

**FROM TH2 POLARIZATION TO IL-17-DEPENDENT INFLAMMATION:
THE CORRELATION STRUCTURE OF POST-IMPLANTATION
REACTIVITY TO METAL-CONTAINING OCCLUDERS IN CHILDREN**

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Abstract. The correlation structure between clinical, allergological and immunological parameters and the grade of post-implantation reactivity was analysed in 126 children after transcatheter closure of congenital septal heart defects. Spearman analysis revealed a hierarchical system of associations in which the strongest links were shown by eosinophil cationic protein ($r=0.739$), IL-13 ($r=0.724$), total IgE ($r=0.712$), IL-4 ($r=0.693$), IL-17 ($r=0.672$) and blood eosinophils ($r=0.661$), all $p<0.001$. The nickel patch test and tryptase showed moderate coupling, whereas IL-5, IL-10, CD19⁺ lymphocytes and basophils formed no stable connections and remained outside the pathogenetic contour.

Keywords. pathogenesis; correlation analysis; Th2 polarization; IL-17; eosinophil cationic protein; tryptase; metal hypersensitivity; occluder; congenital heart disease; children.

Background and relevance. Hypersensitivity to implanted metal-containing devices is traditionally interpreted within the framework of type IV contact sensitization or of classical Th2-mediated atopy, yet neither model fully explains why in some children the reaction resolves spontaneously while in others it becomes persistent and relapsing despite pharmacological correction. Published data confirm the participation of humoral activation, eosinophils, mast cells and Th2 cytokines, but these components are usually studied separately, so the sequence in which they are recruited and the point at which a reversible reaction converts into a stable one remain undefined. Establishing the internal correlation architecture of these markers is a prerequisite for understanding which of them drive the process and which merely accompany it. Such an analysis is also of direct practical value, since only variables belonging to the true pathogenetic contour deserve inclusion in preoperative predictive models applied to children.





Aim. To analyse the clinical, allergological and immunological interrelations and to substantiate the pathogenetic pattern of the formation of reactivity to metal-containing occluders.

Materials and methods. The study covered 126 children aged 3 to 18 years who underwent primary transcatheter closure of a congenital septal heart defect and were followed for no less than six months, after which they were retrospectively divided into groups without reactivity ($n=45$), with transient ($n=42$) and persistent ($n=39$) reactivity. Allergological history, nickel patch testing, total IgE, blood eosinophils, eosinophil cationic protein, tryptase, CD19⁺ lymphocytes, basophils and the cytokines IL-4, IL-5, IL-6, IL-10, IL-13 and IL-17 were assessed preoperatively. Because several immunological variables deviated from normal distribution, associations with the grade of reactivity were evaluated using the Spearman rank correlation coefficient, with significance accepted at $p<0.05$.

Results. Increasing reactivity was accompanied by the formation of a coordinated system of associations between markers of allergic and inflammatory activation, with coefficients for the leading variables ranging from $r=0.661$ to $r=0.739$. Eosinophil cationic protein showed the closest link ($r=0.739$; $p<0.001$), reflecting not the mere presence of eosinophils but the intensity of their effector realization; IL-13 ($r=0.724$) and total IgE ($r=0.712$) followed. IL-4 demonstrated a strong association ($r=0.693$), and IL-17 ($r=0.672$) occupied a distinct position outside the classical atopic markers. The nickel patch test and tryptase showed moderate coupling, while IL-5, IL-10, CD19⁺ lymphocytes and basophils formed no stable connections.

Conclusion. Post-implantation reactivity to metal-containing occluders develops as a multistage process arising on a background of pre-existing allergic predisposition. Th2-associated cytokines, primarily IL-4 and IL-13, initiate humoral restructuring and sustain the allergic response, after which activated eosinophils and mast cells are recruited, manifesting as rising eosinophil cationic protein and tryptase levels. The subsequent increase in IL-17 marks the addition of an inflammatory component that broadens and stabilizes the immune response and determines the transition to a persistent variant. Parameters that form no stable associations, namely IL-5, IL-10, CD19⁺ lymphocytes and basophils, remain outside this contour and possess limited diagnostic and prognostic value.

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