Storage of sperm and embryos

Cryopreservation of sperm should be offered to men with testicular cancer

EDITOR,—Patients with testicular cancer often become infertile as a result of the disease and its treatment. It has been argued that all such patients should be offered cryopreservation of semen,¹ but in 1980 Braken and Smith reported that only 4% of patients had semen of suitable quality for a fertility programme.² The advent of intracytoplasmic sperm injection now allows even low quality sperm to be used successfully,³ but many clinicians are unaware of recent advances and the facilities available.

To determine the awareness and availability of this service we sent a questionnaire to 292 consultant urologists, of whom 197 (67%) replied; we also contacted the 41 cryopreservation centres in the United Kingdom. We found that 71 urologists routinely used cryopreservation facilities, while 123 left the oncologists to organise this. Of the 71 who routinely used the services, most (48) recommended storage of semen samples obtained after unilateral orchidectomy that was performed within one week of diagnosis; only a minority (23) thought that a short delay between diagnosis and orchidectomy would have an adverse effect on the clinical outcome. Of the 41 cryopreservation centres, only five offered storage on the NHS, but a further 10 had contracts with oncology services at preferential rates. All of the centres offered immediate access to facilities, so that the treatment of patients with cancer would not be greatly delayed.

Cryopreservation of semen has been available for over 20 years in the United Kingdom but is still used by a minority of urologists. Infertility after the treatment of testicular cancer may be a cause of litigation, and this will become an increasingly important issue. Low cost storage of sperm is readily available in most of the United Kingdom and should be offered to patients with testicular cancer at the start of their treatment.

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Storage facility exists for sperm from patients positive for antibody to hepatitis C virus

EDITOR,—We recently encountered considerable difficulties in arranging the storage of sperm

from a 19 year old man with severe haemophilia A who was positive for antibodies to hepatitis C virus after an infusion of infected pooled blood products. He had normal transaminase activities and had developed no other viral complications. He had been diagnosed as having stage IIE Hodgkin's disease and needed to start chemotherapy. He had a good prospect of being cured of this disease and was keen to have the option of starting a family later. Ten fertility centres with facilities for long term storage of sperm were approached. Only two were able to offer help, albeit with some delay.

As a result of this case, the University College Hospital Trust has set up a separate storage facility at the Thorn Institute at the Middlesex Hospital, London. It is disappointing that such a service is not provided more widely, and until this action was taken no such facility was available at all. Hepatitis C virus has a low rate of sexual and intrafamilial transmission,^{1 2} and we are not aware of any cases in which it has been transmitted by stored bone marrow or semen. A case of hepatitis B acquired from stored bone marrow was recently described,³ and hence vigilance is required for all potentially transmissible agents. With isolated storage facilities now provided, all patients who are positive for antibody to hepatitis C virus should be able to preserve their long term fertility.

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Couples having IVF should be asked their wishes about spare embryos before egg retrieval

EDITOR,—The recent mass destruction of embryos in Britain could have been prevented if couples had been asked to give their consent for embryo donation before cryopreservation.¹ Many couples who are unable to have children could have benefited from the donation and transfer of these embryos.

Since 1986 the state of Louisiana, uniquely in the United States, has had a law (Civil Code Article La RS 9:121-133) that allows the anonymous donation of embryos but prohibits the deliberate destruction or sale of unimplanted embryos and the culture of embryos solely for research. In disputes arising between any parties about the embryo after in vitro fertilisation the judicial standard is to decide in the best interest

of the embryo. This law does not supersede the decision in the case of *Roe v Wade*, whereby women may obtain a legal abortion of an intra-uterine embryo or fetus.

To ensure that legal rights would extend to the embryo the statute declares the embryo to be a juridical person. This law, which was enacted before the first cryopreservation procedure was performed in Louisiana, was written with the aid of attorneys, embryologists, and directors of in vitro fertilisation programmes, representing both Roman Catholic and Protestant points of view. In the view of the law and many people of all faiths in the state of Louisiana, the embryo is a human being (J Krentel, R P Dickey, Vth world congress on in vitro fertilisation and embryo transfer, April 5-10, 1987).²

All couples who are considering in vitro fertilisation are informed that, once their embryos have been frozen, they cannot be purposefully destroyed but must be given a chance of survival; the couple are also told that they may select a host uterus or allow the clinical staff to select an infertile recipient for anonymous donation. Alternatives, such as immediate donation of fresh eggs or embryos, donation of excess eggs for research, and insemination of a limited number of eggs, are also offered. Couples are contacted annually about their wishes regarding their embryos. We have found that many couples are willing to receive the donated embryos and to have the chance of having a child.

Clearly, the time for the biological parents to indicate their wishes in all eventualities, including death or loss of contact with the clinic for years, is before egg retrieval. Had this been done

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in Britain, many of the difficult decisions would not have been necessary.

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Counselling will be needed when embryos are donated as well as when they are stored

EDITOR,—We agree with Alan Trounson and Karen Dawson that the ability to cryopreserve embryos has presented both opportunities and dilemmas.¹ The authors suggest that consent be obtained at the time of storage, and this may have organisational advantages. Nevertheless, we have misgivings about this suggestion because many units may not have screened couples for HIV infection, cystic fibrosis, and hepatitis B. It is also possible that, in future, additional screening may be deemed necessary. We suggest that couples who consent to the storage of embryos for donation should be told that at the time the embryos are donated they will need to be further counselled and screened and will need to give their consent again. Our present experience is that couples do not wish to return to the unit for further screening, possibly because we did not counsel them about this at the time that their initial consent was obtained.

If a couple who wish to donate frozen embryos return for screening and are found to be positive for HIV or hepatitis B virus then another potential problem arises: there is currently some concern that cross contamination is possible between tissues held in liquid nitrogen storage.²

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Postmenopausal cystitis

Bladder cancer may be a cause, but interstitial cystitis is an unusual differential diagnosis

EDITOR,—Linda Cardozo is right to draw attention to the problem of postmenopausal cystitis and the use of topical oestrogens in its treatment.¹ Topical oestrogens are almost certainly underused in this condition. From the urological perspective, however, certain important points should be emphasised.

Firstly, ultrasonography is probably preferable to intravenous urography for imaging. Ultrasonography will quantify residual urine and detects renal and bladder calculi better than plain radiography. Ureteric stones (which ultrasonography will probably miss) are virtually never the isolated cause of recurrent infections.

Ultrasonography spares the patient irradiation and the finite risk of a reaction to contrast medium.

Secondly, bladder cancer is an important consideration in postmenopausal women who present with irritative voiding symptoms. There can be few urologists who have not seen patients referred late with bladder tumours after inappropriate management for other presumed causes of lower urinary tract symptoms. In all patients whose urine is not free of cells after treatment of a confirmed urinary tract infection, repeat cytological examination of urine and flexible cystoscopy should be carried out. Cytological examination will detect those patients with carcinoma in situ whose bladder looks normal cystoscopically.

Thirdly, interstitial cystitis is an unusual differential diagnosis in this group of patients. We accept that it creates considerable controversy both in its diagnosis and in its treatment. The putative role of mast cells in this condition is debated; some studies have reported greater numbers of these cells in the detrusor muscle of patients with interstitial cystitis than in normal detrusor muscle, though the value of counting mast cells for diagnostic purposes is still doubted.² Indeed, overlapping values are found when the control group includes patients with other types of chronic cystitis³; differences are at the statistical, rather than the individual, level. The issue is further confused by the fact that mast cell counts that are related to the surface area of the detrusor muscle will be affected by the state of contraction or distension of the bladder wall and the procedures for tissue fixation and processing. For these reasons, many uropathologists would not routinely count mast cells when presented with a biopsy specimen in this clinical condition⁴; the main value of the biopsy is to exclude neoplasia.

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Should be managed in urological units

EDITOR,—We take issue with several points in Linda Cardozo's editorial on postmenopausal cystitis.¹ The comment that "for those women in whom oestrogen therapy is ineffective or inappropriate, it is important to exclude underlying pathology" is misleading as it implies that oestrogen should be given before adequate assessment and investigation. The author should have mentioned that urothelial carcinoma should be excluded by microscopical examination of urine for red cells, followed if indicated by cytological examination of urine and flexible cystourethroscopy, before oestrogen is started after antibiotic treatment for bacterial cystitis.²

The coexistence of vaginal and urethral stenosis with atrophic vaginitis is well known and is best treated with a combination of urethral dilatation and intravaginal oestrogen for long term success.³

Bacterial cystitis can be difficult to distinguish from bladder carcinoma, especially carcinoma in situ. Interstitial cystitis has clearly defined diagnostic criteria,⁴ including a particular symptom complex, a systemic response to endoscopic cystodistension, and specific histological appearances on biopsy. The suggested treatment options for interstitial cystitis are incomplete. The therapeutic effects of cystodistension and cystodiathermy are not mentioned; nor is the role of intravesical instillation of silver nitrate, dimethyl sulphoxide, or newer agents such as hyaluronic acid.

This editorial emphasises that postmenopausal cystitis is best investigated and managed in urological units.

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Sensitivity testing for *Helicobacter pylori* should be more widely available

EDITOR,—Greg Rubin and Richard Stevens are right to ask for the wider availability of non-invasive diagnostic tests for managing *Helicobacter pylori* infection in primary care.¹ We believe that the implementation of management guidelines for peptic ulcer disease also requires the wider availability of tests to determine the sensitivity of *H pylori*, because increased prescribing of antimicrobial drugs to treat the infection may be associated with increased drug resistance. Furthermore, our data indicate that if the global eradication of *H pylori* is deemed desirable then simpler and more effective regimens need to be developed for infected patients.

Table 1 (see overleaf) gives details of seven patients with gastric or duodenal ulcer who received at least three different courses of eradication treatment, including the most commonly used drugs, in an attempt to eradicate *H pylori*. In all cases we used either histological examination (Giemsa staining) plus the rapid urease test or breath testing to evaluate the patients' *H pylori* status at least six weeks after the completion of the treatments. All the patients were fully informed and complied with the treatments.

Failure of treatment may be due to the different antibiotic susceptibilities of the various strains of *H pylori*; phenotypically and genotypically different strains of *H pylori* can be present in the stomach at the same time.² We do not yet know whether, in an individual patient, drug resistance occurs through the selection of resistant strains within a mixed population (that is, primary resistance) or through previously sensitive strains becoming resistant (that is, secondary resistance). Because we found that a patient might have to be treated three or more times for *H pylori* to be eradicated, both mechanisms may act in the same patient. In some cases, after the selection of organisms that are primarily resistant to certain antibiotics, secondary resistance to other drugs might develop.

Before treating patients with *H pylori* infection it is thus always important to consider the results of culture and sensitivity tests.³ The problem is that at present the tests are unavailable in most centres. In addition, the routine isolation of