limitations with respect to correcting concentrations of urinary nicotine metabolites with the creatinine concentration have been detailed by Watts et al. (5).

Undoubtedly, the differences between the various studies, particularly those of Peach et al. (2) and ourselves, relate directly to the subjects investigated. In our case, a group of patients, mostly aged, with diabetes mellitus and associated complications such as nephropathy and hypertension were assessed; Ellard’s focus, in contrast, was directed at predominantly healthy subjects, where the validity of his methodology has been established. However, as our results imply, generalization of Ellard’s methodology to other patient groups, and in our case to hospital patients with multiple disorders, may not be appropriate. More-specific procedures (ELISA, HPLC, gas chromatography, or gas chromatography/mass spectrometry) may be necessary.

References

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Mild Course of Cystic Fibrosis in an Adult with the D1152H Mutation

To the Editor:

Diagnosis of cystic fibrosis (CF) is based on the presence of chronic pulmonary lung disease, pancreatic insufficiency, and increased concentrations of electrolytes in sweat. Measurement of sweat sodium or chloride remains the laboratory confirmation of diagnosis. The disease begins early in life, so the diagnosis is usually made in childhood, although a few adult patients with a mild course of disease are identified later. The cloning of the CF transmembrane conductance regulator (CFTR) gene permits the identification of mutations in CF patients. The ΔF508 deletion accounts for ~70% of CF chromosomes; in the remaining CF chromosomes, 500 rare mutations have been described so far, to the CF Gene Analysis Consortium. Only two mutations have been reported in CF patients with normal concentrations of sweat chloride: two patients homozygous for G551S (1) and patients homozygous for 3849 + 10 kb or composite heterozygous 3849 + 10 kb/ΔF508 (2).

We report here a patient with a mild clinical syndrome of CF, equivocal sweat test results, and the genotype ΔF508/D1152H. The procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 1983.

The patient, a nonsmoking 46-year-old woman complaining of moderate dyspnea, had been suffering from bronchitis since childhood with a progressively increased frequency of acute respiratory tract infections. At age 42, a bronchographic study demonstrated the presence of bilateral bronchiectasis, mainly in the upper lobes. Cytologic investigation of the sputum showed methicillin-sensitive Staphylococcus aureus. On admission to hospital, her weight was 60 kg and her height was 1.7 m; she had no symptom related to the gastrointestinal tract. The respiratory symptoms included only moderate dyspnea. Respiratory function tests showed moderate obstruction: forced expiratory volume in one second (FEV1) was 21 (70% of predicted), FEV1/vital capacity was 67% of predicted, functional residual capacity was 2.25 L (125% of predicted), and pulmonary capacity was normal. Treatment with β₂-agonist did not improve the respiratory function.

Repeated measurements of sweat chloride concentrations gave results of 30 and 56 mmol/L by a skin chloride system (Orion Research, Boston, MA) and 24, 79, and 72 mmol/L by the pilocarpine iontophoresis method of Gibson and Cooke with sweat samples >0.1 g (normal values <60 mmol/L).

Denaturing gradient-gel electrophoresis of amplified exon 18 of the CFTR gene from the patient showed an abnormal pattern. Direct DNA sequence analysis showed a heterozygosity for a G to C substitution at nucleotide 3586. The substitution results in replacing Asp 1152 with histidine. The ΔF508 mutation was found in the other allele.

This D1152H mutation has been previously observed in one CF family with a mild phenotype (by W. Highsmith et al.; personal communication) and in patients with congenital bilateral absence of vas deferens (CBAVD) (3). In conclusion, this report shows the importance of mutation screening in uncertain CF diagnosis.

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Highly Specific Immunoassay for Cardiac Troponin I Assessed in Noninfarct Patients with Chronic Renal Failure or Severe Polytrauma

To the Editor:

Cardiac troponin I (cTnI) has recently been defined as a new marker for the diagnosis of myocardial injury detectable by selected monoclonal antibodies (1, 2). The particularity of this isoform is its presence exclusively in cardiac muscle. Several articles (2–6) report studies on the spec-

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Specificity of cTnI in myocardial infarction. In other pathologies such as renal failure (7, 8) without cardiac disease, cTnI was not detected, whereas cardiac troponin T (cTnT) was increased. Furthermore, Bodor et al. (9) recently demonstrated that cTnT is expressed in patients with polymyositis or Duchenne muscular dystrophy as well as in normal skeletal muscle.

To confirm the high specificity of a recently developed immunoassay for cTnI, we tested the sera of patients with severe polytrauma, patients with chronic renal failure, and hemodialyzed patients before and after treatment. In these noninfarct patients, we compared the specificity of cTnI with that of CK-MB mass and myoglobin. We used the cTnI Pasteur assay (Sanofi Diagnostics Pasteur, Marnes la Coquette, France), commercially available since July 1994, to measure cTnI in sera obtained from 12 patients (two samples per patient) with severe polytrauma, 49 patients with chronic renal failure, and 20 patients before and after hemodialysis; none of the patients had cardiac disease. CK-MB mass and myoglobin were assayed with the Access® automated test immunoassay system (Sanofi Diagnostics Pasteur).

This cTnI assay involves two cardiac-specific monoclonal antibodies (2). The first, used as capture antibody, is adsorbed onto polystyrene tubes, and the second is labeled with peroxidase. Assay time is 30 min; concentrations of the calibrators range from 0.1 to 1.5 μg/L; and the cutoff value is set at 0.1 μg/L. The assay showed no cross-reactivity with skeletal isoforms of Tnl, even at 500 μg/L, was negative for 392 healthy donors; and had a diagnostic sensitivity of 100% in 43 patients with acute myocardial infarction 6 h after the onset of chest pain.

Among the 24 sera obtained from patients with severe polytrauma, 58% had CK-MB mass positive for myocardial damage (>6 μg/L) and myoglobin results were positive (>90 μg/L) in 88%. (The values for CK-MB mass in these samples ranged from 2.4 to 29.5 μg/L, and myoglobin ranged from 87.9 to >3533 μg/L.) All of these serum samples were negative for cTnI (Table 1). Among the 49 patients with renal failure, 8% had CK-MB mass >6 μg/L and 88% had myoglobin >90 μg/L; the respective ranges were 0.9 to 11.9 μg/L and 38.7 to 749.7 μg/L. Again, all the serum samples were negative in the cTnI assay (Table 1). The 20 hemodialyzed patients with chronic renal failure were assayed before and after dialysis for cTnT only. Whatever the sampling time, no cTnT was detected in the sera. These results confirm the high specificity of the cTnI Pasteur immunoassay and the specificity of this marker for myocardial damage.

We conclude that this immunoassay for cTnI is a remarkable tool to differentiate between patients with myocardial damage and those with other clinical disorders such as skeletal muscle damage or renal failure without cardiac injury.

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