ADVANCES IN MEDICAL GENETICS PROSPECTIVES AND ETHICAL PROBLEMS

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The astonishing and troubling appeal of Nobel Laureate H.J. Muller [1] to human geneticists, convened at the Third International Congress of Human Genetics in Chicago in 1966, to engage in a strong "offensive for the control of human evolution" was founded upon the premise that "modern culture by maximal saving of lives and fertility, unaccompanied by a conscious planning which takes the genetic effects of this policy into account, must protect mutations detrimental to bodily vigor, intelligence or social predisposition" (p. 526).

A few years later, 1972, his statement was confirmed by a Technical Report of the World Health Organization. [2] A group of geneticists estimated that, if in the next generations all the subjects who up to now could not reach the age of fertility would reproduce, then the incidence of polygenic diseases should have increased 3-5% per generation, and the incidence of monogenic diseases should have increased 15% per generation, and would be doubled after seven generations.

Muller's appeal and proposal were echoed and supported by other distinguished geneticists, [3] among whom T.M. Sonneborn and J. Lederberg. The offensive for the control of human evolution had to move along three main lines: rigorous genotype selection, germinal choice and gene manipulation.

Medicine felt inevitably involved in that enterprise, and medical genetics developed as a new branch of human genetics. [4] From that time on, many important and beautiful pages were written in the history of medicine as a result of close collaboration between clinics and the newly developing areas of genetics: cytogenetics, mathematical and population genetics, immunogenetics, biochemical genetics and molecular genetics, to mention only a few. But many ethical problems emerged also.

Our aim, here, is firstly to give a glance to the main scientific achievements of medical genetics and to the great prospectives open to medicine, and secondly to briefly analyse a few hot spots where the ethical tension is stronger, in order to understand its underlying reasons.

Conquests of medical genetics

In the 1960s and 1970s an extraordinary number of new genetic diseases and congenital anomalies were discovered due to either *chromosomal aberration* [5] or to *single gene mutations*, with the number of the latter increasing from 1487 in 1966 to 2811 in 1978. [6] Most important, with the use of new biochemical techniques it was possible to demonstrate, in a number of genetic diseases, either a reduction or accumulation of certain metabolites, or a deficit of functionally significant proteins, suggesting that defect of *enzymes* or *structural proteins* were the primary effect of gene alteration. [7]

By 1980 the responsible molecular defect had been elucidated for about 200 genetic diseases: a great step forward indeed, although this represented less than 10% of the conditions proved or suspected to be due to single gene mutation. Furthermore, for many of these diseases not only the *etiology* could be studied extensively but also the *pathogenesis*; [8] and valuable genetic parameters, like *gene frequency, heterozygote incidence* in the populations and *segregation patterns* in the families had been established. [9] Attempts to identify heterozygotes for deleterious genes had also been made: but they frequently proved unsuccessful, due to ample estimates overlappings between controls and carriers, or unjustified because of their rarity, or even impossible, because of a lack of reliable detection methods. Finally the cytological observation of the presence of chromosomal abnormalities in tumour cells had opened the way to the study of the *genetics of human cancer*. [10]

No effective treatment or cure for genetic diseases was then possible. Yet, remarkable improvements in *ultrasonography* and *fetoscopy* had paved the way for the introduction and diffusion of *prenatal diagnosis* [11] in medical practice. By the end of 1977, two largest surveys on prenatal diagnosis of pregnancies at risk reported from United States and Canada (13,785 pregnancies) [12] and from Western Europe and Israel (11,334 pregnancies) [13] had shown that the number of fetuses affected by genetic diseases in the second trimester of pregnancy is approximately 4-6%.

In the 1980s the explosion of new technologies, [14] that followed the brilliant discovery of *recombinant DNA* by the Nobel Laureate P. Berg, [15] caused the *molecular revolution* in medical genetics, that altered altogether the direction of the search: the major target was no longer the defective products of mutated genes,

but the genes themselves, their precise error and their direct effects. The 127 papers presented at Cold Spring Harbor in 1986 under the title "Molecular Biology of Homo Sapiens" [16] give an idea of the exciting successes of this new era of human and medical genetics.

In less than ten years, more than 450 disease genes, [17] including oncogenes and tumor suppressor genes, [18] and approximately 3300 anonymous polymorphic DNA sequences [19] were mapped into human chromosomes, the latter representing extremely useful markers for locating coding genes through linkage studies. [20] The ten volumes reporting on the International Workshops on Human Genome Mapping are a testimony of the immane efforts accomplished, and of the great successes obtained. H. Ruddle and K.K. Kidd [21] while announcing in the tenth volume the formalization of the "Big Science" Human Genome Project that was increasing the hope "to view the human gene map in its largely completed form some years hence" (p. 2), could be very proud and satisfied for the great success already obtained by the 'little science' in the discovering and analysis of human genetic information.

In the time span of approximately six years from the starting of the Human Genome Project (1989-1995) in the United States and in other countries, [22] its knowledge increased exponentially. The first goal was the preparation of a sufficiently precise *physical map* of the *chromosomes* that is of the 24 volumes containing the human genetic information, by ordering the thousands fragments, in which the chromosomes had been broken. [23] The main efforts are still being devoted to a second goal, that is, the discovering of all the *coding genes* and the construction and continuous adjournment of the *genetic map*: to date, more than 15,000 *markers* were localized at an average distance of 200 kilobases along the chromosomes; and *sequence data* are available for approximately 5,000 *coding genes*, while 25,000 additional genes are represented by *Expressed Sequence Tags* (EST). [24] A major step has been the characterization of 87,983 unique partial complementary DNA sequences expressed (ESTs) in 37 human tissues at various stages of development, [25] 124 of which represent *oncogenes* or *tumor suppressor genes*.

Contemporaneously the *molecular analysis of mutated genes* [26] - such as those of the hemoglobinopathies, hemophilia, cystic fibrosis, muscular dystrophies, miotonic dystrophy, spino-cerebellar ataophy, Huntington Chorea, Fragile-X syndrome and Retinitis pigmentosa, oncogenes and suppressor genes - not only

disclosed the great number of *mutations*, either at a given locus or at different loci, that may be responsible for a given disease, but also led to the discovery of the *specific products* of the normal genes,[27] thus facilitating the understanding of the *pathogenesis* of *single gene*, and also *poligenic*, diseases. [28]

Prospectives of Medical Genetics

As a consequence of these uninterruptedly continuing advances, the *identification* of both *patients* and *heterozygous carriers* of deleterious genes became relatively easy by *postnatal, prenatal* and *pre-implantation* diagnosis. [29]

The enthusiasm of medical geneticists went still further. Tissue culture and *in vivo* animal experiments had shown that purified genes could be transferred into mammalian cells, function sufficiently well in them, and even cure them. [30] Thus, the prospective of *somatic cell gene therapy* appeared attainable. [31] Further investigation, aimed at making the transfection more regulated and the risk of insertional mutations minimal, could finally substantiate the proposal of the first projects of human gene therapy in 1991. [32] By the end of October 1994 [33] more than 200 protocols for gene therapy experimentation in humans were approved in United States and the patients treated were over 300, mainly for cancer, genetic diseases - cystic fibrosis, Gaucher disease, ADA deficiency, hypercholesterolimia 1, alpha-1-antitrypsin deficiency 1, Fanconi's anemia 1, Hunter syndrome - and AIDS.

It must be stressed, however, that we are still in a phase of "cautious optimism", as W.F. Anderson stated in 1991, and with still greater emphasis confirmed in 1994 [34] when, concluding an Editorial, he wrote: "The long term potential of genome science and gene therapy is extraordinary great. I have repeatedly argued that gene research should be strongly supported because it is the best prospect that we have for curing, and preventing the scourges that now claim so many lives: cancer, heart diseases, etc. Those of us in this field need to be careful, however, to provide realistic appraisals of the potential benefits and risks, as well as realistic estimates of how long it will take before society will see significant benefits. If we generate false hopes, the backlash when we cannot produce on schedule could be significant" (p. 1078). Indeed, as he stated more recently [35] "the results from the dozens of clinical trials are very encouraging in one sense, but discouraging in another (...) The gene transfer technology itself appears extraordinarily low in risk

at this point in time. Nonetheless, what we want to see is efficacy - we want to see patients getting better. We still only have two little girls with ADA deficiency, one familial hypercholesterolemia patient, and a few scattered cancer patients who have shown positive response" (p. 1432).

This situation, very well recognized by thousand researchers in the field, continues as yet: on May 1996, D.T. Zallen, [36] while underlining the vigor of scientific and biotechnology research and the encouraging signs of the field, made clear that "human gene therapy is still in its embryonic stages", that, "despite all the hope, promising results are scarce and the difficulties are legions" (p. 796), and that there is the need to "bring the troubling ethical and scientific questions to public view" in order "to proceed carefully and to flourish with broadly based public support" (p. 797).

Simultaneous to these developments, refinement of gene transfer, including *direct microinjection of genes into cell nuclei*, and progress in embryology allowed a major advance toward the goal of gene therapy. [37] It was shown that cloned DNA could be found in the cells of newborn mice when it was injected into the pronuclei of fertilized mouse eggs, and that the newly acquired genes were transmitted to the germ lines of these *transgenic* mice. Subsequently, their quantitative and tissue specific expression appeared controllable, and accurately designed experiments explored, in mice, the potential, of gene microinjection in germ cells for gene therapy. A number of successes were obtained. To recall only a few: [38] a partial correction of murine hereditary growth disorder; the cure of beta-thalassaemic mice by transfer of human adult beta-globin gene; the restoration of reproductive functions in expected hypogonadal mice, deficient of the gonadotrophin-releasing hormone because of the absence of normal gene, after germinal microinjection of the cloned wild-type *GnRH* gene. Yet, here also, a rigorous analysis of the results obtained so far in experimental animal models shows that the prerequisites for good success - that is, that gene transfer be harmless, efficient, and certain to result in physiologically significant expression - are all far from being satisfied.

While the search for gene therapy via somatic and germinal cell lines continues actively despite the rare successes, other techniques are being developed on the germe line with the aim of *preventing implantation*, or even *conception*, of embryos carrying disease genes: the DNA of one or two cells biopsied from 8 to 16 cell embryos, or of the first polar body of a mature oocyte, can now be easily analized

for the presence of a suspected abnormal gene. [39] The introduction of these techniques into medical practice is now largely spreading.

The ethical tension

All these advances in Human and Medical Genetics and their actual or attempted application in clinical practice deserve admiration and consideration. However, it is undeniable that a strong *ethical tension* did and still does accompany this tremendous progress. Very wisely the founders of the Human Genome Project [40] decided, from the very start, that at least 3% of the annual financial funds for the Project should be spent to support the Ethical, Legal and Social Implications (ELSI) Program, an amount that increased to 5%-7% in subsequent years. Indeed, it was perfectly clear that a project which: a) would have afforded knowledge and possibilities for diagnosis, treatment and prevention of genetic disorders and diseases; b) would have thrown light on the evolution of the human species and the development of human individuals; and, finally, c) would have set bases for the exploration of the biological components of human behaviour, should have also included potential risks of abuses of the acquired knowledge.

Some dissent on this point and think that actually no new ethical problems are to be faced. [41] J. Maddox, [42] for instance, in his paper "New genetics means no new ethics", contended: "There is also a temptation to believe that new laboratory techniques mean new applications and thus new ethical problems. But this is not the case (...) This new knowledge has not created novel ethical problems, only ethical semplifications (...) Is it not a welcome improvement ... that, when the impending birth of a child with a genetic disease can be determined by amniocentesis, most governments should allow abortion?" (p. 97).

Others, [43] because of incorrect or incomplete information and/or emotional excitement were led to an irrational condemnation and indiscriminate ban on these new scientific approaches to very serious human problems.

However, an increasing number of well-informed humanistic groups and scholars, and even a number of the most enthusiastic leaders in the development and application of the new technologies to medical genetics, show a deep-rooted concern about the possibility of misuses, and demand clear lines to be drawn between what is permissible and what is not. [44] An example is the letter that C. Thomas

Caskey, [45] President of the ASHG and chairman of the ASHG Human Genome Committee, wrote to J. Watson, at that time Director of the National Center of Human Genome Research at NIH. "The acquisition of new information - he writes - does not guarantee its use in a way that is to the benefit of mankind, respecting the prevailing views of society and the dignity of the individual. Members of the ASHG deal with such issues on a daily basis in their role as physicians, genetic counselors, and laboratory directors, providing sensitive and highly personal information about the future health of the individual and the family. There is need for resources to fund a continuing dialogue on the ethical, social and legal implications of the genome project. In addition to the workshops and symposia on this topic, there is a need both for careful research to establish the exact nature of the problems to be anticipated and for educational programmes to prepare experts in legal and ethical decision making in the field of medical genetics. These needs arise not only out of the genome project itself; they are with us already as a result of the cloning of several of the most important disease genes. The genome project will, however, exacerbate the problem as the availability of diagnostic reagents for the common multifactorial diseases brings the technology to a much larger segment of the population, and as screening programs for common genetic disorders bring the genetic knowledge to a majority of the population" (p. 689).

This highly sensitive attitude toward the ethical problems emerging from the development of the Human Genome Project and genetic engineering is constantly increasing and spreading among scientists, technologists and the public. However, the different ethical views render consensus difficult, whichever the proposed solution might be, or even impossible: wherefore the ethical tension must necessarily arise. Here we shall briefly touch on three hot spots.

The "early embryo" *a disposable* object *for experimentation?*

Research on the human genome has essentially two main aims: 1) the knowledge of the genome's *physical* and *genetic structure*, through the sequencing of the total DNA and the complete mapping of genes; and 2) the structural and functional analysis of single normal and abnormal genes, and their interactions.

The first type of investigation is generally done on the somatic cells' DNA, and does not entail particular ethical problems. It only demands professional honesty that, in some cases, may impose a rapid communication of available new data,

mainly of those that might accelerate new applications for a better knowledge and treatment of genetic diseases.

However, since 1987, *preimplantation embryos* are not excludable from the second type of experimentation. Their DNA is being used for many scientific purposes, among which: 1) the discovering of the main causes of failure in assisted reproduction; [46] 2) the setting up of easy diagnostic techniques for the pre-implantation detection of abnormal genes; [47] and 3) the analysis of activation and function of genes in the very early phases of human development, [48] as a premise to germ-line and/or early embryo gene therapy.

W.H. Anderson himself, [49] the pioneer of gene therapy, while remarking that "on medical and ethical grounds a line should be drawn excluding any form of enhancement engineering" (p. 689), stresses the idea that "as experience is gained, the line should be moved to include possibly germ line gene therapy for specific diseases" (p. 690). Actually, by the end of September 1994, 70 experimental protocols on this line of research were already in the hands of special Committees for approval. [50]

The reasons of those who insist that research on pre-implantation human embryos is a necessary step for the good of man cannot be disregarded. They are summarized in a note entitled "Embryo research: why the Cardinal is wrong", [51] issued by the President of the British Medical Association and the Royal Society of Medicine soon after the English Houses had approved the law allowing early embryo experimentation: "The potential benefits to society and to suffering humanity will be uncalculable. To have rejected its sensible and humane provisions would have dealt a devastating blow to the future of medicine and biological science, and, I believe sincerely, to that fundamental principle of Christian ethics of aiding those less fortunate than ourselves" (p. 186).

With sincere respect for all those who have such a profound convinction we think, nonetheless, that one cannot ignore the following considerations. In every experimentation on fetuses and mainly - at least in current practice - on newborns or on grown up people, where genetic engineering is applied for diagnostic or therapeutic purposes, the *human being* during all steps of experimentation is always considered and treated as a ***human subject***, respecting his dignity and rights, among which the rights to life and to integrity. A proof of this are the rules published by many Committees for the revision and approval of submitted experimental protocols

and for the patient's consensus. [52]

The *experimentation on very early human embryos*, on the contrary, appears subtracted to this principle. Whichever the origin of the embryos, either purposely facbricated or selected among the spare ones from assisted reproduction, they are considered and treated as pure ***producible and disposable objects***, which - according to laws already existing (England) or in preparation (United States and France) [53] - must be *destroyed* between the 14th and the 18th day after fertilization. Evidently the human embryo's *dignity* and *rights* as a real ***human being***, who is autonomously developing and exploiting its potentialities, are violated.

The reasons advanced by those who support the need to experiment on human early embryos for the advancement of science and medicine are understandably only *within a logic* where the human embryo is absolutely *deprived of humanness* and, consequently, of its corresponding *moral value* as a *human subject*. This position, however, has neither biological nor metabiological foundation. [54]

The explicit conclusion reached on this respect by the Warnock Committee [55] is very clear: "While, as we have seen, the timing of the different stages of development is critical, once the process has begun, there is no particular part of the developmental process that is more important than another; all are part of a continuous process, and unless each stage takes place normally, at the correct time, and in the correct sequence, further development will cease. Thus biologically there is no one single identifiable stage in the development of the embryo beyond which the in vitro embryo should not be kept alive. However, we agreed that this was an area in which some precise decision must be taken, in order to allay public anxiety" (p. 65). The decision was: "The legislation should provide that research may be carried out on any embryo resulting from in vitro fertilisation, whatever its provenance, up to the end of the fourteenth day after fertilisation" (p. 69). Without any doubt, in this decision socio-political reasons prevailed on both the logical coherence and the ethical reason!

The view of the Catholic Church on this point can now appear in its true significance and value. Consistently with Her ethical perspective, and in accordance with the scientifically based conclusion that *from the zygote state a true human subject starts its own life cycle*, she declares: [56] "Thus the fruit of human generation, from the moment of its existence, that is to say from the moment the zygote is formed, demands the unconditional respect that is morally due to human

being in his bodily and spiritual totality. The human being is to be respected and treated as a person from the moment of conception; and therefore from the same moment his rights as a person must be recognized, among which in the first place is the inviolable right of every innocent human being to life" (pp. 13-14).

As a consequence and coherently, the Catholic Church cannot consider ethically right any kind of experimentation on very early human embryos conducted with the *exclusive* aim of research. If, and only if, the scientific progress, made by respecting the above mentioned requirements, could reach the point of permitting a safe and effective gene therapy also in very early human embryos, then and only then an experimental therapeutic approach would licitly be applied, given all the conditions and warranties requested for any therapeutic experimentation in human beings. Quoting from her document: "In the case of experimentation that is clearly therapeutic, namely, when it is a matter of experimental forms of therapy used for the benefit of the embryo itself in a final attempt to save its life, and in the absence of other reliable forms of therapy, recourse to drugs or procedures not yet fully tested can be licit" (p. 17).

The «genetically mistaken» *fetuses: should they be born?*

The possibility of discovering, through prenatal or pre-implantation diagnosis, a human subject who has a *wrong gene* that, sooner or later, will seriously affect the quality of its life, is steadily increasing. Suffice here to recall the easy detectability of genes as those involved in Mediterranean anaemia, sickel cell anaemia, cystic fibrosis, Tay-Sachs disease, Duchenne and Becker muscular dystrophy, myotonic dystrophy, spinal muscular atrophy, spinal cerebellar atrophy, Huntington's chorea, Fragile-X syndrome and a number of tumours.

Negative eugenics, through selective termination of affected embryos or fetuses is, at present, the policy of choice, to such an extent that most feel this practice as a *social obligation*. A great exacerbation of this policy is expected as a consequence of the new advances in gene mapping. Yet, the ethical tension in this area is still considerable.

To some people this practice is *good* and, in some case, *compulsory*. According to H.D. Aiken [57] of the Department of Philosophy of Brandeis University at Waltham (Mass) "claims regarding the right to biological survival are entirely

contingent upon the ability of the individual in question to make, with the help of others, a human life for himself. This means that in circumstances where there exists no possibility of anything approaching a *truly* human life, the right to biological or physical survival loses its own *raison d'être* and hence that the merciful termination of life, in the biophysical sense, is acceptable or perhaps even obligatory" (p. 180).

To some others, among whom the council of Churches, [58] the "decision for foetal diagnosis and abortion is a *weighty decision*, as the foetus, although still dependent, has a potential existence as a human being. The decision to deprive it of that potentiality depends on a conclusion that the *detriments* resulting from its birth *outweigh the benefits*" (p. 207). Here, the ethical principle is more restrictive, but the conditional criterion practically cancels any limitation, thus opening the door to unlimited relaxation. As a matter of fact, what only a few years ago was considered ethically wrong - such as the selective termination of a Klinefelter or a Turner fetus or a fetus of an undesired sex - is now becoming a routine; and there are pressures to extend prenatal selective termination to heterozygous carriers of defective genes.

The Catholic Church, on her side, is not against prenatal diagnosis itself. To the question: "Is prenatal diagnosis morally licit?", she answers: [59] "If the prenatal diagnosis respects the life and integrity of the embryo and the human foetus, and is directed towards its safeguarding or healing as an individual, then the answer is affirmative" (p. 14). Those who, in the Catholic Church, are responsible for the doctrine are well aware of the anxiety of many women during gestation, due mainly to their cultural environment, and of the relief that most of these women can receive from prenatal diagnosis. She is also aware of the dramatic situation of the parents in the case of a «*bad*» diagnosis. In her view, however, even in such a dramatic circumstance an unhealthy unborn human subject, and - *a fortiori* - a healthy foetus that will or may become ill later in life, both are *innocent human beings* who have absolute right to life. Therefore, she teaches that abortion, even in these cases, is morally illicit.

The «bad gene» *carriers: what their future?*

In *families* where there is a case of genetic disease, in general - unless it is due to casual mutation - there are, because of segregation, *healthy carriers* of the deleterious gene, who can be at risk of transmitting the disease and/or of becoming ill themselves.

In *a population,* one can also find *healthy carriers* of many bad genes that are nowadays detectable, and whose number will greatly increase in the years to come. For instance: in Europe, approximately 1 over 20-25 subjects carries the cystic fibrosis gene; in certain Mediterranean countries 3-5 over 30 subjects are carriers of a serious anaemia gene; in Ashkenazic Jews 1-2 over 100 carry the Tay-Sachs disease gene. All the healthy carriers have an appreciable probability of forming families at high genetic risk for their children.

The identification of *bad gene carriers* became progressively easier through the advances in the Human Genome Project and the growth of industrial genetic engineering. Therefore the interest in *predictive testing* and *presymptomatic screening* is exponentially growing, among both specialists and the public, due mainly to commercial pressure. To give but one example, according to sources of the Office of Technology Assessment (OTA), the number of cystic fibrosis carrier tests in the United States increased from 1,854 in 1989 up to 63,000 in 1992. [60]

The diagnostic application of genetic knowledge undoubtedly opens new perspectives for *preventive medicine*. The identification of subjects at risk coupled with competent and responsible counselling in order to inform and enlighten carriers concerning, first of all, their reproductive personal choices, could lead: 1) to a *primary prevention* for genetic diseases, that is to avoid the conception of human subjects who will be affected by serious disorders, thus contributing to the preservation and promotion of the quality of life in families and populations; 2) to a *psychological relief* for all those who could be assured that they do not carry a specific bad gene; and 3) to the *alleviation of unavoidable distress* for those who are indeed bad gene carriers and should - with high probability - become ill later on, by suggesting possible preventive measures and, hopefully in the near future, also providing convenient and effective therapies.

However, serious ethical problems arose also from such important advances in the effort to safeguard the health of persons, families and society.

1. The *assisted reproduction*, that is offered not only to families suffering because of *sterility* or *infertility* but also to those *at risk* of having *children affected by genetic disorders*, is a new field full of emerging ethical problems. Actually it is a medical practice that is rapidly spreading and becoming more and more common, supported by national and international bioethics Committees and, in many countries, guaranteed by law.

Although it is commonly accepted, there are different views on the many correlated ethical and deontological aspects. Most rigorous is that of the Catholic Church. It is condensed in the following statements:[61] "Conception in vitro is neither in fact achieved nor positively willed as the expression and fruit of a specific act of the conjugal union. In homologous IVF [in vitro fertilization] and ET [embryo transfer], therefore, even if it is considered in the context of 'de facto' existing sexual relation, the generation of the human person is objectively deprived of its proper perfection: namely that of being the result and fruit of a conjugal act in which the spouses can become cooperators with God for giving life to a new person" (p. 30). The Church teaches, indeed, "the inseparable connection, willed by God and unable to be broken by man on his own initiative, between the two meanings of the conjugal act: The unitive meaning and the procreative meaning" (p. 26).

At the same time, however, the Catholic Church, after noting that "a medical intervention respects the dignity of persons when it seeks to assist the conjugal act either in order to facilitate its performance or in order to enable it to achieve its objective once it has been normally performed", urges scientists and physicians to continue their research in order to find more human ways to relieve the anxieties of those families which are sterile or at risk for genetic diseases. It is, indeed, to be hoped that further progress in the search for the *selection of genetically healthy oocytes* and of ***in vivo** fertilization techniques* will provide a human as well as morally acceptable way.

2. The application of *predictive* and *presymptomatic tests* in view of epidemiological genetic surveillance is the second field where many ethical and deontological problems are being opened. There is a strong pressure to start or to accelerate, *at the population level* [62], at least some of the possible screenings, mainly in order to find healthy carriers of defective genes - among which those for cystic fibrosis, Duchenne muscular distrophy, myotonic dystrophy, phenylketonurea and some tumours. In this area, possible *conflicts* of the *individual's rights* to freedom of choice and privacy with other people or *community rights* are to be expected, and in fact do exist.

The ethical controversy is still pending [63] and no general solution appears to be possible. However, in the light of the basic ethical principles of *justice*, *equity*, and *respect of the dignity* of every human being, efforts are being made to establish some rules that could help meet these requirements [64]. The Recommendations relative to «genetic screening» promulgated by a Committee of the Institute of

Medicine of the National Academy of Sciences in United States [66] - constituted by medical geneticists, genetic counsellors, pediatricians, ethicists and lawyers - are consistent with the above mentioned requirements. Among those Recommendations the following are declared as absolutely necessary: *voluntary participation*; genetic information and counselling about the benefits and risks of testing procedures, the possible outcomes and the available options; more rigorous education and training of health care providers in the area of genetic testing and counselling; restriction, for single gene disorders, to conditions of a relatively high frequency either preventable or treatable; caution over the use of genetic tests to determine a person's susceptibility or predisposition to genetic disorders that can occur later in life; finally, protection of individuals against discrimination from health insurers and employers.

As to the last requirement, the results of rigorous surveys are very impressive. [67] The Division of Genetic Medicine of the California Pacific Medical Center at S. Francisco [68] has overtly denounced that "genetic discrimnination exists and is manifested in many social institutions, especially in the health and life insurance industries. Stigmatization, and denial of services or entitlements to individuals who have a genetic diagnosis but who are asymptomatic, or who will never become significantly impaired is noted" (p. 476).

Here we have yet a further and clear example showing that progress, if it is not constantly accompanied by appropriate ethical considerations, can easily turn against man himself.

The Catholic Church for the respect of human dignity and rights

One reason that could explain at least part of the ethical tension in this era of profound cultural changes is the lack or difficulty of understanding the teaching and the proposals of the Catholic Church. She [68], as well as all other religious groups [69], feels the urgency of facing the above issues and all others involving man. She recognizes and highly appreciates the intrinsic value of basic scientific research, and attributes great importance to applied investigation: indeed, as far as her religious view of the world is concerned, both *research* and *technology* "constitute a significant expression" of "the dominion over creation" (p. 5), which is entrusted by the Creator to man. At the same time, however, she feels as her essential duty: firstly, to examine all the aspects concerning human responsibility

in the manner of acquiring knowledge and in the applications that inevitably follow new discoveries; and secondly, to help - through her teaching - the Catholics first of all, and then anybody else who so wishes, to see the reasons why some ways of acquiring knowledge can be incorrect, and for what reasons some applications of scientific results may be ethically unacceptable.

While doing so, however, she is *profoundly respectful* of all those who, with a sincere - although often uninformed or scarsely informed - conscience, may hold and/or follow other opinions. She is aware of the fact that the cultural background upon which individuals or societal groups base their ethical principles of human behaviour may be greatly at variance; and, moreover, that this cultural background, whichever its origin, constitutes for every human person a true fundamental heritage, both intellectual and emotional, that has indeed for each one of us a great significance and value, and is therefore difficult to remove or even to question. It is with this sense of respect that she wants to fulfill her duty.

The *general ethical perspective* of the Catholic Church is, certainly, far from that of those [70] who think that "ethics as such is not an objective discipline", but "represents and reflects the customs accepted by a society", which under the impact of the scientific and technological development "will continue to modify" and, therefore, "tends to employ principles that vary with time and people" (p. 14). It seems quite obvious that, for all those who agree with this view, no general common principles can be found from which one can derive common ethical imperatives. If, however, one could consider man's *nature* and *dignity*, that is *the human person's* integral reality he would certainly recognize that it is his or her innermost self that can dictate the laws for the right behaviour. This principle was vigorously reiterated by John Paul II in a recent address to the Members of the Pontifical Academy of Science [71]: "One must not allow himself to be fascinated by the myth of progress, as if the possibility to make a research or to set up a technique could immediately qualify them as morally good. The moral goodness of any progress is measured from the genuine good that it affords to man taken in his double corporal and spiritual dimension. When man is the point of interest, the problems overflow the field of science, which can neither give any reason of his transcendence nor dictate moral laws that derive from the central position and his primordial dignity in the universe" (p. 5).

Conclusion

The progress and great promises of science and technology in the very frontier fields of human and medical genetics are stupendous and exciting. All the steps were accompanied by the emergence of many ethical problems, which are still a matter of controversy.

The desire of the Catholic Church is to offer a contribution to the ethical reflection on the new problems that are continuously emerging from this scientific and technological progress. In this study we have simply proposed her essential thoughts concerning a few ethical problems that have arisen in the field of human genetic research, and of the medical application of new genetic technologies, which are expected to grow and expand very quickly under the powerful impulse of the rapidly developing Human Genome Project.

Undoubtedly, one cannot help having the impression of a *rigorous* and seemingly *intransigent* doctrine. This is probably one of the reasons for the resistance and opposition to her teaching. Yet, the *true spirit* underlying that doctrine is emphasized in the following few lines in the introduction of the Document «Donum Vitae», here abundantly quoted: "The Church's Magisterium having taken account of the data of research and technology, intends to put forward, by virtue of its evangelical mission and apostolic duty, the moral teaching corresponding to the dignity of the person and to his or her integral vocation. It intends to do so by expounding the criteria of moral judgment as regards the applications of scientific research and technology (...) These criteria are the respect, defence and promotion of man, his primary and fundamental right to life, his dignity as a person who is endowed with a spiritual soul and with moral responsibility. The Church's intervention in this field is inspired also by the love she owes to man, helping him to recognize and respect his rights and duties" (p. 6).

It seems, however, that, independently of the intervention of the Catholic Church, the *ethical tension* that permeates the most advanced frontiers of medical genetics would not easily subside, due to the predominant pluralistic cultural structure of our society. Given this situation, all the efforts to find rules, to establish deontological codes, and to dictate laws in these areas might be helpful for preventing gross abuses. But only a profound sense of *human responsibility*, within the *scientists* involved in the making of science, as well as among *physicians* and *society* as they apply new scientific achievements, will be the best guarantee for a *real* and *respectful*

service to man. It is to this sense of responsibility that R.N. Proctor, [72] an historian of science, was strongly appealing after revealing the pitfalls of a «value-free-science»: "It is the duty of science, in the face of its public, to understand the conditions of its freedom, but also the responsibilities brought forth by that freedom" (p. 271).

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