Staphylococcal enterotoxin specific IgE in serum is linked to severe asthma and nasal polyposis

Tomassen, Peter¹; Cardell, Lars-Olaf²; De Ruyck, Natalie¹; Foerster, Ulrike³; Fokkens, Wytske⁴; Gevaert, Philippe¹;
Hellings, Peter⁵; Hox, Valerie⁵; Katainen, Elina⁶; Kowalski, Marek⁷; Mullol, Joaquim⁸; Olze, Heidi³; Olzewska,
Agnieszka⁹; Reutherborg, Ann²; Segboer, Christine⁴; Toskala, Elina¹⁰; Van Bruaene, Nicholas¹; Van Drunen,
Cornelis⁴; Van Zele, Thibaut¹; Bachert, Claus¹

¹Ghent University, Upper Airways Research Laboratory, Gent, Belgium; ²Karolinska Institutet, Division of ENT diseases, CLINTEC, Stockholm, Sweden; ³Charité-Universitätsmedizin Berlin, Department of Otorhinolaryngology, Berlin, Germany; ⁴Academic Medical Centre, Department of Otorhinolaryngology, Amsterdam, Netherlands; ⁵University Hospitals Leuven, Department of Otorhinolaryngology, Head and Neck Surgery, Leuven, Belgium; ⁶Helsinki University Hospital, Helsinki, Finland; ⁷Medical University of Lodz, Department of Immunology, Rheumatology and Allergy, Berlin, Poland; ⁸IDIBAPS, Clinical and Experimental Respiratory Immunoallergy, Barcelona, Spain; ⁹Medical University of Lodz, Department of Immunology, Rheumatology and Allergy, Lodz, Poland; ¹⁰Finnish Institute of Occupational Health and Helsinki University Hospital, Helsinki, Finland

Background: Staphylococcus aureus produces enterotoxins which have potent polyclonal immunostimulatory effects. IgE directed to these enterotoxins has been detected in serum of asthma, nasal polyp, allergic rhinitis, and atopic dermatitis patients, but also in serum of healthy subjects. The aim of the study was to assess the association of sensitization to enterotoxins with chronic rhinosinusitis (CRS), asthma, and atopy presence and severity. **Method:** The study was designed as a multicenter, non-matched case-control study, and recruited CRS with (CRSwNP) and without (CRSsNP) nasal polyps, and controls undergoing septoplasty or conchotomy. Serum was analyzed for total IgE and for SAE-IgE (SEA, SEC and TSST-1). Sensitization was defined as SAE-IgE > 0.35 kU/L. Asthma severity was classified according to medication use based on NHLBI guidelines.

Result: 794 serum samples were collected. Of these, 189 were controls, 378 were CRSsNP and 189 were CRSwNP. Asthma was present in 11.1% of controls, in 19.2% of CRSsNP, and in 39.2% of CRSwNP. Moderate to severe asthma was present in 7.4% of controls, in 10.2% of CRSsNP and in 28.3% of CRSwNP. SAE-IgE levels were positive in 15,7% of controls, in 19.6% of CRSsNP and in 29.6% of CRSwNP. Non-asthmatics had in 19.4% SAE sensitization, compared to 19,1% of intermittent to mild asthmatics and 40.2% of moderate to severe asthmatics. Binary logistic regression revealed significant and independent associations of SAE-IgE presence with moderate-severe asthma and nasal polyposis. When taking in account the titer of SAE-IgE using multinomial logistic regression, moderate levels of IgE (0.35-1 kU/L) were associated with nasal polyposis and moderate-severe asthma, whereas high levels (>1 kU/L) were associated with moderate-severe asthma. After controlling for asthma and sinus disease, atopy was not associated with SAE-IgE.

Conclusion: Serum presence of IgE to staphylococcal enterotoxins was strongly associated with moderate to severe asthma and nasal polyposis, independently of the presence of atopy. This underlines a potential role for staphylococcal superantigens in the pathogenesis of severe asthma, nasal polyposis and in their systemic interaction.