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 in his histochemical and biochemical evidence of mitochondrial respiratory chain dysfunction. These investigations are often abnormal in patients with neurological abnormalities resulting from mtDNA defects, 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.1 Therefore, although the clinical evidence presented by Dr Chinnery is consistent 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.

PFC is a Wellcome Trust Research Fellow. RA is a MRC (UK) Research Fellow. NH is supported by the Wellcome Trust, The National Eye Institute (RO1 EY107509), and the John Sealy Memorial Endowment Fund.

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“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
euromuscular 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 disc muscle wasting in two affected brothers, aged 15 and 14 years at the time of our report.1 In that report, we described the frequent occurrence of generalised epileptic seizures without pathognomonic epileptic elements on EEG. For the age of 6 years, 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 tonic-clonic convulsions and were precipitated by being tired; as in case 1 reported by Crow et al,1 these episodes were precipitated by a loud noise or excitement. The frequency and severity of these abortive attacks worsened with age and was correlated with a further progression of the peripheral muscle wasting and a severe throracolumbar tonus scoliosis, which finally resulted in acute cardiopulmonary 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 boy suddenly dropped, always in a forward position, hurting himself. No epileptic discharges have ever been noted on 24 hour EEG monitoring. Also, a progressive thoracolumbar scoliosis was noted. We, however, 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 with age and was correlated with a further progression of the peripheral muscle wasting and of a severe thoracolumbar torsion scoliosis, which finally resulted in acute cardiopulmonary failure.

In conclusion, our experience in CLS males confirms that “cataplexy” is not that rare in XLRM syndrome, as we observed it in three of 22 male patients. The aetiology and pathogenesis of this sudden, acute 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, when they had a severe 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 MELAS 3243 mutation. 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 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), very long chain fatty acid intolerance, and the NARP 8993 mutation. One has also been successfully used for identification purposes by DNA fingerprinting. In a study of a large number of blood spots in the West Midlands Region for the common MCADD mutation, a failure rate of PCR of only 0.3% was obtained.1

Hence there is no reason to believe that autoclaving 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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