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UK centres are not following the Royal College of Pathologists’ recommendations for storage of Guthrie cards: a national policy is needed

Stored neonatal blood spots are a valuable source of DNA for retrospective diagnosis. A recent working party of the Royal College of Pathologists recommended storage of neonatal screening test (Guthrie) cards for at least 20 years provided that no deterioration of the sample has occurred. Our recent attempts to trace such cards convince us that a UK national policy and central funding for storing these cards is necessary.

Mitochondrial encephalopathy with stroke-like episodes (MELAS) is frequently associated with a mitochondrial DNA point mutation, A3243G. Segregation and proliferation of this mutation in human lymphoblastoid cell lines is not well understood. Levels of the 3243 mutant in blood are usually lower than in muscle and cross sectional data suggest that the level of mutant in blood may fall with increasing age. There is concern that cases of MELAS may be missed if diagnosed using the polymerase chain reaction (PCR) on blood. Longitudinal studies are necessary to clarify this issue. We have carried out a European collaborative study using Guthrie cards to compare levels of the 3243 mutant mtDNA in blood at birth and at diagnosis, under the auspices of the European Neuromuscular Centre. When we attempted to include patients with MELAS born in the UK after 1970 and, with the informed consent of the patients or parents or both as appropriate, sought their Guthrie cards, we met with no co-operation. Three hospitals have their own laboratories; a telephone survey of the 25 UK neonatal screening laboratories showed marked variability in practice between regions. Two centres use serum for screening rather than blood spots, and one stores blood spots for five months only. Only 12 centres store cards for longer than 10 years, and the trend is towards shorter periods because of financial pressures. We suggest that a national policy for storage of neonatal blood spots is needed and that this may require central funding. Centralisation of cards and records would be an advantage as families now move between regions frequently and do not always recall their previous addresses. Cards should be stored in such a way as to prevent cross contamination, particularly if PCR is to be used in analysis of the blood spot.

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Cyclopia and siringenemia in a liveborn infant

Recently, Chen et al1 published the case of a stillborn infant who presented with cebocephaly, spina bifida, cyclopia, and siringenemia. We would like to describe a liveborn infant with cyclopia and siringenemia, identified by the Spanish Collaborative Study of Congenital Malformation (ECEMC) group. This case is similar to that the one published by Chen et al, although with a more severe form of clinical holoprosencephaly with cyclopia, absent nose with presence of a proboscis, and without any evidence of spina bifida. In 1992, we participated in an epidemiological study in an international collaboration, providing data from the ECEMC to the study group. A picture of the case being described here in detail was published in the paper by Källén et al2 just to illustrate the title of that paper (The cyclops and the mermaid) but the case, which was included in the epidemiological analysis, was not described in full. In 1994, in a Letter to the Editor,3 we commented that we had observed a case with cyclopia and siringenemia that may be a clinical representation of a case described by Modenier of Ravena, but the case was not described.

The infant was the product of the second pregnancy of a 29 year old mother and a non-consanguineous 33 year old father, both healthy. The family history was unremarkable. The first pregnancy ended, a year earlier, in a normal male infant. In 1978, the proband was born spontaneously at 39 weeks of a previously healthy, otherwise uncomplicated pregnancy, apart from a respiratory tract infection during the first 15 days of gestation. The mother denied any exposure to known teratogens, including alcohol and tobacco. She also denied having had problems in conceiving. At birth, the infant’s weight was 1600 g (<3rd centile). The infant died at 15 minutes and had microcephaly, absent nose with presence of a proboscis, cyclopia, siringenemia and a clinical right forebrain deficiency. No external genitalia or anus were visible. The umbilical cord contained only an artery and a vein. It was not possible to perform any radiological study, karyotype, or necropsy.

The prevalence of any type of holoprosencephaly in the series of 1 245 863 births monitored by the ECEMC between 1980 and 1996 is 0.83 per 10 000 births, while the prevalence of cyclopia and siringenemia is 0.10 and 0.08 per 10 000 births, respectively. In an epidemiological study on the association of holoprosencephaly and caudal dysgenesis,4 we showed that both conditions tend to be preferentially associated. That is, both are associated in the same child with a frequency that is significantly higher than would be expected by chance. However, the combination of the two most extreme forms of alteration of the cephalic and caudal part of the embryo, cyclopia and siringenemia, is very infrequent. In fact, our case was identified among a total of 12 863 births and it appears that this case is the first one published with cyclopia and siringenemia, bringing to three the total published cases with different degrees of holoprosencephaly and siringenemia.5 Cyclopia and siringenemia are gross alterations of early blastogenesis. Thus, as Opitz postulated6 and we reported,7 the combination of the two conditions, which is lethal, is a polytopic response of the alteration of the primary field, mostly affecting the midline. We have also observed8 that mothers of infants with blastogenic defects have a higher proportion of previous abortions that may mask the recurrence risk. However, we consider that in cases of holoprosencephaly (with different degrees of severity) and siringenemia, in the absence of abnormalities of the mother and abnormal maternal diabetes, the recurrence risk at birth should be very low.

We think that it is important to present this case in detail since, at present, it is the only one that has the two most severe forms of alteration of the cephalic and caudal part of the embryo (cyclopia and siringenemia), and also because it was identified among a series of consecutive births, which allows the estimation of the birth prevalence of this entity.

This work was supported in part by a grant from “Fundación 1000 para la investigación sobre defectos congénitos”, Spain, and by a grant from Dirección General de Salud Pública, Ministerio de Sanidad and Consumo, Spain.

1 Chen CP, Shib SL, Liu FF, Jan SW. Cebocephaly, alobar holoprosencephaly, spina bi-