

OPINION

Towards an efficient medical eugenics: is the desirable always the feasible?

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Classical eugenics was, it is well known, essentially of a negative nature. It was not only aggressive and brutal in practice but, as its positive counterpart, inefficient as well. In fact, any eugenic plan may be blighted by biological, sociological or psychological events beyond our control. Thus, as an effect of the usual unexpected mutations and of meiosis, an uncontrollable natural lottery, even those individuals encouraged to procreate by positive eugenics using adult people as target could suffer the birth of defective babies. The factors which determine the choice of two individuals to form a couple and to procreate are also beyond biological determinism. Also, no-one can predict which of the 200×10^6 spermatozoa will fertilize or furthermore the genetic identity of the oocyte then encountered. Moreover, since humans have a low fertility rate compared to other mammals, their reduced number of offspring constitutes a limit for eugenic programmes. It is also naive to choose genetic determinism when we know that the majority of genes interact with environmental factors (Strohman, 1994). Finally, imposing negative eugenics is in opposition to human liberty and dignity and has become unacceptable in the majority of democratic societies.

It is due to recent technical advances that eugenics can re-emerge as a social project. In particular, two research disciplines have been in active development: molecular genetics on the one hand, and medically assisted procreation (MAP) on the other. These two disciplines have already provoked a number of public debates separately, but it will be their encounter that will be truly explosive. The hypothesis of a voluntary modification of human embryos with the aim of producing 'supermen' or 'infra-human' beings is not in question. 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 it be realistic to fear germinal genetic therapy for correction of embryos carrying defective genes because the simultaneous availability of several embryos (of which the majority do not carry the anomaly) obviates the need for such a therapy.

The major point to consider is whether a new medical eugenics—that which would be acceptable to our developed

and democratic nations—is currently emerging and will involve the selection of the genome, not its manipulation. For this, the techniques of contemporary genetics can be used to select the best embryos amongst those growing in our test tubes, as they are too numerous to be transformed into children. This eugenics would have several characteristics which the other eugenics does not have: it will be beneficial and normal, painless and efficient. These qualities make it a social means of regulating health and of defining normality according to more and more restrictive conditions. Once applied clinically, embryo selection will not only be irreversible but increasingly practised, hence we must consider its implications now.

From quantitative to qualitative mastery of procreation

The last few decades have seen the emergence of revolutionary solutions for the adaptation of family-size according to a couple's desire. On the one hand, birth control allows us to suppress or to delay births in order to find sexual fulfilment without undesired procreation. On the other hand, MAP allows infertile couples to achieve a live birth. Furthermore, in extreme cases of infertility, MAP can be carried out using sperm donors, egg donors or surrogate mothers. In this way medicine proposes procreational solutions to almost all sterile couples, even after physiological ageing, 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 lasting >3 months result in the birth of a living infant, with this individual becoming a person within the family.

It is thus that the quantitative mastery of procreation has emerged, leading couples in industrialized countries to produce only 1.6–1.8 children in the course of their lives but with the risk of 'reification' of the child. There now arises, as is the case for all objects of consumption, the problem of qualitative mastery (Testart, 1986). The simultaneous availability of numerous embryos is made possible by MAP, either in the event of 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 analysed. There is also the possibility, within the technical limits which are to be examined, of choosing a 'good' embryo, i.e. it is almost always possible to discover embryos free from serious genetic defects, and even to retain a few embryos conforming to parental desire in respect of sex, risk factors for certain afflictions, or even aesthetic criteria. The elimination

of unsuitable embryos is facilitated by two factors: firstly, the slight emotional weight given to these fertilized eggs, also called 'pre-embryos', and secondly, their availability outside the maternal body.

The eugenic methods already advocated will now have to be compared with regard to their impact (Table I). Our societies can no longer accept the elimination at birth of malformed babies, as was once practised in ancient Greece or that of babies with undesirable sex, as still practised in certain Asiatic countries. Imposed sterilization is poorly accepted, as is late abortion when ultrasonographic or genetic examinations reveal an anomaly. In contrast, genetic counselling is well tolerated socially, as is the transfer into the uterus of only certain of the embryos produced by IVF. While the satisfaction of the couples undergoing classical eugenics was always low, embryo selection appears now to be the only technique which does not itself oppose their desire to have a child but, in fact rather guarantees certain characteristics of that child. While genetic load is unaffected by the various methods of eugenics, pre-implantation diagnosis can however have strong eugenic implications due to the number of embryos available. Pre-implantation diagnosis is the only non-violent means available to a couple desiring to have, without delay, a baby which is not only 'normal' but in accordance with their wishes (Testart, 1994).

Embryo pre-implantation diagnosis: an original tool for eugenics

The consequence of a large number of available embryos is fundamental if we compare prenatal diagnosis, practised in the course of pregnancy, with pre-implantation diagnosis, an in-vitro technique (Table II). Prenatal diagnosis is performed on one fetus at a time, and its application cannot be required more than once a year for a given couple. When the single screened embryo does not appear satisfactory, the birth of another baby could be delayed for ≥ 1 year. In contrast, pre-implantation diagnosis may concern more than one and even several dozen embryos simultaneously, and this screening may be repeated several times a year. In addition, pre-implantation diagnosis always gives the opportunity for the birth of a baby by discovering one or more 'normal' embryos.

The question then arising is that of the practicability of this pre-implantation diagnosis and its ability to recognize genetic characteristics. After only a few years of experimental removal of blastomeres for human early embryos, it has been established that the technique is easy, not time-consuming and that nearly all the experimental embryos survive. The subsequent genetic screening of the sampled blastomeres may be performed in just a few hours. Embryo freezing during screening therefore appears to be unnecessary. In only 5 years, following the results published by Handyside *et al.* (1989), pre-implantation diagnosis has advanced and can now propose efficient and viable techniques despite the restricted number of cells available for analysis. These results have been obtained with polymerase chain reaction (PCR)-amplification of a single gene or with multiple PCR, allowing several genes to be simultaneously amplified. This approach has also involved

Table I. Advantages of negative eugenic procedures according to the respective target

Target for the eugenic action	Social acceptability	Couple's satisfaction	Effect on genetic load
Adult			
Sterilization	±	-	0
Genetic counselling	+	±	0
New-born (suppression)	-	-	0
Fetus (abortion)	±	±	0
Embryo (no replacement)	+	++	+

+ = positive; - = negative; 0 = no effect.

Table II. Quantitative efficiency of prenatal versus pre-implantation diagnosis. Comparative numbers of potential children submitted to screening

Diagnosis	No. embryos/feti simultaneously screened	No. screenings per year	No. embryos/fetuses screened per year
Prenatal (CVS, amniocentesis, ultrasonography)	1	1	1
Pre-implantation (genetic screening of IVF embryo)	4-20	3-6	12-120

CVS = chorionic villus screening; IVF = in-vitro fertilization.

fluorescent in-situ hybridization (FISH) to reveal the presence of one or several chromosomes. The two techniques, PCR and FISH, have also been used successively on the same cell. These pioneering projects open significant eugenic perspectives since it appears possible to evaluate aneuploidy for five different chromosomes (Munné *et al.*, 1993) and, above all, to look for mutations in 20 different genes (Xu *et al.*, 1993) from a single blastomere. Moreover, initial concerns that the screening of embryos with only 4-8 cells frequently results in errors, have revealed themselves to be largely unfounded. Current work on the conditions of co-culture of the embryo with somatic cells has allowed the in vitro development of the majority of embryos for up to 5 days. It thus becomes easy to improve the reliability of screening carried out on several sampled cells. By cloning the early embryo it should also be possible, as demonstrated in animals (Modlinsky and Smorag, 1991), to obtain several monozygotic embryos available for genetic screening. Furthermore, by isolation and culture of totipotent inner cell mass (ICM) cells from human blastocysts, several millions of identical cells can be obtained (Bongso *et al.*, 1994).

A limit is introduced by the observation of ploidy mosaics, but the future of embryo screening is the detection of mutant genes, and not the establishment of karyotypes. This role will be rapidly confirmed with the application, to the embryo, of ever more numerous diagnoses adapted from those performed on the fetus, the child or the adult.

Let us examine the future conditions of pre-implantation diagnosis with the example of a selection procedure applied

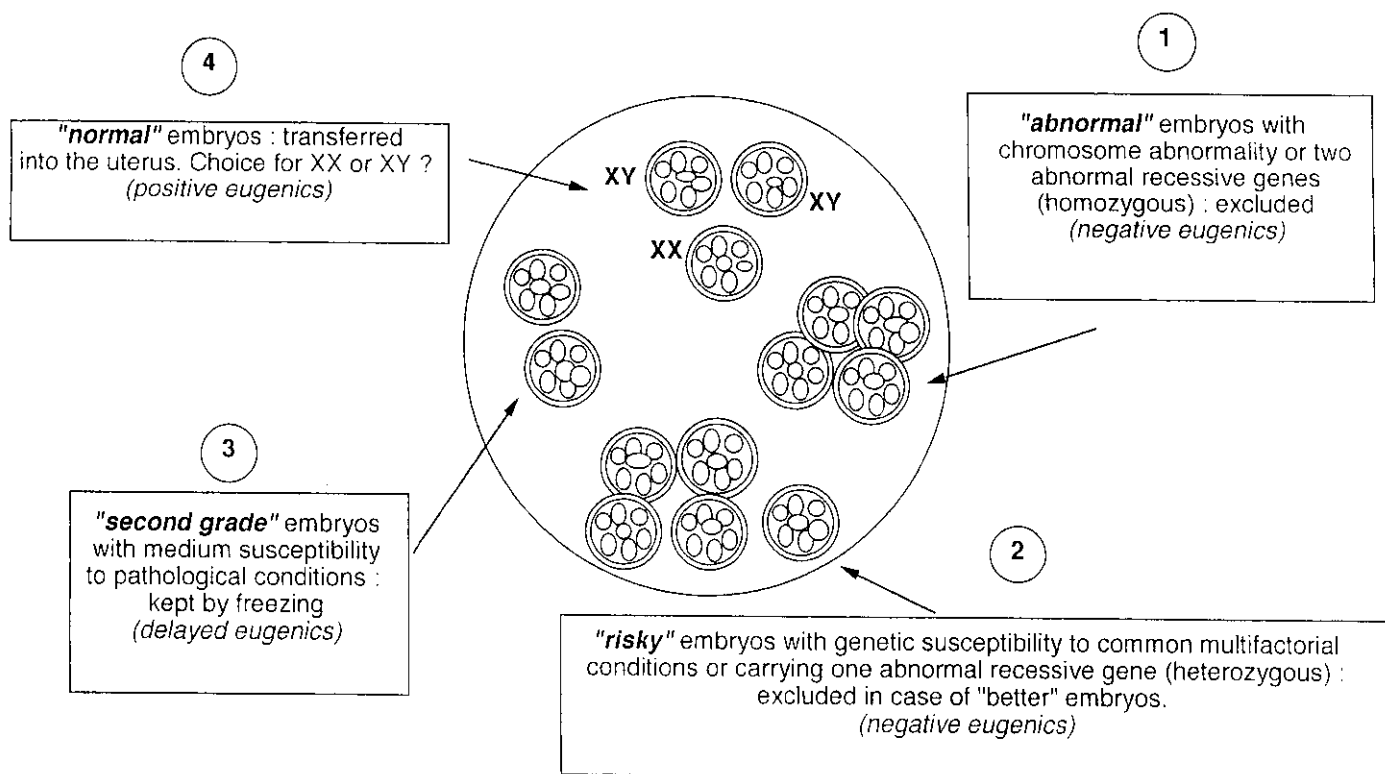


Figure 1. Consequences of positive-negative eugenics applied to embryos simultaneously recovered from one couple.

Table III. Forseeable evolution of pre-implantation diagnosis according to the couple's fertility and the presence of genetic risk

Couple's situation	1	2	3	4
Infertility	No	Yes	Yes	No
Known genetic risk	Yes	Yes	No	No
Medical justifications for pre-implantation diagnosis	Elimination of hardship due to medical termination of pregnancy	Opportunity taken at the time of IVF	Genetic guarantee IVF efficiency (selection of viable embryos)	Personalized request
Limitations to medical action	Couple's medical history/ severity of risk	Severity of risk	Number of embryos available	Inconvenience/ cost of intervention

IVF = in-vitro fertilization.

to 14 embryos obtained through a single IVF attempt, not rare when a woman is young (Figure 1). At first the four embryos which carry very bad characteristics are excluded, in particular those which are homozygous for a serious recessive illness. Then five 'risky' embryos are found for which the failing might be the carrying of some genes statistically associated with pathologies such as diabetes, cancers or cardio-vascular illnesses. (In fact we all possess such genes and that is, by the way, why we are and will remain mortal.) In such cases, the issue is not an automatic relationship between genes and pathology, as other factors like environment later modulate the expression of these genes. But eugenics can take account of those risk factors only because healthier embryos almost always exist in the same series of test tubes. The risk avoided by this approach can also be that of transmitting to future generations the gene of a serious illness; for that reason, a heterozygotic embryo can be discarded, even though its evolution would have resulted in the birth of a healthy child carrier. Once again, that elimination is possible only because other

embryos, free of the incriminating gene, are available. In contrast, this elimination is not possible by using conventional antenatal diagnosis, because the choice involves only one fetus and is based on the phenotypical binary system. It is this element of choice that makes this approach an innovation in eugenic policy. In the same example, two 'second grade' embryos can be identified, which will be acceptable if the transfer into the uterus of the best embryos did not result in pregnancy. Therefore they will be frozen until a future choice. Finally, three embryos will be judged 'normal', which is not to say that they are perfect, as the perfect embryo exists only as a phantasm. Since two males and one female were discovered amongst these three embryos, it would be a lack of kindness to oblige the couple to have a girl rather than a boy.

In this simultaneous screening of numerous embryos, both negative and positive eugenics are applied since, on the one hand, some 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.

From genetic counselling to common eugenics

The average couple desires the production of only one or two babies in the course of their life, which justifies their exigence concerning the 'quality' of these babies. Thus pre-implantation diagnosis, already available to couples suffering from a known genetic risk, could be soon requested by individuals treated for infertility by IVF (Table III); >100 000 embryos already produced by IVF could potentially be analysed each year in France.

Such a derivative has already been observed in France by the introduction of genetic screening for sperm donors and recipients in order to detect their respective genetic risk factors before anonymous matching. According to this policy, a minimum conceptus quality can thus be offered to the infertile patient request (Jalbert *et al.*, 1989). More recently, a case was reported of male embryo elimination after sex determination by FISH, in a woman treated for tubal infertility and fortuitously carrying haemophilia (Veiga *et al.*, 1994). This demonstrates that an initial need for IVF can lead to the prevention of any disease, independently of its severity, by embryo selection.

Genetic screening of embryos will also favour the policy of embryo transfer following IVF; the correct number of embryos for introduction into the uterus will be better defined after elimination of non-viable embryos discovered in the course of screening. Thus pre-implantation diagnosis will also be justified as a way of limiting the incidence of multiple pregnancies, one of the most serious consequences of IVF.

Finally, the new possibility of guaranteeing a certain embryonic quality will also be an incitement for numerous fertile couples to have recourse to MAP. As the access to MAP 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 defects to take advantage of IVF.

Human selection: are we at liberty to choose?

Since pre-implantation diagnosis presents advantages from the medical and eugenic points of view, we should also examine its potential dangers. It is impossible to predict the impact of embryo screening on the human genome since this impact will depend on the number of couples treated as well as on the number of generations involved. The project for the eradication of unfavourable genes is utopian as incessant mutations renew such genes within the population. We know, however, that certain mutant genes are beneficial to the heterozygote: the genes for Tay-Sachs disease, sickle-cell anaemia and cystic fibrosis confer resistance to tuberculosis, resistance to malaria, and increased life-expectancy respectively. In addition, pre-implantation diagnosis can have unknown consequences. In fact, our capacity for genetic manipulation is becoming too large compared to our real knowledge and could lead to the creation of irreversible situations. As demonstrated by Hubbard and Wald (1993), the gene myth is associated with simplistic

explanations while reality is much more complex than molecular genetics tells us. Contemporary ecological problems in various parts of the world caused by exoticism—for instance the importation in the 19th century of would-be beneficial plants—should serve as an example of the danger we pose to our genetic heritage.

We can ask ourselves whether the possibility of choosing, in the embryo, the sex of one's child belongs to the concept of woman's liberation or whether it does not flow from choices which 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 which 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, this would be seriously compromised by the obligation to gratify the parents by giving them their choice. If such embryonic sorting has to be considered beneath the dignity of humanity it is not because it can be assimilated to an 'in-vitro abortion'. Rather it is because it 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 of humanity.

If the choice that parents impose upon their children is not truly their own, then whose is it? For reasons associated with economy and 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 pseudo-scientific 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 that it can foresee the risk of pathology and to evaluate 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 their maintenance. These perspectives, 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 the citizen whose lack of competence would lead him 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 led to an examination of the various means of restraining the use of pre-implantation

diagnosis. We cannot place our confidence in medical guidelines since doctors are exposed to the extreme pressure exerted by patients and industry. Moreover, like all human beings, physicians and geneticists are sensitive to their personal interests which operate by their impact on financial success or the search for power. It has been said that patients' innate sense of responsibility will 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 is also their right to choose their child, as soon as this becomes possible. In countries like France, where the social security system takes responsibility for the entire cost of MAP, the citizens may consider that their contribution to the system gives them the right, too, to be taken care of, both technically and financially, in the production of quality children.

It was also proposed that medical screening of embryos should 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 and for the dignity of all human beings proclaimed by our societies and even in conflict with the concept of human rights.

Rather than limiting the medical indications, it has then been suggested that the right to screen embryos should be limited to a short list of doctors and geneticists. Experience proves that the certification thus accorded to certain practitioners renders difficult any eventual control over their activity. Moreover, this exclusive right to a medical practice reserved to a select few could, in the absence of competition, provoke their excessive financial demands and poses the risk of a medico-genetic monopoly which would invent its own rules.

Therefore the creation of controlling committees has been suggested. But how can criteria be applied 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 which would evaluate each medical request even before embryonic screening. This proposal is the least bad if several conditions exist: the committee must include others beside professionals of genetic screening, biomedical acts without the committee's authorization must be considered as illegal, and the committee would have to produce a full public report annually. Moreover, such regulation of eugenics could only be effective if all countries abide by the same rules. Otherwise, medical tourism would limit access to eugenics only to those who could afford it.

In conclusion, the scenarios inspired by the imminent union of MAP with genetics are in line with our society's mode of development (Testart, 1993). 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 species, normally monovulatory has become polyovulatory and even polytocous. Until the present, eugenic refinement of social competition has been only approximately achieved with IVF: the viable embryos are transferred into the uterus, those not viable are eliminated from the human reproductive circuit, and the doubtful ones are in a stand-by unemployment population, in laboratory freezers. The new possibilities offered by the genetic screening will allow the elaboration of the criteria of choice, and promise, not without some illusions, to produce individuals who conform better to the social and economic ideal. What is in the making is a veritable revolution in ethics transcending the frontiers of any given country. It is up to us to respond, as we are today responsible for the production of future generations. This response must be realistic insofar as it concerns our true mastery of the genome. We have to recognize that we know very little about the functioning of what we are preparing to modify without scruples. 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 performance, individual interest and naive desire, the problems are more complex than we are led to believe. We ought to approach these problems with a concerted effort and determined humility to uphold the ethical dimension of human life.

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