family. First, it allowed the diagnosis of SMA to be confirmed, since the affected child carried a homozygous deletion of SMN exons 7 and 8, as previously reported in more than 90% of SMA patients. Second, the direct analysis of the SMN gene and its flanking markers C212–C217 provided strong evidence for a de novo deletion of maternal origin and rejected the hypothesis of genetic heterogeneity since the affected and unaffected children carried different genotypes at the SMN locus. The risk for the mother of bearing another affected child should therefore be considered to be very low. Indeed, analysis of 41 families with two affected children did not provide any evidence for germinal mosaicism using microsatellite DNA markers, suggesting that this situation is very rare (data not shown, available on request).

For this reason, the combined analysis of SMN and its flanking markers C212 and C217 are still of interest for detecting de novo deletions, estimating their actual frequency, and delivering accurate prenatal prediction in SMA.

In conclusion, the use of SMN gene testing has important implications for genetic counselling in SMA families. First, it allows the diagnosis of SMA to be confirmed when a proband harbour a homozygous SMN gene deletion. In contrast, the absence of a homozygous deletion may suggest either a misdiagnosis or the presence of intragenic mutations in the SMN gene, as previously reported. A clinical re-evaluation of the proband and the search for intragenic mutations by screening of each SMN exon should be undertaken before making prenatal diagnosis feasible. Second, the use of SMN and the closest genetic markers as probes enables detection of de novo deletions in the probands. Establishing the status of the parents at the SMN locus should be helpful in estimating the actual frequency of de novo deletions at this locus. Finally, several reports have estimated the frequency of homozygous SMN deletions in asymptomatic carriers to be below 1% (0.8%). Moreover, these observations have been reported in the mildest form of the disease only. Consequently, fetuses harbouring homozygous SMN gene deletions should be predicted to be affected in families with severely affected probands.

This work was supported by the Association Française contre les Myopathies (AFM) and the Assistance Publique, Hôpitaux de Paris.


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Correction

In the November 1996 issue of the journal, on page 940, the current affiliation of Dr F M Pope as MRC Connective Tissue Genetics Group, Strangeways Research Laboratory, Worts Causeway, Cambridge CB1 4RN, was inadvertently omitted.