Uterus transplants and their ethical implications

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Abstract
Early experiments in womb transplants have increased interest in the possibility of performing this procedure in women who have no womb, usually for congenital reasons. The present article describes past experiments and summarises the most relevant reference documents before indicating the key ethical implications involved in womb transplants.

INTRODUCTION
Clinical and ethical considerations do not apply equally to all the organs that can be transplanted in humans. While some organs are vital for survival (heart, liver, lung), others that are not necessary for survival nonetheless raise ethical, anthropological and emotional issues that involve not only – and in any case to a lesser degree – the physical well-being of the recipient, but also the perception of the self and of one’s body.

While a hand or face transplant clearly does not constitute a life-saving procedure, both imply significant problems regarding the patient’s self-perception. The present article concerns womb transplants which, because of the particular importance of the womb in female reproductive functions, belongs to the same category. A womb is the place where a new human being settles, is formed and develops, invisible to the world until an ultra-sound reveals it and perceived as growing only by the woman who carries it: a womb transplant – involving only women – is thus the only “gender transplant” performed to date.

We are, therefore, not talking about the usual bioethical problems that accompany new methods of medically assisted procreation (such as the beginning of a person’s life or the moral status of the embryo), but rather about the symbolic value attached to the womb. Although the present article addresses the problem from the point of view of the state of the art of the procedure in clinical terms and in regard to the more typically bioethical issues involved in transplants in general, it is nonetheless important to keep in mind the peculiarities of the womb, its functioning and purpose, that are unique characteristics.

Womb transplants were performed in animals as long ago as the 1960s [1]; in humans they have to date been performed in women born without a uterus (Mayer-Rokitansky-Kunster-Hauser), but could be appropriate for other pathologies that involve the uterus.

The first experimental womb transplant in a woman was performed in 2000 [2]. The uterus was taken from a 46-year old living donor and transplanted into a 26-year old woman. It responded to treatment with oestrogen and progesterone and could thus potentially have been stimulated to achieve endometrial proliferation. However, the development of thrombosis in the anastomosed blood vessels led to necrosis of the graft and it had to be removed.

A second attempt was made in 2011 in Turkey [3]. A 20-year old woman received a uterus taken from a deceased donor of the same age. Twenty days later the patient had her first menstrual cycle, which was followed by two early spontaneous abortions following two embryo transfers.

In 2012-2013 the first clinical trial was conducted, involving eight women with uterine agenesis and one who had had a hysterectomy [4, 5]. The organs were removed from living donors, in most cases the mothers of the recipients. Post-operative complications included: thrombosis in the uterine arteries (1 case in 9) pleural effusion (2/9), intrauterine abscess (1/9) retroperitoneal haematoma (1/9). The only post-operative complication in a donor was one case of urethral-vaginal fistula (1/9). Two of the transplants were unsuccessful: bilateral uterine artery occlusion and persistent endometriosis required hysterectomy. In the remaining cases menstrual cycles were regular after 6 months.

In 2013, at the Sahlgrenska University Hospital in Gothenburg (Sweden), a 35-year old women suffering from Rokitansky syndrome was given a womb taken from a living 65-year old donor. Prior to the transplant in vitro fertilisation had been performed using oocytes from the recipient and spermatozoa from her partner, and 11 em-
bryos had been frozen. Forty-three days after the transplant the recipient had her first menstruation and one year after the first embryo was transplanted. After 31 weeks and 6 days the woman gave birth to a boy of normal weight for his gestational age [6]. Subsequently, the transplants in Sweden resulted in four other births [7, 8].

Table 1 shows a summary of the womb transplants reported to date in the specialised literature.

Although New York’s Downtown Hospital had announced plans to perform a womb transplant in January 2007 [9], the first operation was performed on 24th February 2016 in Cleveland. The recipient was a 26-year old who had been included in an experimental trial aiming for 10 transplants, and the womb was taken from a deceased 30-year old donor (in contrast to the Swedish trial, which used living donors). On 8th March 2016 the transplanted womb had to be removed in an emergency operation, as a result of complications [10].

The Swedish cases encouraged several surgical teams in various countries to plan womb transplants. Such plans are usually announced in press conferences or through press agencies. For example:
• in France a womb transplant is planned for 2016 in Limoges [11];
• in Italy, the Ethical Committee of the Italian Health Institute has approved a womb transplant protocol at the Umberto I Hospital in Rome, in accordance with the regulations governing the authorisation of such trials [12];
• in the United Kingdom the UK Womb Transplant Research Team led by Richard Smith, consultant gynaecologist at Queen Charlotte’s and Chelsea Hospital in London, received authorisation in September 2015 to conduct trials with 10 patients [13].

INSTITUTIONAL DOCUMENTS

In 2008 a report by the International Federation of Gynecology and Obstetrics (FIGO) found that the lack of sufficient data on the safety and efficacy for the recipient meant that womb transplants were not acceptable from the ethical point of view. The FIGO therefore made the following recommendations:

1. uterine transplantation, which may reach human clinical experimentation stage, should only occur after significant and adequate research in appropriate large animal models, including primates;
2. the lengths to which some women will go to experience uterine transplantation, even with the availability of such options as adoption and surrogacy in some cultures, can lead to a conflict of interest and pressure on researchers to move prematurely to human application;
3. ut is unethical to remove a uterus for transplantation from a young woman who did not complete having the desired number of children or a uterus with a deformed cavity;
4. given the lack of data on safety and the known hazards to live donors, the procedure is considered ethically inappropriate [14].

In 2012 a working group from McGill University (Montreal, Canada) proposed the "Montreal criteria for the ethical feasibility of uterine transplantation" [15], which were updated the following year [16]. The revised Montreal criteria for the ethical feasibility of uterine transplantation are:

1. The recipient
   a. is a genetic female of reproductive age with no medical contraindications to transplantation,
   b. has documented congenital or acquired UFI that has failed all current gold standard and conservative therapy,
   c. (c1) has a personal or legal contraindication to surrogacy and adoption measures and desires to have a child, or (c2) seeks the UTx solely as a measure to experience pregnancy and adoption measures and desires to have a child,
   d. has not had her decision to undergo UTx deemed as irrational by expert psychological evaluation, and has no psychological comorbidity that interferes with diagnostic workup or treatment,
   e. does not exhibit frank unsuitability for motherhood,
   f. is likely to take antirejection medication and follow up with the treating team in a responsible manner, and
   g. is responsible enough to consent, informed enough to make a responsible decision.

2. The donor
   a. is a female of reproductive age with no medical contraindications to donation,
   b. (b1) has repeatedly attested to her conclusion of parity, or (b2) has signed an advanced directive for post mortem organ donation,

Table 1

Summary of the womb transplants reported to date in the specialised literature

<table>
<thead>
<tr>
<th>Author</th>
<th>N. patients</th>
<th>Age</th>
<th>Donor/s</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fageeh et al. [2]</td>
<td>1</td>
<td>26</td>
<td>living</td>
<td>Hysterectomy for vascular occlusion 3 months after transplant</td>
</tr>
<tr>
<td>Ozkan et al. [3]</td>
<td>1</td>
<td>21</td>
<td>deceased</td>
<td>Pregnancy and abortion</td>
</tr>
<tr>
<td>Brännström et al. [4]</td>
<td>10</td>
<td>31.5 (average)</td>
<td>living</td>
<td>7 cases: viable uterus (of which 3 with sub-clinical rejection treated effectively with corticosteroids)</td>
</tr>
<tr>
<td>Johannesson et al. [5]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brännström et al. [6]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dahm-Kähler et al. [7]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brännström et al. [8]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleveland Clinic [10]</td>
<td>1</td>
<td>26</td>
<td>deceased</td>
<td>Hysterectomy 12 days after transplant for complications</td>
</tr>
</tbody>
</table>
c. has no history of uterine damage or disease, and
d. is responsible enough to consent, informed enough
to make a responsible decision, and not under coercion.

3. The health care team
a. is part of an institution that meets Moore’s third cri-
teron as it pertains to institutional stability,
b. has provided adequate informed consent to both par-
ties regarding risks, potential sequelae, and chances of
success and failure,
c. has no conflict of interest independently or with ei-
ther party; and
d. has the duty to preserve anonymity if the donor or
recipient do not explicitly waive this right”.

On 23rd June 2015 the French Académie Nationale
de Médecine published a report on “La transplantation
uterine” [17]. The report noted the data published
so far, and in particular those relating to the birth in
Sweden in 2015; pointed to the uncertainties, risks and
problems; noted that transplants from both living and
deceased donors raised serious issues; indicated the un-
certainties surrounding the long-term health conditions
of children born from a transplanted womb, and made
the following recommendations:
1. research programmes that are conducted strictly in
accordance with regulations laid down in law and by the
Agence de la Biomédecine in regard to all innovations
in the matter of organ transplantations and medically
assisted procreation should continue;
2. clear and detailed information that takes into ac-
count the drawbacks and risks associated with womb
transplants should be given to living donors and recipi-
ents participating in these research programmes, who
should be given appropriate assistance before, during
and after the procedure;
3. data on research conducted in France and in other
countries should be collected with a view to ensuring
the validity of womb transplants and, in due course, to
assess the possibility of extending the procedure, with
respect for the ethical principles that apply in all organ
transplantations and medically assisted procreation, in
order to avoid deviations”.

More recent documents, as we can see, are less wary
of the concept of womb transplants. However, the
FIGO has still not amended the opinion it published in
2008 [18], notwithstanding the availability of additional
results.

ETHICAL ASPECTS
General criteria for experimental surgery
With very few exceptions new surgical techniques
do not enter clinical practice as a result of randomised
clinical trials; they evolve gradually from existing tech-
niques or, more rarely, from bold divergences from com-
mon practice adopted by a surgical team on the basis of
experience [19].

Francis D. Moore has proposed three criteria that
should be met in order for innovative surgical procedures
to become acceptable, including from the ethical point
of view. The first is laboratory experience that optimally
should precede a surgical innovation; the second is “field
strength” meaning the intellectual and technical expert-
tise available in the institution where the work is being
done; and the third is “institutional stability” based on its
resources, support systems, and staff [20, 21]. All three
were cited in the “Montreal criteria for the ethical feasibil-
ity of uterine transplantation” mentioned above [15, 16].

Donation from deceased and living donors
There are pros and cons for transplants from de-
deceased donors:
Pros:
• no risk for the donor;
• less time needed for removal;
• technically easier, thanks to longer peduncles and
easier anastomosis.
Cons:
• difficult in making a complete pre-operative appraisal;
• logistic issues: distances, etc.;
• informed consent calls for special attention. When
transplanting unusual organs (e.g. face, hands) it is ad-
visable to ask for specific consent in addition to the ge-
neric declaration of consent to the donation of organs
[21]. This is particularly advisable before removing a
womb, given the special significance and symbolic na-
ture of the organ;
• very little clinical experience;
• there are pros and cons for transplants from living
donors.
Pros:
• increased certainty that the organ will function.
Cons:
• highly complicated procedure for the donor: Brän-
nström reported surgical procedures lasting more than
10 hours, involving considerable risks [6];
• the age of living donors is a further problem. To in-
crease the chance of success the donor should be of
childbearing age. It is clearly problematic, to say the
least, to remove the womb of a fertile woman, even she
has already born children;
• it could be feasible to transplant a womb taken from
a living donor with a pathology that does not directly
involve the uterus (which therefore continues to func-
tion) but prevents her procreating;
• a particular problem arises with transsexual women
who wish to have their wombs removed. The Acadé-
mie Nationale de Médecine has suggested that in these
cases a womb transplant could be possible provided two
conditions are met: the transplant should be performed
in the interest of the transsexual and for the therapeutic
benefit of the recipient (i.e. procreation) [17]. On this
point it should be noted that some lesbian, gay, bisexu-
al, transsexual (LGBT) associations are campaigning to
abolish the need for surgical sterilisation as a requisite
for gender reassignment. Clearly, while such cases fall
within the category of transplants from living donors,
the unusual nature of the donor’s personal journey calls
for an even more specific form of informed consent;
• current legislation requires that there should be a
family connection between the donor and the recipient.
Cases of undue influence (such as a mother who feels
responsible for her daughter’s inability to procreate)
and other forms of interference cannot be ruled out.
The recipient

Although womb transplants are seen in some quarters as being relatively simple in comparison with the transplantation of other organs, the procedure is a complex one. The operation described by Brännström lasted 10 hours and 7 minutes for the donor and 4 hours and 55 minutes for the recipient [6].

A womb transplant is not a life-enhancing event for the recipient (in fact, it has the opposite effect), though it does enable her to procreate.

To avoid the need for lifelong immunosuppressive therapy, a womb transplant requires two further operations: a caesarean section for delivery, followed by a hysterectomy.

The possibility of rejection during pregnancy means that an exit strategy is more complicated in a womb transplant than in other organ transplantation procedures.

Issues of distributive justice also arise, given that the high costs of these interventions make them inaccessible to most people.

There is a considerable imbalance between the large number of potential recipients and very few potential donors. The main source should be young, brain-dead donors with healthy wombs, of whom there are very few.

Recipients should receive detailed information regarding: the surgical risks, probable need to remove the transplanted uterus, complex preparation process (pre-operative hormone therapy), possible failure to procreate and the effects of immunosuppressive therapy.

Womb transplants and medically-assisted procreation

The two are linked because to date post-transplant pregnancies have been initiated only after in vitro fertilisation.

Womb transplants pose many problems similar to those posed by other assisted procreation procedures: rights of the donor, health consequences for the foetus and child, interventions on a woman’s body, the role of the state in regulating procreation, etc.

There are considerable regulatory problems. Current regulations in most states do not mention womb transplants either in the context of assisted procreation or among types of transplants performed to date.

Womb transplants could be considered as a means to counter the perverse phenomenon of surrogacy, though in the current circumstances it is too experimental a procedure to be an alternative: this could change if and when womb transplants become a part of consolidated clinical practice. For the sake of clarity, the lack of a “medical” alternative to surrogacy does not make this phenomenon ethically legitimate; it remains an unacceptable exploitation of women and a violation of the rights of the child. In the current state of knowledge the requisite cited in the “Montreal criteria for the ethical feasibility of uterine transplantation” – that the recipient should have “a personal or legal contraindication to surrogacy” – is ethically highly controversial and, in the authors’ opinion, quite unacceptable.

There could be a higher risk of trade in wombs than in other organs. This risk is heightened by the fact that while there exist international conventions against the trade in organs for transplantation [22] (which unfortunately is nonetheless present in some states), some countries allow the legal sale of gametes. This, combined with the current legalisation or, in some states, mild acceptance of surrogacy, could lead to the treatment of the womb as a “separate” case associated with female reproduction, an area that is already more susceptible to market criteria and less protected.

Pregnancy

Because the objective of womb transplants is conception, these procedures pose highly specific problems linked to the wellbeing of the product of conception, that are not associated with the transplantation of other organs. In ethical terms the risks are of primary concern.

Currently available figures do not point to short-term risks for the child as a consequence of immunosuppression, but risks associated with premature birth cannot be excluded, nor can long-term risks such as haemophilia, cancer, retarded growth or other pathologies.

There is the possibility of psychological risks for children on learning they were born from a transplanted womb.

CONCLUSIONS

The transplantation of a womb is the first all-female “gender transplant” performed to date: it stands alone in the world of transplants, also because of the emotional and symbolic importance attached to the functioning and purpose of the womb. In ethical and clinical terms, it is the opinion of the authors that in the current state of knowledge womb transplants are still a highly experimental procedure and should be subject to all the risk/benefit assessments normally applied in similar circumstances. It should also be recalled that this is not a life-saving procedure and that the womb should in any case be removed after any pregnancy in order to permit the interruption of immunosuppressive therapy; the risk/benefit assessment should be performed in this light. The state of the art for the moment excludes the possibility that womb transplants can be considered as an alternative to other forms of pregnancy, which in any case are highly controversial in ethical, social and psychological terms (and unacceptable in the authors’ opinion), such as surrogacy, or even as an alternative to legitimate means of achieving parenthood such as adoption. In brief, in ethical terms womb transplants from a deceased donor, in specific, carefully controlled and clinically assessed circumstances and bearing in mind that such procedures are currently highly experimental, could be acceptable, while the removal and transplantation of a womb from a living donor presents for now such major issues and contra-indications as to render it unacceptable.

Conflict of interest statement

None.

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REFERENCES


