HIV Vaccine: Ethics and Human Rights

Justice Kirby Collection

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VACCINES IN CONTEXT

It is exactly two hundred years since Edward Jenner released his study on the first vaccine against smallpox[2]. One by one, other conditions have responded to immunisation: yellow fever, plague, polio, diphtheria, tetanus, typhoid, whooping cough, rabies. Most of these conditions are produced either by bacteria (such as typhoid) or by a comparatively stable virus (such as smallpox). HIV/AIDS presents particular challenges to vaccine development. Those challenges stem from the features of HIV itself and of the social context in which this particular virus manifests itself.

One of the first lessons I learned in evaluating the ethical issues presented by HIV/AIDS, the prevention of its spread and response to its outcomes, was taught to me fifteen years ago by Dr June Osborn. Good ethics on this, as on most similar issues, will grow out of good science - a thorough understanding of the scientific facts. Because our knowledge about the HIV virus, and the particular strains[3]by which it differentially manifests itself, is constantly expanding, it is inevitable that ethical perceptions will also be in a constant state of evolution. Like the virus itself, they are unstable and continuously mutating.

Some elements of stability, can, however, be introduced into ethical discourse on this subject by constantly returning to fundamental principles. Relevantly, these may be found in the great charter of human rights known as the *Universal Declaration on Human Rights* and in the *Declaration of Helsinki*[4]. These and other international statements of principle establish three central requirements to govern the ethics of prophylactic or therapeutic research into HIV involving human beings:

- First, respect for persons: their autonomy in decision-making and self-determination;
- Secondly, beneficence: maximising benefits and minimising harms; and
- Thirdly, distributive justice: that is equitable distribution of both the burdens and benefits of participation in research[5].

The defects and suggested inadequacies of the *Helskini Declaration* to respond to the complex problem of HIV/AIDS, the human genome and so on has led to controversial suggested changes in the *Declaration* which are before the World Medical Assembly[6]. The late Jonathan Mann pointed out that the *Helsinki Declaration* makes no specific reference to issues related to patients' rights or to medical treatment as a fundamental human right[7]. But he also taught that the HIV/AIDS pandemic has, from the start, been concerned with ethics. Ethics at a national level by reason of the modes of transmission of this virus and the stigma,

shame, prejudice and legal sanctions which acquisition of the virus involves. But also macro-ethics: looking at the pandemic from a global perspective. Such a perspective demands access to HIV prevention and therapy in developing countries as a global issue of equity and basic human rights[8].

THE BASIC GUIDING PRINCIPLES

In considering the ethical issues presented by HIV vaccines, it is easy to lose one's way. These two guideposts should therefore be remembered:

- Base your judgements on the best available science, recognising that science is constantly changing and that its subject matter, HIV/AIDS, not only produces different pathological strains of the virus in different countries but also different pathologies of social prejudice, fear and stigma; and
- When in doubt about a particular issue, return to universal norms. There are not two global statements of fundamental human rights - one for the developed world and another for developing countries[9]. There are only universal principles, although their application may sometimes vary in different environments.

Out of recognition of the need to develop global principles which will be in place as vaccine trials are multiplied in both developing and developed countries, UNAIDS has been preparing a "Guidance Document" on *Ethical Considerations in HIV Preventive Vaccine Research*[10]. The preparation of this document has involved a long and complex process reflecting the controversies which such an attempt inevitably produces. We should not be surprised about such controversies and the differences they reflect. They arise out of the many tensions which exist in this area:

- Between the perspectives and sense of urgency of developing countries and those of developed societies which feel that the worst phase of the pandemic may be behind them;
- Between those who see the priority as the development of a prophylactic vaccine and those who view vaccines as part of the strategy of therapy to help those already infected with HIV;
- Between governments and agencies which want immediate action and pharmaceutical corporations fearful of civil liability, dubious of short-term profits, inclined to hasten slowly, and vice versa;
- Between old time vaccinologists looking for an answer to HIV/AIDS in the tried and trusted medical model and the communities with long-term experience of this pandemic who fear any diversion of funds and energy from education, behaviour modification and prevention of spread which has been the strategy to date in default of an effective vaccine and affordable therapy; and
- Between the politicians and others looking for a quick fix that will relieve them from having to deal with stigmatised groups - homosexuals, sex workers, injecting drug users and the like. And those groups, energised by the pandemic, into demands for wider reforms of the law and of social attitudes.

The resolution of these debates will yield the answers to some of the ethical questions presented by the development, testing and use of HIV vaccines.

A THRESHOLD QUESTION: A VACCINE AT ALL ?

A threshold question is whether the development and trial of an HIV vaccine at this stage can be supported on ethical principles? There are those who express doubts. They suggest, for example:

- That we do not know enough about this unstable virus to be progressing to the risky undertaking of a trial of a vaccine to prevent its spread. Already the attempt of French vaccine researchers in the former Zaire indicated the risks of premature intervention[11]. There is also the peril of researcher egos and political pressure[12]and the special complications with this virus because of its mutations and local variations[13].
- That trials in the United States have been discontinued because legal liability for mishaps would be scrupulously enforced in the courts[14]. They look suspiciously on the shift to developing countries where official approvals are more readily secured, individual consent can be obtained by community deals and legal liability if things go wrong is no big problem[15];
- That we may see a repetition of the scientific imperialism which marked the Tuskagee study that denied penicillin to indigenous victims of syphilis even after it was widely available in the United States[16]or the radiation of human subjects which exposed living people to unknown and dangerous risks[17];
- That there is a peculiar possibility that this virus, because of its high volatility, may "unattenuate" from an attenuated strain, such that a dead virus may come back to life threatening the person vaccinated with it[18].

These are legitimate ethical concerns which have to be answered. The response to some of them will depend upon the best available scientific knowledge. Clinical trials on animal subjects must first be attempted. Yet these have clear limits in HIV because, as in the past, the human response cannot be exactly replicated, or replicated at all, even in the animal closest to the human species, the chimpanzee[19]. In the end, it is essential to take some measured risks[20]. These should be taken with a clear appreciation of the urgency which faces humanity. That urgency derives from three basic factors:

- HIV is the fastest spreading new pathogen threatening life in the world today. It is estimated that every day 16,000 new HIV infections occur[21];
- Behaviour modification is a very slow and imperfect process. For any degree of effectiveness, it is necessary to challenge entrenched religious, moral, social and other sources of resistance and this is never easy or wholly successful; and
- In developing countries there is no time to overcome social resistance. As one Health Minister observed "If you don't get on with this soon there will be no one left to test"[22].

This is why, on a macro level, it has been declared that the only "realistic" way to deal with the HIV/AIDS epidemic in many parts of the world is by vaccines[23]. It is why in recent years there

has been a renewed commitment of governmental leaders to the development of HIV vaccines[24].

We must recognise that *not* to take a decision to trial scientifically promising vaccines is itself to make an ethical decision. Even a low efficiency limited impact vaccine, used in places of major spread of HIV and protecting some individuals at primary risk to spread and receive the virus would, on mathematical population models, have a huge impact on this particular pandemic[25]. In any case, vaccine trials are now beginning. If too long delayed the energy, investment and interest of the private sector entrepreneurs, essential for their practical success, might be lost[26]. In these circumstances, some risks may ethically be taken. Indeed, they will be taken as the trials progress. However, especially because many or most of the trials will take place in developing countries[27]it is essential that those countries themselves, UNAIDS and voices of principle everywhere should insist upon the observance of fundamental ethical principles that respect the human dignity and rights of those involved in the trials without forgetting the human dignity and rights of those who will benefit, even only partially at first, should the trials (or some of them) prove successful.

ETHICAL RULES FOR THE CONDUCT OF TRIALS

It is impossible to outline more than the main ethical considerations which must inform trials of HIV vaccines. Useful checklists for the conduct of vaccine trials in developing countries have been produced[28]. In approaching these questions, we can learn from the responses to analogous ethical quandaries:

- From the testing of HIV drugs in developing societies where there is no real prospect that such drugs will become commonly available in the societies concerned[29]; and
- From the suspension of the Human Genome Diversity Project because some of the developing societies subject to experimentation and study felt that they would be unfairly excluded by patent laws from any benefit as a result of their cooperation[30]

At the risk of arbitrary choice of some only of the priorities for ethical reflection in this context I would mention five:

- The need for close community involvement and education in vaccine development to ensure the recruitment of informed volunteers, true informed consent of those involved, continuing HIV education and health and other support for those participating in trials, particularly should they sero-convert;
- The development of health infrastructures generally, to improve the provision of basic healthcare to those in the target populations in developing countries. In short, host countries that participate in such trials, as well as the people who take part in them, must reap a just return ("the vaccine dividend") if, as a result of the trials, commercial vaccine development goes ahead;
- Those who participate in trials must continue to receive the HIV education messages because such messages are the only certain and available means of reducing their risk. Indeed, education of the community generally is essential as vaccine trials are carried out. There must be no let up in the general effort, to promote behaviour

modification generally, as well as in the trial group, which has produced measurable results in countries such as Thailand and Uganda;

- Informed consent for entry into trials requires sensitive attention to local customs and values. It is here that, in developing countries, the involvement of community representatives in the development of protocols will sometimes take a different direction than occurs in developed societies. Yet the individual is precious and has fundamental human rights in every society. The same basic norms must be observed. This will require an ethical commitment which is unwavering for the support and welfare of vaccine trial participants and their families;
- For those trial participants who sero-convert during the trial it is essential that they then be offered the best known standard of treatment (although exactly what this means is debatable). In advance of the trial beginning, those in charge should fix and publish the circumstances of termination of their trial and the provisions they will make for any that may suffer or be disappointed[31]. They must address the compensation package for those who sero-convert. They must specifically address the problems of discrimination against, and stigma towards, people participating in trials[32]and people who, after the trial, present as HIV positive (even if not sero-converted) with all of the practical and legal disadvantages that that can entail[33].
  It is essential that every HIV trial should have a guardian, a human rights ombudsman, to remind the politicians, scientists, investors and all concerned that HIV is a virus with special implications and dangers for human rights and ethics.

A FURTHER AIDS PARADOX

What is the basic reason for renewed vigilance about ethics in connection with the trials of a HIV vaccine? To answer that question requires us to acknowledge a new AIDS paradox. Years ago, before vaccines, we came to know the first AIDS paradox. This is that, paradoxically, the most effective way to promote behaviour modification essential to reducing transmission of HIV is not criminal law and punishment. It is protection of the vulnerable who are at risk and effective defence of their basic human rights. Only then will such persons be receptive to the messages and means necessary for self-protection and the protection of others.

Now we have a new HIV paradox. Ethics requires that those participating in HIV vaccine trials must be alerted, counselled and reinforced in the lessons of behaviour modification. They must not put their faith in the vaccine. Whether receiving the experimental product or the placebo, they must be constantly reminded of the messages about avoiding exposure to the virus. Yet, paradoxically, the effectiveness of the trial will only be proved if some participants do not receive or ignore these messages and become infected[34]. In this sense those promoting a vaccine have, potentially, an interest in the sero-conversions of those receiving the placebo. They have an interest in the exposure to risk of those who have received the vaccine. No one would suggest that scientists engaged in vaccine development would promote the risk or act unethically to bring it about. But objectively the vaccine trial will only be successful if some exposure to the virus occurs. There lies the paradox. In non-life threatening vaccine trials (mumps, measles and so on[35]) such potential conflicts of interest may be tolerable. Where HIV/AIDS is concerned, they are not. They require the greatest

possible vigilance. An ethical respect for the human rights of trial participants must place life before quick results; informed consent and thorough counselling before long term profits; the uninfected today before the uninfected tomorrow.

HIV/AIDS is a challenge full of dilemmas and paradoxes, scientific and ethical. Whoever we are, scientists or laity, we have imperfect understanding. We see the road ahead, including the ethical road, through a glass darkly; yet we must respond to the puzzles urgently face to face. Our hopes and prayers must be that we have "enough wisdom to make the right decisions, strength and courage to continue to discuss and confront the hard issues and luck to make it all work"[36].

ABSTRACT OF JUSTICE KIRBY'S PAPER ON HIV VACCINES

In the 200 year history of vaccines there have always been ethical dilemmas. ut they are especially acute in the case of an HIV vaccine because of the dangerous and unstable features of the virus itself and the social setting of prejudice and stigma in which the virus operates.

The only safe way of responding ethically to the trialling and use of HIV vaccines is by mastering the science concerning the vaccine, and its target HIV, and by applying universal human rights principles - such as those stated in the *Universal Declaration on Human Rights* and the *Helsinki Declaration*. These require attention to respect for the individuals involved; beneficence in the trial and distributive justice - so that those who participate stand to gain just benefits for doing so and not simply risks and burdens.

After reference to the UNAIDS draft *Ethical Considerations in HIV Preventive Vaccine Research* this paper analyses the tensions and differences that arise in this field and examines two basic questions.

The first is whether there should be HIV vaccine trials at all in present conditions of knowledge and given that most trials would be conducted in developing countries. The author reviews various criticisms and risks based on past experience. However, he concludes that the decision *not* to undertake vaccine trials may itself involve an ethical decision given the rapid spread of HIV (approx 16,000 new infections each day) and the severe difficulty of securing behaviour modification to reduce this spread. In any case, trials are beginning so it is timely to lay down some basic ethical ground rules about how they should be conducted.

These ground rules include: the need to closely involve the communities concerned in such trials; to ensure that a "vaccine dividend" is paid to developing countries which participate; to ensure that there is no let up in investment in educational messages designed to prevent the spread of HIV; to demand informed consent from participants in trials; and to ensure that those who take part are afforded the best known standard of treatment, particularly if their involvement is followed by HIV sero-conversion.

The need for vigilance is doubly important in this area because of the serious potential of sero-conversion and the needs of those trialling a vaccine to ensure that a number of those in the trial are actually exposed to the virus. Nothing else will effectively test the efficacy of

vaccines. Yet that risk needs to be minimised out of respect for human life. Herein lies a new AIDS paradox.

The paper concludes with the needs of humanity in this enterprise - hope and prayers - wisdom, courage, caution, and a measure of luck to devise vaccines that will help humanity's response to the most dangerous new pathogen in the world today.