## International research ethics : some issues

■ What are the odds of a poor Guatemalan getting entry into a trial for the latest AIDS drug cocktail - and of continuing those drugs once the trial is over? Can a placebo control be used where the local standard of care does not include a proven treatment? Does the answer differ depending on whether the study is collaborative or locally funded?

This article identifies and discusses some ethical issues in international research. Research collaboration with developing countries is plagued by differing interpretations of ethical standards and by inequitable funding. Only 10 per cent of global research funding goes to diseases comprising 90 per cent of the global burden. Collaborative research can exacerbate the poor state of local research environments by diverting local scientific expertise from more important to less important areas of research, and neglecting national research networks.

The awareness that the success of research collaboration should not be judged solely on the results of scientific research activities must be coupled with a learning approach to craft a sustainable, mutually beneficial working relationship that, aside from advancing science, must address inequity and put local priorities first, develop capacity with a long term perspective, and preserve the dignity of the local people by ensuring that the benefits of research will truly uplift their status.

**Edejer T: North-South research partnerships: the ethics of carrying out research in developing countries *BMJ* 1999;319:438-441**

## Revising the Declaration of Helsinki : one opinion

■ Should the control group of a research study in a poor country receive the best possible treatment or the standard of care - which might be nothing at all? Two articles inthe *New England Journal of Medicine* debate the question. The first author states that the proposed revisions of the Declaration of Helsinki may "inappropriately cause a shift to an efficiency-based standard for research involving human subjects and weaken the principles of the investigator's moral commitment to the research subject and the just allocation of the benefits and burdens of research. The revisions will also logically lead to an explosion of research in developing countries that would be intended mainly to benefit developed countries — another affront to current notions of ethical research."

The proposed changes are subtle. They would allow a waiver of written informed consent if the ethics committee determined that the risks posed by the research are slight or if the procedures to be used in the research are customarily used in medical practice without informed consent. It does not insist on consent being obtained by a physician who has no conflicts of interest. And it will permit the control group to receive "the local standard of care", which could be no care at all. Finally, it dilutes the prohibition against publishing unethical research.

**Brennan T A: Proposed revisions to the Declaration of Helsinki — will they weaken the ethical principles underlying human research? *The New England Journal of Medicine* 1999; 341 (7):**

## ...and another opinion

■ The second author argues that the Declaration of Helsinki makes a spurious distinction between therapeutic and non-therapeutic research, resulting in errors not intended by the authors. Second, it includes several provisions out of touch with contemporary ethical thinking. As a consequence, many researchers routinely violate its requirements. Such routine violations and their associated attitudes rob the declaration of its credibility.

For example, insistence on active controls would increase expense, decrease efficiency and actually violate international ethical guidelines which require that research is responsive to the health needs and the priorities of the community in which it is carried out. Referring to the placebo-controlled trials of short-course AZT to prevent maternal-foetal transmission in developing countries, the author argues that the placebo control meets ethical requirements: what people in developing countries need to know is whether the short-course regimen is better or worse than that which is currently available.

Countries which cannot afford all the treatments available to residents of industrialised nations must be allowed to develop affordable preventive and curative interventions. Research sponsors in industrialised countries should not be prevented from assisting developing countries in their efforts. The Declaration of Helsinki should be revised to reflect this understanding.

**Levine RJ: The need to revise the Declaration of Helsinki *The New England Journal of Medicine* 1999; 341 (7):**

## Standards for mandatory programmes

■ Mandatory public health programmes are justified in limiting the rights of individuals because they benefit the community as a whole. The authors suggest that any mandatory programme should meet certain requirements: failure to implement it would negatively affect the rights of others; it is the least restrictive feasible alternative, and it is fairly and equitably administered. They evaluate 10 TB programmes in the US using mandatory Directly Observed Therapy (DOT) to see if they fulfilled these criteria. Their findings: "DOTS was *not* shown to be consistently more effective than ... a high-quality self-administered treatment program. Within DOT programs, the least restrictive

alternative was not consistently used (as demonstrated by variations in frequency, duration, and location of treatment), nor was DOT always applied equitably."

**Jeymann SJ and Sell RL: Mandatory public health programs: to what standards should they be held? *Health and human rights* 1999; IV (1): 193-203.**

## Conflict of interest: some findings

■ In an editorial in the issue of *BMJ* containing a collection of material on conflict of interest, the author notes the accumulation of evidence that financial benefit makes doctors more likely to refer patients for tests, operations, or hospital admission, or to ask that drugs be stocked by a hospital pharmacy. Reviews acknowledging sponsorship by the pharmaceutical or tobacco industry are more likely to draw conclusions favourable to the industry.

The author refers to two significant papers documenting the consequences of conflict of interest. A study of 70 journal articles on calcium channel antagonists for treating cardiovascular disorders showed that authors were more likely to support the drug if they had a financial relationship with a manufacturer. Two thirds of the authors had financial relationships with manufacturers, but "only two of the 70 articles ... disclosed the authors' potential conflicts of interest." As many as 96% of the supportive authors had financial relationships with manufacturers, compared with 60% of neutral authors and 37% of critical authors.

Second, of 106 review articles on passive smoking looking at characteristics determining their conclusions, 37% concluded that passive smoking was not harmful and the rest that it was. A multiple regression analysis controlling for article quality, peer review status, article topic, and year of publication found that the only factor associated with the review's conclusion was whether the author was affiliated with the tobacco industry. Only 23% disclosed the sources of funding for research.

**Smith Richard: Editorial : Beyond conflict of interest: transparency is the key *BMJ* 1998;317:291-292**

## Medicine and human rights

■ 1999 marks the 50th anniversary of the 1949 Geneva Convention and the 100th anniversary of the Hague Convention, and follows by one year the 50th anniversary of the Universal Declaration of Human Rights. These anniversaries offer the *BMJ* the opportunity to explore a number of ethical and policy dilemmas that face medicine and science when issues of moral choice arise in war and in peace.

Discussions through case example, historical analysis, analysis of clinical data, or assessment of current and anticipated issues, seek to illuminate the relevance of key points in international humanitarian law and human rights to those whose work is guided by the more familiar principles of medical and research ethics.

It is hoped that readers deliberating on these questions of medicine, moral choice, and international law will appreciate that in the sphere of international humanitarian law and human rights there is not only room for the moral voice of physicians but an outright imperative that it should be heard.

**Leaning Jennifer: Medicine and international humanitarian law: Law provides norms that must guide doctors in war and peace. Editorial *BMJ* 1999; 319: 393-394**

## Applying guidelines rationing health care

In 1997, a 63-year-old Maori man with moderate dementia was taken off dialysis for end stage renal disease, applying a New Zealand health service guideline that 'moderate to severe dementia' is a factor 'likely to determine that an individual is not suitable for treatment.' since 'there must be ability to co-operate with active treatment.' He died after an unsuccessful effort to get the Human Rights Commission to review the decision. The commission ruled that the guidelines were legitimate and used correctly. The case has been described as "discrimination leading to death." This essay notes that the questions raised by this decision are central to the concerns of people with disabilities: "It would be thought unacceptable to withhold dialysis from patient who are blind or have an intellectual disability, yet the rationale underpinning the 'mental function' guideline applied to Mr Williams - 'there must be ability to comply with active treatment' - could also be applied to such patients."

**Paterson R: Rationing access to dialysis in New Zealand. *The newsletter of the network on ethics and intellectual disabilities* 1999 winter; IV (1): 5.**

## Defining limits

■ What does the researcher do when the group that s/he wishes to study is incapable of giving informed consent? Not doing research would deny that particular part of the population the benefits of research-dependent care. The author discusses the limits to research and therapeutic intervention on perinatal patients.

Starting with a discussion on therapeutic innovation, the prelude to systematic research, he goes on to consider consent in therapeutic and non-therapeutic research. The problems with accepting parental consent for non-therapeutic research are pointed out. The author presents guidelines for designing research involving perinatal subjects: it should be worthwhile and the goals realisable; and it should involve only "minimal risk to the research subject", a subject which is defined in some detail.

Regarding limits to therapeutic interventions, the decisive factor is the interest of the patient. However, when a clinician is eager to evaluate a new

technique and a parent is faced with losing a child, the cost to the child in need may get overlooked. The author concludes by referring to a four-year-old child who spent "the last months of her life undergoing harrowing heroic procedures. This raised the question of whether some paediatricians felt there was no point at which to call a halt to innovative practice."

**Evans D: Research on perinatal patients. *Otago bioethics report*. 1999 March; VIII (1): 5-7.**

## Deaf-mute or brain dead?

■ The author, a nephrologist, comments on the public response to the report of Prakash, a mentally disabled deaf-mute man, whose kidney was transplanted into his brother who had renal failure (see *IME* VII [2]: 38 VII [3]: 70). The consent form was signed by the man's mother. The author writes: "Had the guardian a right to give consent to the surgery? This boy was treated like an animal, not like a human being with some rights. He was subjected to the risk of death, albeit very small, and to considerable pain..." Some letter writers made surprising observations. One wrote that the transplant would "fill the hollowness in (Prakash's) heart and unknowingly or knowingly add a new meaning to his silent existence." Another, the president of the Indian Society of Organ Transplantation, declared that Prakash was "suffering from brain death due to loss of his higher sensory faculties," and in any case, if he were a "sane man, (he) would have been most happy to donate a kidney to his own brother." The author notes, "Almost half the perfectly sane, prospective, related donors decide that they do not wish to donate a kidney to their brother or sister, son or daughter. ...If we throw ethics to the wind, where will it end? Our mental health institutions are full of mentally incompetent people. Why not take their kidneys, and maybe lungs, hearts and liver as well, and thereby give some meaning to their lives?"

**Mani MK: Letter from Chennai. *National Medical Journal of India* 1999 May-June; XII (3): 128-130.**

## Love and medical ethics

■ The March 1999 issue of the Eubios journal contains papers from one of the sessions at the TRT4 in October 1998, looking at bioethics and the love of life. A number of the articles discuss the relation of love and medical ethics: as a general concept as well as in specific cultures such as the Philippines, south Asia, India, Iran, Thailand and China. Of the many valuable essays, one of them is particularly useful. The author discusses the question of bioethics and the love of life through the five central questions for bioethical theories: the meta-ethic, the normative questions of what is value, what is virtue, what are the principles of right conduct; and the relation between principles and causes.

**Veatch RM: Theories of bioethics. *Eubios journal of Asian and international bioethics* 1999 March; IX (2): 35-38.**

## CALENDAR

**October 28-31, 1999, Philadelphia, USA:** Second annual meeting of the American Society for Bioethics and Humanities. Contact: Jennifer Reinard, SSBH Second Annual Meeting, 470 W Lake Avenue, Glenview, IL 60025-1485 USA

**October 28-31, 1999, Edmonton, Canada:** Expanding the Boundaries of Ethics. The Canadian Bioethics Society's 11th annual conference. See the conference website at http://www.ualberta.ca/~cbs1999. Tel: +1 780 492 6676. Email: CBS1999@ualberta.ca.

**November 10-12, 1999, Philadelphia, PA, USA:** Complementary and Alternative Therapies in the Academic Medical Center: Issues in ethics and policy. Contact: University of Pennsylvania Office of Continuing Medical Education, (215) 898 6400.

**November 18-19, 1999, Charlottesvile, VA, USA:** Healthcare organization ethics. Contact: Ann Mills, University of Virginia, Center for Biomedical Ethics, amh2r@virginia.edu.

**January 13-15, 2000, Sacramento, CA, USA:** Health care systems: Ethical and economic considerations. Contact: Cristal Sumner, UC Davis School of Medicine Alumni Association, 2315 Stockton Blvd, Sacramento, CA, 95817, USA. chsumner@ucdavis.edu

*Issues in Medical Ethics* can also be seen on the internet, at:

http://www.healthlibrary.com/reading/ethics/index.htm