-epsilon receptor test – is one of the most reliable tests on the market. CCD cross-reactivity only occurs in the (almost) entirely highly positive seasonal allergy test and the hymenoptera and concerns all the allergy tests available on the market.

Perennial allergens are not affected. Once the result of the seasonal allergy test indicates the existence of carbohydrate antibodies in this animal (CCD-positive = cross-reactive carbohydrate determinant – cross-reactive carbohydrate side chains), we do a CHO blocking. The seasonal allergens are repeated using a CCD blocker to avoid selecting wrong allergens for ASIT because of false positive reactions. This exclusively applies to seasonal allergens and hymenoptera in dogs and cats; perennial allergens are not affected by this phenomenon. Please send in sufficient material as more material might be needed due to the additional steps.

Literature

Altmann (2007) The role of protein Glycosylation in allergy. *Int Arch Allergy Immunol* 142: 99-115.

Altmann (2016) Coping with cross-reactive carbohydrate determinants in allergy diagnosis. *Allergo J Int* 25 (4): 98-105.

Holzweber et al. (2013) Inhibition of IgE binding to cross-reactive carbohydrate determinants enhances diagnostic selectivity. *Allergy* 68: 1269-77.

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