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Association of Biomedical Andrologists; Association of Clinical Embryologists; British Andrology Society; British Fertility Society; Royal College of Obstetricians and Gynaecologists

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## UK guidelines for the medical and laboratory screening of sperm, egg and embryo donors (2008)

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### Abstract

This article updates the 1999 British Andrology Society (BAS) guidelines for the screening of sperm donors and the 2000 British Fertility Society (BFS) guidelines for the screening of egg and embryo donors and combines the new recommendations into a single document. This was achieved by a multidisciplinary working group composed of representatives from the Association of Biomedical Andrologists, the Association of Clinical Embryologists, the BAS, the BFS and the Royal College of Obstetricians and Gynaecologists. The major changes to the guidelines include a requirement to consider a donor's risk of transmissible spongiform encephalopathies and the recommendation to screen for human T cell lymphotropic viruses 1 and 2. The role of nucleic amplification tests for the detection of blood borne viruses such as HIV is discussed, but it remains the recommendation that this be achieved by serological testing to detect antibody or antigen as appropriate with a quarantine period of 180 days.

**Keywords:** *Sperm, egg, embryo, donation, UK, guidelines*

### Introduction

UK guidelines for the medical and laboratory screening of sperm donors have previously been drawn up by the British Andrology Society (BAS) (1999) with guidelines for the screening of egg and embryo donors being developed by the British Fertility Society (BFS) (Aird et al., 2000). Since the publication of each of these guidelines, the landscape of donor-assisted conception in the UK has changed markedly. Firstly, there has been a reduction in the use of donor sperm as a consequence of the increasing use of ICSI (Human Fertilisation and Embryology Authority, 2006) but also potentially through a general shortfall in the number of donors (Hamilton, 2008). There has also been increasing demand for donor eggs and the widespread development of egg sharing programmes (Simons & Ahuja, 2005). Secondly, following the removal of donor anonymity (HMSO, 2004) and the recommendations of the SEED Review (Human

Fertilisation and Embryology Authority, 2005a), there has been an apparent change in the UK donor profile, particularly of sperm donors, who are now more likely to be older men (Human Fertilisation and Embryology Authority, 2005b). Thirdly, there have been major advances in the use and availability of molecular techniques to diagnose infectious diseases (Ratcliff et al., 2007) as well as increased knowledge and availability of genetic testing (McPherson, 2006). Finally, the incorporation into UK law of the EU Tissues and Cells Directive (European Union, 2006) encourages increased emphasis on the use of validated testing methods as well as introducing testing strategies not originally considered in the previous BAS and BFS Guidelines.

In response to these issues, a cross-organisational working party was formed to review the current BAS and BFS guidelines with the objective of producing a single, combined document to encompass the medical and laboratory screening of sperm, egg and

embryo donors. The working party comprised the individuals outlined in the Acknowledgements and the programme of work began with an initial meeting in May 2006. The workload was shared amongst the representatives who undertook a series of comprehensive literature searches and consultations with professionals in their own and other disciplines, as listed. Progress was monitored by a series of telephone conferences throughout 2006/7 during which time a revised document was drafted which was in turn submitted into the peer review process of each stakeholder group in the latter part of 2007 and early 2008. Final work to address the respective comments was carried out during mid-2008.

The primary objectives of these guidelines are twofold: (1) to protect the recipients of donor sperm, egg and embryos from acquiring an infection from the donor; and (2) to protect any donor-conceived people from being born with an infection or acquiring a serious heritable disorder from the donor. They also include a section of best practice recommendations. These guidelines are not intended to address the non-medical counselling of potential donors, because such guidelines are already available from the British Infertility Counselling Association (British Infertility Counselling Association, 2007).

### **Clinical assessment**

All prospective donors should be generally healthy and assessed by a medical practitioner as to their suitability to donate. This assessment should consider the age of the potential donor, as well as relevant medical and surgical history, reproductive and sexual history, genetic history, family genetic history and the risk of transmissible disease including blood-borne viral infections and spongiform encephalopathies. It should also include a physical examination.

#### *Age limits*

All potential donors should be above the age of 18. The recommended upper age limit for donation is 40 for males and 35 for females as outlined below.

With regard to egg donors, it has been shown that the outcome of donation relates to the age of the donor (Cohen et al., 1999), as would be predicted from experience with assisted conception where success rates relate to the age of the female partner and there is a significant decline in fertility after the mid-30s (Human Fertilisation and Embryology Authority, 2006). Fertile egg donors may not have the same poor outcome as age-matched infertile women, but there is, nevertheless, a marked reduction in fecundity with age (Menken et al., 1986), so

that older women are less suitable as donors. There is also an increasing risk of miscarriage with maternal age (Andersen et al., 2000) and the risk of chromosomal abnormality in children conceived by older women is also well recognised (Cuckle, 1999). Because the success of egg donation relates to the age of the donor, and a child born from the egg of an older donor may carry a higher risk of genetic abnormality, it is recommended that egg donors should be no older than 35 years at the time of donation.

With regard to sperm donors, the BAS (1999) guidelines proposed that sperm donors should be less than 40 years old at the time of donation. This was underpinned by the argument that advanced paternal age is associated with new mutations of the paternal genome (e.g. Crow, 1997) and that this was associated with an increased frequency of genetic problems in any individuals born (e.g. dyskinetic cerebral palsy – Fletcher and Marsden, 1996). Although current shortages of donor sperm are an obvious reason to consider increasing the upper age limit for donation (Hamilton, 2008), following the publication of the BAS (1999) guidelines there has been further evidence published to show that reproductive failure through infertility or miscarriage is more common in men above the age of 40 (see De La Rochebrochard et al., 2003 for review) as well as an increase in the incidence of congenital malformations (Bille et al., 2005; Zhu et al., 2005) and autism spectrum disorder (Reichenberg et al., 2006) in their children. This is probably as a result of greater levels of DNA damage in the sperm of older men (Singh et al., 2003), the consequences of which have recently been reviewed (Aitken & De Iuliis, 2007). It is therefore recommended that the upper age limit for sperm donors should remain at no greater than 40 years. This is similar to the recent decision reached by the Practice Committee of the American Society of Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology (2006).

#### *Medical and surgical history*

This should be obtained through a face-to-face interview as well as with reference to medical records when required. Contact with the potential donor's General Practitioner is strongly advised in order to obtain an independent assessment of their suitability as a donor, and appropriate consent to achieve this should be obtained. Particular attention should be paid to identifying any factor that might increase their risk of transmitting an infection or genetic disease or any evidence of high-risk behaviour such as recreational drug use or multiple sexual partners (see below). Consideration should also be given to

the potential donor's lifestyle, and in particular, the potential genotoxicity of tobacco smoke (DeMarini, 2004). There should also be an assessment of an individual's ability to donate. In the case of egg donation, this should include an assessment of the risk to the donor in terms of the superovulation and egg collection procedures, for example because of a thrombo-embolic history or estrogen-dependent tumor or recent pelvic inflammatory disease.

#### *Reproductive and sexual history*

Prospective donors with evidence of risk behaviour, such as multiple episodes of bacterial sexually transmitted disease or unprotected sexual intercourse with multiple partners during the period of donation, should not be accepted. Donors with a history of sexually transmitted infection should be assessed carefully. A distant past history of bacterial sexually transmitted infection is not an exclusion criterion as long as the donor is shown to be negative at the time of donation and adequate treatment has been given. However, a history of acute or chronic pelvic inflammatory disease increases the risk of complication following egg collection. Potential sperm donors with a history of genital warts or herpes should be rejected, although this is of less importance for egg donors.

#### *Genetic history*

The donor should not have any significant heritable condition; this being defined as one that has a major adverse effect on lifestyle or life prognosis. When taking the medical history, enquiries should be made to establish that the potential donor does not have:

- familial disease with a major genetic component, such as cleft lip or palate, congenital hip dislocation, neural tube defects, congenital heart malformation, clubfoot or (in the male) hypospadias. These have an increased chance of occurring in the offspring of an affected individual;
- any significant Mendelian disorders, such as (but not exclusively) albinism, hemophilia, hemoglobin disorders, hereditary hypercholesterolemia, neurofibromatosis or tuberous sclerosis;
- familial disease with a known or reliably indicated major genetic component, such as debilitating asthma, juvenile diabetes mellitus, epileptic disorder, severe hypertension, a psychosis, rheumatoid arthritis or a severe refractive disorder;
- a chromosomal rearrangement that may result in unbalanced gametes.

Furthermore, the potential donor should ordinarily not:

- be heterozygous for an autosomal recessive gene known to be prevalent in the donor's ethnic background. This includes: cystic fibrosis in Caucasian populations, glucose-6-phosphate dehydrogenase deficiency or  $\alpha^0$  or  $\beta$ -Thalassaemia in Mediterranean populations, sickle cell disease in African & Afro-Caribbean populations and Tay-Sachs disease in Jews of Eastern European descent.

But in exceptional circumstances (e.g. in cases of known donation where the donor is known to the recipient) the presence of a recessive gene disorder may not necessarily be a contraindication to donation provided that when the donation is used, all parties are fully informed and the view of an appropriately qualified clinical geneticist is obtained. This should take into account the type of treatment being offered as well as the genetic profile of the donor and recipient couple.

#### *Family genetic history*

Enquiries should also be made to establish that the potential donor's genetic parents, siblings and offspring are free of:

- any of the major malformations outlined in the first bullet point above;
- non-trivial disorders showing Mendelian inheritance in the following categories:
  - autosomal dominant or X-linked disorders, such as Huntington's disease;
  - autosomal recessive disease particularly if it has a high frequency in the population such as, for example, cystic fibrosis;
- a chromosomal abnormality (unless the donor has a normal karyotype);
- a history of any mitochondrial disorders (egg and embryo donors only).

If there is any evidence of the above, then an appropriately qualified clinical geneticist should evaluate the risk and the donor offered any relevant screening.

#### *Transmissible spongiform encephalopathies*

The previous BAS (1999) and BFS (Aird et al., 2000) guidelines made no mention of the risks of transmissible spongiform encephalopathies (TSEs) such as Creutzfeldt-Jakob disease (CJD) through sperm, egg and embryo donation. However, the Practice Committee of the American Society for

Reproductive Medicine (2006) has recently suggested a number of exclusions to avoid transmission of TSEs through donated sperm, egg or embryos. Furthermore, the US Federal Food and Drug Administration has excluded any man from donating sperm if they have spent more than 3 months in the UK during the period 1980–1996, or more than 5 years (cumulatively) in any European country since 1980 (Food and Drug Administration, 2004).

Recent guidance from the Advisory Committee on Dangerous Pathogens and the Spongiform Encephalopathy Advisory Committee (2003) documents assumed levels of infectivity in different human tissues and body fluids but makes no specific mention of semen, gametes and embryos. However, embryos and semen are included in the list of samples of ‘no detectable infectivity’ in animals. European Union Directive 2006/17/EC details screening tests required for donations of human cells and tissues (European Union, 2006), but makes no specific mention of CJD for reproductive tissues and cells. However, it makes a general statement that ‘assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, such as the possibility of transmitting diseases’.

Given the indeterminate risk of transmitting TSEs through sperm, egg and embryo donation, it is suggested that donors should not be accepted who have:

- been diagnosed with a prion-related disease or have first degree family members similarly diagnosed;
- undergone invasive neurosurgical procedures;
- received human pituitary-derived growth hormone, cornea, sclera or dura mater.

Unfortunately, there are no agreed means of identifying risk factors or testing potential donors to exclude those at risk of developing variant CJD. Until such time that these are developed, it is suggested that the above exclusion criteria are a realistic safeguard without having a significant negative effect on donor recruitment.

### Physical examination

Donors should be given a physical examination by an appropriately trained clinician. This is to assist in the detection of sexually transmitted infections (e.g. urethral discharge or genital warts in males), identify inherited congenital abnormalities (e.g. hypospadias) and evidence of high-risk behaviour (e.g. intravenous drug abuse). Because there are currently no validated test methods to detect human papilloma virus or herpes simplex virus, the physical examination of

males should include an examination to detect any genital warts or sores associated with these infections.

Egg donors should undergo pelvic examination and trans-vaginal ultrasound to exclude gynecological conditions that would contraindicate ovarian stimulation and egg collection. This includes ovarian cysts, hydrosalpinges or large uterine fibroids. Ultrasound assessment should include ovarian accessibility and morphology. Potential donors with polycystic ovarian morphology are at increased risk of ovarian hyperstimulation syndrome and should be managed accordingly (National Institute for Clinical Excellence, 2004).

### Screening tests for potential donors

All donors should undergo appropriate genetic/cytogenetic testing, as well as basic blood typing, rhesus status and screening for blood-borne viruses and sexually transmitted infections.

#### *Karyotyping*

It is recommended that all donors should be screened for chromosomal abnormalities. Although the frequency of balanced translocations is <2 per 1000 (Evans et al., 1978), it has been shown that previously unsuspected cytogenetic abnormalities may be detected during routine screening of oocyte (Wallerstein et al., 1998) and semen donors (Ravel et al., 2006). A donor found to have a significant chromosomal abnormality should be rejected.

#### *Autosomal recessive conditions*

Potential donors should screen negative for the following conditions according to their ethnic background:

- $\alpha^0$ - and  $\beta$ -Thalassaemia (e.g. Mediterranean, Middle East, Indian subcontinent);
- Sickle-cell disease (e.g. African and Afro-Caribbean);
- Tay-Sachs disease (e.g. Jews of Eastern European descent);
- Common mutations of the cystic fibrosis gene (e.g. Caucasian).

All genetic testing should be performed in collaboration with a suitably qualified geneticist and follow the strategy agreed by the UK Genetic Testing Network (<http://www.ukgtn.nhs.uk>). Testing for hemoglobinopathies should follow the procedures outlined in the sickle cell and thalassemia handbook for laboratories (Worthington, 2006). In both cases, all testing should be carried out in an accredited

laboratory and adequate pre-test information and counselling as well as post-test support should be available. As outlined earlier, donors who screen positive for autosomal recessive conditions may be accepted under exceptional circumstances (e.g. for known donation) after appropriate consultation with a qualified clinical geneticist and consultant hematologist as appropriate.

#### *Blood group and rhesus antigen*

The use of donor gametes and embryos creates the potential for rhesus incompatibility. All donors should have their blood group and rhesus status recorded for matching purposes when required.

#### *Bacterial infections*

To minimise the risk of transmission of bacterial infections, all prospective donors should, prior to donation, screen negative for:

- Syphilis (*Treponema pallidum*);
- Gonorrhoea (*Neisseria gonorrhoea*);
- Chlamydia (*Chlamydia trachomatis*).

All screening should be carried out in consultation with a suitably experienced genito-urinary medicine (GUM) physician and testing of specimens be performed by an accredited laboratory using validated methods. As with blood-borne viruses, the timetable of screening should be sufficient to cover any latent period between infection and detection (see below). Guidelines for test specimens and testing strategies have been developed by the British Association for Sexual Health and HIV (2006) and should be followed. Donors should be asked to inform the clinic if they experience any clinical sign of sexually transmitted infections during the donation period. In such cases, the donation should be stopped and advice from a GUM physician obtained.

#### *Cytomegalovirus*

The requirement to recruit only cytomegalovirus-negative (CMV) sperm donors was one of the most controversial aspects of the BAS (1999) guidelines, stimulating correspondence (Curson & Karakosta, 2000) and debate (Liesnard et al., 2001; Matson, 2001) on whether this was a reasonable decision. The BFS guidelines for egg and embryo donation (Aird et al., 2000) concluded that it was 'not known if CMV could be transmitted via egg donation and whether the risks are greater or less than those associated with sperm donation' and therefore proposed that the decision to allow seropositive donors to donate to seropositive recipients should be

a matter of clinical judgement, because the exclusion of all seropositive donors would 'exacerbate further the already acute shortage of donors'.

In reviewing the data available, it is clear that the risk to the neonate of a maternal CMV infection during pregnancy can be significant (Raynor, 1993; Hemmings et al., 1998) and therefore should be avoided if at all possible. Of the infants born to mothers primarily infected with CMV during pregnancy, 13% have mental retardation and 8% bilateral hearing loss (Fowler et al., 1992). Over 700 babies each year in the UK are damaged as a result of CMV infection acquired during pregnancy and, although the risk associated with donor assisted conceptions is not known, it has been proposed that the only way to avoid iatrogenic transmission is to screen gamete donors to exclude those who are infectious by this route (Griffiths, 2002). However, it has been pointed out that women could be exposed to multiple possible sources of CMV infection during pregnancy and these other sources will not be prevented by the sole use of seronegative donors (Liesnard et al., 2001).

It is therefore recommended that prospective sperm, egg and embryo donors should continue to be screened for the presence of cytomegalovirus IgG and IgM antibodies using the appropriate serological test, noting that:

- it is always preferable to recruit CMV-negative donors (i.e., those who are IgG and IgM negative). If there are sufficient numbers of CMV-negative individuals willing to donate then CMV-positive donors should not be recruited;
- in situations where insufficient CMV-negative donors are available, CMV IgG positive (IgM negative) donors may be recruited but their use should be limited to CMV IgG positive recipients (see below);
- individuals who are CMV positive with IgM antibodies, indicating an active infection, should defer donation;
- a donor who is initially seronegative and who seroconverts while donating must not be used for treatment purposes. The screening timetable and quarantine period (if applicable) must therefore take account of this.

The decision to treat a patient with a seropositive donor should be a matter of clinical judgement. Although the risks associated with CMV transmission during egg or embryo donation are arguably lower than those encountered during treatment with donor sperm, there are no data to determine the relative risk of infection. Centres should be aware that CMV recurrence in a previously infected woman is more likely if she is repeatedly exposed to CMV by

sexual activity prior to pregnancy (Shen et al., 1993). Despite a relatively low risk, congenital infection following insemination with semen from a seropositive donor cannot be ruled out (Liesnard et al., 1998) and it has long been established that CMV may be present in human semen (Mansat et al., 1997). The matching of CMV positive semen donor samples to CMV seropositive recipients is consistent with the views of the British Transplantation Society (2000) concerning kidney donation and the Practice Committee of the American Society for Reproductive Medicine, Practice Committee of the Society for Assisted Reproductive Technology (2006).

#### *Other blood-borne viruses*

To minimise the risk of transmission of viral infections all prospective donors should, prior to donation, screen negative for:

- human immunodeficiency virus (HIV) 1 and 2;
- human T cell lymphotropic viruses (HTLV) 1 and 2;
- hepatitis B & C.

All screening should be carried out in consultation with a suitably experienced virologist and testing be performed by an accredited laboratory using validated methods. The timetable of screening should be sufficient to cover any latent period between infection and detection as discussed below.

With regard to the most appropriate testing methods, the BAS (1999) recommended that testing and quarantining for blood borne viruses in sperm donors be undertaken using serological testing to detect antibody or antigen as appropriate. In contrast, the BFS guidelines (Aird et al., 2000) made no specific recommendation on preferred methods, only that egg and embryo donors should be tested. The recent guidelines from the Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology (2006) has recently outlined a list of approved tests for use in sperm, egg and embryo donation, whereas the European Tissues and Cells Directive (2004/23/EC) allows that if nucleic amplification tests (NAT) were used for initial screening, repeat testing may not be required and therefore, by inference, the quarantining of reproductive tissues may not be necessary (European Union, 2006).

Although the serological testing for blood-borne viruses is well established and widely available, it does have the disadvantage that there is latency between the time of infection and the appearance of serological markers. In some individuals,

seroconversion can be extremely rapid and antibodies to HIV can be detected in the majority of individuals within 2–4 weeks (Stekler & Collier, 2004) and 6–12 weeks after infection with Hepatitis B and C (Lau & Wright, 1993; Chiavetta et al., 2003; Offergeld et al., 2005). However, in a small but significant proportion of individuals, the antibody response may be delayed or insufficient and thereby increase the risk that an infected individual might go undetected (Busch & Satten, 1997; Netski et al., 2005). Blood transfusion, which has a relatively low residual risk of an undetected infection owing to the many exclusion criteria imposed, can now be made even safer by a combination of NAT with standard serological tests. For example, in Germany for the reporting period 2000–2002, 11 HCV positive blood donations were detected as a result of additional NAT testing and the residual risk reduced to 1 in 4,400,000. For HIV, the residual risk was reduced to 1 in 5,540,000 and for Hep B 1 in 620,000 by additional NAT testing (Offergeld et al., 2005).

With regard to the possible use of NAT testing in sperm, eggs and embryo donation there are as yet few published studies from which any experience can be drawn. As such, advice from the Expert Advisory Group on AIDS has been obtained in order to evaluate if NAT testing could be used instead of serological markers, and in the case of sperm donation, whether the current 180 day quarantine period (British Andrology Society, 1999) could potentially be reduced. The advisory group concluded that HIV NATs were ‘quantitative assays designed for monitoring infection’ and although their ‘negative predictive value would be high when taken in conjunction with a negative serology test’ there are currently no data to confirm whether a NAT that was negative for HIV in plasma would necessarily be negative for HIV in semen, although natural history studies have suggested a generally good correlation between plasma and seminal viral load (Expert Advisory Group on AIDS, 2007).

It is therefore recommended that the detection of blood-borne viruses in sperm, egg and embryo donors should continue to be carried out by using serological testing to detect antibody or antigen as appropriate.

#### **Recommendations for good practice**

The following sections outline three areas for good practice for the initial recruitment of sperm, egg and embryo donors. They include recommendations on screening tests for fertility, quarantining procedures for donations that are cryopreserved and important information about monitoring and surveillance.

### Screening tests for fertility

Prior to donation, the semen quality of prospective sperm donors should be assessed according to World Health Organisation (1999) methods. There is a well-described relationship between the features of semen (such as sperm concentration) and the probability of conception in natural family planning (see Bonde et al., 1998), although this relationship does not seem to exist for the use of thawed-cryopreserved sperm following intra-cervical insemination (Barratt et al., 1998). The BAS (1999) guidelines for the screening of sperm donors did not recommend minimum acceptance criteria for donors based on semen quality or post-thaw survival rates, although the Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology (2006) have recommended that the World Health Organisation (1999) minimum criteria for normal semen can be applied. There is growing awareness of the relationship between traditional values of semen quality and the integrity of sperm DNA (e.g. Irvine et al., 2000) and likewise the relationship between sperm DNA quality and embryo quality (Tomsu et al., 2002; Seli et al., 2004). Therefore, although it may be possible to accept sperm donors based on their intended use (e.g. specifically for use in IVF or ICSI cycles), this is not encouraged. It is recommended that only those men whose fresh (pre-freeze) semen quality is above that described in Appendix 1A of the World Health Organisation (1999) laboratory manual should be accepted as donors.

With regard to the assessment of potential fertility in egg donors, the BFS guidelines (Aird et al., 2000) suggested that the ideal egg donor would already have proven fertility and have completed their own family. The advantage of these criteria is that such women will have already proven they can produce viable eggs and embryos, and that should they experience adverse consequences of treatment, such as pelvic infection, their own reproductive future would not be altered. However, the encouragement of egg sharing (Simons & Ahuja, 2005) has allowed infertile women to choose to become egg donors. Because they are already undergoing IVF for their own benefit, they should not be exposed to any additional medical risk by donating. The egg-sharing donor should be selected carefully if the recipient is to have a good chance of pregnancy and this effectively restricts the egg sharing option to donors from young couples with male infertility and those in which the woman has undergone sterilisation. Ovarian reserve testing of potential egg-sharers may be used to predict the likelihood of collecting sufficient oocytes. Ovarian reserve testing has not

been thoroughly validated in the non-infertile population, but is nevertheless usually undertaken as part of donor selection procedures (Mirkin et al., 2003), both for exclusion of potential poor responders and identification of donors at risk of ovarian hyperstimulation.

### Quarantine

Quarantine is an important part of donation because its primary purpose is to protect the recipient (and any donor-conceived offspring) from bacterial or viral infection. However, the principles of quarantine cannot be applied equally to sperm, eggs and embryos because of inherent differences in their ability to be frozen and thawed and there are clearly different levels of risk that need to be considered when assessing the best strategy for quarantine, based upon the likelihood of infection.

Of all donated material, leukocyte-rich semen represents the highest risk of infection. Fortunately, strategies for the effective cryopreservation of sperm are well established and are sufficiently effective to allow sperm to be frozen for many years. The BAS (1999) guidelines recommended that only ejaculates that had been in storage for > 180 days at the time of re-testing should be released for clinical use and this has similarly been recommended by the Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology (2006). Although there is obvious pressure to use NAT to be able to release semen specimens from quarantine earlier, current advice from the Expert Advisory Group on AIDS (2007) is that because donated sperm can adequately be quarantined for 180 days, this precautionary principle should remain, irrespective of the testing method employed (see earlier). For all sperm donors, donated samples should therefore continue to be quarantined for at least 180 days and the following should be seen as the minimum testing schedule prior to the release of gametes:

- HIV 1 and 2 antibody, hepatitis B (HbsAg), hepatitis C (HVC), HTLV 1 and 2, CMV – prior to donation and 180 days following last donation;
- *Treponema pallidum* (syphilis), *Neisseria gonorrhoea*, *Chlamydia trachomatis* – prior to donation and every 6 months until donation is complete. Immediately after last donation, Gonorrhoea and Chlamydia should be repeated. A repeat Syphilis should follow 1 month later;
- Genital warts or herpes should again be excluded at the end of donation by physical examination and medical history.

As a minimum all centres recruiting sperm donors should:

- perform risk assessments with respect to quarantine practice to include: the need for physical separation of samples; the integrity of the plastic containment used in cryopreservation, whether samples are stored in the liquid or gaseous phase of nitrogen and the total duration of the donation period;
- follow published practical guidance on the use of materials for cryopreservation and storage such as those produced by the Association of Biomedical Andrologists ([www.aba.uk.net](http://www.aba.uk.net));
- be mindful and take account of any developments in the detection of all sexually transmitted infections and take the advice of their local accredited laboratory when appropriate;
- be aware that the longer the quarantine period for gametes prior to final screening, the lower the risk to any recipient of subsequent transmission of blood-borne viruses;
- implement effective checking procedures in order to prevent premature release of gametes for therapeutic use i.e., before completion of testing or before an appropriate 'window of detection' has passed;
- have a documented referral/care pathway for dealing with prospective donors who are found to be positive upon re-testing.

The relative risk of transmitting infectious agents through egg or embryo donation is undocumented but intuitively is likely to be less than that associated with donated semen. Because the current technology for freezing eggs remains associated with low success rates (Gosden, 2005), it is clear that the requirement for the freezing and 180 day quarantine that applies to sperm donation (see earlier) cannot be applied to egg donation and give a realistic chance of success. Although the next best alternative would be to freeze and quarantine any embryos created in the egg donation IVF cycle (Hamer et al., 1995), the known reduction in success rates of frozen embryo replacement (Pados et al., 1992) makes this a less attractive option. In the BFS guidelines (Aird et al., 2000) it was suggested 'such pragmatic considerations mean that embryo cryopreservation and quarantining before transfer, although advisable, are not mandatory at the present time'. The present guidelines continue to support this view, although if the technology of egg freezing improves substantially with the development of vitrification (Jain & Paulson, 2006), this position must be reviewed. Clearly, in the absence of cryopreservation and quarantine, the recipient in egg donation cycles should be informed of the theoretical risk of transmission of infection through

the transfer of fresh embryos, although it is acknowledged that this is currently unquantifiable.

Because embryos which are normally donated are taken from those which remain in storage after a couple have completed their own treatment, it would be unusual for either of the gamete providers to have been screened as donors at the time their embryos were placed in storage. This was recognised by the BFS guidelines (Aird et al., 2000) where it was considered best practice to ask the provider of the gametes from which the embryo was created to undergo retrospectively the full screening process as recommended for egg and sperm donors described before embryo donation takes place. This remains the view of the working party in the present revised guidelines. However, it is recognised that in some rare circumstances (e.g. the death of one of the gamete providers) this may not be possible. In such cases, donation may still take place, but a review of the relevant medical records should be undertaken to identify any risk factor that may have ruled out the individual as a gamete donor. The lack of any screening results should be discussed with the recipient couple so that they are fully informed. The significance of any missing results should be explained to them.

#### *Monitoring and surveillance*

It was recommended in the BAS (1999) guidelines that serum from all sperm donors should be collected and stored in the event that a currently unidentified viral or bacterial pathogen became detectable in the future. Although there was no similar recommendation for egg donors in the BFS guidelines (Aird et al., 2000), Gazvani et al. (2002) discussed the value of storing samples of DNA from all donors in order to facilitate the future provision of genetic information to the donor-conceived in the event that advances in technology meant that information about late onset genetic diseases became available after the time of donation. It is not clear how many UK centres that recruit donors retain serum and/or DNA from donors (either themselves or through a third party agreement with a laboratory carrying out the testing), but it is recommended that this should now be viewed as best practice. Moreover, recruitment centres should have mechanisms in place to manage any information they may generate. In addition, the outcome of all donor pregnancies should be closely monitored with particular reference to birth abnormalities in donor conceived offspring. Any such abnormality should be carefully documented and discussed with a clinical geneticist so that the risk to other donor-conceived siblings and the donor's own children (if applicable) can be assessed. The decision to inform a donor and/or the parents of any donor

conceived children about any new genetic information should be a matter of clinical judgement.

### Revision of guidelines

The Terms of Reference of the multidisciplinary group responsible for drafting these guidelines include an agreement to review them annually and if necessary issue further updates.

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