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OPINION ETHICS OF RESEARCH AND CARE EN

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OPINION ON MEDICALLY ASSISTED REPRODUCTION FOR HIV-DISCORDANT COUPLES IN WHICH THE MALE PARTNER IS HIV-POSITIVE

At the request of Professor Michel Kazatchkine, Director of the French National AIDS Research Agency (ANRS), the National AIDS Council (NAC) studied the ethical issues raised by **the desire for a child in HIV-discordant couples in which the male partner is HIV-positive**. The NAC and the French National Advisory Committee on Ethics in Life and Health Sciences (CCNE) had already addressed this issue in an Opinion issued jointly in February 10, 1998.

Following evidential hearings arranged by the National AIDS Council, it appeared necessary at the present time to specify the **conditions** under which it would be possible, in the near future, **to offer, as professional medical context, some of the techniques involved in medically assisted reproduction using the male partner's sperm** (rather than that of a third party donor) for HIV-discordant couples who wish to have a child, but in which the male partner is HIV-positive. Irrespective of the precise method used, artificial insemination in the uterus or injection into the cytoplasm of a single spermatozoon, all the techniques currently employed under research protocols (techniques for the preparation and isolation of spermatozoa, measurement of the viral load in the sperm) are characterized by the fact that they enable selection of spermatozoa free of any detectable trace of HIV, thus making it possible to reduce as far as possible any risk of HIV transmission to the mother and her child.

It is important to remember at the outset that the option of artificial insemination by donor is a real alternative for HIV-discordant couples in which the male partner is HIV-positive. As was emphasized in the Opinion of February 10, 1998, artificial insemination by donor has the advantage of guaranteeing all the conditions of safety for the mother and the child : "the exclusion of the HIV-positive male partner from the reproductive process rules out in principle any risk of infection for the mother and the child. Furthermore, despite the fact that the complexity of the medical procedure involved prevents acceptance of all couples applying for such artificial insemination, it is nevertheless provided with success for several couples of this kind every year, whereas adoption is in practice virtually impossible. Nevertheless, as in the case of adoption, artificial insemination by donor cannot by definition fulfil the desire of the HIV-positive male partner for biological paternity.

THE PRESENT SITUATION WITH RESPECT TO THE PROVISION OF MEDICALLY ASSISTED REPRODUCTION FOR HIV-DISCORDANT COUPLES IN WHICH THE MALE PARTNER IS HIV-POSITIVE

Drafted in accordance with the recommendations of the joint Opinion issued by the NAC and CCNE on February 10, 1998, the ministerial order of January 12, 1999 concerning the rules governing good clinical and biological practice for medically assisted reproduction stipulates as follows in Article 1.2.4.a. paragraph 2 :

> *"with respect to HIV infection, treatment of couples can only be provided within the framework of a protocol of multidisciplinary research pursuant to the prescriptions of the Huriet law, including the opinion issued by the CCPPRB, and validated by the CNMBRDP"*

At present, **two research protocols** funded by the ANRS are in progress in Paris (ANRS 092, Cochin-Necker hospitals) and in Toulouse (ANRS 096, La Grave General Teaching Hospital) for HIV-discordant couples in which the male partner is HIV-positive. Each one is treating sixty couples. The common goal of these protocols is **to evaluate the feasibility of medically assisted reproduction for HIV-discordant couples** in which the male partner is HIV-positive, in order to propose an **alternative** to natural reproduction which **reduces the risk of HIV infection as far as possible**. There are some differences between these facilities, most notably the impregnation technique used (intrauterine artificial insemination in Toulouse, injection of spermatozoa into the cytoplasm in Paris) and the criteria for eligibility of HIV-positive male partners (CD4 higher than 350/mm3 in Toulouse, higher than 200/mm3 in Paris). The results of these protocols will be available at the end of 2001.

According to all of the experts from which evidence was heard, whose views are based most notably on data deriving from work done by Italian and Spanish teams, **no HIV infection** should be observed in women and their children by completion of the Paris and Toulouse protocols, and the estimated successful impregnation rate is 20 % to 30 %. Furthermore, the **number** of couples applying for such medical assistance is unanimously estimated to be higher than the number of research places available, despite uncertainty as to the precise number of couples applying.

Given this, and assuming that the results of the protocols are as expected, it is appropriate to begin to reflect now on the conditions which, in 2001, should govern the shift from the present scientific research protocols to actual medical treatment. It would also be advisable to put in place the means to enable accurate evaluation of the extent of the demand for such procedures.

THE CONDITIONS GOVERNING GOOD MEDICAL PRACTICE FOR MEDICALLY ASSISTED REPRODUCTION PROVIDED TO HIV-DISCORDANT COUPLES IN WHICH THE MALE PARTNER IS HIV-POSITIVE.

1. The first condition relates to the official order of January 12, 1999. As soon as the two protocols of Paris and Toulouse are completed, it will be necessary **to amend Article 1.2.4 of this order** by deleting the paragraph on HIV-infection quoted above, which stipulates that medically assisted reproduction is to be provided under research protocols.

However, it is appropriate to observe that, due to the formulation used, ("with respect to HIV infection"), the provisions stipulated cover all HIV-discordant couples, and therefore not only those couples in which the male partner is HIV-positive and the woman HIV-negative, but also those in which the man is HIV-negative and his female partner HIV-positive. But, as has been pointed out by certain experts giving evidence to the National AIDS Council, the situation of couples in which the female partner is both HIV-positive and sterile is especially problematic at the present time, insofar as no research protocol exists to cover them, despite the fact that medically assisted reproduction would provide their only chance of having children. Rapid expert consultations are thus necessary in order to look closely at the conditions in which such medical assistance could be provided to such couples. It should not be forgotten that the issue raised by their situation is more one of ethics than of science, since it is known how the risk of mother/foetus transmission can be reduced in pregnant HIV-positive women.

2. The second condition is the establishment in 2001 of a specific HIV **approval procedure** for a certain number of **teams providing medically assisted reproduction**.

Such approval will need to be based **on biological and clinical criteria**, since all equipment and virus-handling techniques must guarantee optimum safety. These criteria must be established by a **committee of experts**, notably including virologists, biologists, gynaecologists and obstetricians specializing in medically assisted reproduction, clinicians specializing in HIV infection, and psychologists.

The **number of clinical and biological teams** must be carefully defined, but all indications are that the number should not be too large : 5 or 6 should be enough.

The **geographical distribution** of the teams should be given close attention, to ensure that all couples applying for the service will have reasonable access to them.

The greatest possible vigilance must be devoted to the **ethical aspects of this medical proc**edure, to ensure that couples applying cannot fall victim to any form of discrimination based on psychological or social criteria.

3. The third condition involves the **funding** of the equipment used and the tests for measuring the viral load in the sperm. Notably, investment must be made to provide dedicated equipment and premises for the teams approved. Also, provisions must be put in place to allow the costs of medically assisted reproduction to be paid by social security.

4. The fourth and last condition relates to the **evaluation of medical practice**. Medically assisted reproduction for HIV-discordant couples in which the male partner is HIV-positive is still in the phase in which data is being gathered. For this reason, procedures for monitoring and evaluation must be established as soon as the treatment is introduced, while continuing to encourage research in this area. Research results should regularly be presented to the responsible authorities.