

# Genetics Is Top of the List of Risk Factors for RA

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SNOWMASS, COLO. — Of the many putative risk factors for rheumatoid arthritis investigated to date, only three—genetics, smoking, and reproductive factors—are supported by strong and persuasive evidence, Dr. Sherine E. Gabriel said at a symposium sponsored by the American College of Rheumatology.

But the evidence remains weak and inconsistent for potential environmental risk factors, which include infectious agents, coffee consumption, red meat intake and other dietary variables, and psychosocial stress, added Dr. Gabriel, professor of medicine and epidemiology at the Mayo Clinic, Rochester, Minn.

Genetics explains roughly 50% of the variation in the incidence of rheumatoid arthritis (RA). Two new genetic risk factors identified in the past several years are STAT4 and a polymorphism of the intracellular phosphatase gene, PTPN22.

Both provide support for the common ground hypothesis, which holds that shared genes confer risk for a number of autoimmune diseases, implying common

2.6-fold relative risks of RA in two studies, whereas quaffing three or more cups of tea per day was associated with a 61% risk reduction in one study. But the massive Nurses' Health Study showed little evidence of an association between the consumption of either beverage and RA risk.

Patients in several surveys have attributed the onset of their RA to stressful life events. However, a rigorous case-control study has failed to show any difference in the number or timing of such events be-

tween RA patients and controls (J. Rheumatol. 2000;27:2123-30).

Infection has long been suspected to be a risk factor for RA. Arguing against this is the lack of a consistent seasonal variation in RA onset, or the documentation of localized RA epidemics. Moreover, data from the Norfolk Arthritis Registry showed only 2.7% of subjects with polyarthritis had serologic evidence of human parvovirus B-19.

Several occupations that were linked to

an increased risk of mortality resulting from RA and other autoimmune diseases were recently identified. Those at increased risk were a diverse assemblage, including elementary and secondary school teachers, farmers, and operators of mining machinery (Arthritis Rheum. 2007;56:3189-201).

"It's interesting hypothesis-generating data, but ... the investigators couldn't explain why these occupational exposures were associated with increased RA mortality," Dr. Gabriel noted. ■



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DR. GABRIEL

disease pathways. A variant allele of STAT4 is associated with increased risks of both RA and systemic lupus erythematosus (N. Engl. J. Med. 2007;357:977-86), whereas the PTPN22 polymorphism confers risk for type 1 diabetes and autoimmune thyroid disease, in addition to RA.

Numerous studies have examined the relationship between use of oral contraceptives (OCs) and subsequent RA. The majority demonstrate that OCs have a protective effect, including a case-control study by Dr. Gabriel and coworkers. They found a 44% reduction in the relative risk of RA in ever-users of OCs, after adjusting for potential confounders (J. Rheumatol. 2004;31:207-13).

The protective effect was much stronger in users of early-generation OCs, which contained far higher estrogen doses than did later versions.

In contrast to OCs, postmenopausal estrogen replacement therapy has, on balance, shown no protective effect against RA in multiple studies.

Breast-feeding for 12 months or longer was associated with a 50% reduction in later RA in an analysis of 121,700 participants in the Nurses' Health Study (Arthritis Rheum. 2004;50:3458-67).

Smoking as a risk factor for RA has been extensively studied. It is clearly associated with increased risk; however, whether smoking by RA patients affects their disease progression is uncertain, she said.

Consumption of four or more cups of coffee daily was associated with 2.2- and

**Cardiac Risk Factors**  
Serving Size: 1 Adult Male  
Servings Per Container: 1

Amount Per Serving	
<b>Age</b>	48
<b>Weight</b>	243
<b>Total Cholesterol</b>	259
LDL	169
HDL	47
<b>Coronary Calcium Score</b>	397
<b>Body Mass Index</b>	37
<b>Waist Circumference</b>	48
<b>Blood Pressure</b>	
Systolic	150
Diastolic	90
<b>Fasting Blood Glucose</b>	146

**Ingredients for Coronary Artery Disease Risk:**  
Family History, Diabetes, Hypertension, Smoker, Occasional Chest Discomfort

**Refer**

**Nuclear stress testing for reliable diagnostic and prognostic results<sup>1,2</sup>**

1. Klocke FJ, et al. *Circulation*. 2003;108:1404-1418.  
2. Hachamovitch R, et al. *Circulation*. 1998;97:535-543.

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