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Historical, ethical, legal, and social issues
(Part I)

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Articoli/Articles

GENETICS AND BIOTECHNOLOGY
IN MEDICINE HISTORICAL, ETHICAL,
LEGAL AND SOCIAL ISSUES

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The ongoing debate on the impact of molecular genetics and biotechnology in medicine is growing more heated and nuanced. As far as future prospects are concerned, the positions are generally reflected by a continuum that ranges, on the one hand, from the theory of an imminent redefinition of all diseases on a genetic-molecular and biochemical basis, that is, starting from events that govern the biology of the disease at a fundamental level, with radical consequences also for clinical practice; and, on the other hand, the hypothesis advanced by those who are doubtful that genetics applied to medicine will trigger a real revolution. Most diseases, say the latter, are multifactorial in nature and genetics still does not possess the necessary tools for finding its way around extremely knotty complex causes or for making predictions of any practical use. Regardless of how things will actually turn out, the process of transferring genetic knowledge to the clinical field has already begun and will speed up over the next few years. This is both because research and commercial pressures act as a stimulus to this transfer process and because strong expectations are being induced in society, as is shown by the constant increase in the demand for genetic testing. These developments in principle represent extraordinary opportunities for enhancing human well-being but at the same time also ethical and educational challenges for medicine and society.

The aim of the present collection of articles is to provide a reappraisal as concrete as possible, untainted by any ideological

bias, in a historical perspective and with several contributions reflecting specific geopolitical aspects such as that of Italy, of certain issues arising out of the application of genetics and biotechnology in medicine. The project is a response to the need for reflection on experiments, clinical cases and emblematic problems as perceived by the writers in the context of their teaching activities carried on at the university and through the bioethics courses run by the Osservatorio sulla Bioetica of the Fondazione Luigi Einaudi. One further aim is to try and stimulate the lukewarm attitude adopted in the scientific and socio-ethical confrontation on these issues in Italy and to stimulate a truly free cultural reflection on the practical implications of genetics and biotechnology in medicine. On the basis of these premises, on 25 October 2002, at the Faculty of Medicine of the "La Sapienza" University of Rome, the authors of the articles published herein presented and publicly discussed the results of original research and thinking concerning the consequences of the application of genetics and biotechnology in medicine.

The collected articles reflect a number of different cultural problems - that is, of a scientific-epistemological, historical-scientific, ethical-social and socio-economic nature - that underlie and characterize the debate on the knock-on effects of genetics and biotechnology in medicine.

Two of the most authoritative protagonists at world level of the process that started after the Second World War and that has involved the application of molecular genetics knowledge and research methods to medicine, define the historical and thematic contexts bearing on the significance of genetic knowledge in relation to the possibility of preventing the negative effects of drug treatment, that is, to improve the efficacy of therapeutic choices based on a conceptual re-foundation of medicine. Arno Motulsky illustrates the evolution of pharmacogenetics as far as the new methods and the new objectives of pharmacogenomics are concerned. The US geneticist warns that we are perhaps creating excessive expectations around pharmacogenomics regarding the actual possibility of systematically using genotyping in clinical practice in order to make drug testing and drug use more efficient.

Barton Childs then examines the conceptual and practical implications of applying functional genomics and genetics in medicine. For the first time, Childs points out, medicine is in a position to build up a unifying definition of all diseases. It will also be able to develop a more organic relationship with biology, above all with regard to the acquisition of an evolutionary perspective that will significantly modify the way disease is conceptualized (the "perceptions") at the pathogenic and clinical level, as well as the prospects of prevention and treatment. Childs's message is that medicine must construct a new theoretical horizon for itself. It must succeed in linking together the concept that genes are the proximal cause of disease and the concept that, insofar as they have been selected in the course of evolution and expressed in relation to specific historical personal life related contexts, genes themselves are also remote causes and thus imply the individuality and heterogeneity of any manifestation of the disease. If medicine can open up to the ideas of the individual uniqueness of pathogenesis, of its clinical expression, of its treatment and prevention, and if these ideas can be applied in the training of future doctors, it may well be possible to enhance communication between physician and patient.

Perhaps the most controversial area is the application of genetics to psychiatry. The article by Alberto Oliverio illustrates the methodological problems involved in research on the genetic bases of behaviour. Oliverio reiterates, on the basis of a wide-ranging analysis of genetic studies of schizophrenia, mood disorders and autism, that psychiatric disorders certainly have a genetic basis. As far as behavioural phenotype determination is concerned it will be very difficult to determine the role of individual genes, isolating them from the context of their relations with other genes, the cellular environment and with external environmental factors.

The prospects are further broadened by the article by Robert Bud, who illustrates the historical origins of biotechnology, also through a reconstruction of the semantic evolution of the term itself, showing how the meaning and perception of the social impact of the techniques described by this term have changed in the various historical, scientific and political-economic contexts

as a function of the relationships between the aims and methods of biotechnology and chemistry. There is no doubt, as Bud demonstrates, that biotechnology (which has now been in existence for nearly one century) has attained an authoritativeness (a "charism" *à la* Weber), just as a prospect of enhanced human well-being free of the undesirable side effects due to the applications of chemistry and that has gradually also gained in power (again *à la* Weber) although becoming a priority investment sector for the chemical industry, has also begun to show signs of crisis in its social acceptability level.

The application of genetics to medicine has shown that it can contribute to reducing the disease load, at the same time avoiding the risk of slipping into the eugenics ideology, while not being deterred from displaying problems concerning the interpretation of the results obtained in the context of two important experiments carried out in Italy and in the United States after World War II against hereditary diseases. Stefano Canali and Gilberto Corbellini reconstruct the history of the first nationwide preventative health campaign in Italy against a genetic disease, thalassemia. Their article analyses the action taken by Ezio Silvestroni and Ida Bianco, who, after contributing to the establishment of the genetic basis of thalassemia, in the immediate aftermath of the war, devised a massive screening campaign and fight against thalassemia, based mainly on programmes of education and premarital consultancy. The difficulties encountered by Silvestroni and Bianco, the organization of the campaigns and their results are discussed in the article, which emphasizes how the plan implemented in Italy served as a model for the campaign actually run in Cyprus in the Seventies.

The evolution of the eugenic contents of genetic disease prevention strategies after World War II is the topic dealt with in the article by Diane Paul on the attitudes towards the prevention of phenylketonuria. In particular, Paul shows how, as a result of the discovery made in the 1980s that the foetuses of women saved by neonatal screening and diet therapy were exposed to serious risk as even very low levels of phenylalanine can damage them, the attitude of clinicians to maternal PKU tends to consider it preferable for the reproductive choice to be directed towards avoiding the risk.

Genetics applications in medicine pass, or should pass, through genetic consultancy, which represents a particularly sensitive dimension of the physician-patient relationship, in the sense that genetic counselling is constantly subjected to surveillance to prevent the risk of it being practised in a directive form or for eugenic purposes. The origins and spread of genetic counselling as a result of the success of prenatal diagnosis by means of amniocentesis are examined by Robert Resta, who illustrates how cost-benefit calculus rather than statistically valid assessments of the risk-benefit ratio was used to justify the choice of the age of 35 as that after which amniocentesis is recommended. The medical justification, Resta claims, derives from the desire of genetic counsellors to distance themselves from eugenic ideas which would be directly implicated in any analysis based on economic cost-benefit ratios.

The theories supporting the legitimacy of using manipulations designed to bring about improvements in genetically controlled features have long since been abandoned in the debate on the use of biogenetic technologies as a function of reproductive choices. Fabio Bacchini and John Harris make a critical analysis of the arguments underpinning the thesis that it is morally wrong to allow positive manipulations, or to select or boost characters in children who come into the world with the help of the new medically assisted reproduction techniques. The conclusion they reach is that no argument against the hypothetical use of positive genetic manipulations has successfully demonstrated that these choices are intrinsically dangerous or that they cause any harm to anyone; indeed, they may have beneficial effects also for the child brought into the world.

The highly topical issue of human genetics marketing is at the centre of the articles by Ari Berkowitz and Daniel Kevles, and by Timothy Caulfield. Berkowitz and Kevles present a historical-comparative analysis of the development of patents legislation concerning human genes in the United States and in Europe, focusing on the absolute novelty of the use and adoption (in Europe) of ethical criteria to regulate the granting of rights to the economic exploitation of gene sequences. Caulfield uses a series of examples of different policies on the subject to compare the

effects of the benefits and risks involved in the process on scientific research conditions, and in particular how the patent-granting policies must be designed to promote innovation without at the same time causing any conflicts, or any concern and discouragement on the part of society at large regarding science and scientists.

The potential of medical applications of biotechnology has been enhanced in recent years by the development of cellular engineering, and in particular in view of the possibility of transferring the nucleus of somatic cells to enucleated oocytes or zygotes to create stem cells capable of differentiating into histocompatible tissues potentially able to repair damaged organs. The prospects of so called therapeutic cloning today lie at the focus of the international ethical-political debate, with special reference to the United States which has apparently decided to forego the potential scientific and applications benefits of the new technique applied to stem cells derived from embryos. Dorothy Wertz attended the meeting and reconstructed the history of the use of embryos and derivatives thereof in biomedical research in the United States, describing the religious and political-cultural factors that at a certain stage contributed to justifying a series of choices opposed to the use of embryos for research purposes.

Andrea Vicini's paper discusses the position of the Roman Catholic Church concerning research involving embryonic stem cells. On the basis of a comprehensive analysis of the technical and scientific problems involved in this research and their contextualization vis-à-vis the ethical-theological problem of material cooperation in the case of the use of cell lines derived from embryos destined for destruction, Vicini considers the decisions by the US President Bush and the German parliament as being in line with Catholic doctrine. The Jesuit theologian draws attention to the need to set research prospects using embryonic stem cells within the context of the broader debate on the promotion of a social justice that reduces healthcare inequalities as a result of which only an elite currently has access to the therapeutic benefits of the so called regenerative medicine. The fact remains, as was said by Cinzia Caporale, who at the meeting reconstructed and analysed the history of the ethical and political

debate on medically assisted fertilization in Italy, that the respect for all persons, starting from those who want children and those suffering from diseases that might one day be cured with the help of therapeutic cloning, are not shaping the regulations currently in the process of being approved.

Bioethics has certainly contributed to alerting public opinion to the impact of genetics and biotechnology and sociological studies and surveys of the way people perceive these innovations still arouse keen interest. Federico Neresini reconstructs the debate on biomedical technologies in Italy, claiming that the issue of identity, that is, the idea that biotechnology applied to medicine possibly threatens human identity and dignity has had a transversal cultural effect on the way these developments were treated in the national media. Massimiliano Bucchi sums up the results of the first two surveys of the public perception of biotechnology carried out in Italy in 2000 and 2001, and characterizes several specific features of the Italian situation. In general, he draws attention to a number of apparently paradoxical aspects of the relationship between levels of understanding of biotechnology and moral judgments passed on the various applications of biotechnological research, as well as the levels of confidence in political regulatory strategies.

As the promoters and organizers of the conference, we wish to thank contributors for their enthusiastic participation in the initiative and for stimulating discussions. We also wish to thank Luciana Rita Angeletti, Director of the History of Medicine Section and of "Medicina nei secoli" who made the journal available for the publication of the contributions, as well as the Head of the Faculty of Medicine of "La Sapienza" University of Rome, Luigi Frati, for the hospitality afforded to the conference. The Luigi Einaudi Foundation has accommodated within the mainstream of the more enlightened liberal tradition of this country this and other initiatives promoted by the Bioethics Observatory. Lastly the Compagnia di San Paolo di Torino, the Sigma Tau Foundation and MIUR helped make the event economically possible.