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, as 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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3 Chinnery PF, Turnbull DM. The clinical features, investigation and management of patients with mitochondrial DNA defects. J Neurol Neurosurg Psychiatry 1997;63:559-63.
9 Terroni A, Petrossi M, D'Urbano L, et al. Haplo- and phylogenetic analyses suggest that one European-specific mtDNA background plays a major role in the expression of Leber hereditary optic neuropathy by increasing the penetrance of the primary mutations 11778 and 14484. Hum Genet 1997;99:1107-21.

"Cataplexy" in Coffin-Lowry syndrome

Crow et al reported an unusual, non-epileptic, cataplexy-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 rapid decline of muscle wasting in two affected boys, aged 15 and 14 years at the time of our report. In that report, we described the frequent occurrence of generalised epileptic seizures without pathognomonic epileptic patterns on EEG. The age of 6 years, when we had occasion to follow these CLS brothers up to their sudden death at the age of 32 and 34 years, respectively. During this follow up it became evident that the "epileptic episodes" were episodic tetraplegic or paraplegic seizures with atonia; as in case 1 reported by Crow et al, these episodes were precipitated by a loud noise or excitement. The frequency and severity of these tonic attacks worsened with age and was correlated with a further progression of the peripheral muscle wasting and a severe thoracolumbar torsion scoliosis, which finally resulted in acute cardiorespiratory failure.

Over the last 25 years we have had the opportunity to examine 20 other CLS males. In one of these patients the same type of sudden, non-epileptic attacks were noted from the age of 4 years, when this affected boy suddenly dropped, always in a forward position, hurting himself. No epileptic discharge have ever been noted on repeated 24 hour EEG monitoring. Also, a progressive thoracolumbar scoliosis developed in the boy, 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 surgery. In conclusion, our experience in CLS males confirms that "cataplexy" 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 cataplexy-like symptoms increased in frequency and severity in the two brothers, together with the progressive thoracolumbar scoliosis and muscle wasting. 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 MECLS 3243 mutaion. They comment that 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 in screening for phenylketonuria (PKU). We have used such blood spots for analysis of the common mutations for medium chain acyl-CoA dehydrogenase deficiency (MCADD), and reported on the throughsteaminution intolerance, and the NARP 8993 mutation. One has also been successfully used for identification purposes by DNA fingerprinting. In a study of these blood spots, it is clear that there was some contamination in the West Midlands Region 7 for the common MCADD mutation, a failure rate of PCR of only 0.3% was observed.

There is no reason to believe that autoclaving blood spots could contribute 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 the storage of this important medical resource.

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Many clinicians who deal with high risk obstetrics or have specialised in maternal-fetal medicine, obstetric physicians, and geneticists with a welcometo the management of patients with genetic disorders who intend to have