Assisted reproductive technologies: psychoneurological, moral-ethical, and socio-cultural aspects

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The paper provides a definition of sexual and reproductive health and infertility and also reflects modern ideas about ways to overcome infertility using assisted reproductive technologies, such as in vitro fertilization (IVF) and surrogacy. It shows the specificity of the impact of an IVF procedure on the mental health of a potential mother. The features of the neonatal health status, as well as neuropsychiatric disorders in babies born using the IVF procedure are described. The authors present two types of surrogacy (traditional and gestational ones) and the features of their use in different countries according to governmental legislative regulation, socioeconomic and religious factors, and cultural traditions in society. They unveil the features of a psychological relationship between the mother (surrogate and presumed one) and the fetus. The consequences of surrogacy for a surrogate mother, genetic parents, and a child himself/herself are noted to be little studied. It is shown that the development of assisted reproductive technologies (IVF and surrogacy), on the one hand, helps fight infertility and, on the other hand, entails a number of problems (moral and ethical, legal, cultural and religious, socioeconomic, and neuropsychiatric ones) that need to be solved in order to prevent psychological, neurological, and mental abnormalities in all the participants (a surrogate mother, an unborn child, and potential parents) in the assisted reproductive process:

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Reproductive and sexual health is fundamental to individuals, couples and families, to every country and society as a whole. As defined by the World Health Organization, human reproductive health is «a state of complete physical, mental and social well-being, and not just the absence of disease or health problems, in all aspects related to the reproductive system, its functions and processes» [1].

Education in the field of reproductive health protection and prevention of infertility are important tasks and determine the need for affordable diagnostic procedures and new reproductive technologies. According to the WHO global strategy for reproductive health, «infertility services» are among the five priority areas for sexual and reproductive health described [2].

More than 180 million couples worldwide suffer from primary or secondary infertility. A marriage is considered sterile when a wife of childbearing age does not become pregnant within one year of regular sexual activity without the use of contraception [3]. The social stigma of childlessness creates conditions for the isolation of people suffering from infertility, and, despite more than 30 years of history of assisted reproductive technologies, the prevalence of infertility is still high.

Assisted reproductive technologies (ARTs) include «all treatments or procedures that include in vitro handling of both human oocytes and sperm, or embryos, for the purpose of establishing a pregnancy. This includes, but is not limited to, in vitro fertilization (IVF) and embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer, gamete and embryo cryopreservation, oocyte and embryo donation, and gestational surrogacy. ARTs do not include assisted insemination (artificial insemination) using sperm from either a woman's partner or a sperm donor.»[4].

The human ability to conceive and bear healthy offspring in case of reproductive health disorders in women and men has been of interest to mankind for a long time. From the late nineteenth century onwards, artificial insemination experiments were carried out on animals.

Positive experience of in vitro fertilization with the participation of experimental animals – rabbits (in 1890 Walter Heap, professor at the University of Cambridge, carried out a rabbit embryo transfer; in 1934 Gregory Pincus repeated this experiment; in 1959 a Chinese scientist Min Che Chang reported the birth of live offspring in a female rabbit after fertilization in a test tube) allowed in the following years to make a breakthrough in solving the problem of infertility.

In 1978, after several unsuccessful attempts to maintain a pregnancy resulting from in vitro fertilization, British scientists Patrick Steptoe and Robert Edwards announced the birth of the world's first child conceived in vitro. For this achievement in 2010 R. Edwards received the Nobel Prize.

Subsequently, scientists from different countries of the world (Australia, USA, France, Sweden, Germany, Austria, Russia) were able to carry out in vitro fertilization of an egg, followed by the birth of one or more live term babies [5].

Advances in assisted reproductive technology (ART) have provided a real parenting perspective for many infertile women, but at the same time resulted in high levels of stress,

anxiety and depression associated with the treatment. In case of unsuccessful IVF, women experience a significantly more severe degree of anxiety and depression compared to their initial level [6]. Other psychopathological manifestations of stress associated with unsuccessful fertility therapy include anger, feelings of powerlessness, frustration, guilt, decreased energy potential, and increased incidence of mental disorders. ART is associated with daily procedures: injections to stimulate ovulation, vaginal ultrasound examination, painful manipulations of oocyte aspiration, which present certain mental and physical difficulties [7].

Fertility specialists consider ART treatment exclusively in the positive light of the onset of pregnancy. As a rule, they ignore potentially negative mental consequences associated with unsuccessful attempts at in vitro fertilization [8]. Infertile individuals hope for the positive result of fertility therapy and will be disappointed if it fails. Despite the existing problems in the field of ART, more than seven million people all over the world were born with the help of IVF, and the procedure itself has become routine.

The IVF procedure can be combined with gestational, or full, surrogacy. The first successful IVF surrogate pregnancy was reported by W.H. Utian et al. in 1985 [9].

Surrogate motherhood is «the use of biological materials of the intended parents and the artificial insemination of the sex cells of the intended parents; the embryo obtained as a result of fertilization is implanted into the uterus of the gestational courier (surrogate mother)». The European Society for Human Reproduction and Embryology (ESHRE) does not indicate the gender of the intended parents [10].

There are two main types of surrogacy: traditional and gestational. It is believed that the very first traditional arrangement of surrogacy took place about 2000 years before the birth of Christ and was mentioned in the Old Testament of the Bible. Sarah and Abraham could not conceive a child, and Sarah asked Hagar to give them a child. After some time, Hagar gave birth to a son Ishmael for Sarah and Abraham [11].

Today, traditional (genetic, or partial) surrogacy is the result of artificial insemination of a surrogate mother with the sperm of an alleged father. This means that the surrogate mother's eggs are used, making her the genetic parent along with the alleged father.

Full, or gestational, surrogacy is a procedure in which an embryo obtained by fertilizing the sex cells of the intended parents or with the participation of the gametes of one of the parents and a donor oocyte or sperm is transferred to the surrogate uterus. A surrogate mother bears and gives birth to a genetically alien child under an agreement with potential parents or a single woman for whom carrying and giving birth to a child is impossible for medical reasons, but whose germ cells are used for fertilization.

A surrogate mother can be a woman between the age of 20 and 35, who has at least one child of her own, a medical report confirming a satisfactory health condition, and who has given a written informed voluntary consent to this medical intervention. However, she cannot be an egg donor [12]. Thus, a woman carrying a child is not its genetic mother [13].

Today, surrogacy is recognized by a number of countries, however, the attitude towards it is ambiguous. Canada, United Kingdom, Australia, Israel allow non-commercial surrogacy. In the Russian Federation, Ukraine, the Republic of Kazakhstan, Belarus, Georgia, the USA, South Africa, surrogacy is allowed and legally enshrined. Austria, Germany, France, some US states (Arizona, New Jersey, Michigan), Sweden, Norway prohibit surrogacy by law.

In the Russian Federation, there are significant gaps and shortcomings in the legislative regulation of surrogacy, especially in terms of protecting the rights of children born to surrogate mothers, since at present, the primary task is to protect the rights and interests of a surrogate mother. Cases of rejection by genetic parents of a child born by a surrogate mother for various reasons have been described, including frivolity and immaturity of genetic parents, onset of pregnancy of the genetic mother, multiple pregnancy of a surrogate mother, physical disabilities in the born children. In all these cases such children remained orphans [14].

If a child born under the surrogate motherhood program, had some health problems or physical defects, genetic parents in some cases motivated their rejection by the detrimental influence of the surrogate mother on the fetus during pregnancy [15]. Currently, there are no scientific works in Russia covering the neuropsychiatric characteristics of children born under the surrogate motherhood program. This can be explained by the fact that in Russia the secret of adoption, as a legal procedure which children born under the surrogacy program go through, is protected by law. Its disclosure can be the cause of moral suffering for both the child and the family as a whole [14].

Currently, existing biomedical technologies, such as gene therapy, cell reprogramming, cloning, genetic modification of embryos, assisted reproductive technologies and others, are created with the aim of solving such social problems as old age, degenerative diseases, infertility. However, their development entailed not only progress in science, but also certain negative consequences, which can be difficult to predict [16].

Among the urgent problems, the issue of the absence of international legislation regulating ART, and surrogacy in particular, is especially acute, which entails such a phenomenon as medical tourism and exploitation of low-income, socially unprotected women [17].

The views of researchers on the widespread use of ART as a way to overcome the demographic crisis in the world and in Russia differ, which is explained by the morbidity rates of such children.

Since surrogacy is always associated with the IVF procedure, the health status of such children can be indirectly assessed by the existing scientific data.

The possibility of assessing the health status of children born with the help of ART is determined by such factors as the age of the parents, their health status, the type and duration of infertility, multiple pregnancy, its pathological course and complications in childbirth. However, here are no special recommendations for monitoring the health of such children. Nevertheless, nowadays there is convincing scientific evidence about deviations in the health status of children born with the help of ART.

In Russia, the first study of the health status of children born as a result of IVF and artificial insemination was carried out by OV Bakhtiarova (1993) [18]. The author found that children born with ART had the following anomalies: intrauterine growth retardation (29.3% of cases), asphyxia at birth (90.5% of cases), neurological disorders, including infantile cerebral palsy

(53.6% of cases), morphofunctional immaturity, ante- and intranatal hypoxia, perinatal lesions of the central nervous system (87.5% of cases), mental disorders (autism, mental retardation, behavioral disorders).

The health status of newborns and overall morbidity of children born with IVF differs from that in general population due to the prevalence of prematurity (24.6% of cases), low birth weight (less than 1.5 kg – 6.2%), mild asphyxia in childbirth (4.3%), intrauterine growth retardation, respiratory disorder syndrome, post-hypoxic conditions, pathological hyperbilirubinemia and congenital malformations [19]. According to the author, total morbidity of children born with the help of IVF is 4 times higher compared to total morbidity of children born through natural conception. Hypoxic damage to the central nervous system and dysplasia of the brain in the projection of the pathways of the visual analyzer causes widespread visual impairment in these children [20].

The analysis of the health status of 104 full-term infants born as a result of IVF showed that 75% of children were healthy or relatively healthy. However, according to the author's data, 48.1% of children still had some neurological disorders, 22.1% of children had psychomotor developmental abnormalities. The neuropsychiatric disorders revealed as a result of the examination more often were functional and included neurotic reactions (8 children; 7.7%), autonomic dysfunction (15 children; 14.4%), and a mild delay in speech development (9 children; 8.6%) [21].

Another aspect of the problem of infertility therapy with IVF is due to a number of moral, social and legal problems associated with this biomedical technology [22]. In this regard, the problem of the moral status of the embryo is acute. In the process of in vitro fertilization, up to several dozens of embryos are created; after that, 2–3 best embryos are selected and implanted into the woman's uterus, and the rest are destroyed or cryopreserved (frozen). This issue is closely related to the issue of human rights, since the embryo, as a potential person, can be endowed with some of such rights.

The moral justification of the IVF procedure closely correlates with the religion attitude; according to religious dogmas human life begins from the moment of conception, and the destruction of «extra» embryos in Christian religion can be considered as murder. In this regard, the so-called "criterion of the fifteenth day" was declared, which is recognized by many European countries and reflected in the literature on bioethics.

According to this criterion, a 2.5–3-week-old embryo formed after the fusion of germ cells is not yet a human being, «is an accumulation of cells that has potential to become a human being, called a pre-embryo». It is possible to destroy, cryopreserve or implant a pre-embryo into the uterus only in the first 14 days after its creation. It is considered ethically unacceptable to grow it for more than 14 days and then destroy it [23].

Modern trends in in vitro fertilization methods are the issues of their use for non-therapeutic purposes, which correlates with the context of moral acceptability of IVF, for example, in the so-called family practices of «co-parenting», when a certain group of people (a homosexual couple and a single woman) unite to give birth to a child through assisted reproduction. A specific feature of this practice is the absence or optional presence of marital, sexual or romantic relationships between the partners. However, the interests of the group participants correlate in terms of upbringing, education, financial status of the intended child [24].

Some European and American researchers have made an attempt to identify the peculiarities of the psychological relationship between mother and fetus in the context of surrogacy. Fischer S. and Gillman I. [25], using the maternal and fetal attachment scale (MFAS), first developed by M.S. Cranley (1981) [26], described the characteristics of maternal and fetal attachment for 21 surrogate mothers and 21 expectant mothers in the United States and found that surrogate mothers were significantly less attached to their unborn children than the alleged ones.

Van den Akker [27] found that surrogate mothers are significantly less concerned about the health and well-being of the fetus and are less positive about it than intended mothers. Other data were obtained in France [28], which confirmed the normative level of attachment to the fetus in both surrogate and non-surrogate pregnant women.

Surrogate motherhood, or gamete donation, is responsible for the disruption of the biological connection between mother and child, which contributes to the disruption of psychological attachment of the surrogate mother to the child, and formation of a special attitude towards the child as «a project or order» [17]. The subsequent weaning of the surrogate mother from the newborn child can explain her risky behavior during pregnancy – smoking, unhealthy diet, etc [29].

The results of studies in the United States and Great Britain have repeatedly shown that most surrogate mothers do not experience problems with the child transfer to the intended parents [30, 31, 32, 33, 34]. It has been suggested that they make a conscious effort to view surrogacy as a job and do not consider this child as their own [35,36]. Payment in surrogacy is a factor contributing to the creation of an emotional distance between the surrogate mother and the developing fetus [36].

The practice of surrogacy, its legislative regulation and cultural characteristics are strikingly different in Western European and developing countries, such as India [37, 38, 11], Latin America [39], most of the countries of Asia and the African continent [40]. A number of works [37, 41, 42, 43, 44] reflect the results of an in-depth study of the characteristics of surrogacy in India (Delhi, Mumbai). Such factors as inclusion of the names of the alleged parents in the birth certificate, the use of the latest methods of reproductive medicine, and low medical costs have contributed to the spread of commercial surrogacy in India [45, 46].

During the period from 2002 to 2015, surrogate mothers in India gave birth to 25 thousand children, and the terms «womb farm» [47], «baby factory» [48], «market pregnancy» have come into use to characterize the growing level of surrogate motherhood [44]. According to preliminary economic estimates, the value of the Indian surrogacy market was estimated at US $ 2.3 billion [49].

In India, surrogate mothers are usually recruited by unofficial agents.

A. Pande described surrogate mothers as «submissive, selfless and caring» women who were trained to be ideal «working mothers» [41]. According to the author, Indian surrogate mothers believe that their relationship with the fetus is due to «blood and sweat», and not a genetic relationship, which is implied in Western European countries. By «blood and sweat» they mean their blood ties with the fetus and the burden of childbearing.

During pregnancy surrogate mothers in India live in a surrogate home, which is a group housing located next to reproductive medicine clinics. Living in such houses allows surrogate mothers to be under constant supervision of medical personnel. Indian surrogate mothers have a special "sisterly" attitude towards each other [42, 43].

In contrast to Western European countries (e.g. Great Britain), a reproductive medicine clinic that provides surrogacy services in India acts as a mediator between intended parents and a surrogate mother, seeking to depersonalize her role. Thus, in most cases surrogate mothers do not interact directly with the intended parents [43], although they hope to establish a strong bond between them and the child, his parents, and rely on the reciprocity and generosity of the intended parents [42]. Other difficulties in establishing warm relationships are language barriers and long distances.

As for the perception of surrogate motherhood in Indian society, it is often concealed by a surrogate mother and her family, since it is considered immoral [50]. Surrogate mothers face humiliation and criticism from the members of their parental families and society as a whole [46].

Members of the parental families, who usually have a low educational level, contribute to sexual stigmatization of surrogate mothers by considering pregnancy without marriage «sex work» or adultery. The growing belly makes it impossible for surrogate mothers to communicate with their parental families and friends during pregnancy, which gives rise to social isolation and lack of moral support. These factors negatively affect psychological well-being of surrogate mothers [49, 50].

A number of studies have revealed the role of stigma in the development of anxiety and depressive disorders in these women [51, 52]. Psychological counseling is not available to Indian surrogate mothers; as a rule, detailed psychopathological screening of surrogate mothers and their relatives is not carried out before pregnancy, which potentially makes them more susceptible to psychological and psychiatric problems [46, 53].

In 2016, India introduced a new law prohibiting commercial surrogacy. A significant difference in the incomes of potential parents and surrogate mothers [54], commodification (reproductive opportunities of women as a market service) of the female body in poor population groups [55], and lack of an alternative way of earning for women [41] made them a vulnerable group for exploitation. Cross-border surrogacy with its legal, ethical, religious and medical implications endangers the well-being of surrogate mothers, intended parents and unborn children [56, 38, 11]. The new bill only allows altruistic surrogacy for infertile Indian couples [57].

Thus, the development of assisted reproductive technologies (IVF and surrogacy), on the one hand, helps to fight infertility, and on the other hand, it entails a number of problems (moral and ethical, legal, cultural and religious, socio-economic, neuropsychiatric), which must be solved in order to prevent psychological, neurological and mental abnormalities in all participants of the assisted reproductive process: a surrogate mother, an unborn child and potential parents.

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