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 perform 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.

“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 profound 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 epileptiform elements on EEG. At 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 epileptic spasms with atonia; as in case 1 reported by Crow et al,2 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 of a severe thoracolumbar 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 stopped, always in a forward position, hurting himself. No epileptic discharges have ever been noted on routine 24 hour EEG monitoring. Also, a progressive thoracolumbar scoliosis was noted during the third male after the scoliosis fusion. In the following year, he developed a further deficit in walking, which was noted to precipitate with standing up. At the age of 15 years, he stopped walking and was noted to have profound muscle wasting in the lower limbs, and it was decided to operate on the scoliosis fusion.

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 phenotype remains unclear. In this perspective, it is of interest to note that these cataplectic-like symptoms increased in frequency and severity in the two brothers, together with the progression of the 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 Poultou (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 mtDNA 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 (PAH) screening for phenylketonuria (PKU). We have used such blood spots for analysis of the common mutations for medium chain acyl-CoA dehydrogenase deficiency (MCADD), respiratory enzyme intolerance, and the NARP 8993 mutation. One has also been successfully used for identification purposes by DNA fingerprinting. In a study of 1000 newborns, 40 blood spots from the West Midlands Region for the common MCADD mutation, a failure rate of PCR of only 0.3% was obtained.3

Hence there is no reason to believe autoclaving will contaminate 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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