

Genetic Susceptibility to RA Trumps Other Risks

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Cigarette smoke and breast-feeding respectively increase and decrease the risk of rheumatoid factor positivity in children who have no genetic susceptibility to rheumatoid arthritis, according to recent study results.

However, among children who do have genetic susceptibility to the disease, these environmental factors are not associated

with rheumatoid factor positivity, reported Kendra A. Young of the University of Colorado at Denver and Health Sciences Center and her colleagues (*Ann. Rheum. Dis.* 2007;66:179-83).

The observation could possibly be related to “a multi-hit aetiology,” suggested the authors, “where those without the genetic susceptibility marker need environmental exposures to convert to autoantibody positivity, whereas those who already have a genetic susceptibility marker

do not need these exposures to become positive.”

The study included 651 children who made up a subgroup of the Diabetes Autoimmunity Study in the Young (DAISY), a prospective study of the natural history of environmental risk factors of type 1 diabetes in genetically predisposed children. Participants in DAISY were selected if they had either a genetic susceptibility to diabetes identified by the presence of HLA-DR4 and -DR3 alleles or a parent or sibling with type

1 diabetes, regardless of their HLA genotype. HLA-DR4 alleles are also associated with an increased risk of rheumatoid arthritis and polyarticular juvenile rheumatoid arthritis (JRA), noted the authors.

The subgroup of children was selected for the current study because they had also had their blood tested for rheumatoid factor—an intermediate phenotype of RA and polyarticular JRA.

All study patients had data collected on sociodemographic factors and perinatal variables including birth order, mother's education, race/ethnicity, mother's age at child's birth, and mother's smoking status during pregnancy. Data on infant diet as well as regular height, weight, and body mass index measurements were recorded. Prospective data were also collected on the child's exposure to tobacco smoke.

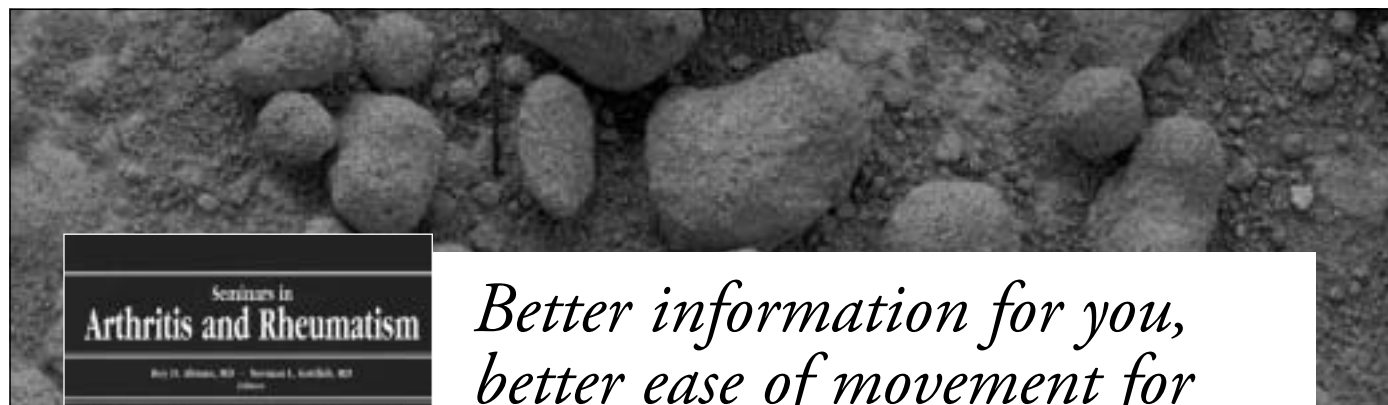
A total of 23 of the 651 children tested positive for rheumatoid factor. An analysis of all variables “strongly suggested that risk factors for autoantibody positivity differed by HLA-DR status,” wrote the authors. They therefore performed separate analyses in children who were and were not HLA-DR4 positive.

The study found that, in children who were HLA-DR4 positive, no risk factors were associated with the presence of rheumatoid factor. But in children with no HLA-DR4 alleles, breast-feeding for more than 3 months was protective (odds ratio 0.18), and caregiver (but not parental) smoking increased the risk (OR 5.38). Additionally, compared with children who were rheumatoid factor negative, children with rheumatoid factor were more likely to be of an ethnic/racial background other than non-Hispanic white (OR 6.94).

“Examination of the risk factors for rheumatoid factor positivity in healthy children may yield important clues as to the early pathogenesis of polyarticular JRA or, potentially, seropositive rheumatoid arthritis in general,” they wrote. “An additional follow-up of this and other cohorts of children is necessary to elucidate whether these influences result in clinical diseases,” they concluded. ■

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