the ACE I/D and G>A polymorphisms, which is consistent with previous findings for ACE I/D. 2 Through the frequency of the 2350A allele was similar in both groups, its distribution was skewed towards severe SLE (SLAM >20). The D and the 2350A alleles were in strong LD and the predominant transmission of the DA haplotype in severe SLE indicated its association with severe SLE. These results support the involvement of ACE polymorphisms with increasing disease severity of SLE.

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Rheumatoid arthritis in Poland and Lithuania: different clinical course and HLA associations despite similar genetic background


A recognised feature of rheumatoid arthritis (RA) is its clinical heterogeneity, which may be caused by HLA factors. This theory is supported by observations that relatively severe and mild RA are associated with, respectively, DRB1*04 and DRB1*01. Further, comparisons between populations show that the disease course in the Mediterranean is milder than in northern Europe, correlating with a higher frequency of DRB1*01 and lower frequency of DRB1*04 in the former than in the latter region.

METHODS AND RESULTS
Poland and Lithuania are neighbouring central European countries. During clinical practice we noticed that RA was less severe in Lithuanian than in Polish patients. To test this observation we prospectively analysed 24 Polish and 20 Lithuanian randomly recruited patients with recent onset RA diagnosed by modified American Rheumatism Association criteria. The patients had a similar mean (SD) age (53.6 (11.4) v 57.0 (14.2) years), mean (SD) age of RA onset (52.2 (11.2) v 55.8 (14.4) years), mean (SD) disease duration (16.9 (13.6) v 13.9 (9.8) months), rheumatoid factor (RF) seropositivity (50% v 40%), and mean (SD) Steinbrocker stage (1.5 (0.5) v 1.5 (0.5)), respectively for Polish and Lithuanian cohorts. The only significant difference was higher frequency of women with RA among the Polish group (22/24 (92%) v 10/20 (50%), p<0.01).

The first assessment of the patients was performed before the start of treatment and then after 2 months and after 1 year. The analysis at baseline indicated significantly more severe disease among Polish than Lithuanian patients (table 1). After 2 months, probably as a result of treatment which was more aggressive in the Poles, disease activity in both groups decreased and most differences present at baseline were no longer seen (table 1). The clinical and laboratory results were similar also after 1 year (table 1), but radiographic analysis performed at that time showed an increase in mean (SD) erosion score and Larsen score in Poles (respectively, 0.7 (1.3) and 4.0 (6.5)), but not in Lithuanians. The difference in Larsen score progression between the two cohorts was significant (p<0.05, t test).

Because of the relative excess of men among the Lithuanian patients we also performed analysis after adjusting for the sex of the patients. We found that all the differences seen between the cohorts at baseline on univariate analysis (table 1) were also present in the multivariate analysis controlling for sex (not shown). The participants of the study and some additional patients (in total 49 Poles and 32 Lithuanians) were genotypically typed for DRB1*01 and DRB1*04, and 158 Poles and 134 Lithuanians fully typed for DRB1 (low resolution) constituted ethnically matched controls. When patients were compared with their respective controls a significant increase
of DRB1*04 (41% v 19%, odds ratio (OR) = 2.9, p<0.002) but not DRB1*01 (6% v 17%, NS) was found in the Polish group, whereas among the Lithuanians there was an increase of DRB1*01 (47% v 21%, OR = 3.3, p<0.003) but not of DRB1*04 (22% v 15%, NS). The increase of DRB1*01 among the Lithuanian patients was significant also when compared with the Polish patients (p<0.00005). No statistically significant differences in the frequencies of any of the HLA-DRB1 alleles were found between Polish and Lithuanian controls (not shown).

**DISCUSSION**

The presented data are interesting in the context of studies of RA features in southern v northern Europe. Although the association of mild (among Lithuanians) and severe disease (among Poles) with, respectively, DRB1*01 and DRB1*04 was consistent with these reports, the lack of difference in distribution of HLA-DRB1 alleles among controls from both populations does not support the hypothesis that variation in population frequency of DRB1*01 and DRB1*04 is a general determinant of geographical differences in RA severity.

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