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.

Ernst L. Wynder
American Health Foundation,
320 East 43 Street,
New York 10017

Steven D. Stellman
American Cancer Society, Inc.,
777 Third Avenue, New York 10017

References

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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 Marquio patients were found to be defective in N-acetylglucosamine-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. Tomà proceeded to the purification and characterization of the two postulated enzymes, some discrepancies with our original results became evident, namely (i) the 6-sulfated hexosaminotol were poor substrates for the postulated enzymes; (ii) [1-3H]-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 14C or 3H, N-acetylglucosamine-6-sulfate β-1 → 3-[1-3H]galactitol, and N-[1-3H]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 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.

Nicola Di Ferrante
1816 Norfolk
Houston, Texas 77098

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N-acetylglucosamine-6-sulfate sulfatase deficiency reconsidered
N Di Ferrante

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