Table 4

Summary of Results of Organic Acid Analyses

Test	Percentage of Laboratories Correctly Identifying Organic Acids	Percentage Correctly Diagnosed	Presumed Diagnosis
1.....	60	60	Normal
2.....	25	0	Succinic semialdehyde dehydrogenase deficiency
3.....	67	67	Glutaric aciduria type 2
4.....	56	50	Respiratory chain defect
5.....	50	75	Propionic acidemia
6.....	...	...	...
7.....	78	78	β-Ketothiolase deficiency
8.....	40	40	Mevalonic aciduria
9.....	100	100	Pyroglutamic aciduria
10.....	69	85	Oxaluria type 1

this training financially. With the higher number of participants, as well as cuts in financial support, this part of the program has suffered and it is perhaps the most important part of the program. Here is clearly a task for professional societies, such as the American Society of Human Genetics, the Society for Inherited Metabolic Disorders, and the Society for the Study of Inborn Errors of Metabolism.

The Clinical Laboratory Improvement Amendments of 1988 (PL 100–578) mandates proficiency testing for every laboratory involved in the analysis of human-body-derived specimens as of January 1, 1990. Since licensure of a laboratory under this law will be dependent on performance in proficiency testing it is of the utmost importance that deficiencies in the performance of laboratories be corrected.

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Analysis of ΔF508 Does Not Confirm a Previously Reported Recombination in a Cystic Fibrosis Family

To the Editor:

We have reported (Farrall et al. 1988) an Italian family

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with three children affected with cystic fibrosis (CF), the eldest of whom apparently showed a recombination between the CF locus and the markers located proximally to it. Haplotype analysis using the RFLPs revealed by probes metH, metD, E6, W3D1.4, XV-2c, KM.19, E2.6, and Mp6d.9 assigned the recombination event to a paternal meiosis (fig. 1). None of the distal markers analyzed in this family was informative in the father, thus precluding the possibility of localizing the recombination breakpoint with respect to them. Diagnosis of CF in each of the three children was based on two or more positive sweat tests; however, the clinical expression of the disease varied markedly among them. The second of the three children (a girl) had severe respiratory and pancreatic insufficiency, whereas the youngest had a milder clinical expression. No clinical sign of the disease was apparent in the eldest.

The identification of the most common mutation causing CF (ΔF508) (Kerem et al. 1989; Riordan et al. 1989) prompted us to reanalyze this family. Results show that the father is a carrier of ΔF508, which he transmitted to both of his younger children but not to his eldest. On the other hand, the mother is a carrier of a different, not yet identified CF mutation; haplotype analysis showed that she passed on the same CF chromosome to the three children. It therefore follows that, in spite of the positive sweat tests, the eldest child is a CF carrier, having inherited the mutant allele from his mother and the normal allele from his father.

This family was extensively studied prior to the isolation of the CF gene because the analysis of recombinant families is extremely useful for ordering markers with respect both to each other and to the disease locus. However, correctness of diagnosis is crucial to this end, because the analysis of linked markers is not always able to discriminate between a heterozygote and a recombinant. In our CF family, this was possible only by direct detection of the mutation in the father and in two of the children but not in the third one. The identification of a larger proportion of mutations causing CF than that already available will allow resolution of many cases with borderline sweat tests or with otherwise clinical features typical of CF but with a negative sweat test.

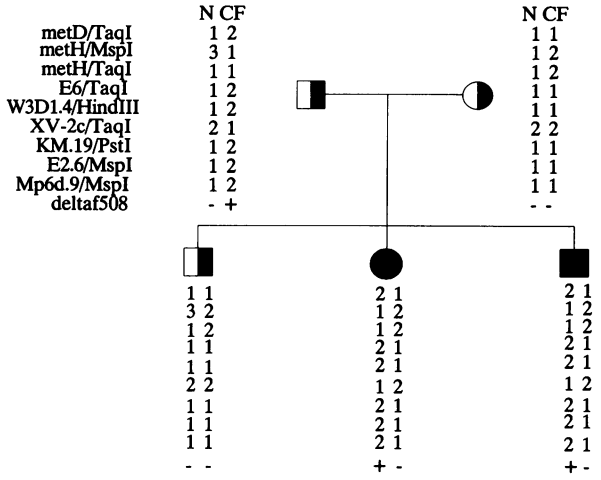

Figure 1 Pedigree of CF family

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