PRENATAL GENETIC TESTS:
MISCONCEPTIONS AND THEIR IMPLICATIONS

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1. INTRODUCTION

The earliest research on prenatal diagnosis was conducted around 1967, and such studies have continued until today, when it is possible to test for more than 100 genetic diseases. The social utility of prenatal diagnosis is focused on the possibility of fetal testing for genetic diseases in which an urgent appropriate intervention can lead to a normal phenotype—or in other cases, to a therapeutic abortion.

Of course, not all women can be subjects of this kind of test. There are two reasons that justify this affirmation:

a. First, all of these techniques imply a risk of fetal loss. In some cases, this risk is higher than the risk of fetal disease. For example, the incidence of Down's syndrome in babies born of women between 30 and 34 years of age is 1.54/1,000; however, the risk of an abortion following the use of the technique is 0.6-0.9% (Hubbard and Henifin, 1985).

b. Second, these tests are very expensive. Because of this, they are restricted to groups of women for whom the probability of finding a fetal anomaly is higher than average. (These are called groups at risk.)

In the early years, it was easy to distinguish between serious and less serious diseases; today, genetic diagnosis gives us the possibility of detecting predispositions (e.g., a tendency to develop bipolar disorder or cancer), and such simple genetic conditions as the sex of an individual. Along this line, in some countries it is common to apply for cytogenetic testing with the only purpose being to select the sex of the fetus (Nelkin and Tancredi, 1989).

The technological possibility of knowing a genetic sequence whose presence predisposes an individual to suffer an illness or simply to manifest a concrete phenotype, in my view, contributes to biasing the balance between

phenotype and genotype, and to reinforcing a biologism present in one way or another in our society.

In other words, when it is possible to detect a relationship between a piece of DNA and illness—for example, certain kinds of cancer—there is a tendency to immediately believe that this sequence irremediably determines the future appearance of an illness. This conception, erroneous in itself, is a consequence of a misunderstanding of the technique and of the diseases in which DNA is involved. Such misconceptions, and their implications, are the focus of this paper.

2. GENETIC DISEASES AND PRENATAL DIAGNOSIS

There are many diseases in which DNA is involved. Although an exhaustive classification of them is beyond the scope of this paper, I want to say several things. From my point of view, the most important conceptual problem in terms of prenatal and postnatal diagnosis is the confusing of monogenetic with multifactorial diseases.

In recent years, more than 350 markers related to diseases or predispositions have been identified. Also, more than 1,500 genes have been located within the chromosomes of human beings. Some of these diseases are monogenetic—for instance, cystic fibrosis, sickle cell disease, and Huntington's disease—but most are multifactorial. In the latter, several genes are implicated, often along with environmental factors. In these cases, all the factors are necessary before the disease appears. As an example, some congenital malformations of the heart are caused by several genes and environmental factors working together.

For the most part, among diseases that affect human beings, most have a genetic component that predisposes an individual to develop the disease only under certain environmental conditions—and, in most cases, the genetic component involves several genes. In other words, the diseases are *polygenetic*.

Most of the tests developed in recent years for prenatal diagnosis are designed to detect monogenetic diseases. Although such diseases represent a tiny fraction of inherited genetic modifications, they represent the nucleus, the largest number of genetic tests for the early detection of disease.

3. TECHNIQUES USED TO OBTAIN FETAL MATERIAL

To make a prenatal diagnosis, it is necessary to obtain fetal cells, to extract the DNA from them, and to test the DNA samples. Obtaining the cells is accomplished in several ways. We can mention the following:

a. *Amniocentesis*: This technique for prenatal diagnosis is the oldest and probably the most widely used—undoubtedly because it is safe and easily performed. The number of abortions caused by use of the technique is no higher than two percent (Fuster, 1980).

The technique involves the extraction of amniotic fluid by transabdominal puncture guided by ultrasound. Within the amniotic fluid, fetal cells are found that can be cultured to remove DNA for testing.

Normally, amniocentesis is performed between the fifteenth and seventeenth weeks of gestation; before that time, the number of fetal cells in the amniotic fluid is not high enough to obtain an adequate culture. This time factor is one of the chief drawbacks of the technique, because in many cases the long delay before the test can be done makes it impossible to take adequate measures if the test is positive.

b. *Chorionic villus sampling*: This technique involves removal of material called chorionic villi, which are fetal membranes that surround the embryo. The villi contain fetal cells from which DNA can be extracted for testing.

Removing chorionic material can be accomplished in several ways. The differences depend on different access paths to the chorion—abdominal or vaginal—and the instruments used to collect the material.

—A chorionic transcervical biopsy employs tongs and is guided by ultrasound (Salvador *et al*., 1988).

—Chorionic biopsy via transabdominal puncture uses a needle and again is guided by ultrasound (Brambati, Oldrini, and Lanzani, 1987).

—Chorionic biopsy via transabdominal aspiration is also guided by

ultrasound (Hogge, Shonberg, and Golbus, 1985).

Chorionic villus sampling has several advantages over other methods—especially earlier diagnosis. It is possible to remove fetal cells between the eighth and twelfth weeks of gestation, so that results can be obtained five or six weeks before they can with amniocentesis. However, there are also disadvantages—for example, higher levels of induced abortion, as high as 4.46 percent (Carrera Maciá, 1990).

c. *Funiculocentesis*: This technique was first described in 1983 (Daffos, Capella-Pavlosky, and Forestier, 1983), and it soon became the most popular technique for removing fetal cells in the late stages of pregnancy.

The normal reason for doing a test at this late stage is because there is evidence or suspicion (often based on ultrasound scans) of fetal malformation. In such cases, the test is used to confirm or disconfirm the suspicion of malformation. The interest that is involved is to avoid a caesarian section or other surgery that could be viewed as unnecessary in cases of serious chromosomal abnormalities (Salamanca and Gonzalez, 1988).

The technique involves extracting fetal blood from a vein in the umbilical cord via transabdominal puncture guided by ultrasound. The risk of induced abortion is estimated to be around two percent (Daffos, Capella-Pavlosky, and Forestier, 1985). Since it is common for fetal blood to be contaminated by maternal blood, more than one puncture may be necessary. The advantage of the technique is speed of diagnosis, and results can be obtained in three or four days.

4. TECHNIQUES FOR ANALYZING THE MATERIAL

After removal of the fetal cells, several kinds of tests can be performed, among which we can mention the following:

a. *Cytogenetic tests*: These tests are done when a fetus has presumed anomalies, implicating either whole chromosomes (trisomies, monosomies, etc.) or fragments (deletions, duplications, translocations) that are detectable when observed under a microscope.

Briefly, the technique involves culturing fetal cells in an appropriate way, after which the culturing process is stopped at a stage of cell division that will allow clear observation of complete chromosomes (called a metaphase). Then the chromosomes are stained, using a special technique that makes it possible to see a characteristic pattern of lines on a screen or film. All of this permits the distinguishing of pairs of chromosomes from one another.

In cases of amniocentesis, the quality of the chromosomes obtained from amniocytes is very good. In general, diagnosis is possible in 98-99% of cases (Carrera Maciá, 1990). For this reason, amniocentesis is the most common means for obtaining cells for chromosomal studies.

In cases of chorionic villus sampling, the fetal material removed is sometimes contaminated with maternal cells. It is also relatively common to find cells with chromosomal abnormalities that do not indicate that the fetus has them; on the contrary, such alterations often simply point to mosaics of placental cells. In such cases, another karyotype study of blood cells or amniotic fluid is needed before issuing a diagnosis. Moreover, I should also mention that the quality of chromosomal material extracted from chorionic villi is lower than what is retrieved from amniocytes. This makes diagnosis more difficult—even impossible in as many as twelve percent of cases.

With funiculocentesis, good results can be obtained in three or four days.

b. *Biochemical tests*: This technique is used when the biochemical alteration caused by a genetic anomaly is known. Many genetic anomalies display a phenotype translation that can be detected by doing tests that examine materials that show up in metabolic products such as urine and blood—or, contrariwise, by noting the absence of other materials. Examples include cases of phenylketonuria, hyperglyconemia, tyrosinemia, and Fanconi's syndrome. If we can detect these metabolic pathologies (some of which are linked to serious mental retardation) in the prenatal period, we can minimize their effects by appropriate dietary changes for the baby. At the present time, almost 200 of these metabolic diseases are known, and about 80 are linked to serious mental retardation.

For these tests to work, the product of the altered gene absolutely must be expressed in the fetal cells—and that does not always occur. For example, in the

case of phenylketonuria, the disease is caused by a defect in the phenylalanine hydroxylase enzyme, and the activity of this enzyme is not manifested in amniocytes; this is because there is no expression of the implicated gene in these cells.

c. *RFLPS (Restriction Fragment Length Polymorphisms) and VNTRs (Variable Number Tandem Repeats)*: As is well known, these tests are based on the sequencing of DNA fragments of genes that are polymorphic with respect to one (or more) restriction enzyme(s). Each of the polymorphisms is linked to a single disease.

This is the test procedure: once DNA is cut using appropriate restriction enzymes, the fragments are separated using the Southern blot technique. Then the fragments are identified either by appropriate probes (these are DNA sequences complementary to the fragments to be identified), whether radioactively marked or not (e.g., digoxygenin), or by immunological tests.

Another type of procedure, more informative than RFLPs, are tandem repeats (VNTRs), which can also be used to detect genetic diseases—though only if the sequences linked to the gene are transmitted.

In either case, RFLP or VNTR, we can trace patterns in families, indicating which members have the particular disease and which ones are carriers. The test for linkage must be carried out with as many family members as possible, including healthy ones. Among the family members, there must be a significant difference either in the length or in the sequence of the restriction fragments. When both sick and healthy family members exhibit the same restriction sequence of materials linked to the gene in question, it becomes impossible to carry out the analysis. In that case, we can say that it is a non-informative family history.

Furthermore, we must be able to identify a gene-related polymorphic pattern to identify a particular gene we want to study. And the tests must be carried out in families with more than one diseased member.

Even so, these tests present some advantages:

—It is not necessary for the gene to be expressed in fetal cells.

—It is not necessary to know in advance either the gene in question or the protein it codes for.

For these reasons, the method permits diagnoses of many genetic diseases having a single cause; it allows us to arrange the particular patterns characteristic of the diseases we are interested in. At present, it is possible to test in this way for 40 genetic diseases (not all of which are related to mental retardation).

The only bad feature of these tests is the length of time they take. In cases where they are done following amniocentesis, the amniotic cultures must be maintained for two or three weeks because, before this time, it is impossible to remove enough DNA to test it. And, as noted earlier, before the fifteenth or sixteenth week of pregnancy, it is impossible to extract amniotic fluid. To this must be added two to four weeks to culture the cells, and the actual time required by the RFLP test itself. In a country like Spain, where abortion law divides pregnancy into rigid periods, the length of the process could make the outcome too late for both parents and physicians to take appropriate measures if the genetic test is positive.

5. SOURCES OF ERROR

Most of the conflicts associated with genetic diagnoses occur with respect to RFLPs and VNTRs. This is because these tests allow us to detect so-called "genetic conditions" as well as genetic diseases. Sometimes, however, critics hold conceptual misunderstandings about the sources of error and the limitations of the tests. In this part of the paper, I review the basic concepts. But I must limit myself to RFLPs.

a. *RFLPs are based on statistical correlations*: For this reason:

1. We can always find a percentage of cases that cannot be appropriately diagnosed. Some of these exceptions will be false positives (the test says yes, but the subject does not have the condition); others will be false negatives (the test says no, but the subject does have the condition). For example, we have known since 1978—when the RFLP method was first used to diagnose sickle cell disease (see Kan and Dozy, 1978)—that there is a polymorphic fragment for the Hpa1 enzyme, located at 5Kb from the 3' end of the beta-globin gene which is linked to the disease. After cutting normal globin genes using Hpa1, in 92% of the cases we find a

restriction point for the enzyme, while the same point is present in only 40% of the altered genes. This is verified by noting the differing lengths of the restriction fragments when the DNA samples of both diseased and normal individuals are cut using Hpa1. (One is labeled 7,6Kb, the other 13Kb.) However, this result does not show up in all cases, but in only 60% of diseased individuals (yielding 40% false negatives) and 8% of normal individuals (false positives).

Such error percentages are not always recognized by the technicians doing prenatal diagnoses. For instance, alpha fetoprotein levels are often used to detect neural tube defects during pregnancy. A high concentration of the protein, in 95% of cases, is linked to a neural tube defect. In the remaining 5% of cases, while the protein level is high, the fetus is normal. But, according to a report of the U.S. Congress's Office of Technology Assessment, while obstetrics departments studied were regularly using these tests, only 10% of the technicians were aware of the false-positives frequencies. This would suggest that it is very likely that some healthy fetuses are being aborted if no other tests are used to confirm the results obtained using the alpha protein method. This is one example of a misunderstanding of the technical limits of a test.

2. The sensitivity of the tests is based on the number of known alleles causing (or markers related to) the biological condition we want to test for. So, if for example all that we know is that three alleles (or three markers) are linked to a genetic disease, all we can determine is those individuals who have versions of the three genes or markers. But if other alleles are related to the same phenotypic condition and they are unknown, we will not, with these tests, be able to detect all the individuals who have the condition. In the case of cystic fibrosis, for example, it is currently possible to detect only 75% of the chromosomes that include an allele related to the disease in a given population (Gostin, 1991).

This source of error is related to the heterogeneity of disease and genetic conditions. Sometimes, the same clinical symptoms are produced by changes or modified conditions in different locations within the chromosome. This means that, in genetic screening, in order to detect a genetic condition or a pathology in a population, we must take into account the possibility that more than one gene could be causing the symptoms (Kinmerling, Fain, and Kenyon, 1988). If we do not take this into account, there could be serious consequences for both fetuses and parents.

3. A statistical correlation between two factors does not necessarily imply a causal relationship. In other words, statistical correlation is not biological causality. For example, if we are studying life expectancy among European and African babies, we will probably discover that the former have a much higher probability of reaching adulthood than the latter. Just as likely, we will discover that almost all Europeans use disposable diapers, and almost no Africans do. That is, we will find a high statistical correlation between the life expectancy of babies and the use of disposable diapers. Now there is an obviously high correlation between a baby's good health and the use of disposable diapers, which—if it were not so obvious—might lead to the absurd conclusion: the use of disposable diapers increases the life expectancy of newborns.

This is especially relevant when we are talking about conditions that are multifactorial. In these cases, statistical correlations are especially misleading and they are the least objective way to establish the heritability of a condition (e.g., cancer, bipolar disorder, alcoholism). Statistical correlations establish a linear relationship with a phenotype, and they can support a causal relationship in cases of monogenetic conditions—although, even then, the correlation is merely probabilistic. On the other hand, most human characteristics are multifactorial, not monogenetic, and wherever that is true relationships are not linear.

For example, in several studies of alcoholism carried out by Cloninger (Cloninger, Theodore, and Samuel, 1975; Cloninger, 1987), the conclusion is reached that the condition is hereditary. The claim is based on the authors' use of statistical correlations. Furthermore, these studies have been confirmed by more recent ones, carried out at the University of California and the University of Texas Health Center, which also establish a correlation—specifically, between a polymorphism in the gene for dopamine receptors and alcoholism.

However, since alcoholism is related to many factors—some of which are affective, social, educational, in short, environmental (Freixa *et al*. 1981)—and since these factors can cause health problems as well as social problems, it is at least possible that focusing on genetic factors, using statistical correlations, could minimize the role of these environmental factors and turn a multifactorial problem into a supposedly biological condition—or, even more reductionistically, into a genetic problem. And a genetic predisposition does seem to exist in early-onset alcoholism, among young people who start drinking to excess at a very early age.

But even in these cases and even if we could demonstrate a linkage between a genetic condition and a certain type of alcoholism, which could thus be passed on from parents to children, the heritability of the characteristic can provide us with information only about a genetic factor in a limited population; it would tell us nothing about environmental variables, and we could predict nothing on this basis about how phenotypes might vary if we were to alter the environment in which these young people were raised (Lewontin, Rose, and Kamin, 1989).

   b. *Expressivity and penetration of genes*: Penetration is the name given to the percentage of individuals, taking into account their genotype, who manifest an expected phenotype. Expressivity is the degree to which inherited characteristics are manifested (Suzuki and Knudsen, 1991). To understand these concepts, we can consider the following:

   —In monogenetic characteristics, a recessive phenotype will be manifest only in recessive homozygotes—not in heterozygotes. And the variability can be enormous. For example, there is a disease called Charcot-Marie-Tooth disease—a nerve disorder—which causes atrophy of the leg muscles. Penetration and expressivity are so variable in these cases that some people having the gene do not display symptoms of the disease at any time in their lives (Billings *et al*., 1992).

   —Monogenetic characteristics, controlled by dominant genes, are manifest in both heterozygotes and dominant homozygotes. However, even if the gene is found, different symptoms can appear, and there can be both incomplete penetration and variable expressivity. One such case occurs with the gene for Huntington's disease. There is incomplete penetration in some cases where it is known that a person is dominant for the gene but never shows any symptoms of the disease (Ayala and Kiger, 1984; Gostin, 1991; Natowicz, Alper, and Alper, 1992). There is also variable expressivity in that symptoms can appear at different ages, from childhood to old age. And repercussions for individuals' lives can be very different, depending on when the symptoms first appear.

   —Finally, in multifactorial diseases and conditions, it does not even make sense to talk about penetration and expressivity, because there are so many factors involved in causing the phenotype, some of them being genetic and others environmental.

c. *Crossing over*: This label is used to describe an exchange of homologous chromatides in DNA during meiosis (i.e., the formation of sex cells). The greater the distance between a marker and a gene, the greater the probability that an exchange will take place between them. If this occurs before prenatal testing, a normal fetus might carry an RFLP sequence linked to a genetic disease, or an affected fetus could have a normal sequence. In the first sort of case, the parents might decide to abort a normal fetus thinking that it is abnormal. In the latter case, they could choose to continue a pregnancy involving an abnormal fetus thinking it is normal. An example: some years ago, the frequency of exchanges between genes and markers in Huntington's cases was determined to be 4%. That yielded an equal percentage of erroneous diagnoses (Lewis, 1987). This is well known to experts in genetic diagnosis, and they deal with the issue by looking for markers close to the gene—if possible, right next to it.

d. *Problems defining what are desirable or undesirable syndromes or genetic conditions*: Classifications of traits as desirable or undesirable are changeable; so are concepts of health and disease (Serrano Gonzalez, 1990). One reason that the defining of advantageous traits is changeable is that it depends upon our considering it a socially valuable thing to have the technological capacity to distinguish one condition from another. For some authors (e.g., Rothschild, 1989), the new techniques of genetic diagnosis are modifying patterns of normality and abnormality, perfection and imperfection, advantage and disadvantage. It is very likely, in this context, that if we do not have a technique appropriate for the task of differentiating between two genetic conditions, we will not say that one is advantageous with respect to the other. On the other hand, as genetic diagnoses improve, the possibility is opened up of separating all kinds of genetic conditions. Many of them—monogenetic recessives, multifactorial conditions—would not have been detectable using older methods. For this reason, it is always important to take into account both what is commonly understood by a phenotype and the conceptual variability of definitions of advantage, normalcy, etc.

Along these lines, it should be recalled that certain genetic conditions that are disadvantageous for homozygotes are advantageous for heterozygotes. This fact, that there are some protective mechanisms in the face of some environmental conditions, can explain the high frequencies of particular alleles in some ethnic groups and not in others. This is especially clear in pathologies affecting hemoglobin—for example, alpha and beta thalassemia, or G6PD deficiency. In

these cases, heterozygotes have an advantage with respect to malaria. In P. Falciparim, non-carrier individuals get infections more often than carriers (Motulsky, 1989). Something similar happens with respect to the sickle cell trait, where a homozygous condition produces an anemic crisis, whereas heterozygotes have an advantage in the face of malaria: the allele for the disease has a high incidence in African populations where malaria is endemic.

In general, it seems that certain alleles in heterozygotes have been evolutionarily selected for and maintained in populations because they provide an advantage to carriers. It has even been proposed that certain HLA alleles generate a resistance in carriers facing Haemophilus influenza infections. It seems clear that high or low susceptibility with respect to viral, bacterial, and other kinds of infections is related to certain alleles which account for a disadvantage in homozygotes whereas they are clearly advantageous in heterozygotes. For this reason, clarifying what is to be considered advantageous or disadvantageous is a serious problem—as in Africa, where to be heterozygous for P. Falciparum is an advantage—as is the question of who decides (and using which criteria) with respect to the conditions to be included in either category.

In our society, there is general support for the idea that industrial or technological development is the basis of social progress, that development promises great benefits at low cost. On the other hand, if the managerial class is defining what is advantageous or disadvantageous, they will always define it in economic terms, whereas others might well define it, for example, in terms of the health of the community (Sanmartín, 1993).

6. SOCIAL CONSIDERATIONS

In order better to understand the social implications of genetic screening, in my view, a good approach is to single out the groups involved and look at the possible risks and impacts in each one separately. Among such groups, we can mention the following:

a. *Parents*: Generally, parents who are expecting a child typically request genetic counselling for several reasons: family history, consanguinity, past abortions, or mother's age. Whatever the test used or the motivation for the test, if a genetic disease is confirmed, a decision must be made about the pregnancy, and

whether to end it or not. Pressure on the parents can come from several sources:

      —Genetic counsellors: In the past, information supplied to parents often came freighted with the ideological preferences of the experts providing it (Lappé, 1987; Nelkin and Tancredi, 1989; Hubbard and Henifin, 1986; Botkin, 1990; Clarke, 1990). This was not necessarily because the experts deliberately wanted to push the parents in one of another direction; rather, it is very difficult to tell parents the result in a noncommittal way. So the information given to parents is likely to be flavored by the particular counselor's ideology no matter what, and this conditions the parents' decision. In Spain, for example, of all the women who should be tested using amniocentesis followed by chromosomal analysis because of their age (more than 35 years old), only 5-7% are actually tested (Dexeus and Carrera, 1989). Among the many reasons for that, surely the ideology of the experts who give information to the parents is a factor, including religious prejudices.

      —Social pressures: By this I mean definitions of normality and abnormality dominant in a culture. Depending on the kind of society in which we live, its values, and the possibilities enhanced by genetic diagnoses, some biological conditions will be favored over others. For example, in cultures in which daughters are perceived as a burden to families and male children are valued positively, the possibility of determining in the prenatal period whether a child will be male or female will logically lead to a situation in which the majority of aborted fetuses will be female (Rothschild, 1989).

      If a technology makes it possible during pregnancy to detect not just diseases but tendencies to biological conditions—e.g., susceptibility to cardiac disease, schizophrenia, or bipolar disorder—it is easy to predict that many couples will decide not to have a child with such susceptibilities on account of the models of biological normalcy dominant in the culture. In this way, particular parents of reproductive age will be making their choices based on social acceptability. And, for that reason, there is a risk that these parents could become instruments of a new kind of eugenics, where ideals about perfect babies, combined with technical possibilities, will be determining which fetuses will live and which will die.

      —Insurance companies: Although in Spain health care is not based on private insurance as it is in the USA, government deficits associated with the economics of joining the European community could mean in the near future that

there will be privatization of health care financing or of health care itself. In either system, public or private, there are social advantages and disadvantages, both with respect to health care and the economy more generally. Privatization might seem to offer advantages in cost/benefit terms, but there are also inconveniences. If we take health care to be a public good or a right of all human beings, the introduction of a new health care system should involve different considerations of advantages and disadvantages, for instance, involving variables such as degree of user satisfaction (Ortún Rubio, 1990). Otherwise, the introduction of a privately financed health care system could end up pressuring citizens, forcing them, for instance, to make certain choices about reproduction which, in my view, ought to be strictly personal.

Along this line, Wexler (1992) and Billings and Beckwith, (1992) both describe the case of an American family who had their funding for health care through a health maintenance organization (HMO). The family had had one child with cystic fibrosis. When they decided to have another baby, they asked for genetic counselling. The results were positive, but they decided to continue the pregnancy anyway. And then the insurance company told them that their policy covered either the cost of prenatal testing or the costs of care for an affected baby but not both. Although in this case the HMO eventually relented, the story highlights the possibility that another couple in a similar situation might decide to abort even a fetus they would want to maintain because of the impossibility of affording care if it is not paid for by the insurance company.

In my opinion, decisions on reproductive issues must be made by the individuals involved, and they should not be subjected to anyone's values or interests other than their own.

b. *Physicians and genetic counsellors*: In Spain, almost half of the pregnant women who should get genetic testing (because of their age, history of prior abortions, etc.) know that there is a risk, but they are unaware of the tests and their utility (Dexeus, 1989). Among these women, 70-80% ask for information about chromosomal tests, but ultimately only 7-8% of the women in this risk group get tested. There are many reasons to explain this, but I will just mention these:

—The limited education of first-line professionals, who provide inadequate answers to requests for information.

—A deficiency of resources. In Spain, there are only about 30 prenatal diagnosis centers. In most of these, an ultrasound can be done, along with chromosome and metabolic tests. But few of them can do DNA tests. For this reason, if all the couples who need testing were actually to ask for it, the health care system would be incapable of absorbing the demand.

—The ideologies of genetic testing personnel mentioned earlier.

c. *The pharmaceutical industry*: At present, many of the major pharmaceutical companies have a biotechnology unit. In 1987 there were already more than 100 products in line for approval from the Food and Drug Administration. But now more than 100 genes have been identified as causes of over 5,000 of the diseases that appear in McKusick's catalogue (Collins, 1992). So it is impossible to doubt that genetic tests will turn out to be good business for major pharmaceutical companies. (I am not questioning the social utility of what they are doing.)

7. EPILOGUE

Efforts to detect genetic conditions early on, during pregnancy, are based on the belief that through knowing an individual's genome, we can determine what his or her future health will be. Underlying this hypothesis is the further belief that an individual's genome determines a person's future, irremediably, without exception.

However, the very concept of a genome is an abstract concept, and it makes no sense to consider it as anything other than a part of the whole picture. Though it is possible today to detect a great many genetic diseases, we must remember that concrete realization of them are not always the same. Also, to confuse genetic diseases with multifactorial conditions can have disastrous consequences, particularly for the affected individuals. It could also lead to changes in our concepts of health and disease—and ultimately, to unpredictable changes in concepts of diagnosis, prevention, and treatment. Although the technology allows us, for example, to detect whether a person has a predisposition to cancer, this does not mean that that person will in fact come down with it in the future. The likelihood is that having a genetic predisposition is a necessary but not a sufficient condition for developing the disease. Furthermore, there are many other necessary (and not sufficient) conditions related to the disease.

For these reasons, whenever genetic diagnosis is used to detect the genetic condition of an individual, it must be remembered that we then have only limited information about that individual—even with respect to monogenetic diseases, and certainly in all multifactorial conditions. All we have is one small piece of a larger puzzle. Being aware of this is the best way to avoid the misconceptions—and their implications—which have been the focus of this paper.

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