

Correspondence

Reply

To the Editor:

We thank Drs Honda and Kabashima for their thoughtful response¹ to our commentary on the study by Msallam et al.² We recognize that mast cells (MCs) in fetal and neonatal skin display less FcεRI expression than those in the adult. Nonetheless, the study by Msallam et al² demonstrates that IgE transferred from dams passively sensitized with monomeric IgE directed against trinitrophenol (TNP) can be detected on cutaneous MCs in E17.5 pups in a dose-dependent manner. Msallam et al² observed that following isolation, cutaneous MCs from these pups degranulated in response to TNP-ovalbumin *in vitro*, and they further noted that cutaneous MCs from these pups were activated after TNP-ovalbumin had been painted on the pups' dorsal skin. Together, these observations indicate that neonatal MC populations within the skin are endowed with FcεRI sufficient to elicit functional responses through transplacental maternal IgE transfer. Honda and Kabashima¹ correctly point out that IgE-IgG complexes form in actively sensitized dams, consistent with their previous studies linking IgE transfer to such complexes. However, the study by Msallam et al¹ also shows transplacental transfer of IgE from passively sensitized dams, in which such complexes are less likely. Definitive proof that IgG is needed to facilitate IgE transfer would

likely require passive IgE transfer studies in mice lacking all endogenous immunoglobulins. Finally, we fully agree that the relationship between maternally transferred IgE and the inheritance of atopic disease is inferential at best. We suspect that the capacity for infant MCs to become armed with maternal IgE may be part of a passive immune mechanism that benefits the host in areas of high endemicity for helminths, ticks, and other pathogens for which IgE and MCs form part of the initial line of defense.

Daniel F. Dwyer, PhD

Joshua A. Boyce, MD

From the Department of Medicine, Harvard Medical School, Division of Allergy and Clinical Immunology, Brigham and Women's Hospital, Boston, MA 02115. E-mail: jboyce@rics.bwh.harvard.edu.

Supported by the following National Institutes of Health grants: R01AI078908, R01HL117945, R37AI052353, R01AI136041, R01HL136209, R01AI130109, and U19AI095219.

REFERENCES

1. Honda Y, Kabashima K. Maternal IgE is transferred to fetuses with IgG and minimally sensitizes fetal/neonatal skin mast cells. *J Allergy Clin Immunol* 2021;148:XXX-XXX.
2. Msallam R, Balla J, Rathore APS, Kared H, Malleret B, Saron WAA, et al. Fetal mast cells mediate postnatal allergic responses dependent on maternal IgE. *Science* 2020;370:941-50.

<https://doi.org/10.1016/j.jaci.2021.05.041>