Environmental and Epigenetic Clues to Twin and Family Risk for Eosinophilic Esophagitis

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ABSTRACT:
Eosinophilic esophagitis (EoE) is an increasingly common and debilitating inflammatory condition of the esophagus, likely involving both genetic and environmental causes. EoE is known to cluster in families, yet associated genes such as CAPN14, TSLP, TSLPR, CCL26, and FLG do not tell the whole story. Environmental exposures, including antibiotics in the first year of life, are also associated with increased risk for EoE. Indeed, epigenetic mechanisms may “turn on” the eotaxin promoter, causing the characteristic eosinophilic inflammation in the esophagus. By comparing nuclear families and a new international registry of twins with severe atopy, Alexander et al. found that environment has a much stronger role than genetics in EoE. Identical and fraternal twin analysis estimated the contribution of the common household environment at 81% and genes at 15%. Environmental risk factors included food allergies, high twin birth-weight difference, and self-reported penicillin allergy. Interestingly, fall birth season and breastfeeding may be protective. Supporting the role of environment, a surprisingly high frequency of fraternal twins (22.0%) and nuclear siblings (2.4%) were concordant for EoE. Early-life exposures may prime genetically susceptible individuals for EoE, highlighting the need to rigorously identify relevant genetic and environmental risk mechanisms. Research focused on identifying modifiable environmental risk factors for EoE may give clinicians tools for evidence-based recommendations to reduce risk in genetically susceptible families. New epigenetic evidence suggests both new risk factors for validation as well as the need for improved non-invasive testing for family-based studies.
BIO:
Eileen Steinle Alexander is a Frank C. Woodside III, M.D., Dinsmore & Shohl Fellow in the Cincinnati Children’s Hospital Medical Center’s Division of Biostatistics and Epidemiology. Ms. Alexander was a 2011 Center for Environmental Genetics New Investigator Scholar, making her eligible for a 2012 CEG Pilot Project award to study genetic and environmental factors contributing to the development of eosinophilic esophagitis, a debilitating food allergy. While a Fellow on the Molecular Epidemiology and Children’s Environmental Health training grant, she received support from the National Institute of Environmental Health Sciences, and the Young Investigator Award from the International Eosinophil Society. As a doctoral student, she co-authored 4 peer-reviewed manuscripts. Her dissertation manuscript, “Twin and Family Studies Reveal Strong Environmental and Weaker Genetic Cues Explaining Heritability of Eosinophilic Esophagitis,” was featured “New Research” by the Journal of Allergy and Clinical Immunology. In 2014, Dr. Alexander received her PhD in epidemiology with Dr. Paul Succop from UC’s College of Medicine Department of Environmental Health, in collaboration with Drs. Erin Haynes, and Marc Rothenberg (Allergy & Immunology), Lisa Martin (Human Genetics), Margaret Collins (Pathology), Vincent Mukkada (Gastroenterology) at Cincinnati Children’s Hospital. She earned her M.S. studying ecological toxicology from the UC Department of Biological Sciences, with Dr. Jodi Shann.

In the Department of Health Services Administration (the MBA of healthcare) at Xavier University, she uses experiential simulations and community projects to teach Public Health and Quality Management. “We are committed to becoming a bridging resource between the families struggling to understand and manage serious diseases that run in their families, the design and analysis of epigenetic studies and the ways that environmental factors change risk. Through interdisciplinary collaboration, we focus on how genetic risk can be reduced by modifying the environment,” says Alexander. Importantly, her passion for pediatric research and public health education stems from her background as a nurse and dedication to empowering families to live healthier, happier lives.