In vitro fertilization and human immunodeficiency virus: review of the current medical and legal issues

T Kalampokas, C Sofoudis*, I Boutas, A Koumousidis, C Anastasopoulos, E Kalampokas, K Panoulis

Abstract

Introduction
The percentage of couples around the world facing infertility problems is especially high, resulting in the acquisition of a child to become an unfulfilled desire. The medical definition of infertility is the failure of a couple to conceive following 12 months of free and frequent intercourse without any type of contraception. This review is divided into two subsections. In the first subsection, we briefly summarize the available methods of the assisted reproduction and deal with the medical procedures when a human immunodeficiency virus carrier wishes childbirth, and in the second subsection we discuss about the spread of AIDS through in vitro fertilization and the responsibility of the physician.

Materials and methods
We searched the medical literature and the relevant nomology on in vitro fertilization and human immunodeficiency virus. The information found in 19 sources of this search was used to form our narrative review.

Results

In vitro fertilization—intracytoplasmatic sperm injection (IVF-ICSI)
It is divided into homologous (when the donor of the sperm is the partner of the couple) and heterosexual (if the donor of the sperm is a third person). If this procedure is attempted, i.e. the circulation of the tubes, then the substitution of fertilization in vitro, by aspiration of oocytes from the ovaries and their placement in special plates with the spermatozoa and nutrient material achieves fertilization. The fertilized ovum is placed in the uterus in time, dependent on the quality and the clinical practice of the physician.

In vitro fertilization with surrogate motherhood
The method of surrogate motherhood constitutes the transfer of embryos or only sperm (after insemination) of donation and preimplantation diagnosis for genital diseases. The issue of HIV and pregnancy was investigated.

Conclusion
Every decision should be taken with a resolution of all criteria, legal or clinical, and always taking into consideration the best service provision to the woman.

Introduction
Globally, the infertility rate, based on the data of the World Health Organization, is up to 15%1–3. Infertility should be treated as a condition concerning the couple, and the investigation appeals to both partners5. The causes of infertility are disaggregated to those that concern the female partner and to those that are related to the male partner. A common agent of female infertility is lesions in the fallopian tubes, which appear either as occlusion or as dysfunction4. Other causes of infertility in women are endometriosis5, polycystic ovarian syndrome5, ovarian failure7, diet and everyday living patterns8. On the other hand, as far as the male is concerned, the main problems related to the quality of the sperm are oligospermia or oligozoospermia (low concentration of sperm), asthenozoospermia (reduced sperm motility), teratozoospermia (sperm with abnormal morphology) and necrozoospermia (dead or immobile spermatozoa in the semen) and varicocele (varicose veins of the testes). Infertility can also be caused by a complication due to an infection or an injury in the area of scrotum9. The aim of this review was to discuss the current medical and legal issues with in vitro fertilization and human immunodeficiency virus (HIV).
the couple in a third woman’s uterus, with prior agreement on the gestation and the delivery of the infant after birth. The methods supportive of assisted reproduction are discussed.

**Cryopreservation of genetic material and embryo**

After the first successful pregnancy with transfer of a frozen-thawed embryo in 1983 by Trouson and Mohr and by Zeilmaker et al. in 1984, this technique, which does not constitute nowadays a method of assisted reproduction, is currently used routinely.

Another technique concerns the in vitro maturation. In 2007, the birth of the first child resulting from immature oocyte, which matured in vitro, frozen and later was fertilized, was announced by the European Society of Human Reproduction and Embryology. The advantage of this technique is that via this implementation, the incidence of ovarian hyperstimulation syndrome is reduced, since the total required amount of gonadotropins is also reduced. As far as the sperm cryopreservation is concerned, this is a method with high frequency of application, especially in cases of testicular removal, chemotherapy, ejaculation failure, difficulty in semen collection or prolonged absence of one partner for social reasons (e.g. times-tables or place of work).

**Oocyte, sperm and embryo donation**

This method, without being a method of assisted reproduction, gives many couples the opportunity of childbearing, namely in cases where the female partner has no oocytes due to premature menopause, ovarian dysgenesis and surgical removal of ovaries and/or the male partner presents lack of sperm or severe sperm disorders. The main difficulty of this method is how to find the available potential donors.

**Preimplantation diagnosis for genital diseases (PGD-PGS-sperm karyotype)**

This method is part of a wider procedure of medically assisted reproduction. It enables the diagnosis of genetic diseases in foetuses within the framework of IVF, so as to prevent the transfer of a fertilized ovum in which abnormalities in composition, structure and number of chromosomes are detected. Via this method, the occurrence of genetic disease is prevented. It is also important to mention the cases of explained infertility, affecting 15–30% of couples. In these couples, inability to conceive is observed, even though all the examined parameters do remain normal. From various current high methodological quality studies, it appears in such cases that IVF/ICSI constitutes the appropriate therapeutic approach.

**HIV and pregnancy**

HIV is a virus that causes the acquired immunodeficiency syndrome, known as AIDS. The modes of transmission are unprotected sexual intercourse, transfusion of contaminated blood or blood derivatives or transplant of organs or tissues, use of non-disinfected tools or hypodermic needles, vertical transmission from mother to child during pregnancy, delivery or even breastfeeding and rarely the exposure of health care professionals to the virus. The infection with HIV leads to an inevitable reduction of cellular immune response. Indicatively, in Greece, the data summarized in Table 1, categorized by gender, were recorded by the Hellenic Centre for Disease Control and Prevention concerning the year 2012.

The transmission rates from mother to infant have declined from 20–30% referred in 1985 to 1–2% in developed countries, with the appropriate antiretroviral treatment and the scheduled delivery via caesarean section. As a decrease in transmission rates is reported, these interventions increase the complexity of prenatal care to HIV-positive women. In USA, approximately 130,000 women are estimated to be infected from HIV, and worldwide this number has raised up to 15 million women. About 6,000 HIV-positive women give birth annually in the USA, and approximately 144 to 236 newborns are not infected due to the specific prenatal care. The improvements in prenatal care, the counselling on HIV, examination, antiretroviral medication and reduction policies of HIV transmission via breastfeeding are vital in order to improve the quality of life of the mother and to achieve an increase in life expectancy and a reduction of HIV transmission. The hormonal changes during pregnancy may increase the risk of toxicity of antiretroviral therapy, in particular by the reverse transcriptase inhibitors. Many cases of lactic acidosis and hepatic failure, some of them resulting in the death of the mother, were reported in women receiving long-term nucleoside therapy during pregnancy. The effect of HIV infection and antiretroviral therapy on the outcome of pregnancy is an issue that should be taken into consideration. Many studies in developed countries indicated an increased proportion of preterm births, low neonatal weight, limited intrauterine growth and neonatal mortality in HIV-positive women. Factors associated with preterm birth and low neonatal weight in HIV-positive women include previous adverse pregnancy outcomes, hypertension, multiple pregnancy, smoking, haemorrhages, alcohol use, low weight, and maternal age.

<table>
<thead>
<tr>
<th>Gender</th>
<th>HIV</th>
<th>AIDS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>928</td>
<td>73</td>
<td>1,001</td>
</tr>
<tr>
<td>Women</td>
<td>159</td>
<td>20</td>
<td>179</td>
</tr>
<tr>
<td>Total</td>
<td>1087</td>
<td>93</td>
<td>1,180</td>
</tr>
</tbody>
</table>
maternal weight and sexually transmitted diseases. The greatest concern of HIV infection during pregnancy is the risk of perinatal transmission of the virus to the foetus. In HIV-positive women, who do not breastfeed, the transmission may occur in 20–30%. In approximately 75% of all cases, the virus is transmitted during the third trimester of pregnancy or during delivery. Specifically, it is estimated that two-thirds of virus transmissions from HIV-positive women, who had not received proper treatment and care, incurred during delivery. The levels of maternal HIV RNA seem to be the main predictive factor of transmission. The antiretroviral treatment during pregnancy and neonatal period reduces the risk of perinatal transmission of HIV. The risk is increased if the mother has a low CD4 count or high viral load. The role of the physician is very important in matters of eugenics of seropositive women/couples in terms of the welfare of the future child. The physician should inform women and couples not only of the risks of HIV infection related to the couple but also the risks related to the child. The question of whether the physician takes into account his responsibility towards the newborn for quality and healthy life may or may not abrogate to HIV-positive parents, access to treatment for infertility or even the possibility of IVF cannot be answered clearly. First, is there any difference in who is affected, the male partner, the female one or both? If only the male partner is a carrier, the procedure—puriﬁcation of the sperm and the cryopreservation can signiﬁcantly reduce the levels of HIV in the fertilized ova. If the female or both partners are carriers, then the risk of transmission of the infection from mother to infant is about 10%. Moreover in this case, there is a high probability that the child will prematurely lose one or even both parents, with the corresponding effects on his psychological development. Of high importance are the medication and the possible side effects to the neonate, since according to studies the odds of being born with low body weight are increased. The ability of motherhood in HIV-positive parents is not a priori morally unacceptable. The requirement to screen for HIV infection, as a prerequisite for the IVF procedure, conﬂicts with the right to respect the autonomy of the patient/client. This policy certainly can be justiﬁed only in the context of responsibility of the physician as far as the health of the newborn is concerned. The argument for the examination for HIV of the candidate is important. Speciﬁcally in favour of the examination include the welfare of the newborn and the right even for the future offspring to a healthy life. Even if the test is positive, with proper therapy the vertical transmission of HIV can be prevented. The consequences of non-diagnostic procedures the parent and the subsequent infection of the infant are very severe, for both the child’s well-being and also for the premature parental mortality with all that entails socially and psychologically. As a drawback of the examination, the disregard of the patient’s autonomy can be mentioned and also that a potential positive result may raise different attitude patterns from the health professionals. It is essential that the medical community is able to undertake any patient wishing motherhood, and even if this seems impossible or unethical, the physicians should argue and inform for every decision.

Discussion
Transmission of AIDS through assisted reproduction techniques and the responsibility of the physician
In Greece as well as internationally, the need of properly managing the medically assisted methods of reproduction appeared, as the right of reproduction is fundamental and directly related to the development of the individual’s personality. The role of the medical and the nursing staff in assisted reproductive procedures is essential; these professionals should be informed and further adopt the new medical methods and the related technologies, so the risk to the patient is reduced. Quite indicative indeed is a case from Canada, where a doctor was familiar with the artificial insemination from 1974, but he was not informed about the risk of AIDS transmission through artificial insemination. The infection of a patient in 1985 leaned against many questions, apart from the legal process, about the range of responsibility of the physician and whether his professional methods could be classified as negligence or ignorance. In particular, in early 1983, first the issue of infection of women from HIV-positive men was raised, in contrary to what was the general belief that heterosexual relationships were safe and there was no correlation between artificial insemination and AIDS. In October 1983, the first concern on this matter was published by Mascola, and in June 1985, a documented study was published by the same author about the risk of disease transmission associated with sexual intercourse through assisted reproduction techniques. The conduct of the assisted reproductive procedure should be provided as safely as possible for all parties involved, as in this way protection can be afforded in terms of physical integrity and dignity not only for the woman but also for the newborn. The responsibility of the doctor and staff associated with these procedures is worth mentioning, due to the risk or harm that may be caused to the legal good of physical integrity and dignified life. The Greek legislation is devoted considerably to the importance of protecting life and safety. In particular, in Article 304 of the Penal Code, it is stated that whoever acts illegally towards a pregnant woman, leading to severe damage of the foetus or displaying heavy medical condition of the body or the mind of the neonate, is punished according
to the fault and the result of his actions. Certainly when it comes to the medical staff, any omission can be interpreted as negligence as the nature of the employment relationship is not supported by the concept of potential fraud. According to Law 3305/2005, Article 26, it is projected that whoever uses the methods of medical assisted reproduction without prior laboratory and clinical tests on genetic material is punished by imprisonment of up to 1 year. Furthermore, whoever, in case of disposal of gametes or embryos proceeds to their use for medical assisted reproduction without the requisite clinical and laboratory testing or use of fresh sperm of donor is punished with imprisonment of at least 2 years. The same law states that laboratory testing on HIV1, HIV2, hepatitis B and C and syphilis is necessary and that donors of fresh sperm must undergo clinical and laboratory tests and cannot be accepted if suffering from inherited, genetic or contagious diseases and also that the use of a third person's fresh sperm is strictly not allowed. This law formalizes a crime in the aspect that the specific laboratory tests and their omissions may have consequences for the woman and the neonate, and also in general for public health—a crime, the prevention of which ensures life and human's physical integrity. Safety is potentially jeopardized by certain diseases and viruses; therefore, the control and the prohibition of fresh sperm’s use is essential, where either by omission or by ignorance there is a possible risk of transmitting a disease in the involved parties.

**Conclusion**

Science is constantly evolving and IVF is a medical aspect growing rapidly. Fertility is a dominant theme for modern women, and also for the state through legislation and educational policy. Every decision should be taken with a resolution of all criteria, legal or clinical, and always taking into consideration the best service provision to the woman.

**Abbreviations list**

HIV, human immunodeficiency virus; IVF-ICSI, *in vitro* fertilization—intracytoplasmatic sperm injection.

**References**

17. Magganas A. The transmission of AIDS through artificial insemination the responsibility of the physician in Canada. Criminal Procedure Law 1/1999 (20 year).

Licensee OA Publishing London 2013. Creative Commons Attribution License (CC-BY)