Should Ethical Issues in Biotechnology Research be Decided by Physician-Scientists or by Lawyers?

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As with clinical practice, the practice of biomedical research is a moral activity. We have to think about what we should do, not just about what we can do, to modify life. We would do well to remember what Peter Medawar called the 'limits of scientific discovery'.[1,2] Also, there are distinct limits to the present understanding of the boundary zone between living things and non-living things, although some researchers are unaware of these limits.

Actually, some researchers may be as misled by the media-generated hyperbole ('hype') as the general public. I believe this is particularly true of the people who work at the interface between experimental biology and industry—the sphere called biotechnology, which includes bioengineering and genetic engineering. Why is this? Chiefly because non-clinical biotechnologists do not see the failures of intervention in living patients; physicians do.[3] The experience of physicians is a crucial counterweight to the unbridled enthusiasm of scientists. As Karl Popper stated, "It must be possible for an empirical scientific system to be refuted by experience ... not the verifiability but the falsifiability of a [scientific] system is to be taken as a criterion of demarcation".[4]

Why do We Need Research Ethics?

Designing and implementing an experimental study often requires us both to ask factual questions ("How does this disease arise? Does this drug produce a clinically important effect?") and to make value judgements ("This intervention is likely to alter the natural course of this type of stomach cancer", or "The unwanted effects of treatment are so severe that we should stop the trial"). As in managing ill patients, therefore, research requires not only scientific and technical knowledge, but also value judgements. These judgements need to be systemically analysed and validated, just as with the results of experiments.

So, ethics or moral philosophy is that set of rules which guides rational and good behaviour. Bioethics is that branch of ethics which deals with biomedical research, specifically with questions related to artificial reproduction, tissue transplantation and genetic engineering. Ethics cannot define absolute right or absolute wrong; even if it could, it may not be valid in all possible types of research. Also, how ethics translates into real behaviour varies according to the religious, socioeconomic and political context. For this reason, I believe we ought to pay greater attention to humanist moral principles that transcend religion, while recognising that any given community's ethical guidelines are influenced by the legal, socioeconomic and political climate of the time.

Thinking Systematically in Ethical Terms

In a widely accepted belief system, there are two general ways of assessing value judgements—the Consequential-Utilitarian method and Duty-based ethics (deontology). Although the terminology of the methods came from Jeremy Bentham and John Stuart Mill, and Immanuel Kant respectively, the systems share many elements with the moral ideas from within the great cultures of humankind. According to Consequentialism, the right action is that which produces the best foreseeable outcomes. By the Utilitarian approach, the important thing is to choose the action that results in the greatest happiness of the greatest number of people. Of course, the devil is in the details, and many experts earn a living defining quality adjusted life years and allocating finite healthcare resources.

According to Kantian duty-based ethics, we should decide what is right according to the nature of our actions, always

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remembering that we owe a duty to respect one another. For example, to a duty-based ethicist, it is immoral to breach confidentiality, regardless of the consequences. It seems to me the gaps between the two methods allow the variations in actual behaviour depending on the current medicolegal regulations.[5] Recently, 4 fundamental principles of human bioethics have become widely accepted, though not applied everywhere—respect for the person (autonomy), beneficence (doing what's best for the individual), non-maleficence (avoiding harm) and justice (balancing the needs of an individual against those of society). The principles are a useful framework for judging validity and morality in bioscience studies.[6]

What Factors Determine Whether a Study is Ethical?

In some experimental studies, the ethical issues are plain. For instance, in 1941 the large bactericidal effect of penicillin on highly sensitive strains of *Staphylococcus aureus* required only careful observation, no randomised, controlled, clinical trials to prove. To refuse a seriously infected patient the benefit of appropriate antimicrobial treatment is unethical. By contrast, a neuroscientist may want to decrease infarct size in stroke through the early injection of, say, a metabolism-modifying drug. The study patients are often so obtunded that informed consent must come from a proxy. A hurried explanation of the need for a randomly assigned inactive control usually fails to obtain consent. If the investigator gives the patient the study drug first, and obtains consent later, the principle of autonomy is broken. But the slow recruitment of participants deprives society of a possibly beneficial treatment (for a time), thereby breaking the principle of justice—therein is the dilemma. Many human studies fall between these extremes.

One of the best justifications for making a treatment study is a true equipoise between the qualitative benefit and the quantified risk of adverse effects associated with an intervention.[7] When there is genuine doubt about the net benefit of intervention, a carefully-designed study provides the technical and ethical foundations for proper action. Conversely, a poorly-designed study is nearly always unethical, because net harm may occur to the participants, the investigators and to society.

In many human studies, both the small size of the treatment's benefit and the rare but serious harmful effects conspire to mandate large studies. Large studies cost much money and resources. This fact is at the root of much of the present troubles in bioscience research, from fraud to bad science. Industrial companies, wishing to save time (= money), may press investigators to cut corners and to ignore bioethical constraints. We should recognise that it is greed for fame and fortune that drives some biotechnology researchers, in particular those dealing with 'therapeutic cloning', which promises large rewards in terms of replacement human tissues. 'Big science' continually threatens to destroy good science.

For all the above reasons, if we are to practise biomedical research in the way we believe is right, we must know what value judgements are important in a specific research setting, understand the relevant bioethical issues, open our views to independent and critical analysis to assure logical and consistent views and amend our views in the light of such analysis.

A Systematic Approach to Making Bioethical Decisions

All the concerned people should resolve bioethical issues jointly: research participants, physicians, biotechnologists, research nurses, families and research managers. But ethical guidelines and moral philosophy may not always resolve disagreements. Two or more persons might disagree even after fully considering the key issues clearly and logically. If conflict is an unavoidable feature of ethical analysis, how should physicians or scientists who wish to practise ethical research proceed?

Researchers and their institutions must be ready to justify publicly their decisions and actions. Therefore, a researcher should attend to the grounds for making decisions and establish a valid process for making the decisions. To improve the quality of the decision, we need to answer questions like—Have we consulted the right people before making the decision? Are we making the decision in the correct forum? Have we discussed the key issues thoroughly? Have we recorded the decision properly? Do we have a proper system for reviewing the decision?

Regulatory Structure

We in Singapore are fortunate that basic regulatory mechanisms are in place. The Faculty of Medicine of the National University of Singapore has run seminars and workshops on good clinical research practice for biomedical researchers since 1997. All hospitals and research institutions have their own research ethics committees, established in accordance with the International Committee on Harmonization guidelines on the composition and function of such committees.[8] The Health Sciences Authority is charged with overseeing the design and implementation of clinical intervention trials. Nonetheless, a defect of any largely self-regulating system is that sometimes it can and will break down at its weakest point, i.e. the conduct of the investigators.

Leave it to the Judiciary?

The Bioethics Advisory Committee (BAC) is an important forum for an open discussion of current dilemmas in bioethics; its broad consultative approach is surely the right way to go. Wide discussion is a key activity for the BAC, as it is for local ethics committees. However, some have argued that it might be best to leave the resolution of conflicts between biomedical science and morality to an independent institution, such as the judiciary.[9] By this argument, no single institution, religious dogma, profession (e.g. biomedical scientists) or financial bloc (e.g. the biotechnology industry) would have an undue influence on debates over bioethical dilemmas. This is a compelling argument, especially because the power of science has radically altered the social environment in which moral decisions occur.

The market place increasingly determines the direction of biomedical research, because private companies pay bigger salaries than public institutions. The more democratic the society, the more empowered the ordinary citizen; if these conditions coincide with a profit-driven economy, we have a potent mix. Furthermore, many people medicalise their unwanted feelings and look for quick fixes. The result is a distortion not only of priorities in life but also of moral values. What better solution than to leave the bioethical dilemmas to the law?

Tension Between Enterprise and Human Rights

Entrepreneurs in many societies will consider the judicial process too sweeping and too slow for resolving bioethical difficulties. To others, the very slowness of the legislative and judicial processes is, to an extent, a virtue. Indeed, seeking guidance from the courts is a useful way of widening the public debate of bioethical issues, in particular of issues at the start and the end of human life. The drawback of this route of resolving dilemmas is that no bill can cover every possible nuance of bioethics, and the interpretation of the laws still requires a thorough understanding of the technology and its likely consequences for the people involved. There is a profound need to transfer very complex information to lawyers and judges. For instance, knowing the correct statistical meaning of DNA fingerprinting evidence from crime scenes is challenging to biologists, never mind lawyers.

The BAC recommended a statutory board to oversee stem cell research and genetic engineering, in particular germline modification. Competent physician-scientists are uniquely able to explain not just the science but also the risks and potential benefits of technologies and treatments. Perhaps, therefore, society should give physician-scientists the main, but not exclusive, responsibility to decide what is right or wrong in biotechnology research of this type. But first, we require a core of physician-scientists with the requisite knowledge and experience to lead debates and make some, if not all, of the crucial bioethical decisions. This will be an expensive long-term enterprise, but surely it is worth investing in a sound system for protecting not only the rights of individuals but also our national reputation as a civilised people?

Conclusion

We cannot stop the urge to unfurl the envelope of life through experimental research. Only the practical constraints of experiment set the ultimate limits of what can be done to radically alter the course of human evolution. Piecemeal biological engineering behaves as if the consequences are beyond its province. The legislative machinery reacts slowly to the growth of bioscience knowledge and technology. Physician-scientists should work in different contexts to promote honest explanation and discussion of issues raised by genetic and biotechnology research. Whenever our collective wisdom does not prevail over greed or emotion, nature has a way of biting back where it hurts most—if not now, later.

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