access during the angiocardiography procedure, raising the suspicion that the peak could be a result of interference from the iodinated contrast agent.

To confirm that the interference on the Capillarays was a result of iomeprol, we enriched a control serum to give a final concentration of 28.6 g/L. On the basis of the known kinetics of the compound, this concentration was anticipated to occur in vivo. CZE revealed a peak in the middle of the β fraction, corresponding to the location of the abnormal peak in the patient (Figs. 1B and 1C).

Thus far, all reports of interference by iodinated contrast agents on CZE have been cases in which the interference was located in the α2 fraction (2, 3). In vitro, Arranz-Pena and coworkers have compared the interference by 13 different iodinated contrast agents on the Paragon by adding the different agents to control serum, and found that most agents caused a peak in the α2 fraction, but some agents (sodium-meclumine ioxaglate, ioversol, and iomeprol) caused interference in the β fraction (4). Here we describe a patient in whom a radio-opaque agent (iomeprol) produced an interference in the β fraction.

Considering that the mean (SD) half-life of iomeprol in the elimination phase is 109 (20) min (drug information sheet), we evaluated the in vivo interference caused by iomeprol in 2 patients with normal renal function who underwent angiocardiography. After receiving approval from the Institutional Ethics Committee, we obtained samples before catheterization, immediately after catheterization, and at 1, 2, 4, 8, 12, and 24 h postcatheterization. For samples from both patients, CZE revealed suspect peaks in the β fraction after angiocardiography that were clearly discernable up to 8 h after angiocardiography in the first patient and up to 4 h in the second patient. The morphology of the β fraction remained disturbed up to 12 h and 8 h after angiocardiography. After 24 h, no residual interference could be observed in either patient. The interference may, however, be expected to persist for more than 24 h in patients with renal dysfunction, because iomeprol is cleared via the kidneys.

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Further Evidence That the UGT1A1*28 Allele Is Not Associated with Coronary Heart Disease: The ECTIM Study

In their recent paper in Clinical Chemistry, Bosma et al. (1) were unable to demonstrate a protective effect of the UGT1A1*28 allele against coronary heart disease (CHD). This was surprising because individuals homozygous for the UGT1A1*28 allele have higher serum bilirubin than do heterozygous or homozygous wild-type individuals and serum bilirubin concentration is inversely related to risk of CHD (2, 3).

We studied UGT1A1 bilirubin uridine diphosphate glucuronosyl transferase genotypes in the ECTIM case-control study of myocardial infarction (MI) (4). The study was conducted on a predefined subsample of the ECTIM Study population. DNA was available for 366 male cases and 314 male controls [from Strasbourg and Toulouse: 181 cases with mean (SD) age 53.7 (8.0) years and 159 controls, with mean (SD) age 52.7 (8.7) years; from Northern Ireland: 185 cases with mean (SD) age 54.8 (8.0), and 155 controls, with mean (SD) age 54.6 (7.8)]. The UGT1A1 genotype was determined for all samples. Body mass index, presence of diabetes mellitus, systolic blood pressure, LDL-cholesterol, and HDL-cholesterol were similar in the total ECTIM case population and the 366 cases selected for this study (data not shown). Serum bilirubin concentrations were not available.

Genomic DNA was extracted from peripheral leukocytes and TATA-box genotyping was performed as described (1).

Odds ratios for MI for the genotypes 6/7 and 7/7 were computed by logistic regression analysis, with the genotype 6/6 as the referent category. The overall UGT1A1*28 effect was tested assuming an additive effect of alleles by entering the genotypes coded as a continuous 0,1,2 variable in the model. A 2nd model was adjusted for country and for established cardiovascular risk factors (smoking habits, body mass index, LDL-cholesterol, HDL-cholesterol, diabetes mellitus, systolic blood pressure). All analyses were done with Stata 8.0 for Windows.

Because there was no significant heterogeneity between Northern Ireland and France with respect to the association between UGT1A1*28 allele and MI (P = 0.48 for interaction), data from the 2 countries were pooled for further analysis. UGT1A1 promoter genotype frequencies are presented in Table 1. There was no significant deviation from Hardy–Weinberg equilibrium in controls (P = 0.33, χ² test with 1 degree of
freedom). Compared with genotype 6/6, the risks of MI were 1.4 (95% confidence interval, 1.0–2.0) for genotype 6/7 and 1.9 (1.1–3.4) for genotype 7/7, \( P \) for trend = 0.005. After adjustment for the risk factors above, the risk estimates were 1.5 (1.0–2.1) and 1.8 (0.9–3.5) for genotypes 6/7 and 7/7 respectively, \( P \) for trend = 0.017.

On the basis of its frequency and its effect on serum bilirubin concentration, the UGT1A1*28 allele was considered a possible protective factor against CHD. Indeed, this allele encodes an enzyme with reduced activity and thus is associated with increased serum bilirubin concentration [although Bosma et al. (5) have demonstrated that genotype 7/7 is necessary but not sufficient to express the Gilbert phenotype with increased bilirubin]. Our results do not support the hypothesis that the UGT1A1*28 allele is protective. We even observed an opposite result, because homozygous and heterozygous carriers of this allele appear to have an increased risk of MI. Moreover, serum bilirubin concentration depends not only on its degradation rate (catalyzed by UGT1A1), but also on its production rate. In connection with this, heme-oxygenase, the rate-limiting enzyme involved in bilirubin production (2), may also play an important role. It has been shown that a decreased activity of heme-oxygenase is associated with an increased risk of CHD in patients with coronary risks (6). It is also worth noting that heme-oxygenase induces the production of nitric oxide, a powerful and active vasodilator, likely to protect against atherosclerosis. Finally, as previously observed in other studies, it is possible that the lower serum bilirubin concentrations observed in patients with CHD simply reflect increased consumption of natural antioxidants as a result of increased oxidative capacity (7).

Our results on UGT1A1*28 are in agreement with those of Bosma et al. (1). This does not rule out the potential protective role of bilirubin, but it means that other factors that result in mild hyperbilirubinemia, such as heme-oxygenase, may play important roles. Further studies should include measurements of serum bilirubin concentrations and liver functions tests to avoid confusing the results, as shown very recently by Ioannou et al. (8).

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