



Ethical questions about preimplantation genetic diagnosis and stem cell research

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Ethical problems with PGD: an overview

- the moral status of the embryo
- the relationship between prenatal and preimplantation diagnosis
- the right not to know (e.g. Huntington, exclusion and non-disclosure testing)
- the application for 'late onset' and multifactorial diseases



Ethical problems with PGD: an overview

- the transfer of carrier embryos
- the transfer of affected embryos
- requests to select affected embryos (e.g. deafness)
- the autonomy of the parents vs the responsibility of the physician



Calculation of genetic risk

1. The gravity or seriousness of the disease (life quality, life expectancy, suffering, disabilities ...)

2. The probability of occurrence

Risk = gravity X probability



Differences between PD and PGD

1. The contribution of the physician is larger
 2. The physician has to act rather than refrain from acting. Acts weigh heavier than omissions
 3. In vitro location shifts the locus of control from the woman to the physician and the partner
- Contribution entails responsibility



Moral responsibility

1. Causal contribution: the person does something.
 - material complicity: actus reus
2. Intentional contribution: the person has the intention to realise the goal.
 - formal complicity: mens rea



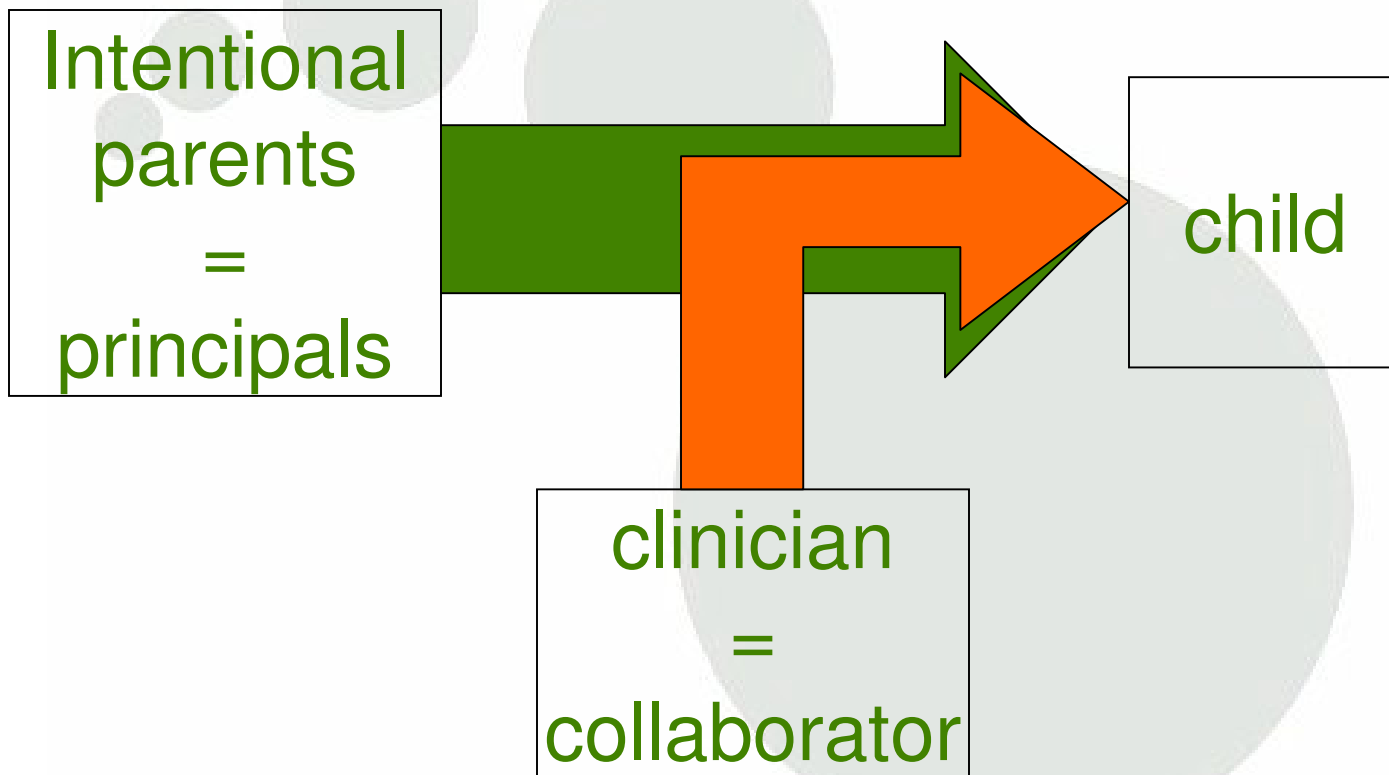
Moral responsibility

1. Principals: intentional parents: who start the project and intend to raise the child
2. Collaborators: who assist when the parents experience problems
 - persons: gamete donors, surrogate, physician ...
 - actions: inform, diagnose, perform technical acts etc.

Collaborator (clinician) performs an act that contributes to the realisation of the parental project of the intentional parents.



Patients-clinician relationship in the parental project





Evaluation of parental project is crucial for the evaluation of the actions of the collaborators

- standard for *responsible parenthood*: the future child must have a reasonable chance of having a reasonably happy life
- conflicts arise because patients and physician use different standards of responsible parenthood.
- main problem: large grey zone



Procreation and assistance is

acceptable

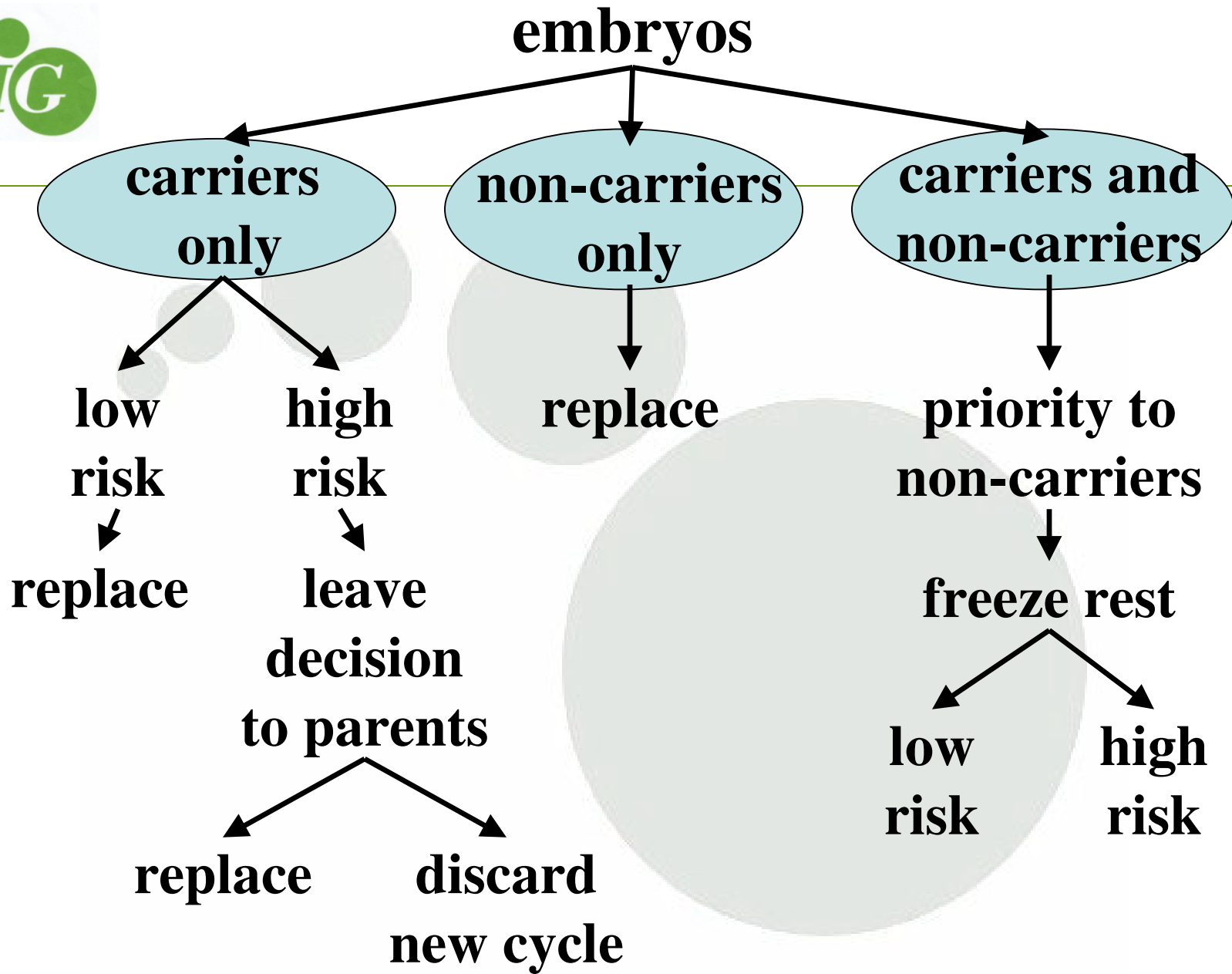
physician *should* assist

wrong but acceptable

physician *can (is allowed to)* assist

unacceptable

physician *must not* assist





Decisional authority about embryos

- Intentional parents have priority



Choose within institutional and/or legal framework

i.e. PGD is not allowed for social sexing

i.e. the center refuses PGD for cleft palate

- Within this framework, patients and clinician negotiate



Run through the most likely outcomes during counselling

i.e. preferential replacement of non-carrier embryos



Patients change their minds

• Advance directives: 'if X happens in the future, Y must be done'

→ Difficulty:

- bring the future situation to mind
- predict new possibilities
- foresee possibilities

→ Consequence: advance directives have a limited value and patients have a right to change their minds



Possible conflict with clinician



Changing the project

- The clinician makes a causal and intentional contribution at the start of an originally determined project.
- The project serves as a context in which the persons are able to foresee and plan the consequences of their actions.
- Patients' decision is a deliberate human intervention that 'cuts off' the clinician's contributions from the final result.



Changing the project

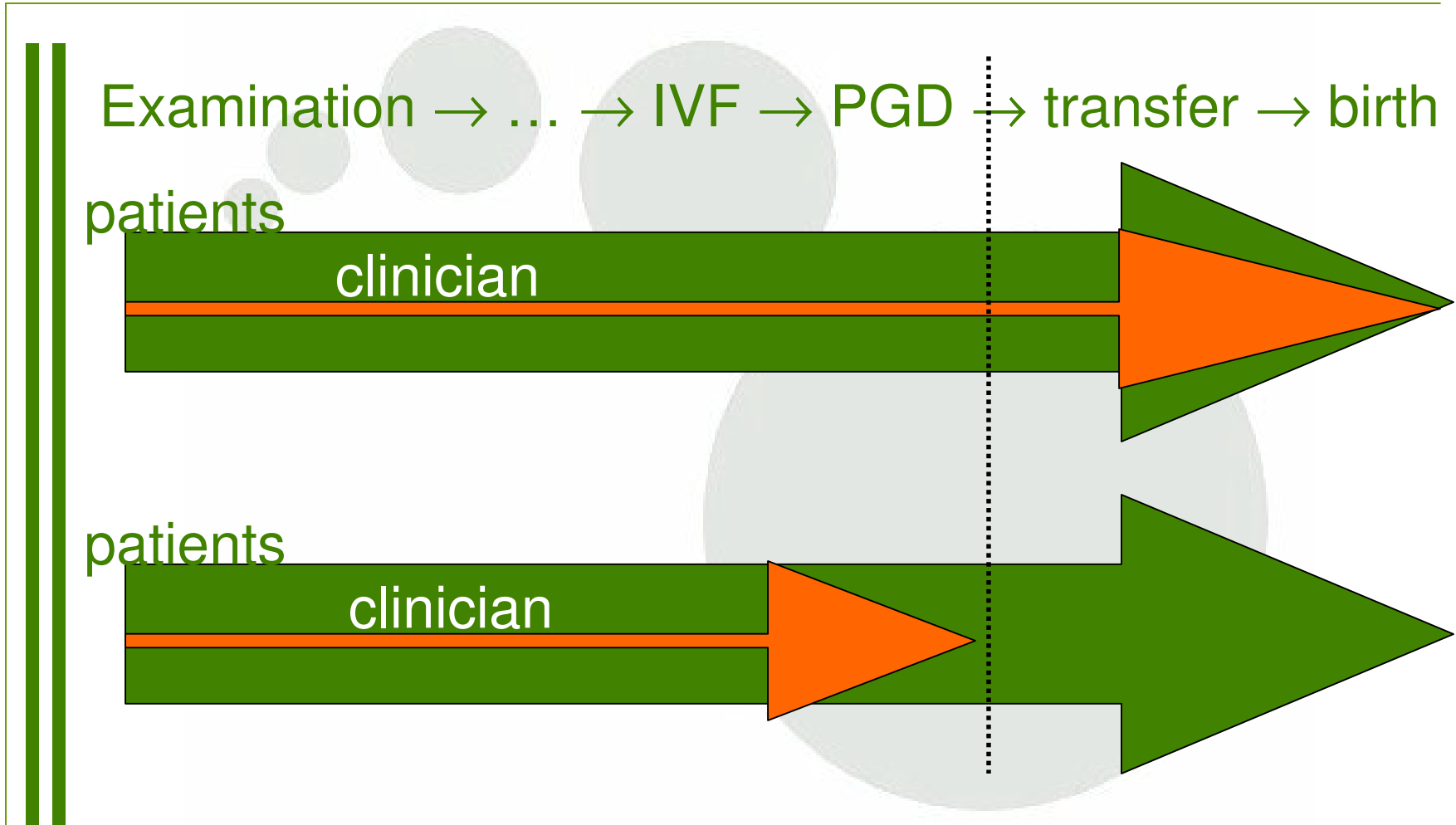
Examination → ... → IVF → PGD → transfer → birth

patients

clinician

patients

clinician





Changing the project

- However, the clinician may feel abused and betrayed because he or she has been ‘tricked’ into participating in a project he or she considers as morally wrong.



- These feelings may generate the wish of physicians to force patients to abide by the original agreement.



Conditional treatment

Imposing conditions is ethically problematic because this conflicts with

- a) the rule of non-directiveness, and*
- b) the couple's reproductive autonomy.*

Goal of conditions: bring the situation in line with responsible parenthood and/or good clinical practice

- reduce risk for future child
- increase the chance of success



Conscientious objections

Making non-directiveness absolute disregards the moral responsibility of the collaborators.

Causal -
intentional
contribution



Partial
responsibility



Possible
objections of
conscience



Conscientious objections

- Conscientious objections only apply to one's own behaviour: integrity.
- No right to prevent patients from realizing their goal by coercion, i.e. discarding the embryos.

Possibly cryopreserve the embryos until the transfer to a colleague.



Conditional treatment

Nevertheless: risk reduction cannot be the sole goal.

i.e. PD after PGD because of risk of misdiagnosis

The risk of patients not complying with the original agreement is fairly high for some acts.

i.e. 25% did not have PD to confirm the PGD result although they accepted this in the informed consent form.



Requests which increase risk of abortion

- at risk embryos after exclusion testing for Huntington's disease
- male embryos after sexing for X-linked diseases

Original theoretical risk: 1 in 4



Known risk after PGD: 1 in 2



Conflicts between the proximate and the ultimate goal

1. Replacement of male embryos in case of X-linked diseases

Possible justification: secondary infertility

2. Incontinentia pigmenti

=> ♀ carrier: mild to serious handicaps

=> ♂ carrier: death in utero

Replacement of male embryos is justified



Goals of PGD

- proximate goal: prevent an abortion
- ultimate goal: prevent birth of an affected child

Normally, the ultimate goal is reached by striving for the proximate goal.



Conclusions

1. The clinician carries partial responsibility for the result as a collaborator in the procreative project of the parents.

2. If the project conflicts with principles of responsible parenthood and good clinical practice, the clinician can impose conditions for his or her collaboration or refuse further assistance.

Counselling and discussion before the start of treatment can prevent most conflicts.



Ethical questions in stem cell research



Two principles

Two principles that have a descriptive and normative function in the debate on the use of embryos for research:

- the subsidiarity principle, and
- the separation principle



I. The subsidiarity principle

Material from an entity with a higher moral status should only be used for research if and only if the same results cannot be obtained by material from an entity with a lower moral status

- Reformulated: the use of the entity with the higher moral status should be **NECESSARY**



Necessary for which goal?

- the fastest path to therapy?
- the safest and most efficient method?
- the cheapest way?
- the most widely applicable method?



The subsidiarity principle

- animals used prior to humans in clinical research
- adult stem cells used prior to embryonic stem cells
- supernumerary used prior to research embryos
see UK and Belgian law on embryo research
- 'low quality' used prior to 'high quality' embryos

The principle expresses degrees of respect due to different organisms



The subsidiarity principle

- “why not take the least offensive moral approach?”
problem: no consensus

Three counter-arguments:

1. Simple destruction of embryos is not morally superior to using them for research
2. Continued cryopreservation of embryos is not morally superior to using them for research now
3. Subsidiarity states priority but without criteria to decide when alternatives should be started, it comes down to an unlimited prohibition of research on embryos



Categories of embryos in ART

A. Genetically affected embryos

B. Genetically at risk embryos

- high risk (X-linked diseases)

- no diagnosis

C. Low quality embryos

Two dimensions (that may overlap) play a role:

- viability (or potentiality)

- quality of life



Absent or reduced viability

- embryos created by SCNT have little or no potential to develop into a healthy human being (Jaenisch, Trounson)

If these embryos are not viable, one does not destroy a future human being. Like parthenotes, these embryos would have the same moral status as teratoma

Recent proposal of Hurlbut to create embryo-like entity by means of Altered Nuclear Transfer

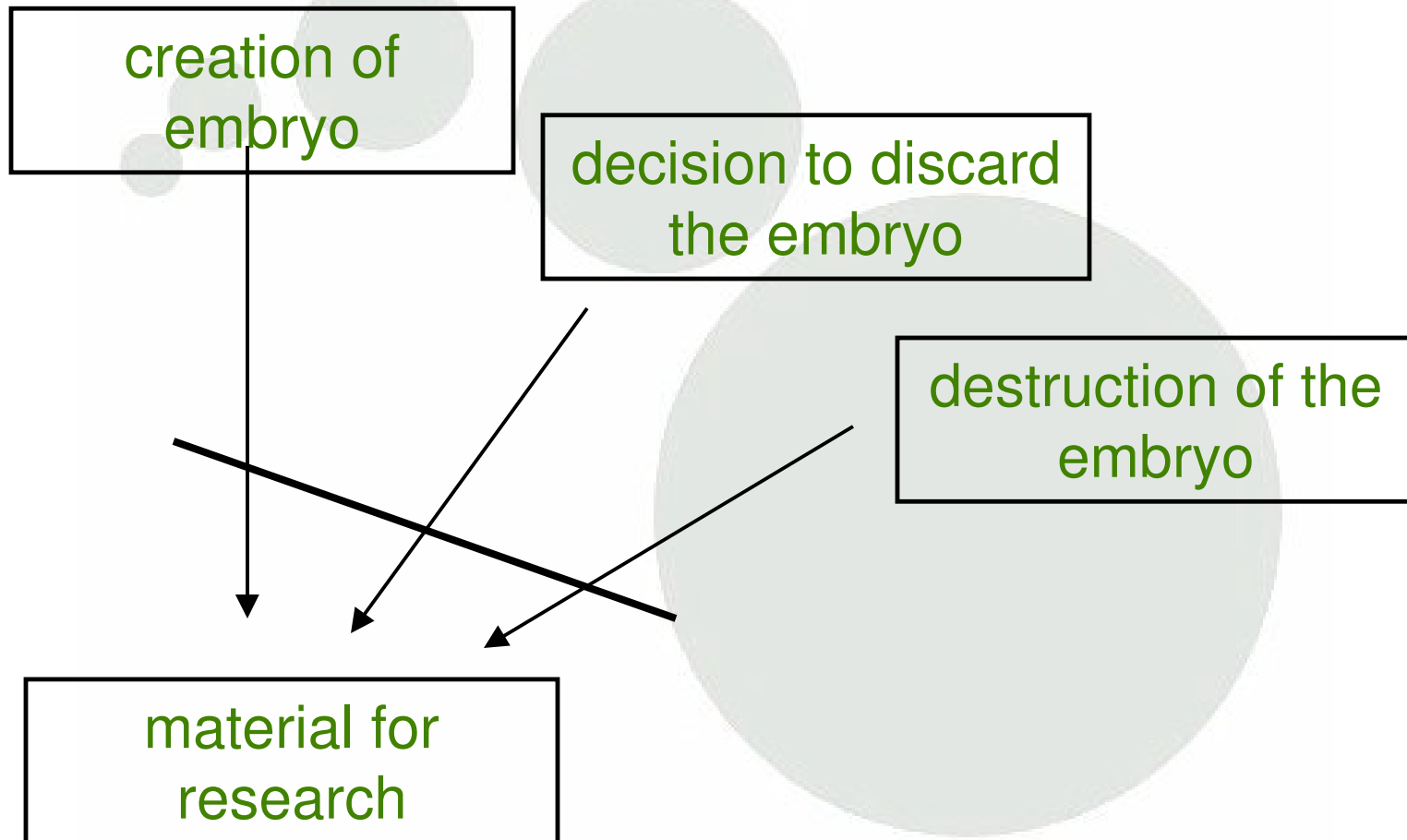


II. The separation principle

The separation cuts the link between research and the wrongful act (the destruction of the embryo) and thus eliminates the complicity before and after the fact of researchers



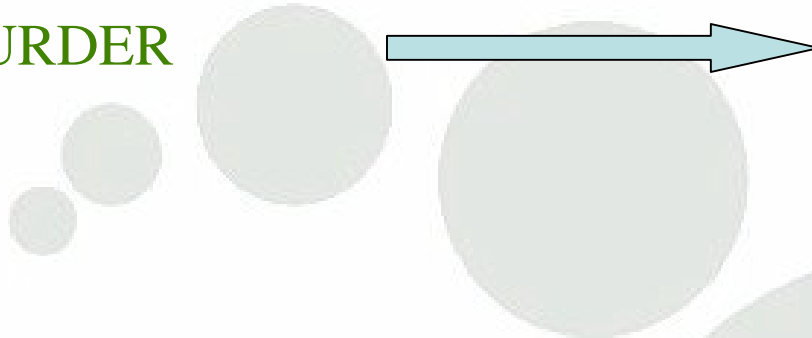
The separation principle





The separation principle

MURDER



transplant organs

↓
surgeon is NOT
accessory to murder

ABORTION



fetal tissue or germline
stem cells

↓
researcher is NOT
accessory to abortion

EMBRYO DESTRUCTION



embryonic stem cells

↓
accessory researcher?



The separation principle

Creation of the embryo // research

- separation principle prohibits the creation of embryos for research since the research determines the creation



The separation principle

Decision to discard the embryo // research

- this separation is not kept: infertility patients have to indicate what shall be done with their embryos after they stop treatment

- strictly speaking they should only be approached for donation for research after they have decided to discard their supernumerary embryos



The separation principle

Destruction of the embryo // research

- taking the ES cells (ICM) is the destruction of the embryo

- Decision to discard the embryo had already been taken
- Blastomere extraction without destruction of the embryo tries to break this link between stem cell collection and embryo destruction



Separation principle in ESC research

Once stem cell lines are established, can research be conducted without a link to the destruction of the embryos from which the stem cells were obtained?

Once stem cell lines are established, can drugs and therapies developed by research be used without a link to the destruction?



Separation

Researcher X



kills embryo z
for stem cells

Country A

private research
institute

Time t

Researcher Y



uses stem cell
line Z

Country B

public research
institute

Time t + 1



Separation principle in regulation

- Germany: import of SC lines established before 1 January 2002 is allowed but no research on embryos
- US: federal funding for research on SC lines established before 9 August 2001 but no derivation

The condition to use SC grown before a certain date is based on the wish to avoid complicity with destruction (the bad already happened) and to guarantee that not more embryos are killed for research (comparable to the 'more abortions' argument)



Death and the separation principle

New proposal: collect stem cells from a dead embryo (Landry & Zucker, 2004)

Death: irreversible loss of integrated organismic functioning i.e., cleavage arrest

Separation principle: the collection of stem cells must be separated from the death (destruction) of the embryo



Additional problems

1. The foreseeable shortage of oocytes for research (at least short term)
 - risk of exploitation of women
2. The safety of clinical trials with stem cells
 - pressure on researchers to lower standards
3. The dangers of commercialisation
 - threat to distributive justice



Conclusions

Both the subsidiarity and the separation principle may offer a solution for people who attribute a high moral status to the embryo. However, apart from some selected situations, they lead to serious and avoidable complications

One should not accept too many adaptations and restrictions in research to accommodate a rare and extreme view on the embryo.