Letters to the Editor

CHANGES IN VERDICT OF SUDDEN INFANT DEATH

SIR,—To investigate how often histological and other detailed studies are done when a death has been registered as sudden infant death syndrome (SIDS) and to find out what is done with any such new information all notifications of SIDS to the coroners in Inner North London and West London for the years 1982 and 1983 have been analysed. Post-mortem reports were examined for every such death between 1 week and 1 year of age. The pathologist was asked if he had done any histological, virological, or other investigations and whether his opinion of the cause of death had changed as a result. He was also asked if any changes had been reported to the Office of Population Censuses and Surveys, the general practitioner, the coroner, and the parents.

56 cases of SIDS were recorded for Inner London and 49 for West London. Necropsies were done at seven hospitals, 38% being by one pathologist. 98 questionnaires were completed, the remaining 7 being from one hospital which did not respond.

Of the 98 cases 84 were investigated histologically, 45 virologically, and 46 were examined in other ways (chromosomal, bacteriological, toxicological, and radiological investigations). One hospital (13 cases) did no further investigations after the coroner's post-mortems. As a result of further investigations, the original diagnosis was changed in 20 cases and added to in 5 (table). Most of the changes in diagnosis (18) were made by one pathologist who, in his 37 cases, did histological, virological, and other investigations in almost every instance.[1] Where histology alone was done the diagnosis was changed only twice.

One pathologist did not change the cause of death but reported abnormalities or associated lesions in 10 of his 20 cases, most of these being recorded as contributory causes on the certificate. He wrote that in 1 case SIDS should probably have been replaced on the death certificate by bronchopneumonia; in another case the post-mortem findings suggested the possibility that the child had been abused but there was no supporting evidence; and in another case both the pathologist and the police suspected abuse.

The coroner was informed of all 20 cases where the diagnosis was altered; doctors (1 general practitioner, 4 paediatricians, and 1 chest physician) were told in 6 cases, and the pathologist expected that the parents would then be informed. In only 5 cases were the parents told directly about the change in diagnosis and the OPCS was not told by the pathologist or, routinely, by the coroner.

These findings support earlier conclusions that many cases of SIDS are due to occult disease[2,3] and that most of these causes come to light because tests other than macroscopic and microscopic investigations were done. Even though revisions in the diagnosis, made after histological and other investigations, were reported to the coroner, there is no certainty that the officially certified cause of death will be changed and neither parents nor family doctors were routinely told that SIDS was no longer thought to be the cause. Parents do become anxious where there is no definite cause of death[4] and are helped by a more accurate diagnosis.[5] By failure to notify general practitioners an important source of help for bereaved parents is being neglected. The SIDS programme in the United States advocates, in cases of sudden unexpected infant death, not only post-mortem studies to determine the cause of death but also a written report to the family.[6] This practice is not routine in the UK, although there is now increasing pressure for specialist paediatric centres to investigate these deaths. What is needed is a strict code of practice, with guidelines not only for investigating further deaths certified as SIDS but also for ensuring that any resulting changes in the diagnosis are reported to everyone concerned.

CHANGES IN AND ADDITIONS TO DIAGNOSIS OF SIDS

Changes in diagnosis:	*Changes in diagnosis (cont'd):*
(1) *E coli* septicaemia and bronchopneumonia	(12) Bronchopneumonia
(2) Endocardial fibroelastosis; *E coli* septicaemia	(13 Streptococcal pneumonia
(3) Acute tracheobronchitis	(14) Acute tracheobronchitis; pneumococcal otitis media
(4) *Haemophilus* pneumonia	(15) Tuberculosis
(5) *Staphylococcus aureus*	(16) Pneumococcal pneumonia
(6) Pneumococcal pneumonia	(17) Carotid body hypoplasia
(7) Bronchopneumonia; gangrenous large intestine; intestinal malrotation	(18) Pneumococcal septicaemia
(8) *Klebsiella* septicaemia	(19) Bronchopneumonia
(9) Pneumococcal pneumonia	(20) Acute bronchitis
(10) Disseminated intravascular coagulation; septicaemia; acute enteritis	*Additions to diagnosis:*
(11) Pneumococcal bronchitis; pneumonia	(21) Pulmonary tuberculosis
	(22) Pneumococcal otitis media
	(23) *Haemophilus* tracheobronchitis
	(24) Pneumococcal otitis media
	(25) Fetal distress

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INOSINE PRANOBEX FOR MUCOCUTANEOUS HERPES

SIR,—Your Jan 26 editorial on the use of inosine pranobex in mucocutaneous herpes contains several misleading statements and conclusions. You refer to five clinical trials in support of your argument that the inosine pranobex looks "clinically useful". None of these have been published in full so it is difficult to assess them properly. Even so some of them are clearly flawed, and any clinical advantages were very slight.

One study[1] inappropriately combined data from patients with primary genital, recurrent genital, and orolabial herpes; more seriously, the mean number of days of illness before the onset of therapy was twice as long in the inosine pranobex patients as in the controls. These two factors invalidate this trial. 61 patients with recurrent genital herpes were entered in the second study.[2] The patients treated with isoprinosine were said to have had a significantly shorter time to healing, but no statistical data were provided. Bouffaut and Saurat[3] also combined oral with genital infections. They used a complex scoring system at some unspecified point in time and claimed that "isoprinosine was very good" again without statistical analysis or any other clinical information.

Galli and colleagues[4] studied recurrent herpes and found a significant reduction in the mean number of recurrences in isoprinosine-treated patients with labial herpes compared with controls, but not in patients with genital herpes. The mean number of recurrences in the year of the trial was 6·04 in isoprinosine patients compared with 7·87 in controls, and this reduction is unlikely to be clinically important. The final clinical trial,[5] in 39 patients with primary genital herpes, reported a reduction in time to healing of lesions (18·1 days compared with 22·3 days) and of viral shedding (7·00 days compared with 11·2 days). These significant effects are only of marginal benefit, particularly when compared with the effects of oral acyclovir in primary genital herpes.[6-8]

The effect of inosine pranobex (if any) on mucocutaneous herpes cannot be assessed from the clinical trial data available. Until the results of properly conducted clinical studies have shown a

significant and consistent effect this drug should not be used to treat patients with either oral or genital herpes.

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LASER-ASSISTED VASCULAR ANASTOMOSIS

SIR,—Dr Quigley and his colleagues (Feb 9, p 334), in their letter on laser-assisted vascular anastomosis, criticise my contribution to your correspondence columns (Oct 6, p 816). My letter was a brief description of the clinical applications of the technique of microvascular anastomosis with the neodymium-YAG laser. The details are given elsewhere.[1–3] To the best of my knowledge, based on my last visit to Northwestern University Medical School in May, 1984, my neodymium-YAG laser technique has not been repeated by Quigley or any of his co-workers. They do not have the micromanipulator described by me and the spot size of 4 mm they mention is ten times bigger than the 0·3 mm spot size I use, and this difference invalidates any comments of Quigley et al on my technique.

Quigley et al are interested in a particular CO_2 milliwatt laser and do not mention the fact that the vascular anastomosis achieved by them is not sutureless, but only supplements the conventional suture technique. I have not been able to find any properly documented publication on the use of the milliwatt CO_2 laser in vascular anastomosis.

Quigley et al are "certain that basic mechanisms of tissue welding is the same for all lasers". This is ridiculous: in the first place, the basic mechanism for laser tissue welding is not fully understood and, secondly, differences in the biological effects of lasers of different wavelengths are well accepted. This is why milliwatt CO_2 lasers achieve poorer results in vascular anastomosis. Those who study my technique and apply it properly will not have any of the problems and doubts Quigley et al mention. Since my technique is not yet fully automated, microsurgical skill is still required for a successful outcome. My technique should not be attempted without proper equipment and training in the safe use of it. Misuse of the neodymium-YAG laser can lead to complications.[4]

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EFFECTS OF CRYOPROTECTANTS ON HUMAN OOCYTE

SIR,—The report from Australia[1] of a pregnancy with subsequent live birth after transfer of an eight-cell human embryo, after cryopreservation, confirms that human embryos can be successfully recovered after storage at −196°C. Cryopreservation of embryos raises many ethical problems, and it may be more acceptable to freeze unfertilised oocytes. With this in mind we have been studying the cryopreservation of human preovulatory oocytes.

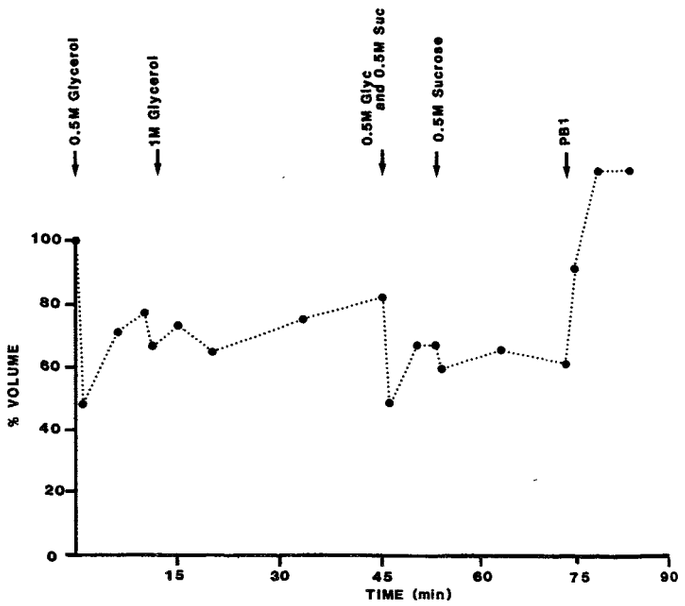

Fig 1—Dimensional changes of human oocytes during addition and removal of glycerol.

PB1 = modified Dulbecco's phosphate.

With low concentrations of glycerol as cryoprotectant and normothermic equilibration temperatures mouse oocytes can be successfully cryopreserved with subsequent culture to expanded blastocysts after thawing and in-vitro fertilisation.[2] Using a similar protocol, we soon found that human oocytes required at least 45 min equilibration time in glycerol with an increase in glycerol removal time (fig 1). After removal of cryoprotectant freshly produced sperm was added to media containing oocytes in an attempt at fertilisation. Fertilisation was not observed in any of the oocytes so treated.

High survival rates of eight-cell mouse embryos is possible after freezing with 1,2-propanediol as cryoprotectant and an

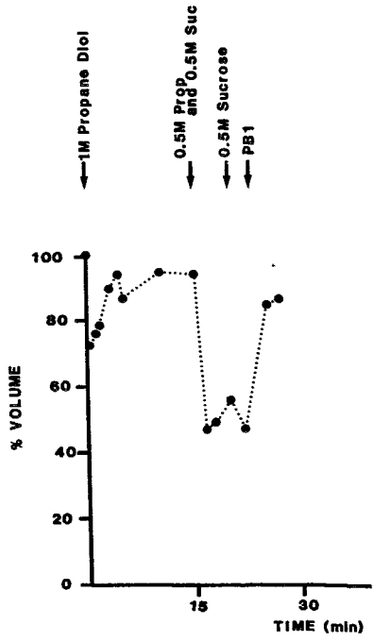

Fig 2—Dimensional changes of human oocytes during addition and removal of 1,2-propanediol.