

Human Genetics: The Molecular Revolution and Its Ethical Consequences

F. Vogel

Institute of Human Genetics, University of Heidelberg, Germany, Im Neuenheimer Feld 328, D-69 120 Heidelberg, Germany

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ABSTRACT Recent progress in molecular human genetics, while opening up new and unexpected prospects for medical diagnostics, prognosis, and therapy, poses a great number of ethical problems. Some of them are discussed in four steps:

1. X-linked mental retardation is taken as one example for progress in molecular diagnostics in one special field. Here, ethical aspects of prenatal diagnostics and abortion are discussed.
2. In a second part, issues such as preimplantation diagnosis, embryonal cloning, and the possible use of embryonic stem cells are reviewed.
3. It is becoming increasingly possible to diagnose disease susceptibilities using molecular methods. This raises questions of patient autonomy, on the one hand, and justice for the population as a whole, on the other. For example: Should a life or health insurance company be allowed to ask for genetic information?
4. The fourth - and possibly most controversial - group of ethical problems is posed by research priorities. Here, studies on molecular aspects of infectious diseases should have high priority.

The enormous progress of human genetics, human genome research, and molecular medicine during the recent decades is posing a great number of ethical problems. Often, the following question is asked: Are we allowed to do everything we can do? Posed in this way, the question is easy to answer: Of course, we are not allowed to do everything we can do. Everything we do should be considered from the viewpoint: Are we allowed to do it? Or are there constraints that should prevent us from the envisaged action? Does this action contravene our - and the society's - basic principles of life and behavior? To say it differently: Ethical considerations are always required. This is true especially if basic aspects of human life are at stake, and if, due to rapid scientific progress, new and unexpected ways of action are opening up. Therefore, it is not surprising that the recent progress in our field has led to a worldwide boom of ethical consid-

erations. It cannot be the purpose of this contribution to give a comprehensive overview over these discussions. Rather, I shall try to outline some basic principles that should be considered before decisions in special cases are made. These principles will be illustrated by examples, - mainly from the practice of the medical geneticist. More complete information may be found in a number of publications (See, for example, Wertz and Fletcher 1989,1993; Wertz et al. 1990; Verma and Singh 1989; Schroeder-Kurth and Hübner 1989; many WHO reports, for example the report on Ethical, Legal and Social Issues of the Human Genome Project, 1992).

In their book "Principles of Biomedical Ethics", (first published in 1979), Beauchamp and Childress proposed four ethical principles that could be used as starting points for decisions in biomedicine. These principles are: Respect for autonomy; nonmaleficence; beneficence; and justice. There appears to be agreement about these principles - irrespective of religious and political affiliations. However, the matter is becoming much more difficult when special - and, especially, new - issues are considered; here, hard controversies are coming up, - especially if long-lasting, traditional principles are challenged. In the following, I shall discuss these problems in four steps: First, I shall describe progress in medical genetics using one specific example: X-linked mental retardation. In a second part, recent issues such as preimplantation diagnostics will be mentioned. Then, specific problems of genetic diagnostics especially of disease susceptibilities in relation to social and personal issues will be mentioned - especially in the context of patient's and doctor's autonomy. At the end, - in the fourth part, - I shall turn to the difficult question of research priorities. Can it be justified from an ethical point of view to have the same priorities in the

industrialized countries of the West and in countries of the Third World?

1. X-linked Mental Retardation as an Example for Progress in Medical Genetics (See also Tariverdian and Vogel 2001)

Mental retardation is a relatively common phenotype. Its causes are highly heterogeneous: About 2 - 3% of the population in Western European countries have an intelligence quotient (I.Q.) of <70. Many exogenous causes such as brain trauma or infections might lead to brain damage resulting in mental retardation, but an increasing number of genetic causes have been identified. We shall discuss only one subgroup: Already at the end of the 19th century, it was observed that more males than females were mentally retarded. Many observers did not regard this sex difference as biologically real; for example, the famous English human geneticist, L.S. Penrose, assumed an ascertainment bias due to social factors and, possibly, a higher aggression potential among male retardates. However, already in 1943, Martin and Bell published a pedigree with 11 retarded males, and the characteristic pattern of X-linked inheritance. Once doctors had been alerted toward such occurrences, an increasing number of pedigrees were observed. It was shown by more detailed analysis that there is not only one type of X-linked mental retardation, but many of them (See, for example, Tariverdian and Vogel 2001).

Analysis was performed at three levels:

1. The phenotypical level: Some affected individuals show, in addition, other external clinical signs.
2. The chromosome level: In some genetic types, the X chromosome shows a fragile site at the long arm of the X chromosome.
3. The molecular level: Genes responsible for the anomaly are located at different sections of the X chromosome, and there are different types of mutation.

Depending on presence or absence of external clinical signs, syndromal and non-syndromal types can be distinguished. Up to the end of the year 2000, no less than 124 syndromal types had been identified; in 57 of them, the responsible gene has been localized, and in 25, this gene has been isolated, and some mutants have been ana-

lyzed. The number of nonsyndromal types cannot be counted. Hence, detailed analysis has revealed an enormous degree of complexity.

Now, I shall mention three examples of syndromic types - a relatively common one, a rare one, and one with a specific and unusual mode of inheritance. The common type is the Frax syndrome. In addition to mental retardation, the male patients show a characteristic face with prominent forehead and jaw, and big testicles. In some of their X chromosomes, a fragile site can be seen. About 30% of female carriers also show mental retardation, although at a milder degree. The responsible gene and its mutations have been analyzed in every detail. This gene determines a protein which is found mainly in the brain and in the testicles; it may play an important role in the formation of the synapses. In distinction to most other mutations which we know, the responsible mutants consist of an unusually high number of repetitive sequences of the base triplet CGG. Normal individuals also have a moderate number of CGG triplets in the same gene; possibly, it helps in fine-tuning of gene action (Brahmachari 1995). But this mechanism is disturbed by an increase in the number of triplets. Some individuals show a moderately increased number of triplets; they are phenotypically normal but have an increased risk for producing a full mutation in their germ cells, and having affected offspring.

The second type of X-linked mental retardation to be shown here is rare. This is the MASA syndrome with mental retardation, aphasia, shuffling gate, and adducted thumb. Many of these patients have a mutation in the MICAM gene which is expressed mainly in neural cells, and encodes a protein involved in cell adhesion. In some cases with an X-linked type of hydrocephalus, mutations in the same gene have been detected. This shows that different mutations within the same gene may lead to different abnormal phenotypes.

Now, let us look at the third example: A mutant on the X chromosome which leads to an unusual mode of inheritance: The Rett syndrome is observed only in females. The male carriers of this gene die in early pregnancy. Affected females suffer from a severe, and very characteristic, type of mental retardation. With an

incidence of about 1 : 10 000, this syndrome is one of the most common causes of genetic mental retardation in females. In addition to the retardation, stereotypic hand movements are characteristic, and in adult life, the patients often get epileptic seizures. Since the males with this mutation die early in pregnancy, and the affected females are severely handicapped, the great majority of all cases are new mutants. But a few concordant MZ twin pairs pointed to a genetic cause, (Tariverdian et al. 1987), and a few pedigrees with affected sibs and half-sibs helped in identification of the gene at the X chromosome. This gene is called MECP2. It determines a common protein which binds to 5-methylcytosin residues in the DNA -especially in promoter regions of genes.

These are three, quite different examples of X-linked mutations leading to mental retardation combined with additional - and quite specific - clinical features. They are shown mainly for two reasons:

1. They point to the complexity of genetic determination of normal brain function, and to the various ways in which it can be disturbed.
2. They show, how genetic analysis of special anomalies with "classical" methods, in combination with the full instrumentarium of molecular biology leads to new insights not only into the anomalies studied, but into mechanisms of gene action and regulation. All ethical considerations are facing a more and more complex situation. They will now be outlined in greater detail.

We all hope that this rapid progress in genetic research will lead to a similar progress in medicine - improved understanding of disease processes. This will help in detailed diagnosis and, hopefully, in the future also in improved therapy. But at present, our diagnostic and prognostic skills are much better than our progress in therapy. This poses some ethical problems. Assume, for example, that a boy has been born with the MASA syndrome. This makes it very likely that the mother is a carrier of this mutant, and that future sons have a risk of 50%. But we know the gene. Therefore, we may offer to the mother for her next pregnancy prenatal diagnosis by amniocentesis or by chorionic villus sampling. If the expected child is a boy, and if this

boy carries the MASA mutant, she may opt in favor of artificial pregnancy termination. But this means killing an embryo in the fourth or fifth month of his lifetime; a very difficult decision for any thoughtful human being,- primarily for the family, but also for the doctor who is educated to preserve life, not to destroy it. Here, I should mention a personal decision of mine, from which I never departed: Prenatal diagnosis can also be used to determine the sex of the expected child - either by chromosome studies, or even - not 100% but with a good probability - by ultrasound examination. I am absolutely against this procedure; in my opinion, it cannot be justified by any ethical or social consideration.

2. Preimplantation Diagnosis

But modern molecular genetics is offering now a different approach to prenatal diagnosis: Preimplantation diagnosis after in vitro fertilization. IVF has become an established technique for treatment of certain types of female infertility,- for example, when the Fallopian tube is blocked. The fertilized oocyte is then implanted in the uterus, and will develop normally in about one quarter or one third of all instances; the success rate is increasing. Now, a recent progress of molecular genetics is coming into play: It has become possible to perform cytogenetic and molecular studies even on one single cell. And if you take one cell from the embryo in the 8 cell stage for examination,- before implantation into the mother's uterus-you can find out whether the future child would be affected by the mutant you are looking for. If it is affected, i.e., in our example, if it is male and carries the MASA mutant, you can abandon this zygote and select a normal one for implantation. For my ethical conscience as a human being and a medical doctor, this is a much better solution than artificial pregnancy termination in the fourth or fifth month of pregnancy,- mainly since the fertilized zygote at the 8-cell stage certainly does not suffer whereas the more mature embryo very probably will suffer.

A short time ago, there was a notice in the press that in France, a mother had given birth to two boys who were severely affected with a genetic disease (The precise diagnosis was not mentioned). The mutant was known, and

preimplantation diagnosis helped in giving her a normal child.- Another example was also published in the press. An American girl suffered from Fanconi's anemia (autosomal recessive). The girl could be helped if it would receive blood stem cells from a normal individual. But stem cells are accepted by the body of the receptor (the child) only when genes of the MHC complex were compatible - and such cells are difficult to find. But each sibling has a chance of 25% to have compatible MHC cells. Therefore, the parents decided to have 16 oocytes fertilized by the father's sperm. From these, a normal embryo without the Fanconi anemia genes and with compatible MHC genes was selected and implanted to the mother. When this little boy was born, blood from the umbilical cord was taken, stem cells were isolated, and injected to his sister. In this way, the little boy has saved his sister's life already at the time when he was born.

Preimplantation diagnosis is now being introduced in many Western countries - for example Great Britain, the U.S.A., and France;- and also in Japan. But in Germany, it is legally prohibited: The cells of this embryo in such an early state of development are "totipotent", i.e. they could develop under suitable conditions into a full individual. Therefore, our embryo protection law ("Embryonen-Schutzgesetz") affords to him full protection (like a complete human individual). I cannot follow this argument.

This discussion of preimplantation diagnosis also points to another ethical problem which will now be discussed: Autonomy of patients and their family members. But in this context, as in the issues discussed above, another problem should also be considered: The medical doctor and the genetic counsellor also has a right to be regarded as an autonomous individual. He cannot act as an elongated arm of his patients and clients.

3. Patients', Family Members', and Doctors' Autonomy

As mentioned, the examples given above constitute a small fraction only of all genetic anomalies that can be diagnosed prenatally, and are posing ethical problems. These anomalies may be classified into three main categories:

- a. Chromosomal aberrations such as trisomy 21. When such a trisomy has been diagnosed prenatally, the parents have to decide whether the pregnancy is to be continued. Within this group, there are instances in which a decision might be very difficult. One example is the Turner syndrome (very often an XO Karyotype). These girls are small and, due to underdevelopment of their ovaries, they cannot have children. But mentally, most of them are practically normal. How will parents decide in such instances? I personally tried to convince them that they should accept such a child. Often it helps to let them come together with adult XO women - for example, in a self-support group.
- b. The second category are children suffering right from birth from a disease with a simple mode of inheritance. The MASA syndrome has already been discussed as one example. In some countries,- including parts of South India,- diseases of the blood such as Thalassemia major or sickle cell anemia are common. In the islands of Sardinia and Cyprus, young people who want to become parents are offered examinations to find out whether they are carriers of these genes. When both are carriers of a thalassemia mutant, every child has a risk of 25% to develop thalassemia major. Therefore, these parents are offered prenatal diagnosis, and pregnancy termination in case this child is affected. In Sardinia, wide acceptance of this procedure has led to a reduction of thalassemia major by more than 80%. According to I.C. Verma (Delhi), a similar procedure is being introduced in some Indian population groups.
- c. A third category of cases is much more problematic, since here, the child is phenotypically normal, but presence of a certain gene indicates that it will very probably develop a severe genetic disease some time in the middle of its life. Huntington's disease is the classical example. This autosomal-dominant disease raises a number of ethical questions: For example, most parents are too young to know whether they will be affected themselves when they have children. They know of their risk mostly because one of their parents is affected. Should they have their genes

examined before they decide in favor of children? Or do they still have the right not to know? And in case their own result is positive - should their children be examined - prenatally or postnatally? These are difficult and often discussed questions.

Similar problems are now being posed by some types of hereditary cancer, - for example breast and ovarian cancer. Genes have been discovered that carry a risk of about 90% for carriers of certain mutations to develop one of these cancers - and not at advanced age when cancers might occur normally but at relatively young age 30, 35, or 40. About 5% of women with breast cancer carry such a gene. Here, something can be done: Individuals at risk can be examined in short time intervals to detect the cancers so early that there is enough time for treatment. - In these cases, it is certainly justified to have children at risk examined in young age, and to inform them when they approach maturity (about 18 years). But what about chorioideremia? This is a degenerative disease of the retina that leads to blindness in young adult age. The mode of inheritance is X-linked, and the disease can be diagnosed early in life - even prenatally. Here, it is necessary to teach the affected boys reading and writing braille and other cultural techniques for the blind already in their teens to prepare them for adult life in blindness.

These few examples show that it is very difficult - and in many cases impossible -to establish general rules for our actions that are valid for all upcoming situations. Often, one should leave the decision whether more precise information should be sought and provided to our clients themselves; - in other cases, complete information is strongly recommended since the future fate of the client depends on this information, and subsequent action. As a rule, genetic information should not be given to children, but even this rule has exceptions, as shown by the example of chorioideremia.

Who should provide genetic information and counseling?

All these examples lead to one conclusion: Information and genetic counseling requires two prerequisites: Excellent expert knowledge of the counselor, and his ability to provide information and help in a psychologically adequate way.

But it cannot be the task to prescribe certain ways of action - especially when ethically controversial issues such as artificial pregnancy termination are at stake. In all these instances, the decision has to be made by the clients themselves; counseling should be, as much as possible, "non-directive". But this "non-directiveness" has certain limits: The doctor should not lend his hand to actions that are illegal in the country in which he works. And he should not be forced to act against his own ethical principles. This has one practical consequence: Providing genetic information and counseling should be limited to specially trained medical doctors who have experience in this difficult field. They can be helped by additional personnel such as social workers or - as in the United States - non-medical genetic counselors. But in my opinion - and in that of my German colleagues - this is a full-fledged specialty within medicine. This rule is now being challenged by some biotechnology companies. They are developing laboratory kits for an increasing number of genetic anomalies, and they might try to sell these kits to practicing physicians, - and even directly to the general public. In principle, this would allow everybody to find out whether he has a certain genetic predisposition or not. But the layman cannot use this information properly; he often will come to wrong conclusions. He does need the human genetics specialist for proper understanding what the test result is really meaning for himself and his family. I am not against developing test kits - and not even against companies performing certain tests. Quite in the contrary: Their work might be very helpful to the doctor's task. But results should only be forwarded to the doctor, - the specialist in human genetics and genetic counseling. Here, clear rules should be established in the interest of our patients, clients, and their families.

Genetic Results and Insurance

One special problem that is discussed very often, and in many countries, is the relationship between genetic information and insurance :(See Bartram et al. 2000) Obviously, a health insurance system undergoes different risks, ensuring either a person with a risk of getting breast cancer at relatively young age, or another one with

a good chance to reach an advanced age in relatively good health. Or another problem: A person has received the information that he will fall ill with Huntington's disease in early middle age. This person, planning to take care for his family, buys a high life insurance. The money which the company will be able to give to his heirs comes, in principle, from the contributions of the insured population. It is calculated from average life expectations. However, the person we talk about has a reduced life expectation; he knows it, and he plans to take advantage of the better expectation of other people. Is the insurance company allowed to ask its clients before an agreement is signed whether the client knows of some special genetic risk? And - to go one step further - is it allowed to require certain genetic tests before the agreement is signed?

European countries and their legal systems answer these questions in different ways. In Belgium, Denmark, France, and Austria, the use of genetic information by insurance companies is strictly prohibited. Norway and the Netherlands are having somewhat milder regulations. In Germany, similar to some other countries, no regulations are existing at present. In Great Britain and Germany, a moratorium has been agreed upon by insurance companies: In the moment, they are not asking their customers for genetic information. Recently, a German expert group has published recommendations that appear to be fair also in my opinion (Bartram et al. 2000):

1. Types of insurance that are legally prescribed for the population as a whole, or for significant population groups, should not be allowed to ask for genetic informations. Here, the rules of solidarity require that all insured persons carry the risk also of specially endangered members.
2. In voluntary insurance,- for example, life insurance-the companies should be allowed to ask for genetic information. In the past, they have always asked their potential clients for special health hazards; smoking is one example.- If the company asks, the client is obliged to give a complete and truthful answer, according to his knowledge. This means: If a test has been performed, and the result points to a special risk, he has to inform the company. However, he cannot be

forced to have himself tested, if he prefers "not to know", - even if other features, for example, his pedigree, point to the possibility of a high risk. In my opinion, this would be a fair compromise between the right of privacy and self-determination of the individual, and the rights of other people within the community. To come back to the principles proposed by Beauchamp and Childress (1979; see above), this solution would agree with their four principles: It would show respect for autonomy of the individual since it would not force him to know more about himself than he wants to know about himself and his personal future; it would be beneficent for this individual without being maleficent for anybody else; and it would be fair for the community of insured persons since it would not permit the individual asking for insurance to hold back information about himself that is known to him. Hence, the requirement of justice would be fulfilled.

Gene Therapy and Cloning

In this context, I wish to mention briefly two other aspects that have little connection with practice in medical genetics,- at least, at present,- but are being discussed in the public, and may become important in the near future: Gene therapy, and cloning. For gene therapy, there are two options: Gene therapy on germ cells and early zygotes, and gene therapy on somatic cells. Since more than ten years, attempts at somatic gene therapy have been made in a great number of hereditary diseases,- and also in cancers caused by somatic mutations,- and some partial successes have been reported. But to the best of my knowledge, a convincing concept for successful treatment even of only one genetic disease is still lacking. Still, I am sure that, sooner or later, success will come. But much more basic research at many levels will be necessary. In principle, however, this approach has never been challenged for ethical reasons; from the ethical viewpoint, it is regarded to be similar, for example, to a blood transfusion or a transfusion of blood stem cells - established methods of medical therapy. Much more controversial, however, is gene therapy in freshly fertilized germ cells. Its purpose would be to replace a mutant gene

by its normal counterpart in the entire individual - including its germ cells. This would mean that not only the individual itself would be free from the disease, but the normal replacement gene would be transferred to the progeny. In mammals such as laboratory rats, such attempts have been successful in special instances, and some scientists, for example, in the U.S.A., are seriously discussing application to human beings. In Germany, such gene therapy on fertilized human egg cells is prohibited by law - and in this case, I agree. It should remain prohibited - at least in the foreseeable future. For me, the reason is not so much ethical - despite the fact that the method is also disputable for ethical reasons. But much more important: The method is simply not necessary. Why? Inheritance of genetic diseases follows Mendel's laws. This means that there is segregation of affected and unaffected offspring among children. For example, if both parents are carriers of the recessive gene for thalassemia major, the risk to be afflicted with this disease would be 25%. Therefore, before starting gene therapy on a fertilized oocyte, it would be necessary to find out whether this oocyte really contains two copies of the mutant gene, and could therefore develop into a thalassaemic child. Such preimplantation diagnosis has become possible. But obviously, it would be much easier to abandon an affected zygote, and to implant another one that contains the normal gene.

It would be quite another matter to "improve" a normal zygote by transfer of genes that might enhance, for example, the intelligence of the future child, - or may alter other aspects of its personality. Here, I would have many concerns also for ethical reasons.

Another aspect of gene technology that is being discussed is cloning. We all remember a photo of the sheep "Dolly" which was produced by fusing the nucleus of a cell from the udder of one sheep with the enucleated egg cell of another sheep, and implanting this fusion product to the uterus of a sheep. It developed into another sheep that was identical genetically with the provider of the udder cell. This production of a genetically identical daughter - "Dolly" - from its genetic mother - "Tracy" - was published in 1997 (Wilmut et al. 1997). As a rule, the idea

behind this experiment has not been mentioned in public discussions: Tracy was a transgenic animal that contained the human gene for alpha-1-antitrypsine, a necessary protein being deficient in some individuals. This protein could now be produced with the milk of Tracy, to be used for medical therapy. But this result stimulated the phantasy not only of journalists but of many people in the general public, as well. For example, will people such as Saddam Hussein in Iraq now be able to produce a genetically identical son who will be able to continue with the same type of tyranny that his father has established? Or: How would the world look like today if such a method would have been available to Hitler or Stalin?

In real life, however, cloning of entire human individuals would be absolutely uninteresting scientifically as well as for practical life. The reason is that we know very well how human clones look like and how they behave: Monozygotic twins are natural clones - they are genetically identical - and their study has been a leading research method in human genetics since almost 100 years. And we know that, as a rule, they do not behave identically at all. Of course, there are many similarities in disease susceptibilities, intelligence, and many other features. But life course and performance might be very different (See Vogel and Motulsky, 1997). For example, Hitler's cloned son might have become a criminal but also a journalist with leftist tendencies, a bad artist, or even a successful businessman - but not another Hitler.

But cloning is now being discussed also in a different context: Organ and stem cell transplantation are being used for treatment of an increasing number of diseases - from kidney failure to leukemia. However, the main problem is always compatibility of genetic tissue types (mainly the MHC system). Would it be possible to create stem cells, cell complexes, or even incomplete human embryos by cloning who will then serve as sources of cells or organs for the donor? Recently, this topic has become very controversial - leading even to political difficulties (For this topic, see, for example, Schroeder-Kurth 2001). In mid-december 2000, the House of Commons in Great Britain passed a law according to which cloning and medical use of embryos should be

permitted up to the 4th week of pregnancy. In this law, the possible medical use is given priority compared with the undisputed fact that even a very young embryo - like a fertilized zygote - is a potential human individual that has to be appreciated as such. In the German public, - including many politicians, - this decision has led to an uproar of indignation. Some people even asked for political action at the level of the European Community. It is my opinion that such a law does not necessarily violate basic ethical principles since no human being will suffer. A 14 days old embryo has no nervous system and does not suffer. There is no malevolence but benevolence for patients who might be helped. But here, different opinions are possible. In my opinion, the (promising) attempts at isolating pluripotent (not necessarily totipotent) stem cells from somatic tissue such as bone marrow should have priority, and should be pursued with energy. Probably, here, non-controversial alternatives could be opened up.

One conclusion can be derived from these discussions: The concrete questions how to tackle such situations will come not all at once but stepwise, one after the other. They require ethical decisions that might be difficult - and controversial between observers with different intellectual and cultural backgrounds.

4. Research Priorities in Industrialized Countries of the West and in Countries of the Third World

Research priorities have a very strong ethical aspect. If there is a choice, scientists and, especially, bioscientists should try to select topics that promise a benefit for human beings; at least in the long run. Problems on molecular genetic diagnosis and therapy mentioned above have been discussed so far mainly from the point of view of Western industrialized countries. Hereditary diseases such as X-linked mental retardation, chromosome aberrations, diseases showing simple Mendelian modes of inheritance, and especially complex diseases such as cancer or coronary heart disease are urgent medical problems in these countries. With the appearance of a new, and relatively well-to-do middle class in some of the Third World countries such as India or China, such problems are becoming

more urgent in these countries, as well. But there is another group of problems that are at least quite as urgent, - genetic aspects of infectious diseases (Hill et al. 1996; Fischer et al. 1998; Chedwick and Cardew 1999). Infections such as tuberculosis, leprosy, infant diarrhea, and many others are still common in many countries of the world. Detailed molecular genetic studies could help in detecting individual, genetically determined differences in susceptibility. Such knowledge might open new ways for protection and even therapy, especially when molecular studies are combined with adequate studies on population genetic theory. Such studies - in addition to being interesting from a purely theoretical point of view - might help in understanding population dynamics of human populations in interaction with infective agents (See, for example, Fischer et al. 1998). One step in this direction is the discovery that certain human beings are resistant against the HIV virus because their cells are lacking the receptor necessary for attaching the virus to the cell, and entering it. (O'Brian and Dean 1997). In the long run, studies on genetic variation in the human host, in combination with investigations on the various infective agents, would also help in solving another problem that all of us are facing - also people apparently living on the "island of the blessed" - in the Western industrialized countries: Big infections are coming back. Resistances are developing for antibiotics and other chemotherapeutical agents, for example, malaria, tuberculosis, and many other germs. (See, for example, Chedwick and Cardew 1999; Eberhard-Metzger and Ries, 1996). A possible solution of these problems is offered by development of antibiotic drugs that have been designed specifically for special genotypes not only of the infective agents, but for the human host, as well. For my understanding, it would not only be an unique scientific chance, but also an ethical duty mainly in countries in which such diseases are still common to concentrate on these problems in cooperation with scientists in the rest of the world.

This review of ethical problems in Human genetics is not meant to be complete: An enormous and ever-increasing literature has accumulated in recent years. The interested reader will

find good access by: Drze 2000. (See the references).

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