

rights mattered far more than those sanctioned by the science, law, and perceived social needs of the era.

The revelations of the holocaust strengthened the moral objections to eugenics and sterilisation, and so did the increasing worldwide discussion of human rights, a foundation for which was the Universal Declaration of Human Rights that the General Assembly of the United Nations adopted and proclaimed in 1948. Since then, the movement for women's rights and reproductive freedom has further transformed moral sensibilities about eugenics, so that we recoil at the majority's ruling in Buck versus Bell. History at the least has taught us that concern for individual rights

belongs at the heart of whatever stratagems we may devise for deploying our rapidly growing knowledge of human and medical genetics.

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## North-South research partnerships: the ethics of carrying out research in developing countries

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The new phase of North-South research collaboration was caught in a snapshot published recently in a popular weekly newsmagazine.<sup>1</sup> The picture is that of a participant in an AIDS study in Guatemala City. He looks jaunty, even confident. In 1997, he participated in a "life-and-death lottery," as the article is entitled, and beat the odds to be entered into a Merck drug trial of different doses of a triple cocktail containing their new drug, Crixivan. He was one of only 59 patients who were lucky enough to be entered into a trial, among the many who join the "scramble for cutting edge medications in a country where there aren't nearly enough of them to go around." The clinic caring for him "takes up the slack—for example, by enlisting its patients in drug studies."

"I felt myself stabilizing [he said]. I had the energy to go back to work." However, his future, as well as the futures of the rest of the participants who participated in and benefited from the study, is uncertain. "The year long study ended last September, and the leftover medicine will run out in the fall. Participants say they were led to believe that the company would supply them the drugs for the rest of their lives. Merck and the clinic doctors say the only promise was that the company would try to offer more drugs after the study, and the company did agree to provide Crixivan for five years. But the patients have to come up with the other two components of the cocktail on their own. That won't be easy. Participants worry that if they go off the drugs the virus will emerge stronger and more resistant to the drugs."

It is perhaps inevitable that AIDS will provide the backdrop for much of the rethinking that is going on with regard to research done by the North in developing countries. In 1998, HIV/AIDS ranked number four among the top 10 causes of the global burden of disease, accounting for 5.1% of the total disability adjusted life years. The burden is borne overwhelmingly, 98.6%, in middle income and low income countries.<sup>2</sup> In developed countries AIDS has become a high profile disease primarily because of strong and persistent advocacy. Aside from being a major burden,

### Summary points

North-South research collaboration is currently plagued by differing interpretations of ethical standards of doing research in developing countries and by inequitable funding, with only 10% of global research funding going to diseases which comprise 90% of the global burden

Health research is a public good, and the burden and benefits of doing health research should be shared equally by the North and South partners.

Three guideposts—Think action. Think local. Think long term—can be used to resolve ethical dilemmas and address inequities in research funding

Scientific advances are not the only yardstick to measure the success of North-South research collaboration: the choice of identified priorities as areas of work, the sustainability of the studied interventions outside the research setting, and the investment in local research capacity are becoming equally important as indicators of success

HIV/AIDS is a highly fatal disease, and the cost of drugs to stall the progress of the disease is high—beyond the reach of many low income countries, where the average per capita expenditure on health is less than half of the \$US12 that the World Bank suggests will fund an essential package of public health and clinical services.<sup>3</sup>

### Claims and counterclaims

Two years ago a controversy erupted over a report and an accompanying editorial that claimed that it was unethical to use placebo controls in studies in developing countries on the prevention of perinatal transmis-

sion of the HIV virus.<sup>4 5</sup> These randomised, placebo controlled trials on alternative and less costly protocols of zidovudine (AZT) were sponsored by the US National Institutes of Health and the Centers for Disease Control and Prevention. They were being conducted at the time that the 076 protocol on the use of this drug in the peripartur period had already been proved to decrease transmission by 65%; it had already been introduced as standard treatment in the United States. The counterclaim was that using placebo controls was not unethical in countries where the standard of care did not include zidovudine. Thus, a placebo controlled trial would be the quickest and most valid way of answering the question on efficacy. Strongly worded letters and editorials on this dilemma were carried in three major medical journals.<sup>6-12</sup> The recent consensus statement on Perinatal HIV Intervention Research in Developing Countries<sup>13</sup> and the 1999 draft revision of the Declaration of Helsinki<sup>14</sup> addressing this issue still arouse strong sentiments and show that resolution is difficult.<sup>15 16</sup>

The "scientific colonialism"<sup>17</sup> that characterised earlier North-South research collaborations has slowly been transformed. Then as now, it is straightforward to condemn research practices of "mosquito" scientists, who come into a country, take blood samples, and fly them out—with the results being learnt only on publication.<sup>18</sup> Likewise it is easy to expose the forgettable contributions of "parachuting" consultants, who land, gobble up a large part of the research budget with their two week stay, and then rehash local wisdom into a thick report.

However, the new phase of North-South collaboration as depicted in the HIV examples have dimensions of complexity and do not readily lend themselves to outright condemnation or resolution. Though they are outwardly a mutually beneficial partnership, some of the new research practices and partnerships have more insidious, subversive ill effects, particularly for the developing country partner. "Clinical investigations [result in problems] because of different and often conflicting cultural constructions of what clinical research is, how it is conducted, and what is to be gained from it."<sup>19</sup>

In Guatemala City, the AIDS patients knew that these were effective drugs, and they joined the study to extend and improve the quality of their lives. The investigators and the pharmaceutical company ran the study to determine which protocol was more efficacious. How are these different expectations dealt with once the study is finished? In anticipation of the outcome, should the study in Guatemala City not have been done at all? By having participated in the trial, are the patients diminished more because of their poverty?

In trials of zidovudine or other drugs run by pharmaceuticals or foreign funding agencies, can a placebo control arm still be used in countries where the local standard of care currently does not include a proved efficacious treatment? The Council for International Organisations of Medical Sciences states that "researchers working in developing countries have an ethical responsibility to provide treatment that conforms to the standard of care in the sponsoring country, when possible."<sup>20</sup> What if the same study was planned and mounted by local investigators solely? Does a mere change in the nationality of the investiga-



Medicine in the tropics is no longer limited to parasitic diseases but encompasses health problems like overpopulation and malnutrition

tors and funders determine whether the trial is ethical or not? The only certainty that emerges from these complex questions is that the rich-poor divide is magnified and felt more acutely in the drama of life and death situations.

### The equity of research funding in developing countries

The North-South axis in health research funding is tilted, reflecting the rich-poor divide in an equally dramatic way. The 10/90 disequilibrium is a term coined to describe the situation where only 10% of the \$50-60 billion spent annually on health research worldwide is directed to diseases which contribute 90% of the global burden of disease.<sup>21</sup> Health research funding is provided mostly by Northern countries, and the burden of disease lies mostly in the Southern countries. Responses to a self administered questionnaire from six out of 10 European research institutions show that collaborative ventures are conceived in varied ways but are mostly Northern initiatives.<sup>22</sup>

Voices from Africa say, "Lack of funds can be understood as lack of funds for local research initiatives. There are funds for Northern initiatives, and consultancies within the framework of Northern research programmes are well paid" and "We have to accept their priorities and interests."<sup>23</sup> Priority setting that is more accommodating of the needs of developing countries, followed by a political will to commit the funding, is needed to redress this imbalance.<sup>24</sup>

### Tropical diseases

Aside from HIV, tropical diseases provide another arena for discussions on North-South research collaboration. The ongoing debate about the future of tropical medicine revolves around whether tropical medicine must widen its scope to include other diseases of poverty and whether the traditional citadels of tropical research in the North should move out to the tropics.<sup>25</sup> Proposals on the questions of what (more) should be funded and where the funding should go provoked a brief flare-up of reaction,<sup>26-28</sup> from which there evolved an admission that medicine in the tropics is no longer limited to parasitic diseases but encompasses health problems such as overpopulation and malnutrition. These call for new skills and disciplines and for more field research rather than gleaming laboratories. There was also an acceptance that Northern partners bring in needed technology and opportunities for advanced training not available in developing countries. These tempered reactions are likely to lead to preservation of the status quo or token changes, unless a new impetus is discovered to develop new models of North-South funding and collaboration.

### Southern priorities

Even the best intentioned funding agencies and developed country partners can exacerbate the poor state of local research environments by competing for the few qualified scientists in the country.<sup>29</sup> Driven by their own priorities, they offer chances for research collaboration, which can bring in resources and prestige to the scientist and his base institution. Because of the widespread prevalence of many diseases and a chronic lack of institutional resources to carry out health research, any research topic can be and usually is justified as a priority, especially in the face of ready funding and partners who come wooing. One informant says: "We have no choice; we have not enough state funding; sometimes we are like poor prostitutes."<sup>23</sup>

Internal brain drain occurs, and local expertise is diverted from the more important areas to the less important areas of research.<sup>30</sup> A more insidious side effect is that developing country researchers work vertically with their Northern partners and become isolated from the other researchers within the country.<sup>23</sup> Thus, national research networks are neglected while North-South or South-South collaborations are promoted by funding agencies.

### Problems and complexities

In summary, despite the good intentions of the North-South partners, clashing agendas and values persist. The simplistic name calling or placing of the blame on the dominant partners of the past cannot capture the complex realities of the present. The problem of doing ethical research in an environment of constrained resources cannot be addressed solely within a discussion of whether or not to use a placebo and other aspects of research design. The inequity of distribution of health research funding requires the adoption of a broader perspective that treats health research as a public good. Finally, unless the model of North-South collaboration changes, the unintended ill consequences on local research structures will continue to

### Principles of research partnership<sup>34</sup>

- Decide on the objectives together
- Build up mutual trust
- Share information, develop networks
- Share responsibility
- Create transparency
- Monitor and evaluate the collaboration
- Disseminate the results
- Apply the results
- Share the profits equitably
- Increase research capacity
- Build on achievements

subvert any efforts to build national capacity; but only national capacity will eventually put the South on an equal footing with its Northern partners.

Increasingly, there is an awareness that the success of North-South research collaboration should not be judged solely on the results of scientific research activities. This awareness 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.

### Ways and means

Mutually beneficial North-South collaboration is not an impossible task. Outstanding examples already exist, such as the Swiss Tropical Institute and the Ifakara Centre of the Tanzanian National Institute of Medical Research.<sup>31</sup> The International Clinical Epidemiology Network has succeeded in developing a sustainable network of clinical epidemiology units in the South with technical assistance from some Northern universities.<sup>32</sup> Funders have already started acknowledging the primacy of demand driven research with the Dutch RAWOO initiative<sup>33</sup> and Swiss enunciation of principles of research partnership with developing countries (box).<sup>34</sup>

Singular efforts have produced local successes but have not succeeded in changing the basic character of North-South collaboration. In October 2000, the World Health Organisation, the World Bank, the Council on Health Research and Development, and the Global Forum and other partners will sponsor an international conference on health research for development.<sup>35</sup> This meeting will assess the impact of major initiatives in health research in the past decade and will help forge the research agenda for the new millennium. This will be an opportune international context to explore and promote new models of North-South collaboration.

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## The Icelandic database—do modern times need modern sagas?

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On 17 December 1998, as a result of legislation instigated by deCODE genetics, a Delaware biotechnology company working in Reykjavik, the Icelandic parliament adopted a law making it legal for a private company to construct an electronic database of the country's health records.<sup>1</sup> deCODE has received an exclusive licence to build a database of Iceland's medical records (including diagnoses and test results, treatments and side effects) and will be able to combine and analyse these with genetic and genealogical data. The act also grants deCODE exclusive rights to commercial exploitation of the database for 12 years. Accordingly, deCODE has entered into a (non-exclusive) arrangement with Hoffmann-La Roche which gives the latter company access to the database for the purpose of researching the genetic origins of 12 common diseases.

### Are the rules out of date?

The debate before and after the bill on Iceland's proposed database has been vigorous. Sigurdur Gudmundsson, Iceland's surgeon general, was quoted in the *New Yorker* as saying, "I don't think this country can just sit here and say, 'Nope, sorry, we are going to stand on rules that existed in a different era for a differ-

### Summary points

The government of Iceland has granted an exclusive licence to deCODE genetics to construct a database of the country's health records

Debate about issues of informed consent, privacy, scientific freedom, benefit, and commercial monopoly is vigorous

The question at issue is whether the rules being applied to the database can deal with the issues raised

A debate that focuses on traditional principles risks ignoring new challenges brought about by advances in medical technology

If the role of commercialism is to be assessed and defined appropriately, benefits to the individual and to public health need to be articulated clearly

ent world.'<sup>2</sup> But are the rules being applied to the database able to address adequately the issues that

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