investigation of these patients, incorporating both clinical and laboratory evidence. It would be of great value to carry out a skeletal muscle biopsy on the patient described by Dr Albin, and to correlate the histochemical and biochemical evidence of mitochondrial respiratory chain dysfunction. These investigations are often abnormal in patients with neurological abnormalities resulting from mtDNA disease, and the characteristic mosaic pattern of cytochrome c oxidase activity in muscle or a biochemical complex deficiency may provide clues as to the nature of the underlying genetic defect. It is often difficult to ascribe pathogenicity to a mtDNA mutation, particularly if the disease has an unusual phenotype. Therefore, although the clinical evidence presented by Dr Albin is compatible with a mitochondrial disorder, the inference that the T4216C and G15257A nucleotide transitions are the primary aetiological factor responsible for Fuch's corneal dystrophy is unfounded.

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Catalepsy in Coffin-Lowry syndrome

Crow et al reported an unusual, non-epileptic, catalepsy-like phenomenon in three males with Coffin-Lowry syndrome (CLS). The authors also provided evidence of neuromuscular dysfunction as part of the phenotype by showing abnormalities on muscle ultrasound in four gene carriers, and they commented on our observation of the red dis of muscle wasting in two affected boys suddenly dropped, always in a forward position, hurting himself. No epileptic discharges have ever been noted on 24 hour EEG monitoring. Also, a progressive muscular atrophy in a new born baby, and after the experience in the two brothers we decided to operate on the scoliosis at the age of 14 years with satisfactory correction and stabilisation of the curvature. On that occasion a muscle biopsy was performed with normal results. Much to our surprise, the frequent episodes of sudden and reversible loss of muscle tone have completely disappeared after the scoliosis fusion.

In conclusion, our experience in CLS males confirms that "catalepsy" is not rare in this XLMR syndrome, as we observed it in three of 22 male patients. The aetiology and pathogenesis of this sudden collapse phenomenon remains unclear. In this perspective, it is of interest to note that these catalepsy-like symptoms increased in frequency and severity in the two brothers, and they may be related to the progression of the aetiological factor. In contrast, the collapse symptoms disappeared completely in the third male after surgical correction of the scoliosis.

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Autoclaving Guthrie cards does not prevent their use in PCR reactions!

Doctors Rahman, Emery, and Poulton (J Med Genet 1998;35:263) point out their problems in obtaining neonatal screening dried blood spots or Guthrie cards from patients with the MELAS 3243 mutation. They comment that they of the four cards they were able to obtain, one had been autoclaved. This, they claim, destroys the DNA.

Dried blood spot cards are commonly autoclaved or steamed before performing the bacterial inhibition assay for phenylalanine HPLC screening for phenylketonuria (PKU). We have used such blood spots for analysis of the common mutations for medium chain acyl CoA dehydrogenase deficiency (MCADD), early infantile epileptic encephalopathy, and the NARP 8993 mutation. One has also been successfully used for identification purposes by DNA fingerprinting. In a study of autodestructed blood spots from patients in the West Midlands Region, the common MCADD mutation, a failure rate of PCR of only 0.3% was obtained.

Hence there is no reason to believe autodestructing newborn spots contributes to a poor PCR. In fact it may be that denaturing contaminating protein by autoclaving may help to reduce the amount of protein carried over during extraction and hence reduce the risk of PCR failure. However, we fully support the authors' suggestions for central funding for the storage of this important medical resource.

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Many clinicians who deal with high risk obstetrics or have specialised in maternal-fee d medicine, obstetric physicians, and geneticists with an interest in the management of people with genetic disorders who intend to have