pairs was dictated by the matched design (*3*). We can imagine that some statistical procedure more powerful than standard Mantel-Haenszel and Miettinen tests might narrow the confidence intervals a bit, but it would not alter these point estimates by much.

Adjustment of the *RR*'s for tobacco use provides an adequate test for confounding. With subjects categorized either as non-, ex-, or current cigarette smokers or as pipe or cigar smokers, the adjusted *RR*'s were 0.97 for males and 0.76 for females, practically unchanged from their original values. Thus, tobacco use was not a confounder.

We appreciate Bross's concern that we not overlook potential artifacts or alternative interpretations of our data, but having reexamined them we see no reason to change any of our conclusions.

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N-Acetylglucosamine-6-Sulfate Sulfatase Deficiency Reconsidered

In 1978 two papers were published by our group (*1*) indicating the existence of two *N*-acetylglucosamine-6-sulfate sulfatases, specific respectively for the glucose or galactose configuration of their substrates. While extracts of skin fibroblasts derived from Morquio patients were found to be defective in *N*-acetylgalactosamine-6-sulfate sulfatase, those of a patient (G.G.) affected by a mucopolysaccharidosis clinically and radiologically different from those already known were reported to be defective in *N*-acetylglucosamine-6-sulfate sulfatase.

During 1978, as S. Toma proceeded to the purification and characterization of the two postulated enzymes, some discrepancies with our original results became evident, namely (i) the 6-sulfated hexosaminitols were poor substrates for the postulated enzymes; (ii) [1-^{3}H]-galactitol-6-sulfate was not hydrolyzed by any preparation of *N*-acetyl-galactosamine-6-sulfate sulfatase, either crude or purified; (iii) fibroblast line GM 2243 (which allegedly represented G.G.'s fibroblasts deposited in the Human Genetic Mutant Cell Repository, Camden, N.J.) was found to have normal *N*-acetylglucosamine-6-sulfate sulfatase activity with several substrates, such as *N*-acetylglucosamine-6-sulfate labeled in the acetyl group with ^{14}C or ^{3}H, *N*-acetylglucosamine-6-sulfate β-1 $\rightarrow$ 3-[1-^{3}H]galactitol, and *N*-[1-^{3}H]acetylglucosaminitol-6-sulfate.

We reviewed all the original data concerning the enzyme studies performed on G.G. and his parents; everything seemed to be in order to justify the original conclusions, except that we found the results of the enzyme measurements performed on a leukocyte extract of G.G.'s father to have been manipulated: what should have been low, defective values had been corrected and presented as "heterozygous" values.

Considering the possibility that an accidental exchange of G.G.'s fibroblasts might have occurred, we secured a frozen pellet of G.G.'s original fibroblasts, derived from a biopsy performed elsewhere about 2 years before the patient came to our attention. Enzyme studies done in parallel with this line and line GM 2243 repeatedly indicated that both had comparable, normal activity of *N*-acetylglucosamine-6-sulfate sulfatase.

By then, R. Matalon informed us that in his laboratory line GM 2243 had shown normal *N*-acetylglucosamine-6-sulfate sulfatase activity, with oligosaccharides derived from keratan sulfate used as a substrate. Recently, H. Kresse provided us with a copy of a manuscript demonstrating the existence of two different *N*-acetylglucosamine-6-sulfate sulfatase enzymes, specific for 6-sulfated residues present in heparan sulfate and in keratan sulfate. In his laboratory, line GM 2243 was normal in both enzyme activities.

We have not found a satisfactory explanation for the original results related to patient G.G., and the possibility that they were fabricated must be considered. If they were, as the senior member of the group I would wish to assume the responsibility for reviewing the original data with excessive enthusiasm and with a criticism not suited to uncover a scientific fraud. At the same time, I would like to apologize for all inconvenience caused to the scientific community.

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