"Immunodeficiency in CHARGE syndrome"
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AUTHORS AND THEIR CONNECTION TO THE CHARGE SYNDROME FOUNDATION:

Sam Mehr, MD is a Consultant Paediatric Immunologist, Allergist and Immunopathologist at the Royal Children's Hospital, Melbourne, Australia. He has a clinical and research interest in allergy, autoinflammation and paediatric immunodeficiency. He is part of a group in Australia (including Dr. George Williams) who have published on immunological aspects of CHARGE syndrome. He is interested in learning more about the variety of immune issues that arise in CHARGE.

Peter Hsu, PhD is a Consultant Paediatric Immunologist and Allergist at the Children's Hospital at Westmead, Australia, and a senior lecturer at the University of Sydney. His research interests include immune regulatory mechanisms in allergy and immunodeficiency. He has published several papers on CHARGE syndrome and has presented at the Australasian CHARGE conferences.

Dianne Campbell, MD is the Chair and Co-head of the Department of Allergy and Clinical Immunology at the Children's Hospital, Westmead, Australia. She has active roles in allergy and immunology research and has published over 90 peer reviewed papers.

SUMMARY OF THE PAPER:

***Abstract*:** Immunodeficiency can occur in CHARGE syndrome (CS). The defects can range from a reduction in T-cell counts to combined T-B cell defects, which may require antibiotic prophylaxis or immunoglobulin replacement, to severe combined immunodeficiency which is fatal without immune reconstitution (such as thymus transplant). However, because it has not been systematically studied, we do not know what percentage of individuals with CS have immunodeficiency. In this review, we examine

the existing literature covering immunodeficiency associated with CS, compare these with immunodeficiencies reported in 22q11.2 deletion syndrome (a condition that shares many characteristics with CS) and suggest future research priorities.

Additional summary: Immunodeficiencies of many types have been described in individuals with CS. They vary from asymptomatic abnormalities in the numbers of T-cells to life-threatening severe combined immune deficiency (SCID or complete DiGeorge anomaly). Section 2 of the paper summarizes the various parts of the immune system and a description of the adaptive system: B-cells, T-cells and how the thymus "educates" the cells produced by the bone marrow. Immune issues in CS are due to abnormalities of thymic development, with absence of thymus being the extreme. The clinical effects of levels of thymic abnormality are described, including infections, lymphopenia, reduced T-cell types and complete absence of thymus. Complete absence of the thymus can only be treated by thymus transplant, which is only being done in two places in the world (Great Ormond Street Hospital in London and Duke University Hospital in the US).

Lesser immune issues may include antibody deficiency. Many individuals with CS have a reduced response to immunizations and may require boosters. A small number may require immunoglobulin infusions. Table 1 summarizes the published reports of immune issues in CS, many of which are isolated case reports. The authors compare the immune issues reported in CS with those reported in 22q11.2 deletion syndrome. Immunodeficiency is reported more often in 22q11.2 deletion syndrome than in CS, but it may be due to what is looked for in each syndrome. Prospective head to head comparison studies are needed to confirm this.

Although there is no consensus in the published literature, the authors make recommendations for immune studies in all individuals with CS: what blood work to do on everyone and when to consider the possibility of significant thymic abnormality or absence. They recommend additional evaluation of older children with recurrent sino-pulmonary infections to detect more subtle immunodeficiency. They finish by recommending four areas that merit further investigation.

WHAT DOES THIS MEAN TO FAMILY/PERSON WITH CHARGE?

This is the first comprehensive summary of immune issues in CS. It is something that may be relevant to the majority of individuals with CS. The information and recommendations could have a big impact on the health and management of many individuals with CS.

SHOULD I READ IT? SHOULD ONE OF MY DOCTORS READ IT?

Yes, and yes. This paper does a lovely job of explaining the basics of the immune system in an understandable way. It summarizes the immune issues that have been reported in CS and makes specific recommendations for both newborns and older individuals with CS. Read the paper yourselves. Take a copy to the primary care physician. If your child is a newborn, ask for the recommended testing. If your child is older and you have any questions about possible immune issues, request a referral to an immunologist and take a copy of this paper with you to give to the immunologist.

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