## ACUTE PHASE REACTANTS, INTERLEUKIN-6 AND THE DEVELOPMENT OF DIABETES MELLITUS-THE ARIC STUDY

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## Abstract 117-OR

Several studies have suggested that a low grade, chronic inflammation precedes and predicts type 2 diabetes. In order to specifically address the question of whether acute phase reactants, an integral part of such inflammation, predict diabetes, we measured C-reactive protein (CRP), orosomucoid, and sialic acid, as well as interleukin-6, a cytokine known to stimulate this reaction, in a case-cohort study of incident diabetes. Incident diabetes was defined by report of a physician diagnosis, anti-diabetic medication use, or a fasting or casual plasma glucose of >= 126 or >=200 mg/dl, respectively, at one of 3 follow-up exams of the Atherosclerosis Risk in Communities (ARIC) Study. Frozen sera were measured on 651 incident cases of diabetes and 643 controls, and associations studied with proportional hazards analyses, weighted to represent the experience of 10397 eligible ARIC participants over an approximately 9 year follow-up period. Relative risk (HR) of developing diabetes for those in the 4th (vs. 1st) quartile of markers, adjusting for age, gender, ethnicity, study center, and baseline fasting glucose (Model 1) and additionally for cigarette smoking, baseline body mass index, waist-hip ratio and fasting insulin (Model 2) are shown below: TABLE

Marker	Model 1		Model 2	
	HR	95% CI	HR	95% CI
Interleukin-6	1.7	1.1 - 2.7	1.3	0.8 - 2.1
CRP	2.1	1.4 - 3.4	1.3	0.8 - 2.3
Orosomucoid	1.5	0.9 - 2.3	1.2	0.7 - 2.0
Sialic Acid	2.3	1.4 - 3.6	1.6	1.0-2.6

Although associations were generally statistically significant in initial models, their magnitude decreased considerably after adjusting for measures of adiposity and other remaining covariates. Exclusion of GAD antibody positive individuals produced only minimal changes in strength of these associations. In conclusion, these data provide further evidence that a mild, chronic inflammatory state precedes and predicts the development of diabetes in adults.