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# Reflections and recommendations on research ethics in developing countries ☆

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**Abstract**

The debate on the ethics of international clinical research involving collaboration with developing countries has achieved a high profile in recent years. Informed consent and universal standards have been most intensively debated. Exploitation and lack of adequate attention to justice in the distribution of risks/harm and benefits to individuals and communities have to a lesser extent been addressed. The global context in which these debates are taking place, and some of the less obvious implications for research ethics and for health are discussed here to broaden understanding of the complexity of the debate. A wider role is proposed for research ethics committees, one that includes an educational component and some responsibility for audit. It is proposed that new ways of thinking are needed about the role of research ethics in promoting moral progress in the research endeavour and improving global health. © 2002 Elsevier Science Ltd. All rights reserved.

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## Introduction

Debates on the ethical requirements for conducting medical research in developing countries have achieved considerable prominence in recent years. To some extent this is the result of growth of interest in research in developing countries since the HIV/AIDS pandemic. It also reflects renewed and encouraging interest in, and concern about, the nature of the relationship between researchers and their subjects. While researchers are generally privileged people many research subjects are among the most vulnerable in our world, living under the worst conditions of deprivation and exploitation. Appreciation of concerns regarding research in developing countries requires some knowledge of the growing global disparities in wealth and health, and of the lifestyle and worldview of potential research subjects. Against such a background it is apparent that the ethical dilemmas faced in conducting collaborative international research can only be addressed satisfactorily if research ethics is seen as intimately linked to health care, to human health globally and to the promotion of social and economic processes that could begin reversing widening global disparities in health (Benatar, 2001a).

## Disparities in wealth and health

At the beginning of the 20th century the wealthiest 20% of the world's population were 9 times richer than the poorest 20%. This ratio has grown progressively—to 30 times by 1960, 60 times by 1990 and to over 70 times by 1997. The extent of absolute poverty has also increased and today almost half the world's population lives on $<$US$2 per person per day. Tens of millions of people, many of them children, die each year of

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starvation and malnutrition—in a world with enough food to feed all (Hobsbawm, 1994; World Health Organisation, 1997; Benatar, 1998a; Falk, 1999).

At the beginning of the 21st century patterns of diseases and longevity also differ markedly across the world. Of the approximately 52 million people who die each year 18 million die of infectious and parasitic diseases (over 16 million of these—many in their youth—in the developing world), 10 million die of diseases of the circulatory system (4.5 million of these in the developing world) and 6 million die of malignant diseases (3.5 million in the developing world). Poor countries bear over 80 percent of the global burden of disease in disability adjusted life years (DALYs). The WHO estimated that in 1998, 11 million children and adults of working age died of six infectious diseases that could have been prevented at $20 per life saved (WHO, 1997). Life expectancy at birth ranges from well over 70 years in highly industrialised countries to below 50 years in many poor countries. Life expectancy is increasing worldwide. However, in 16 of the world's poorest countries it has fallen in recent years. In sub-Saharan Africa gains in longevity achieved during the first half of the 20th century are rapidly being reversed by the HIV/AIDS pandemic.

Poverty (defined as lack of economic resources, lack of education, lack of access to basic life resources such as food water and sanitation, and lack of control over the reproductive process) directly accounts for almost one-third of the global burden of disease. It is now well established that there is a definite relationship between wealth/poverty and health/disease, although this relationship is not linear (Wilkinson, 1996). For example, one of the wealthiest nations in the world—the USA—has worse health statistics (infant mortality and longevity) than some other industrialised countries; and a particularly poor state—Kerala in India—has achieved lower infant mortality rates and greater longevity than many wealthier nations. Despite having the largest per capita health expenditure in the world the US is ranked 24th in overall population health as judged by the disability-adjusted life expectancy, 37th in efficiency of its health care system, and 54th alongside Fiji in how fairly the financial burden of health care is distributed (WHO, 2000).

Since the 1960s major advances in medicine and technology have been associated with greatly increased expenditure on health care—most of this in highly industrialised countries. Annual per capita expenditure on health care ranges from $4000 in the US to less than $5 in the poorest countries in Africa. Half the world's population lives in countries, which cannot afford annual per capita health expenditures of more than $5–10, which is less than the World Health Organisation's recommended minimum $12 for a basic health care package.

Erosion of the economies of many poor countries, under the impact of globalisation and debt, has prevented the introduction of effective forms of modern medicine into deprived communities and thus prevented achievement of widespread access to even basic health care for billions of people. In the 1990s, 89% of annual world expenditure on health care was spent on 16% of the world's population who bear 7% of the global burden of disease in DALYs (Iglehart, 1999), and of the estimated US$56 billion spent annually on medical research much $<10\%$ is spent on health problems of the developing world (Commission on Health Research for Development, 1990). These are examples of global injustice that should surely be intolerable if there were genuine commitment to universal human rights and human dignity. Regrettably little attention is given to such issues in the voluminous literature on human rights.

The world at the beginning of the 21st century is thus characterised by widening economic and health disparities between rich and poor (within and between countries), and by suffering, conflict and alienation associated with pervasive social forces Hobsbawm, 1994; Benatar, 1998a; Falk, 1999). This scenario provides a strong case for viewing the emergence of new diseases such as AIDS that afflict predominantly those marginalised by poverty (80% of HIV positive persons live in the poorest countries in the world), as directly related to the ecological niches created and sustained by the nature of the global political economy and its ideology (Lee & Zwi, 1996).

Problems of such magnitude, starkly illustrated by the AIDS pandemic, require that ethical considerations extend beyond the interpersonal level. It is vital now for the ethics debate to include the best interests of whole populations, the ethics of how institutions (including multinational drug companies) should function, and the ethics of international relations—especially those between rich/strong and poor/weak countries. In the same way that racism, paternalism, gender discrimination and interpersonal abuse have become discredited, so too should autocratic/unaccountable institutions and exploitation be actively contested.

## Contextual considerations—an illustrative narrative

When those in privileged positions and in wealthier countries consider undertaking collaborative research with colleagues in developing countries it is necessary to understand both their own framework of thinking, and the implications of very different mind-sets and environments in which research projects may be carried out in developing countries. The mind set of researchers from industrialised countries, and in which the debates on research ethics are taking place, is characterised by a

biomedical approach to disease, and by a neoliberal approach to economics and trade (Benatar 1998a; Lee & Zwi, 1996). These powerful forces shape the world and a dominant worldview. There is a need to be sensitive to the fact that not all, and especially not those who are disadvantaged or who have been exploited, will see the world through the same lenses—as illustrated by the following narrative.[2]

> Ntombi is in her middle twenties. She has received little if any formal education and spends a large part of her day collecting fuel and water, and preparing food for the daily survival of her family. Like many rural Africans she has no access to electricity or piped water. During her short life she has witnessed, and been the victim of, more suffering and misery than any of us could imagine or bear. She has lost many of her close family—parents, siblings and children—to violence, poverty, and disease. Despite her misfortunes and multiple deprivations she copes with her lot with courageous acceptance, and continues to make contributions to her family and her society.
>
> Ntombi lives on a continent that contains 33 of the 50 poorest countries in the world. Its 690 million people represent 10% of the world's population who live on <1% of annual global GNP, and who have access to less than the World Health Organisation recommended minimum annual health care expenditure of US$12 per capita. Two-thirds of Africans live in absolute poverty: more than 50% lack safe water and 70% are without proper sanitation. Of all people in the world who are HIV-positive almost 80% are in sub-Saharan Africa. This region bears the burden of 90% of the 2 million annual deaths from malaria in the world—and 90% of these are young children. Africa also accounts for 22% of global deaths, 34% of global DALYs from tuberculosis and 24% of global DALYs from malnutrition. The number of unnecessary deaths on the continent is equivalent to the loss of life, that would occur from dropping more than 10 Hiroshima and Nagasaki sized nuclear bombs annually. Much of this disease, suffering and premature death is preventable and at a cost that is not unaffordable in the global context.
>
> Ntombi lives on an annual sum of money approximately equivalent to the amount that a person from the modern western world lives on for less than a day. She is aware of the disparities in wealth between the people within her country. She may also possibly be aware from the television set in a local store of the life styles of people in other parts of the world. Those whom she sees as living comfortable lives are mostly white, while those who live like her are mostly black. The differences she sees in the other ways of life are awe inspiring, incomprehensible and unimaginable for her.
>
> Ntombi is pregnant with her third child and is receiving care from a local midwife. During her pregnancy a team of health care workers that includes people from her own country and others who are visiting from abroad approaches her. She is told that there is a significant possibility that she is infected with the human immunodefficiency virus and that her child may acquire this infection during childbirth or breast-feeding. She is asked if she would be willing to be tested for HIV infection and, if positive, to participate in a trial of a drug which may reduce the chances of transmission of infection to her child. She is also told that she should not breast feed her child if she tests positive in order to reduce the risk of transmission.
>
> She is both bewildered and afraid. She does not feel ill. Who are these people? What is their real intention? Why are health care facilities so inadequate in her village? Why is such a large team of people with access to seemingly vast resources coming to study her? Is it for her benefit or for theirs? How will her life change if she discovers she is HIV-positive? What will happen to her if she refuses to participate? If she accepts what will happen to her and her baby when the study is completed? Will she or her baby really be better off as a result of this study? What effect will failure to breast-feed have on her baby? What will her spouse say about her participation in the trial? Whom can she ask for answers to these questions? Can she rely on all the explanations given by the researchers? Should she consult the leaders she respects within her community? Should the community play a role in deciding whether its members should participate in the trial, or should she decide for herself? If she is encouraged by the research team to decide for herself how may this affect her relationship with the community?

Do any of these questions really matter to researchers? To what extent have researchers tried to understand the mind-set of potential research subjects? Does the way in which their subjects see researchers and the privileged world matter to them? Have resources been allocated to train local health care personnel to participate constructively in evaluating and dealing with the questions research subjects may ask, or do researchers merely want to get on with the study as quickly and as economically as possible? How does this square with respect for the autonomy of research subjects?

[2] The use of narratives to teach bioethics is increasingly being appreciated. See for example Narrative in bioethics. Hudson Jones A. Brit. Med. J. 1999; 318: 253–56.

How many privileged people can see the world through the eyes of someone like Ntombi? Have they questioned the extent to which their privileged lives have been constructed and maintained through modern and sophisticated methods of exploitation of people across the globe? Have they questioned the foreign policies pursued by their countries? Are they aware that Africa has been eliminated from the foreign policy agenda of many industrialised nations following decades of financial and arms trading practices that have impoverished and crippled the continent? Do they really care? If not, what psychological processes allow them to see themselves apart from fellow humans in misery?

What are the lives of privileged researchers all about? How will they be viewed by future generations? What would a Global Truth and Reconciliation Commission reveal about the unethical and exploitative practices of powerful nations? Do physicians, bioethicists and others have responsibilities for developing approaches to ethics that go beyond the micro level of interpersonal relations? Should they be considering the ethics of how institutions, including multinational drug companies operate, how nations relate to each other and what implications such relationships have for the lives and health of billions of people? If these issues about the lives of the "wretched of the earth" have not been sufficiently considered they are raised here to promote introspection and activism.

## Excellence in research

Many moral lessons have been learnt from the history of medical research. Regrettably, 50 years after the Nuremberg trials and the Nuremberg code, unethical medical research on humans continues, even in highly privileged countries (Katz, Capron, & Glass, 1972; President's Advisory Commission, 1998; Brody, 1998). Similarly, the extent to which human rights abuses continue 50 years after the Universal Declaration of Human Rights, even in wealthy industrialised countries, illustrates how difficult it is to achieve such universal moral aspirations (Amnesty International 1990, 1998; Cassese, 1996). How research should be regulated to avoid the errors and indiscretions of the past, and how to avoid new forms of discrimination and victimisation in the increasingly complex era of biotechnology, thus remain important issues worldwide.

In undertaking research on humans the scientific merit of a project must be matched by the ethical merit of the work. Scientific merit requires study designs and methods that attempt to falsify hypotheses, or reliably and efficiently develop answers to the questions being posed. The methods used today have evolved from less adequate methods in the past and scientific methodology is continuously being improved.

Ethical merit embraces respect for the dignity of research subjects (their integrity, privacy, safety, and human rights—hence the need for informed consent), the imperative to minimise risk, to balance risks against benefits, to make appropriate recompense for time, to provide compensation for any injury which may occur during the research, to protect confidentiality (Council for the International Organisations of Medical Sciences—CIOMS, 1993; Royal College of Physicians, 1996; South African Medical Research Council, 1993, Anonymous, 1997b; Levine, 1988) and to avoid conflicts of interest (Emanuel & Steiner, 1995; Spece, Shimm, & Buchanan, 1997). Within many, but not all, industrialised countries the understanding and implementation of these requirements has also continued to evolve and improve over several decades.

Because there is the danger, even in societies with aware and vocal citizens, that the views of researchers who have control over large resources may dominate, ethical merit requires that research subjects: (i) understand the nature and purpose of the research; (ii) have the opportunity to have their questions answered; (iii) can give truly informed consent; and (iv) can make uncoerced decisions to participate. Coercion should not be equated with incentives. Incentives to participate in research, such as guaranteed access to otherwise unavailable health care, and modest financial recompense for time and travel, are appropriate and should not be viewed as constituting coercion. It is clear that in developing countries the major incentive to participating in research may be access to otherwise unavailable health care. This is acceptable if the potential benefits of the research to the subjects and their community outweigh the potential harms in the long term as well as in the short term.

In "developing" countries, where cultural, linguistic, economic and other barriers may prevail between researchers and subjects, it is especially important to ensure effective communication. Anthropologists and others have documented the many pitfalls and difficulties that need to be faced in obtaining meaningful informed consent under these circumstances (Marshall, 2001; Lindegger & Richter, 2000). Work in Uganda has suggested that (i) socio-economic inequalities between researchers and subjects result in subjects feeling that they have no choice when asked to participate in research; (ii) the legacy of colonialism evokes covert ethnic divisiveness between researchers and subjects, and (iii) the tyranny of the Amin regime that eroded a previously admired health care system has left a lingering suspicion that HIV was brought to Africa by foreigners. For these and other reasons Ugandan researchers have had difficulty in applying the widely recommended principles of bioethics (Loue, Okello, & Kawama, 1996). Problems identified with research in Latin America include (i) failure to involve local health

care professionals in protocol design; (ii) difficulties with the language in which protocols are written; (iii) errors in translation; (iv) problems associated with the co-option of prominent local principal investigators untrained in research; (v) the allocation by such investigators of duties to subservient juniors who cannot speak out, and (vi) pressure to meet recruitment sample sizes (Hardy, 1996).

Despite these problems it should not be assumed that disadvantaged people cannot grasp the concepts involved in research and it is important to recognise that most of the goals of ethical research can be achieved when dealing with impoverished and illiterate people if sufficient time, skill, interest and resources are devoted to communication and consultation.

*Achieving universal standards*

While the source of, and justification for, universal ethical standards remain the subject of complex debates (Wilson, 1993; Thomas, 1989; Nagel, 1991; Macklin, 1999) it is generally accepted that there is a need for universal ethical standards for research on humans, and considerable progress has been made towards achieving this goal (CIOMS, 1993; Royal College of Physicians, 1996; South African Medical Research Council, 1993; Levine, 1998). Achieving universality in ethical standards requires reflection on such issues as: (i) what constitutes the best interests of subjects—with insightful recognition that individual and cultural preferences, and what can be achieved in any particular context, may differ significantly; (ii) what distinguishes the truly universal from imperialistic notions; and (iii) the relevance of contextual issues that can be taken into consideration on moral grounds without resorting to ethical relativism. As the facts of the case have an influence on the nature of any ethical dilemma and on how it is to be solved, there is a need to recognise and deal with contextual differences on rational grounds. Contextual differences constitute the starting point for rational discourse, and it should be possible to reasonably justify any differences required in the conduct of research in different contexts. Clearly, the challenges here are to avoid both ethical imperialism and ethical relativism (London, 2000, 2001)

*Informed consent and conflict of obligations*

Informed consent has become established as the cornerstone of research ethics. In addition to the difficulties described in obtaining informed consent in cross-cultural settings, it is also important to recognise that there are differences between informed consent for participation in research and informed consent in the realm of patient care (Levine, 1983; Taylor, 1987). In clinical practice obtaining informed consent is a somewhat informal, friendly and unhurried procedure in a context characterised by patients seeking medical advice from medical professionals whom they perceive to be concerned primarily with the best interests of patients. The process lacks rigidity, encompasses consideration of the fact that autonomy may be impaired, and makes some allowance for tailoring of treatment according to patients' wishes. Such a process, if conducted appropriately, can enhance patient confidence and the doctor/patient relationship (Levine, 1983; Taylor, 1987).

In contrast, informed consent procedures in the research context are both formal and regulated. Characteristically, the encounter is between an investigator seeking patients to include in a study, within a relationship resembling a brief encounter between strangers in a quest for the pursuit of knowledge and the need to do so with scientific rigor. The information disclosed and the method of doing so are more impersonal, detailed and harsher than in the clinical context. Professional ignorance is exposed to enable patients to understand why randomisation to different forms of treatment is justified. While patient autonomy may be preserved, the rigidity of the protocol does not allow for patient choices (other than withdrawal) once the research has been embarked on. Such a relationship has potentially adverse effects on researchers and patients (Levine, 1983; Taylor, 1987).

A conflict of obligations may thus arise when the doctor is both the investigator and the provider of patient care. The pursuit of knowledge in the best interests of science and society may not be compatible with protecting the best interests of the patient (Levine, 1983; Taylor, 1987). This conflict may be particularly difficult to resolve in developing countries where it may be impossible to separate the roles of investigator and carer, and where grossly inadequate health care resources and the pressures to enrol research subjects may overshadow concern for patients' best interests (Loue et al., 1996; Hardy, 1996).

*Protecting research subjects—beyond informed consent*

The fact that influential researchers (individuals and corporations) may have much more to gain than any single research participant has correctly resulted in considerable attention to designing studies that protect research subjects. Unfortunately, most of this protection has focused on informed consent and on reviewing research protocols, with inadequate attention paid to monitoring studies, trying to improve the actual conduct of research, and to promoting justice in the distribution of the burdens and benefits of research.

This focus on informed consent and relative lack of attention both to how research is actually conducted and to the implications of the research for the community in which the study is being conducted, may reflect any or

all of the following: (i) acceptance that researchers will do what they say they will do; (ii) willingness to believe that obtaining informed consent in practice meets up to the high moral level implied by the concept, rather than merely meeting legal requirements; (iii) confidence that conflicts of interest between the provision of care and the desire to advance knowledge can be balanced; (iv) lack of concern for justice in balancing the benefits and burdens both for the participants and more broadly; and (v) that in reality the interest in making medical progress takes precedence over the desire to protect the interests of research subjects (Benatar, 1998a, b).

Lack of attention to how research is actually being conducted is a serious shortcoming, requiring critical attention. This applies especially in an era of expanding research, growing links with industry and commercial organisations, documented inadequacies in the protection of research subjects and with growing recognition of the need to avoid exploitation. Recent endeavours to seek justice in research beyond informed consent are to be welcomed (Kahn, Mastroianni, & Sugarman, 1998), although not uncritically as many pitfalls remain to be negotiated (Woodward, 1999; Ellis, 1999; Benatar & Singer, 2000a, b).

## Debates on recent studies

In recent debates about HIV transmission studies in Thailand, South Africa and elsewhere the use of placebos and the implications of the Helsinki Declaration for the standard of care required for research subjects have been fiercely debated (Angell 1997; Lurie & Wolf, 1997; Anonymous, 1997a; Aaby et al., 1997; Bulletin of Medical Ethics, 1999; Varmus and Satcher, 1997; Fairchild & Bayer, 1999; Harvard University CD Rom). The recommendation from the Council for the Organisation of Medical Sciences (CIOMS) that studies should not be done in developing countries if they can be done in better-resourced nations has also been contested.

In response to these important questions some editors of medical journals have delivered dogmatic ethical prescriptions. Superficial and inaccurate analogies have also been drawn in support of their views, for example between the Tuskegee syphilis experiment in the US and HIV transmission studies in developing countries. Making these inadequate analogies trivialises the Tuskegee experience and disregards the meaningful differences between these examples (Benatar, 1998b; Fairchild & Bayer, 1999).

Contrasting views have been expressed regarding whether the standard of care for research subjects should be equivalent to that available in the host country, or merely meet the best local standards. This controversy has not been resolved, and heated debates will continue. If it is insisted that the best standard drug regimen must be used it can also legitimately be asked why ethical considerations are limited to the best available standard drug treatment. Why not include the best standard medical, nursing and hospital facilities, and follow up care? If expense is not a consideration for drugs why should it be for such other aspects of treatment? Such considerations reveal a complexity that cannot adequately be dealt with merely by reference to synoptic statements from guidelines in the belief that these can be precisely applied in any and all circumstances (Benatar, 1998b; Benatar & Singer, 2000; London, 2000).

However, it must be surely be agreed that standards of care during clinical trials should neither be set at levels that are impossible to achieve, nor should research subjects be denied higher levels of care than may be available within their country if much higher standards can be achieved during the research process. A balanced approach—as so often required when dealing with ethical dilemmas—is needed, based on the merits of the case in question, and the fullest possible expression of respect for human dignity in the context (Benatar & Singer, 2000).

Regarding the use of placebos it is also clear that it is simplistic to imagine that the legitimacy of using a placebo arm can be determined solely on the basis of an all encompassing rule, or to consider that all the ethics of research can be deduced for all contexts from such guidelines as the Helsinki Declaration. Guidelines are not intended to cover every possible circumstance and, like laws and constitutions, require thoughtful interpretation (Hurwitz, 1998). Whether or not a particular drug regimen can be considered the best standard or whether a placebo arm is ethical will be determined by such issues as: (i) the strength of evidence that any treatment has been shown to be superior; (ii) the ability to extrapolate the results of drug treatment in one context to another in which the drugs may have a different profile of side effects—for example in the presence of genetic disorders such as porphyria or G6PD deficiency that may have implications for drug metabolism and action; (iii) whether the drugs can be safely taken and monitored in a radically different environment; (iv) whether the study is being done primarily to benefit the local population; (v) what study design can best achieve this; and (vi) the implications of the outcome of the study for the subsequent implementation of a national policy to make the new treatment available to the community(Benatar, 1998a, b; Benatar & Singer, 2000; Tramer, Reynolds, Moore, & McQuay, 1998).

For example, in the HIV transmission studies the best proven drug regimen (0 7 6) would have had to be given for 14 weeks prior to delivery and intrapartum to the mother, and to the infant for 4 weeks, omitting breast feeding—a difficult regimen to satisfy in dealing with

women in developing countries who first present only few weeks before delivery and whose infants may be placed at considerable risk if not breast fed. The use of a placebo in such a situation can be justified, if the drugs used in wealthy countries could not be a feasible option because of expense, difficulties in their administration and monitoring, or dangers associated with their use. The reasons for new drugs not being available and whether or not such feasibility might change in the near future could of course become influencing factors. A recent study of directly observed treatment for tuberculosis (which has been widely recommended as the gold standard) has illustrated that the standard method may not be the best means of delivering treatment in some settings (Zwarenstein, Shoeman, Vundule, Lombard, & Tatley, 1998).

It would thus seem that good reasons could sometimes be provided for the different structure of studies in different contexts without having to accuse researchers of moral relativism. Indeed it is often ethical considerations that require that such studies be structured differently (Beauchamp, 1996). Those who dogmatically insist that what is ethical can be simply deduced from declarations, have failed to understand that just as constitutions may require complex legal interpretation, so declarations about ethics may require moral interpretation. Lack of insight into the way in which formal ethical principles have to be implemented with appropriate specification in different contexts, leads to 'cookbook' application of abstract principles and obstructs deeper understanding of what can be justified through ethical reasoning (Beauchamp, 1996).

## Exploitation or compensation and partnership?

World history is filled with examples illustrating the pervasiveness of exploitation. Although exploitation today may be less crude and less overt than in the past, the extent of covert exploitation under sophisticated guises continues to devastate the lives of billions of people (Hobsbawm, 1994; Benatar, 1998a; Falk, 1999; Lee & Zwi, 1996). Against this background, with the widening disparities described, and with acknowledgement of the potential for research to be exploitative, it can be argued that research should bring significant benefits to research subjects (de Jesus Mari, Lozano, & Dudley, 1997; Benatar, 2000a, b).

Information gained from clinical trials conducted efficiently and expeditiously in developing countries may allow early registration of drugs in developed countries thus considerable enhancing profits. It does not seem unreasonable to expect that such profits should also benefit the citizens of developing countries in which the research was undertaken. The colonial model of exchange of 'trinkets for ivory' must be avoided. The notion that it is acceptable to give a gift of minimal intrinsic in exchange for extracting valuable goods should be transformed into a commitment to giving fair recompense for sharing in the development of knowledge that may translate into great profits for pharmaceutical companies. For example, in addition to the direct benefits of the treatment regimens being studied for individuals within the study, it is being claimed (with justification in the view of many) that such benefits should include the provision of proven treatments following completion of trials, and use of the research project to empower the community (de Jesus Mari et al., 1997; Benatar, 2000a). While it may be difficult to undertake harm/benefit calculations in advance of knowing what research will reveal and how valuable the information may be, the debate that is beginning on how safeguards can be built into the contract to promote justice in the distribution of benefits at a later time must be encouraged in the quest to achieve greater fairness in the international research endeavour. Such considerations in the ethics of research have not yet evolved to the same level as some of the other ethical requirements that have been the focus of more attention.

## Research ethics committees

The role of research committees is briefly reviewed here to illustrate that for moral progress to be made, the functions of such committees need to be broadened. Their first, now well developed and implemented task, is to evaluate research proposals with special attention to risk/benefit ratios, equity in distribution of benefits and burdens, potential conflicts of interest, the adequacy of information provided for subjects, and the protection of freedom: (i) within the consent process; (ii) for subjects to withdraw without prejudice to care; and (iii) of investigators to publish.

Their second, equally important but less widely implemented role is to educate and assist faculty, researchers and the community in understanding and appreciating the ethics of research. This can be achieved by reflecting on and discussing the history of unethical research in many countries, by encouraging discussion of controversial projects with researchers and the community on whom research is being undertaken, by allowing as many faculty as possible to participate by rotation in the work of the committee, by the inclusion of lay members as full committee members, and by ensuring that all research students have experienced mentors and access to mechanisms of due process for resolving conflict. Formal courses in research ethics within postgraduate education could promote this ambitious goal.

A third, increasingly acknowledged but even less widely implemented, function is to monitor and audit

research, and to provide accountability to the public. Suspected unethical or fraudulent behaviour should be drawn to the attention of specific committees appointed to investigate allegations of abuse of scientific integrity, take appropriate action against unscrupulous researchers and publicise this.

Ethics has received only patchy attention in many "developing" countries. There is little uniformity in the structure and function of research ethics committees and minimal if any public accountability. Additional shortcomings in some countries include the existence of self-appointed private ethics committees lacking in expertise and accountability, the absence of open-minded dialogue and public deliberation, and possibilities of undeclared conflict of interest between the roles of physicians as carers for patients and as medical researchers. The depth and pervasiveness of this conflict are not sufficiently widely appreciated (Emanuel & Steiner, 1995; Spece et al., 1997). Resources thus need to be made available, in some countries more than others, to develop the expertise and infrastructure required to (i) evaluate ethical problems, (ii) educate practitioners and researchers, and (iii) facilitate development of policy. Understanding and promoting science requires scientific training and expertise. Understanding and dealing with ethical dilemmas similarly requires scholarship and skill.

## Towards more comprehensive guidelines for research ethics in developing countries

The categories of issues thus requiring special consideration in formulating new Guidelines for Biomedical Research on Human Subjects in "developing" countries include:

*Conditions in developing countries*

- A disproportionately heavy burden of disease (particularly infectious diseases); the breadth and depth of poverty; and high levels of illiteracy.
- Wide disparities in health and in access to health care; and imbalance between the often-ample resources available for research and the meagre resources available for even basic health care.
- The meagre resources in the developing world to do such research-making international collaboration necessary.
- Inadequate scientific and ethics infrastructures for the required reviewing process.
- The extent of disempowerment of the poor in their personal and communal lives.
- Knowledge of the ways in which people of other cultures traditionally view themselves as individuals embedded in communities and with respect to the changing boundaries between perceptions of the self that differ from the classical western notion.
- The need to understand what it means to be ill in contexts very different from those known to researchers and what can be expected from those one consults for help under those circumstances.

*The research agenda of the industrialised world*

- The fact that 90% of health research expenditure is on diseases that cause 10% of the global burden of disease, and that diseases that afflict many very poor people are minimally researched reflects a research agenda driven largely by the profit motive.

*Informed consent*

- The relevance of the above considerations to the complexity of obtaining informed consent—with due regard for respect for persons as they see themselves, within their cultural, familial and social contexts while simultaneously seeking to empower them to become more autonomous, and to reduce the power gap between researchers and subjects. Given the greater difficulty in achieving informed consent, more resources, education and training need to be dedicated to this aspect of research programs in "developing countries."
- The gap between the motives of external funders/researcher, and those of local institutions/researchers.
- The even larger gap between the scientific worldview and expectations of both these research groups and the mind-sets of their research subjects.

*Justice in the distribution of knowledge and resources flowing from research*

- The need to improve the lives of the vulnerable and disadvantaged; and to ensure that research on them results in beneficial results being made available to individuals and their communities through influences on policy makers.
- The sensitivity to appreciate the extent to which exploitation has contributed to existing disparities and to how these may be perpetuated through selective promotion of the interests of researchers/professionals, and through insistence on exclusive ownership of data and intellectual property rights.
- The need to build capacity in research ethics as part of the research endeavour; and the great need for research into diseases of limited interest to the industrialised world.

The debate on these issues cannot be undertaken solely within industrialised countries. The inclusion of scholars and others from diverse societies will enable all to see themselves and what they value in a clearer light. Such a

collaborative process is required for moral progress and for the achievement of human well being across the globe. Collaborative research should also include the enhancement of local capacity for grappling with these ethical problems in ways that allow the quest for universalism to include all who have something to contribute to collective understanding and to the reasoning process (Tan Torres Edejer, 1999; Macaulay, Commanda, & Freeman, 1999).

## Making scientific and moral progress in the quest for human flourishing

Scientific and moral progress are dependent on: (i) the ability to be critical of the status of current knowledge, method and dogma; (ii) the willingness to raise critical questions on any issue; (iii) acquiring an understanding of one's own base within a specific cultural context; (iv) the sensitivity to recognise the limitations of one's own world view—that one's own insights are not necessarily correct or better than those of others and (v) the willingness to debate differences with an open and scholarly attitude. While there may be uncertainty on substantive aspects of the ethics of a particular project, ensuring a scholarly, open and deliberative process about the project within the framework outlined above offers the greatest potential for making moral progress in understanding and dealing with the substantive issues at stake.

The tensions between the views of westerners and those with alternative world views are illustrated by consideration of some covert reasons for why the South African government may have taken the decision not to implement a national drug-based programme for the prevention of HIV transmission (Benatar, 2001b). Such potential tensions also need to be kept in mind when addressing complex ethical issues in relation to testing AIDS vaccines (Benatar, 2000b; Lindegger & Richter, 2000; Slack et al., 2000), and to appreciate the fears of some that the haste to test as yet very imperfect vaccines in developing countries may largely reflect the concerns of wealthy nations for themselves. It is also appropriate to acknowledge that there is justification for scepticism that vaccines will be the solution to the HIV/AIDS pandemic. While scientific advances, and the search for vaccines must continue with vigour and integrity, and science should receive maximal support, it must simultaneously be borne in mind that science alone will not solve the problem of infectious diseases.

For example, the proximate cause of tuberculosis has been known since 1882, and effective chemotherapy has been available since the late 1940s. With the introduction of rifampicin and short course chemotherapy in the 1960s it became possible to cure almost any patient with tuberculosis. Indeed the hope existed at that time that tuberculosis might be eradicated from the world. Today the spectre is faced of tuberculosis becoming an untreatable disease due to the emergence of multi-drug resistant organisms and lack of development of new drugs. This situation has arisen because inadequate attention has been given to the fundamental causes of poverty and human suffering and to the context within which lives are lived and diseases need to be treated (Benatar, 1995). Against this background it is evident that a vaccine against HIV will not eliminate AIDS if this were to be used as ineffectively as anti-tuberculosis treatment has been used.

Tuberculosis and malaria are rampant largely because those who suffer from these conditions are out of sight, their lives are not valued and there is an insufficient profit motive driving treatment regimens. If there is no humanistic drive to providing treatment for malaria and tuberculosis then why should there be faith that when a vaccine has been developed for HIV/AIDS this will be made widely available? Those who travel with missionary zeal to undertake research on subjects they have not bothered to understand or care about, beyond their immediate research value, need to be reminded of these issues. Science must be associated with making public policy and with an ethics of international relations that will help promote processes to ameliorate the miserable conditions in which the majority of the world's population live (Hobsbawm, 1994; Benatar, 1998a; Falk, 1999; Benatar & Singer, 2000).

Robertson has eloquently argued for a language of public health that "speaks to the reciprocity and interdependence which characterise community." She describes how such a language can be found in a "moral economy of interdependence" (defined as the collectively shared basic moral assumptions constituting a system of reciprocal relations) rather than one of "moral nihilism and radical individualism" (Robertson, 1998). The ability to undertake HIV vaccine trials and other international collaborative research ethically will thus require extensive public debate and education on the balance between individual rights and the common good. It will be essential to involve the community to be researched in the design of protocols and in the conduct of collaborative research. Public education must be coupled to methods of protecting individuals from stigmatisation or abuse.

## Conclusions

Reflection on a century that has been characterised by both amazing scientific progress and intense human suffering on a vast scale makes it clear that new ways of thinking are now required about illness, human suffering, health care, international relations and other forces that shape the world and profoundly affect health. These

include a better understanding of why disparities in wealth and health are widening; a greater commitment to social justice within nations and between nations; a deeper understanding of the interdependence of all people and of the ecological threats to the planet from environmental overload—threats which should lead to a new concept of security that focuses on the benefits of widespread human flourishing rather than on military might. It should also be acknowledged that it is neither beneficence nor altruism that are required to address national and global problems, but rather rational self-interest and a longer-range view than we currently seem willing to take. Progress will require transdisciplinary approaches that embrace a wide range of knowledge, skills, insights and abilities provided by philosophers, anthropologists, sociologists, physicians, theologians and others; and the promotion of public debates that enable participation in decision making.

As indicated earlier, problems of the magnitude we face, so starkly illustrated by the AIDS pandemic, require that ethical considerations extend beyond the interpersonal level. It is vital now for the ethics debate to include the best interests of whole populations, the ethics of how institutions (including multinational drug companies) should function, and the ethics of international relations—especially those between rich/strong and poor/weak countries. Neglect of the health and well being of the poorest and most disadvantaged threaten the health of all. Failure to learn profound lessons about interdependence from the HIV/AIDS pandemic, and to develop new paradigms of thinking about health and human flourishing will almost certainly lead to other, and perhaps worse, pandemics in the future.

The central recommendation in this presentation is for the ethics debate to be extended to the macro level. Achieving a higher public profile for such considerations, as with the battle against slavery, oppression and apartheid, is the first step towards resolving complex global problems. Use of the concept and the language of a "moral economy of interdependence" offer hope for making such progress (Robertson, 1998).

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