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 storage of 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 a family with a maternal pattern 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 cord 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 conducted 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.

We examined blood spots from 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. A panel of laboratories was asked to measure the load at birth. It has been possible to locate only four cards, and one of these has been autoclaved (this destroys DNA). Hence, the failure rate was 87%, despite cooperation from both patients and relatives. 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 sirenemla in a liveborn infant

Recently, Chen et al published the case of a stillborn infant who presented with cecolo- malencephaly, sirenemla, spine bifida, and sirenemla. We would like to describe a liveborn infant with cyclopia and sirenemla, identified by the Spanish Collaborative Study of Congenital Malforma- tions (ECEMC). The case is similar to the one published by Chen et al, although with a more severe form of clinical holopros- encephaly with cyclopia, absent nose with presence of a proboscis, and without any evi- dence of spine bifida.

In 1992, we participated in an epidemiologi- cal study in an international collaboration, providing data from the ECEMC to the study group. A picture of the case is described here in detail was published in the paper by Källén et al just to illustrate the title of that paper (The cyclops and the mermaid) but the case, which was included in the epidemiologi- cal analysis, was not described in full. In 1994, in a Letter to the Editor, we commented that we had observed a case with cyclopia and sirenemla that may be a clinical represen- tation of a postulated Mendelian disease, 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. There was no family history of congenital malformations. The first preg-
BOOK REVIEW

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It is a salutary experience to open the index of a history book and find oneself cited (albeit only once, and then only in parenthesis), if for no other reason than that it reinforces one's awareness of the passage of time. The events related in Errol Friedberg's book took place within living memory and the author deserves credit for eliciting for us the accounts of those who were responsible for them. The discoveries themselves are, of course, fascinating. While the need for living things to have means of dealing with the chemical and physical threats to their genomes is old hat to us, and the ways in which they achieve genomic stability and fidelity are not conceptually difficult today, this was not the case in the early days of DNA repair. It was first necessary to know the gene's composition, its structure (established by Dan Brown and Lord Alexander Todd in 1952), and its conformation (as shown by Watson, Crick, and Wilkins in 1954). Indeed there is a subtext to the story in that the giants in the field of molecular genetics (as it came to be known) were in general little interested in genomic repair and tended to regard such work as second-rate, largely because it was often done in national laboratories established and maintained for the purposes of supporting atomic energy and weapons research. Yet DNA repair has contributed more than its fair share of major discoveries, excision repair, mismatch repair, and the SOS coordinated inducible response being the most exciting with implications that extend to modern clinical medicine. Even the classic work of Avery, McLeod, and McCarty in 1944 showing that genes are made of DNA was antedated by Hollaender and Emmons in 1941, who showed clearly that the wavelength of ultraviolet light that was most effective in inducing changes in genes coincided with the peak of absorption by nucleic acid.

Various controversies are dealt with as fairly as appears possible. It is understandable that Friedberg has no wish to disturb the amicable relations that he has with his colleagues. One senses, however, that there could be another even more entertaining history written that gave more prominence to the paranoidas, suspicions, and personal animosities of the characters involved in the "natures and all".

While the field up to, say, 1970 is covered well, after that the coverage is selective. There is, for example, no more than a paragraph about the repair of ionising radiation induced double strand DNA breaks, despite the fact that the field is of major importance, and the commonality of mechanism with immunoglobulin gene rearrangement foreseen since around 1980 has been spectacularly demonstrated in the last few years. Although there is a full and almost complete discussion of the inducible SOS system (lacking only an acknowledgement of the contribution of Peter Emmerson in Newcastle), there is no account of the discovery of the molecular mechanism by which mutations are made by the SOS gene products. Obviously, a second and updated edition will be needed before Friedberg himself retires.

One final thought in the reviewer's mind concerns the conceptual nature of the really significant advances described in this book. They were frequently made by bright people thinking beyond the confines of their field, often beyond what they were being paid to do, going out of their way to interact with other bright people who were needed for mental cross fertilisation. The advances were more often than not predictable only with hindsight. Rarely would they have been the subject of a successful grant application in today's world.

BRYN BRIDGES

NOTICE

Embryos, Genes, and Birth Defects
The Institute of Child Health and Great Ormond Street Hospital for Children NHS Trust will hold a Short Course on "Embryos, Genes, and Birth Defects" on 5-7 May 1998. Course organisers: Professor Peter Thorogood and Professor Robin Winter. Speakers will include Steve Brown, Andrew Copp, Dian Donnai, Patrizia Ferretti, Ieuan Hughes, Robin Lovell-Badge, Willie Reardon, Peter Scambler, Cheryll Tickle, Veronica Van Heyningen. Themes to be covered: Research strategies, Mapping syndromes to genes, Use of dysmorphology databases, molecular genetic approaches, Transgenic technology, Teratology as an analytical tool, Developmental mechanisms, Analysis of birth defects of selected organ systems. Fee £175. For further information, please contact: Courses and Conferences Office, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK. Tel: 0171 829 8692, fax:0171 831 0488, e-mail: Courses@ic.hal.ccl.ac.uk

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