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Policy and ethical issues in applying medical biotechnology in developing countries

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Summary

A brief review of some of the key issues in policy relating to the ethical issues raised by medical biotechnology in developing countries is presented, using India as an example. A series of some key issues is discussed, including information obtained from interviewing Indian government policy makers. Some of the issues discussed include: Economic and social incentives to encourage biotechnology; Health policy and ethics review; Patents on drugs; Medical genetics; Relationship to traditional medical practices; Positive public attitudes to biotechnology; Limited public participation; Infrastructural hurdles; Indian progress in stem cell research; and dilemmas of expensive technologies. The results show that although the needs of developing countries are different to those of rich countries, government policy utilizing guidelines and ethics committees has evolved as mechanisms to aid ethical health care delivery in India. In all countries there may be some of these concerns that are raised here, however, the integration of traditional medicine and advanced medical technology, and access to medical services by people in need, are particularly important challenges in developing countries. Better public involvement in policy making will require education and infrastructural organization as well as mutual willingness on the part of policy makers and citizens.

key words: India • policy • bioethics • biotechnology • developing country

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1. BACKGROUND TO BIOETHICS AND MEDICAL BIOTECHNOLOGY

Human beings have been using nature and its products throughout history. We can define biotechnology as the use of living organisms or parts of them to provide goods or services. Medical biotechnology is applied to the diagnosis or treatment of a disease. Use of technology in living organisms has been subject to debate, and has often posed questions of medical ethics and policy.

In the 1970s the field of medical ethics evolved into a more philosophical analysis called bioethics [1]. Bioethics emerged as an independent field when developments in medical and biological sciences started challenging the ethical implications of scientific progress and established principles of medical ethics were unable to satisfactorily answer them. Bioethics encompasses both medical ethics and environmental ethics, including areas like public health. It is a multidisciplinary subject including medicine, environmental sciences, humanities and philosophy. Balancing of ethical principles can aid rational decision making; and the four fundamental principles of bioethics include autonomy (self rule), justice (love of others), non-maleficence (do no harm or loving life), beneficence (loving good) [2,3].

Although the principles of bioethics and moral theories are universal at one level of comparison because of the common biological and social heritage of every culture, there are subtle cultural differences. Ethics in Asia focuses more on human attitudes to nature and relationships with other members of the biological community rather than a modern North American concept that the basic social unit is a human person as an autonomous unit [4]. Societies vary in their emphasis on individuals or families as units that interact with health professionals. Societies are also under transition from paternalistic systems of relationships between health professionals and patients to choice-based societies.

2. METHODOLOGY OF INTERVIEWS IN INDIA

India is usually referred to as a 'developed developing country', so it faces problems of both developed and developing countries. India is country of more than one billion people and the main reason for promoting biotechnology and medical research is not only to reduce the burden of disease in the nation but also to be equally compatible with the world in scientific research. In order to provide some perspectives on how policy is being debated in India interviews were conducted with government officials on various biotechnology issues in different ministries and government institutions. This paper includes some example comments that were given during interviews in November 2001. The interviews focused on the bioethical challenges these 24 policy makers faced in developing policies in biotechnology and genetics research in India. Only 4 of the subjects were female, and 15 of the 24 subjects agreed to being tape recorded. Interestingly most of those who did not

wish to be recorded were in more junior positions, as they were more fearful of being quoted, although we guaranteed their anonymity. Some of the interviewees were members or having observer status in the different ethics committees or review boards set up by the government or its institutions.

The institutes that were surveyed included the All India Institute of Medical Sciences (AIIMS), which is the biggest government hospital in India; the Department of Biotechnology (DBT) under the Ministry of Science and Technology which serves as a nodal point for all biotechnology related research; Indian Council of Medical Research (ICMR), the apex body in India for the formulation, coordination and promotion of biomedical research; the Ministry of Health and Family Welfare; and National Institute of Science Technology Advanced Development, an Institute responsible for transfer of technology, linking people to technology and promoting federal efforts at local level.

3. ECONOMIC BARRIERS TO MEDICINE

As the world's largest democracy with more than half the population below middle class, there are many infrastructural problems that face developing countries, such as bureaucratic structures, corruption, lack of universal health care access. Above all the lack of funds for medical care experienced by so many people is dominant for a developing country and limits the choices open to its citizens [5].

Many administrative hurdles make it difficult to keep pace with international research, as was observed by one doctor, stating, '*Personally I feel that finance is not a major constraint. DBT has put lot of money in it, the main problem is the bureaucratic hassles. First is the approval and then it takes months to release the funds*'. There is a three tier health system, the rich, the middle class, and those who cannot afford to pay who must rely on the generosity of hospitals and donors. Discrepancies over private and public hospitals were raised as one interviewee said, '*Government hospitals are cheaper but less equipped with good facilities, and private clinics apply good services to patients*'. *People have to pay, as a public medical practitioner said, 'Government sector gets choked because of the rush of patients, even then anyway 90% of the money patients still have to pay, theoretically it may be free but still you are asked to buy small things*'.

There is much enthusiasm among scientists and government in India about the prospects of genome research and stem cell research in India. There is a specific government Department of Biotechnology, reflecting the positive attitude of the government. There is some sense of national pride to try to use the resources available within the country considering the great diversity of genetic resources that could be 'tapped' for genetics research because of the diverse ethnic groups (over 300 official ethnic groups) and the multi-cultural social system in the country. The motivation is also economic development, something that has not been a priority for many smaller developing countries.

There are a number of critics of this emphasis however, and many criticize that any venture into genomics will not be considered as a first priority for India. As one person said, *'strategically genomics does not fit into our priorities, it has a long gestation period, we can't expect results in an year or two, so it would not be good to divert resources from ensuring primary and secondary health care to genomics'*. This is a practical dilemma facing health care professionals in their choice of vocation also, i.e. whether to devote their time to the immediate needs around them or to contribute to a long term research project with uncertain rewards for society. Nevertheless, there needs to be health research in order for developing countries to overcome the burden of disease and accidents that afflict them [6]. Because the needs of a developing country are particular, a local system of health research is necessary for development of capacity, knowledge, utilization and management of knowledge and for the mobilization of resources [7]. These research systems often do not include sufficient resources for examining the social and ethical dimensions of health, although this type of research is within the financial means of most developing countries.

Global inequity is not a new problem but it is of central importance. Because of the importance of international protection of intellectual property rights (IPRs) for technological and cultural exchanges and promotion of free trade there is an international system for IPRs. IPRs regarding biotechnology have been discussed at various international forums including WIPO, WTO, UNESCO [8], and UPOV, as well as at each national patent office. By April 1998, 132 countries had signed the Trade Related Aspects of Intellectual Property Rights (TRIPs) agreement, discussed under the General Agreement on Tariffs and Trade (GATT) and the WTO. There have been possible conflicts observed in article 27 of the TRIPs agreement by the United Nations Commission on Human Rights [9]. The right of governments to impose compulsory licensing in medical interventions to protect public health was affirmed by WTO in the Doha Declaration [10]. India has been involved in several international disputes related to U. S. companies claiming patents on agricultural and medical products extracted from plants long known to be medicinal, such as the Neem tree. This issue has been raised in agriculture, considering rewards for farmers for their innovations in the development of plant and animal varieties. There may be knowledge that should be global commons, but it is a complex issue [11].

On the issue of generic drugs and multi-national companies involvement, one person observed, *'there is lot of noise about patents now because we are signatory to GATT and patents are going to effect local pharmaceutical industry a lot. We produce drugs at low cost which is affordable to people and also a source of foreign income, which will vanish after 2005'*. Another person said, *'Local pharmaceuticals are trying to have collaborations with MNCs because they think anyway 80% of the core drugs are out of treatment, then better drugs through recombination technology will come through and would be costlier if imported. So they are gearing up for joint venture with MNCs'*. The government has a difficult job to make

compromises between various voices in Indian industry and the tradition of many NGOs in India to be leaders of global campaigns against patenting. India and China are huge countries that have a local drug industry, and are not only recipients but is also donors of drugs. Most developing countries are dependent upon drug donations, and there are WHO guidelines on these [12].

4. ETHICAL REVIEW OF MEDICAL RESEARCH AND PUBLIC PARTICIPATION

Governments continue to devote increasing proportions of their gross national product to medical care, whether rich or poor. Concerns were raised by respondents interviewed primarily in the provision of infrastructure facilities, equity, poverty and other socio-economic concerns. One interviewee said, *'There are people who can afford medical facilities with all kinds of luxuries at their door steps and there are people who can't afford safe food or safe drinking water. So this kind of heterogeneity which is very enormous is a big ethical challenge'*.

In order to meet with these challenges appropriate applications of modern biotechnology need to be continually developed. However, for the majority of peoples in the world, who live in developing countries, the implementation of established therapies would alleviate much human suffering, both for infectious and non-infectious diseases. This means that critics inside many developing countries would prefer to put more funding into implementation of therapies and disease control rather than investment into new technology.

In India, an IEC (Institutional Ethics Committee), which is equivalent to what is called an Institutional Review Board (IRB) in many countries, approves all the projects involving human subjects. If the IEC has some questions, the proposal is forwarded to the Drug Controller General of India (DCGI) for clearance. DCGI is considered equivalent to the US FDA. In the case of controversies or if the trials are of national importance they are referred to the national ethics committee under ICMR, which is decided by the Drug Controller General of India. The national bioethics committee looks at all the issues related with human research clinical trials.

However, issues related to basic research regarding gene therapy come under the authority of DBT. In the case of gene therapy, somatic gene therapy is permitted in India, but germ-line gene therapy or gene therapy for enhancement is not allowed. A gene therapy trial consists of two parts. The first part is preparation of the gene construct to be administered, and the second part is evaluation of the efficacy and safety of the administered gene (construct). As far as the first part is concerned, the guidelines and clearance for it is to be regulated by the National Bioethics Committee under DBT and for the second part clearance from the local IEC and Central Ethical Committee (CEC) of the ICMR shall be obtained. Children could be candidates for therapy if it is meant for a childhood disorder. For comparison, issues related to stem cell research are first cleared by

institutional ethics committee and then referred to the national bioethics committee for final approval.

The ICMR has taken the lead in developing ethical guidelines for selected areas of medical biotechnology, including reproductive technologies and medical genetics, and these are on-line [13]. There is no concrete legislative framework at the federal level on some very sensitive issues like genetic privacy, although there are guidelines provided by the Medical Council of India (MCI) for practitioners and surgeons. There are a number of ethical issues for research in general in developing countries [14].

A common difficulty in making policy was cited as lack of knowledge and public enthusiasm for policy recommendations. Public participation is at a very low level in government matters; although many people will express an opinion when they are personally asked. One reason for the absence of much public uproar against stem cell research or any other genetic technology is that the scientific research is usually conducted quietly; away from ordinary lives. Around 70% of the Indian population lives in villages and there is wide gap in between the lifestyles of people living in villages with those dwelling in the cities. This is also a major obstacle in the flow of information among people. Comments on pro or against technology are left for the NGOs and media; rather than ordinary people.

People living ordinary lives are unaware of such developments. Lack of interest among people stems out of very fundamental ethical question of education. Lack of education results in lack of interest and consequently lack of public participation. This is a serious ethical issue when human lives are involved. Active public participation is necessary for interactive bioethics. An example was given by a person saying, *'We made draft ethical guidelines in 1998 and send to more than 1000 medical professionals for comments, but only 120 replied. Following that we had regional debates, we advertisements in the local newspapers so that public can come and attend, hardly 2 or 3 persons came. Public participation is limited to journalists who write on such issues'*.

Even NGOs, who bridge the gap between people and power are thought to be too radical of any government's decision, because of their protests. Sometimes their views are alienated rather than a combined mutuality. One person dealing with NGOs said, *'NGOs put a lot of pressure on government to review its decisions. But which pressure would work more is likely to be determined by all. If they are right for one thing, they may be wrong on many other things'*. There were concerns raised on the lack of institutional ethics committees and also lack of central accreditation system for medical research and agriculture research, although major efforts are being taken for decentralization of responsibilities. Decentralization with proper controlling or regulatory mechanism was considered an urgent concern in policy making. International collaboration and private sector collaboration is considered very important for development in biotechnology as they have the knowledge and resour-

ces for advance research. Although government has promoted private sector collaboration, fears were raised over a total takeover by the private sector in the process of globalization that could make things more difficult for the general public.

Another important factor which contributes to difficulties in policy making is Indian cultural diversity makes it easier as well as sometimes very difficult to resolve issues. One person said, *'it would be extremely difficult to come out with something that can satisfy everybody. There is an upper crust that is ambitious but there is lot more below. Then there are cultural differences from one region to another. We can only inform people let them decide what they want. We would have to bring something that can satisfy most if not all'*.

5. CHALLENGES OF TRADITIONAL MEDICINE AND NEW TECHNOLOGY

Traditional medicines are generally exempt from review for new drugs. The philosophy of traditional medicine is based on the thought that nature is the mother for all kinds of treatments and provides therapies for all diseases and illnesses. This approach has been universally found in all cultures of the world, although the extent to which traditional medicine is used varies widely between cultures. According to WHO, traditional medicine is 'the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness [15]. In some African countries up to 80%, and in India 65%, of the population depends on traditional medicine to help meet their health care needs. In developed countries, the percentage of the population that has used complementary and alternative medicine at least once is 48% in Australia, 40% in Belgium, 70% in Canada, 75% in France and 42% in USA. Traditional medical practitioners, like Ayurvedic doctors, require six years of study, which is similar to Western medical practitioners, and can be equally professional.

Flexibility is essential as new diseases are emerging everyday which may not be able to be combated with traditional medicine, for example AIDS. In some cultures, for example in many African countries, there may not only be a lack of funding for drugs to combat AIDS but also beliefs in traditional therapies. Some of the extreme social practices in South Africa include men raping young children because of a belief that sleeping with a virgin will cure them of AIDS. In India persons with HIV have been killed by some communities, despite the high prevalence of HIV [16].

The rejection of modern technology due to of cultural beliefs and practices is not a novel phenomenon for medicine, or other aspects of life. An example can be seen in the 19th century in India when people rejected Western treatment for cholera and other epidemic diseases because of lack of a religious basis to the therapies. Whether it is Islamic medicine, Unani medicine,

Chinese medicine or Indian medicine the approach has been largely experience based.

Perhaps even more important for the ethical issues of practice of medicine in developing countries is the lack of informed consent in many countries. In India the courts have recognized the concept of informed consent and it would be an accepted norm, however exercise of consent and choice is limited by the situation of poverty as in all developing countries. The cultural practices may also make it difficult to have effective first person informed consent [17], but at least familial level informed consent should be practiced. The time constraints on medical consultations are a problem even in rich countries, so the practice of counseling is important. Perhaps this human interaction found with some traditional medical healers is the reason they are so popular still. Still access to modern medicines is important for people's health, as found in a recent Indian clinical trial for mental disorders, which found affordable antidepressants were more effective than psychiatric care [18].

Abortion and infanticide are medical practices that have traditional roots, given that plant extracts are common sources of the drugs that are still used in parts of India. Modern technology has been combined with these to allow selective termination of pregnancy. In a 1993 survey 41% of Indian people strongly disagreed to abort a 4 months old fetus if it was not suffering from any diseases; the highest among the ten countries in Asia and Oceania that were surveyed [19]. This shows the sanctity of life is a major ethical issue for Indian people. Nevertheless, 38% agreed to abort if the fetus was suffering from some congenital malformations, showing some pragmatism. This and other surveys have showed that there were not major religious differences in Hindus, Christians and Muslims in India when it comes to decisions over prenatal diagnosis. In Verma's survey (N=1404), 50% of the respondents agreed that the handicapped fetus does not have a right to life [20]. If there was a high risk of recurrence of the handicap, one third of the parents in such a circumstance said they would prefer to adopt a child.

Regarding the reasons behind the support for prenatal genetic screening, let us consider why the opinion changed so much for a fetus with abnormality. Despite rejection of abortion in general (15% for, 71% against), there was conversely high support for selective abortion of fetuses with congenital abnormalities (67% for, 19% against). There was support for prenatal genetic screening under government funding (80% yes, 8% no) and for personal use (71% yes, 17% no) [21]. Half of the persons who gave a reason made a comment suggesting economic benefits of such screening and that health care was a right or that the government should pay for the poor. There was also relatively high reasoning based on improvement of genes (15% of those who answered). In India there are well documented abuses of amniocentesis for sex selection [22]. A few respondents made comments that it should not be used for sex selection, but otherwise the issue was not addressed here. Some

would argue sex selective abortions are one step better than female infanticide, but it is a controversial issue.

Although many people use traditional medicine, when asked in surveys about the use of applications of modern biotechnology, people in developing countries, including India, are among the most positive countries in the world [23]. This enthusiasm is even more marked when asked about the use of genetic enhancement technologies like making children more intelligent or physically stronger [24]. Unlike respondents to surveys in Australasia, Europe or Japan, more than half the respondents in China, India or Thailand approve of these hypothetical examples. The acceptance of biotechnology may be because they perceive science and technology will alleviate the burden of disease. Thus although traditional medicine is popular, it may be sometimes the chosen therapy because of its cost, availability, and the absence of anything more effective. Also the government and media promotion of science and biotechnology may have influenced people's opinions to be favourable.

Especially after US federal funding in stem cell research for the two leading research organisations in India, namely National Centre for Biological Sciences (NCBS) in Bangalore, and a recently created private research laboratory called Reliance Life Sciences (RLS) in Mumbai which is ranked 3rd among the top 10 laboratories for stem cell research in the world by NIH. They possess 2 and 7 stem cell lines, respectively. They are both attempting to make more.

Concerns were raised on the use of foetal tissue for stem cell research. Because abortion is legal, as is private reproductive clinics offering IVF, there are a large number of fertility clinics across India. As the Deputy Director General of ICMR puts it, *'the fear is that since we have lot of spare embryos because of bloom of IVF clinics, there is going to be great clamor of exporting embryos to get money. Even if you try to stop it, it is not going to stop. So the government has decided to allow to continue stem cell research but with certain conditions'*. The pragmatic attitude of Indian society to allow abortion, ES cell research and prenatal diagnosis, despite of the sanctity of human life (as discussed for medical genetics above) may be a reflection on how Indian society has survived in some form for thousands of years, adapting traditional ideals to allow the use of new technologies.

India does perform many organ transplantations, though concerns over paid kidney transplant markets are high. However only a few percent of the patients who need kidneys live. Heart transplants occur rarely. Intensive care is a more common technology, which presents problems as another person said. *"hospitals hardly have any heart-lung machines or artificial respirators. How can an earlier patient be taken off when a patient comes?"*

6. CONCLUSIONS

Around 80% of the world population lives in developing countries where people don't even have access to basic

medical facilities and health care[6]. Health care policy needs to be considered in the proper environmental, cultural, social and economic context. As we can see from the results of the interviews the particular health structures and socio-economic conditions of developing countries may not only lessen the emphasis placed on developing research in biotechnology, but at the same time desperate situations may make people grasp at any new tool that is perceived to be a panacea to relieve the burden of disease.

Although there is a general positive attitude for biotechnology research, the discrepancies and difficulties to get public support and involvement are serious issues to be addressed. Although it can be argued that the basic moral principles can be redefined by public debates or voting, the culture is important in how society makes a decision on the use of new technology. In this environment the open availability of ethical guidelines through the Internet and in printed copy provides an essential guide for health care professionals. In this way the development of guidelines that are appropriate for the particular country are essential for the proper utilization of medical biotechnology. Still we are concerned that the access to commercial services such as amniocentesis for sex selection, reproductive technology, and to drugs and hormones made by modern biotechnology like human growth hormone, in a developing country means it is very difficult to limit the use and misuse of these technologies by some members of the community.

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