Recommended Ethical Principles Regarding the Use of Assisted Reproduction in HIV Infected Individuals

(Committee on Promoting Acceptance of People Living with HIV/AIDS (CPA) of the Hong Kong Advisory Council on AIDS, April 2004)

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Background

1. The desire of HIV positive individuals to procreate has become increasingly witnessed in the HAART era when the morbidity and mortality of HIV infection have been dramatically reduced. To acknowledge their procreative rights, assisted reproductive therapy (defined as *all treatments or procedures that include the in vitro handling of human oocytes and sperm or embryos for the purpose of establishing a pregnancy* [1]) has been in use for HIV positive patients overseas to prevent HIV transmission to the HIV negative partners and their offspring. None of the 3000 women and 400 children undergoing the procedures worldwide has been tested HIV positive so far. Albeit appearing a safe procedure, the possible risks of infecting the partners and the offspring associated could not be eliminated.

2. The birth of the first baby conceived by assisted reproductive technology in Hong Kong took place in 1986. Since then, Queen Mary Hospital, Prince of Wales Hospital, Kwong Wah Hospital and some private practitioners have been offering assisted reproduction to their clients. Although there has been no documented case of its use in HIV positive patients locally, requests of such were noted recently. In view of the possible demand in the future, the committee put forward the following recommended ethical principles to be observed regarding the use of assisted reproduction in HIV infected individuals in Hong Kong.

Ethical Principles Regarding the Use of Assisted Reproduction in HIV Infected Individuals

3. **HIV infected individuals should enjoy equal right to access assisted reproductive treatment in Hong Kong as to those who are HIV negative.** Although there is a lack of local experience in using assisted reproduction in HIV infected individuals in Hong Kong, this should not constitute a reason for declining such request given that it is technically feasible. People with HIV/AIDS are protected under the *Disability Discrimination Ordinance*.[2] According to its section 26, it is unlawful to refuse to provide a person with disability (i.e., *a person with HIV/AIDS*) with services of any profession (i.e., *assisted reproductive treatment*), unless the provision of such services would impose unjustifiable hardship on the service providers.

4. When seeking advice on their reproductive options, **HIV infected individuals should be given comprehensive information and appropriate counselling on their reproductive options** (refers to Appendix 1) **and the pros and cons on each of the options** (refers to Appendix 2). A multidisciplinary team, consisting of HIV physicians, assisted reproduction specialists, nurse counsellors and medical social workers should be equipped with such knowledge. They should adopt a **supporting attitude** by providing appropriate and unprejudiced information and medical assistance when necessary. The common goal is to minimize the possible risks of procreation and the use of assisted reproduction, and maximize the well-being of the child and the couples[3].

5. To evaluate possible clients for assisted reproduction, **the same principles under *the Code of Practice on Reproductive Technology & Embryo Research* should be applied irrespective of their HIV status** (refers to Appendix 3), and in particular, the *welfare of the child* will be of paramount importance. The latest ethical guidelines set out by overseas authorities should be referred to. (Examples of such are attached in Appendix 4). A set of criteria and recommendations recently published by overseas authorities for the use of assisted reproduction among HIV infected men and women should also be taken as a reference (refers to Appendix 5).

6. **The final decisions as to procreate or not and which reproductive options to opt for should be made by the couples themselves** after counseling. The decisions made should be free from coercion of any kind from any health care providers.

Conclusion

7. To conclude, HIV infection per se should not be an exclusion criteria for access to assisted reproduction. The HIV positive individuals should enjoy equal access to such service and be evaluated using the same principles as applied to the uninfected people. Health care workers should preferably be equipped with knowledge to provide appropriate information and counselling in a non-discriminatory manner. The dogma in medical ethics, namely autonomy, beneficence, nonmalefeasance and justice should be considered at all times and the final decisions concerning the procreative choices should always be made by the patients and be respected by the health care providers.

Appendix 1

Summary of Reproductive Options for HIV Infected Individuals

The basic concern for HIV infected individuals to procreate is to prevent HIV infection of the uninfected partners and the offspring. The following table summarizes the reproductive options for HIV Infected Individuals.

Reproductive Options for HIV Infected Individuals

HIV status / Reproductive options		HIV discordant couples		both are HIV positive
		HIV positive men	HIV positive women *	
Unprotected intercourse ^		YES	YES	Yes or unknown
Artificial insemination using	Washed sperms	YES	YES	
	Donors' sperms	YES		
Adoption		YES	YES	

* PMTCT (using antiretrovirals &/ C- Section, avoiding breastfeeding) should be employed

^ The chances of the female and the male being infected during an unprotected vaginal intercourse are estimated to be 0.05 to 0.15% and 0.03% to 0.09% respectively

To wash semen free from HIV, three basic methods are currently being used. Sperm washing separates the cells from seminal fluid by repeated cycles of centrifugation. Swim up method further separates the sperms, which are motile, from other cells by adding an overlying medium to the cell pellets. Only the sperms would be able to swim up and be collected in the medium. The third technique employed density gradient columns and centrifugation to obtain isolated sperms. Sperm samples are then tested for viral particles using immunoflorescence, HIV RNA and HIV DNA PCR. Only HIV negative sperms are used for insemination.

Combinations of the above methods have often been used overseas; and experience so far has shown a 0.9%-6% chance of obtaining a positive PCR test. More than 3000 intrauterine inseminations on about 1200 HIV negative women have been performed in Italy, Spain, German, United Kingdom and some centres in the United States resulting in almost 400 children being born. About 300 cycles of intracytoplasmic insemination (ICIS) and in-vitro fertilization (IVF) have also been performed giving birth to 50 children. None of these women or children has been found HIV positive.[4] The only single documented case of HIV transmission during assisted reproduction in 1990 in the United States was presumed to be due to inadequate washing.[5]

Insemination with HIV negative donors' sperms and adoption are the only risk-free methods to ensure giving birth to a HIV negative child but the genetic relationship to either or both parents are removed.

The use of assisted reproductive treatment in HIV positive women avoids HIV transmission to the male partners but not the offspring. There is no report on the use of assisted reproduction in HIV positive women to-date. Only one review paper documented its use in some centres in France for HIV infected women, especially those with subfertility.[6]

The options are all applicable to couples which both the man and woman are HIV positive. The use of reproductive technologies avoids unprotected sex and hence HIV superinfection. There is a possible risk of the infant to become orphaned prematurely and no optimal guideline is currently available.

Appendix 2

Risks and Benefits of Assisted Reproduction in HIV Infected Individuals

Possible risks involved in using assisted reproduction in HIV infected individuals include

(a) HIV infection of the children,
(b) early orphanage of the children,
(c) HIV infection of the uninfected partners,
(d) HIV infection of the staff,
(e) contamination of other embryos in the laboratory, and
(f) the risk of assisted reproductive reproduction itself.

Risks (a), (b) and (c) were often the main deterrents in the past but the outlook has been changing because of (i) the advance of HAART in decreasing the morbidity and mortality associated with HIV infections, (ii) the improvement in prevention of mother to child transmission, and (iii) the apparent success of using assisted reproduction in HIV infected individuals as described above. These risks have been much reduced but not removed.

Local experience in the use of HAART in HIV infection and prevention of MTCT is accumulating and encouraging. Currently about 1000 patients are regularly receiving treatment at one of the two HIV specialist services, where HAART is prescribed according to clinical indications. All six babies born to HIV positive women during the first year of implementation of the Universal Antenatal HIV Antibody Testing Programme have been tested negative so far. Despite of the lack of local experience in using assisted reproduction in HIV infected individuals, the technologies and techniques required are apparently available.

At present, there is no evidence to suggest risks (d) and (e) justify as reasons to withhold treatment when specific infection control guidelines and universal precautions are straightly followed.[7] For risk (f), most studies have shown a negligible or only a slight excess risk of major and minor birth defects in babies conceived by assisted reproduction. However, the associations of assisted reproduction with increased risks of major birth defects, low birth weights and congenital abnormalities have been reported[8].

Possible benefits of using assisted reproduction in HIV infected individuals include

(a) an apparent lower chance of HIV infection in the uninfected partners and the children compared to unprotected intercourse,
(b) promotion of protected intercourse[9],
(c) psychological benefit of the couples[10].
(d) meeting the needs of HIV positive patients in an appropriate and non-discriminatory manner.

Appendix 3

Assessment of Clients for Reproductive Technology Treatment in Hong Kong [11]

Clients should be offered fair and unprejudiced assessment. Client's medical condition should be fully assessed to determine the most appropriate treatment option.

In assessing clients' suitability for reproductive technology treatment, the welfare of the child is of paramount importance. The assessment should take into account the clients' physical, mental and social well-being, including the following factors -

(a) their commitment to having and bringing up a child or children;
(b) their ability to provide a stable and supportive environment for any child born as a result of treatment;
(c) their medical histories and the medical histories of their families;
(d) their ages and likely future ability to look after or provide for a child's needs;
(e) their ability to meet the needs of any child or children who may be born as a result of treatment, including the implications of any possible multiple births or disability;
(f) any risk of harm to the child or children who may be born, including the risk of inherited disorders, problems during pregnancy and of neglect or abuse.

Code of Practice on Reproductive Technology & Embryo Research, Council on Human Reproductive Technology, December 2002

Appendix 4

Latest ethical guidelines on the use of assisted reproduction in HIV infected individuals by ACOG and ASRM

1. **2001 The Committee on Ethics of American College of Obstetrics and Gynaecology (ACOG)** commented that 'offering ART to HIV patients is consistent with balancing respect for autonomy with fetal beneficence. There is also precedent for offering ART to individuals with other chronic and potentially lethal diseases. With the emerging consensus that ART may be offered to some couples with HIV, practitioners who have knowledge and expertise in this field should are ethically obliged to provide care to them.'[12]

2. **2001 Ethics Committee of American Society of Reproductive Medicine (ASRM, formerly The American Fertility Society)** suggested that 'individuals are no acting unethical in proceeding with reproduction if they have taken all reasonable precautions to prevent diseases transmission and are prepared to love and support the child, regardless of the child's medical condition. Likewise, health care workers are not acting unethical if they have taken all reasonable precautions to limit the risk of transmitting HIV to offspring or to an uninfected partner. Patients should be referred to tertiary centre with the facilities that can provide the most effective evaluation treatment and follow up, or alternatively, advised to look to options and consider donor sperm, adoption or not having child.'[13]

Appendix 5

Criteria and Recommendations for the Use of Assisted Reproductive Technologies among HIV Infected Men and Women [14]

- Disclosure of serostatus between partners
- Preconception counselling
- Informed consent (risks, benefits, and alternatives must be explained and documented)
- Absence of opportunistic infections or prophylaxis
- CD4 cell count >350 cells/mm^3 and HIV RNA level <50,000 copies/ml
- Patients receiving HAART:
  - HIV RNA level <400 copies/ml
  - Regimen without teratogenic drugs
  - Adequate tolerance to the regimen
  - Antiretroviral therapy for at least 1 year with appropriate follow up (stable viral load and CD4 cell count)
- Semen samples analyzed for HIV by PCR before insemination (only negative samples should be used)
- Close follow-up and appropriate therapy during pregnancy and after birth
- Intrapartum zidovudine chemoprophylaxis
- Follow up of the child (strongly recommended)
- HIV infected women
  - normal results of Pap's smear or at most low grade squamous intraepithelial lesion with confirmed colposcopy and appropriate follow up
- HIV hepatitis C virus coinfected women
  - hepatology consultation, stable liver enzymes for >1 year and no evidence of liver cirrhosis

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Al-Khan A, Colon J, Palta V & Bardeguez A. Assisted Reproductive Technology for Men and Women Infected with Human Immunodeficiency Virus Type 1. Clinical Infectious Diseases 2003; 36 : 197

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Test paper - Recommended Ethical Principles Regarding the Use of Assisted Reproduction in HIV Infected Individuals

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1. Which of the following statements is true regarding the risk of HIV infection from unprotected sexual contact?
   (a) risk of catching HIV from vaginal intercourse with an infected opposite sex partner is lower for female than male
   (b) anal sex is a less risky act because it is potentially less traumatic
   (c) HIV cannot be transmitted through oral sex
   (d) Estimates of infection risk in female for vaginal sex with HIV-infected male are 0.05-0.15%
   (e) Women having sex with women is less at risk than men having sex with men

2. Which of the following is not a reproductive option for HIV-infected people to minimize the risk of infecting spouse/partners during conception?
   (a) Unprotected intercourse
   (b) Artificial insemination
   (c) Sperm washing
   (d) Adoption
   (e) In-vitro fertilization

3. Which of the following is not useful in reducing mother to child HIV transmission?
   (a) Antiretroviral prophylaxis
   (b) Breastfeeding
   (c) Prevent mother from becoming infected
   (d) Elective caesarean section
   (e) Assisted reproduction

4. The first baby conceived by assisted reproduction technology in Hong Kong was born in year:
   (a) 1985
   (b) 1986
   (c) 1987
   (d) 1988
   (e) 1989

5. Which of the following is not a recommended ethical principle for the use of assisted reproduction in HIV infected subjects in Hong Kong?
   (a) Provide adequate information and counseling
   (b) Ensure equal access to service
   (c) Give final decision to the couple
   (d) Apply the *Code of Practice on Reproductive Technology & Embryo Research*
   (e) None of the above

6. Which of the dogma in medical ethics should be applied when considering reproductive options in HIV-infected individuals?
   (a) Autonomy
   (b) Beneficence
   (c) Nonmalefeasance
   (d) Justice
   (e) All of the above

7. The only documented case of HIV transmission during assisted reproduction occurs in the United States in year:
   (a) 1990
   (b) 1991
   (c) 1992
   (d) 1993
   (e) 1994

8. Which of the following is true regarding the advances of HIV treatment and use of assisted reproduction in HIV-infected patients?
   (a) HAART (highly active antiretroviral therapy) has greatly reduced morbidity and mortality of HIV/AIDS patients
   (b) Early orphanage of children born to HIV infected parents is uncommon nowadays with the improved treatment
   (c) Successes of employing assisted reproduction to minimise HIV transmission from infected father to uninfected spouse and his child have been witnessed
   (d) The risk of infecting her child by an infected mother has been much reduced with the advances in mother-to-child HIV prevention
   (e) All of the above

9. Which of the following is an insurmountable barrier in using assisted reproduction for HIV-infected patients?
   (a) HIV infection of the staff
   (b) Contamination of other embryos
   (c) Health care provider being unethical if it results in infection of partner
   (d) Health care provider being unethical if it results in infection of child
   (e) None of the above

10. Which of the following statement is false regarding assessment of a client's eligibility for reproductive treatment in Hong Kong?
   (a) The welfare of the child is of paramount importance
   (b) The parents' commitment to having and bringing up the child should be considered
   (c) HIV infection status of the parent is an exclusion criterion
   (d) Medical histories of the clients and their families are factors to consider
   (e) Physical, mental, and social well-beings of the clients should be considered