

Ethical Issues of Medical Research in the Developing World

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Concluding Remarks

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It is a great pleasure for me to conclude these two days. It has been a real privilege to participate in this conference on ethical issues of medical research in the developing world, but it is quite a challenge to capture the quintessence of the exchange that took place.

Ethics of research is a developing and even a booming theme, according to the number of publications and meetings. Yet, despite the enormous body of literature and the impressively long list of founding texts and guidelines referred to by the articles and projects submitted to evaluation, we still find ourselves in an experimental phase. All of us are aware of the importance of medical research for the enactment of the "Right to Health", but we still have to invent the ways of promoting medical research that are not only unceasingly more inventive and fruitful, but also more and more sensitive to human values and specific needs of the populations, in a word a more ethical research.

The ethical character of research can be legitimately considered as a marker for justice and progress in societies, as the microcosm of medical research reflects the whole society where it is embedded. Accordingly it was tempting for us, while discussing how to reform the doings of ethics, to extend our scope to the reform of the society itself. The presentations frequently emphasized the necessity of maintaining golden standards, in conformity with an ideal model, bordering on utopia. But, despite the frequent reference to universally admitted values and standards, the process of making ethics a reality across developed and developing countries still faces many obstacles and is submitted to numerous factors of frailty.

History bears testimony to the experimental and fragile character of ethics.

Some historical background to the development of research ethics was discussed, in particular during the last day. The emergence of the topic is frequently tracked back to the Nuremberg events. In fact, if it is true that for centuries, the investigator's personal morals and dedication to patients were considered to be the main safeguard in the labyrinth of research; the

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Nuremberg code of 1947 was far from being the starting point for the elaboration of ethical guidelines for doctors. Influenced but not triggered by the BCG trial at Lübeck in 1930 Germany, some precise guidelines for doctors, with explicit mention of the subject's consent, had been put forth in 1931, which unfortunately by no means prevented crimes from being committed by the medical profession in the following years.² These past events prove how research ethics is a crucial but fragile link.

Our meeting was permeated by the common conviction that the improvement of ethics in research is not only a moral requirement but also a decisive step in the way to progress and social development. Which explains both the concern about keeping high standards but also the repeated caveats about context and realities, emanating from researchers working in India, Cameroon, China, Morocco, Senegal...

I do not have enough time to survey all examples of the persisting gap between laws and norms, on the one hand, and the reality of the situation on the other. (We call this in Arabic *_hukm al waq'a*", which means testing something through examination of reality). I will mention only two blatant examples of such gaps and distortions.

The first example is the debated matter of free and informed consent, considered as a key moment of research involving human subjects. This notion reflects the importance given to the individual over the collective will, a source of difficulty in numerous countries with a prevailing community or family-based ethos. Providing accurate, intelligible and adapted information may be a real challenge. The qualification of free consent also requires close attention. While exploring this issue in a comparative way, we have recognized that the context often jeopardized the efforts to implement procedures for the collect of valid informed consent. For example, when effective treatments for a disease are not available or affordable in a country, and participation in a trial is the only way of having access to a cure, the validity of the consent and its volunteer character are questionable. A forthcoming book by the Canadian anthropologist and doctor Nguyen Vim Kinh, called *The Republic of Therapy*, addresses this specific issue in the context of clinical trials for AIDS in Ivory Coast and Senegal. More generally, how to insure a free consent in a context of scarce therapeutic resources? This question leads to consider the embryonic development of national pharmaceutical companies in most developing countries, the monopoly of drug firms and the political decisions by governments to avail themselves or not of international agreements (ADPIC), allowing them to go astray of the strict application of patents.

Another particularly thorny issue relates to what happens once the research is over. Generally speaking, almost everywhere, the restitution of the results of experimental trials is often unsatisfactory, their communication and discussion in the public biased or inexistent. The

² Bonah C., Lepicard E., Roelcke V., *La médecine expérimentale au tribunal*, Paris, Editions des Archives Contemporaines, 2003; Menut P., The Lübeck catastrophe and its consequences for the anti-tuberculosis BCG vaccination, in *Singular Selves. Historical debates and controversial issues in Immunology*, AM Moulin and A Cambrosio eds., Mérieux Foundation, Elsevier 2001.

way the results are translated into tangible benefits (drugs or vaccines or recommendations for disease prophylaxis) is another source of frustration.

Progress is badly needed in this domain. The participants have repeatedly expressed their concern about the fate of the enrolled population (or village or community or group), when the research is over, and emphasized the fact that for them this assessment represented an integral part of the Committees' activities. But can Ethics Committees follow up the successive phases of the research, and specifically ensure that the one succeeding the trials is managed correctly?

How to deal with the issue of time scale?

One of the main problems at stake, something which has perhaps been downplayed in our discussions, is the time scale, which impedes a sustained mode of action. On the one hand, experimental situations require permanent watch, and decisions may need to be taken at short notice (with the appearance of undesirable events in the course of the trials or new developments in the field, for example), while ethicists' activity is intermittent at best and in any case incompatible with continuous follow up of the scene.

On the other end, we must acknowledge that the time scale for the release of useful products exceeds often a period of 10 years and may approximate a generation leap. The researchers who started the whole process are often no longer in a position to influence the decisions some twenty years later. My countryman Maupas, who passed away unexpectedly in the course of his pioneering work on hepatitis B vaccine in Tours, was no longer there to watch the scandalous lag in providing the first anticancer vaccine to the Senegalese population where the trials had been conducted.

In the long term, it might be the responsibility of historians rather than ethicists, to be concerned and to remind the academic community, political body and industrial partners, of unfulfilled promises. It is also their duty to call attention to the mentality shifts and the sensitivities to new norms and social expectations, and make an issue of it.

Unfortunately, the list is long of scientific mistakes or gross moral faults linked to events that sometimes passed initially unnoticed and were far from immediately fostering critical reactions and reflections. I will mention only the late coming scandal of the Tuskegee Affair, a story of clinical survey on black syphilitic patients left untreated, and pursued for years in the south of the United States, long after the arrival of penicillin³, or the Thalidomid disaster. The so-called "Cutter incident", cases of post-vaccine polios in children, which occurred after the happy end of the great Francis vaccine trial in 1954, has recently been revisited.⁴ The story illustrates how scientific doubts on safety (in this case, on virus inactivation and vaccine innocuousness) can be swept aside when facing political agendas, and the difficulty of raising dissenting voices in the scientific community, once an official consensus has been obtained. In

³ J Jones, *Bad Blood, The Tuskegee Syphilis Experiment*, New York, Free Press 1993.

⁴ P.A. Offit, *The Cutter Incident*, Yale University Press, London and Newhaven 2005.

retrospective, it can be argued that the threat of polio epidemics weighed so much on the authorities, that hasty release of imperfect vaccines, at the cost of a few casualties, might have seemed preferable to postponing unduly the general distribution of the precious vaccine and optimizing safety. Recently, we faced a similar debate and a different choice. The withdrawal of a licensed rotavirus, held as responsible for intussusception cases in the US, has triggered a heated debate on its consequences in the Third World, deprived of a tool for curbing its infant mortality linked to diarrheas. There is no doubt that the increasing use of the precaution principle will generate many similar questioning in the coming years.

Working on the history of revision and debates on texts promulgating ethical and scientific norms at the international level, historians wish an easier access to the oral or written archives of the involved institutions, in order to learn more on the dissonances in the midst of apparent harmony. In the sphere of the committees of ethics working at the level of international organizations (WHO, the European Commission, for example), the tendency may be strong, even if legitimate, to avoid clash-making assumptions in their reports and to favor a diplomatic consensus at the end. Some historical and anthropological work on committees would tell us much on the underlying stakes and the exchanged arguments prior to the writing of the final report. Committees tend to take for granted the respect of the written norms in the field, refraining their curiosity about the way these norms are translated. Again we are fighting with time. The first comprehensive book on the doings of the French National Committee of ethics went out only twenty years after its creation.⁵

Is the legalization of Research Ethics the ultimate answer?

My last point will be that with a growing body of literature and jurisprudence, we seem to have entered the era of ethics legalization, with legally binding authoritative texts. Judge Byk and our chairman have reminded me that France has followed the European guidance in this respect by giving to ethical reviews the meaning of a legal seal of approval.

Our conference has been tensely polarized between the seductive voice of utopia and the stringent call of reality, as its members refused to choose between binding legal judgments and consultative advice, "l'esprit et la lettre" (I could go on this way with a long list of oppositions). I stress again that, on the one hand, we made the choice of sticking to high standards potentially out of reach, and that, on the other hand, especially in our workshops, we have urged the necessity of bringing attention to a broad range of conflicting positions and controversial experiences.

⁵ AM Moulin, "Medical Ethics in France", *Theoretical Medicine*, 1989, 9, 271-285 ; D. Memmi, *Les gardiens du corps*; Paris, EHESS, 1996.

The role of social sciences

To conclude, I would like to emphasize the importance, in order to balance the "transcendent power of science" over the minds, of deploying good and active research in social sciences, assuming a critical function. The role of social sciences, whether they be in the field of political sciences, sociology or anthropology, is to investigate decision-making processes, and explore the diversity of behavior patterns and beliefs, a diversity which has been addressed repeatedly by the speakers.

I am well aware of the fact that social sciences introduce an inquisitive look into the sanctuaries of science, that may be frowned upon by the people concerned. In the last few years, history, sociology and anthropology of sciences, have pointed to the necessity of understanding the scientific practices in context. Researchers have been encouraged in scrutinizing the multiplicity of pathways, the turning points, the dramatic changes in scientific choices, the divergences among the team members and the scientific leaders, and between the sponsors, the promoters and the investigators of clinical trials. The intervention of social scientists may resemble an unpleasant form of Medical Nemesis, a title once chosen by Ivan Illich for his very controversial review of the responsibility of medical research⁶ in the improvement of life expectancy in the 20th century. Social sciences may be taxed for a purely negative impact when pointing to the hesitations and doubts, the conflicts of interests, the personal quarrels, the commercial concerns and even corruption. I would like to plead that this negative function of embracing the real can be viewed as a healthy counterpart to an idealistic view of harmony in our global world, which in reality is contradicted by facts.

Touching base with reality may be a necessary preliminary step before making progress in this area. Sociological analyses may be sobering or refreshing. They often lead to iconoclastic questions. As an example, I remember my past enthusiasm when listening to the late Jonathan Mann, a companion of the Foundation who has since passed away, as he advocated passionately his choice of a strategy against AIDS, pivoting on the defence of human rights. At the time it seemed to us and to me the best possible way of dealing with the terrible epidemic. Ethics was engaged in the fight against AIDS as it was in the fight for the essential rights of minorities, of women, of all vulnerable people. Ethics, research, human rights and development were irresistibly geared together in the most possible coherent way...

In the country where I presently live, Egypt, it seems to me, to the risk of shocking some of you, that the strategy of human rights is not necessarily the most appropriate and effective. Some intellectuals have currently expressed their disagreement with the language of Human Rights, suggesting the cultural superiority in the West and accommodating the Western interests, an idiom that has recently covered infringements on national and individual liberties. For me, the best strategy against AIDS in Egypt, in a context of relative denegation of the epidemic by the government,⁷ seems, rather than invoking the imperfect implementation of

⁶ I Illich, *Medical Nemesis. The Expropriation of Health*, London, Marion Boyars, 1975.

⁷ J-N Ferrié and S Radi, "Moralisme et identité", *Journal du Sida*, 996, 92, 50-51.

human rights, to press the improvement of individual welfare, which would occur if the government led a policy of real assessment of the epidemics. For example, if the government facilitated voluntary anonymous testing for AIDS (in conditions of strict confidentiality) by developing free access to treatment after passing agreement with companies which sell antiretroviral drugs at a low cost; or better supported the creation of local factories, a point that conducts us back to the core of the development question. There is no African country, apart from South Africa, which possesses an autonomous pharmaceutical industry.

This meeting was clearly a great success in articulating the declarations from the chair and the collective work of the groups, the many voices from the associations, the press, the industry, voices from different countries and continents. This meeting represented a subtle mixture of positive information and the exploration of the difficulties and the obstacles to overcome, a mixture of traditional hospitality and scientific brainstorming, an opening on new ventures, all clearly a long-lasting specialty of the Mérieux Foundation.