

Parents' choices in banking boys' testicular tissue

Timothy F Murphy

Correspondence to

Professor Timothy F Murphy,
Department of Medical
Education m/c 591, 808 S.
Wood St, University of Illinois
College of Medicine, Chicago IL
60612-7308, USA;
tmurphy@uic.edu

Received 8 April 2010

Revised 2 July 2010

Accepted 8 July 2010

Published Online First

26 August 2010

ABSTRACT

Researchers are working to derive sperm from banked testicular tissue taken from pre-pubertal boys who face therapies or injuries that destroy sperm production. Success in deriving sperm from this tissue will help to preserve the option for these boys to have genetically related children later in life. For the twin moral reasons of preserving access and equity in regard to having such children, clinicians and researchers are justified in offering the option to the parents of all affected boys. However, some parents may wish to decline the option to bank tissue from their boys because the technique may seem too unfamiliar or unusual, but over time people may become more comfortable with the technique as they have done with other novel assisted reproductive treatments (ARTs). Other parents may wish to decline the option because of moral or religious reasons. A prominent natural law theory holds, for example, that the ARTs that would be involved in using sperm derived from banked tissue to produce a child are morally objectionable. Some parents might not want to bank tissue in order to shield their son from using ARTs they see as objectionable. Clinicians and researchers should respect parents who wish to decline banking tissue, but parents should ordinarily embrace choices that protect the possible interests their sons may have as adult men, including the wish to have genetically related children.

Because of accidents, disease and treatment for disease, some boys lose the capacity to produce sperm after puberty. For example, some boys lose their testes to injuries, others have disorders that require the removal of their testes, while others face radiological and chemotherapy treatments that kill spermatogonial cells, the cells that will produce sperm after puberty. Boys who have already gone through puberty have an advantage when seeking to preserve their ability to have genetically related children later in life since they can bank sperm for later use before incurring permanent testicular damage. However, most childhood cancers are pre-pubertal, and pre-pubertal boys facing radiation and chemotherapy have no such option available to them.

Advances in fertility medicine may soon make it possible to derive sperm from testicular tissue from pre-pubertal boys of any age. This has been done successfully with animals, and the sperm has been used to produce live offspring in mice.^{1 2} In fact, some clinicians already counsel parents of boys facing certain therapies to bank testicular tissue in anticipation of the day when it can be used to derive sperm.³ While research in this area is still preliminary for humans, so long as certain ethical cautions are observed in how the tissue is collected and used, there is nothing in medical ethics that makes it

impermissible to bank testicular tissue in the hopes of offering affected boys an option that would help them have genetically related children later in life. In fact, the key ethical concern may go in the other direction: Given the options it preserves, would it be permissible to decline the banking of testicular tissue since doing so would limit the hope of having genetically related children later on? Providing an answer to this question requires balancing parents' interests and the interests of their children's future adult lives.

OFFERING TO BANK TESTICULAR TISSUE

Given that sperm derivation from banked human spermatogonial cells is only a future possibility at this point, who—if anyone—should be approached about banking this tissue?

Not all adult men want or will have children, for reasons of choice and accidents of fate, and not all men will have children who are genetically related to them. Some men adopt children or marry women who already have children, and they are not bothered by a lack of genetic relation to those children. Some men accept as their own children who are conceived by their wives during extra-marital affairs. In view of these facts, might it be appropriate to offer tissue banking only to *some* parents on behalf of their boys? While it is true that some adult men will not want children or will accept genetically unrelated children, there is no way to identify which boys—as adults—will express those preferences. It would be unfair for clinicians to make judgements about their young patients' future desire for children based on their own perceptions, since these parties cannot foretell the future better than anyone else.

Another way to decide how to offer tissue banking would be to make the option available for all boys who face loss of testicular function to disease or treatment. This option has the benefit of treating all boys equally, so that neither fallible estimates of the future nor favouritism enter the picture. However, human sperm has not yet been derived from pre-pubertal tissue, and even researchers who are optimistic about deriving sperm cannot be certain how long it will be before they are able to derive sperm and use it to produce children reliably and safely. In general, medical ethics does not require clinicians to carry out procedures that have no demonstrated benefit, and it might be argued that banking tissue at this time for all boys overstates the value of the venture and could give the boys and their families unfounded hope about fertility in the future.

In light of the experimental nature of this venture, one might even argue that the option of tissue banking should be withheld from all boys, especially since banking might trigger hopes of

genetically related children that may not be realised. This approach would, however, also close the door to doing the research necessary to achieve sperm derivation. Perhaps, then, the option of tissue banking should be offered to only as many boys as is necessary to conduct the essential research. If we follow this approach, clinicians and researchers would not offer tissue banking to all eligible boys, but only to a relatively small subset. The exact number would depend on the amount of tissue necessary to carry out the research. However, this approach carries a significant moral cost. If an effective technique of sperm derivation were to emerge within 15 or 20 or 25 years, the technique could benefit all boys who had banked tissue, not just the subjects involved in the research properly speaking. Depending on how young they were at the time of banking and assuming they survived to adulthood, boys could take advantage of research developments that took place decades after originally banking their tissue. Using only a subset of boys who would be eligible for this kind of study would orphan the larger number of boys (and the adults they will become) from the benefits of the research should sperm derivation techniques become generally successful.

One thing above all stands out in this analysis: without tissue banking, pubertal boys will lose this promising prospect by which they could father children using their own sperm. (Another kind of sperm derivation will be discussed later.) Most people say they want children, which fact—as a general assumption—seems to support the idea that banking would be an important option for most families, so long as the research involved is eventually successful. The risks (possible harms in the excision of the tissue and possible unfounded expectations) seem more than tolerable when measured against the possible benefits (having genetically related children later in life). In view of this estimate of risks, clinicians are justified in offering tissue banking to all prepubescent boys facing imminent loss of testicular function, whether or not that banking also involves an additional agreement to make some of the tissue available for research.⁴

As clinicians and researchers approach parents and boys about banking spermatogonial cells, they should, of course, observe caution in order to avoid two possible misunderstandings: first, that the option is a guarantee of survival or, second, that it guarantees success in having genetically related children. Most children do survive cancer if treated in a timely fashion and with appropriate methods, and survival rates have increased over time, but—even so—not all children survive.⁵ Moreover, no children have yet been born through the use of banked pre-pubertal testicular tissue, and there are no guarantees that it might happen within the child's lifetime. Even so, there is nothing about tissue banking that must necessarily lead to these misunderstandings; a thorough informed consent process seems capable of de-coupling survival and future fertility from tissue banking itself.⁴ Moreover, going to a family with the option of banking tissue expresses concern for the welfare of the child, no matter what happens later on, and that is valuable for the relationship between clinician and patient in its own right.

Given its potential benefits, should law and policy mandate tissue banking as a standard practice for all boys facing loss of testes or testicular function? Mandatory interventions may make sense in minors where there is a clear benefit, such as a life-saving blood transfusion, but the benefits of tissue banking for sperm derivation have not yet been proved, and it is unclear when they might emerge. It is hard to make the case that banking should be compulsory in the absence of demonstrated benefit. Even if techniques for sperm derivation were more

advanced than they are now, mandatory tissue banking would erode respect for parents' wishes in regard to their minor children, respect it is important to preserve except when parents' choices threaten children's health or welfare in fundamental ways. Exploring the different reactions parents can have to this tissue banking can help illustrate why.

THE ROLE OF PARENTS

Banking tissue offers a way to preserve a biologically characteristic capacity of human males, sperm production, which would exist in boys except for injury or iatrogenic damage. The banking preserves not only a biologically characteristic function but also the option of having genetically related children, which is an aspirational ideal for many if not most people. Helping to establish a technique of sperm derivation works to preserve equal access to genetic fatherhood for boys who lose testicular tissue through accidents of fate. The benefit here is not only for the boys, but also for their parents who may look forward to genetically related grandchildren as well. These outcomes seem to me persuasive reasons to bank tissue, but others might not see things this way. Some parents might be so stressed by the medical condition of their child and the speed at which they have to make a decision about banking that they may recoil from the option altogether. Other parents may believe that moral or religious considerations require them to decline banking the tissue.

First, parents might want to decline banking because they find the prospect unsettling because it appears too futuristic and unfamiliar. This is not, of course, a moral objection, but a question of psychological familiarity. Techniques such as gamete donation, in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI) and embryo donation were extraordinary at the outset and yet are now used worldwide. Almost no two countries have the same rules and regulations, but even where assisted reproductive treatments (ARTs) are restricted or forbidden, people engage in reproductive tourism to bypass limitations on access at home.^{6, 7} The broad embrace of ARTs shows that even radically novel techniques can become acceptable—and routine—because of increased familiarity, and the same might eventually hold true for testicular tissue banking.

Second, some parents who have declined taking testicular tissue from their children have indicated being overwhelmed by their child's diagnosis and the limited time available in which to make a decision. The issue here seems to be not familiarity per se but the compressed time period in which a significant decision must be made. This reaction is, however, not a moral argument against tissue banking per se, so much as it is an artefact of stressful circumstances. Yet as the option of testicular tissue banking becomes better known, parents may find themselves less unprepared for having to make a decision under stressful circumstances. The informed consent process can also help parents evaluate the option even under stressful conditions as they consider its significance for their son and for themselves. One practical way to help manage stress might be to stage the decision-making process, perhaps to authorise excision of the tissue for banking first but deferring decisions about its ultimate disposition until later on. This staging would solve certain problems, of course, but create others, since it might be more difficult to opt for disposal of the banked tissue later on, if that is what parents ultimately decide what they wanted to do. In other words, the fact that tissue has been banked might constrain parents' more fully considered wishes, but the staging process would at least offer one way to introduce longer opportunities for reflection about final decisions.

Some parents might yet object to tissue banking not for reasons of unfamiliarity or stress but for moral or religious reasons. These parents would probably not object to banking of tissue *per se*; tissue is excised from human bodies and stored across the breadth of medicine for a vast number of clinical and research purposes. Most commentators raise few moral objections to banking itself, even if important concerns about access and use remain.⁸ Yet if the offer of testicular tissue banking is going to extend across the breadth of boys who are eligible for medical reasons, there is no reason to expect uniform responses, let alone acceptance under all circumstances. In fact, some parents have indicated moral and religious concerns as reasons not to bank their son's testicular tissue.

No study has identified the specific moral and religious concerns for which parents have declined banking, but—for the sake of the discussion—let us imagine one possible objection, that some parents believe that the ARTs involved in the future use of their boy's sperm would be objectionable on moral grounds. For example, some Natural Law moralists argue that the conception of a human being should occur only through the intercourse of married couples.⁹ Relying on Natural Law arguments, the Vatican defends the view that insemination, IVF and ICSI—among other treatments—are morally objectionable.¹⁰ Some of these techniques would certainly be in store for men using sperm derived from banked tissue, and not even their use in trying to prevent heritable cancer susceptibility in a child would justify them. Parents who hold similar views may wish to withhold permission for tissue banking in order to protect their son in his future years from turning to choices they believe to be inherently wrong.

In another area of concern, some parents might also believe that trying to derive sperm from banked tissue represents an undesirable pathway for biomedical research. For example, they might hold that it is more important to find treatments for pre-pubertal cancer that do not have damaging effects on gonadal tissue than to perfect techniques of sperm derivation. Or they might favour research that somehow restores testicular tissue after damaging therapies. Even if these alternative therapies are not pursued or are unlikely to help people now living, the Vatican argues, for example, that it would still be better to decline all ARTs. In its 1987 'Donum Vitae', it said, for example, 'Physical sterility in fact can be for spouses the occasion for other important services to the life of the human person, for example, adoption, various forms of educational work, and assistance to other families and to poor or handicapped children' (2.B.5). It went on to say that for married couples unable to conceive through intercourse that 'Spouses who find themselves in this sad situation are called to find in it an opportunity for sharing in a particular way in the Lord's Cross, the source of spiritual fruitfulness' (2.B.5).

This counsel can be respected for what it is, a sincere exhortation to pursue certain religious and moral values, and many people want to pursue exactly that kind of life. Even so, for the same combination of humane and practical reasons that clinicians offer ARTs to people looking for help in have children, they should certainly be free to offer the option of testicular tissue banking to boys and their families so long as they do not misrepresent its prospects and so long as clear standards are in place regarding the storage and future use of the tissue. Certain effects of banking will have to be thought through, including what should happen to the sperm if the son dies. Should that sperm be made available to the boy's parents to produce a child through a surrogacy arrangement, if they wanted a grandson that way? This topic of post mortem fatherhood of prepubescent

boys is a topic that deserves its own discussion separate from the question of whether parents may decline banking in the first place.^{11 12} For this discussion, it is enough to recognise that people are entitled in democratic societies to make these kinds of decisions, without regard to the objections of others, especially since the practice of ARTs have a moral integrity in their own right, especially in preserving the option to have children.

It must be noted, however, that tissue banking need not always lead to violations of Natural Law or an upset of parents' expectations. Upon reaching the age at which he would be entitled to use his banked testicular tissue and the ARTs involved in producing a child, a man will be able to understand the arguments raised against the procedures involved. If persuaded by these views, he would be entirely free to decline using the sperm. In that case, he may simply authorise the use of banked tissue in research or direct its disposal, and no harm—as Natural Law sees things—will have been done by him or by his parents in banking the tissue in the first place. By contrast, it should be noted that not banking tissue will not prevent a sterile man from turning to ARTs for help having children, except that he will not be able to use own sperm. In fact, not having that sperm available would only increase the total number of allegedly objectionable practices involved in ARTs, insofar as—in addition to whatever other ARTs were necessary to have a child—the man would also have to turn to donor sperm.

As a matter of circumspection, parents should recognise, of course, that their adult son may not share their objections to assisted conception. Indeed, no one can know what degree of respect for the Natural Law or for religious arguments a child will have decades ahead. Parents make many choices they hope will direct their children towards certain moral and religious values, but sometimes those choices lead to unforeseen outcomes. The adult son might repudiate the views he was raised to respect, either in whole or in part, and he may welcome the options banked tissue keeps open for him, ARTs included. The moral question that parents must ask themselves is whether they are willing to accept tissue banking on behalf of their child, which may enable a choice that they reject in principle but which their son as an adult might see as highly beneficial and not at all immoral. In short, there are no guarantees that children will embrace the views parents wish them to have, but neither is it true that parents and children must necessarily be estranged from one another when these differences emerge. Parents and children can disagree about other important matters without necessarily damaging their relationship. In regard to tissue banking, the open question is whether parents will take steps to help protect their boys in a variety of possible futures they might have and not only a single, idealised future they envision.

PARENTS' CHOICES ARE NOT THE WHOLE STORY

Clinicians have taken testicular tissue from boys as young as 3 months of age.¹³ At very young ages, no child can understand the implications of clinical decisions, or what tissue banking might mean to him in the future. Older boys can, of course, be brought into these discussions as they are able to understand the nature and significance of the banking, in much the same way maturing children are brought into discussions about their clinical care. But how should we treat the preferences these boys express? Looking at parallel standards in research ethics can help frame an answer. In the US, parents are entitled to make choices about their children's participation in research, but children must be consulted, as appropriate to their age and understanding, for

their 'assent' as well. But their unwillingness to assent can be overridden in some circumstances if the 'intervention or procedure holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research'.¹⁴ It can be plausibly argued that the intervention to bank the testicular tissue—in a now or never way—of an 8-year-old child is important to a child's later welfare even if he says he now does not want it. In other words, it is difficult to believe that the boy can fully understand the implications of declining to bank the tissue for his later welfare. In any case, even if tissue were banked over the child's non-assent, he would retain the right to dispose of the tissue later on.

To consider the other potential conflict, what if the boy wants the tissue banked, but the parents do not? In this circumstance, clinicians should engage in a certain amount of conflict resolution and offer a staging process. If those approaches fail to bring about agreement and the parents remain unwilling to bank the sperm, their view should prevail since they are better situated than the boy to gauge the impact of this banking on their family, which is another way of stating the same rationale for overriding a young boy's objections to the banking, should that happen. Not banking testicular tissue may not be the end of the story as far as sperm derivation is concerned for boys whose choices to bank are overridden by parents. Researchers have used certain pluripotent stem cells to produce gametes.¹⁵ Should this venture succeed in humans, it could restore to an adult man the option lost if his parents declined to bank testicular tissue prior to radiation or chemotherapy.

Both moral philosophy and the law grant parents wide latitude over decisions that affect their children's futures, and decisions about banking testicular tissue are not out of line with all the other profound responsibilities they exercise. At this point, parents who decline to bank tissue are only declining to offer tissue for research, since that is all that is currently possible. When the day comes that banked testicular tissue can be used to produce sperm, parents should still be respected in their wishes if they want to decline tissue banking for their son, even if clinicians and researchers believe those decisions to be a mistake, just as parents are free to accept or decline other significant opportunities that come their children's way. Because children's moral and religious lives can diverge from those of their parents in significant ways, parents should, however, work to protect the possible selves their children will become. Some of the boys who lose the ability to produce

sperm will become men who will harbour no moral or religious objections to tissue banking or the choices it opens up in having children later in life. Even though banking tissue may give sons choices their parents would find morally dubious, banking tissue does enlarge their sons' future choices and thereby better preserves access and equity for them in regard to having genetically related children, and parents should keep those moral goals in mind as they exercise the privilege they have to make decisions about banking tissue.

Competing interests None.

Contributors Timothy F Murphy is the sole author.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Wyns C**, Curaba M, Martinez-Madrid B, *et al*. Spermatogonial survival after cryopreservation and short-term orthotopic immature human cryptorchid testicular tissue grafting to immunodeficient mice. *Hum Reprod* 2007;**22**:1603–11.
2. **Sadri-Ardenkani H**, Mizrak SC, van Daalen SK, *et al*. Propagation of human spermatogonial stem cells in vitro. *JAMA* 2009;**302**:2127–34.
3. **Lee SJ**, Schover LR, Partridge AH, *et al*. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *J Clin Oncol* 2006;**24**:1–15.
4. **Ginsberg JP**, Carlson CA, Lin K, *et al*. An experimental protocol for fertility preservation in prepubertal boys recently diagnosed with cancer: a report of acceptability and safety. *Hum Reprod* 2010;**25**:37–41.
5. **Pulte D**, Gondos A, Brenner H. Trends in 5- and 10-year survival after diagnosis with malignancies in the United States, 1990–2004. *J Natl Cancer Inst* 2008;**100**:1301–09.
6. **Pennings G**. International evolution of legislation and guidelines in medically assisted reproduction. *Reprod Biomed Online* 2009;**18**(Suppl 2):15–18.
7. **Murphy TF**. Access and equity: international standards and assisted reproductive technologies. *Reprod Biomed Online* 2007;**14**(Suppl 1):12–18.
8. **Dierickx K**, Borry P, eds. *New challenges for biobanks: ethics, law, and governance*. Mortsels, Belgium: Intersentia, 2009.
9. **Finnis J**. Law, morality, and 'sexual orientation'. *Notre Dame J Law Ethics Public Policy* 1995;**9**:11–39.
10. **Congregation for the Doctrine of the Faith**. Donum vitae: instruction on respect for human life in its origin and on the dignity of procreation. Replies to certain questions of the day. 1987. http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_19870222_respect-for-human-life_en.html (accessed 16 August 2010).
11. **Murphy T**. Sperm harvesting and postmortem fatherhood. *Bioethics* 1995;**9**:380–98.
12. **Iserson K**. Sperm donation from a comatose, dying man. *Camb Q Healthc Ethics* 1998;**7**:209–17.
13. **Van den Berg H**, Reeping S, van der Veen F. Parental desire and acceptability of spermatogonial stem cell cryopreservation in boys with cancer. *Hum Reprod* 2007;**22**:594–7.
14. U.S. Department of Health and Human Services, 45 Code of Federal Regulations 46.408, 2009–2010. <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm> (accessed 16 August 2010).
15. **Editorial**. New sources of sex cells. *Nature* 2008;**452**:913.