



## **Eugenics and medicalized reproduction Conceptual, historical, medical, and ethical considerations**

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From science to health

Inserm Ethics Committee

**“Embryo and  
Developmental  
Research”  
Working group**

**Eugenics and medicalized  
reproduction. Conceptual,  
historical, medical, and  
ethical considerations.**

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## Eugenics and medicalized reproduction

### Conceptual, historical, medical, and ethical considerations

Bernard Baertschi, Pierre Jouannet and the Embryo and Developmental Research group of the Inserm Ethics Committee

#### Abstract:

The classic eugenics of the late 19<sup>th</sup> century sought to improve the human race by relying on the coercive power of the state. This practice has been discredited, but it is sometimes argued that “liberal” or “private” eugenics has outlived it, particularly in the context of medically assisted reproduction (MAR). Indeed couples can resort to *in vitro* fertilization (IVF) when they wish to have a child who does not have certain serious genetic diseases in the name of reproductive freedom and the interest of the unborn child.

“Liberal” or “private” eugenics is currently the subject of much debate. The main arguments underlying the current thinking are as follows: (a) even if the aim (not having a child with a serious genetic disease) is laudable, not all means of achieving it are necessarily so; (b) by choosing which embryo(s) to transfer, a choice is made as to the people who deserve to exist; (c) there is a risk of applying arbitrary or even immoral selection criteria; (d) some MAR practices involve the transmission of genetic mutations or chromosomal abnormalities (dysgenics); (e) the practice of genetic testing with the aim of choosing embryos without genetic diseases expresses a stigmatizing attitude towards people with disabilities (expressivist argument); (f) couples and the medical institution have a moral duty not to transfer an embryo carrying a deleterious gene; (g) couples are under a great deal of pressure to undergo testing, a pressure that could undermine their autonomy and their ability to choose freely; (h) the good of the child, a cardinal ethical and legal consideration, could be threatened by “private” eugenics; and (i) an alternative to embryo selection could be germline gene therapy, which is currently prohibited.

Today, genetic testing and criteria can be used in a wide variety of ways when reproduction is medicalized. These may include genetic factors sought in gamete and embryo donors to avoid the transmission to the child of a genetic pathology when the risk is known; chromosomal analysis of embryos to avoid transferring into the uterus those that will not develop to term; a preimplantation diagnosis on the embryos to avoid transmitting to the offspring genetic characteristics of the future parents that are likely to seriously harm the health of the unborn child; selection of embryos on the basis of polygenic scores to detect those less at risk of developing a pathology after birth; and selection of the child’s sex without any medical indication.

Male sterility, for example, may be due to a chromosomal factor (Y-chromosome micro-deletion) or a genic factor (mutations of the *CFTR* gene or genes involved in spermatogenesis). When spermatozoa can be used in ICSI, sterility can be bypassed, but chromosomal or genic modifications can be transmitted to offspring and cause sterility in boys. If no spermatozoa are available, an *in vitro* correction of the defective gene by genomic engineering in germ cells could be considered for the treatment of male infertility.

As classical eugenics has been unanimously discredited, labeling a practice as eugenist is tantamount to condemning it. The law is currently doing the same. However, this was not always the case: before World War II, it was often viewed positively.

The notion of eugenics was therefore devised at a time when genetics, in the sense of determinism and the process of transmitting inheritable traits, was not yet understood. Nowadays, a return to “genetic determinism” or “genetic program” sometimes resurfaces, often simplistically or erroneously based on the most recent data from knowledge acquired in genetics.

The cumulative effect of couples’ decisions has some effect on the composition of future generations, albeit quantitatively minimal. However, there is no eugenist intention as such. A distinction must therefore be made between eugenics as a consequence and intentional eugenics. The first is not truly eugenics, so the term “eugenist” should be used only for interventions that promote the deliberate, intentional transmission of genetic traits or characteristics to offspring.

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## 1. Introduction

Over the past decade, discussions within the *Embryo and Developmental Research* working group of the INSERM Ethics Committee and the resulting Briefs<sup>1</sup> have been based on questions submitted by researchers and/or physicians working in the field of reproduction. This was not the case this time around but the topic of eugenics complemented the issues previously discussed by the group. The decision was made to rely primarily on scientific and medical considerations and not on legal, philosophical, or other aspects. To this end, we interviewed scientists and physicians working in the field, including outside the human species, without ignoring the point of view of specialists in human and social sciences.

Today, genetics is present in multiple aspects of biomedical research and practice across all stages of human life. We have chosen to address only issues relating to the period usually considered by the group, ranging from gametes to the implantation of the embryo in the uterus after *in vitro* conception. We have therefore addressed matters concerning the use of genetic analysis or tests conducted to choose or select either the gametes used for insemination or *in vitro* fertilization or the embryos intended to be transferred into the uterus as part of medically assisted reproduction (MAR) processes, when the MAR is intramarital or with a third-party donor and when recourse to MAR is motivated by a medical indication or not. As such, we have not addressed, except in passing, the issues raised by a genetic diagnosis conducted before natural reproduction (preconception testing) or those raised by the prenatal diagnosis conducted during the course of pregnancy. On the other hand, we have discussed the issues relating to the potential implementation of new technologies in the future, such as germline gene therapy.

The selection of a partner to start a family and have children can be motivated by many factors, foremost among which we find what is in the domain of attraction or emotion. However, many other criteria: whether cultural, social, economic, or otherwise, may occupy a more or less important place,.

Genetic criteria can also come into play when it comes to reproduction or carrying out a parental project. They can be *direct* or *indirect*, *individual* or *collective*. As such, when couples chose to terminate a pregnancy or even kill a child at birth to obtain offspring of the desired sex, the choice was made on the basis of sex-related morphological criteria but actually corresponded to genetic selection. When the *Lebensborns* breeding program brought Aryan women together with SS men to produce children who would form the “elite of the future,” the reference was above all “racial” and therefore indirectly genetic or supposedly so. At the beginning of the 20<sup>th</sup> century, in countries such as Sweden and the United States, forced sterilization programs were implemented for the mentally ill and prisoners to prevent the transmission of presumed genetic traits deemed harmful to society. Whether individual or collective, freely chosen or imposed by states or other social structures, these behaviors were

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1. They are available on the INSERM website: <https://www.inserm.fr/ethique/les-groupes-de-reflexion-thematique-du-comite-dethique/#embryon-et-d%C3%A9veloppement>.

considered eugenic or eugenist,<sup>2</sup> but *none were implemented using the tools of modern genetics*.

During the last 50 years, the genetic knowledge and tools have developed considerably. At the same time, the possibilities for medical intervention in human reproduction processes have increased. The combination of the two approaches, serving a variety of purposes, raises issues about their legitimacy, when they are used to carry out a parental project with the help of medicine and science.

We will begin by clarifying what is meant by “eugenics” and propose some conceptual distinctions (section 2) before elaborating on the historical and scientific aspects of the subject (sections 3 and 4). We will then present the various phases or procedures of MAR possibly involving genetic testing or criteria, including the case of male infertility since it is a good model for understanding the role of genetic criteria when reproduction is medicalized (section 5). Lastly, we will devote most of our discussion to the ethical issues raised by eugenics in the selection of gametes and embryos (section 6).

## 2. Conceptual considerations

### *a) Classical eugenics*

The word “eugenics” was coined by Francis Galton in 1883 (therefore before the principles of heredity were understood in terms of Mendelian laws) to refer to the “science” of improving the human race by acting on hereditary characteristics or those presumed as such.<sup>3</sup> In 1883, he defined it as “the science of improving stock, which is by no means confined to questions of judicious mating, but which, especially in the case of man, takes cognizance of all influences that tend in however remote a degree to give to the more suitable races [...] a better chance of prevailing [...] over the less suitable [...]” and clarified in 1904 that “it is the study of the agencies under social control that may improve or impair the racial qualities of future generations either physically or mental.”<sup>4</sup>

From the outset, eugenics was a movement based on “scientific” knowledge – erroneous, hence the quotation marks – with the aim of influencing the composition of the human species. The methods advocated and used were often coercive on the part of states that had adopted a eugenics policy in order to prevent “degenerate” individuals from procreating, assuming that characteristics deemed deleterious could be transmitted across generations. This was deliberate or intentional eugenics: humanity was faced with an “*attempt to influence the genetic endowment of future generations*,” according to Giulia Cavaliere.<sup>5</sup> In summary, it could be said that classical eugenics:

C1. Sought to act at the population level or even the species level (improve it or

2. We will use these two terms synonymously.

3. “The word *eugenics* was coined by the Englishman Francis Galton in 1883 (from the Greek *eugenès*, ‘wellborn’) to denote the ‘science’ of the biological improvement of the human kind” (M. Adams, *The Wellborn Science*, Oxford, OUP, 1990, p. 3).

4. Cited in D. Aubert-Marson, *Histoire de l’eugénisme*, Paris, Ellipses, 2010.

5. “Looking into the Shadow: the Eugenics Argument in Debates on Reproductive Technologies and Practices,” *Monash Bioethics Review*, vol. 36, 2018, p. 8.

stop its degeneration).

C2. Resorted to the coercive power of the state, professional institutions, or other bodies.

C3. Did not, therefore, recognize the reproductive freedom of individuals.

C4. Selected the progenitors, not the embryos.<sup>6</sup>

*b) Liberal or private eugenics*

Currently, most states no longer advocate a eugenics policy. They are even openly hostile to it. However, for many authors, eugenics has not disappeared and survives in the form of *liberal eugenics*: this new eugenics, as Diane Paul points out, is the result of a multitude of individual decisions and couples' requests for testing and screening and not a social policy designed with eugenics in mind.<sup>7</sup> Some couples who are carriers of serious genetic diseases want to avoid having children afflicted with them. Although fertile, they use *in vitro* fertilization (IVF) followed by a preimplantation genetic diagnosis (PGD) so that only unaffected embryos are transferred into the uterus, or they resort to MAR with a third-party donor.

As Jean Gayon explains: "Between the 'old' and the 'new' eugenics, there is a significant difference in the purpose of the practices. Pre-war eugenics was based on public programs to selectively improve the hereditary qualities of populations and thus aimed for long-term modification of the genetic makeup of a population (a particular 'race,' a particular nation, or even the entire human species). The new eugenics is based on the notion of reproductive autonomy of the woman (or couple) and is concerned with the immediate qualities of the individual progenitor and the ability of the parents to cope with disabilities."<sup>8</sup> For some, this is a sufficient reason not to talk about eugenics in this case: PGD and preventing of diseases due to modifications of mitochondrial DNA would be in the scope of good medical practice of preventing serious illness, not eugenics.<sup>9</sup>

There are other cases where infertile couples using IVF agree to have chromosomal tests performed on the embryos to increase their chances of having a child. In this case, though, we generally do not speak of eugenics.<sup>10</sup> In short, it could be said that liberal eugenics:

L1. Does not seek to act at the population or species level.

6. B. Baertschi, *De l'humain augmenté au posthumain*, Paris, Vrin, 2019, p. 162-163; see also CEI, *L'évaluation préimplantatoire de l'aptitude au développement embryonnaire (EPRADE)*, June 2021, p. 21, available at: <https://www.hal.inserm.fr/inserm-03268622v1/document>.

7. "The new eugenics will result from a multitude of voluntary decisions, or even demands for tests and screens, rather than from social policy designed with eugenic aims in view." ("Is Human Genetics Disguised Eugenics?," 1994, in D. Hull & M. Ruse, dir., *The Philosophy of Biology*, Oxford, OUP, 1998, p. 539). Jacques Testart had warned about the practice in 1986 in *L'Œuf transparent* (Paris, Champs-Flammarion, p. 131 sq), but not yet using the term "eugenics."

8. "L'eugénisme, hier et aujourd'hui," *Médecine/Science*, vol. 15, 1999, p. 4. The end of the quotation raises the controversial issue of how to deal with disability. It should also be noted that Jürgen Habermas defines liberal eugenics very broadly as "a practice that entrusts interventions into the genome of an embryo to the discretion of the parents" (*The Future of Human Nature*, Cambridge, Polity Press, 2003, p. 78), thus encompassing genetic engineering.

9. "Like PGD, preventing mitochondrial DNA disease falls within the good medical practice of preventing serious illness, not eugenics." (A. Murdoch, in M. Cook, "UK to Allow Research into Three-Parent Embryos," BBC, June 29, 2013, p. 14).

10. Cf. CEI, *Evaluation of PReimplantation embryo Aptitude for DEvelopment (EPRADE)*.



L2. Does not resort to the coercive power of the state, professional institutions, or other bodies.

L3. Recognizes, therefore, the reproductive freedom of individuals.

L4. Does not select the progenitors, but the gametes or the embryos.<sup>11</sup>

In its opinion on this topic, the French National Consultative Ethics Committee (CCNE) considers that one should not speak of “eugenics” here and that “the term ‘private eugenics’ contains a contradiction,”<sup>12</sup> firstly because the intention of the future parents is not to modify the composition of the human race or improve it – they simply want to have a healthy child – and secondly because eugenics is inextricably linked to a state policy. We can agree with this statement but unfortunately we will not prevent opponents of periconceptional genetic testing using the word “eugenics” to condemn it because, as we will say again, “eugenics” is a term with a very negative connotation. In an earlier opinion, the CCNE also used the term: “Individual eugenics or micro-eugenics or private eugenics or even liberal eugenics,” which it characterized as follows: “It corresponds to a phenomenon of selection where decisions are made at the individual or family level. One example is a couple’s decision to avoid the conception, implantation, or birth of a child carrying a genetic abnormality leading to a physical and/or mental disability.”<sup>13</sup>

### c) Positive and negative eugenics

When one is concerned about the “quality” of unborn children – which, it should be noted, is not usually the case when one chooses their gender – it can be done in two ways: either, in the case of classical eugenics, by encouraging “superior” individuals to procreate (abundantly) or by preventing “degenerate” individuals from having children (which is how it was expressed back then) or, in the case of liberal eugenics, by selecting embryos with particular qualities or discarding embryos carrying serious diseases. The first case refers to *positive eugenics*, and the second refers to *negative eugenics* (positive and negative have no connotation of value here). Laurence Perbal puts it this way about classic eugenics: “Eugenics studies and implements ways to improve the human race by seeking either to promote the appearance of certain traits (positive eugenics) or to eliminate hereditary pathologies (negative eugenics).”<sup>14</sup> In this sense, some medical practices can be considered negative eugenics – inevitably, according to Hallvard Lillehammer – and this will continue in the future.<sup>15</sup>

11. In L4, this involves the selection of the embryo to be implanted and the selection of the gamete and/or embryo donor.

12. “L’eugénisme: de quoi parle-t-on ?,” Opinion 138, 2021, p. 14.

13. “Avis sur les problèmes éthiques liés aux diagnostics anténatals : le diagnostic prénatal (DPN) et le diagnostic préimplantatoire (DPI),” Opinion 107, 2009, p. 12. In Belgium, the Ethics Advisory Committee (CCBB) also addressed the issue of eugenics in 2005 in its opinion 33 entitled *Opinion on somatic and germline gene modifications for therapeutic and/or improvement purposes*, and in Switzerland, the National Ethics Commission (CNE) addressed it in 2005 and 2007 in two statements of position (10 and 14) on *preimplantation diagnosis*.

14. Art. “Eugénisme,” in G. Hottois & al., eds, *Encyclopédie du transhumanisme*, 2015, p. 278; see also Jean-Noël Missa, “L’individu n’est rien, l’espèce est tout,” in J.-N. Missa & C. Susanne, eds, *De l’eugénisme d’État à l’eugénisme privé*, Brussels, De Boeck, 1999, p. 14.

15. H. Lillehammer, “From Genes to Eugenics,” *Studies in History and Philosophy of Biological and Biomedical Sciences*, 2001, vol. 32/4, p. 597.

Another way of describing this opposition is to speak of *selection* of a characteristic for positive eugenics and *counter-selection* for negative eugenics.

*d) Eugenist intention and effect*

Diane Paul's proposed definition of new eugenics speaks of "results": the multiple individual decisions regarding the selection of the embryo to be transferred into the mother's uterus have, when added together, a certain effect on the composition of future generations, albeit quantitatively minimal.<sup>16</sup> This is without any eugenist *intention* on the part of couples, since they only want to have a healthy child. Some definitions of eugenics describe it solely in terms of effects or consequences, eliminating the intentional factor; this can be referred to as *eugenics as a consequence*. Any practice that, having an impact on who will be born and who will not, therefore has an *effect* on the composition of future generations is eugenist or eugenic in this sense: "Adopting eugenic practices means determining who should or should not exist, i.e. in this case, come into existence as a result of their birth."<sup>17</sup> Classical eugenics is eugenist in intention and consequence; liberal eugenics is generally eugenist only in consequence or result, in the sense that the underlying intention concerns only the unborn child, an individual. Sometimes the intention is more difficult to characterize, such as when people who consider themselves "high potential" seek partners in the same category to have offspring with the same "qualities" as the parents.<sup>18</sup> This is true of any approach to reproduction, whether natural or resorting to MAR technologies.

When we interviewed Françoise Baylis, she told us that the effects are what matter and that she therefore considers liberal eugenics to indeed be eugenics. Simply, it does not act "*en masse*", but individually: the composition of the human race is ultimately changed, but it is through the selection of one individual at a time. It is then the aggregate results of individual decisions that change the composition of future generations. This is what can be considered liberal eugenics.

In ethical debates, this opposition is often encountered between positions that favor results (consequentialist positions) and those that favor intentions (non-consequentialist positions). However, it is impossible to leave intentions completely aside, and the consequentialists themselves distinguish between intended and unintended, foreseen and unforeseen effects. So, not every bad state of affairs has to be morally bad; for it to be so, it must have been brought about by human action (of an individual or a group) who actively wanted it or at least who considered it to be a genuinely possible consequence of the action undertaken.<sup>19</sup> It is therefore doubtful whether it makes sense to speak of eugenics if no intentional element is present, unless it is considered that there is no need to assess eugenics morally, which would be contrary to

16. This is not, strictly speaking, the case when the embryo is selected to minimize the risk of miscarriage, because a trait of the future person is not selected there.

17. J.-Y. Goffi, "La notion de vie préjudiciable et l'eugénisme," in J.-N. Missa & C. Susanne, *op. cit.*, 1999, p. 73.

18. As Jean-Pierre Siffroi pointed out during his hearing.

19. For many authors, intention lies at the heart of our conception of morality: it is the source of the morality or immorality of our actions (B. Baertschi, "Neuroethics: A Renewed View of Morality? Intentions and the Moral Point of View," in É. Racine & J. Aspler, eds., *Debates About Neuroethics*, Springer, 2017, p. 109-127).

the way this term is currently used.

There is also a very good reason not to speak of eugenics for eugenics as a consequence that would be devoid of any intentional component. This is because, as Jonathan Glover points out, any political decision with a social effect inevitably changes the composition of future generations: “It is hard to think of any social change which does not make some difference to who survives or who is born. [...] [E]ugenic policies [aim to alter] breeding patterns or patterns of survival of people with different genes. [...] [T]he difference is only that the genetic impact is intended.”<sup>20</sup> If we were to ignore intention, any policy decision affecting reproduction (think of family allowances or China’s one-child policy) would have to be considered eugenicist, which borders on the absurd.

Consequently and in short, *any intervention that intentionally promotes or prevents the transmission of genetic traits or characteristics to offspring* by selecting or counter-selecting these traits could be said to be *eugenic or eugenist*.

Finally, it is relevant to distinguish between practices that have significant consequences on offspring<sup>21</sup> and others that have few, such as in the case of rare genetic diseases where few embryos are involved. On the one hand, there is what is statistical or quantitative and, on the other, what is symbolic. What is quantitatively tiny, though, remains symbolically important. We will see this later in the case of cystic fibrosis, a disease that makes men sterile, but for which one of the gene mutations responsible is transmitted through the use of ICSI.

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20. *What Sort of People Should There Be?*, London, Penguin Books, 1984, p. 27.

21. Some involve the transmission of harmful variants responsible for serious diseases, such as cystic fibrosis, while others do not, such as trisomy 21, which has virtually no risk of transmission to subsequent generations.

- The classical eugenics of the late 19<sup>th</sup> century sought to improve the human race by relying on the coercive power of the state.
- This practice has been discredited, but it is sometimes argued that “liberal” or “private” eugenics has outlived it, particularly in the context of MAR.
- It is in the name of reproductive freedom that couples can ask for IVF when they wish to have a child who does not have certain serious genetic diseases.
- Discarding embryos carrying factors responsible for serious diseases is negative eugenics, while wanting children with desired qualities is positive eugenics.
- The cumulative effect of couples’ decisions has some effect on the composition of future generations, albeit quantitatively minimal.
- There is often no eugenist intention as such. A distinction must therefore be made between eugenics as a consequence and intentional eugenics.
- The first is not truly eugenics, so the term “eugenist” should be used only for interventions that promote the deliberate transmission of genetic traits or characteristics to offspring.

### 3. Historical considerations

#### *a) Current negative view*

Currently, labeling a practice as eugenic is tantamount to condemning it: “The word is now so loathed that simply describing an idea or practice as ‘eugenist’ is often tantamount to condemning it.”<sup>22</sup> The law itself attests to this, referring to “Crimes of eugenics and reproductive cloning” (Article 214-1 of the French Criminal Code) and specifying that “any eugenic practice aimed at organizing the selection of persons is prohibited” (Article 16-4 of the French Civil Code). “Eugenist” is thus an epithet with a very negative connotation; it is the equivalent of a red flag (like “contrary to human dignity or contrary to human rights, ...”), and as with any flag of this type, there is a risk that it masks a lack of arguments: when someone has run out of arguments but is unwilling or unable to agree with their opponent, it is not uncommon for them to wave such a red flag.

However, there are very good reasons for condemning classical eugenics, so it is hardly surprising that opponents of certain MAR practices label them as eugenist to cast the same stigma on them without any need to argue. In this note, we examine the arguments, not the polemical uses.

It should also be noted that negative eugenic screening programs remain encouraged by some countries and are viewed positively by many authors: Geoffrey Roche points out that, using PGD and preconception screening, the Christian community of Cyprus has successfully eradicated thalassemia and the Ashkenazi Jewish community has largely eradicated Tay-Sachs disease. He goes on to mention that for the advocates of these programs, bringing children with normal abilities into the world is morally laudable, even morally required, so much so that not using the available technologies

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22. J. Gayon, *art. cit.*, p. 1.

would be immoral.<sup>23</sup>

Positive eugenics is also not condemned in all its forms. PGD with HLA typing has been authorized in France when it involves “helping a seriously ill child by transplanting stem cells from the cord blood of his or her future brother (sister).”<sup>24</sup> This is the situation that corresponds to what has been called “savior sibling” or, more positively, the “double hope child.” Here, an embryo with a specific “quality” is selected.

A much more problematic type of positive eugenics is explicitly endorsed by certain pronatalist groups in the United States who promote the selection of partners with a high IQ and embryos with “high potential,” further placing hopes in genetic engineering to improve the human race by modifying its genome in a transmissible way (genetic enhancement).<sup>25</sup>

*b) Formerly positive view*

Eugenics did not always have a negative connotation. Before World War II, it was often viewed positively, even if it was sometimes in rather abrupt terms, as in the writings of Georges Hardy (pseudonym of Gabriel Giroud): “One question that is now being discussed openly and frankly is how to improve the species. Two methods lead to the goal, whose action must be parallel. One is to prevent all defective births, any reproduction of degenerates, through sterilization. The other, through hygiene measures, aims to preserve and improve the physical and mental health of individuals. [...] Such precautions are being taken in America [...] and it is desirable that they be taken everywhere.”<sup>26</sup> Since that time, our values have changed: the submission of the individual to social and collective goals became morally problematic in a fairly short period. Jean-Noël Missa also observes that “in the first decades of the ongoing century, there was little to distinguish eugenics from the new human genetics. Most of the great geneticists are also eugenicist.”<sup>27</sup>

- As classic eugenics has been unanimously discredited, labeling a practice as eugenicist is equivalent to condemning it. The French law is currently doing the same.
- This was not always the case: before World War II, it was often viewed positively.

23. “Using PGD, the Christian community of Cyprus has succeeded in eradicating thalassemia; likewise, the Ashkenazi Jewish community [...] has largely eradicated Tay-Sachs disease. For advocates of such programs, bringing optimally enabled children into the world is morally admirable, or even morally required [...]. As such, *not* using available technology is, arguably, immoral.” (G. Roche, “Closing One’s Eyes to Danger: Against the Disability Rights Critique of Genetic Screening,” in K. Ishihara & S. Majima, eds, *Applied Ethics*, 2008, p. 106).

24. H. Chneiweiss, “Sur les sentiers escarpés des montagnes de bioéthique: aux confins de l’eugénisme,” *Médecine/Science*, 2003, vol. 19/5, p. 635. See also CCNE, “Réflexion éthique sur l’évolution des tests génétiques liée au séquençage de l’ADN humain à très haut débit,” Opinion 124, 2016, p. 69-70.

25. P. Myers, “Pro-natalists, long-termists, the Church of the Future Police... what a nightmare,” *Pharyngula*, January 3, 2023, available at: <https://freethoughtblogs.com/pharyngula/2023/01/03/pro-natalists-long-termists-the-church-of-the-future-police-what-a-nightmare/>

26. G. Hardy, *L’avortement*, Paris, éd. du Malthusien, 1913, p. 158-159.

27. J.-N. Missa, “L’individu n’est rien, l’espèce est tout: analyse historique de l’évolution de l’eugénisme au XX<sup>e</sup> siècle”, in J.-N. Missa and C. Susanne, eds, *De l’eugénisme d’État à l’eugénisme privé*, Bruxelles, De

#### 4. Scientific considerations

The notion of eugenics was devised at a time when genetics, in the sense of determinism and the process of transmitting inheritable traits, was not yet understood. However, this approach, which was intended to be scientific, was based on the underlying assumption that the targeted traits were inheritable or characteristics of a population and that counter-selection was possible by excluding people from reproduction (negative eugenics) or, conversely, by promoting others (positive eugenics).

The genetic determinism of phenotypes presents a continuous range from strictly Mendelian characteristics (a single gene is responsible for the variation of the characteristic) to polygenic traits (many genes have more or less significant effects on the characteristic). In addition, for certain phenotypes, an environmental component, alone or in interaction with the genetic component, can play an important role. Height, for example, is a characteristic with high heritability (the transmissible part of the characteristic), but this genetic component involves a very large number of genes, each with small effects.<sup>28</sup> Variants of these genes may differ from one population to another, with complex interactions between them (epistasis). However, environmental factors, such as nutrition or health, can also influence growth. Height has thus increased significantly in some human populations over the last century, under the effect of environmental changes, without evidence of significant genetic changes at the same time.<sup>29</sup>

However, in conjunction with advances in genetic and genomic knowledge of human populations, a return to “genetic determinism” or “genetic program” sometimes resurfaces.<sup>30</sup> Applied to complex and sometimes questionable characteristics, this approach is similar to that of early eugenics.

Numerous genome-wide association studies (GWAS) have been conducted to identify genetic variations that could explain complex and highly varied traits, such as athletic performance, education level, psychiatric illness, religiousness, violence, delinquency, smoking or other drug use, and food preferences.<sup>31</sup> Currently, the UK Biobank project<sup>32</sup>, whose main aim is to gain a better understanding of the genetic basis of the most common diseases, also includes an ambitious program to link genetic data with a very wide range of other individual traits. Often, the phenotypes analyzed in these studies are complex and poorly defined and do not necessarily take into account stratification or confounding factors such as population or socio-economic characteristics. In addition, the underlying statistical models take very little account of epistasis (interactions between genes) or pleiotropic effects (on other traits). Lastly, there is often confusion between the statistical robustness of the genetic association between a trait and a gene (the significance) and the proportion of variation explained by this

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Boeck, 1999, p. 11.

28. L. Yengo & al., “A saturated map of common genetic variants associated with human height,” *Nature*, 2022, vol. 610, p. 704-712.

29. NCD Risk Factor Collaboration, (NCD-RisC), “A century of trends in adult human height,” *eLife*, 2016, vol. 5, e13410.

30. S. Foucart, “L’inquiétant retour du gène roi,” *Le Monde*, January 21, 2023, p. 28-29.

31. N. R. Yaseen & al., “Genetics of vegetarianism: A genome-wide association study,” *PLoS One*, 2023, vol. 18, e0291305.

32. <http://www.ukbiobank.ac.uk/>

gene, which may be very small. Despite all these reservations, the results of these studies can be used to calculate a polygenic score of a given characteristic from a person's genome or an embryo.

For example, the GWAS conducted on IQ, a highly controversial phenotypic "characteristic" that is supposed to measure intelligence on models and populations and with different methods, often have discordant results, which does not prevent them from being highly publicized. Critics of these approaches point to their many weaknesses.<sup>33</sup> Moreover, the complexity of our bodies does not always make it easy to identify possible correlations between different phenotypic traits. One study, for example, found a statistical correlation between a high IQ (or high education level) and the risk of developing Parkinson's disease.<sup>34</sup> In addition to the ethical issues raised by calculating a polygenic score for complex characteristics, this approach is particularly likely to be ineffective and could even unintentionally select genetic variants with potentially adverse effects on other traits.

Lastly, these genomic studies are conducted mainly in very small subsets of populations that do not represent the global diversity of genetic structures of complex characteristics. The results obtained for one population are therefore not necessarily interpretable or usable for another. This is an important ethical issue for research into the genetic components of complex diseases in populations underrepresented in genomic data. To assume that genetic association results based on large cohorts should lead to universal results would be to underestimate the role of the environmental and cultural components of certain traits and to disregard the different genetic structures between populations. As a caricatural example on this subject and for a trivial phenotype, a recent preprint (article not yet peer-reviewed in november 2023) compared the genetic associations and correlations identified for coffee consumption between two very large cohorts in the United States (23andMe) and the United Kingdom (UK Biobank), and the observed genomic associations were almost entirely different between these two cohorts, despite the fact that the studied populations have a largely common ancestry.<sup>35</sup>

- The notion of eugenics was devised at a time when genetics, in the sense of determinism and the process of transmitting inheritable traits, was not yet understood.
- In conjunction with advances in genetic and genomic knowledge about human populations, a return to "genetic determinism" or "genetic program" sometimes resurfaces.

33. K. Richardson, "GWAS and cognitive abilities: Why correlations are inevitable and meaningless. GWA studies to identify genetic factors for educational achievements largely ignore underlying social structures and dynamics," *EMBO Report*, 2017, vol. 18, p. 1279-1283.

34. C. Fardell & al., "High IQ in Early Adulthood Is Associated with Parkinson's Disease," *Journal of Parkinson Disease*, 2020, vol. 10, p. 1649-1656.

35. H. Thorpe & al., "Genome-Wide Association Studies of Coffee Intake in UK/US Participants of European Ancestry Uncover Gene-Cohort Influences," *medRxiv*, 09.09.202, <https://doi.org/10.1101/2023.09.09.23295284>.

## 5. Medical considerations

Since it has become possible to intervene medically in reproduction, combining eventually more or less sophisticated genetic tests, issues relating to the deliberate transmission of genetic traits or characteristics to offspring have taken on a new dimension, sometimes leading to the suspicion that MAR is promoting “new eugenics” or being at “eugenic risk,” without it being clear how the exact nature of the acts in question and their effects on offspring justify these qualifiers.

After briefly reviewing the various types of MAR and the situations involved, we will discuss the issues raised by male infertility management in more detail. The measures implemented to help infertile men become fathers are an interesting and a rarely examined model for discussing how genetic criteria are taken into account or not in MAR procedures, their consequences, and the ethical issues they raise.

### 5.1 The various types of MAR involving genetic testing and/or criteria

When reproduction is medicalized, the use of genetic testing and criteria can occur in a wide variety of ways, whether depending on the type of MAR performed, the intentions, or the consequences. It can be performed on people, gametes, or embryos.

In the case of third-party MAR (TMAR), the donors' spermatozoa, oocytes, or embryos used to enable a person or couple to realize their parental project are not chosen at random. In most centers, the choice is made on the basis of phenotypic and genetic criteria of donors and recipients. In commercial banks, where the choice can be made directly by recipients, sociological, cultural, and financial criteria can be added. In the United States, for example, the oocytes of a white donor studying at Harvard cost much more than those donated by an African-American cashier in a supermarket.

In France, the CECOS have developed a gamete selection strategy that takes into account the genetic risk for the health of children.<sup>36</sup> In practice, it is based on the results of a karyotype and the collection of family data from donors, possibly supplemented by specific genetic tests. The aim is to assess the risk of transmission of a disease to the child. At the end of this assessment, either a major risk is identified, and the donor gametes and/or embryos are excluded from donation, or no risk is identified, and their gametes and/or embryos can be used for all recipient women and couples. When a relative risk is identified (multifactorial diseases), the donated gametes are not used in recipients with the same risk factor, which means that a genetic assessment is also conducted in them. This strategy was confirmed in the good practice guide published by the French Ministry of Health: “When data from the medical history and the clinical examination reveal a relative risk factor, care is taken not to allocate the donor’s gametes to a couple whose recipient presents the same risk factor” (GBEA AMP Order of August 3, 2010).

When IVF or ICSI is performed on infertile individuals, it is not impossible for

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36. P. Jalbert, C. Leonard, J. Selva & G. David, “Genetic aspects of artificial insemination with donor semen: the French CECOS Federation guidelines,” *American Journal of Medical Genetics*, 1989, vol. 33, p. 269-275.



chromosomal or genic alterations to be transmitted to the child and therefore potentially to subsequent generations. This is particularly the case when sterility is due to a genetic factor, as we will see. In addition, a chromosomal analysis of embryos is sometimes suggested in order to give priority to transferring those without aneuploidy. This procedure, which aims to increase the chances of carrying a pregnancy to term, is used in many countries. Its usefulness is currently being evaluated by a multicenter protocol in France that was the subject of a previous IEC brief.<sup>37</sup>

Analysis of embryos may not be limited to identifying markers indicating an inability to develop *in utero* but may aim to select, through a more or less extensive analysis of the genome, embryos that would be less at risk of developing a pathology after birth. With this in mind, US commercial companies offer to search for mutations and variants of genes enabling them to establish polygenic scores to select the embryos least at risk.<sup>38</sup> The ability of this approach to achieve the desired goal has not been scientifically validated and remains widely debated.<sup>39</sup>

MAR is not always done to help infertile people carry out a parental project that they cannot achieve naturally. It can also be requested by fertile people who wish to avoid transmitting genetic characteristics that could seriously harm their child. Future parents can either ask for MAR using donated gametes or, when possible, undergo IVF followed by an analysis of the embryos to look for chromosomal or gene alteration (PGD) of which the future parents are carriers and transfer into the uterus only embryos that are free of the genetic disease.

MAR can also be used for people who are not infertile or at risk of transmitting a pathology to their child but want to choose the sex of their child. Various techniques have been proposed for sorting -spermatozoa carrying X or Y chromosome, but the effectiveness of the procedure in producing a child of the desired sex has not really been demonstrated when the selected spermatozoa are inseminated into the woman.<sup>40</sup> On the other hand, the goal can be achieved much more reliably when the chromosomal sex is determined on the embryo before it is transferred into the uterus. A survey conducted in 2017 in the US showed that more than 70% of MAR centers in the country agreed to perform this sex selection method at the request of couples, including outside any medical indication. However, this type of MAR is a controversial subject in the United States.<sup>41</sup>

Lastly, the extraordinary advances in gene engineering technologies in recent years have led to discussions on their use on embryos and germ cells. However, this prospect cannot be envisaged in humans until the efficacy and safety of the procedures

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37. *Evaluation of Preimplantation embryo Aptitude for DEvelopment (EPRADE)*, August 2021.

38. R. Pells, "Genetic Screening Now Lets Parents Pick the Healthiest Embryos," *Wired*, 2022.

39. F. Forzano O. Antonova, A. Clarke & al., "The use of polygenic risk scores in preimplantation genetic testing: an unproven, unethical practice," *European Journal of Human Genetics*, 2022, vol. 30/5, p. 493-495, and M. Kozlov, "The controversial embryo tests that promise a healthier baby," *Nature*, 2022, vol. 609, p. 668-671.

40. A. Botchan, R. Hauser, R. Gamzu & al., "Sperm separation for gender preference: methods and efficacy," *Journal of Andrology*, 1997, vol. 18/2, p. 107-108.

41. Ethics Committee of the American Society for Reproductive Medicine, "Use of reproductive technology for sex selection for nonmedical reasons: an Ethics Committee opinion," *Fertility and Sterility*, 2022, vol. 117/4, p. 720-726.

have been validated. This led to the unanimous condemnation of a Chinese researcher when he announced in 2018 that he was responsible for the birth of two children after a gene had been modified in them at the embryonic stage. However, any possibility of editing the germline genome in human clinics in the future has not been ruled out from a medical and scientific perspective.<sup>42</sup>

Genetic testing and criteria can be used in a wide variety of ways when reproduction is medicalized:

- In the case of third-party MAR, the donors' gametes and embryos can be chosen in order to avoid as much as possible the transmission of a genetic pathology to the child when the risk is known.
- When IVF or ICSI is performed for infertile individuals, chromosomal analysis of embryos may be performed to avoid transferring those that will not develop to term into the uterus.
- IVF followed by an analysis of the embryo prior to its transfer can also be undertaken by fertile individuals who wish to avoid transmitting to their offspring genetic characteristics of which they are carriers that are likely to seriously harm the health of the child.
- Commercial companies sometimes propose selecting embryos based on a more or less extensive genome analysis to detect those that are less at risk of developing a pathology after birth. This approach, which has not been scientifically validated, remains widely discussed.
- IVF followed by chromosomal analysis of embryos can be performed, without any medical indication, in people who wish to choose the sex of their child, which is a relatively common practice in the United States.

## 5.2 A model: male infertility

### a) *Transmission of various paternal genetic and/or pathological traits*

#### *Chromosomes*

Men who are carriers of Robertsonian<sup>43</sup> or reciprocal<sup>44</sup> translocations may have more or less marked alterations in spermatogenesis. They can sometimes conceive naturally. However, there is a risk that the sperm may carry a chromosomal imbalance that could be transmitted to the embryo and will be a source of major physical or mental pathologies in the child.<sup>45</sup> This situation is one of those in which a PGD can be

42. G. Q. Daley, R. Lovell-Badge & J. Steffann, "After the Storm – A Responsible Path for Genome Editing," *New England Journal of Medicine*, 2019, vol. 380/10, p. 897-899, and R. Lovell-Badge, "CRISPR babies: a view from the centre of the storm," *Development*, 2019, vol. 146, dev175778.

43. Robertsonian translocation is characterized by the fusion of two acrocentric chromosomes (13,14,15,21,22). Its frequency is around 1 in 1,000 in the population. The individuals involved are in good health, but their gametes carry chromosomal modifications that could lead to an unbalanced chromosomal abnormality in the offspring.

44. Reciprocal translocation is characterized by the reciprocal exchange of segments between two non-homologous chromosomes. It can also cause significant pathological congenital abnormalities in the offspring, especially if it is unbalanced.

45. R. H. Martin, "Cytogenetic determinants of male fertility," *Human Reproduction Update*, 2008, vol. 14/4, p. 379-390.

performed in France, particularly when male infertility requires the use of ICSI. The genetic tests performed are a karyotype in men and a targeted analysis of chromosomes by FISH in embryos produced by IVF/ICSI followed by non-transfer of the affected embryos.

Most aneuploidies in adult men involve sex chromosomes. The XXY aneuploidy responsible for Klinefelter syndrome is the most common and is accompanied by a major spermatogenesis defect. This defect is rarely a total defect, and it is often possible to perform ICSI with spermatozoa taken from the semen or surgically in the genital tract or testes. Children born after ICSI generally do not carry their father's aneuploidy, which is explained by the fact that only euploid spermatogonia would be able to achieve complete spermatogenesis. However, several studies have shown that a high proportion of embryos obtained in these circumstances were carriers of gonosomal and/or autosomal abnormalities.<sup>46</sup> The possibility of then performing a PGD is an open question.<sup>47</sup>

Male sterility may be due to a more or less extensive Y-chromosome microdeletion. Indeed functional spermatozoa cannot be produced in the absence of the genes controlling spermatogenesis. In some cases, it is nevertheless possible to collect spermatozoa to perform ICSI, which may lead to the formation of embryos and the birth of children. If the child is a boy, he will carry his father's Y-chromosome microdeletion, which may be even more extensive.<sup>48</sup> This is therefore a case where the vertical transmission of a chromosomal abnormality that was naturally impossible becomes a reality thanks to MAR. This indication for ICSI is commonplace and performed in most countries in the world.

### Genes

A few decades ago, most people with cystic fibrosis did not reach adulthood. Thanks to the considerable progress made in their medical care and the possibility of lung transplantation, their life expectancy has increased significantly. Today, many patients want to become parents, but men with cystic fibrosis are naturally sterile. The dysfunction of the *CFTR* protein disrupts the development of the genital tract between the head of the epididymis and the urethra. The spermatozoa produced by the testes cannot reach the sperm at the moment of ejaculation, hence azoospermia and sterility due to the bilateral absence of vas deferens (BAVD).<sup>49</sup>

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46. C. Staessen, H. Tournaye, E. Van Assche et al., "PGD in 47,XXY Klinefelter's syndrome patients," *Human Reproduction Update*, 2003, vol. 9/4, p. 319-330 and S. Kahraman, N. Findikli, H. Berkil et al., "Results of preimplantation genetic diagnosis in patients with Klinefelter's syndrome," *Reproductive Biomedicine Online*, 2003, vol. 7/3, p. 346-352.

47. C. Krausz & F. Cioppi, "Genetic Factors of Non-Obstructive Azoospermia: Consequences on Patients' and Offspring Health," *Journal of Clinical Medicine*, 2021, vol. 10/17, p. 4009. See also P. Jouannet, O. Claris & Y. Le Bouc, "Santé à moyen et à long terme des enfants conçus par fécondation in vitro (FIV)," *Bulletin de l'Académie Nationale de Médecine*, 2023, vol. 207, p. 695-705.

48. C. Y. Deng, Z. Zhang, W. H. Tang & H. Jiang, "Microdeletions and vertical transmission of the Y-chromosome azoospermia factor region," *Asian Journal of Andrology*, 2023, vol. 25/1, p. 5-12.

49. E. Bieth, S. M. Hamdi & R. Mieuisset, "Genetics of the congenital absence of the vas deferens," *Human Genetics*, 2021, vol. 140/1, p. 59-76.

Men with cystic fibrosis may be homozygous for one of the most harmful mutations in the *CFTR* gene, such as deletion  $\Delta F508$ , but there may be a combination of two different mutations on both alleles, both involved in cystic fibrosis.

Other sterile patients have BAVD without symptoms of cystic fibrosis; in general, they have a severe *CFTR* mutation on one allele and a less severe mutation such as *IVS8-5T* on the other allele. Lastly, in some sterile patients with BAVD, no mutations in the *CFTR* gene are found, but others have been identified as mutations in the X-linked *ADGRG2* gene.<sup>50</sup>

The same sterility can therefore be due to a wide variety of genotypes.

From a clinical point of view, how can we intervene to allow these men's fertility to express itself? In general, it is possible to collect a good number of spermatozoa upstream of the obstacle, as the testicular function is not impaired or only slightly so. However, these spermatozoa cannot lead to the formation of embryos, either by artificial insemination or by conventional *in vitro* fertilization. They lack the molecular equipment acquired during transit through the epididymis to be able to interact with the oocyte and fertilize it. Everything has changed since the development of ICSI. Micro-injected into the oocyte, the spermatozoon makes it possible to obtain an embryo and the birth of a child. However, there is a risk that the child may have cystic fibrosis if the woman also carries a heterozygous mutation in the *CFTR* gene. This is why a search for mutations is undertaken in her before ICSI, and a PGD can be conducted if necessary.

This type of ICSI is performed in most countries in the world. Here again, this is a situation where gene mutations (alterations/modifications) are inevitably and knowingly transmitted to the next generation through MAR when this is naturally impossible. Hence the symbolic weight of these cases, even if they remain rare.

*b) Reproduction and/or restoration of fertility in cases of gene-induced spermatogenesis deficiency*

When a few spermatozoa can be recovered from the semen, genital ducts, or testes, ICSI may be considered to help infertile men become fathers. However, this is not always possible, either in the total absence of spermatozoa or because all the produced spermatozoa have characteristics incompatible with the formation and/or development of the embryo.

Genome analysis of infertile men has developed considerably over the last thirty years, and more than 120 genes more or less strongly associated with the male infertility phenotype have been identified.<sup>51</sup> The responsibility of some of them, such as *STAG3*, *SYCP2*, and *TEX11*, whose mutations block meiosis, has been confirmed in animal models and in several cohorts of infertile men.<sup>52</sup> Other genes are involved in qualitative alterations in spermatogenesis, such as *AURKC*, whose mutation results in the production of spermatozoa that are all tetraploid, or *DNAH1*, whose dysfunction

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50. *Ibid.*

51. B. J. Houston, A. Riera-Escamilla, M. J. Wyrwoll & al., "A systematic review of the validated monogenic causes of human male infertility: 2020 update and a discussion of emerging gene-disease relationships," *Human Reproduction Update*, 2021, vol. 28/1, p. 15-29.

52. *Ibid.*

is responsible for multiple flagellar abnormalities.<sup>53</sup> The incidence of this monogenic sterility is very low but tends to increase in certain regions of the world because of inbreeding.<sup>54</sup>

When functional spermatozoa are available, ICSI may be considered. Otherwise, the only options available to these sterile men to become fathers are adoption or a partner's MAR performed with a donor's spermatozoa.

Insofar as the cause of sterility is monogenic, a correction of the defective gene in the germ cells could be a possible treatment for male infertility.<sup>55</sup> Cell lines could be formed *in vitro* from spermatogonia taken from the testes. The defective gene could be corrected using a CRISPR-Cas9-type technique. Spermatogenesis could then be restored *in vivo* or *in vitro* from these corrected gonads to produce functional spermatozoa.

This approach, which is similar to that used for blood cells, would have the advantage of testing the safety of genome editing on germ cells *in vitro* before their use. The concept has already been successfully demonstrated in mice,<sup>56</sup> including by correcting a mutation in a gene that causes meiotic blockade in humans.<sup>57</sup>

From a clinical perspective, the main difficulties are not those relating to germ cell genome editing, but those relating to the means used to induce functional spermatogenesis. This last subject has been extensively researched, particularly to restore fertility from cryopreserved testicular tissue before sterilizing treatment.<sup>58</sup> Positive results have already been obtained in mice and rats,<sup>59</sup> as well as in a non-human primate.<sup>60</sup> There is no doubt that the technique will be clinically usable in the coming years. And when no germline cells are available in infertile men, it is not out of the question that genetically modified gametes could be produced from iPS cells one day.<sup>61</sup>

Here again, the number of cases would be minimal, but the symbolic weight of

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53. P. F. Ray, A. Toure, C. Metzler-Guillemain & al., "Genetic abnormalities leading to qualitative defects of sperm morphology or function," *Clinical Genetics*, 2017, vol. 91/2, p. 217-232.

54. L. Ounis, A. Zoghmar, C. Coutton & al., "Mutations of the aurora kinase C gene causing macrozoospermia are the most frequent genetic cause of male infertility in Algerian men," *Asian Journal of Andrology*, 2015, vol. 17/1, p. 68-73.

55. C. L. Mulder, Y. Zheng S. Z. Jan SZ & al., "Spermatogonial stem cell autotransplantation and germline genomic editing: a future cure for spermatogenic failure and prevention of transmission of genomic diseases," *Human Reproduction Update*, 2016, vol. 22/5, p. 561-573.

56. Y. Wu, H. Zhou, X. Fan & al., "Correction of a genetic disease by CRISPR-Cas9-mediated gene editing in mouse spermatogonial stem cells," *Cell Research*, 2015, vol. 25/1, p. 67-79.

57. Y. H. Wang, M. Yan, X. Zhang & al., "Rescue of male infertility through correcting a genetic mutation causing meiotic arrest in spermatogonial stem cells," *Asian Journal of Andrology*, 2021, vol. 23/6, p. 590-599.

58. C. Wyns, M. Kanbar, M. G. Giudice & J. Poels, "Fertility preservation for prepubertal boys: lessons learned from the past and update on remaining challenges towards clinical translation," *Human Reproduction Update*, 2021, vol. 27/3, p. 433-459.

59. S. Takashima & T. Shinohara, "Culture and transplantation of spermatogonial stem cells," *Stem Cell Research*, 2018, vol. 29, p. 46-55.

60. G. Shetty, J. M. Mitchell, T. N. A. Lam & al., "Postpubertal spermatogonial stem cell transplantation restores functional sperm production in rhesus monkeys irradiated before and after puberty," *Andrology*, 2021, vol. 9/5, p. 1603-1616.

61. F. Fang, Z. Li, Q. Zhao & al., "Human induced pluripotent stem cells and male infertility: an overview of current progress and perspectives," *Human Reproduction*, 2018, vol. 33/2, p. 88-195.

the practice – genome editing – is enormous.

- Male sterility may be due to a chromosomal factor (Y-chromosome microdeletion) or a genic factor (mutations of the CFTR gene or genes controlling spermatogenesis).
- When spermatozoa can be used in ICSI, fertility can be restored, but chromosomal or genic modifications can be transmitted to offspring and cause sterility in boys.
- If no spermatozoa are available, an *in vitro* correction of the defective gene by genomic engineering in germ cells could be considered in the future for the treatment of male infertility.

## 6. Ethical considerations

The four aspects of classic eugenics mentioned on page 2 (C1 to C4) raise moral objections, but for different reasons: C2 and C3 because they violate the autonomy of the progenitors, C1 and C4 because the interests of the progenitors (individual persons) are subject to debatable collective goals. In the case of classical eugenics, there is therefore an instrumentalization of individuals to achieve a social objective that is a source of discrimination. Here, liberal eugenics is in direct opposition to classical eugenics. Is this ethically acceptable, or does it have negative moral and social consequences?

### a) Importance of means

Negative eugenics (rejecting embryos or gamete donors carrying genetic diseases) is generally considered less problematic than *positive* eugenics (choosing “superior” embryos). This raises the issue of the *means* used in the pursuit of eugenic goals. Even if an aim is good and pursued with good intentions, it is always possible that the means used to achieve it are morally reprehensible. Some means of having a healthy child are clearly laudable, such as refraining from smoking or alcohol, while others were implemented in the past without any opposition, but would no longer be acceptable today, such as controlled marriages: “This idea is widespread among many peoples and has sometimes been applied (in Sparta, for example)”.<sup>62</sup> Still others, used by our states, remain widely accepted. According to Stephen Wilkinson and Eve Garrard, there are ways “in which people and societies may reasonably pursue aims that may ultimately be (at least partly) eugenic. These include avoiding incest; providing genetic counseling to people with inherited genetic disorders; discouraging cousin marriage; or encouraging women to have children only in the optimum years for doing so (avoiding both teenage pregnancy and ‘post-menopausal motherhood’).”<sup>63</sup> That said, the question before us is whether using a PGD, rejecting an embryo or gametes carrying a serious disease, genetically modifying them for the same purpose, or even choosing the sex of the unborn child is morally acceptable.

62. J. Gayon, *art. cit.*, p. 2.

63. S. Wilkinson & E. Garrard, *Eugenics and the Ethics of Selective Reproduction*, Keele University, 2013, p. 11.

*b) Selection of people*

The CCNE refuses to speak of eugenics when it comes to the reproductive choice of couples selecting one embryo to be implanted over another; however, for this committee, it does not follow that this practice does not raise ethical questions. In particular, this practice amounts to choosing who will be born, which is a cause for moral concern: “These practices raise the issue of the ‘selection of people.’ How can we ensure that the elimination of certain embryos following a PGD or MTP does not result in the preventive elimination of future individuals considered ‘undesirable’ in a society of performance and efficiency?”<sup>64</sup> This is also what Jean-Yves Goffi asserted, as we have seen, who raises the issue of the selection criteria (the “right” embryo, the “right” gamete donor).

Here, we need to be very careful about how we express ourselves. Strictly speaking, the choice is not made between individuals, but between embryos that are not (yet) people – for the law and for the CCNE and the IEC, they are *potential* people.<sup>65</sup> Embryos do not have the moral status of a person, and it is generally accepted in our societies that embryos conceived by IVF and not used to realize the parental project of those who created them can be given to another couple or scientific research or be destroyed. Even if they are not the “owners” of them, it is generally accepted that it is those who are at the origin of the embryos who must choose between these different destinies. This is also the case under French law. The same should apply to embryos that are not transferred following genetic testing.

What sometimes underlies this confusion is what Alex Mauron has called the Paradox of the Platonic Boarding Gate.<sup>66</sup> The reasoning here is as if all potential persons were waiting for the opportunity to be implanted and born, so much so that if parents reject an embryo, they are denying it this possibility of existence. As such, future and even possible persons would already exist in a Platonic world and would be impatiently waiting to embark on their journey to terrestrial existence. Discarding them would therefore cause them harm (an analogous argument could be made for gametes, but it would be even less relevant, since a gamete cannot be considered a potential person).

However, the fact remains that it is still possible to object to the practice of choice that, while it is not reprehensible from the perspective of the status of the embryo, it could be reprehensible from the perspective of the attitude of couples, who would choose on the basis of morally unacceptable criteria.

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64. Opinion 138, p. 17. However, the CCNE also states in the same opinion: “Genomics now offers a technology that avoids the selection of individuals, replacing it with the selection (or modification) of genes” (p. 26).

65. IEC, *Research on Embryos and Embryonic Models for Scientific Use (EMSUs)*, January 2019.

66. “Choosing among possible persons: The ethics of prenatal selection in the postgenomic age,” *Comptes rendus biologiques*, vol. 338, 2015, p. 568: “It is as though we believed implicitly that the souls of future persons are sitting at a kind of virtual boarding gate, holding their boarding passes for the journey towards terrestrial existence. They have every reason to be anxious: will next flight not be overbooked? [...] And what about health? Is a life heavily burdened by illness and/or disability still desirable? Is it better to live at all costs rather than wait for eternity at the boarding gate?”

### c) Selection criteria

To choose the embryo to transfer among multiple embryos, morally robust criteria are needed. Those that are used today are medical, but the choice could be based on societal criteria, i.e. those that represent qualities valued in the conception of the human being that we maintain personally or socially, such as being tall or being intelligent (if there were a way to make such criteria operational, which is currently not the case, except for sex where it is valued).

When it comes to preventing the transmission of a hereditary pathology, the only criterion accepted and used is the detection of a gene modification linked to an incurable or particularly serious disease. When an embryo is discarded for that reason, the criterion is certainly medical, but it is often also partly societal, given that in our society, having a child with disabilities is a burden and is very often considered a misfortune. However, some people or schools of thought ask whether what we consider a disability is really an obstacle to leading a fully human life or whether it is just a variation that we should accept as part of our appreciation of human diversity. As the CCNE notes: "The question is whether these mutations represent a pathology or a simple difference contributing to the diversity of the human race."<sup>67</sup> The answer obviously depends on the seriousness of the disability or disease.

A similar question pertains to the selection of *donors' gametes*. What are the admissible criteria here? Should we rely solely on genetic criteria, and how far should we go in taking them into account? The dividing line is not always clear or simple, and Jean-Pierre Siffroi told us that the choice are discussed collectively on a case-by-case basis within the CECOS. Should the choice also take into account the morphotype of those who donate the gametes and those who receive them? Lastly, in most commercial sperm banks, particularly in the United States and especially when it is the users who choose, it is customary to include educational and social characteristics in the data used for donor selection.

### d) Dysgenics

The question of the selection criterion took a particularly acute turn when, in the United States, a deaf lesbian couple sought a sperm donation in order to be able to have an embryo that would lead to the birth of a deaf child.<sup>68</sup> The idea was to maintain better relations with their future child, as deafness is also conceived by the community of non-hearing people not as a disability, but as a cultural variant, since the deaf have their own language. This could be referred to as "dysgenics," insofar as it involves choosing a characteristic considered to represent a disability by the general population.

What can we think of this request on a moral level? Does respect for the reproductive autonomy of parents require that this requirement be met or not, and what

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67. Opinion 138, p. 26.

68. "In 2002, an American lesbian couple, Sharon Duchesneau and Candy McCullough, both of whom were deaf, deliberately chose to have a deaf baby." (S. Wilkinson & E. Garrard, *op. cit.*, p. 18) See also M. Spriggs, "Lesbian Couple Create a Child Who is Deaf like Them," *Journal of Medical Ethics*, 2002, vol. 28, p. 283.



about the good of the child? This case has been hotly debated in the bioethics literature. For those who believe that deafness is truly a disability and not part of normal human functioning (which is a classic definition of health),<sup>69</sup> there are, of course, good reasons to disagree with this request. Who is right?

The following tale might help mobilize our moral intuitions.<sup>70</sup> Following a nuclear accident or chemical disaster that left few survivors, the human race has become genetically deaf. Fortunately, thanks to the deaf people who survived, all the survivors were able to learn sign language and now live in a rich culture, even if nobody is able to appreciate Mozart or the Beatles anymore. One day, because of some genetic mutation or viral infection, certain individuals recovered their hearing. Their numbers have grown, and they now form a community with their own subculture. Unfortunately, because of social pressure (to succeed in a deaf culture, sign language must be mastered because any other language is useless), their children make no effort to assimilate their hearing culture. To remedy this and to promote their own culture, the leaders of the hearing community demand that their children be genetically modified to become blind. Their argument is that if they are blind, they will no longer be able to learn sign language and will be forced to use spoken language, the only language accessible to a blind culture. Do you think this claim is morally acceptable, or do you think these children would be harmed by being rendered blind?<sup>71</sup> If the answer is yes, then the argument of (cultural) (neuro)diversity has its limits.

Apart from the case of a couple of deaf women, which is certainly striking but remains singular, there are far more frequent cases of gene mutations and chromosomal abnormalities affecting infertile men, which were never transmitted naturally, are nowadays passed on to the next generation through ICSI. This admittedly unintentional dysgenics is interesting in that it shows that MAR technologies not only generate *eugenics*, but can, on the contrary, lead to what seems a paradox in genetics, namely the hereditary transmission of a factor of infertility or even sterility. This is a point that is unfortunately never raised by those who comment on or discuss ethical issues in this field.

#### *e) Expressivist argument*

This argument states that the practice of genetic testing with the aim of choosing embryos unaffected by a genetic disease would express a stigmatizing attitude not only towards disability, but also towards people with disabilities, whose lives would be perceived as having less value. Thus, PGD would express a discriminatory attitude towards people with disabilities themselves, which could ultimately lead to worse care for these patients and stigmatize them socially, as well as their parents who “let them be born” and thus imposed a burden on society.

The argument can be countered with empirical evidence that parents who use

69. Cf. N. Daniels, *Just Health Care*, Cambridge, CUP, 1986, p. 46.

70. B. Baertschi, *L'éthique à l'écoute des neurosciences*, Paris, Les Belles-Lettres, 2013, p. 219-220.

71. Those who are uncomfortable with the use of genetic engineering on humans can replace the modification of embryos in this tale with their selection.

reproductive technologies are not motivated by a quest for perfection or by discriminatory attitudes.<sup>72</sup> It should be added that being in favor of not transferring a Down syndrome embryo if it is the choice of the parents does not prevent us from wishing that all possible medical and social means be made available to Down syndrome people who are born so that they have the best possible life. However, even without stigmatizing intention, stigmatizing effects can occur, and we must remain vigilant to avoid them.

*f) Responsibility of future parents and institutions*

Any choice implies the responsibility of the one who chooses. As such, future parents are responsible when they request the use of gametes or the transfer of one embryo rather than others, even if they do not decide alone. This is why authors such as John Savulescu and Guy Kahane have spoken of a duty of beneficence consisting of, at the very least, not choosing an embryo carrying a deleterious gene.<sup>73</sup> Institutions and the state also have their share of responsibility in that they regulate and therefore limit the choice of couples or sometimes try to encourage or promote certain choices.

The question remains as to whether and to what extent the medical teams are liable. What would we say if the parents of a child born through a sperm donation sued the physicians because their child has an inherited condition linked to a genetic factor that was known or easily accessible in the donor<sup>74</sup> but was deliberately not taken into account by the physicians? Is it ethically acceptable to deliberately ignore a genetic trait that could have prevented the occurrence of a pathology in children? That's doubtful.

*g) Social pressure*

In a culture that defends broad reproductive autonomy, social pressure must be taken into consideration because it can jeopardize this autonomy. Indeed, social pressure pushes couples to undergo prenatal, preimplantation, and preconception diagnoses and, in the event of an unfavorable result, to abandon a parental project, terminate a pregnancy, or choose not to transfer an embryo with even a mild pathology where legislation allows it (as in Belgium, but not in France<sup>75</sup>): "The offer of testing tends to lead to acceptance in that women anticipate their own feelings of guilt, should they decline and subsequently discover that the fetus is affected by a genetic disorder."<sup>76</sup> In this way, social pressure may be exerted on parents at risk of having an affected child to undergo a test or not transferring in the uterus an embryo carrying certain genetic predispositions deemed undesirable. If reproductive autonomy is to

72. "Empirical data have shown that parents who make use of reproductive technologies are not driven by a quest towards perfection or by discriminatory beliefs" (G. Cavaliere, *art. cit.*, p. 16).

73. "The Moral Obligation to Create Children with the Best Chance of the Best Life," *Bioethics*, 2009, vol. 23/5, p. 274-290.

74. To find out, it is not necessary to conduct a genome analysis (currently illegal in France). A simple interview to learn the family history of donors or by analyzing their family tree is often sufficient.

75. B. Baertschi, "Le diagnostic préimplantatoire (DPI) à l'ère de la médecine prédictive," *Médecine/Science*, 2019, vol. 35, p. 72-77.

76. D. King, "Preimplantation Genetic Diagnosis and the 'New' Eugenics," *JME*, 1999, vol. 25, p. 177.

preside over parental decisions, this pressure can undermine it and be no less psychologically burdensome than a state constraint.

However, this would only be a reason to challenge or limit this autonomy if the pressure exerted here was much greater than in other areas of our existence, because whenever we have an important decision to make, we do so in context, and pressures are never absent. That said, the existence of pressures is a good reason, during genetic counseling, to try to identify with the couple whether and how they are subjected to them, with the aim of eventually freeing themselves from them and favoring their autonomy.

Respect for the autonomy of future parents has a corollary: their responsibility for the reproductive choices they make. For some time now, however, there has been a tendency on the part of certain professionals to invoke this responsibility to influence parental choice: a 1997 study by Dorothy Wertz and John Fletcher revealed that 20% of geneticists in certain countries (English-speaking countries and Northern Europe) believe that, given the availability of prenatal testing, it is not right for parents to knowingly agree to bring a child into the world with a serious genetic disease, and in the rest of the world, a majority of geneticists support this view.<sup>77</sup> The risk is that this attitude could extend to the parents of a child with disabilities if they refused to undergo the PGD offered to them or even to those who chose to transfer an embryo carrying a genetic disease because there were none without it.

That said, it should be stressed that wanting a healthy child is not necessarily an effect of social pressure and that even if it is, it does not follow that this pressure is to be deplored. Fritz Mann points out that “encouraging the birth of perfectly healthy children and restricting the number of newborns with disabilities as much as possible corresponds to common sense and the spontaneous feelings of parents.”<sup>78</sup> Mark Hunyadi agrees: “The dream of health for oneself and one’s children is a lifelong dream. [...] According to the criteria made available to us by our objective moral context, negative eugenics is not in itself reprehensible.”<sup>79</sup>

#### *h) Good of the child*

The good of the child is a compass for law and ethics. In this case, however, as in general in MAR, this is not a very judicious consideration, as the child does not yet exist and therefore cannot have any interest to be protected. If the embryo is discarded, no harm will have been done to the child since it will never exist. Of course, if we consider that existence is a good, we will say that harm has been inflicted on the embryo, but it will be exactly the same as that inflicted on all embryos that are never transferred in the uterus. On the other hand, if it is discarded because it was a carrier of a serious disease, a future child will have been prevented from suffering, which cannot go against its good.

The difficulty here lies in the harm that could be done to a child with a serious disease who comes from a transferred embryo when the child was known to carry this

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77. D. King, *art. cit.*, p. 177.

78. F. Mann, in J.-N. Missa & C. Susanne, *op. cit.*, p. 137.

79. *Je est un clone*, Paris, Seuil, 2004, p. 109.

risk. Bioethicists have argued that certain lives are not worth living, with arguments that deserve discussion,<sup>80</sup> but in France, existence is never considered a harm, at least in the legal sense of the term. In the case of the choice of deliberately giving birth to a deaf child through an AID and admitting that non-existence is not a state of the individual, Stephen Wilkinson and Eva Garrard argued that when the alternative is deafness or non-existence, choosing to have a deaf child cannot harm him or her, since his or her situation has not been aggravated.<sup>81</sup> To suffer harm implies that we can compare two states of affairs. This is not possible here, though, because non-existence is not a state of affairs and therefore neither a good nor an evil.

However, one question remains unanswered when it comes to choosing gametes: is it acceptable to knowingly pass on to one's offspring gene or chromosome alterations that are never naturally transmitted, even when they are responsible for an alteration in the children's health (for example, in the case of Y-microdeletion)? This raises the broader question of whether and to what extent anything that runs counter to natural processes is morally permissible. There is a short answer to this question: it is the very mission of medicine to interfere with the natural processes of life. MAR does nothing else, but this does not eliminate the ethical concern not to ignore the potential danger to the child's wellbeing, remembering, however, that inheriting a fatal disease is not the same thing as inheriting a rare and more or less incapacitating genetic disease, but for which the father's or mother's life has shown that it is possible to "live with it."

#### *i) Use of genome editing*

So far, only the selection of an embryo or gametes has been discussed. However, in the future, it may be possible to "cure" germ cells or an embryo through genome editing. This could be referred to as *corrective eugenics*. It is true that French law, based on the Oviedo Convention, currently prohibits tampering with the germinal heritage of the human race,<sup>82</sup> but this could change if the process becomes safe.<sup>83</sup> It would then become legal, for example, to modify a gene on germ cells to restore fertility. This modification would obviously be transmitted to the offspring – this is one of the current prudential grievances against germline gene therapy – but one might ask why we should condemn any transmission of edited genes enabling an offspring to exist with an unaltered phenotype when the transmission of naturally mutated genes or chromosomal alterations potentially responsible for altered phenotypes is commonly practiced.

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80. Cf. J.-Y. Goffi, *art. cit.*

81. "When the choice is between deafness and non-existence, we can't say that the deaf child has been harmed by being chosen for existence: she hasn't been harmed because she hasn't been made worse off." (S. Wilkinson & E. Garrard, *op. cit.*, p. 18).

82. *Oviedo Convention*, art. 13: "An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic, or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants." The text speaks of a "aim", but what if it were just an *effect*?

83. Cf. Council of Europe, *The use of new genetic technologies in human beings*, doc. 14328, May 20, 2017: "The scientific consensus at the moment is that these techniques are not yet 'safe' enough, leading to a *de facto* moratorium until a germline intervention could meet the risk/benefit standard for authorising clinical trials."

There is another difficulty here, because if we can modify an embryo's genome to cure it, we could also do so to improve it, i.e. endow it with characteristics deemed beneficial that it does not have naturally (think of the US pronatalist movements mentioned earlier). Without repeating what has been said in the literature about the human enhancement project that can be undertaken after birth by hormonal, pharmacological, or other means or even transhumanism,<sup>84</sup> it should be noted that such possibilities would increase the social pressure on parents and that this is not welcome. Jonathan Glover illustrates this with this anecdote: "John Mackie, arguing once in a discussion, [...] said that if the Victorians had been able to use genetic engineering, they would have aimed to make us more pious and patriotic."<sup>85</sup> It is indeed morally unacceptable to want to impose our values on future people beyond what is inevitable (and that is already a lot) because this would be to consider that what we currently value in human beings or our current conception of good and accomplished life have definitive value. As the example of piety and patriotism shows, this is not the case. This would be a form of instrumentalization of the child, designed to meet the goals of the parents. Thus, Jürgen Habermas refers to the "instrumentalization of conditionally created human life according to the preferences and value orientations of third parties,"<sup>86</sup> which, in his view, still contravenes the equality of people.

"Liberal" or "private" eugenics is currently the subject of much debate. The main arguments underlying the current thinking are as follows:

- Even if the goal (not having a child with a serious genetic disease) is laudable, not all means of achieving it are necessarily so;
- By choosing which embryos to transfer, a choice is made as to the people who deserve to exist;
- There is a risk of applying arbitrary or even immoral selection criteria;
- Some MAR practices involve the transmission of genetic mutations and chromosomal abnormalities (dysgenics);
- The practice of genetic testing with the aim of choosing embryos without a genetic disease expresses a stigmatizing attitude towards people with disabilities (expressivist argument);
- Couples and the medical institution have a moral duty not to transfer an embryo carrying a deleterious gene;
- Couples are under a great deal of pressure to undergo testing, a pressure that could undermine their autonomy and their ability to choose freely;
- The good of the child, a cardinal ethical and legal consideration, could be threatened by "private" eugenics;
- An alternative to embryo selection could be germline gene therapy, which is currently prohibited.

84. Cf. B. Baertschi, *op. cit.*

85. *Op. cit.*, p. 149.

86. J. Habermas, *op. cit.*, p. 30.

## 6. Conclusion

The intervention or consideration of genetic testing or factors is an inescapable reality when reproduction is medicalized. In particular, it can manifest itself through the deliberate or unintentional transmission to the child of identified genetic traits (chromosomal or genic) that could influence the child's phenotype and life.

Any such intervention cannot be prohibited or encouraged *a priori* in the name of philosophical, social, or political principles. However, the nature and effects of this intervention and the intentions behind it cannot be ignored.

Regarding the transmission of genetic traits to offspring, there are four types of MAR:

1° MAR is used to enable an infertile person or couple to carry out a parental project, and the possible transmission of the genetic trait is an unintended but conscious side effect (gene mutation, Y-microdeletion, etc.).

2° MAR is used to enable an infertile person or couple to carry out a parental project, and genetic tests on the embryo (aneuploidy or other) are undertaken to increase the chances of carrying the pregnancy to term. The non-transmission of a genetic trait that has been identified in the embryo and could therefore have been passed on to subsequent generations is an unintended side effect.

3° MAR is used to enable a fertile person or couple to avoid the birth of a child with a hereditary condition whose genetic cause is known in either or both of the future parents. This is counter-selection, and non-transmission of the genetic disease is the main effect sought.

4° MAR is used outside any medical context (infertility, hereditary risk) to obtain the birth of a child with the desired phenotype (sex, deafness, etc.).

Can these four types of MAR be given the same label of eugenics, possibly accompanied by the terms "liberal," "new," or "private"? We don't think so. Given that only interventions promoting the *deliberate* transmission of genetic traits or characteristics to offspring are eugenic or eugenist, only the last two categories can be described in this way, and, of the two, only the last is likely to raise moral objections, particularly when its aim is to give offspring a particular advantage (this is positive eugenics).

Even this is controversial and open to debate. For example, it is clear that the choice of sex for convenience by MAR, as practiced in the US, does not obey any state or professional injunction and is not a source of discrimination or modification of the sex ratio, since almost as many boys as girls are born when this method is used.<sup>87</sup> Of course, the same would not be true if the method were widespread, as is the case (by other methods) in some Asian countries, with significant demographic and social consequences. One way to avoid this would be to allow the procedure only for a second or third child of the same sex.<sup>88</sup>

Regardless of the type of MAR, the considered procedures should only be

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87. P. Colls, L. Silver, G. Olivera & al., "Preimplantation genetic diagnosis for gender selection in the USA," *Reproductive Biomedicine Online*, 2009, vol. 19, Suppl. 2, p. 16-22.

88. This is, for example, what the law in Israel says.

undertaken on the basis of the free choice of the future parents, i.e. with respect for their reproductive autonomy. For it to be exercised responsibly and independently, people need to be well informed – hence the importance of genetic counseling – and as free as possible from social, religious, or other pressures.

Prioritizing the responsibility of people undergoing MAP when it involves choices based on genetic criteria does not prevent the medical teams performing the MAP from responsibility. It would thus be totally irresponsible not to take into account any known or identified genetic factors in gamete or embryo donors that could cause major health problems in children.

However, the risk of deviations should not be ignored. At present, this risk is mainly linked to the commoditization and commercialization of procedures (including when they have not been validated, such as polygenic scores). This has led several authors, including ethicists, to recommend that these highly sensitive procedures be performed only in the public or non-profit sector, as is already the case in France in other medical fields (such as organ transplantation and blood donation) and also in MAR (such as gamete and embryo donation and PGD).

### **Acronyms**

BAVD: Bilateral Absence of Vas Deferens

MAR: Medically Assisted Reproduction

TMAR: Third-Party Medically Assisted Reproduction

CCNE: French National Consultative Ethics Committee

CECOS: Center for the Study and Conservation of Human Eggs and Sperm

IEC: INSERM Ethics Committee

iPS Cells: Induced Pluripotent Stem Cells

CRISPR-Cas9: Clustered Regularly Interspaced Short Palindromic Repeats

PGD: Preimplantation Genetic Diagnosis

FISH: Fluorescent In Situ Hybridization

IVF: In Vitro Fertilization

AID: Artificial Insemination with Donor Sperm

ICSI: Intracytoplasmic Sperm Injection

MTP: Medical Termination of Pregnancy

### **Interviewees:**

- Jean-Pierre Siffroi, physician, professor at Sorbonne Université
- Françoise Baylis, philosopher, professor at Dalhousie University (Canada)
- Luc Berlivet, sociologist and science historian, staff scientist at the CNRS (Pitié Salpêtrière and Armand Trousseau Hospitals)
- Delphine Héron, physician, head of clinical genetics units in Paris
- Jean-Louis Mandel, geneticist, professor at Collège de France
- Pascal Salvetti, agricultural engineer and head of an experimental farm at Eliance
- Julie Steffann, geneticist, professor at Université de Paris

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