Special Section: Designs on Life:
Choice, Control, and Responsibility
in Genetic Manipulation

The New Eugenics and Medicalized Reproduction

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We know today that classical eugenics, of an essentially negative nature, was not only an aggressive and brutal practice but, like its positive counterpart, inefficient as well. In fact, numerous biological, sociological, and psychological events beyond our control arise to prevent the realisation of any eugenic plan. Thus, like all human beings, individuals whose procreation is encouraged by positive eugenics suffer unexpected mutations that are transmitted to their offspring by their gametes. Gene distribution among the gametes at meiosis is the result of an uncontrollable, natural lottery. As an effect of this lottery, positive eugenics could allow the birth of defective babies whereas negative eugenics precludes the birth of normal babies.[1]

Determinant factors in the reciprocal choice of two individuals to constitute a couple and to procreate are beyond biological determinism. No one can also predict which spermatozoon of 200 million will fertilize or the genetic identity of the oocyte thus encountered. Moreover, the low fertility of human beings compromises eugenic programs because of the low number of children produced. We know, too, that to privilege genetic determinism is naive when the majority of genes interact with environmental factors.[2] Finally, negative eugenics, imposed in opposition to human liberty and dignity, has become unacceptable in the majority of democratic societies.

It is, therefore, due to a novel technical context that eugenics can reappear as a social project. Two research disciplines are in active development: molecular genetics and medically assisted procreation (MAP). These two disciplines have already provoked a number of public debates. My opinion is that the encounter of the techniques of medically assisted procreation with those of genetics is explosive. However, my objective is not sensationalism nor do I share with the media their pet hypothesis of a voluntary modification of human embryos with the aim of producing superhuman or infrahuman beings. It would be misleading to call scientific and technical progress into question by evoking situations in which democracy could be abrogated: history has shown that in such situations the most despicable and enormous crimes do not require the assistance of science. Neither would I envisage germinal genetic therapy for the correction of defective embryos carrying the genes for a serious disease: the simultaneous availability of many embryos, of which the majority do not carry the anomaly, obviates the need for such a germinal therapy.

What I do want to show is that the new eugenics—that which would be acceptable to our developed and democratic nations—is currently emerging and will consist not of manipulation of the genome but in its selection. For selection we need only to use the techniques of contemporary genetics to determine the best

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embryos among those contained in our test tubes and which are too numerous to be transformed into children. This eugenics will have several characteristics that the old eugenics did not have: the new eugenics will be benevolent and learned, painless and efficient. These qualities make it a social means of regulating health and defining normality according to more and more restrictive conditions. Because embryo selection, once applied clinically, will be not only irreversible but increasingly practised, we must now consider the implications.

From Quantitative to Qualitative Mastery of Procreation

In the last few decades revolutionary solutions to adapt family size to the couple's desires have emerged. Birth control allows the suppression or delaying of births so that each person may find sexual fulfillment without undesired procreation. By contrast, medically assisted procreation intervenes to treat infertility and, in extreme cases, makes an appeal to sperm and egg donors or surrogate mothers. Thus medicine proposes procreational solutions to almost all sterile couples, even after physiological aging, so that today a woman may become a mother after menopause. Finally, the quality of obstetric and perinatal care has made such progress that the majority of pregnancies result in the birth of an infant.

Thus the quantitative mastery of procreation has emerged, leading couples in industrialized countries to produce 1.6–1.8 children in the course of their lives. This mastery of human procreation is assured at the risk of reification of the child.

Now arises, as is the case for all objects of consumption, the problem of qualitative mastery. The simultaneous availability of numerous embryos is made possible by MAP, either in the event of an *in vitro* fertilization (IVF) or after uterine washing following internal fertilization. Thus the range of genetic characteristics presented by these embryos is much larger than in the case of a natural pregnancy where only one fetus may be analyzed. The possibility exists, within the technical limits that we will examine, of choosing a good embryo, that is, it is almost always possible to discover embryos free of serious genetic defects and, beyond this, to retain a few embryos that conform to parental desire with respect to risk and sex factors for certain afflictions or even aesthetic criteria. The elimination of unsuitable embryos is facilitated by two factors: the slight emotional weight attributed to these very early embryos, also called pre-embryos, and their availability outside the maternal body.

Let us recall that the average couple desires the production of only 1 or 2 babies in the course of their lives. This restriction justifies their exigence concerning the quality of these babies. Thus preimplantation diagnosis (PID), already available to couples presenting a known genetic risk, could soon be requested by individuals treated for infertility by IVF. Over 100,000 embryos already produced by IVF are thus potentially analyzable each year in the United States, as in France. Finally, because the access to IVF is not controlled (even in France where biological and medical expense are entirely assumed by the social security system), there will be a strong incitement for all wishing to have a baby without faults to take advantage of IVF.

It is important to compare the impact of the diverse eugenic methods that have already been advocated (Table 1). Our societies can no longer accept the suppression at birth of malformed babies as practised in ancient Greece or in certain Asiatic countries where little girls are still eliminated. Nonvoluntary sterilization is poorly accepted, as is late abortion when ultrasonographic or genetic examinations reveal

Table 1. Advantages of Various Negative Eugenic Procedures According to Respective Target.

Target for Eugenic Action	Social Acceptability	Couple Satisfaction	Human Genetic Improvement
Newborn (suppression)	−	−	0
Adult			
Genetic counselling	+	±	0
Sterilization	±	±	0
Fetus (abortion)	±	±	0
Embryo (no replacement)	+	++	+

an anomaly. On the other hand, genetic counseling is well-tolerated socially, as is the transfer into the uterus of only certain embryos produced by IVF.

However, the satisfaction of the couple on whom the eugenic act is practised is always low, with the exception of those benefitting from embryo selection because this technique is the only one that does not oppose itself to the desire to have a child but, in fact, rather guarantees certain characteristics of that child.

As for the genetic improvement of the population, we know that the methods of classical eugenics are without effect. By contrast, due to the number of embryos available, PID can have truly eugenic implications. PID is the only nonviolent means available to any couple that can result in a baby that is not only "normal" but conforms to their wishes.

New Prospects in Eugenics

The importance of a large number of available embryos is clear if we compare prenatal diagnosis, practised in the course of pregnancy, with PID, as *in vitro* technique (Table 2). Prenatal diagnosis is performed on a single fetus at a time, and we cannot envisage its application more than once a year for a given couple. In contrast, PID may involve more than one and even several dozen embryos at a time, and this screening may be repeated several times a year. Thus, it is up

Table 2. Quantitative Efficiency of Prenatal Versus Preimplantation Diagnosis: Comparative Numbers of Potential Children Submitted to Screening.

Diagnosis	Number of Embryos/Fetuses Simultaneously Screened	Number of Screenings Per Year	Number of Embryos/Fetuses Screened Per Year
Prenatal (CVS, amniocentesis, ultrasonography)	1	1	1
Preimplantation (genetic screening of IVF embryos)	4–20	3–6	12–120

CVS, chorionic villus sampling; IVF, *in vitro* fertilization.

to a 100 times more efficient because it can involve as many as a 100 embryos each year. In addition, PID always gives the opportunity for the birth of a baby by discovering one or more normal embryos. Prenatal diagnosis could delay the birth of a baby for 1 year or more when the only screened embryo does not appear satisfactory.

The question that then presents itself is that of the practicability of PID and its ability to recognize certain genetic characteristics. First is the analysis sampling of a blastomere in a 2-day-old embryo containing four blastomeres or of several cells from a 5-day-old blastocyst after IVF. This removal of cells for analysis does not appear to alter the embryo's developmental possibilities, especially in the human species in which half embryos are naturally created and frequently become homozygotic twins. After only a few years of experimental removal of blastomeres from human early term embryos, it is clear that the technique is easy, quick, and nearly all the experimental embryos survive. The subsequent genetic screening of the sampled blastomere may be performed in just a few hours. Embryo freezing during screening therefore appears to be unnecessary.

In only 5 years, since the first results published by AH Handyside *et al.*,[3] PID has advanced and can now propose efficient and viable techniques despite the restricted number of cells available for analysis (Table 3).[3–12] Thus results have been obtained with polymerase chain reaction (PCR) amplification of a single gene or with multiple PCR, where several genes have been simultaneously amplified. This approach has also involved fluorescent *in situ* hybridization (FISH) to reveal the presence of one or several chromosomes. And the two techniques, PCR and FISH, have also been used successively on the same cell. These pioneering projects open significant eugenic perspectives because (according to Jack Cohen's team in New York) we can, in a single blastomere, evaluate aneuploidy for five different chromosomes[11] and, above all, look for mutations in 20 different genes.[7]

Table 3. Human PID: First 5 Years of Medical Use of PID Techniques with 2–5 Day Embryos.

	Medical Investigation		
Methods for PID	Sex Determination	Aneuploidies	Genetic Diseases
PCR	Y chrom.[3]		CF[4] Sickle cell anemia[5]
Simultaneous multiple PCR	X and Y chrom.[6]		X chrom. and CF gene[7]
FISH	Y chrom.[8]	Chrom. 18[9]	
Simultaneous multiple FISH	X and Y chrom.[10]	Five chromosomes[11]: X, Y, 18, 13, 21	
Successive multiple PCR and FISH	X and Y chrom.[12]		

PID, preimplantation diagnosis; PCR, polymerase chain reaction; CF, cystic fibrosis; FISH, fluorescence *in situ* hybridization.

Moreover, initial concerns that the screening of embryos with only four or eight cells result in frequent errors have proved to be largely unfounded. Current work on the conditions of coculture of the embryo with somatic cells has permitted the *in vitro* development of the majority of embryos for up to 5 days. It thus becomes simple, in order to augment the reliability of screening, to carry it out on several sampled cells.[13] By cloning the early embryo it should also be possible, as demonstrated in animals,[14] to obtain several monozygotic embryos available for genetic screening.

Another criticism is based on the observation that haploid, diploid, and polyploid cells coexist in the young embryo. However, these observations of mosaic embryos were made on those IVF embryos that were not representative in that they had been judged to be of insufficient quality for transfer into the uterus. Moreover, the future of embryo screening is not the establishment of karyotypes; the future is the detection of mutant genes. This role will be rapidly confirmed with the application, to the embryo, of more numerous diagnoses adapted from those performed on the foetus, the child, or the adult.

Let us examine the future conditions of PID with the example of a selection procedure applied to 14 embryos obtained through an IVF, a situation which is not rare when a woman is young (Fig. 1). We would start by excluding four embryos that carried very bad characteristics, in particular those that were homozygous for a serious recessive illness. We would then find five risky embryos. The failing might be the possession of certain genes statistically associated with certain pathologies like diabetes, certain cancers, or cardiovascular illnesses for

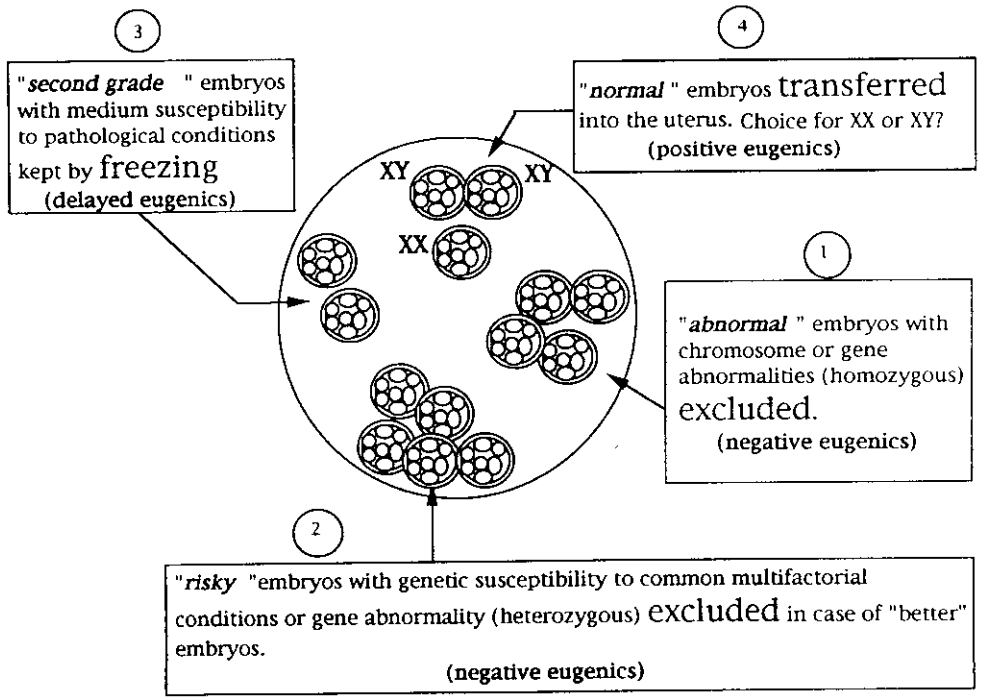

Figure 1. Special meaning and consequences of positive-negative eugenics when applied to the embryo population from one couple.

example. (We would remind ourselves that we all possess such genes and that this, by the way, is why we are and will remain, mortals. . . .) In such cases, the issue is not one of an automatic relationship between genes and pathology, because certain factors like the environment later modulate the expression of these genes. It should also be noted that eugenics can only consider those risk factors because healthier embryos almost always exist in the same series of test tubes. The risk addressed by this approach can also be that of transmitting to future generations the gene of a serious illness: the heterozygotic embryo could be eliminated even though its evolution would have resulted in the birth of a healthy child carrier. Once again, that elimination is possible only because we have available other embryos free of the incriminated gene. It is this fact, the element of choice, that makes this approach an innovation in eugenic politics.

In the same example, we would discover two "second grade" embryos that would be acceptable if the transfer into the uterus of the best embryos did not result in pregnancy. We would therefore freeze these embryos against a future choice. Finally, three embryos would be judged normal, which is not to say that they were perfect (the perfect embryo exists only as a phantasm). Because the screening would have revealed, apart from the pathologies, the sex of each embryo, the couple could request the transfer into the uterus of only embryos of a certain sex or, eventually, even those embryos carrying certain characteristics of aesthetic value.

It will be noted that, in this simultaneous screening of numerous embryos, both positive and negative eugenics are applied because, on the one hand, certain embryos are eliminated and, on the other, the development of others is favoured. This situation, where eugenics is applied to a human population to become at the same time positive and negative, is novel. But this does not signify that eugenics is becoming neutral. It will be noted, too, that genetic screening of embryos will be an element that favours the politics of embryo transfer following IVF: the correct number of embryos for introduction into the uterus will be better defined after elimination of nonviable embryos discovered in the course of screening. Thus PID will also be justified as a way to limit the incidence of multiple pregnancies, one of the most serious consequences of IVF.

Human Selection

Because PID presents very real advantages from the medical and eugenic points of view, we should also examine the potential dangers. It is impossible to predict the impact of embryo screening on the human genome because this impact will depend on the number of couples thus treated as well as on the number of generations involved. The project for the eradication of unfavourable genes is utopian because incessant mutations renew such genes within the population. We know, however, that certain mutant genes are beneficial to the heterozygote: thus the genes for Tay–Sach's disease, sickle-cell anaemia, and for cystic fibrosis confer resistance to tuberculosis, malaria, and increase life expectancy, respectively. In addition, PID can have unknown consequences. Seen globally, embryo screening places us in the position of apprentice sorcerers. In fact our capacity for genetic manipulation is becoming too large in comparison with our real knowledge and could lead to the creation of irreversible situations. As demonstrated by Ruth Hubbard and Elijah Wald[15] the gene myth is associated with simplistic explanations while reality is much more complex than molecular genetics tells us. Contem-

porary ecological problems in various parts of the world caused by exotic, would-be beneficial flora and fauna imported by a naive nineteenth-century biology should serve as an example of the danger we pose to our genetic heritage.

The new possibility of guaranteeing a certain embryonic quality will also be an incitation, for numerous couples, to have recourse to IVF as well as provoking a banalization of instrumental methods of procreation. We can ask ourselves whether the possibility of choosing the sex of one's child belongs to the concept of choices that conform to the ruling social order. In a more general fashion, the value of the majority of genetic characteristics, rather than being intrinsic, is relative to a given society. The liberty that we appear to give to couples to choose their children would therefore appear to be illusory. Insofar as the liberty of the child is concerned, that liberty would be seriously compromised by the obligation to gratify the parents by assuming their choice. Personally, if I consider such embryonic sorting beneath the dignity of humanity, my reasoning is not because eliminating certain undesirable embryos would be "*in vitro* abortion." Rather it is because to do so would result in the production of survivors of this choice, escapees, and obligatory servants of an ideology of performance and exclusion. Thus this ideology will lead to an ever greater rejection of handicapped people, to the extent that their birth could have been avoided. We see, therefore, the construction, supported at once by technical competence and theories of competition, of a more and more restrictive definition of normality and humanity.

If the choice that parents would impose on their children is not truly theirs, then whose is it? For reasons associated with the economy and the market, normality of human beings will be more and more defined according to the needs of industry and insurance contracts. Embryonic screening is a tool for the social exclusion of deviants and for the exacerbation of competition between human beings. The impact upon society of the pseudoscientific demonstration of biological hierarchies, and reduction of individual relevance in these terms must not be underestimated. For the first time, genetics, allied with computerized data handling and statistics, will claim itself capable of foreseeing the risk of pathology and of evaluating its degree in the case of each individual and thus for each embryo. In the long term, one can imagine that embryo screening will be the object of economically inspired pressure, in the context of public health, for example, in which the elimination of certain deviants would appear less costly than to maintain them. These perspectives, which are barely futuristic, show the role that will be played by social engineering, between biomedical power and social planning. Moreover, the complexity of choices offered by molecular genetics could well reduce the liberty of citizens whose lack of competence would lead them to rely more and more on the social engineer. The social engineer is then the specialist, still to be invented, for mediation between biomedical interests and available techniques and the social aspiration to which individuals will conform.

Mastering the New Eugenics: Is It Possible?

The fear of these perspectives, the elaboration of which I have contributed to for the past 8 years[16] has led, in France, to an examination of the various means of restraining the use of PID.

We cannot place our confidence in medical guidelines because doctors are the objects of the extreme pressure exerted by patients and industry. Moreover, like all human beings, doctors and geneticists are sensitive to their personal interests

that are influenced by the impact on financial success or the search for power. It has been said that patients' innate sense of responsibility will enable us to avoid the encroachment of abusive genetic screening. However, we cannot eliminate from consideration the desire for the ideal baby, which existed long before molecular genetics. The parents responsible are justly anxious over the future of their children and know that their chances of success depend on their conformity to the received model. Finally the citizens of our industrialized countries demand the right to share the fruits of progress, which include their right to choose their child, as soon as choice becomes possible. In countries like France, where the social security system takes responsibility for the entire cost of MAP, the citizens consider that their contribution to the system also gives them the right to be taken care of, both technically and financially, in the production of quality children.

Also proposed is that medical screening of embryos be limited to serious illnesses of which a list will be legally established. But the official production of such a list implies that persons thus designated as ill are thereby also designated undesirable. This proposition is in conflict with the wish for tolerance, for the dignity of all human beings proclaimed by our society, and even with the concept of human rights.

Rather than limiting the medical indications, it has then been suggested that the right to screen embryos be restricted to a limited list of doctors and geneticists. Experience proves that the certification thus accorded to certain practitioners renders difficult any eventual control over their activity. In addition, this exclusive right to a medical practise reserved for a select few could, in the absence of competition, provoke excessive financial demands and pose the risk of a medicogenetic monopoly that would invent its own rules.

Therefore the creation of controlling committees has been suggested. But the question is how to apply criteria in this sphere of activity where informal and official criteria are absent. The absence of political decisions would then encourage certain abuses of power. In addition, it is well-known that such committees lack a decisive impact on actual practices. There remains the proposition of a committee that would evaluate each medical request even before embryonic screening. This proposal has several conditions: that it include not only professionals in genetic screening but others as well; that biomedical acts without the committee's authorisation be illegal; and that the committee produce a public and transparent annual report.

In conclusion, the scenarios inspired by the imminent union of MAP with genetics are in line with our society's mode of development.[17] At first, MAP invented biological productivism by increasing the number of eggs and thus embryos that a woman could produce in the course of a menstrual cycle. In this way, our normally monovulatory species has become polyovulatory and even polytoccous. Until the present, eugenic refinement of social competition has been only approximately achieved with IVF: the best embryos are transferred into the uterus, the worst are eliminated from the human reproductive circuit, and the doubtful are put in the "unemployment" queue in laboratory freezers. The new possibilities offered by the genetic inquisition will allow the elaboration of the criteria of choice and promise, not without certain illusions, to produce individuals who conform better to the social and economic ideal. What is in the making here is a veritable ethical revolution that transcends the frontiers of any given country. We must respond because we are responsible today for the production of the future generations. This response must be realistic insofar as it concerns our true mastery of

the genome. We must recognize that we know little about the functioning of what we are preparing, without scruples, to modify. We must also evaluate whether the well-being that embryonic selection could bring to certain people justifies the risks that it carries for all the others. The response cannot be given by genetic practitioners alone. Beyond technical performances, individual interest, and naive desire, the problems are more complex than we are led to believe. They can be resolved only by a reflective effort that conforms to the interests of humanity, by determined humility in the face of this complexity, and in respect for the dignity of all human beings.

Notes

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