

Choosing children

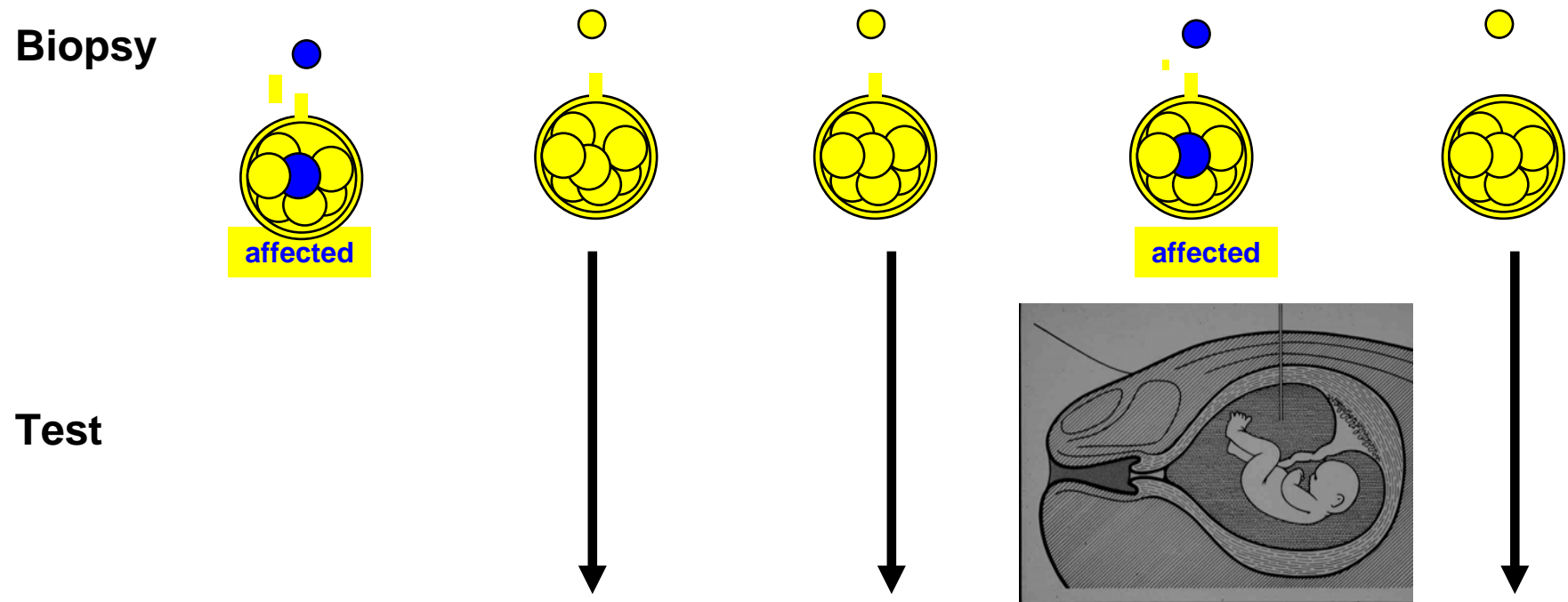
Practical and Moral Choices in the Practice of Preimplantation Genetic Diagnosis

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Preimplantation Genetic Testing

Detection of genetic information in an embryo made by examining a representative sample taken at a preimplantation stage of development

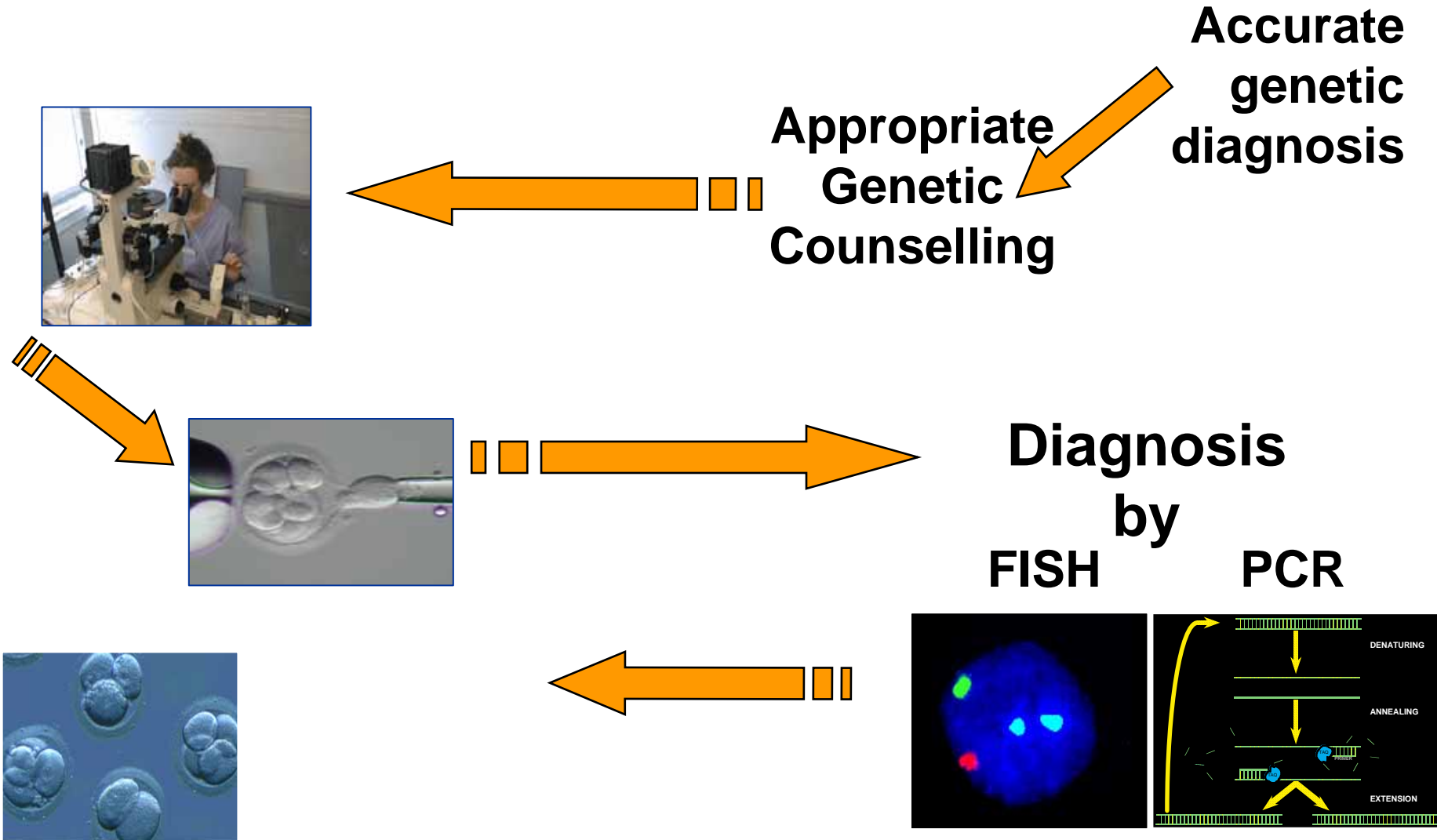
PGD principle



transfer only unaffected embryos back to the patient

Assisted Conception Unit

Genetics Centre



Steps to PGD

Types of genetic disorders

Autosomal disorders (PCR)

- Spinal Muscular Atrophy
- Cystic Fibrosis
- Huntington's Disease
- Sickle cell disease
- EB

Chromosome rearrangements (FISH)

64 Reciprocal translocations
14 Robertsonian
6 Inversions

Sex Linked disorders

e.g. OTC, Hunter's, ALD, DMD,
Fragile X

Types and Use of Preimplantation Genetic Testing

Preimplantation genetic diagnosis (PGD)

To reduce a known genetic risk

Preimplantation genetic screening (PGS)

To improve IVF outcome

Preimplantation HLA testing (with PGD)

To reduce genetic risk and help a sick sibling

Preimplantation HLA testing (without PGD)

IVF Biopsy & HLA test to provide tissue matched sibling

PGD in Numbers

	ESHRE PGD Consortium Reports 1-7 Report 8		GSTT 1997- 2008
Cycles started	Not reported	Not reported	695
Cycles to OR	5107	1128	606
Cycles to ET	3719 (73%)	816 (72%)	470 (68%)
CPR per OR	18%	17%	28%
CPR per ET	25%	24%	35%

Ethical concerns regarding PGD

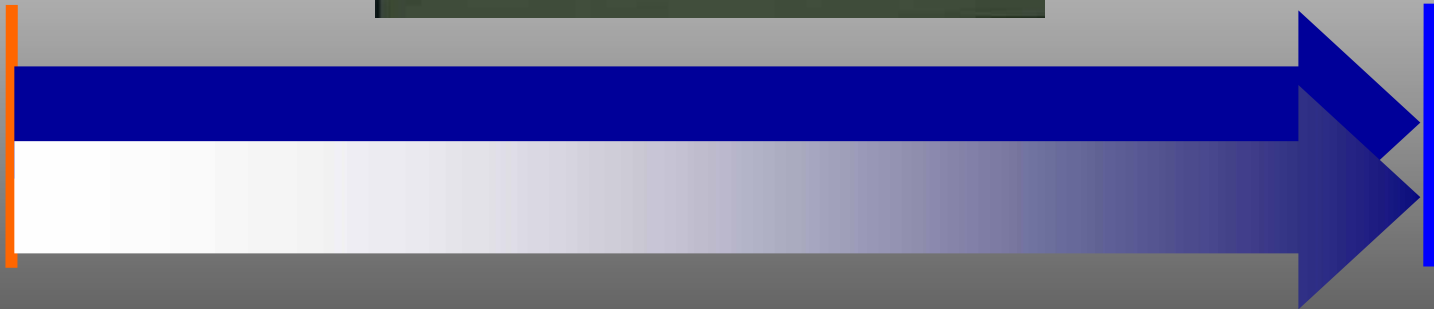
- Different views of **moral status of the embryo** at preimplantation stages
- Fear and concern about **manipulating humans genetically** – choosing our offspring
- Use of the **embryo (or the person) as a commodity**
- Worry where it will all lead; getting out of control (**slippery slope**)

Moral Status of the Embryo

Fertilisation



Birth



Different values for sanctity of life and
start of personhood

Where will it all end?



COMMENTARIES

Preimplantation Genetic Diagnosis for Cancer Syndromes A New Challenge for Preventive Medicine

Perspective
AUGUST 10, 2006

Preimplantation Diagnosis for Genetic Susceptibility

Peter Braude, M.B., B.Ch., Ph.D.

Designer baby to beat risk of Alzheimer's

Sarah-Kate Templeton
Health Correspondent

DOCTORS are planning the first British "designer baby" free from the risk of developing Alzheimer's disease in middle age. A couple with a strong family history of early-onset Alzheimer's will select embryos free from a gene that predisposes people to developing the condition in their forties or fifties.

Under the plan, Charl and Danielle de Beer from London will undergo IVF to create the embryos even though they have no fertility problems. The de Beers say embryo screening offers them the chance to have healthy children and end

the tragedy Alzheimer's has brought to their family.

However, critics warn that screening embryos for the disease is a dangerous step towards creating "perfect" babies.

The de Beers, who are in their early thirties, were considering adoption before they heard of the technique, called pre-implantation genetic diagnosis (PGD), which can screen out embryos carrying the genes that predispose people to Alzheimer's.

The couple's doctors at the Bridge Centre fertility clinic in London will this month apply to the Human Fertilisation and Embryology Authority (HFEA) for a licence to perform the treatment in Britain. It is already used in America.

Doctors are already screening embryos here using PGD to create babies free

from fatal children. Hi for genes th is controver an illness of Alzheimer's their forties sufferers of develop it i about 60%, patients in l

Opponen to a situatio afford it are disability ar the basis of

Dr David King, director of Human Genetics Alert, said he sympathised with

IVF may allow wor daughters breast c

James Randerson, science corresp
Tuesday May 9, 2006
The Guardian

Designer babies' fear in genetic screenings

TWO HUNDRED women being treated for infertility have had their embryos screened for genetic defects, and 20 children have already been born in what critics warn could be the first step towards designer babies. The figures were revealed yesterday by the Human Fertilisation and Embryology Authority in a consultation document. It is seeking views on how tight the rules of the technique should be. The authority has banned sex selection for social reasons in 1993 but allowed it for medical reasons in couples with sex-linked diseases such as haemophilia and Duchenne's muscular dystrophy, which occur only in boys. Now it is seeking views on how tight the rules of the technique should be.

BY JEREMY LAURANCE
Health Editor

Genuinely difficult practical issues to confront

- **Rights and duties of a doctor**
- **Rights wishes and expectations of parent**
 - For themselves
 - For their as yet unborn (potential) offspring
- **Rights of the child once born**

All influenced by society mores
and sanctity of life arguments

Rights and duties of a doctor

- **Welfare of the Child:**
Limiting a child's right to an open future
- Long term **safety** of embryo biopsy
- **Restricted access** to expensive technology

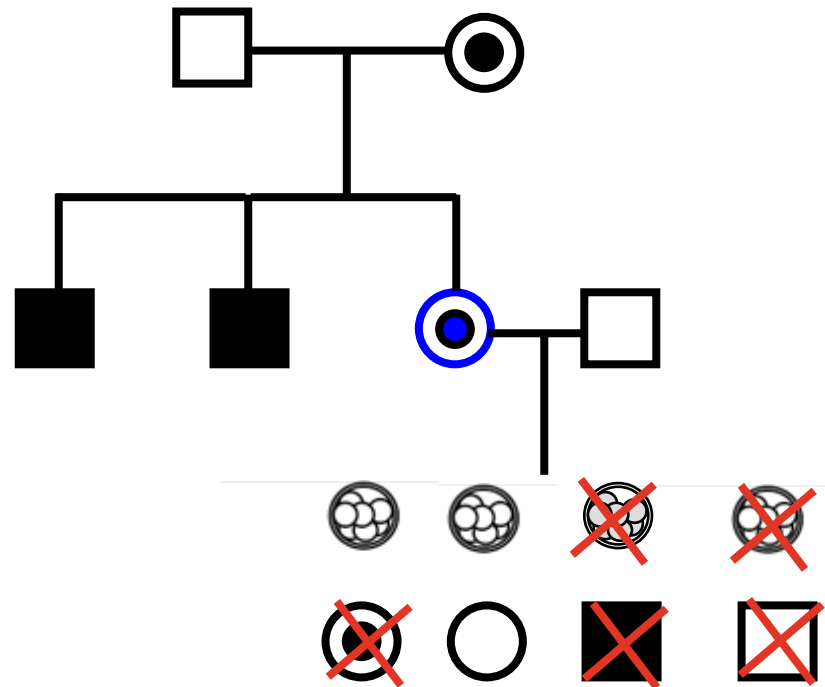
What might parents want?

- Child health in the face of a lethal disorder
- Prevention of a late onset disease
- Avoiding ToP

- Eliminating disease from blood line
- Attaining a physical advantage for the child
- Attaining health for a sibling
- Just being more like them – even selecting for disease trait

Transfer of carrier embryos

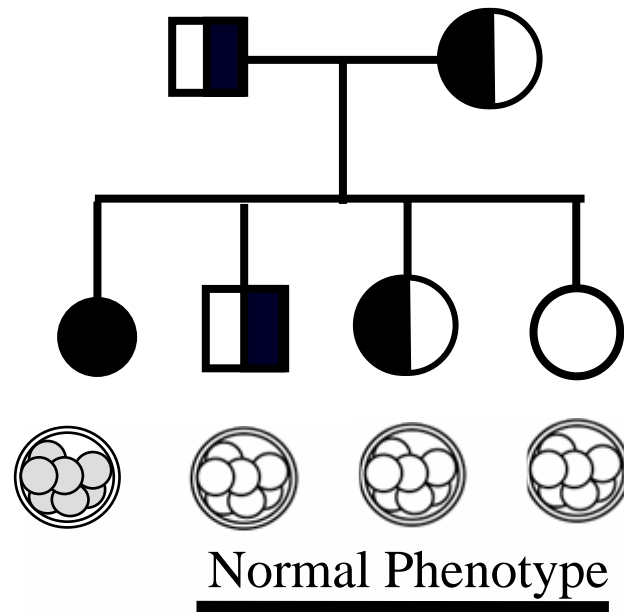
(Alport's disease: Sex selection against males)



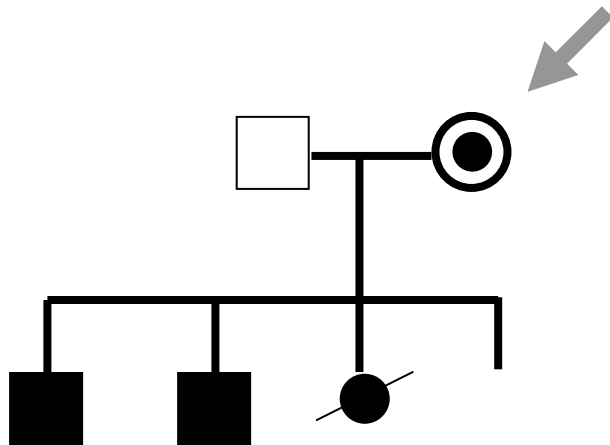
Centre for Preimplantation Genetic Diagnosis

Transfer of carrier embryos

(recessive disorder: CF)

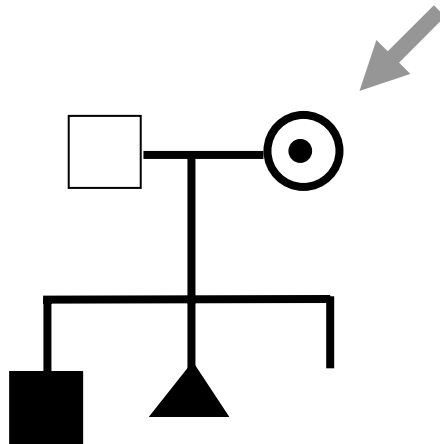


Impact of affected child on parental choice



- Carrier of X linked muscular dystrophy
- Boys will die in late teens or early 20s
- Requests **sexing for female embryos only**

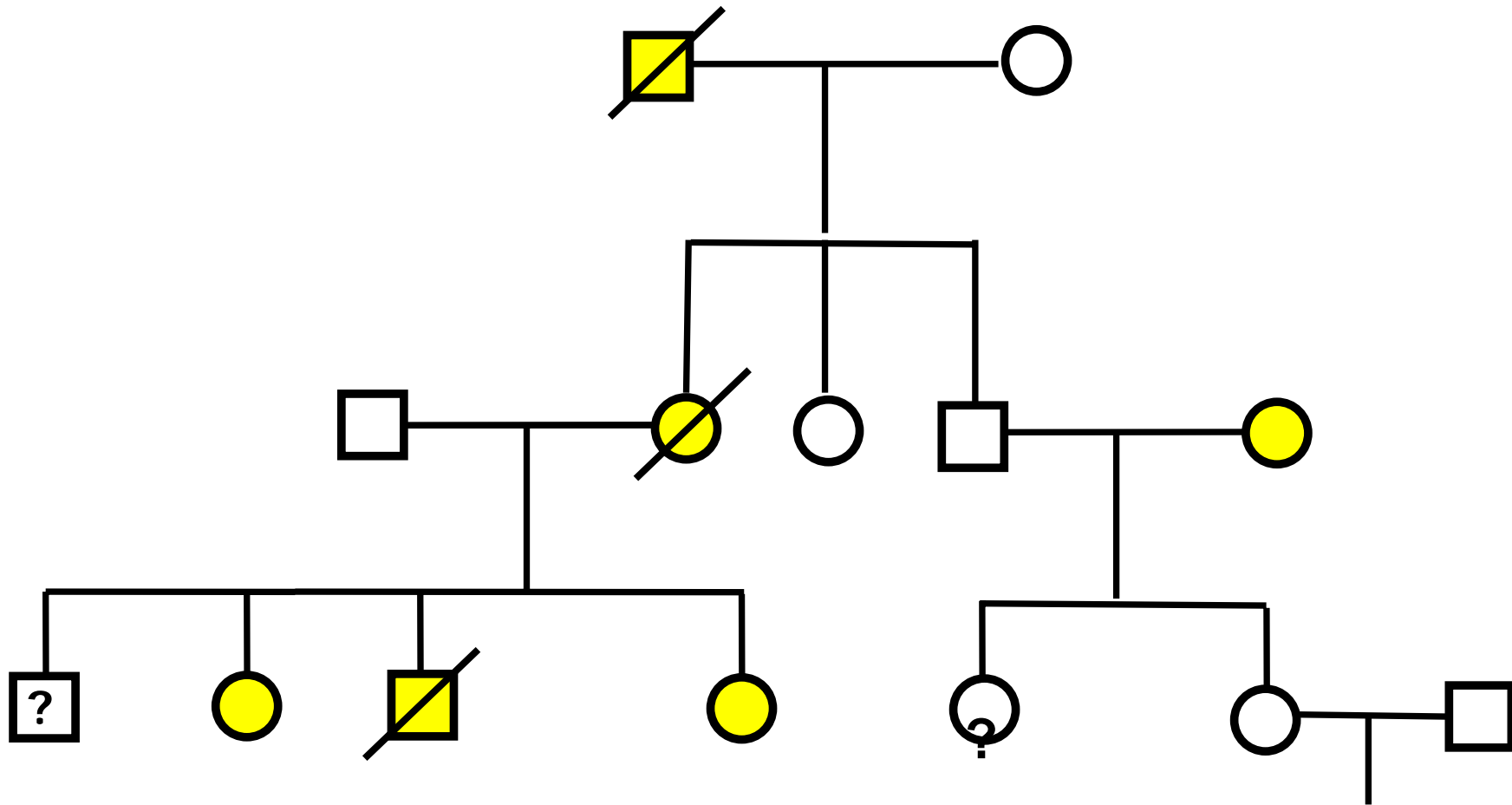
Impact of affected child on parental choice



- Carrier of X-linked haemophilia
- George has haemophilia and loves football which he will be stopped playing at age 10
- **Wants sexing for female** so as not to compete with George
- **Refused** use of test which would identify **normal males**

Late onset disease

(example: HD autosomal dominant)

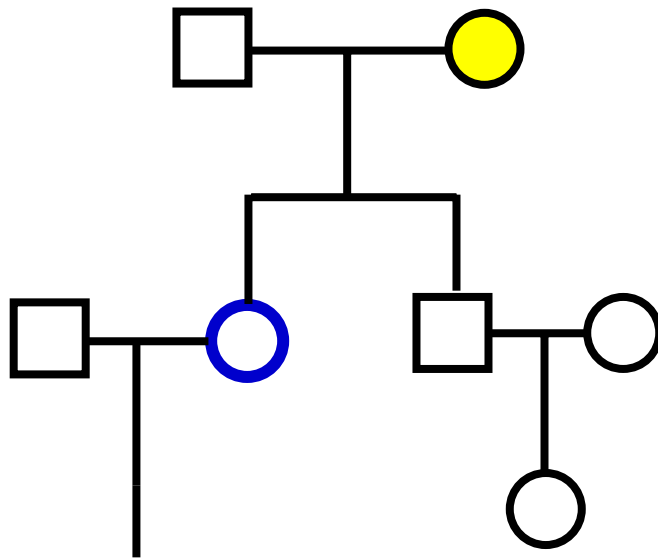


Difficulties of late onset disease

Example: Huntington's disease

- Many years of disease free life
- Knowledge of genetic status changes personal and reproductive prospects
- Desire not to know genetic status has implications for testing and children born
- Termination not undertaken after PND changes child's freedom not to know his status

HD family dynamics



She at risk of HD gene, but no symptoms yet

Progressive degenerative disorder

Will develop symptoms age 35-45 years old

Her mother dying of the disorder

Brother is normal and has family

Wants a family but the child could inherit the disease

What should she do?

patients with HD risk

- Reproduce at 50% risk
- Prenatal diagnosis & TOP
- Remain childless
- Gamete donation
- Adoption
- **PGD**



know, HD status & PGD

Decision to reproduce but
Against Termination of Pregnancy

Know - affected



**Direct testing of
embryos for HD
expansion**

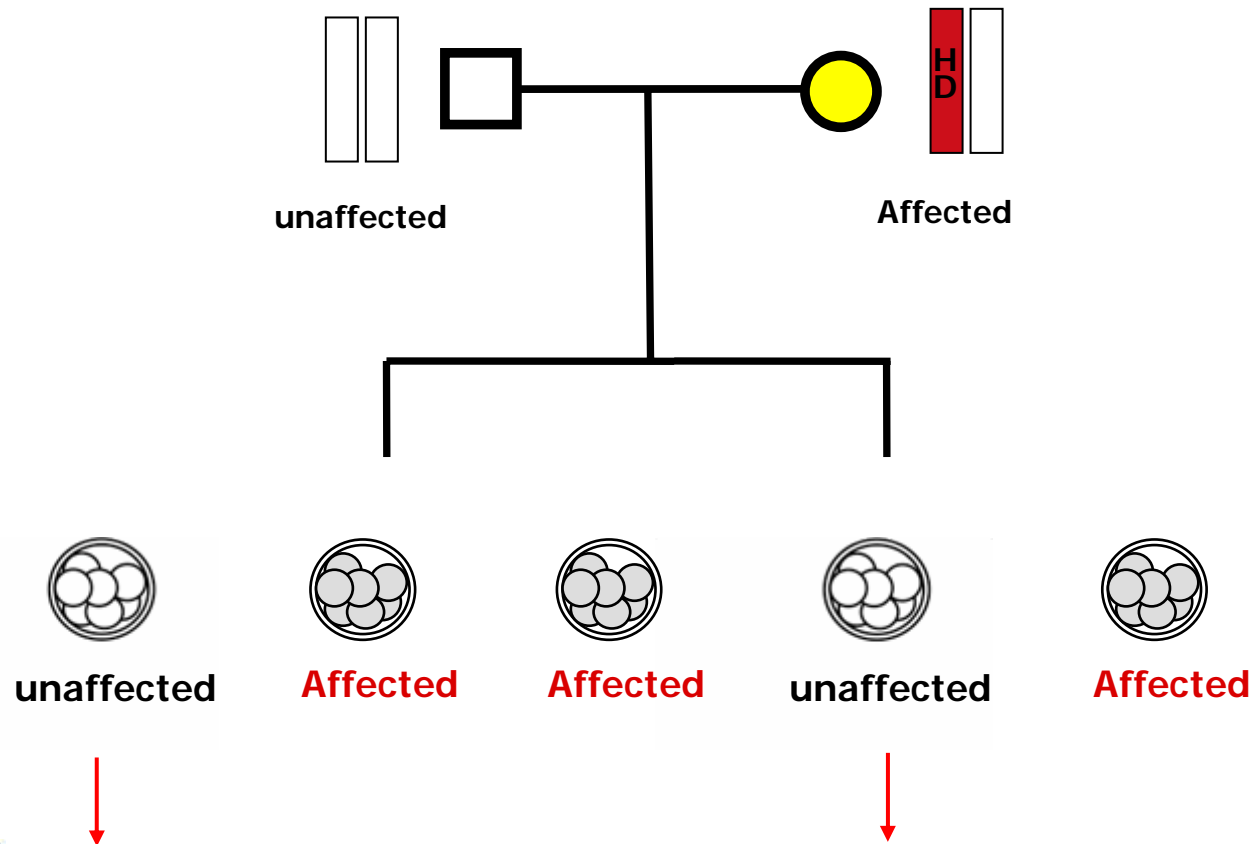
Don't wish to know



**Direct testing of
embryos for HD
expansion
BUT result NOT
to be revealed**

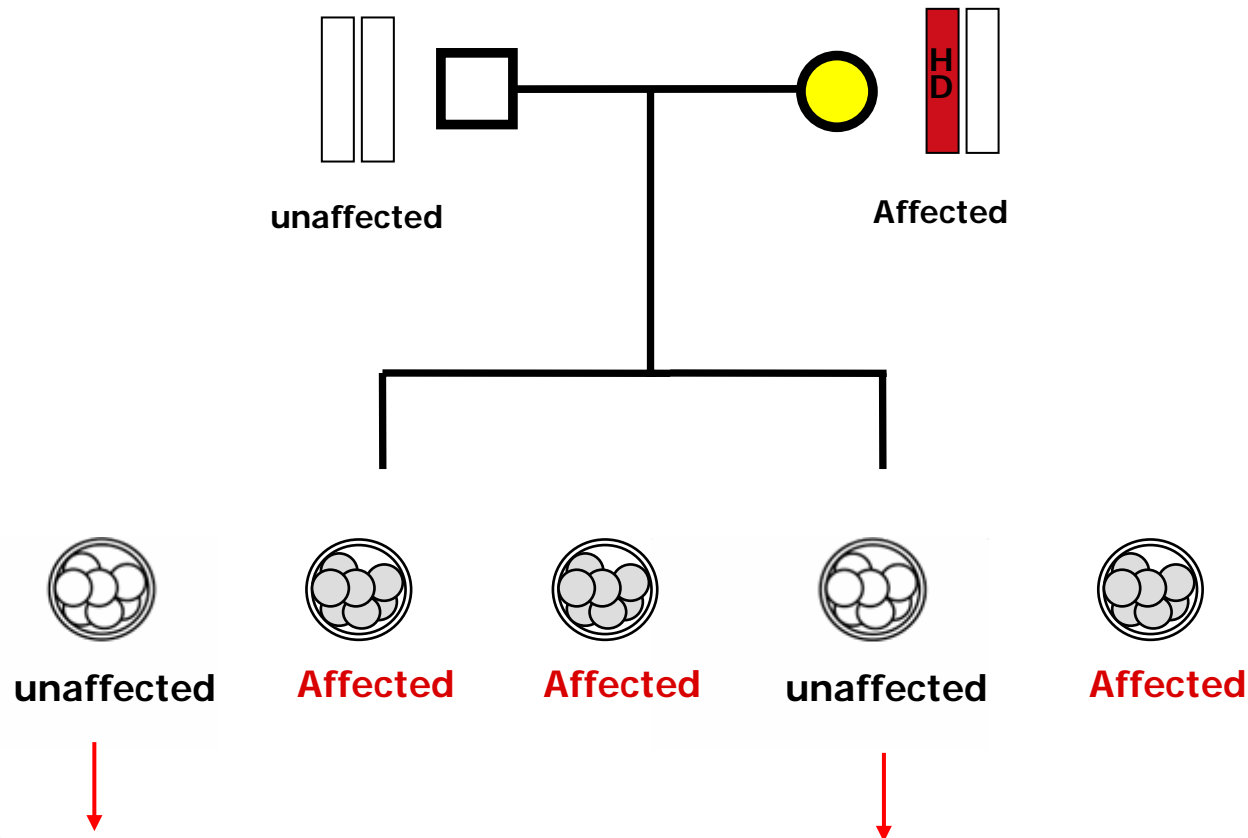
Direct Testing for Huntington's Disease

(patient knows her HD status)



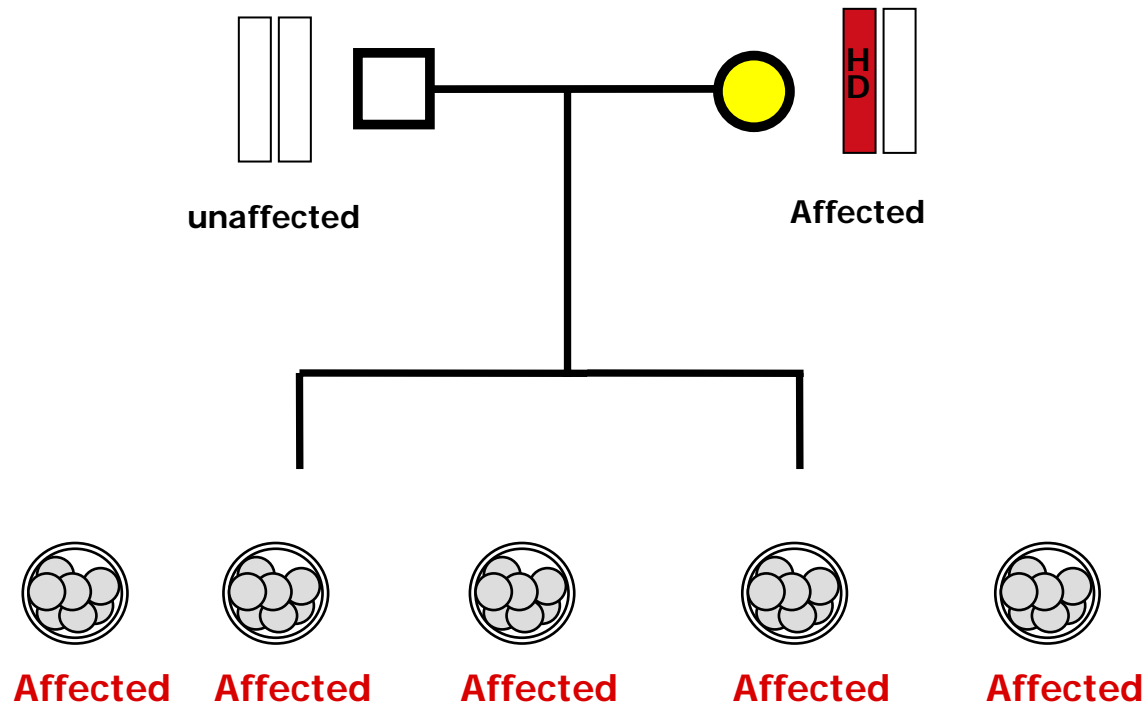
Non-disclosure Direct Testing of Embryos for Huntington's

(patient does **NOT** wish to know HD status but lab and ART centre know!)



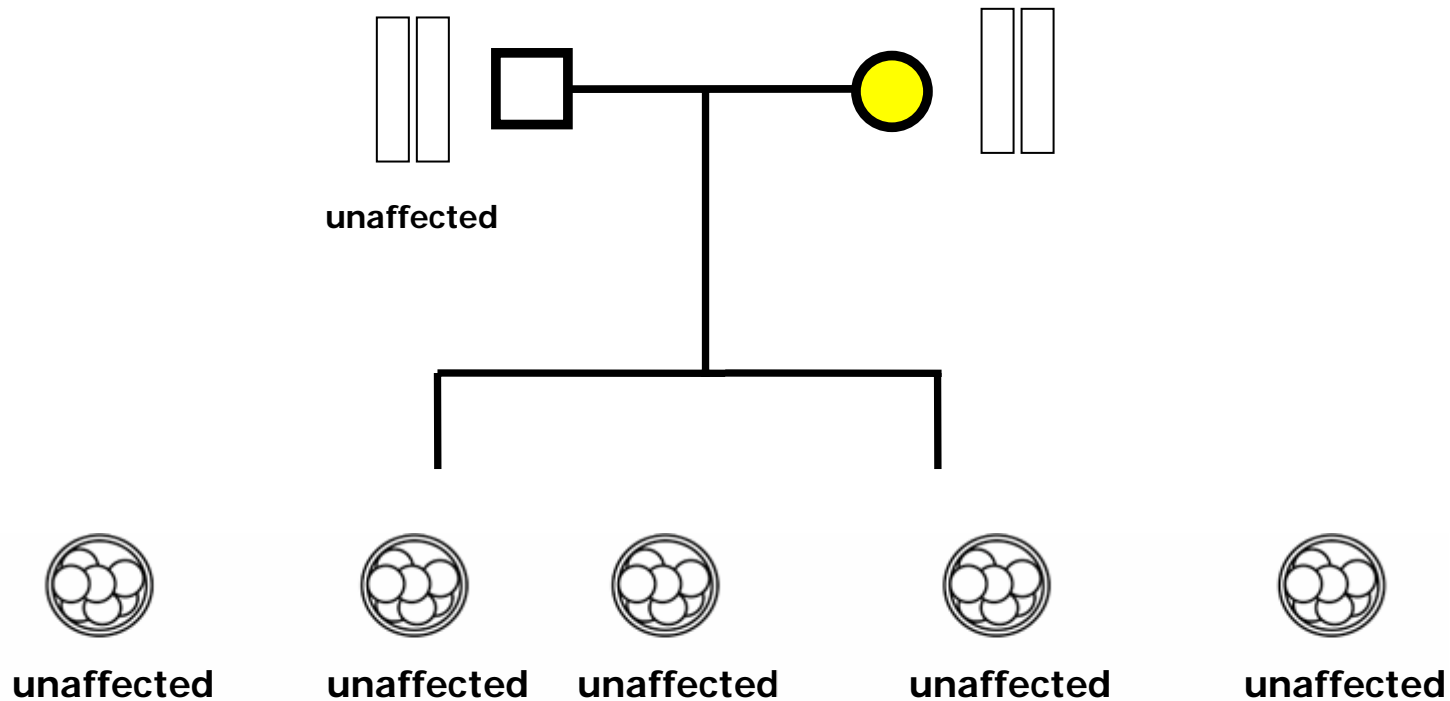
Non-disclosure Direct Testing of Embryos for Huntington's

(patient does **NOT** wish to know HD status but lab and ART centre know!)



Non-disclosure Direct Testing of Embryos for Huntington's

(patient does **NOT** wish to know HD status
but lab and ART centre know!)



To know, or not to know, HD status & PGD

Decision to reproduce but
Against Termination of Pregnancy

Know - affected

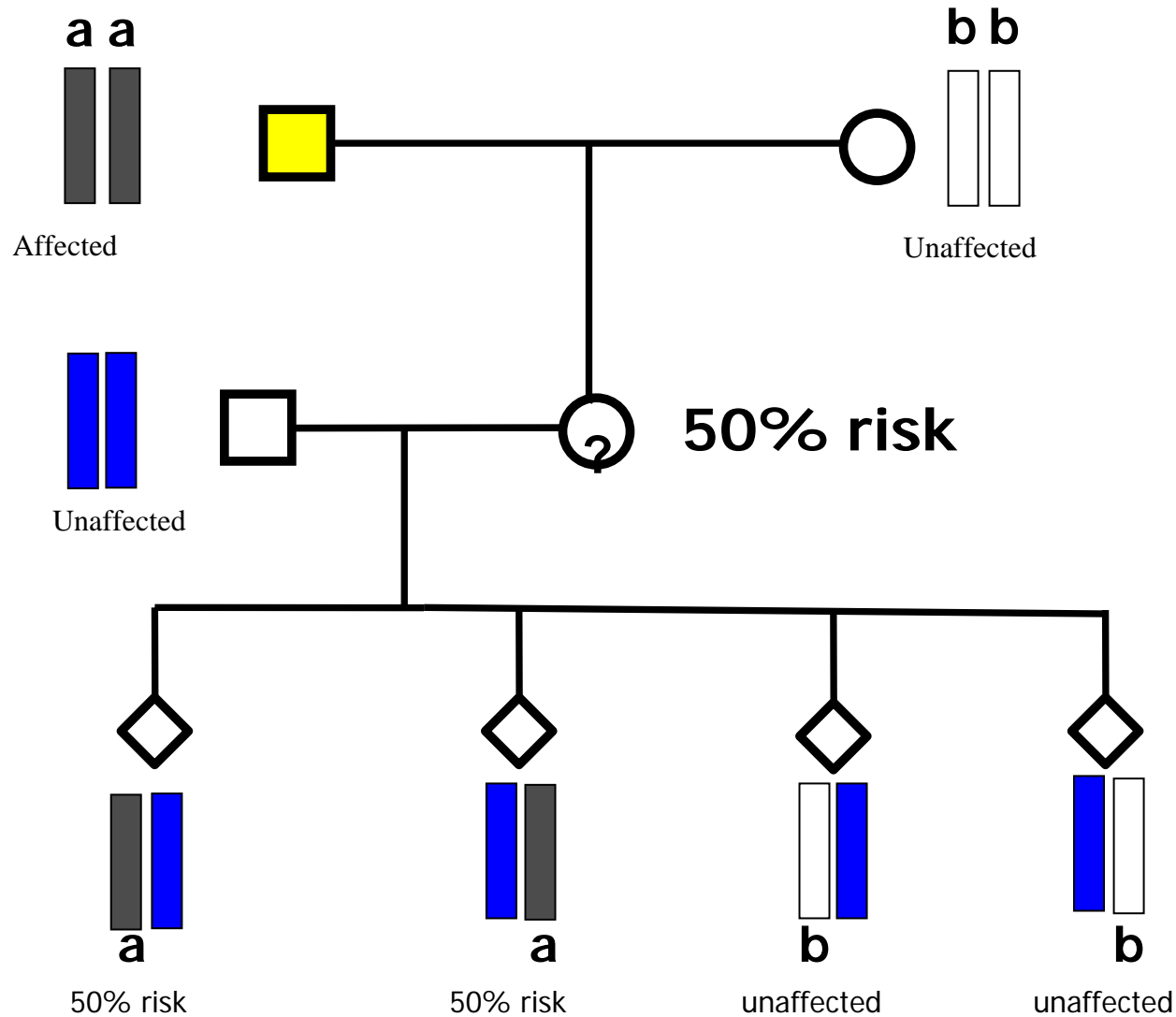
Don't wish to know

**Direct testing of
embryos for HD
expansion**

**Direct testing of
embryos for HD
expansion
BUT result NOT
to be revealed**

**Testing of embryos
using linkage to
grandparental alleles**

Exclusion of Huntington's using Linkage testing of Embryos



Other “late onset” disorders Suitable for PGD?

- **Muscular dystrophies**
- **Spinal Muscular Atrophy type II or III**
- **Familial cancer predisposition**

Predisposition and penetrance

Familial Adenomatous Polyposis Coli [100%]

Retinoblastoma [90%]

HNPCC [70-90%]

Breast malignancy (BRCA1, BRCA2) [50-80%]

Von Hippel Lindau disease [40%]

Hypercholesterolaemia ??

Short stature??

Test-tube baby warning

DON'T WORK WITH THIS MAN



Dr Edwards holds the first test tube baby

THE British Medical Association yesterday urged doctors not to co-operate with test-tube baby pioneer Dr Robert Edwards in experiments with human embryos.

The wait-and-see warning came after Dr Edwards revealed that he experimented on 17 "spare" embryos, just tiny dots consisting of a few cells.

He defended his "observations" as ethically acceptable and said the work could eventually help doctors understand abnormalities such as Down's syndrome.

The BMA is very much in favour of the treatment for otherwise infertile couples. But it is worried about reports...

By CLARE DOVER
Medical Reporter

ments which could involve freezing and cloning.

Dr Hayward said there could be advantages in the cure of disease and the prevention of abnormalities. There were also "great possibilities of disaster."

Dr Edwards and gynaecologist Mr Patrick Steptoe made the test-tube breakthrough with the birth of Louise Brown four years ago. They run a private clinic, Hourn Hall, near Cambridge.

Dr Edwards is a physiologist, and not a medical doctor. His province is the laboratory side of the work, fertilising and culturing the eggs.

He said: "In a few patients, three or four eggs are fertilised and two or three retained. The remaining embryos will grow for three or four days longer, and it must be ethically acceptable to observe them during this period with the patient's consent."

He added: "These embryos could be frozen, although we are not doing this work."

"We have observed 15 embryos aged five days and two up to four-days older. These observations have helped to ensure that the babies born in our work were fully normal, which has encouraged the introduction of similar work into many other clinics."

He agreed that ethical decisions must be taken before embryos are allowed to grow for longer periods in test tubes.

At the storm of protest grew last night, Mrs Nicola Scarbrick, of the anti-abortion group IFR said: "It seems that Dr Edwards is making human embryos in the laboratory and then throwing them away. He is playing God."

Dr Walter Hedgecock, a former BMA official and now scientific adviser to the Bishop of Norwich, said that helping women have test-tube babies was perfectly acceptable—but experimenting on spare human embryos was not.

"These are potential human beings. It is really like planting a baby down on a boat and doing experiments on it," he said.

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Embryo farmers: the children of Mengele

IT IS difficult to oppose medical research for we all have an interest in health, and in the knowledge which helps us to restore it. It may therefore seem as though opposing such research to increase medical knowledge is a benefit and everything done to impede it a harm, and such a view would be too simple.

In the extermination camp of Auschwitz, Dr Mengele carried out experiments on living people, in order to gain information useful to medical science. From the scientific point of view the experiments were a genuine contribution to our knowledge.

It could even be said that the long-term medical benefits of Dr Mengele's actions exceed the short-term costs to human suffering. Nevertheless, he should never have done what he did and people were right to condemn him as a criminal.

Why did Dr Mengele behave in this way? Not because he did not regard his victims as human. If they had not been human his experiments would have been quite welcome for scientists to discover medical facts about the human body, using methods which had been previously forbidden. His experiments required him to believe—and that propaganda denied—that Jews are normal examples of our species.



by ROGER SCRUTON

in it. There is only a small chance of survival for such an embryo and the operation, if carried out, involves multiple fertilisation, producing superfluous embryos which—being in excess of the sympathy of their scientific creator—are eventually washed down the sink.

What kind of attitude to human life does this imply? Are we really to accept that human beings can be created in this way and then disposed of when they do not answer to our purposes? If our sympathy for the infant really to override our natural revulsion towards the mass production and mass destruction of human beings?

Or consider embryo research. Medicine justifies this on a strictly utilitarian basis. Through such research, we shall learn how to avoid deformities, we shall make new discoveries that will arm us in the fight against cancer, Parkinson's disease and AIDS. The question, however, is not whether

there are benefits to be obtained from this research, but whether it should be permitted at all. Are we really entitled to treat the human embryo as we would the embryo of any other animal—as a piece of matter to be used for the purpose of those with power to exploit it? Does not the inevitability of the human adult extend to its infant predecessor and to the little dot of life from which it begins?

WHEN you ask such questions, you generally receive from the medical establishment nothing but the alibi of expediency. We are invited to distinguish the embryo from the "pre-embryo", and told that we do not really begin until the third week. This kind of casuistry fills us with indignation, and the worst, compromising where compromise is impossible.



Dr Mengele's criminal experiments

The Warnock report would allow the sale and possible use of human embryos, and research and experimentation on embryos up to a period of 14 days, with the stipulation that the victims of such research should then be destroyed. If such recommendations are followed, we shall have accepted for the first time in our history that human beings can be used for research and experimentation without their consent.

We shall also have involved a new crime: that of keeping one of those human beings alive after 14 days. It will become obligatory to kill members of our own species. Can we really avoid that? Consider research, however beneficial, justified by this change in attitude?

Whatever the rights and wrongs of abortion, nobody has ever suggested that there are any advantages of the unborn child that must be killed—or that it would be crime to let it die.

The fact is we are acquiring the habit of disposing of human embryos as we would see fit for the sake and selfish purpose of staying alive as long as possible.

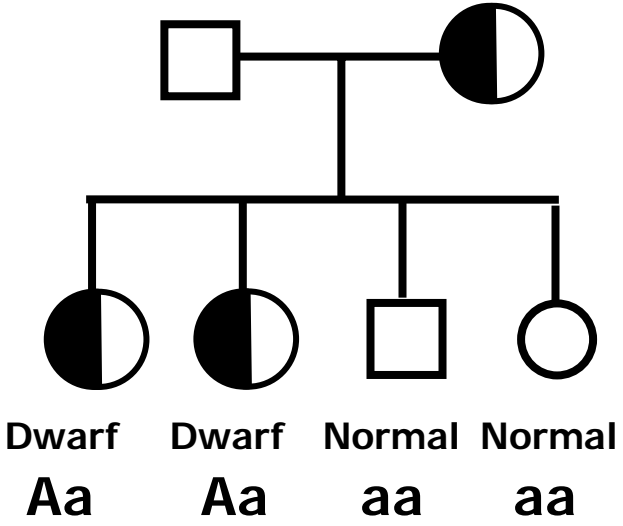
Embryo research in modern medicine, by shifting its sights from cure to prevention, tries to avert death of its prey. The result is a gradual genetic mutation of society and a sacrifice of future generations for the sake of those who will shortly be dead. This constitutes a sacrifice of the true moral order.

The idea of the sanctity of life is, at bottom, a device for encouraging sacrifice; it is the notion that human beings are made in the image and likeness of God and which causes them to deprive themselves of the sake of their children. That is the pattern of conduct upon which the human race depends: the sacrifice of the old for their offspring. Modern medicine, with its scheme of "options" and "choices", inevitably leads in the opposite direction: to the sacrifice of the younger generation for their parents.

This costs a new and sinister light on embryo farming for medical purposes. What is this if not the birth of human life in its youngest manifestation, so that those who should be preparing for the grave can postpone their day of reckoning? Embryo research is the cynicism of our scientific generation—the world's resources—eyes of human life itself—for the sake of our own bodily survival.

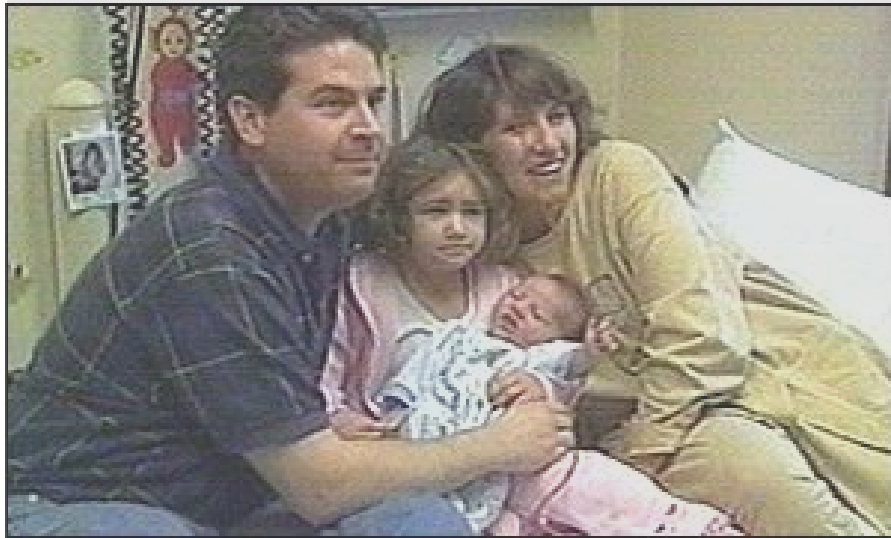
The author is Professor of Architecture at Brunel College, London.

Screening in vs screening out disorders?



Curing Sibling Genetic Disease PGD and HLA typing

Wednesday, 4 October, 2000, 07:37 GMT 08:37 UK
Baby created to save older sister



The Nash family have created medical history

- Fertile couple with **serious genetic risk** undergoes ICSI to produce embryos in vitro
- Embryos are biopsied and screened for genetic defect as well as HLA match to affected sibling chance
- Embryo (s) transferred to produce child who can be a bone marrow match for affected sibling

3:4 unaffected / carrier embryo
1:4 embryo HLA matches sibling
= 3:16 chance of both matching

Curing sibling non genetic disease - HLA typing embryos

- Fertile couple without substantial genetic risk undergoes ICSI to produce embryos in vitro
- Embryos are biopsied and screened for HLA match to affected sibling (1:4) chance
- Embryo (s) transferred to produce child who can be a bone marrow or tissue match for affected sibling

Thursday, 1 August, 2002, 17:35 GMT 18:35 UK
Couple closer to creating 'designer baby'



Charlie needs a transplant within 18 months

A couple are to get help from the United States so they can create a 'designer baby' to save the life of their seriously-ill son.

IVF undertaken and embryos created and biopsied to alleviate disease in a sibling – parent? – uncle or aunt? – good friend?

A child has a right to an open future



“Choosing between Possible Lives”

Rosamund Scott

Centre for Preimplantation Genetic Diagnosis