Ethical considerations on pharmacogenomics

Emilio Mordini*

Secretary of the Bioethical Commission of the National Research Council (CNR) Centre for Science, Society and Citizenship, Rome, Italy

Accepted 7 April 2003

Abstract

Pharmacogenetics offers the prospect of an era of safer and more effective drugs, as well as more individualized use of drug therapies. The effect of human genetic variance on responses to therapy will influence drug-development clinical trials and the use of products in clinical practice. It also promises to raise new ethical challenges, in particular in the fields of research and therapy. Last but not least, pharmacogenetics is likely to fulfil the old dream of an individualised medicine, but in a totally unexpected way.

© 2003 Published by Elsevier Ltd.

Keywords: Pharmacogenomics; Bioethics; Personalised medicine; Tailored drug; Clinical trial

1. Introduction

We are rapidly advancing towards the post-genomic era in which genetic information will be part of our everyday life. With the anatomy of the human genome at hand, the whole of society is facing a new challenge. We are increasingly able to interfere with or diagnose diseases, detect genes for monogenic disorders pre-symptomatically, uncover genetic predisposition to common disorders (including cancer and psychiatric disorders), anticipate normal phenotypic traits, and, in the near future will even be able to foresee behavioural traits, such as novelty-seeking behaviour, antisocial behaviour or sexual orientation. The main paradigm shifts provoked by the genomic era in biomedical research have been recently synthesized by Peltonen and McKusick. This genetic and biological revolution will undoubtedly also change clinical trials and clinical practice in the future. Genomics is likely to provide the opportunity to design and develop new drugs. Most pharmaceutical companies expect that the most future drug developments will come from the field of genomics. Along with the design of new drugs, genomics also will provide opportunities to predict responsiveness to drug interventions, since variations in these responses are often attributable to the genetic endowment of the individual. Examples have been identified where common variants in genes involved in drug metabolism or drug action are associated with the likelihood of a good or bad response.

The expectation is that such correlations will be found for many drugs over the next 10 years, including agents that are already on the market. In the long term, it promises to individualise prescription practices by narrowing the target populations exclusively to those for which the medication is safe and effective. The terms 'pharmacogenetics' and 'pharmacogenomics' (which can be considered to be almost synonymous) reflect this merging of pharmacology and genetics.

Any advancement in terms of knowledge also implies greater levels of complexity and an increasing number of problems; many ethical issues arise in the research and clinical application of pharmacogenetics. In a recent review of the ethical implications of pharmacogenomics, Buchanan at al. pointed out six ethical issues: (1) regulatory oversight, (2) confidentiality and privacy, (3) informed consent, (4) availability of drugs, (5) access, and (6) clinicians’ changing responsibilities [1]. In March 2001, an expert group convened in the International School of Pharmacology of Erice (Italy) issued the “Dichiarazione di Erice sui principi etici della ricerca farmacogenetica” (Erice Declaration of the Ethical Principles of Pharmacogenetics Research). Following that initiatives, in November 2001, the Italian Society of Hospital Pharmacy (Società Italiana di Farmacia Ospedaliera—SIFO) published a proposal of guidelines for the ethical review of clinical trials in pharmacogenetics. SIFO’s guidelines mainly focus on data collection and storage (http://www.sibce.it/documenti/pdf/lineeguida.html). The document addresses the issues of confidentiality, consent, anonymity and subject protection. An important chapter is also devoted to risks of stigmatisation and commercial
2. Research

Genomic knowledge is assisting drug discovery in several ways: (1) by identifying new targets for traditional drugs; (2) by helping us understand why certain drugs work for some people but not for others; (3) by helping explain drug side-effects; and (4) by allowing the introduction of new classes of drug, such as therapeutic proteins. More than one hundred protein-based drugs are now at advanced clinical trials stages and many more are being developed in laboratories [2].

Several positive ethical implications are expected from the application of pharmacogenomics to the process of development and discovery of new medicines. First of all, human subjects enrolled in clinical trials are likely to be more protected thanks to pharmacogenetics. An important ethical tenet in medical research involving human subjects is to minimize risks for participants by optimising the risks/benefits ratio for each participant. The European Convention on Human Rights and Biomedicine states that "Research on a person may only be undertaken if all the following conditions are met: (i) there is no alternative of comparable effectiveness to research on humans, (ii) the risks which may be incurred by that person are not disproportionate to the potential benefits of the research [...]" (art. 16). The application of pharmacogenetic analysis could refine selection criteria allowing to exclude from the study those who are at risk of developing adverse reactions. In particular, people who are at risk of developing side-effects could be excluded from phase I and II studies. During these preliminary phases, the risk of clinical trials will be reduced by targeting people to be investigated according to their genetic make up. In addition, more homogeneous groups of people could be enrolled in phase III, therefore allowing to reduce the numbers of people involved in studies. Indeed, another important positive consequence, from the ethical point of view, of the application of pharmacogenomics in medical research concerns the possibility of reducing the number of people enrolled in phase III studies. By identifying people who would not respond on the basis of genetic variation, researchers could improve the design of clinical trials by testing drugs only on people who would be likely to respond, thus conducting smaller but more effective trials. The drug approval process should be facilitated as trials are targeted for specific genetic population groups—providing greater degrees of success. Effectiveness is not only a scientific requirement of any clinical trial but is also an ethical pre-requisite of any research involving human subjects.

However, some controversial issues still need to be addressed, the regulation of pharmacogenomics probably being the most important of these. To date, no regulatory authority has specifically addressed the management of pharmacogenetic tests in the research, development and licensing of medicines [3]. Biomedical research involving DNA banking is governed by numerous legal and ethical guidelines, while we lack specific regulations on genetics research in clinical drug trials. The need to establish clear procedures for generating and handling genetic information in the context of pharmacogenetic research has led to a cross-industry group proposing standard definitions under which such research can be carried out. Indeed, ethics committees and regulatory authorities could find the current diversity of terminologies and approaches quite confusing. In 2000, the European Agency for the Evaluation of Medicinal Products (EMEA) set up a working party with the aim of harmonising genetic terms required for pharmacogenetics trial protocols and guidelines (www.emea.eu.int/pdfs/human/regaffair/148300en.pdf). In 2001, the US National Institute of General Medicine assigned a similar task to the Pharmacogenetics Research Network.

Tests are another important issue in research. To develop a drug that is effective for a particular sub-group of patients, genetic tests will be necessary for the identification of a specific population, but it is not clear at all whether these tests should become a regulatory requirement in the future. If this is to be the case, pharmaceutical companies will be expected to store an enormous amount of genetic information for the purpose of pharmacogenetic analysis. Genetic testing involves very sensitive and intimate items of information. Unlike most general medical information, it possesses an individual, a familial and a collective dimension. Even if genetic material is, by nature, specific and unique to each individual, it can also reveal personal information about blood relatives and indicate some medical trends encountered in a particular population. The integration of pharmacogenomics into drug development adds new dimensions to the process. The fact that genetic data are manipulated, analysed and stored in this context, calls for the adaptation of legal and ethical standards. We need to address the issues of the level of anonymity that should be accorded to this ge-
netic information. We also need to decide whether pharma-
caceutical companies which collect samples in the course of
research in pharmacogenetics may ask for a generic consent
from the donor or whether donor consent should be restricted
to specific usage. Finally, we need to establish whether re-
searchers should provide individual feedback about genetic
information obtained from participants in research in phar-
macogenetics.

Last but not least, we should address the issue of com-
mercial exploitation and intellectual property of pharmacoge-
netics databanks. The European Group on Ethics addressed
the general issue in its advice number 11 of 21 July 1998 on
“Ethical Aspects of Human Tissue Banking”. In point 2.8,
the IGE states: “In principle, tissue bank activities should
be reserved to public health institutions or non-profit mak-
ing organisations. […] Nevertheless given the current state
of development of the sector, it is difficult to exclude tis-
ue banking activities by commercial organisations, such as
large private laboratories”. In the case of pharmacogenetics,
data will be stored in private labs and used for commercial
reasons. In the context of clinical trials, it would seem wise
to subsequently destroy genetic samples taken specifically
for a pharmacogenetic test. However, one cannot exclude the
use of modern communication tools, such as the Internet,
to allow patients to provide samples for future research yet
retain control over them in the light of future developments.

Some possible approaches currently being considered in-
clude having DNA samples and patient contact details held
by an independent third party, who can then release DNA
for research after contacting patients using email or the In-
ternet [4].

In conclusion, it would be advisable for all the guaran-
tees currently in place for biomedical research (clinical trials
and genetic research) to also be adopted in pharmacogenet-
ics research. However, the most relevant ethical implication
of pharmacogenetics on research is likely to concern the
way in which clinical trials are designed and conducted. A
larger number of patients will probably be enrolled in phase
I and II studies in order to find the markers of polimor-
phism that can predict responses, while a smaller number
of patients will be investigated in phase III. Ethics commit-
tees and institutional review boards should take into account
these changes in order to correctly evaluate research proto-
cols. Another emerging issue is genetic tests for detecting
those people who are at risk of developing adverse reactions
to tested drugs. One day it may be considered unethical not
to carry out such tests routinely in clinical trials to avoid
exposing individuals to drugs that could be harmful to them.

3. Therapy

The promise of pharmacogenomics in reconfiguring ap-
proaches to drug use has considerable currency. Pharma-
cogenomics is expected to improve, even to overturn, current
approaches to drug treatment by reducing adverse reactions,
increasing drug efficacy and refining prescribing practices.
Pharmacogenomics is already being used in therapy. For ex-
ample, a test for common variants of the gene for thioruine
methyl transferase—an enzyme that affects the metabolism
of two antiblastic drugs, azathioprine and mercaptopurine—
is coming into use for the determination of the right dosage
of these two medications in acute lymphoblastic childhood
leukaemia [5]. In Alzheimer’s disease, genetic variations in
apolipoprotein E not only predict the onset of the disease,
but also give clues towards the right treatment to slow down
its progress. The drug tacrine seems to slow the disease’s
progress in patients who do not have two copies of the gene
for apolipoprotein E4. Other drugs may benefit patients with
Alzheimer’s disease who have different gene profiles for
apolipoprotein E4 [6]. Indeed drugs are designed and pre-
scribed on a population basis, but each patient is an individ-
ual. Current therapies are based on a trial-and-error method
of matching patients with the right drugs and right dosage. In
the future—at least in the rosy scenario described by many
scientists—doctors will be able to analyse a patient’s genetic
profile, define his/her appropriate patient group for a partic-
ular medicine and prescribe the best available drug therapy
from the beginning. Current methods of basing dosages on
weight and age will be replaced with dosages based on a
person’s genetics. This will maximize the therapy’s value
and decrease the likelihood of overdose. However, it is dif-
ficult to ascertain to what extent the enthusiasm of scientists
towards discovery—and sometimes their direct involvement
with pharmaceutical companies—may affect their forecasts.
Perhaps in the future we may all carry a “gene chip assay
report” that contains our unique genetic profile that would be
consulted before drugs are prescribed, but at present chips
allowing the genetic profiling of patients are still science fic-
tion. There are few doubts that genetic information will be
able to identify those who cannot take a particular drug, yet
we are far still far from developing technologies such as a
genetic cards or similar devices. At present, what we can rea-
sonably forecast is that tests will become available for deter-
mining which patients will benefit and which will be harmed
by certain drugs. This will in any case comprise an impor-
tant breakthrough; knowing whether a patient will respond
is important so that the best treatment can be given straight
away and because of the high cost of some treatments. Dis-
covering variations in responses is particularly important in
drugs for psychiatric conditions such as schizophrenia and
depression and other chronic or recurrent diseases. Major
cost savings could come from testing for genetic variations.
Ultimately economic issues will drive pharmacogenomics
into conventional practice: the cost of drug failures—drugs
given to people that don’t work, that delay proper treatment,
that increase the cost of care, the expense of treatments for

toxicity and the expense of return visits. Adverse drug reac-
tions occur in a substantial proportion of patients: accord-
ing to a recent study, about two million Americans are hos-

pitalised each year because of drug interactions, and about
106,000 die [7]. Until recently, the only way to identify a pa-

YPHRS 1284 1–5
 PATIENT WITH A GENETIC RISK FACTOR FOR A PARTICULAR ADVERSE DRUG REACTION WAS TO CARRY OUT TEDIOUS PROCEDURES INVOLVING THE ADMINISTRATION OF A SPECIFIC MARKER DRUG OR TEST SUBSTANCE.

MODERN DNA-BASED TESTS REQUIRE ONLY A SMALL SAMPLE OF TISSUE BLOOD FROM A FINGER PRICK, CELLS FROM A MOUTH WASH OR HAIR FOLLICLE CELLS. ALL THESE ELEMENTS PRESENT SEVERAL POSITIVE ETHICAL IMPLICATIONS. THE USE OF GENETIC TECHNOLOGIES TO REDUCE THE UNCERTAINTY SURROUNDING HEALTH STATUS AND HEALTH RISKS WILL INCREASE INDIVIDUAL’S AUTONOMY. CITIZENS WILL BE EMPOWERED BY HAVING THE INFORMATION THEY NEED WHEN THEY NEED IT TO MANAGE THEIR OWN RISK. SIMILARLY, THE APPLICATION OF PHARMACOGENOMICS IN PLANNING MEDICAL TREATMENT WILL ALLOW TO MAXIMISE BENEFITS AND MINIMISE RISKS, RESPECTING THE ETHICAL TENETS OF BENEFICENCE AND NON-MALFEICENCE.

AT A TIME WHEN HARMFUL DRUG REACTIONS ARE THOUGHT TO RANK JUST AFTER STROKES AS A LEADING CAUSE OF DEATH IN THE US, THE POTENTIAL BENEFITS OF TAILORING DRUGS TO A PATIENT’S GENETIC MAKEUP SHOULD NOT BE UNDERESTIMATED EVEN FROM AN ETHICAL POINT OF VIEW.

YES, IN SPITE OF THIS POSITIVE SCENARIO, SOME HURDLES REMAIN. FIRST OF ALL, SOME SCIENTIFIC QUESTIONS NEED TO BE ASKED ABOUT THE EFFECTIVENESS OF THE APPLICATION OF PHARMACOGENETICS IN THERAPY. THE CLINICAL APPLICABILITY OF PHARMACOGENETIC TESTING DEPENDS ON THE RELATIVE IMPORTANCE OF EACH POLYMORPHISM IN DETERMINING THERAPEUTIC OUTCOME. AS WELL AS HAVING GENETIC VARIATIONS, INDIVIDUALS ARE IN DIFFERENT STATES OF HEALTH, EAT DIFFERENT DIETS, TAKE DIFFERENT DRUGS—ALL OF WHICH MAY AFFECT RESPONSES TO DRUGS. DOCTORS NEED TO BE AWARE OF WHETHER A DRUG THEY ARE PRESCRIBING IS SUBJECT TO PHARMACOGENETIC VARIABILITY WITHOUT TAKING IT FOR GRANTED THAT GENETICS PLAY THE MAIN ROLE IN DETERMINING A PATIENT’S RESPONSE TO TREATMENT. A GENERAL WARNING IN THIS RESPECT APPEARED IN THE VERY ISSUE OF SCIENCE WHICH ANNOUNCED THE SEQUENCING OF THE HUMAN GENOME: “THE SUCCESSES OF MEDICAL GENETICS AND GENOMICS DURING THE LAST DECADE HAVE RESULTED IN A SHARP SHIFT TOWARD AN ALMOST COMPLETELY GENETIC VIEW OF OURSELVES.

I FIND IT STRIKING THAT 10 YEARS AGO, A GENETICIST HAD TO DEFEND THE IDEA THAT NOT ONLY THE ENVIRONMENT BUT ALSO GENES SHAPE HUMAN DEVELOPMENT. TODAY, ONE FEELS COMPelled TO STRESS THAT THERE IS A LARGE ENVIRONMENTAL COMPONENT TO COMMON DISEASES, BEHAVIOUR, AND PERSONALITY TRAITS! THERE IS AN INSIDIOUS TENDENCY TO LOOK TO OUR GENES FOR MOST ASPECTS OF OUR “HUMANNESS”, AND TO FORGET THAT THE GENOME IS BUT AN INTERNAL SCAFFOLD FOR OUR EXISTENCE” [8].

THE THERAPEUTIC APPLICATIONS OF PHARMACOGENOMICS MAY ALSO RAISE SOME ETHICAL QUESTIONS. ONE FACT WHICH MAY HAVE ETHICAL IMPLICATIONS IS THAT MANY GENETIC VARIANTS CLUSTER IN RACIAL GROUPS. AS A RESULT, IT IS INEVITABLE THAT SOME FAIRLY SMALL RACIAL POPULATIONS HAVE GENETIC VARIANTS THAT MAKE THEM PARTICULARLY VULNERABLE TO SOME DRUGS. THIS CAN CREATE STIGMATION AND DISCRIMINATION AND, IN SOME CASES, DRUG MANUFACTURERS MAY NOT FIND IT ECONOMICAL TO DEVELOP A NEW DRUG TO AID A POTENTIALLY SMALL MARKET. THE RISK OF CREATING INEQUITIES WHEN DEVELOPING DRUGS TO AVERT PROBLEMS CAUSED BY NATURAL GENETIC DIFFERENCES LINKED TO RACE IS AN IMPORTANT ONE. FRAGMENTATION OF THE MARKET INTO SMALLER AND SMALLER GROUPS MAY NOT JUSTIFY RESEARCH AND DEVELOPMENT EXPENDITURES ON WHAT WOULD BECOME ORPHAN DRUGS. IN EUROPE AND IN THE USA, THE ‘ORPHAN MEDICINE’ STATUS IS GRANTED IF THERE ARE FEWER THAN 200,000 POTENTIAL PATIENTS. THE ‘ORPHAN MEDICINE’ STATUS IMPLIES VARIOUS LEGAL AND FINANCIAL INCENTIVES TO PROMOTE RESEARCH AND DRUG DEVELOPMENT. OBVIOUSLY EXISTING REGULATIONS ARE NOT BASED ON PHARMACOGENOMICS: ONE MAY WONDER WHAT WILL HAPPEN WHEN PHARMACOGENETIC ANALYSIS CREATES HUNDREDS OF NEW “ORPHAN” DISEASES AND MEDICINES. THERE IS A RISK THAT THIS NEW SITUATION MIGHT CREATE A NEW GROUP OF DISEASES AND PATIENTS WHO WILL BE TOLD BY DOCTORS THAT A DRUG CANNOT BE ADMINISTERED IN THEIR CASES. WE NEED NEW REGULATORY MEASURES TO ENCOURAGE THE DEVELOPMENT OF CLINICALLY DESIRABLE BUT ECONOMICALLY UNPROFITABLE MEDICINES, OTHERWISE THE APPLICATION OF PHARMACOGENETICS MIGHT EXACERBATE INEQUALITIES IN THE PROVISION OF HEALTHCARE.

GENETIC EQUITY DOES NOT ONLY CONSTITUTE POTENTIAL NEW “ORPHAN” MEDICINES, BUT ALSO THE OBLIGATION TO TREAT THOSE WHO HAVE DIFFERENT GENETIC MAKEUPS. FOR INSTANCE, VAXGEN HAS RECENTLY ANNOUNCED THAT A GENETICALLY-ENGINEERED AIDS VACCINE, WHICH HAS BEEN UNDERGOING PHASE III TRIALS FOR THE PAST THREE YEARS, HAS FAILED TO SHOW A SIGNIFICANT REDUCTION IN THE DEVELOPMENT OF HIV AMONG THE THOSE WHO WERE VACCINATED. HOWEVER, THE VACCINE HAS INDEED SHOWN A SIGNIFICANT SUCCESS RATE, BUT ONLY IN CERTAIN ETHNIC GROUPS, INDICATING THAT BLACK AND ASIAN VOLUNTEERS MAY HAVE PRODUCED HIGHER LEVELS OF ANTIBODIES AGAINST HIV THAN WHITE AND HISPANIC VOLUNTEERS. THE VACCINE IS THUS OF SOME INTEREST FOR CERTAIN ETHNIC GROUPS, EVEN IF THEY ARE DIFFERENT FROM THE GROUPS TARGETED BY THE STUDY.

4. International justice and pharmacogenomics

THE GENOMICS REVOLUTION WILL BRING ABOUT NEW CURES, NEW SCREENING DEVICES, AND NEW WAYS TO ADDRESS MEDICAL PROBLEMS. YET THE APPLICATION OF THE NEW GENETICS WILL COME WITH A HIGH PRICE TAG, AT LEAST IN THE SHORT TERM. EVEN IN RICH, DEVELOPED COUNTRIES, UNLESS STEPS ARE TAKEN TO PREVENT IT, WE MAY SEE A REPETITION OF THE “DIGITAL DIVIDE”, AS GENETIC TECHNOLOGIES BECOME AVAILABLE FIRST TO THE WEALTHY OR WELL-INSURED. WHETHER THE GREAT HUMAN ACHIEVEMENT OF UNLOCKING AND CONTINUING TO UNDERSTAND THE SECRETS OF THE HUMAN GENOME TURNS OUT IN THE SHORT TERM TO BE A GREAT STEP FORWARD FOR HUMANITY OR A LUXURY FOR THE WEALTHIEST OF THE PLANET DEPENDS ON THE SOCIAL CHOICES WE MAKE IN THE NEXT FEW YEARS. IF EFFORTS ARE NOT MADE TO SPREAD THE BENEFITS TO THOSE MOST IN NEED OF THEM, THEN THIS GREAT ACHIEVEMENT WILL NOT TRULY BE REALIZED FOR MANY YEARS TO COME. THIS HOLDS TRUE EVEN FOR PHARMACOGENETICS. BIOMEDICAL RESEARCH IS INCREASINGLY BECOMING A COLLABORATIVE Venture BETWEEN RESEARCHERS IN DIFFERENT COUNTRIES WITH DIFFERENT LEVELS OF WEALTH. THE RESULTS OF RESEARCH DONE IN ONE COUNTRY WILL BE UTILIZED TO SEEK REGULATORY APPROVAL IN ANOTHER COUNTRY. THERE IS THEREFORE AN URGENT NEED FOR A HARMONISATION OF INTERNATIONAL GUIDELINES AND RULES GOVERNING BIOMEDICAL RESEARCH ALSO RELATING
to pharmacogenetics. The first ethical tenet should be to apply to pharmacogenetic research the current guidelines that rule the ethics of international clinical trials. In particular, it seems important to consider the CIOMS’ “International Ethical Guidelines for Biomedical Research Involving Human Subjects” (revised August 2002). In Guideline 1 (Ethical justification and scientific validity of biomedical research involving human beings) it is stated: “The ethical justification of biomedical research involving human subjects is the prospect of discovering new ways of benefiting people’s health. Such research can be ethically justifiable only if it is carried out in ways that respect and protect, and are fair to, the subjects of that research and are morally acceptable within the communities in which the research is carried out. Moreover, because scientifically invalid research is unethical in that it exposes research subjects to risks without possible benefit, investigators and sponsors must ensure that proposed studies involving human subjects conform to generally accepted scientific principles and are based on adequate knowledge of the pertinent scientific literature”. This means that pharmacogenomics analysis is ethically acceptable only if the drugs which have been developed for administration in conjunction with a pharmacogenetic test are also distributed to host countries in which testing facilities are not available.

5. Personalised medicine?

In the long run, the development of pharmacogenetics will provide a mechanism to move prescription away from its current empiricism towards a more “individualised” kind of drug treatment. There are two sides to this coin; while on the one hand, the use of pharmacogenomics analysis can have a positive impact on drug discovery and therapy, on the other it also entails the risk of promoting “cosmetic medicine”. In the media debate the phrase “cosmetic medicine” evokes the concept of consumer satisfaction, and acts at the borderline of the realm of health, in areas such as the use of medication for improving social and working skills, physical appearance, etc. For instance, many sports scientists warn that current performance-enhancing drugs may be a thing of the past once pharmacogenomics are introduced. We live in a world where people are always seeking to improve their performances (working, social, athletic, intellectual, sexual, etc.) as much as possible. Drugs offer a simple, technical, solution to do the job. Genetic enhancement is not only a science fiction dream, it is also an important drive of current research. It has also been said that we live in an addicted society, at least in the sense of a society where biochem-icals are used to find easy solutions to societal problems. With drugs tailored reliably to an individual’s genome and biochemical symptoms, many of the skills that doctors now deploy will have become automated. This will not apply to all areas, of course, but those operating in many branches of medicine may find that their jobs have been superseded by chips. Technology has significantly altered the form and meaning of the medical relationship. Increasingly, technical aspects dominate the doctor–patient relationship. Now these aspects may even come to determine the possibility of individualising therapy. The appropriateness of using technical procedures as a way of dealing with societal problems is always highly debatable, and this trend is one which needs to be carefully checked.

However, the paradox inherent in pharmacogenomics is that technological medicine is creating a new personalised medicine. There is a certain irony in this, considering that one of the main outcomes of the genetic revolution will be to see an aphorism often used to criticize modern technological medicine come true, that is, that you should treat the patient, not the disease—or, at least, that you can and should tailor treatment to the patient. This perhaps will have us remember that, as usual, there are things in heaven and earth than are dreamt in our philosophy!

Acknowledgements

This work was partly funded by a grant from the European Commission—DG Research—Contract number QLG6-CT-2002-01796.

References


YPHRS 1284 1–5